

628. Bipyrrroles. Part III.^{1, 2}

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A study of the ultraviolet, infrared, and nuclear magnetic resonance spectra of a range of 2,2'-bipyrrroles has enabled certain conclusions to be drawn regarding the conformations of these molecules. Intramolecular hydrogen bonding exists in the 2,2'-bipyrrrole-3,3'-dicarboxylic esters. The preparation of some new 2,2'-bipyrrroles and related compounds is described.

In Part I¹ we described the synthesis of 2,2'-bipyrrrole esters by subjecting 2-iodopyrrole esters to the Ullmann reaction, and reported that by use of *NN*-dimethylformamide as solvent the condensation could be effected even at room temperature. Using diethyl 5-iodo-3-methylpyrrole-2,4-dicarboxylate³ (I) we have examined the effect of variation of solvent in the Ullmann condensation and obtained the following results (yields of 2,2'-bipyrrrole in parentheses): dimethylformamide, 2 hours at room temperature (61%); benzene, 8 hours at 80° (77%), and nitrobenzene, 4 hours at 100° (38%). In the last case it seemed possible that the intermediate free radical might have coupled with the solvent, but no such product was detected. The preparation of several new 2,2'-bipyrrrole esters is recorded in the Experimental section.

The position and intensity of bands in the infrared spectra of dipyrromethanes and dipyrromethenes has been used as a measure of the nature and strength of hydrogen bonding within these molecules,⁴⁻⁶ although the interpretations of the results are at variance. We

¹ Grigg, Johnson, and Wasley, *J.*, 1963, 359, is taken to be Part I.

² Bullock, Grigg, Johnson, and Wasley, *J.*, 1963, 2326, is taken to be Part II.

³ Kleinspehn and Corwin, *J. Amer. Chem. Soc.*, 1953, **75**, 5295.

⁴ Badger, Harris, Jones, and Sasse, *J.*, 1962, 4329.

⁵ Kuhn and Kleinspehn, *J. Org. Chem.*, 1963, **28**, 721.

⁶ Castro, Marsh, and Nakata, *J. Org. Chem.*, 1963, **28**, 1943.

have measured the infrared spectra of a number of 2,2'-bipyrroles in carbon tetrachloride and the bands associated with the NH group are shown in Table 1. The compounds fall into three groups which accord with their ester substitution pattern.

TABLE 1.

Carbonyl and N-H bands (cm.^{-1}) in the infrared spectra of substituted 2,2'-bipyrroles

No.	Group	Substituents			Free	Bonded	Free	Bonded C=O	
		5,5'	4,4'	3,3'	N-H	N-H	C=O	Intra	Inter
1	I	CO ₂ Et	Me	CO ₂ Et	—	3150	1720	1676	—
2	I	CO ₂ Et	Et	CO ₂ Et	—	3152	1720	1678	—
3	I	CO ₂ ·CH ₂ Ph	Me	CO ₂ Et	—	3151	—	—	—
4	II	CO ₂ Me	CO ₂ Et	Me	3436	3283	—	—	—
5	II	CO ₂ Et	Me	Me	3464, 3454	3295	1715	1693	1672sh
6	II	CO ₂ ·CH ₂ Ph	Me	Me	3463	3299	—	—	—
7	II	CO ₂ Et	Me	Et	3464, 3451	3291	1716	1692	1675sh
8	III	Me	CO ₂ Et	Me	3461	3299	1703	—	1673
9	III	Me	CO ₂ ·CH ₂ Ph	Me	3461	—	—	—	—
10	III	H	Et	H	3486	—	—	—	—

The single band at 3150—3152 cm.^{-1} , corresponding to a strongly bonded NH group in the bipyrroles of group I, does not change in either frequency or intensity on dilution of the solution. This band is close to the C-H stretching bands near 3000 cm.^{-1} and a similar displacement of N-H bands has been noted with β -amino- $\alpha\beta$ -unsaturated ketones.⁷ Each of the bipyrroles of group I is a 3,3'-diester, and the position of the N-H band, together with its independence of concentration, is interpreted on the basis of the conformation (II), emphasizing the intramolecular hydrogen bonding.

