# Synthesis of Pyrrolo[2,3-b]azepine-4,7-dione Derivatives

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The Dieckmann reaction has been successfully applied for the first time in the synthesis of pyrrolo[2,3-b]azepines.

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As part of a program to prepare potential antineoplastic (2) and antimalarial agents, we became interested in the synthesis of various substituted pyrrolo[2,3-b] azepines (1), which could possibly act as antimetabolites of riboflavin. In contrast to the numerous reports (3,4) which have appeared for the synthesis of benzazepines, few references are prevalent for preparation of pyrroloazepines. Synthesis of several pyrroloazepinones was accomplished by

Beckmann (5-8) or Schmidt (9) type ring-enlargement reactions on the corresponding pyrrolocyclohexanones. Intramolecular cyclization of amino esters has also been employed to yield pyrroloazepinones (10,11).

The Dieckmann reaction (12) does not appear to have been utilized in the synthesis of pyrroloazepinones, and to our knowledge no pyrroloazepinediones (1) have been synthesized by application of any of the procedures mentioned. Scheme I outlines a route which can be utilized to synthesize various substituted derivatives of 1.

2-Amino-3,4-dicarbethoxypyrrole (2) was prepared by the method of Gewald and co-workers (13). Protection of the N-1 position was achieved by two different methods. Initially, the phthalimido derivative (3) was prepared followed by N-1 alkylation (4) and hydrazinolysis (5). Subsequently, it was possible to alkylate 2 directly with dimethylsulfate in the presence of base to obtain 5a. Acylation of 5 with 3-carbomethoxypropionyl chloride gave the diesters (6), which could be presented for Dieckmann cyclization. However, upon cyclization the mixed ester functionality present in 6a led to a low yield of product con-

taining the ethyl ester (8a) and the methyl ester (8c). When 6 was subjected to transesterification, the resulting product 7 was cyclized without difficulty to give good yields of the desired pyrroloazepinedione (8). To avoid possible formation of succinimide derivatives (9), it was necessary to utilize at least two equivalents of sodium metal or sodium hydride in pyrroloazepinedione synthesis from 6 or 7.



In order to increase the hydrophilicity of **8a**, compound **8e** was proposed (16). The procedure in Scheme I was readily adapted to the preparation of **8b**. Catalytic hydrogenolysis of **8b** (17) failed to produce the hydroxymethyl derivative. Similarly, treatment of **8b** with hydrobromic acid at room temperature had no effect, and the starting compound was recovered intact.

When 8c was heated in 0.2N hydrochloric acid, the material obtained was indicated by its spectral and analytical data to be the product of ring contraction (10), rather than the product of hydrolysis and decarboxylation.



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This observation was in agreement with the literature reports (14,18,19) relating to attempted hydrolysis and decarboxylation of benzazepinediones.

The monomethyl derivative (12) of 5a was prepared by sodium borohydride reduction of the alkyl imidate (11) prepared from triethyl orthoformate (20) (Scheme II). Acylation with 3-carbomethoxypropionyl chloride (13) and Dieckmann cyclization (14) proceeded as previously described. Further studies utilizing the procedure successfully applied in this report should consider the use of a variety of substituents in order to establish meaningful structure-activity relationships.



## **EXPERIMENTAL**

Melting points were determined on a Thomas-Hoover apparatus (capillary method) and are uncorrected. Infrared spectra were determined on a Perkin-Elmer 467 Grating Spectrophotometer. The nmr spectra were determined on a Hitachi Perkin-Elmer R20A High Resolution nmr spectrometer using Tetramethylsilane (TMS) as internal reference. Mass spectra were determined on a Dupont 21-490 mass spectrometer. Elemental analyses were determined by Atlantic Microlab, Inc., Atlanta, Georgia.

