Research on Nitrogen Heterocyclic Compounds. XII. Synthesis of 5*H*-Pyrrolo[1,2-*b*][2]benzazepine Derivatives

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Several routes to the synthesis of the unknown 5*H*-pyrrolo[1,2-*b*][2]benzazepine ring system have been explored. 1-(2-Cyanobenzyl)pyrrole was useful as starting material to obtain 1-(2-carboxymethylbenzyl)pyrrole and 1-(2-chloromethylbenzyl)-2-pyrrolecarboxaldehyde. Polyphosphoric acid catalyzed intramolecular cyclization of the former substance and treatment of the latter compound with potassium cyanide led to 11-oxo-10,11-dihydro-5H-pyrrolo[1,2-*b*]-[2]benzazepine and to 10-cyano-5*H*-pyrrolo[1,2-*b*][2]benzazepine, respectively. Starting from these materials the synthesis of the parent nucleus 5*H*-pyrrole[1,2-*b*][2]benzazepine and its 10,11-dihydro- and 1,2,3,10,11,11a-hexahydroderivatives has been realized.

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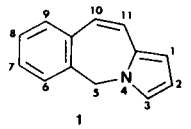
In connection with our studies on nitrogen heterocyclic compounds (1-6) related to alkaloids and antibiotics possessing antitumor activity, we were interested in the synthesis of 5*H*-pyrrolo[1,2-*b*][2]benzazepine **1**, a nitrogen heterocyclic ring isomeric with the 1*H*-pyrrolo-[2,1-*b*][3]benzazepine moiety **2**, which is incorporated into the naturally occurring antileukemic cephalotaxine **3** (7-9).



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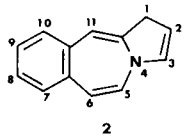

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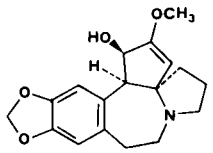

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The synthesis of the 5*H*-pyrrolo[1,2-*b*][2]benzazepine ring system has not to date been reported in the literature. We therefore decided to synthesize this novel nitrogen-containing ring and selected as potential starting material three compounds, namely, 1,2-bis(bromomethyl)benzene, 2-bromomethylphenylacetonitrile and 1-(2-cyanobenzyl)-pyrrole. The latter compound has been synthesized by one of us in a previous work of this series (10).

Attempts to prepare 1-(2-bromomethylbenzyl)pyrrole, a key intermediate to the required 5*H*-pyrrolo[1,2-*b*][2]-benzazepine, by reaction of 1,2-bis(bromomethyl)-benzene and the potassium salt of pyrrole under different reaction conditions led only to the symmetrical bis-pyrrolyl derivative **4**.

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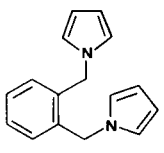
On the other hand, attempted preparation of 2-(2-formyl-1-pyrrolyl)methylphenylacetonitrile by condensation of 2-bromomethylphenylacetonitrile with pyrrole-2-carboxaldehyde potassium salt was unsuccessful because of the formation of 2,2′-bis(cyanomethyl)stilbene **5** by self condensation of the starting material.



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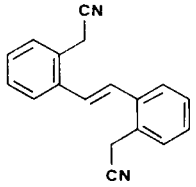