The bipyrroles of group II showed two N-H bands, one at 3283—3299 cm.^{-1} associated with an intermolecularly bonded group and the other at 3436—3464 cm.^{-1} associated with a non-bonded group. The relative intensity of the lower-frequency band decreased on dilution, as expected for a system showing intermolecular hydrogen bonding. The slight splitting of the higher-frequency peak in compounds 5 and 7 (Table 1) is probably due to weak intramolecular hydrogen bonding involving the 5,5'-ester groups. Bipyrroles of group III contain neither 3,3'- nor 5,5'-ester groupings and are therefore incapable of intramolecular hydrogen bonding. Compound 8 showed a band at 3299 cm.^{-1} associated with intermolecular bonding (dilution experiments supported this view), and the fact that a similar band was not observed in the spectrum of compound 9 was probably due to its low solubility in carbon tetrachloride which entailed the use of very dilute solutions. The introduction of an α - or β -ester group into the bipyrrole nucleus causes the free NH frequency to shift from 3486 (compound 10) to *ca.* 3461—3464 cm.^{-1} .

TABLE 2.

Carbonyl and N-H bands (cm.^{-1}) in the infrared spectra of substituted pyrroles.

Substituents	Substituents				Free	Bonded	Free	Bonded C=O	
	5	4	3	2	N-H	N-H	C=O	Intra	Inter
CO ₂ ·CH ₂ Ph	Me	CO ₂ Et	H	Free N-H	3453	3300	1723, 1701	—	1681sh
CO ₂ Et	Me	CO ₂ Et	H		3466sh, 3451	3297	1724, 1697	—	1676
CO ₂ Et	Me	Me	H		3486, 3468	3325	1716	1692	1678sh
Me	CO ₂ Et	Me	H		3476	3345	1701	—	1683sh

The infrared spectra of certain pyrroles (Table 2) were relevant to the above discussion. Thus, the lowest N-H frequency for pyrrole-3,5-dicarboxylic esters was in the region 3297—3300 cm.^{-1} , and this was shown to be associated with intermolecular hydrogen bonding by dilution studies. The absorptions at 3150—3152 cm.^{-1} in group I of the bipyrroles did not

⁷ Cromwell, Miller, Johnson, Frank, and Wallace, *J. Amer. Chem. Soc.*, 1949, **71**, 3337.

involve the 5,5'-ester (*i.e.*, α -ester) groupings, as a similar effect would have been observed in the spectra of the pyrrole esters. The slight splitting of the free N-H absorption in two cases is probably again associated with weak intramolecular hydrogen bonding (see ref. 5).

A study of the effect of hydrogen bonding on the carbonyl absorptions of 2,2'-bipyrroles was limited by the low solubility of these compounds in carbon tetrachloride and by solvent interference in this region when larger cells (>2 mm.) were used. It appears (Table 1) that a non-bonded α -ethoxycarbonyl group in a 2,2'-bipyrrole has a stretching frequency about 1715—1720 cm^{-1} whilst that of a β -ethoxycarbonyl group is about 1703 cm^{-1} . These values are almost identical with those observed for pyrrolic esters (Table 2). Bipyrroles containing 3,3'-ester groupings did not show absorption in the carbonyl region at the position expected (1703 cm^{-1}) for free β -ester groupings, but instead the spectrum contained a band at 1676—1678 cm^{-1} , the intensity of which did not change on dilution and which was therefore ascribed to an intramolecularly bonded carbonyl group.

Evidence for intramolecular hydrogen bonding involving an α -ester group was obtained for two bipyrroles and one pyrrole, and in all three cases the N-H band showed evidence (Tables 1 and 2) of splitting. The expected absorption associated with the intramolecularly bonded α -ester groups of the two pyrrole-3,5-dicarboxylic esters (Table 2) is probably obscured by the carbonyl absorption of the non-bonded β -ester group. Contrary to the results obtained using chloroform solutions,⁸ it seems that it might be possible to distinguish pyrrolic α - and β -esters in carbon tetrachloride by the position of the infrared carbonyl absorption band.

