sulfate, and evaporated to dryness. Crystallization from methanol gave 0.05 g (60%) of **34** as pale yellow rods, mp and mmp with a sample prepared as above 192–195 °C.

**Acknowledgment.** We are indebted to the following members of our Physical Chemistry Department under the direction of Dr. R. P. W. Scott: Dr. W. Benz, Dr. F. Scheidl, Dr. V. Toome, Mr. S. Traiman, and Dr. T. Williams for the spectral and elemental analysis. We also wish to express our gratitude to Professor G. Büchi and many of our co-workers for invaluable advice and discussions.

**Registry No.**—**1,** 4393-72-0; **2,** 41963-51-3; **3,** 58-25-3; **4,** 62167-14-0; **5,** 62167-11-7; **6,** 5969-98-2; **7,** 62167-15-1; **9,** 62167-16-2; **10,** 4951-07-9; **11,** 62167-17-3; **14,** 62167-12-8; **15,** 62167-18-4; **16,** 5220-83-7; **17,** 62167-19-5; **21,** 62167-20-8; **22,** 4647-62-5; **23,** 3489-63-2; **24,** 62167-21-9; **25,** 62167-22-0; **28,** 62167-23-1; **29,** 62197-70-0; **30,** 62197-71-1; **31,** 62167-13-9; **32,** 62167-24-2; **33,** 62167-25-3; **34,** 62197-72-2.

**Supplementary Material Available.** Table of the positional and thermal parameters for **5**, **14**, and **31** (8 pages). Ordering information is given on any current masthead page.

## References and Notes

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# Synthesis and Acylation of Pyrrolinones

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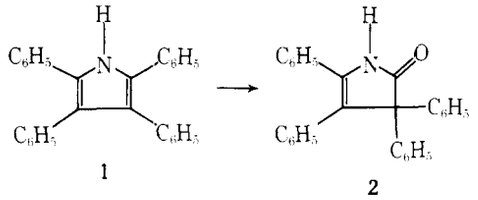
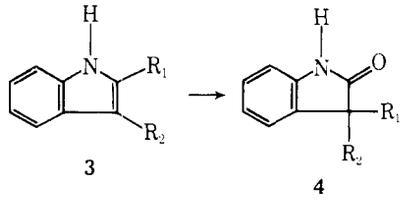
Ethyl 5-acetyl-2,4-dimethylpyrrole-3-carboxylate (**5a**) reacted with concentrated nitric acid to give pyrrolinone **6a** and nitropyrrole **7**. Several pyrroles related to **5a** were also oxidized to pyrrolinones. Diethyl 2-acetyl-3-methylsuccinate reacted with ammonia to give a mixture of ethyl 4,5-dihydro-2,4-dimethyl-5-oxo-1*H*-pyrrole-3-carboxylate (**13b**) and its $\Delta^3$ isomer (**14b**). Acylation of **13b** and its *N*-methyl analogue **13a** with various reagents was studied. The reaction products were formulated as pyrrolinones or 5-acyloxypyrroles on the basis of spectral ($^1$H and $^{13}$C NMR, UV, and IR) properties.

Wasserman and Liberles have described the oxidation of tetraphenylpyrrole (**1**) to pyrrolinone **2**;[1] related reactions



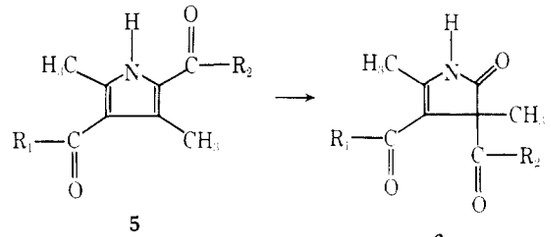
**1** **2**



**3** **4**

a, $R_1 = R_2 = C_6H_5$
b, $R_1 = COOC_2H_5$; $R_2 = CH_3$

leading to indolinones **4a** and **4b** have also been described.[2-4] In this paper we report additional examples of this oxidative rearrangement in which the migrating group is acetyl, carboalkoxy, or dialkylcarbamoyl. We have found that pyrroles **5a–i** react rapidly with concentrated nitric acid to give pyrrolinones **6a–i.** We have synthesized related 4,4-disubstituted pyrrolinones by acylation of **13a** and **13b** and also report iso-



**5** **6**

a, $R_1 = OC_2H_5$; $R_2 = CH_3$
b, $R_1 = OCH_3$; $R_2 = CH_3$
c, $R_1 = CH_3$; $R_2 = OC_2H_5$
d, $R_1 = OCH_3$; $R_2 = OCH_3$
e, $R_1 = OCH_3$; $R_2 = OC_2H_5$
f, $R_1 = OC_2H_5$; $R_2 = OC_2H_5$
g, $R_1 = OCH_3$; $R_2 = N(CH_3)_2$
h, $R_1 = OCH_3$; $R_2 = N(CH_3)(C_2H_5)$
i, $R_1 = OCH_3$; $R_2 = N(C_2H_5)_2$