## 3,4-Dicarbethoxy-2-phthalimidopyrrole (3).

In a 1000 ml. round-bottomed, three-neck flask, a mixture of 3.4 g. (0.015 mole) of 2-amino-3,4-dicarbethoxypyrrole (2) (13) and 2.25 g. (0.015 mole) of phthalic anhydride in 250 ml. of xylene was heated to reflux. Water from the reaction was collected in a Dean-Stark apparatus. Reflux was continued for 12 hours. After cooling to room temperature, the crude product was collected by filtration and recrystallized from benzene (80-90%), m.p. 199.5-201.5°; ir (potassium bromide): 3240, 2980, 1790, 1720, 1560, 1512, 1443, and 1055 cm<sup>-1</sup>; mmr (DMSO- $d_{h}$ ):  $\delta$  8.8 (s, 4H, aromatic H's), 7.6 (s, 1H, H at C-5), 4.15 (2q, 4H, CH<sub>2</sub>'s of -CO<sub>2</sub>C<sub>2</sub>H<sub>3</sub>), 1.29 and 0.95 (2t, CH<sub>3</sub>'s of -CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>).

Anal. Calcd. for  $C_{18}H_{16}N_{2}O_{6}\!\!:$  C, 60.67; H, 4.53; N, 7.86. Found: C, 60.60; H, 4.54; N, 7.87.

#### 3,4-Dicarbethoxy-1-methyl-2-phthalimidopyrrole (4a).

A 250 ml. three-neck, round-bottomed flask was fitted with a nitrogen inlet and a dry-ice-2-propanol condenser. A solution of 3.56 g. (0.01 mole) of **3** in 200 ml. of dimethylformamide was placed in the flask and the mixture cooled in an ice-bath. Potassium t-butoxide (1.23 g., 0.011 mole) was added to the chilled solution. After 15 minutes, the mixture was treated with 2 ml. of methyl iodide. After stirring the mixture overnight (20 hours), the solution was concentrated *in vacuo*. The crude solid was suspended in chloroform and filtered to remove potassium iodide. Evaporation of the chloroform yielded a dark solid which was washed with cold 95% ethanol to yield a white solid. The product thus obtained was recrystallized from benzene-petroleum ether to yield **4a** as a white

crystalline solid (75%), m.p. 144-145.5°; ir (potassium bromide): 2980, 1787, 1724, 1700, 1533, 1451, and 1232 cm<sup>-1</sup>; nmr (DMSO- $d_b$ ):  $\delta$  7.94 (m, 4H, aromatic H's), 7.31 (s, 1H, H at C-5), 4.2 (2q, 4H, CH<sub>2</sub>'s of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>), 3.54 (s, 3H, NCH<sub>3</sub>), 1.30 and 1.00 (2t, 6H, CH<sub>3</sub>'s of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>).

Anal. Calcd. for  $C_{19}H_{18}N_2O_6{:}$  C, 61.62; H, 4.90; N, 7.56. Found: C, 61.52; H, 4.92; N, 7.56.

1-Benzyloxymethyl-3,4-dicarbethoxy-2-phthalimidopyrrole (4b).

The compound was prepared in the same manner as 4a using *N*benzyloxymethyl chloride (17,21) as the alkylating agent. The oily product was purified by passing through a silica gel column, using benzene as eluent. The oil was used directly in the synthesis of **5b**.

2-Amino-3,4-dicarbethoxy-1-methylpyrrole (5a).

## Method A.

A refluxing solution of 2.0 g. (0.0054 mole) of **4a** in 300 ml. of absolute ethanol was treated with 10 ml. (0.026 mole) of 85% hydrazine hydrate. Within 5 minutes, a thick precipitate appeared. Refluxing was continued for 2.5 hours. The solvent was evaporated off at reduced pressure. The white solid was chilled in an ice-bath and treated with 20 ml. of 50% potassium hydroxide. The basic solution was extracted with three 250 ml. portions of ether. The organic layer was dried over sodium sulfate. Removal of the solvent, *in vacuo*, yielded an oil which solidified upon standing. The crude product was recrystallized from benzene-petroleum ether (80%), m.p. 84.5-86°; ir (potassium bromide): 4360, 3348, 1705, 1645, 1520, 1316, and 760 cm<sup>-1</sup>; nmr (deuteriochloroform):  $\delta$  6.79 (s, 1H, H at C-5), 5.25 (s, 2H, NH<sub>2</sub>), 4.25 (q, 4H, CH<sub>2</sub>'s of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>), 1.30 (two overlapping t's, 6H, CH<sub>3</sub>'s of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>).

Anal. Calcd. for  $C_{11}H_{16}N_2O_4{:}\,$  C, 54.99; H, 6.71; N, 11.66. Found: C, 54.96; H, 6.72; N, 11.66.