The degree of twist of the rings about the 2,2'-bond in bipyrroles is an important factor when the use of these compounds as intermediates for the formation of macrocyclic systems is under consideration. The resolution⁹ of 1,1',3,3',5,5'-hexamethyl-2,2'-bipyrrole-4,4'-dicarboxylic acid indicates that 1,1',3,3'-tetramethyl-2,2'-bipyrroles are appreciably sterically

TABLE 3.
Ultraviolet spectra of 2,2'-bipyrroles.

No.	Substituent			$\lambda_{\text{max.}}$ (m μ) *	ϵ *
	5,5'	4,4'	3,3'		
1	H	H	H †	277, 283	17,300, 16,700
2	H	Me	H	284	13,320
3	H	Et	H	286	13,650
4	H	Me	Me	263	11,770
5	H	Me	Et	256	9780
6	Me	CO ₂ Et	Me	228, 259	37,700, 13,480
7	CO ₂ Et	Me	Me	203, 217, 250, 314	6825, 8640, 8640, 25,120
8	CO ₂ Et	Me	Et	222, 248, 294	8620, 9510, 17,500
9	H	Me	CO ₂ Et ‡	242, 280, 293, 343	15,450, 5130, 5140, 22,360
10	CO ₂ Me	CO ₂ Et	Me	230, 302	20,450, 18,980
11	CO ₂ Me	Me	CO ₂ Me ‡	252, 291, 350	28,600, 15,350, 22,250
12	CO ₂ Et	Me	CO ₂ Et ‡	252, 292, 352	26,500, 15,100, 21,300
13	CO ₂ Et	Et	CO ₂ Et ‡	252, 293, 352	26,000, 15,600, 22,300
14	CO ₂ -CH ₂ Ph	Me	CO ₂ Et ‡	253, 293, 352	27,300, 15,650, 21,800
15	CO ₂ Et	Me	CO ₂ -CH ₂ Ph ‡	253, 291, 354	30,000, 15,500, 22,400
16	CO ₂ -CH ₂ Ph	Me	CO ₂ -CH ₂ Ph ‡	255, 294, 355	30,000, 16,600, 22,400

* Inflections in italics. † Ref. 10. Shoulders at 273 and 297 $\text{m}\mu$ (ϵ , 16,700 and 8200). ‡ In chloroform.

hindered. Indication of the existence of steric hindrance can be obtained from ultraviolet spectra, and the spectra of a number of bipyrroles (Table 3) and related pyrroles (Table 4) in ethanol have been determined.

Alkyl substitution in the pyrrole ring lowers the intensity of the absorption at about

⁸ Eisner and Erskine, *J.*, 1958, 971.

⁹ Webb and Threlkeld, *J. Org. Chem.*, 1953, **18**, 1406, 1413.

¹⁰ Rapoport and Holden, *J. Amer. Chem. Soc.*, 1962, **84**, 635.

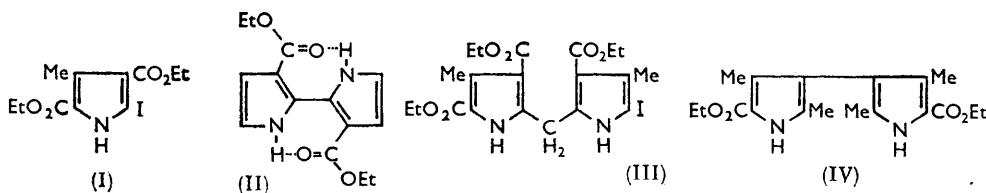
TABLE 4.
 Ultraviolet spectra of pyrroles.