**Table I. Substituted Pyrrolinones and 5-Hydroxypyrroles**[a]

| Compd | Registry no. | Mp or bp, °C (mm) | Yield, % | $^1$H chemical shifts ($CDCl_3$) 2-$CH_3$ | 4-$CH_3$ | Ring H | $\lambda_{max}$ (EtOH) ($\epsilon$) | IR ($CHCl_3$), $cm^{-1}$ |
|---|---|---|---|---|---|---|---|---|
| | | | | $\Delta^2$-Pyrrolinones[b] | | | | |
| **6a** | 62264-77-1 | 81–84 | 26[c] | 2.48 | 1.55 | 9.35 | 282 (10 250) | 1740, 1690, 1625 |
| **6b** | 62264-78-2 | 100–102 | 10[d] | | | | | |
| **6c** | 62264-79-3 | 93.5–96.5 | 32[e] | 2.47 | 1.60 | 9.25 | 224 (2650), 295 (12 400) | 1740, 1710, 1610 |
| **6d** | 62319-73-7 | 146–147 | 13 | 2.45 | 1.61 | 9.00 | | |
| **6e** | 62264-80-6 | 104–107 | 42 | | | | | |
| **6f** | 62264-81-7 | 126–128 | 45 | 2.43 | 1.61 | 9.10 | 283 (12 400) | 1755, 1720, 1700, 1650 |
| **6g** | 62264-82-8 | 203–206 | 44 | 2.31[f] | 1.38[f] | 10.8[f] | 281 (10 000) | 1735, 1695, 1645 |
| **6h** | 62264-83-9 | 154–157 | 42 | 2.47 | 1.63 | 9.55 | 282 (10 450) | 1725, 1690, 1635 |
| **6i** | 62264-84-0 | 184–188 | 80 | | | | | |
| **8** | 62264-85-1 | 162 (0.1) | 32 | 2.90[g] | 1.57 | 9.30 | | |
| **13a** | 23657-69-4 | 115 (0.2) | 74 | 2.42[h] | 1.38[i] | 3.0[j] | 220 (4750), 289 (10 000) | 1700, 1680, 1625 |
| **13b** | 4030-28-8 | 120–125 | 59 | 2.38[h] | 1.40[i] | 3.27,[j] 9.40 | 218 (4150), 281 (11 850) | 1720, 1685, 1640 |
| **15a** | 62264-86-2 | 115 (0.1) | 29[k] | 2.47 | 1.30 | | 284 (11 400)[l] | 1710, 1680, 1625 |
| **15b** | 62264-87-3 | 96–101 | 35 | 2.51 | 1.65 | | | 1730, 1695, 1635 |
| **15c** | 62264-88-4 | 46–49 | 48[m] | 2.54 | 1.51 | | | 1745, 1700, 1640 |
| **15d** | 62264-89-5 | 34–37 | 71[n] | 2.53 | 1.56 | | 285 (10 200)[l] | 1740, 1710, 1685, 1630 |
| **17** | 4027-37-6 | 163–165 | 15 | 2.40 | 1.35 | 9.40 | 272 (10 900)[l] | 1715, 1680, 1630 |
| | | | | $\Delta^3$-Pyrrolinones | | | | |
| **14a** | 62264-90-8 | 95 (0.05) | 20 | 1.50[i] | 2.19[h] | 4.20[j] | 228 (12 300), 271 (2350) | 1700, 1680 |
| **14b** | 62264-91-9 | 94–97 | 6 | 1.44[i] | 2.21[h] | 4.30,[j] 8.40 | 228 (13 500), 288 (1000) | 1700 |
| **18** | 62264-92-0 | 130 (0.1) | 26 | 1.54[i] | 2.16[h] | 4.75[j] | 231 (14 450) | 1785, 1730 |
| | | | | 5-Hydroxypyrroles | | | | |
| **16c** | 62264-93-1 | 81–83 | 40 | 2.43 | 2.03 | | | 1765, 1700, 1525 |
| **16d** | 62264-94-2 | 54–56 | 61 | 2.44 | 2.06 | | 226 (9000), 253 (4550)[l] | 1750, 1680, 1525 |
| **16e** | 62264-95-3 | 125–127 | 18 | 2.46 | 2.07 | | 227 (10 200), 256 (5000)[l] | 1730, 1690, 1530 |
| **19a** | 62264-96-4 | 150 (0.1) | 32 | 2.70 | 2.05 | | 215 (16 650), 232 (8300), 260 (2150)[l] | 1760, 1700, 1550 |
| **19b** | 62264-97-5 | 84–86 | 16 | 2.67 | 1.97 | | 226 (20 300)[l] | 1780, 1730, 1700, 1550 |
| **20** | 62264-98-6 | 115–118 | 9[o] | 2.37 | 2.02 | | 217 (13 700), 256 (7400)[l] | 1750, 1680, 1530 |