## Method B (22).

2-Amino-3,4-dicarbethoxypyrrole (2) (11.3 g., 0.05 mole) was dissolved in 100 ml. of dry tetrahydrofuran (distilled from lithium aluminum hydride) and placed in an ice-bath. Potassium t-butoxide (6.3 g., 0.055 mole) was added to the cold solution. After a few minutes, the mixture was treated with dimethyl sulfate (6.9 g., 0.055 mole) and the ice-bath was removed. The mixture was stirred at room temperature for 15 minutes, and then it was refluxed for 1 hour. The tetrahydrofuran was removed in vacuo, the residue was treated with water, and the compound was extracted with chloroform. The chloroform layer was passed through a short silica gel column and concentrated in vacuo. The product (50.4%) was recrystallized from benzene-petroleum ether and found to be identical to **5a** obtained by Method A.

#### 2-Amino-1-benzyloxymethyl-3,4-dicarbethoxypyrrole (5b).

This compound was prepared in the same manner as compound **5a** (Method A). The crude product was purified by passing through a silica gel column and the oil was used directly in the next step; ir (neat): 3470, 3370, 3000, 1725, 1670, 1615, 1212, 740 and 690 cm<sup>-1</sup>; nmr (deuterio-chloroform)  $\delta$  7.3 (s, 5H, aromatic H's), 6.75 (s, 1H, H at C-5), 5.4 (s, 2H, NH<sub>2</sub>) 5.1 (s, 2H, Ar-CH<sub>2</sub>-O), 4.42 (s, 2H, N-CH<sub>2</sub>-O), 4.25 (q, 4H, CH<sub>2</sub>'s of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>), 1.31 (t, 6H, CH<sub>3</sub>'s of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>).

Anal. Calcd. for  $C_{18}H_{22}N_2O_3$ : C, 62.41; H, 6.40; N, 8.09. Found: C, 62.13; H, 6.38; N, 7.97.

2-(3-Carbomethoxypropionamido)-3,4-dicarbethoxy-1-methylpyrrole (6a).

To a refluxing mixture of **5a** (2.4 g., 0.01 mole) and anhydrous potassium carbonate (2 g., 0.015 mole) in 200 ml. of dry toluene, 1.65 g. (0.011 mole) of 3-carbomethoxypropionyl chloride was carefully added. The reaction mixture was refluxed for 2 hours, cooled, and filtered. The filtrate was washed with 4N hydrochloric acid, 5% sodium bicarbonate, and water. After drying over sodium sulfate, the solvent was removed *in vacuo* to yield an oil (76%) which crystallized from benzene-petroleum ether as a white solid, m.p. 76.5-78.5°; ir (potassium bromide): 3270, 2970, 1730, 1683, 1550, 1292 and 1065 cm<sup>-1</sup>; nmr (deuteriochloroform):  $\delta$  7.05 (s, 11H, H at C-5), 8.35 (broad, 1H, NH), 4.28 (q, 4H, CH<sub>2</sub>'s of CO<sub>2</sub>C<sub>2</sub>H<sub>3</sub>), 3.70 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 3.50 (s, 3H, NCH<sub>3</sub>), 2.70 (s, 4H,

-COCH2CH2CO-), 1.31 (t, 6H, CH3's of CO2C2H5).

Anal. Calcd. for C16H22N2O7: C, 54.23; H, 6.25; N, 7.90. Found: C, 54.32; H, 6.26; N, 7.89.

## 2-(3-Carbethoxypropionamido)-3,4-dicarbethoxy-1-methylpyrrole (7a).

To a solution of **6a** (4.1 g., 0.0115 mole) in 450 ml. of absolute ethanol was added 10 drops of concentrated sulfuric acid. The reaction flask was fitted with a Soxhlet extractor charged with type 3A molecular sieve (80 g.) and the mixture was refluxed for 24 hours. Ethanol was removed in vacuo and the residue was dissolved in 100 ml. of chloroform. The chloroform solution was washed with 50 ml. of water, dried over magnesium sulfate, and concentrated in vacuo to yield an oil (4.0 g., 94%). The oil was crystallized from ether-petroleum ether to yield white needles (2.7 g.), m.p. 76-78°; ir (potassium bromide): 3350, 2980, 1740, 1695, 1550, 1440, and 1290 cm<sup>-1</sup>; nmr (deuteriochloroform): 8 8.35 (s, 1H, NHCO), 7.06 (s, 1H, H at C-5), 4.30 (q, 4H, CH2's of C-3,4 CO2C2H5), 4.15 (q, 2H, CH<sub>2</sub> of aliphatic CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>), 3.51 (s, 3H, NCH<sub>3</sub>), 2.72 (s, 4H, -COCH2CH2CO-), 1.34 (t, 6H, CH3's of C-3,4 CO2C2H5), 1.28 (t, 3H, CH3 of aliphatic CO,C,H,).