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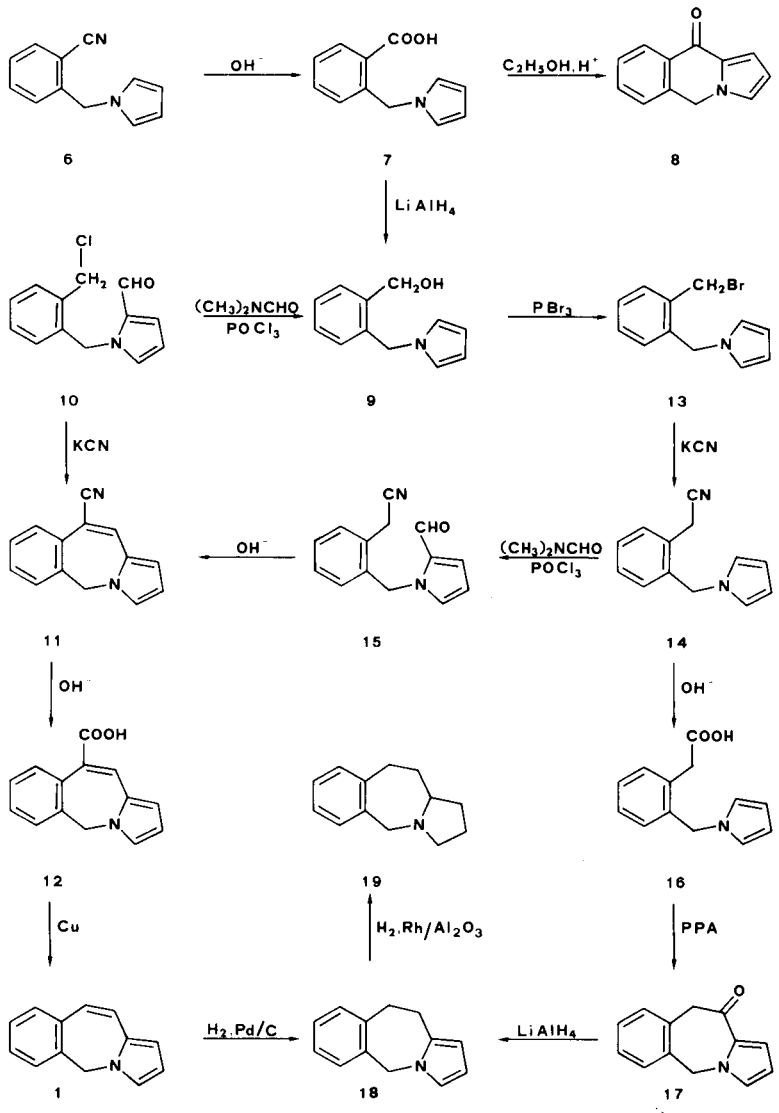
Only 1-(2-cyanobenzyl)pyrrole proved to be a good starting material for our purposes. Starting from this compound the sequence leading to 5*H*-pyrrole[1,2-*b*][2]-benzazepine and other related compounds is outlined in the Scheme.

Alkaline hydrolysis of 1-(2-cyanobenzyl)pyrrole **6** in ethylene glycol by refluxing for 3 hours gave, after acidification of the solution, 1-(2-carboxybenzyl)pyrrole **7**. When this acid was heated in anhydrous ethanol in the presence of concentrated sulphuric acid, instead of the expected ethyl ester, pyrrolo[1,2-*b*]isoquinolin-10(5*H*)-one **8** (11) was formed by intramolecular ring closure. The tricyclic compound **8** was also prepared from **7** by the action of polyphosphoric acid by a standard procedure.

Lithium aluminum hydride reduction of 1-(2-carboxybenzyl)pyrrole **7** in anhydrous dioxane by refluxing for 20 hours furnished 1-(2-hydroxymethylbenzyl)pyrrole **9**. From this material two routes led to 5*H*-pyrrolo[1,2-*b*]-[2]benzazepine derivatives.



The Vilsmeier-Haack condensation between **9** and *N*,*N*-dimethylformamide in the presence of phosphorus oxychloride afforded 1-(2-chloromethylbenzyl)-2-pyrrolecarboxaldehyde **10** as the result of formylation at the 2-pyrrole position with concomitant chlorination of the alcoholic function. When the chloroaldehyde **10** was heated with potassium cyanide in dimethylsulfoxide at 90° for 5 hours, 10-cyano-5*H*-pyrrolo[1,2-*b*][2]benzazepine **11** formed directly.

Hydrolysis of the nitrile **11** with potassium hydroxide in ethylene glycol led to 10-carboxy-5*H*-pyrrole[1,2-*b*]-[2]benzazepine **12**. This compound was then converted into the parent compound **1** by removal of the carboxylic group on heating at reflux with copper powder in quinoline medium.