[a] Satisfactory chemical analyses (± 0.3%) were obtained for all compounds and are presented in the supplementary material for this article. [b] The pyrrole intermediates used in the preparation of compounds **6a–i** and **8** had the following melting points (°C): **5a,** 142–143;[20] **5b,** 161–163; **5c,** 143–144;[20] **5d,** 175–176;[22] **5e,** 130–132;[21] **5f,** 127–130;[22] **5g,** 149–151;[23] **5h,** 115–119;[23] **5i,** 135–136;[23] intermediate for **8,** mp 117–119.[7] [c] Nitropyrrole **7** (36%) was also isolated in this reaction. [d] Methyl 2,4-dimethyl-5-nitropyrrole-3-carboxylate (31%, mp 183–186 °C) was also obtained in this reaction. [e] Ethyl 3,5-dimethyl-4-nitropyrrole-2-carboxylate (18%, mp 202–204 °C) was also obtained in this reaction. [f] $Me_2SO$-$d_6$ used as solvent. [g] Multiplet for 2-$CH_2$. [h] Doublet, $J$ = 2 Hz. [i] Doublet, $J$ = 7 Hz. [j] Multiplet. [k] Isolated yield from the methylation of **13b;** also obtained in 85% yield by methylation of **13a.** [l] UV spectra taken in hexane. [m] Prepared from **6a;** also obtained in 23% yield by acetylation of **13a.** [n] Prepared from **6e;** also obtained in 6% yield by reaction of **13a** with ethyl chloroformate. [o] Yield from **13b;** also obtained in 43% yield by heating **13b** with acetic anhydride.

lation of the hitherto unreported pyrrolinones **14a** and **14b,** the double bond isomers of **13a** and **13b.**

Fischer and Zerweck[5] have reported that nitropyrrole **7** was formed when **5a** was dissolved in concentrated nitric acid. In repeating this work we found that two products were formed in the reaction. Compound **7** precipitated when the reaction mixture was diluted with ice/water, while extraction of the diluted reaction solution with chloroform afforded the pyrrolinone **6a.**

Pyrrole ketones **5b** and **5c** also reacted rapidly with concentrated nitric acid to give mixtures of nitropyrrole and pyrrolinone, while pyrrole esters (**5d–f**) and amides (**5g–i**) gave pyrrolinones as the only isolated products (Table I).[6] Diethyl 3-methyl-5-propylpyrrole-2,4-dicarboxylate[7] was oxidized to **8** by concentrated nitric acid.

Pyrrolinone **6f** has already been prepared in low yield (19%) by chromium trioxide/acetic acid oxidation of Knorr's pyrrole (**5f**), but the product has been incorrectly formulated as **9** by

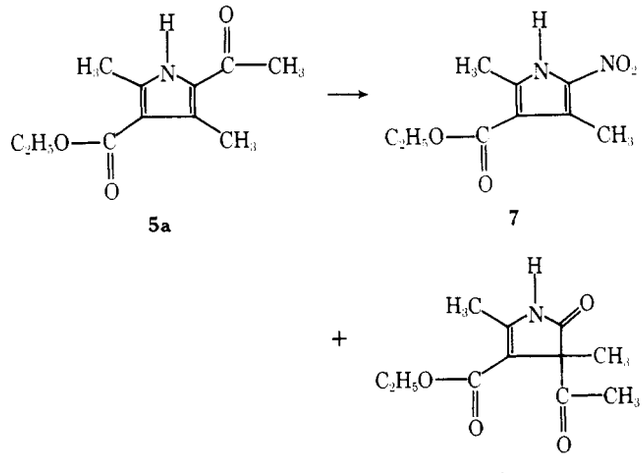
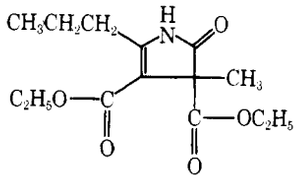