Anal. Calcd. for C17H24N2O7: C, 55.52; H, 6.37; N, 7.61. Found: C, 55.50; H, 6.61; N, 7.58.

1-Benzyloxymethyl-2-(3-carbethoxypropionamido)-3,4-dicarbethoxypyrrole (7b).

To a refluxing mixture of 5b (10.4 g., 0.030 mole) and dicyclohexyl methylamine (5.9 g., 0.030 mole) in 200 ml. of dry benzene, 3-carbomethoxypropionyl chloride (5 g., 0.033 mole) was added dropwise. The reaction mixture was refluxed for 4 hours and then 200 ml. of cold water was added. The benzene fraction was separated, washed one time with water (200 ml.), dried over magnesium sulfate, and concentrated in vacuo. The residue (6b, quantitative yield) was subject to transesterification in the same manner as **6a**. Crude **7b** (14 g., 97%) was passed through a silica gel column using ether as eluent. The solid obtained upon evaporation of the ether was recrystallized from ether (88%); m.p. 73.5-75°; ir (potassium bromide): 3340, 3000, 1730, 1170, 740 and 691 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 7.12 (s, 5H, aromatic H's), 7.08 (s, 1H, H at C-5), 5.2 (s, 2H, Ar-CH2-O), 4.38 (s, 2H, OCH2N), 4.21 (q, 4H, CH2's of C-3,4 CO2C2H3), 4.05 (q, 2H, CH2 of aliphatic CO2C2H3), 2.62 (s, 4H, COCH2CH2CO), 1.32 (t, 6H, CH3's of C-3,4 CO2C2H3), 1.22 (t, 3H, CH3 of aliphatic CO2C2H5).

Anal. Calcd. for C24H30N2O8: C, 60.75; H, 6.37; N, 5.91. Found: C, 60.76; H, 6.36; N, 5.89.

3,5-Dicarbethoxy-1-methylpyrrolo[2,3-b]azepine-4,7-dione (8a).

### Method A.

Compound 6a (3.0 g., 0.008 mole) in 15 ml. of dry toluene was added dropwise over a period of 15 minutes to a 200 ml., three-necked, roundbottomied flask, equipped with a reflux condenser, dropping funnel, nitrogen inlet, and magnetic stirrer, containing 0.5 g. (0.021 g. atom) of sodium metal in 20 ml. of toluene at a temperature of 95-100° and under an atmosphere of nitrogen (15). The brownish red mixture was heated at this temperature for 8 hours, cooled and filtered. The crude solid, free of any solvent, was then added to 200 ml. of water and the pH of the mixture was adjusted to 1 with 2N hydrochloric acid (pH Hydrion paper.)

The gummy precipitate was extracted with chloroform and the organic layer was dried over sodium sulfate. Evaporation in vacuo of the chloroform gave a solid product which was purified on a silica gel column eluted with a mixture of chloroform-hexane (7:3). Two products, 8a and 8c were obtained from the column.

The first compound (8a) obtained was crystallized from benzenepetroleum ether (30%), m.p. 196-198°; ir (potassium bromide): 3115, 1980, 1720, 1600, 1195 and 1072 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 12.6 (s, 1H, enolic OH), 10.1 (s, 1H, NH), 7.18 (s, 1H, H at C-2), 4.3 (q, 4H, CH<sub>2</sub>'s of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>), 3.65 (s, 3H, NCH<sub>3</sub>), 3.12 (s, 2H, H's at C-6), 1.32 (t, 6H, CH<sub>3</sub>'s of CO<sub>2</sub>C<sub>2</sub>H<sub>s</sub>); ms: molecular weight Calcd. 322; Found 322. Anal. Calcd. for C13H18N2O6: C, 55.90; H, 5.63; N, 8.65. Found: C,

55.73; H, 5.66; N, 8.65.