Another phase of the synthetic approach to 5*H*-pyrrolo[1,2-*b*][2]benzazepine derivatives started once more from the alcohol **9**, which was treated with phosphorus tribromide in anhydrous ethyl ether to afford 1-(2-bromomethylbenzyl)pyrrole **13**. This compound was then transformed into 1-(2-cyanomethylbenzyl)pyrrole **14** by stirring for 4 days at room temperature with potassium cyanide in methanol.

Formylation of **14** by the Vilsmeier-Haack method gave 1-(2-cyanomethylbenzyl)-2-pyrrolecarboxaldehyde **15**. Compound **15** was then cyclized to the above described 10-cyano-5*H*-pyrrole[1,2-*b*][2]benzazepine **11** by refluxing in benzene in the presence of concentrated potassium hydroxide solution. Alkaline hydrolysis of **14** by heating for 3 hours at reflux in ethylene glycol furnished, after acidification of the solution with diluted hydrochloric acid, 1-(2-carboxymethylbenzyl)pyrrole **16**. Compound **16** was in turn subjected to intramolecular cyclization by treatment with polyphosphoric acid under a nitrogen

atmosphere to afford 11-oxo-10,11-dihydro-5*H*-pyrrolo-[1,2-*b*][2]benzazepine **17**.

Lithium aluminum hydride reduction of **17** in an anhydrous ethyl ether-tetrahydrofuran mixture led to 10,11-dihydro-5*H*-pyrrolo[1,2-*b*][2]benzazepine **18**, identical with the material obtained by 5% palladium on carbon catalyzed hydrogenation of the parent nucleus **1**.

When **18** was reduced with hydrogen in glacial acetic acid in the presence of 5% rhodium on alumina as a catalyst, 1,2,3,10,11,11a-hexahydro-5*H*-pyrrolo[1,2-*b*][2]-benzazepine **19** was formed. This compound was characterized as its hydrochloride.

The structure of the tricyclic compounds here described have been supported by their spectroscopic properties. Data concerning nmr and ir spectra are reported in the Experimental.

EXPERIMENTAL

All melting points were taken on a Fisher-Johns apparatus and are uncorrected. Infrared spectra (nujol mulls) were run on a Perkin-Elmer model 157 spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Varian EM-390 instrument (TMS internal standard). The mass spectrum was recorded on a Hewlett-Packard 5908–A mass spectrometer with an electron beam energy of 70 eV. Merck acc. to Brockmann alumina and Merck silica gel 60 were used for chromatographic purifications. Elemental analyses were performed by A. Pietrogrande, Padova, Italy.

1-(2-Bromomethyl)phenylacetonitrile.

To a boiling suspension of 35.60 g. (0.2 mole) of *N*-bromosuccinimide and 0.50 g. of benzoyl peroxide in 250 ml. of carbon tetrachloride, a solution of 26.20 g. (0.2 mole) of 2-methylphenylacetonitrile in 100 ml. of the same solvent was added by dropping under vigorous stirring. The mixture was heated at reflux for 12 hours, then cooled to room temperature and filtered. Evaporation of the solution *in vacuo* and trituration of the oily residue with ligroin gave 18.30 g. (43.6 %) of 1-(2-bromomethyl)phenylacetonitrile, m.p. 83-84° after recrystallization from ligroin; ir: 2250 cm^{-1} (CN); nmr (deuteriochloroform): δ 3.90 (s, 2, CH_2CN), 4.50 (s, 2, CH_2Br), 7.40 ppm (m, 4, aromatic H).

Anal. Calcd. for C_9H_8BrN: C, 51.45; H, 3.84; Br, 38.04; N, 6.67. Found: C, 51.47; H, 3.85; Br, 37.94; N, 6.57.

1,2-Bis(1-pyrrolylmethyl)benzene (**4**).