No.	Substituent				$\lambda_{\max.}$ (m μ) *	ϵ *
	2	3	4	5		
1	H	H	H	H †	210, 240	15,000, 300
2	H	Et	Me	H ‡	ca. 203	5670
3	H	Et	Et	H §	ca. 208	5900
4	Me	H	Me	H §	218	4700
5	Me	Et	Me	H §	214	7000
6	Me	CO ₂ Et	Me	H	205, 232, 259	14,030, 8580, 4860
7	CO ₂ Et	Me	Me	H	250, 272	8275, 14,650
8	CO ₂ Et	Me	Et	H	248, 272	7975, 14,670
9	CO ₂ Me	CO ₂ Et	Me	H	205, 275, 281	8515, 5150, 9070
10	CO ₂ Et	Me	CO ₂ Et	H	219, 253, 263	28,700, 11,510, 13,320
11	CO ₂ -CH ₂ Ph	Me	CO ₂ Et	H	218, 252, 264	31,700, 12,600, 15,400

* Inflections in italics. † Ref. 11, in hexane. ‡ Ref. 12. § Ref. 13.

[Added in Proof (July 7th, 1964). While this Paper was in the press, R. L. Hinman and S. Theodoropoulos (*J. Org. Chem.*, 1963, **28**, 3052) reported $\lambda_{\max.}$ 201 m μ ; ϵ , 7300 for pyrrole in 95% ethanol and $\lambda_{\max.}$ 209 m μ ; ϵ , 5800 for 2,5-dimethyl pyrrole in water.]

210 m μ and causes the weak absorption at 240 m μ to disappear^{12,13} (Table 4, Nos. 1–5). The same effect is also observed in the bipyrrrole series (Table 3, Nos. 1–5) and the decrease in intensity of absorption and the hypsochromic shift in the alkylbipyrrroles (Table 3, Nos. 2–5) is consistent with increasing twist about the 2,2'-bond as the size of the 3,3' substituents increases. The same effect also occurs in the bipyrrrole esters (Table 3, Nos. 7 and 8). The spectra of the bipyrrrole-3,3',5,5'-tetracarboxylic esters (Table 3, Nos. 11–16) show no change with increasing size of the 3,3'-ester substituents, which provides further evidence for the preferred conformation (II). Comparison of corresponding spectra in Tables 3 and 4 suggests that there is conjugation between the pyrrole rings in all the bipyrrroles.



The nuclear magnetic resonance (n.m.r.) spectra of several bipyrrroles in chloroform solution have been measured (Table 5). Particularly noteworthy is the shift of the N-H band with increasing number of electronegative substituents, an electronic effect which may be augmented by increasing conjugation between the rings caused by intramolecular hydrogen bonding. For comparison, the n.m.r. spectrum of diethyl 2,2',4,4'-tetramethyl-3,3',5,5'-dicarboxylate (IV), measured in chloroform-trifluoroacetic acid, showed bands at 0.31 (singlet; NH), 5.55 (quartet; methylene groups of ethyl esters), 7.85 (singlet; methyl groups), and 8.54 τ (triplet; methyl groups of ethyl esters).

A number of extensions of the 2,2'-bipyrrrole synthesis have been investigated. For example, an attempt to couple two moles of triethyl 4,4'-dimethyl-5-iododipyrromethane-3,3',5,5'-tricarboxylate (III) (prepared from the corresponding 5-carboxylic acid¹⁴) by the Ullmann reaction was unsuccessful and resulted only in hydrogenolysis of the iodine atom. The 3,3'-bipyrrrole (IV) was reported¹⁵ to be formed, along with the pyrroles (V; R = H,

¹¹ Bowden, Braude, and Jones, *J.*, 1946, 948.

¹² Cookson, *J.*, 1953, 2789.

¹³ Eisner and Gore, *J.*, 1958, 922.

¹⁴ Corwin and Buc, *J. Amer. Chem. Soc.*, 1944, **66**, 1151.

¹⁵ Treibs and Kolm, *Annalen*, 1958, **614**, 176.

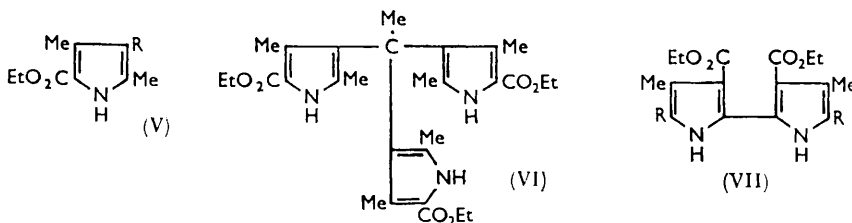
TABLE 5.