**Table II. $^{13}C$ Chemical Shifts for Ring Carbon Atoms in Substituted Pyrrolinones**

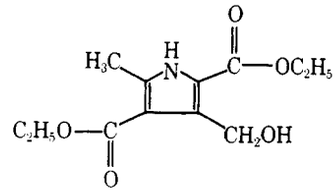
| Compd | C-2 | C-3 | C-4 | C-5 |
|---|---|---|---|---|
| | | $\Delta^2$-Pyrrolinones | | |
| **6a** | 153.7 | 111.7 | 64.5 | 163.4 |
| **6c** | 152.7 | 122.5 | 57.6 | 168.9 |
| **6f** | 153.4 | 111.6 | 57.5 | 163.5 |
| **6g** | 153.0 | 110.1 | 56.4 | 163.2 |
| **6h** | 151.8 | 112.2 | 57.3 | 163.7 |
| **8** | 157.8 | 111.8 | 57.6 | 163.3 |
| **13a** | 153.6 | 109.3 | 41.8[a] | 164.3 |
| **13b** | 151.7 | 110.2 | 43.1[a] | 164.4 |
| **15a** | 152.5 | 113.8 | 45.9 | 164.3 |
| **15b** | 154.4 | 112.6 | 59.8 | 163.1 |
| **15c** | 155.5 | 110.8 | 63.3 | 163.3 |
| **15d** | 154.9 | 111.0 | 56.3 | 163.3 |
| **17** | 150.1 | 114.6 | 47.3 | 164.3 |
| | | $\Delta^3$-Pyrrolinones | | |
| **14a** | 58.3[a] | 141.6[b] | 143.6[b] | 163.2 |
| **14b** | 53.8[a] | 143.4[b] | 143.9[b] | 163.4 |
| **18** | 56.6[a] | 141.2[b] | 144.3[b] | 162.8 |

[a] Doublet in the off-resonance decoupled spectrum. [b] Assignments for C-3 and C-4 may have been inverted.

Fischer and Triebs,[8] and as **10** by Triebs and Grimm.[9] That compounds **6a–i** and **8** are pyrrolinones is supported by spectral and chemical data. All of the compounds show a signal



**8**



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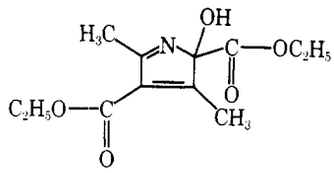
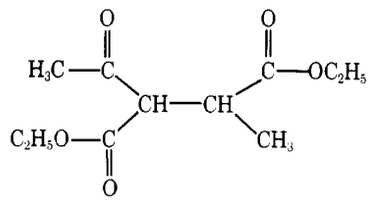


**10**

for the C-4 methyl group near $\delta$ 1.6 in the NMR spectrum (Table I); in the intermediate pyrroles the signal for this group is displaced downfield by about 0.9 ppm. Similar chemical shifts were found for the ring carbon atoms in these pyrrolinones (Table II).

The structure of **6a** was further indicated by its conversion, through N-methylation and hydrolytic removal of the acetyl group, to an isomeric mixture of **13a** and **14a.** This mixture of isomers was also prepared by allowing diethyl 2-acetyl-3-methylsuccinate (**11**) to react with methylamine to give **12a,**[10] which was then cyclized by heating at 190 °C. Only **13a,** the major isomer (75%) in this reaction, has been previously reported.[11–13] Two groups have described the related synthesis of **13b** from **11** and ammonia;[14,15] again, the isomeric pyrrolinone **14b** and intermediate **12b** were not isolated. We have found that cyclization of **12b** also gives a mixture of double bond isomers **13b** (85%) and **14b** (15%). Both isomer mixtures were readily separated into their components by chromatography on silica gel, and the isomers could be further purified by distillation (**13a** and **13b**) or by crystallization (**14a** and **14b**). While the compounds were stable to chromatography



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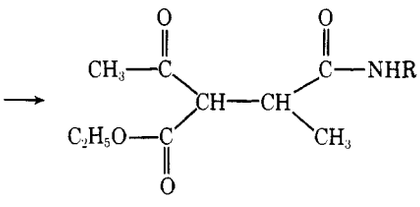
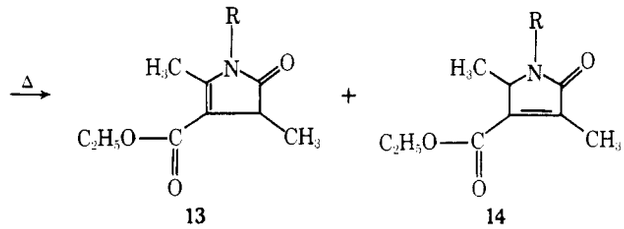