A solution of 23.60 g. (0.089 mole) of 1,2-bis(bromomethyl)-benzene in 200 ml. of anhydrous tetrahydrofuran was dropped into a well stirred suspension of potassium pyrrole [prepared from 6.00 g. (0.0895 mole) of pyrrole and 3.495 g. (0.0895 g.-atom) of potassium metal] in 200 ml. of anhydrous tetrahydrofuran. The mixture was heated for 6 hours, then poured onto crushed ice. Extraction with ethyl acetate gave a solution which was dried on anhydrous sodium sulphate and then evaporated *in vacuo*. The residual dark oil was dissolved in benzene and passed through alumina. Removal of benzene from the filtered solution gave 17.10 g. of crude material which was chromatographed by passing on a silica gel column eluting with petroleum ether. The first eluates contained 8.90 g. of 1,2-bis(bromomethyl)benzene. Subsequent elution with benzene-petroleum ether (1:1) gave, after evaporation of the solvents, 7.80 g. of 1,2-bis(1-pyrrolylmethyl)benzene, m.p. 70-71° after crystallization from ligroin; nmr (deuteriochloroform): δ 4.85 (s, 4H, CH_2), 6.10-7.30 ppm (m, 12, pyrrole and benzene ring H).

Anal. Calcd. for $C_{16}H_{16}N_2$: C, 81.32; H, 6.83; N, 11.86. Found: C, 81.53; H, 6.81; N, 11.92.

2,2'-Bis(cyanomethyl)stilbene (**5**).

This product formed when potassium pyrrole-2-carboxaldehyde (6.65 g.; 0.05 mole) and 1-(2-bromomethyl)phenylacetonitrile (10.50 g., 0.05 mole) in anhydrous tetrahydrofuran were heated at 80° under stirring in an atmosphere of nitrogen. Treatment of the reaction mixture with crushed ice and extraction with ethyl ether gave a residue, which by chromatographic purification on alumina afforded three main fractions: unidentified material (0.80 g.) and *o,o'*-bis(cyanomethyl)stilbene **5** (2.20 g.), eluting with benzene, and unreacted pyrrole-2-carboxaldehyde from further elution with ethyl acetate. The stilbene **5** crystallized from benzene-petroleum ether and melted at 193°; ir: 2230 cm^{-1} (CN); nmr (deuteriochloroform): δ 3.23 (s, 4, CH_2), 4.60 (s, r, CH=), 7.10 ppm (m, 8, aromatic H); ms: m/e 258 (M^+) and 129.

Anal. Calcd. for $C_{18}H_{14}N_2$: C, 83.69; H, 5.46; N, 10.85. Found: C, 83.73; H, 5.58; N, 10.82.

1-(2-Carboxybenzyl)pyrrole (**7**).

A suspension of 9.11 g. (0.05 mole) of 1-(2-cyanobenzyl)-pyrrole **6** (9) in 50 ml. of ethylene glycol containing 11.20 g. (0.2 mole) of potassium hydroxide pellets was heated at reflux for 3 hours under stirring. The solution was poured onto crushed ice, then filtered. Addition of concentrated hydrochloric acid furnished 1-(2-carboxybenzyl)pyrrole as a crystalline solid (6.60 g., 65.6 %). Recrystallization from acqueous ethanol gave an analytical sample, m.p. 159-162°; ir: 1690 cm^{-1} (COOH).

Anal. Calcd. for $C_{12}H_{11}NO_2$: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.63; H, 5.56; N, 7.04.

Pyrrolo[1,2-*b*]isoquinoline-10(5*H*)-one (**8**).

A mixture of 4.00 g. (0.02 mole) of 1-(2-carboxybenzyl)-pyrrole **7**, 100 ml. of absolute ethanol and 5 ml. of concentrated sulfuric acid was refluxed for 4 hours, then poured into crushed ice and the organic material extracted with chloroform. The solution was washed with water, dried on anhydrous sodium sulfate and evaporated *in vacuo*. The residue was purified by passing through a silica gel column eluting with chloroform. The first eluates were discarded, then the central fractions were collected and evaporated under reduced pressure to afford 0.50 g. (27.3%) of pyrrolo[1,2-*b*]isoquinoline-10(5*H*)-one, m.p. 118-120° (11,13).