The second compound (8c) was recrystallized from benzene-petroleum ether (10%), m.p. 176-178.5°; ir (potassium bromide): 3200, 1720, 1676, 1550, 1440, 1352, 1278 and 1072 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 12.5 (s, 1H, enolic H), 10.1 (s, 1H, NH), 7.2 (s, 1H, H at C-2), 4.3 (q, 2H, CH<sub>2</sub> of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>), 3.85 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 3.78 (s, 3H, NCH<sub>3</sub>), 3.14 (s, 2H, H at C-6), 1.35 (t, 3H, CH<sub>3</sub> of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>); ms: molecular weight Calcd. 308; Found 308.

Anal. Calcd. for C14H16N2O6: C, 54.54; H, 5.23; N, 9.09. Found: C, 54.77; H, 5.34; N, 8.98.

## Method B.

Compound 7a (2.35 g., 0.0064 mole) in 30 ml. of dry toluene was added over a period of 20 minutes to a mixture of 50% sodium hydride dispersion (0.62 g., 0.0129 mole) in 20 ml. of dry toluene under a constant flow of nitrogen. The slightly brown reaction mixture was heated at 110° for 8 hours. After cooling the mixture in an ice-water bath, 2 ml. of acetic acid in 20 ml. of toluene was added dropwise, followed by 30 ml. of water. The toluene layer was separated, dried over sodium sulfate, and concentrated in vacuo. The crude product was recrystallized from benzenepetroleum ether to yield a white powder (53.5%); m.p. 195-197°. The spectral (ir, nmr, ms) and analytical data confirm the product to be identical to that obtained by Method A.

1-Benzyloxymethyl-3,5-dicarbethoxypyrrolo[2,3-b]azepine-4,7-dione (8b).

This compound was prepared in the same manner as 8a (Method B). The product was recrystallized from absolute ethanol (75%), m.p. 157-160°; ir (potassium bromide): 3150, 3000, 1740, 1680, 1200, 1065, 730 and 690 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 9.32 (s, 1H, NH), 7.3 (s, 5H, aromatic H's), 7.2 (s, 1H, H at C-2), 5.28 (s, 2H, ArCH<sub>2</sub>O), 4.47 (s, 2H, NCH<sub>2</sub>O), 4.3 and 4.25 (two q, 4H, CH<sub>2</sub>'s of C-3,5 CO<sub>2</sub>C<sub>2</sub>H<sub>s</sub>), 3.15 (s, 2H, CH, at C-6), 1.33 (t, 6H, CH,'s of C-3,5 CO,CO,H,).

Anal. Calcd. for C22H24N2O7: C, 61.67; H, 5.65; N, 6.54. Found: C, 61.79; H, 5.67; N, 6.47.

3-Carbethoxy-4,6-dihydroxy-1-methylpyrrolo[2,3-b]pyridine-5-acetic Acid (10)

A suspension of 8c (0.8 g., 0.0025 mole) in 0.2N hydrochloric acid was stirred vigorously at 80-85° for 2 hours and then cooled in the refrigerator. A solid was removed by filtration. The crude product was recrystallized from methanol to yield the rearranged product (10) as a white solid (68.5%), m.p. 265-266°; ir (potassium bromide): 3420, 2700, 1700, 1650, 1590 and 1150 cm<sup>-1</sup>; nmr (DMSO-d<sub>6</sub>): δ 11.4 (broad s, 1H, OH at C-6), 11.3 (s, 1H, OH at C-4), 7.8 (s, 1H, H at C-2), 4.35 (q, 2H, CH<sub>2</sub> of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>), 3.65 (s, 3H, NCH<sub>3</sub>), 3.48 (s, 2H, CH<sub>2</sub> at C-5), 1.2 (t, 3H, CH<sub>3</sub> of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>); ms: molecular weight Calcd. 294; Found: 294.

Anal. Calcd. for C13H14N2O6: C, 53.06; H, 4.79; N, 9.52. Found: C, 52.91; H, 4.81; N, 9.49.