**12**



**13** **14**

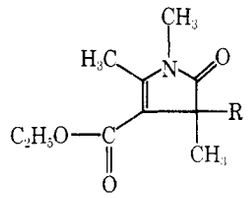
a, R = $CH_3$
b, R = H

and distillation, brief treatment of **13a** or **14a** with base regenerated the isomer mixture in which **13a** predominated. The greater stability of the $\Delta^2$ isomer (**13a**) is consistent with the findings of Atkinson et al.[15] The structures for the isomers have been assigned from spectral information. Compounds **13a** and **13b** have ultraviolet maxima near 285 nm and show a signal for the C-4 ring hydrogen near $\delta$ 3.3 in the NMR spectrum.[13,15] The pyrrolinone ring $^{13}C$ resonances for these compounds (Table II) are similar to those found for **6a–i.** The signal for C-4 is shifted upfield (ca. 15 ppm) as expected, for this position no longer bears an exocyclic carbonyl function. The isomeric pyrrolinones **14a** and **14b** show a lower wavelength UV maximum ($\lambda_{max}$ 228 nm) and an NMR signal for the C-2 ring hydrogen near $\delta$ 4.2.[13] The $^{13}C$ chemical shifts for the ring carbon atoms (Table II) are consistent with the proposed structures and readily allow the compounds to be distinguished from their $\Delta^2$ isomers.

We have investigated the alkylation and acylation of **13a** and **13b** in an attempt to find alternate procedures for the synthesis of pyrrolinones of structure type **6.** Various structures, a result of C-, O-, or N- (**13b** only) acylation, can be proposed for the products formed in these reactions. Products of all the possible structure types have been isolated (Table I) and their structures have been assigned from spectral considerations. The acylation reactions occasionally gave a single product, but more often mixtures containing two major products were formed. To ensure that all products formed in significant amount in these reactions were identified, the crude product was analyzed by TLC and VPC, and the major components were identified after purification on silica gel.

The anion of **13a,** formed from **13a** and lithium diisopropylamide, reacted with methyl iodide and benzoyl chloride to give **15a** and **16a,** respectively. C- and O-acylation products were formed in the reaction of **13a** with acetyl chloride (**15c** and **16c,** 1:2 mixture) and ethyl chloroformate (**15d** and **16d,** 1:9 mixture); compounds **15c** and **15d** have also been prepared in high yield by reaction of pyrrolinones **6a** and **6f** with methyl iodide. Dimethylcarbamoyl chloride reacted with **13a** to give a low yield of the O-acylated product **16e.**

Mixtures of mono- and diacylated products were formed



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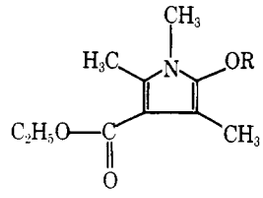
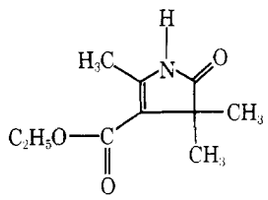


16

a, R = $CH_3$
b, R = $COC_6H_5$
c, R = $COCH_3$
d, R = $COOC_2H_5$
e, R = $CON(CH_3)_2$

when the anion of **13b**, formed from **13b** and sodium hydride, was treated with various reagents. In the reaction with methyl iodide **13a**, **17**, and **15a** were the major products, while with ethyl chloroformate **18** and **19a** were obtained. Acetyl chloride reacted with **13b** to give a mixture of **19b** and **20**; compound



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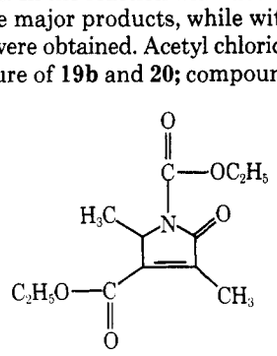
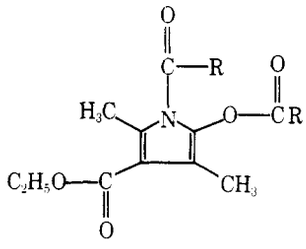
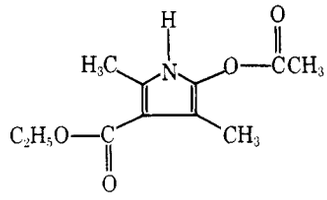


18



19a, R = $OC_2H_5$
b, R = $CH_3$



20

**20** has also been prepared by refluxing **13b** in acetic anhydride.[16,17]

The $^{13}C$ NMR spectra for compounds **20**, **16c–e**, **19a**, and **19b** resemble those of other pyrroles,[18] and show four resonances between $\delta$ 105 and 135 for the ring carbon atoms. An IR band near 1550 $cm^{-1}$ also is characteristic of the pyrrole structure and is not found for any of the pyrrolinones (Table I). The structures assigned to pyrrolinones **15a–d**, **17**, and **18** are in agreement with their spectral properties (Tables I and II).