1-(2-Hydroxymethylbenzyl)pyrrole (**9**).

A solution of 20.10 g. (0.1 mole) of 1-(2-carboxybenzyl)-pyrrole **7** in 150 ml. of anhydrous dioxane was dropped onto a well stirred suspension of 7.60 g. (0.2 mole) of lithium aluminum hydride in 150 ml. of the same solvent. After completion of the addition, the mixture was heated at reflux for 20 hours, then cooled to room temperature and treated with crushed ice. Filtration of precipitate gave a solution, which was dried on anhydrous sodium sulphate. Removal of the solvent *in vacuo* furnished an oily product, which was distilled under reduced pressure to give 16.00 g. (85.5%) of pure 1-(2-hydroxymethylbenzyl)pyrrole, b.p. 126° at 0.06 mm; ir: 3450 cm^{-1} (OH).

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.97; H, 7.00; N, 7.48. Found: C, 76.84; H, 7.16; N, 7.54.

1-(2-Chloromethylbenzyl)-2-pyrrolecarboxaldehyde (**10**).

To 7.30 g. (0.1 mole) of *N,N*-dimethylformamide cooled in an ice-bath, 15.30 g. (0.1 mole) of phosphorus oxychloride were added by dropping while stirring. Then a solution of 9.36 g. (0.05 mole) of 1-(2-hydroxymethylbenzyl)pyrrole **9** in 50 ml. of *N,N*-dimethylformamide was added in small portions during 30 minutes. The mixture was heated at 60° for 16 hours, cooled at room temperature, treated with crushed ice and basified with concentrated ammonium hydroxide. The solution obtained after extraction with chloroform was dried on anhydrous sodium sulphate, then evaporated to give a brownish oil, which was purified by passing through a silica gel column (chloroform as eluent). The collected eluates were evaporated *in vacuo* to afford an oil (7.80 g., 66.7 %) which on standing solidified. After crystallization from light petroleum ether 1-(2-chloromethylbenzyl)-2-pyrrolecarboxaldehyde melted at 58-59°; ir: 1660 cm^{-1} (CHO).

Anal. Calcd. for $C_{13}H_{12}ClNO$: C, 66.81; H, 5.18; Cl, 15.17; N, 5.99. Found: C, 66.66; H, 5.24; Cl, 15.34; N, 6.28.

10-Cyano-5*H*-pyrrolo[1,2-*b*][2]benzazepine (**11**).

From **10**.

A mixture of 11.68 g. (0.05 mole) of 1-(2-chloromethylbenzyl)-2-pyrrolecarboxaldehyde, 6.51 g. (0.1 mole) of potassium cyanide and 40 ml. of dimethylsulfoxide was heated at 90° under stirring for 5 hours. The oil, which formed after cooling and subsequent treatment with crushed ice, was extracted with ethyl acetate and the organic solution was dried on anhydrous sodium sulphate. After removal of solvent *in vacuo* the dark oil obtained was chromatographed on a silica gel column eluting with benzene. The eluates were collected and evaporated to give a liquid which solidified on standing in a cool place. After crystallization from ligroin 10-cyano-5*H*-pyrrolo[1,2-*b*][2]benzazepine, 4.50 g., was isolated (43.6 %), m.p. 98-99°; ir: 2220 cm^{-1} (CN); nmr (deuteriochloroform): δ 4.90 (s, 2, CH_2), 6.20 (m, 1, C_2-H), 6.35 (m, 1, C_3-H), 6.80 (m, 1, C_{11}-H), 7.30 (m, 4, C_1-H and C_6-C_8 benzene-ring H), 7.70 ppm (m, 1, C_9-H).

Anal. Calcd. for $C_{14}H_{10}N_2$: C, 81.53; H, 4.89; N, 13.58. Found: C, 81.23; H, 5.10; N, 13.72.

From **15**.