Nuclear magnetic resonance spectra of 2,2'-bipyrroles.

No.	Substituents			Absorption bands (τ values) *			
	5,5'	4,4'	3,3'	N-H	5,5'	4,4'	3,3'
1	H	Me	H	1.03 s	3.5 s	7.84 s	3.94 s
2	H	Me	Me	2.96 s	3.5 s	8.06 s	8.19 s
3	H	Me	Et	2.93 s	3.60 s	7.89 s	7.61 q 8.99 t
4	Me	CO ₂ Et	Me	1.70 s	7.45 s	8.61 t 5.66 q	7.82 s
5	CO ₂ Et	Me	Me	0.95 s	5.68 q 8.63 t	7.66 s	7.94 s
6	CO ₂ Et	Me	Et	0.44 s	5.84 q 8.72 t	7.67 s	7.54 q 8.98 t
7	CO ₂ ·CH ₂ Ph	Me	Me	0.86 s	4.75 s †	7.71 s	7.99 s
8	CO ₂ Me	CO ₂ Et	Me	-0.61 s	6.32 s	5.62 q 8.61 t	7.9 s
9	CO ₂ Me	Me	CO ₂ Me	—	5.99 s	7.35 s	5.99 s
10	CO ₂ Et	Me	CO ₂ Et	-3.89 s	5.57 q 8.53 t	7.40 s	5.57 q 8.53 t
11	CO ₂ Et	Et	CO ₂ Et	-3.93 s	5.57 q 8.55 t	6.83 q 8.71 t	5.57 q 8.55 t
12	CO ₂ ·CH ₂ Ph	Me	CO ₂ Et	-4.52 s	4.60 s †	7.37 s	5.59 q 8.60 t
13	CHO	Me	CO ₂ Et ‡	-4.25 s	-0.01 s	7.12 s	5.31 q 8.39 t

* s = singlet; t = triplet; q = quartet. † Corresponding to CH₂ grouping of the benzyl ester.
‡ Measured in methylene chloride-trifluoroacetic acid.

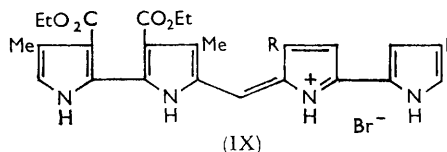
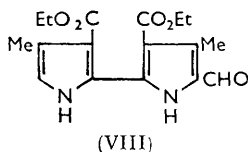
CO·Me), when the iodopyrrole (V; R = I) was heated with acetic acid. In order to test the scope of the Ullmann reaction as applied to 3-iodopyrroles, compound (V; R = I) was synthesised but was found to be less reactive than the 2-iodopyrroles. A dimethylformamide solution of the pyrrole (V; R = I) was unchanged after treatment with copper-bronze at room temperature for 16 hours but when the reactants were heated under reflux



for $\frac{1}{2}$ hour, the 3,3'-bipyrrole (IV), m. p. 246—247.5°, was obtained. Analytical data, molecular weight, and spectral properties all agree with structure (IV), but the compound clearly differed from that, m. p. 186°, obtained by Treibs and Kolm.¹⁵ As the German authors did not report the molecular weight of their product it was considered that it might be the tripyrrolylmethane (VI). However, in our hands, the reaction of (V; R = I) with acetic acid gave only the pyrroles (V; R = H, CO·Me), and an attempt to synthesise (VI) by reaction of (V; R = H) with (V; R = CO·Me) in acetic acid in the presence of hydrogen bromide yielded only unchanged starting materials.