Thus, 4,4-disubstituted pyrrolinones may be prepared by alkylation of **13a** and **13b** or by acylation of **13a**. The value of the acylation approach, however, is limited owing to formation of O-acylated products in several of the reactions. Acylation of **13b** did not afford 4,4-disubstituted pyrrolinones, but gave 5-acyloxypyrroles as the major reaction products.

## Experimental Section[19]

**General Procedure for Pyrrole Oxidation.**[6] The pyrrole (**5**) was added with stirring to concentrated nitric acid (10 mL/g of pyrrole) at 10 °C. The reaction was kept at 10–20 °C until TLC (4:1 benzene/ethyl acetate) showed complete conversion of the pyrrole to the slower moving pyrrolinone; once the pyrrole had completely dissolved in the acid, reaction was usually complete in 5–15 min. The reaction mixture was diluted to four times its volume with ice/water, and any precipitate was removed by filtration and washed with water. The filtrate was extracted three or four times with chloroform, the combined chloroform layer was washed with water, and the chloroform was evaporated to give the pyrrolinone (**6**). This was purified by crystallization or by chromatography on silica gel followed by crystallization to constant melting point.

**Oxidation of diethyl 3,5-dimethylpyrrole-2,4-dicarboxylate (5f)**[21] gave diethyl 4,5-dihydro-2,4-dimethyl-5-oxo-1*H*-pyrrole-3,4-dicarboxylate (**6f**, 45%): mp 126–128 °C from ethyl acetate; NMR $\delta$ 1.22 (t, 3, $CH_3$), 1.28 (t, 3, $CH_3$), 1.61 (s, 3, $CH_3$), 2.43 (s, 3, $CH_3$), 4.17 (q, 2, $OCH_2$), 4.20 (q, 2, $OCH_2$) and 9.10 (s, 1, NH); $^{13}C$ NMR $\delta$ 13.4 (q), 14.1 (q), 14.3 (q), 19.2 (q), 57.5 (s), 60.0 (s), 61.8 (t), 111.6 (s), 153.4 (s), 163.5 (s), 168.6 (s), and 177.9 (s); IR 1755, 1720, 1700, and 1650 $cm^{-1}$; $\lambda_{max}$ (EtOH) 283 nm ($\epsilon$ 12 400).

Anal. Calcd for $C_{12}H_{17}NO_5$: C, 56.46; H, 6.71; N, 5.49. Found: C, 56.14; H, 6.79; N, 5.60.

**Ethyl 2-Acetyl-3-[(methylamino)carbonyl]butyrate (12a).** Aqueous methylamine (10 mL of 40% solution) was added to a stirred solution of diethyl 2-acetyl-3-methylsuccinate (20 g, 0.088 mol) in ethanol (20 mL). After 20 h the solution was partitioned between chloroform and water, the chloroform was evaporated, and the residual oil was recrystallized from ethyl acetate/Skellysolve B to give 8.1 g (43%) of **12a**, mp 101–104 °C. The analytical sample was recrystallized from ethyl acetate: mp 104–107 °C; NMR $\delta$ 1.20 (d, 3, $CH_3$), 1.32 (t, 3, $CH_3$), 1.69 (s, 3, $CH_3$), 2.67 (d, 1, $J$ = 10 Hz, CH), 3.08 (m, 1, CH), 4.26 (q, 2, $OCH_2$), and 4.59 (s, 1, NH); IR 1690 $cm^{-1}$.

Anal. Calcd for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51. Found: C, 56.04; H, 8.27; N, 6.63.

The reaction was repeated using **11** (69 g), anhydrous methylamine (30 mL, liquid), and ether (50 mL) as solvent to give 40.8 g (63%) of **12a**.

**Cyclization of 12a.** Compound **12a** (40.0 g, 0.185 mol) was heated at 190 °C for 15 min and then cooled. The oil obtained was dissolved in benzene and chromatographed on silica gel. Elution of the column with benzene/ethyl acetate (4:1) gave 27.5 g (74%) of ethyl 4,5-dihydro-1,2,4-trimethyl-5-oxo-1*H*-pyrrole-3-carboxylate (**13a**). The analytical sample was distilled: bp 115–120 °C (0.2 mm); NMR $\delta$ 1.28 (t, 3, $CH_3$), 1.38 (d, 3, $CH_3$), 2.42 (d, 3, $J$ = 2 Hz, $CH_3$), 3.0 (s, 3, $CH_3$), 3.0 (m, 1, CH), and 4.20 (q, 2, $OCH_2$); $^{13}C$ NMR $\delta$ 12.4 (q), 14.5 (q), 15.4 (q), 26.2 (q), 41.8 (d), 59.5 (t), 109.3 (s), 153.6 (s), 164.3 (s), and 179.8 (s); IR 1700, 1680, and 1625 $cm^{-1}$; $\lambda_{max}$ (EtOH) 220 nm ($\epsilon$ 4750) and 289 (10 000).

Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.89; H, 7.67; N, 7.10. Found: C, 61.00; H, 7.79; N, 7.11.

Continued elution of the column gave 7.6 g (20%) of ethyl-2,5-dihydro-1,2,4-trimethyl-5-oxo-1*H*-pyrrole-3 carboxylate (**14a**). The analytical sample was distilled: bp 95 °C (0.05 mm); NMR $\delta$ 1.37 (t, 3, $CH_3$), 1.50 (d, 3, $CH_3$), 2.19 (d, 3, $J$ = 2 Hz, $CH_3$), 3.02 (s, 3, $CH_3$), 4.20 (m, 1, CH), and 4.32 (q, 2, $OCH_2$); $^{13}C$ NMR $\delta$ 11.1 (q), 14.3 (q), 16.7 (q), 26.9 (q), 58.3 (d), 60.8 (t), 141.6 (s), 143.6 (s), 163.2 (s), and 169.5 (s); IR 1700 and 1680 $cm^{-1}$; $\lambda_{max}$ (EtOH) 228 nm ($\epsilon$ 12 300) and 271 (2350).

Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.89; H, 7.67; N, 7.10. Found: C, 61.02; H, 7.94; N, 7.27.

**Ethyl 2-Acetyl-3-(aminocarbonyl)butyrate (12b).** Liquid ammonia (30 mL) was added to a stirred solution of diethyl 2-acetyl-3-methylsuccinate (69 g, 0.3 mol) in ether (200 mL). After 6 h the precipitate of **12b** (39.5 g, mp 92–98 °C) was filtered off and washed with ether. The analytical sample was recrystallized from ethyl acetate: mp 99–106 °C; NMR $\delta$ 1.18 (d, 3, $CH_3$), 1.32 (t, 3, $CH_3$), 1.68 (s, 3, $CH_3$), 2.75 (d, 2, $J$ = 10 Hz, CH), 3.06 (m, 1, CH), 4.22 (q, 2, $OCH_2$), 4.92 (s, 1, NH), and 7.62 (s, 1, NH); IR 1715 $cm^{-1}$.

Anal. Calcd for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96. Found: C, 54.01; H, 7.74; N, 6.93.

**Cyclization of 12b.** Compound **12b** (128 g, 0.64 mol) was heated at 190 °C for 15 min. The solid obtained on cooling was recrystallized from ethanol (100 mL) to give 75 g (59%) of ethyl 4,5-dihydro-2,4-dimethyl-5-oxo-1*H*-pyrrole-3-carboxylate (**13b**), mp 120–125 °C. A sample was recrystallized twice from ethyl acetate for analysis: mp 125–128 °C; NMR $\delta$ 1.30 (t, 3, $CH_3$), 1.40 (d, 3, $CH_3$), 2.38 (d, 3, $J$ = 2 Hz, $CH_3$), 3.27 (m, 1, CH), 4.22 (q, 2, $OCH_2$), and 9.4 (s, 1, NH); $^{13}C$ NMR $\delta$ 13.6 (q), 14.5 (q), 15.2 (q), 43.1 (d), 59.7 (t), 110.2 (s), 151.7 (s), 164.4 (s), and 182.8 (s); IR 1725, 1685, and 1640 $cm^{-1}$; $\lambda_{max}$ (EtOH) 218 nm ($\epsilon$ 4150) and 281 (11 850).

Anal. Calcd for $C_9H_{13}NO_3$: C, 59.00; H, 7.15, N, 7.65. Found: C, 59.13; H, 7.16; N, 7.50.

Evaporation of the ethanol mother liquors gave 35 g of a mixture of **13b** and **14b**. This was dissolved in ethyl acetate and chromatographed on silica gel. Elution of the column with ethyl acetate gave additional **13b** (12.2 g) followed by ethyl 2,5-dihydro-2,4-dimethyl-5-oxo-1*H*-pyrrole-3-carboxylate (7.2 g, 6%). The product was recrystallized from ethyl acetate/Skellysolve B to give 5.1 g of **14b**, mp 90–94 °C. The analytical sample was recrystallized twice from ethyl

acetate: mp 94–97 °C; NMR δ 1.37 (t, 3, $CH_3$), 1.44 (d, 3, $CH_3$), 2.21 (d, 3, $J$ = 2 Hz, $CH_3$), 4.37 (q, 2, $OCH_2$), 4.3 (m, 1, CH), and 8.40 (s, 1, NH); $^{13}C$ NMR 10.8 (q), 14.3 (q), 18.8 (q), 53.8 (d), 60.9 (t), 143.4 (s), 143.9 (s), 163.4 (s), and 172.9 (s); IR 1700 $cm^{-1}$; $\lambda_{max}$ (EtOH) 228 nm (ε 13 500) and 288 (1000).