To a solution of 4.48 g. (0.02 mole) of 1-(2-cyanomethylbenzyl)-2-pyrrolecarboxaldehyde **15** in 250 ml. of benzene were added 5 ml. of 30% of acqueous potassium hydroxide and the mixture was heated at reflux for 3 hours. During this time water was azeotropically removed. When heating stopped the solution was evaporated *in vacuo* to small volume and then passed on a silica gel column eluting with benzene. Evaporation of solvent from collected eluates gave 3.60 g. (87.3%) of **11**.

10-Carboxy-5*H*-pyrrolo[1,2-*b*][2]benzazepine (**12**).

A suspension of 4.12 g. (0.02 mole) of 10-cyano-5*H*-pyrrolo[1,2-*b*][2]benzazepine and 4.48 g. (0.08 mole) of potassium hydroxide pellets in 25 ml. of ethylene glycol was refluxed for 3 hours under stirring. The mixture was then poured onto crushed ice. Acidification of solution with concentrated hydrochloric acid gave a precipitate (3.60 g., 79.9%) of 10-carboxy-5*H*-pyrrolo[1,2-*b*][2]benzazepine, which crystallized from benzene-petroleum ether, m.p. 203-204°; ir: 1680 cm^{-1} (COOH).

Anal. Calcd. for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.32; H, 4.79; N, 6.29.

5*H*-Pyrrolo[1,2-*b*][2]benzazepine (**1**).

A mixture of 2.00 g. (8.88 mmoles) of 10-carboxy-5*H*-pyrrolo[1,2-*b*][2]benzazepine **12**, 4.00 g. of quinoline and 0.4 g. of copper powder was heated at reflux for 2 hours under nitrogen atmosphere. After cooling, chloroform was added and the organic solution was separated, washed with dilute hydrochloric acid, then with water and finally dried on anhydrous sodium sulphate. The residue obtained on removing the solvent *in vacuo* was dissolved in benzene and passed through an alumina column.

The benzene eluates after evaporation gave 1.20 g. (74.7%) of 5*H*-pyrrolo[1,2-*b*][2]benzazepine, m.p. 127-129° after crystallization from ligroin; nmr (deuteriochloroform): δ 4.80 (s, 2, CH_2), 6.20-6.80 (superimposed multiplets, 5, pyrrole and azepine-ring H), 7.10-7.30 ppm (m, 4, benzene-ring H).

Anal. Calcd. for $C_{13}H_{11}N$: C, 86.16; H, 6.12; N, 7.73. Found: C, 86.24; H, 6.31; N, 7.68.

1-(2-Bromomethylbenzyl)pyrrole (**13**).

A solution of 3.62 g. (0.0134 mole) of phosphorus tribromide in 100 ml. of anhydrous ethyl ether was dropped onto a well stirred solution of 3.74 g. (0.02 mole) of 1-(2-hydroxymethylbenzyl)pyrrole **9**. During addition the temperature was maintained at 0-5°, then the mixture was stirred for 13 hours at room temperature. The ethereal solution was treated with methanol, then washed with bicarbonate solution and finally with water to neutrality. After drying on anhydrous sodium sulphate the solvent was removed *in vacuo* on a steam-bath and an oily material was obtained. On standing overnight in a cool place the oil crystallized giving 3.50 g. (69.9%) of 1-(2-bromomethylbenzyl)-pyrrole, m.p. 55° after crystallization from ligroin; nmr (deuteriochloroform): δ 4.36 (s, 2, CH_2Br), 5.20 (s, 2, CH_2N=), 6.15 (m, 2, pyrrole β-H), 6.63 (m, 2, pyrrole α-H), 6.80-7.30 ppm (m, 4, benzene-ring H).

Anal. Calcd. for $C_{12}H_{12}NBr$: C, 57.62; H, 4.84; N, 5.60; Br, 31.95. Found: C, 57.60; H, 4.88; N, 5.53; Br, 31.77.

1-(2-Cyanomethylbenzyl)pyrrole (**14**).