Although the 2,2'-bipyrrole-3,3',5,5'-tetracarboxylic ester (VII; R = CO₂Et) was shown¹ to yield the corresponding 5,5'-dicarboxylic acid (VII; R = CO₂H) on treatment with sodium hydroxide in aqueous ethanol, substitution of methanol for ethanol as the solvent gave the corresponding tetramethyl ester by ester interchange. The acid (VII; R = CO₂H) was decarboxylated, and the ultraviolet spectrum of the product was observed (Table 3; No. 9) to resemble those of other 2,2'-bipyrrole-3,3'-dicarboxylic esters (Table 3; Nos. 11—16), rather than those of the 5,5'-dicarboxylic esters (Table 3; Nos. 7 and 8), thus supporting the view that the 5,5'-ester groups of (VII; R = CO₂Et) are hydrolysed

preferentially. Diethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3'-dicarboxylate was converted by the action of phosphorus oxychloride and dimethylformamide into the 5-formyl derivative



(VIII) ² and this condensed with 4,4'-dimethyl- or 4,4'-diethyl-2,2'-bipyrrole, in the presence of hydrogen bromide, to yield the 5,5'-dipyrrolyldipyromethene hydrobromides (IX; R = Me, Et).

EXPERIMENTAL

Ultraviolet spectra were determined on a Unicam S.P. 700 spectrometer. Infrared spectra were determined on a Perkin-Elmer Infracord, model 137 (denoted by P.E.) or on a Unicam S.P. 100 spectrometer fitted with a grating attachment, and refer to chloroform solutions unless otherwise stated. N.m.r. spectra were determined on an A.E.I. RS2 instrument operating at 60 Mc./sec. using tetramethylsilane as internal reference. Molecular weights were determined by the Rast method unless otherwise stated. Light petroleum refers to the fraction, b. p. 60—80.°

Pyrrole-2-carboxylic Acids.—3,5-Dimethoxycarbonyl-4-methylpyrrole-2-carboxylic acid. The acid was prepared by oxidation of dimethyl 3,5-dimethylpyrrole-2,4-dicarboxylate ¹⁶ by the method used ¹ for the oxidation of 2-benzyl 4-ethyl 3,5-dimethylpyrrole-2,4-dicarboxylate. The acid (75.3%) formed needles, m. p. 208—210° (from ethanol) (Found: C, 50.1; H, 4.9; N, 6.2. C₁₀H₁₁NO₆ requires C, 49.8; H, 4.6; N, 5.8%).

5-Benzylloxycarbonyl-3,4-dimethylpyrrole-2-carboxylic acid. Benzyl 3,4,5-trimethylpyrrole-2-carboxylate ¹⁷ (48.6 g.) in dry ether (300 ml.) was treated as before ¹ with bromine (10.5 ml., 1.02 mol.) and then sulphuryl chloride (43 ml.). The acid (21.75 g., 40%) formed plates, m. p. 212—214° (decomp.) (from ethanol) (Found: C, 66.3; H, 5.3; N, 4.85. C₁₅H₁₅NO₄ requires C, 65.9; H, 5.5; N, 5.1%). The neutral fraction was an oil and was not further investigated.

4-Benzylloxycarbonyl-3,5-dimethylpyrrole-2-carboxylic acid. 4-Benzyl 2-ethyl 3,5-dimethylpyrrole-2,4-dicarboxylate ¹ (60 g.) was dissolved in ethanol (410 ml.), sodium hydroxide (7.95 g., 1 mol.) in water (80 ml.) was added, and the resulting solution boiled under reflux for 6 hr. The ethanol was distilled off, water (450 ml.) added, and the solution was heated to 60° and acidified with dilute hydrochloric acid. The precipitated acid was separated, washed with water, and dried at 80° (42.5 g., 78%), m. p. 176° (decomp.). Crystallisation from ethanol gave small needles, m. p. 186° (decomp.) (Found: C, 65.9; H, 5.2; N, 5.3%).