## 3,4-Dicarbethoxy-1-methyl-2-methylaminopyrrole (12).

The amine 5a (2.4 g., 0.01 mole) and 15 ml. of triethyl orthoformate was refluxed with vigorous stirring for 2 hours (20). Excess triethyl orthoformate was removed in vacuo. The residue was dissolved in 40 ml. of ethanol and chilled in an ice-bath. Sodium borohydride (2.2 g.) was added over a 10 minute period. The ice-bath was removed in 0.5 hour and the mixture was stirred at room temperature for 35 hours. The ethanol was removed in vacuo, and the residual solid was covered with ethyl acetate and washed with water until a neutral pH was observed. The ethyl acetate layer was dried over sodium sulfate and concentrated in vacuo to an oil. The oil was purified on a silica gel column using benzene-chloroform (3:1) as eluent (73%); ir (neat): 3340, 2980, 1720, 1663, 1430, 1205 and 1055 cm<sup>-1</sup>; nmr (deuteriochloroform): δ 6.8 (s, 1H, H at C-5), 5.6 (broad m, 1H, NH), 4.25 (q, 4H, CH<sub>2</sub>'s of C-3,4 CO<sub>2</sub>C<sub>2</sub>H<sub>3</sub>), 3.51 (s, 3H, NCH<sub>3</sub> at N-1), 2.78 (d, 3H, NCH<sub>3</sub> at C-2), 1.32 (t, 6H, CH<sub>3</sub>'s of C-3,4 CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>).

Anal. Calcd. for C12H18N2O4: C, 56.68; H, 7.14; N, 11.02. Found: C, 56.41; H, 7.19; N, 10.93.

3,4-Dicarbethoxy-2-[N-methyl-N-(3-carbomethoxypropionyl)]amino-1methylpyrrole (13).

This compound was prepared in the same manner as **6a**. The oil product was chromatographed on a silica gel column using benzene-chloroform (1:1) as eluent (78%); ir (neat): 2988, 1730, 1680, 1530, 1435, 1205 and 1050 cm<sup>-1</sup>; nmr (deuteriochloroform):  $\delta$  7.34 (s, 1H, H at C-5), 4.3 (q, 4H, CH<sub>2</sub>'s of CO<sub>2</sub>C<sub>2</sub>H<sub>3</sub>), 3.69 (s, 3H, CO<sub>2</sub>CH<sub>3</sub>), 3.60 (s, 3H, NCH<sub>3</sub> at N-1), 3.15 (s, 3H, NCH<sub>3</sub> at C-2), 2.3 (m, 4H, COCH<sub>2</sub>CH<sub>2</sub>CO), 1.3 (t, 6H, CH<sub>3</sub>'s of CO<sub>3</sub>C<sub>4</sub>H<sub>4</sub>).

Anal. Calcd. for  $C_{17}H_{24}N_2O_7$ : C, 55.42; H, 6.57; N, 7.60. Found: C, 55.22; H, 6.63; N, 7.54.

3,5-Dicarbethoxy-1,8-dimethylpyrrolo[2,3-b]azepine-4,7-dione (14).

To a cold (0.5°) suspension of 2.4 g. (0.02 mole) of potassium t-butoxide in 600 ml. of dry ether, a solution of 7.0 g. (0.019 mole) of 13 in 50 ml. of ether was added over 45 minutes. Stirring was continued at 0-5° for 7 hours. The mixture was treated with 200 ml. of 2N hydrochloric acid and the ether layer was separated and washed with water. The organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent in vacuo yielded 4.5 g. of an oil which was chromatographed on a silica gel column using hexane-chloroform (3:2) as eluent. The light brown oil crystallized from benzene-petroleum ether (65%); m.p. 102-106°; ir (potassium bromide): 3125, 1780, 1700, 1522, 1433, 1285 and 1205 cm<sup>-1</sup>; nmr (deuteriochloroform): & 7.12 (s, 1H, H at C-2), 4.2 (m, 4H, CH2's of CO2C2H5 and 1H, H at C-5), 3.64 (s, 3H, NCH3 at N-1), 3.09 (s, 3H, NCH<sub>3</sub> at N-8), 2.95 (m, 2H, H's at C-6), 1.3 and 1.32 (2t, 6H, CH<sub>3</sub>'s of CO<sub>2</sub>C<sub>2</sub>H<sub>5</sub>); nis: molecular weight Calcd. 336; Found: 336. Anal. Calcd. for C16H20N2O6: C, 57.18; H, 5.99; N, 8.33. Found: C, 56.93; H, 6.00; N, 8.35.

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