A mixture of 20.00 g. (0.08 mole) of 1-(2-bromomethylbenzyl)pyrrole **13**, 10.42 g. (0.16 mole) of potassium cyanide, 400 ml. of benzene and 200 ml. of methanol was stirred at room temperature for 4 days. After dilution with ethyl acetate the solution was washed more than once with water, dried on anhydrous sulphate, then evaporated *in vacuo*. The oily residue was dissolved in benzene and passed through a silica gel column. The central eluates were collected and evaporated under reduced pressure to afford a liquid (14.70 g., 93.6%), which solidified on standing in a cool place. After crystallization from petroleum ether 1-(2-cyanomethylbenzyl)pyrrole melted at 36-37°; ir: 2250 cm^{-1} (CN).

Anal. Calcd. for $C_{13}H_{12}N_2$: C, 79.56; H, 6.16; N, 14.28. Found: C, 79.35; H, 6.15; N, 14.29.

1-(2-Cyanomethylbenzyl)-2-pyrrolecarboxaldehyde (**15**).

In a similar manner as above for **10**, the treatment of 1-(2-cyanomethylbenzyl)pyrrole **9** (9.80 g., 0.05 mole) with *N,N*-dimethylformamide and phosphorus oxychloride at 60° for 3 hours gave a residue which was purified by chromatography on a silica gel column. The first elution with benzene (2 l.) was discarded, then ethyl acetate was used as eluent and the collected fractions were evaporated to give 8.00 g. of the aldehyde **15**. Further purification of this compound through alumina (benzene as eluent) furnished 7.00 g. (62.4%) of pure product, which crystallized from benzene-petroleum ether and melted at 96-97°; ir: 2230 cm^{-1} (CN), 1650 cm^{-1} (CHO).

Anal. Calcd. for $C_{14}H_{12}N_2O$: C, 74.99; H, 5.38; N, 12.49. Found: C, 75.11; H, 5.58; N, 12.35.

1-(2-Carboxymethylbenzyl)pyrrole (**16**).

A mixture of 17.00 g. (0.087 mole) of 1-(2-cyanomethylbenzyl)pyrrole **14**, 19.40 g. (0.346 mole) of potassium hydroxide pellets and 50 ml. of ethylene glycol was refluxed for 3 hours under stirring. The cooled solution was kept on water, filtered and made acidic with concentrated hydrochloric acid. The gummy precipitate was extracted with ethyl acetate. The organic solution was washed with cold water, then dried on anhydrous sodium sulphate. Removal of the solvent *in vacuo* gave a liquid, which slowly solidified on standing in a cool place. 1-(2-Carboxymethylbenzyl)pyrrole weighed 16.40 g. (87.9%) and melted at 91-92° after recrystallization from cyclohexane; ir: 1700 cm^{-1} (COOH).

Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.51; H, 6.15; N, 6.36.

11-Oxo-10,11-dihydro-5*H*-pyrrolo[1,2-*b*][2]benzazepine (**17**).

A mixture of 15.00 g. (0.0697 mole) of 1-(2-carboxymethylbenzyl)pyrrole **16** and 12.00 g. of polyphosphoric acid was heated at 90° with stirring under nitrogen atmosphere for 2 hours. After cooling, the reaction mixture was treated with cold water, then made alkaline with concentrated ammonium hydroxide. The precipitate which formed was extracted with chloroform. The solution after drying on anhydrous sodium sulphate was evaporated to a small volume and then passed through an alumina column (chloroform as eluent). Removal of the solvent from the collected eluates afforded 7.50 g. (54.6%) of 11-oxo-10,11-dihydro-5*H*-pyrrolo[1,2-*b*][2]benzazepine as a solid melting at 174-176° after crystallization from benzene-petroleum ether; ir: 1610 cm^{-1} (CO); nmr (deuteriochloroform): δ 4.00 (s, 2, CH_2CO), 5.30 (s, 2, CH_2N=), 6.00 (m, 1, C_2-H), 6.76 (m, 1, C_3-H), 7.00 (m, 1, C_1-H), 7.12 ppm (m, 4, benzene-ring H).