2-Benzyl 4-ethyl 5-methyl 3-methylpyrrole-2,4,5-tricarboxylate and 4-ethoxycarbonyl-5-methoxycarbonyl-3-methylpyrrole-2-carboxylic acid. 5-Benzylloxycarbonyl-3-ethoxycarbonyl-4-methylpyrrole-2-carboxylic acid (50 g.) was dissolved in dry methanol (250 ml.) containing dry hydrogen chloride (3 g.). The solution was boiled under reflux for 1 hr. and poured into a stirred solution of sodium hydrogen carbonate (12 g.) in water (1 l.). A light brown oil precipitated which solidified after keeping overnight (45.5 g., 85.5%). A sample of the triester formed needles, m. p. 90—92° (from ethanol) (Found: C, 62.9; H, 5.55; N, 4.2. C₁₈H₁₉NO₆ requires C, 62.6; H, 5.55; N, 4.05%). The impurity in the crude product was unchanged starting material.

The crude triester (40 g.) was dissolved in ethanol (300 ml.) and hydrogenolysed over Raney nickel (W4; 40 ml.) at 80°/25 atm. for 5½ hr. The catalyst was separated and washed with ethanol. The combined filtrate and washings were evaporated to give the acid, plates (24.2 g., 82%), m. p. 204.5—205° (from ethanol) (lit., ¹⁸ 204—205°).

2-Iodopyrroles.—3-Ethyl 2-methyl 5-iodo-4-methylpyrrole-2,3-dicarboxylate. 4-Ethoxycarbonyl-5-methoxycarbonyl-3-methylpyrrole-2-carboxylic acid (22 g.; m. p. 194—198°) and sodium hydrogen carbonate (21.1 g.) in ethanol (120 ml.) and water (240 ml.) were heated to 65—70° and treated with a solution of iodine (22.85 g.) and potassium iodide (23 g.) in water

¹⁶ Küster, *Z. physiol. Chem.*, 1922, **121**, 135.

¹⁷ Johnson, Markham, Price, and Shaw, *J.*, 1958, 4254.

¹⁸ Corwin and Straughn, *J. Amer. Chem. Soc.*, 1948, **70**, 1418.

(265 ml.) as described previously.¹ An oil separated out and the mixture was kept overnight. The slightly gummy solid (24.1 g., 83%) was separated and gave the *iodo-ester*, needles (15.1 g., 52%), m. p. 134—135° (from aqueous ethanol) (Found: C, 35.7; H, 3.8; I, 37.0; N, 3.7. $C_{10}H_{12}INO_4$ requires C, 35.5; H, 3.6; I, 37.5; N, 4.1%).

Dimethyl 5-iodo-3-methylpyrrole-2,4-dicarboxylate. Obtained from 3,5-dimethoxycarbonyl-4-methylpyrrole-2-carboxylic acid (71%) as described above, the *iodo-compound* crystallised as square plates, m. p. 198—200° (from ethanol) (Found: C, 33.6; H, 3.4; I, 39.5; N, 4.6. $C_9H_{10}INO_4$ requires C, 33.45; H, 3.1; I, 39.3; N, 4.3%).

Benzyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate. Prepared from 5-benzyloxycarbonyl-3,4-dimethylpyrrole-2-carboxylic acid as above, the *iodo-compound* formed plates (51%), m. p. 126—128° (from ethanol) (Found: C, 47.3; H, 4.05; I, 35.0; N, 4.0. $C_{14}H_{14}INO_2$ requires C, 47.35; H, 4.0; I, 35.75; N, 3.95%).

Benzyl 2,4-dimethyl-5-iodopyrrole-3-carboxylate. Prepared from 4-benzyloxycarbonyl-3,5-dimethylpyrrole-2-carboxylic acid, the *iodo-derivative* formed needles (96%), m. p. 146—148° (from ethanol) (Found: C, 47.7; H, 4.4; I, 35.9; N, 3.65%).

Bipyrrolecarboxylic Esters.—The general procedure for the Ullmann condensations of iodopyrroles was the same as described earlier.¹

Tetramethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3',5,5'-tetracarboxylate. The crude product was triturated with light petroleum, washed, and dried at 80°. This bipyrrole (60%) formed needles, m. p. 249—251° (from chloroform-ethanol), and was identical with the sample obtained by transesterification (described below).

