797. *The Structure of Pyrrole Trimer.*

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Structure (I), proposed for pyrrole trimer in 1923 by Pieroni and Moggi, is confirmed by degradation.

THE structure of pyrrole trimer, a compound first obtained by Dennstedt and his collaborators [1] by the action of aqueous hydrochloric acid on pyrrole, has not been satisfactorily settled. Of the five structures proposed,[2-6] only (I), proposed by Pieroni and

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[1] Dennstedt and Zimmermann, *Ber.*, 1887, **20**, 857; *ibid.*, 1888, **21**, 1478; Dennstedt and Voigtländer, *Ber.*, 1894, **27**, 476.

[2] Ciamician and Zanetti, *Ber.*, 1893, **26**, 1711.

[3] Tchelinzev, Tronov, and Voskressenski, *J. Russ. Phys. Chem. Soc.*, 1915, **47**, 1224.

[4] Pieroni and Moggi, *Gazzetta*, 1923, **53**, 120.

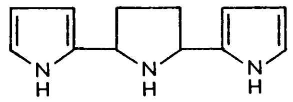
[5] Tronov and Popov, *J. Russ. Phys. Chem. Soc.*, 1926, **58**, 745.

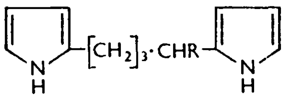
[6] " Organic Chemistry of Nitrogen," Sidgwick, revised by Taylor and Baker, Oxford Univ. Press, 1937, p. 487.

Moggi,[4] seems plausible. This structure, which has been adversely criticised by Tronov and Popov [5] and by Taylor and Baker,[6] was based only on the formation of succinic acid by chromic acid oxidation; we therefore carried out a degradation of pyrrole trimer to establish its structure.

The presence of two unconjugated pyrrole nuclei in the molecule was clearly demonstrated by the ultraviolet absorption [single band at 219 mμ (ε 17,500)]. Pyrrole trimer formed a neutral monoacetyl derivative, whose ultraviolet absorption was practically identical ($\lambda_{max.}$ 217 mμ, ε 17,500) with that of the parent base: this indicates a primary or secondary amino-group out of conjugation with the pyrrole nuclei. Pyrrole trimer also forms a quaternary methiodide in good yield, whose ultraviolet absorption spectrum ($\lambda_{max.}$ 230 mμ, ε 27,000) is appreciably different from that of the trimer; similar increase in the value of ε with change of position of the $\lambda_{max.}$ has been observed in the quaternisation of the dimers of indole and skatole.[7] The formula, $C_{14}H_{20}N_3I$, of the quaternary iodide from pyrrole trimer showed that two methyl groups had been introduced, and strongly suggested that the basic nitrogen of pyrrole trimer is secondary. Hofmann degradation of the quaternary hydroxide failed to yield a homogeneous product, but sodium in dry liquid ammonia effected practically quantitative hydrogenolysis to give a crystalline base, $C_{14}H_{21}N_3$, whose ultra-violet absorption again indicated the presence of two pyrrole nuclei ($\lambda_{max.}$ 215, ε, 16,000). That this base has structure (II; R = NMe_2) was demonstrated by oxidation with chromic acid to a mixture of succinic and glutaric acids, and by catalytic hydrogenolysis, best with Raney nickel,[8] to a neutral compound, $C_{12}H_{16}N_2$, shown by mixed melting-point and by comparison of infrared and ultraviolet spectra to be identical with 1 : 4-di-2′-pyrrolylbutane (II; R = H), prepared by the reduction with lithium aluminium hydride of 1 : 4-di-2′-pyrrolylbutane-1 : 4-dione.

(I)

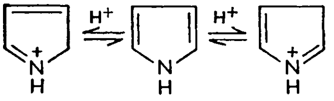




(II)

Degradation to the butane (II; R = H) proves that pyrrole trimer has structure (I).

A mechanism for the formation of the trimer (I), analogous to that suggested for the dimerisation of indole,[9] is very likely: this would involve *C*-protonation of pyrrole as the first step to give a strongly electrophilic cation, which attacks an unprotonated pyrrole molecule. *C*-Protonation of pyrrole can occur in two ways to give cation (III) or (IV).

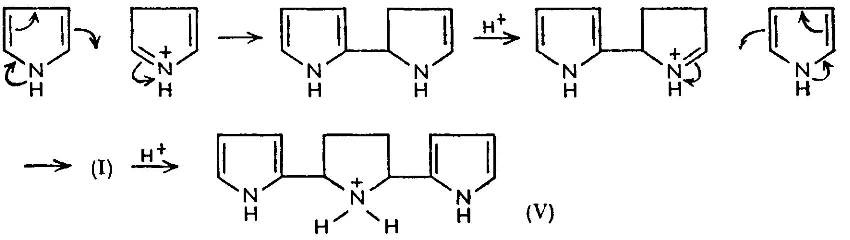


The well-known α-reactivity of pyrrole suggests that cation (III) will predominate. That the concentration of cation (IV), however, will not be negligible, is indicated by the recent observation by Anderson [10] that the mononitropyrrole formed by nitration of pyrrole with nitric acid–acetic anhydride contains 7% of the β-isomer.