Anal. Calcd. for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10. Found: C, 79.40; H, 5.78; N, 7.24.

10,11-Dihydro-5*H*-pyrrolo[1,2-*b*][2]benzazepine (**18**).

From **17**.

A solution of 3.94 g. (0.02 mole) of 11-oxo-10,11-dihydro-5*H*-pyrrolo[1,2-*b*][2]benzazepine **17** in 150 ml. of anhydrous tetrahydrofuran was dropped into a well stirred suspension of 1.51 g. (0.04 mole) of lithium aluminum hydride in 100 ml. of anhydrous ethyl ether. When adding stopped the mixture was heated at reflux for 6 hours (12). After cooling at room temperature crushed ice was added and the precipitate formed was filtered. The organic layer was separated, washed with water and dried on anhydrous sodium sulphate. Evaporation *in vacuo* of the solvents afforded an oil, which was passed through an alumina column eluting with chloroform. The main eluates were collected and evaporated to give 3.20 g. (87.3%) of 10,11-dihydro-5*H*-pyrrolo[1,2-*b*][2]benzazepine, which crystallized from ligroin, m.p. 81-82°.

From **1**.

A suspension of 1.20 g. (6.62 mmoles) of 5*H*-pyrrolo[1,2-*b*][2]-benzazepine **1** and 200 mg. of 10% palladium on carbon in 200 ml. of ethanol was hydrogenated at 55° under 4 atmospheres of pressure for 1 hour. Removal of the catalyst by filtration and evaporation of solvent *in vacuo* furnished 1.20 g. (92.2%) of **18**, which crystallized from light petroleum ether, m.p. 81-82°; nmr (deuteriochloroform): δ 3.13 (s, 4, CH_2-CH_2), 5.10 (s, 2, CH_2-N=), 5.80-6.60 (multiplets, 3, pyrrole-ring H), 7.10-7.30 ppm (m, 4, benzene-ring H).

Anal. Calcd. for $C_{13}H_{13}N$: C, 85.20; H, 7.15; N, 7.64. Found: C, 85.39; H, 7.11; N, 7.82.

1,2,3,10,11,11a-Hexahydro-5*H*-pyrrolo[1,2-*b*][2]benzazepine (**19**) Hydrochloride.

To a solution of 1.00 g. (5.45 mmoles) of 10,11-dihydro-5*H*-pyrrolo[1,2-*b*][2]benzazepine **18** in 100 ml. of glacial acetic acid, 250 mg. of 5% rhodium on alumina were added and the mixture heated at 55° and hydrogenated at an initial pressure of 4 atmosphere for 3 hours in a Parr apparatus. After removal of the catalyst by filtration the solution was evaporated *in vacuo* on a steam-bath. The residue was treated with diluted sodium hydroxide (4*N*) and the solution extracted with ethyl acetate. The extracts were dried on anhydrous sodium sulphate and evaporated. The oily material obtained was purified by passing on an alumina column eluting with chloroform. The eluates were evaporated and the residue dissolved in anhydrous ethyl ether into which gaseous hydrochloric acid was bubbled. The precipitated 1,2,3,10,11,11a-hexahydro-5*H*-pyrrolo[1,2-*b*][2]benzazepine hydrochloride weighed 750 mg. (61.8%) and melted at 248-249° after crystallization from an anhydrous ethanol-ethyl ether mixture.

Anal. Calcd. for $C_{13}H_{17}ClN$: C, 70.10; H, 7.69; Cl, 15.92; N, 6.29. Found: C, 69.85; H, 7.57; Cl, 15.81; N, 6.37.

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(12) When heating at reflux was reduced to 2 hours, the presence of a mixture of **18** and **1** was evidenced by nmr spectral data examination. Catalytic reduction (hydrogen, palladium on carbon) of the mixture gave **18** as the only product.

(13) Intramolecular cyclization of **7** with polyphosphoric acid in a similar manner as reported for **17** furnished **8** in 43.7% yield.