Anal. Calcd for $C_9H_{13}NO_3$: C, 59.00; H, 7.15; N, 7.65. Found: C, 59.28; H, 7.24; N, 8.07.

**Equilibration of 13a and 14a.** The purified compound (**13a** or **14a**, 1.0 g) was dissolved in ethanol (10 mL) containing sodium methoxide (10 mg). After 5 min the product was partitioned between benzene (200 mL) and water (50 mL). Evaporation of the benzene layer gave 0.95 g of product, which by TLC and NMR analysis was a mixture of **13a** (75%) and **14a** (25%).

**General Procedure for Acylation of Pyrrolinones Using Sodium Hydride.** Sodium hydride (1.3 g, 0.027 mol, 50% in oil) was added to a stirred solution of the pyrrolinone (0.025 mol) in tetrahydrofuran (50 mL) at 25 °C. After 5 min the acylating reagent (0.03 mol) was added and the reaction mixture was stirred for 30 min. The product was partitioned between benzene and water. Evaporation of the benzene gave an oil which was analyzed by TLC and VPC,[19] and purified by column chromatography on silica gel (initial eluent 9:1 benzene/ethyl acetate). The purified compound was then distilled or recrystallized to constant melting point.

**Ethyl 4-acetyl-4,5-dihydro-1,2,4-trimethyl-5-oxo-1*H*-pyrrole-3-carboxylate (15c)** was prepared from **6a** and methyl iodide; VPC of the crude product showed 88% conversion to **15c**, retention time 7.1 min.[19] Recrystallization from Skellysolve B gave 48% of **15c**: mp 46–49 °C; NMR δ 1.25 (t, 3, $CH_3$), 1.51 (s, 3, $CH_3$), 2.00 (s, 3, $CH_3$), 2.54 (s, 3, $CH_3$), 3.14 (s, 3, $NCH_3$), and 4.18 (q, 2, $OCH_2$); IR 1745, 1700, and 1640 $cm^{-1}$.

Anal. Calcd for $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; N, 5.85. Found: C, 60.52; N, 7.40; N, 5.73.

**Hydrolysis of 15c.** Compound **15c** (250 mg) and sodium methoxide (10 mg) were dissolved in ethanol (5 mL). After 5 min acetic acid (15 mg) in ethanol (1 mL) was added and the product was partitioned between benzene and water. Evaporation of the benzene gave an oil (190 mg), identified as a mixture of **13a** and **14a** by TLC, NMR, VPC, and IR analysis.

**General Procedure for Acylation of 13a Using Lithium Diisopropylamide.** Compound **13a** (0.025 mol) in tetrahydrofuran (25 mL) was added to a stirred solution of lithium diisopropylamide (0.03 mol) in hexane/tetrahydrofuran (1:4, 100 mL) at −40 °C. The resulting slurry was allowed to warm to room temperature, the acylating reagent (0.05 mol) was added, and the solution was stirred for a further 30 min. Workup, analysis, and purification were carried out as described above for acylation reactions using sodium hydride as base.

**Registry No.**—**5a,** 6314-22-3; **5b,** 62264-99-7; **5c,** 2386-26-7; **5d,** 5448-17-9; **5e,** 21898-57-7; **5f,** 2436-79-5; **5g,** 40593-29-1; **5h,** 40593-32-6; **5i,** 40593-54-2; **7,** 23314-05-8; **11,** 1113-77-5; **12a,** 62265-00-3; **12b,** 62265-01-4; ethyl 3,5-dimethyl-4-nitropyrrole-2-carboxylate, 5463-44-5; diethyl 3-methyl-5-propylpyrrole-2,4-dicarboxylate, 27093-52-3; 4,5-dihydro-2,4-dimethyl-5-oxo-1*H*-pyrrole-1,3,4-tricarboxylate triethyl ester, 62265-02-5; methyl iodide, 74-88-4; ethyl chloroformate, 541-41-3; acetic anhydride, 108-24-7; benzoyl chloride, 98-88-4; acetyl chloride, 75-36-5; dimethylcarbamoyl chloride, 79-44-7; methyl 2,4-dimethyl-5-nitropyrrole-3-carboxylate, 62265-03-6.

**Supplementary Material Available.** Information on the preparation and purification of the remainder of the compounds described in the paper and their elemental analyses and full spectral information (8 pages). Ordering information is given on any current masthead page.

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