Cation (III), being predominant, might be expected to be involved in formation of the trimer. However, it is not possible to devise a plausible reaction sequence which leads

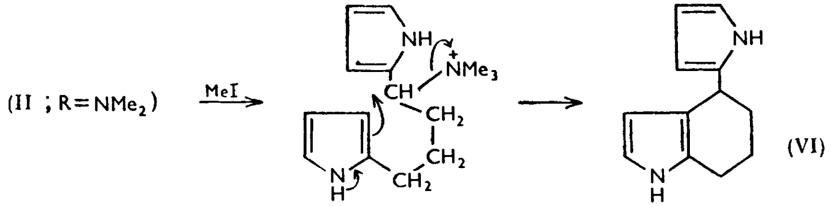
[7] Hodson and Smith, unpublished work.
[8] Treibs and Zinsmeister, *Ber.*, 1957, **90**, 87.
[9] Smith, *Chem. and Ind.*, 1954, 1451.
[10] Anderson, *Canad. J. Chem.*, 1957, **35**, 21.

from cation (III) to trimer (I). On the other hand, cation (IV) leads to trimer (I) in a straightforward and plausible manner:

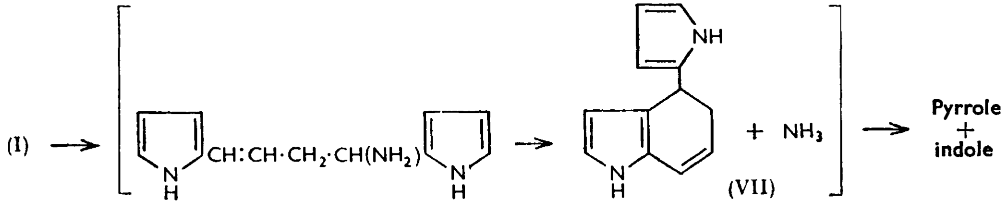


It follows that cation (IV) must be a much more powerfully electrophilic reagent than (III).

Under the acid conditions of the polymerisation, the trimer (I) is immediately protonated to (V), making isolation of the trimer possible, for the formal positive charge on the pyrrolidine nitrogen lowers the susceptibility of the pyrrole nuclei to further protonation, and thus considerably slows further reaction. The failure of gramine and tryptamine to dimerise in aqueous acid, whereas β-propylindole dimerises rapidly, provides an analogy.[11]



An interesting reaction was observed in an attempt to prepare the methiodide of the amine (II; R = NMe_2): the base reacts with methyl iodide at room temperature, best in the presence of anhydrous potassium carbonate, to give trimethylamine, tetramethylammonium iodide, and a neutral compound, $C_{12}H_{14}N_2$, whose ultraviolet absorption ($\lambda_{max.}$ 216 mμ, ε 16,000) again indicates two unconjugated pyrrole nuclei. This, and the formation of succinic and glutaric acids on oxidation with chromic acid, leads to its being formulated as (VI). Its formation is similar to the last step in the trimerisation of indole.[9]



Pyrrole trimer breaks down on pyrolysis into pyrrole, indole, and ammonia:[1] this can be accounted for quite easily in terms of structure (I). The break-down of the pyrrolylindole (VII) into pyrrole and indole finds a close analogy in the pyrolysis of indole dimer into 2 molecules of indole.[12]

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[11] Hodson, Smith, and Walters, unpublished work.

[12] Schmitz-DuMont and Nicolojannis, *Ber.*, 1930, **63**, 323.

EXPERIMENTAL

M. p.s are corrected.

Pyrrole Trimer.—Dennstedt's method [1] has been simplified. A mixture of freshly distilled pyrrole (25 g.) and 20% aqueous hydrochloric acid (100 c.c.), added at 0°, was swirled vigorously for 30 sec., then poured on an excess of aqueous ammonia–ice, and immediately extracted with ether (2 × 100 c.c.). The ether extract gave the pyrrole trimer (10·5 g.), m. p. 99—100° (from ether). We never obtained the higher-melting material (m. p. 120°) reported by Dennstedt [1] and by Pieroni and Moggi.[4]

Methylpyrrole Trimer Methiodide.—Methyl iodide (1 c.c.), saturated aqueous potassium hydrogen carbonate (1 c.c.), and pyrrole trimer (212 mg.) were shaken for 1·5 hr. The *methiodide* was filtered off and washed with water (277 mg.; 72%); it had m. p. 165—170° (decomp.) (from ethanol) (Found: C, 46·9; H, 5·8; N, 11·75. $C_{14}H_{20}N_3I$ requires C, 47·05; H, 5·9; N, 11·75%).

1-*Dimethylamino*-1 : 4-*di*-2′-*pyrrolylbutane* (II; R = NMe$_2$).—To the above methiodide (3·57 g.) in dry liquid ammonia (100 c.c.) sodium was added until the deep blue colour persisted. The excess of sodium was then destroyed by ammonium chloride, the ammonia boiled off, and the residue partitioned between water and ether. The ether extract gave practically pure 1-*dimethylamino*-1 : 4-*di*-2′-*pyrrolylbutane* (2·28 g.; quantitative yield), m. p. 83—85° (Found: C, 73·5; H, 8·9; N, 17·9. $C_{14}H_{21}N_3$ requires C, 72·8; H, 9·1; N, 18·1%). No suitable solvent was found for further purification.

1 : 4-*Di*-2′-*pyrrolylbutane* (II; R = H).—(*a*) The base (II; R = NMe$_2$) (310 mg.) was hydrogenated in ethanol (100 c.c.) at 100 atm. and 80° in the presence of Raney nickel (0·5 g. approx.) for 4 hr. The ether-soluble material (210 mg.) was put on an alumina column and eluted with benzene: the first few fractions were non-crystalline and were rejected; the main fraction (116 mg.) consisted of 1 : 4-*di*-2-*pyrrolylbutane*, m. p. 104—105° (Found: C, 75·4; H, 8·6. $C_{12}H_{16}N_2$ requires C, 76·55; H, 8·6%).

(*b*) A suspension of 1 : 4-di-2′-pyrrolylbutane-1 : 4-dione [13] (1·024 g.) in ether (50 c.c.) was refluxed with excess of lithium aluminium hydride for 5 hr. The excess of reducing agent was destroyed by dropwise addition of water, and the whole partitioned between ether and 40% aqueous sodium hydroxide. The ether-soluble product (568 mg.) crystallised from benzene to give a compound, m. p. 128—130° (101 mg.) which contained hydroxyl groups (infrared) and was not investigated further. The benzene mother-liquor was chromatographed on alumina with benzene as eluant; only 1 : 4-di-2′-pyrrolylbutane, m. p. and mixed m. p. 104—105° (203 mg.) was eluted (Found: C, 75·6, 75·6, 75·5; H, 8·55, 8·3, 8·5; N, 14·8. Calc. for $C_{12}H_{16}N_2$: C, 76·55; H, 8·6; N, 14·9%). We cannot explain the fact that both the product obtained from (II; R = NMe$_2$) and that obtained from the dipyrrolylbutanedione should give analytical results for carbon about 1% low: this corresponds to about 0·12 atom of oxygen per molecule, which cannot be due to water or hydroxyl group (infrared spectrum) or to carbonyl [since the products have identical infrared spectra, and that derived from (II; R = NMe$_2$) cannot possibly contain a carbonyl group].

4 : 5 : 6 : 7-*Tetrahydro*-4-2′-*pyrrolylindole* (VI).—To the base (II; R = NMe$_2$) (177 mg.) in dry acetone (20 c.c.) were added anhydrous potassium carbonate (200 mg.) and methyl iodide (1 c.c.). After 3 hours' refluxing the solvents were removed under reduced pressure, and the residue partitioned between ether and water. The ether extract gave 4 : 5 : 6 : 7-*tetrahydro*-4-2′-*pyrrolylindole* (126 mg., practically quantitative yield), m. p. 131—132° (from benzene) (Found: C, 77·4; H, 7·6; N, 14·9. $C_{12}H_{14}N_2$ requires C, 77·4; H, 7·5; N, 15·05%).

Oxidation of 1-*Dimethylamino*-1 : 4-*di*-2′-*pyrrolylbutane* (II; R = NMe$_2$).—A mixture of the base (295 mg.) and a solution of sodium dichromate (0·25 g.) in 50% aqueous sulphuric acid (5 c.c.) was heated on the steam-bath for 1 hr. After reduction of the excess of chromic acid with sodium sulphite, the mixture was extracted with ether (3 × 25 c.c.). Crystallisation of the extract from ether yielded first succinic acid, m. p. and mixed m. p. 184—185° (42·5 mg.), and then glutaric acid, m. p. and mixed m. p. 97—98° (19 mg.).

Oxidation of 4 : 5 : 6 : 7-*Tetrahydro*-4-2′-*pyrrolylindole* (VI).—The compound (203 mg.) was oxidised with chromic–sulphuric as above, and a small portion of the ether-soluble product chromatographed on Whatman No. 1 paper, with aqueous ethanolic ammonia as the moving phase. The main spots corresponded with succinic and glutaric acids.

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[13] Godnev and Narishkin, *J. prakt. Chem.*, 1929, **121**, 369.

Acetylpyrrole Trimer.—A solution of pyrrole trimer (256 mg.) in acetic anhydride (1 c.c.) was left overnight at room temperature, then warmed on the steam-bath for 5 min. The excess of acetic anhydride was boiled off under reduced pressure, and the residue crystallised from ethanol; pure *acetylpyrrole trimer* (193 mg.), m. p. 174—193° (decomp.), was obtained (Found: C, 68·8; H, 7·15; N, 16·8. $C_{14}H_{17}ON_3$ requires C, 69·15; H, 7·05; N, 17·3%).

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