4,4'-Diethyl 5,5'-dimethyl 3,3'-dimethyl-2,2'-bipyrrole-4,4',5,5'-tetracarboxylate. The oily product solidified during removal of solvent under reduced pressure. It was triturated with ether-light petroleum, separated, washed with ether, and dried at 100° (1.31 g., 21%); it formed needles, m. p. 206° (from ethanol) (Found: C, 57.4; H, 6.1; N, 6.8%; *M*, 424. $C_{20}H_{24}N_2O_8$ requires C, 57.1; H, 5.75; N, 6.65%; *M*, 420.4).

Dibenzyl 3,3',5,5'-tetramethyl-2,2'-bipyrrole-4,4'-dicarboxylate.—The dark brown semi-solid product was triturated with ether-light petroleum, filtered, washed, and dried (1.15 g., 17.9%), m. p. 194—199°. Crystallisation from chloroform-ethanol (charcoal) gave prisms, m. p. 205.5—206.5° (Found: C, 73.5; H, 6.45; N, 6.4%; *M*, 446. $C_{28}H_{28}N_2O_4$ requires C, 73.65; H, 6.2; N, 6.15%; *M*, 456.5), λ_{max} (CHCl₃) 260 m μ (ϵ 15,500). The ether-light petroleum mother-liquors were not investigated.

Dibenzyl 3,3',4,4'-tetramethyl-2,2'-bipyrrole-5,5'-dicarboxylate. The product (3.7 g., 57%), isolated as described above, formed needles, m. p. 219—220° (from chloroform-ethanol) (Found: C, 73.8; H, 6.45; N, 6.25%; *M*, 427), λ_{max} (CHCl₃) 325 m μ (ϵ 24,900). The mother-liquors were not investigated.

Diethyl 2,2',4,4'-tetramethyl-3,3'-bipyrrole-5,5'-dicarboxylate (IV). Ethyl 2,4-dimethyl-3-iodopyrrole-5-carboxylate¹⁵ (V; R = I) and copper-bronze in *NN*-dimethylformamide were stirred under reflux for $\frac{1}{2}$ hr. and the crude product (4.45 g.) isolated as previously described. Recrystallisation from ethanol and sublimation at 210°/0.1 mm. gave the *ester* (1.48 g.; 25%), m. p. 246—247.5° (Found: C, 65.4; H, 7.15; N, 8.7%; *M*, 312. $C_{19}H_{24}N_2O_4$ requires C, 65.05; H, 7.3; N, 8.45%; *M*, 332.4), λ_{max} (CHCl₃) 255 and 285 m μ (ϵ 15,600 and 34,000). The mother-liquors were not investigated.

Effect of Solvent on the Ullmann Condensation of Diethyl 5-Iodo-3-methylpyrrole-2,4-dicarboxylate (I).—The reactions were carried out with the iodopyrrole (5 g.) and copper-bronze (5 g.).

(a) *Dimethylformamide*. The reactants were stirred in dimethylformamide (25 ml.) for 1 $\frac{1}{2}$ hr. The copper-bronze turned dark brown after 1 hr. (usual sign that reaction is complete). The crude product (2.5 g.; m. p. 152—162°), was isolated as described previously¹ and crystallised from ethanol as needles (1.94 g., 61%), m. p. 179.5—181°.

(b) *Benzene*. The reactants were stirred and boiled under reflux in benzene (50 ml.) for 8 hr. The copper-bronze did not darken. The crude product (2.84 g., m. p. 166—171°) crystallised from ethanol as needles (2.45 g., 77%), m. p. 179.5—181.5°.

(c) *Nitrobenzene*. The reactants were stirred in nitrobenzene (100 ml.) at 100° for 4 hr. The copper-bronze did not darken and the product was isolated, as described above, as needles (1.22 g., 38.4%), m. p. 174—176° (from ethanol). Fractional crystallisation of the mother-liquors afforded a small amount (0.65 g.) of unchanged 2-iodopyrrole.

Tetramethyl 4,4'-Dimethyl-2,2'-bipyrrole-3,3',5,5'-tetracarboxylate.—The tetraethyl ester¹ (VII) (7.5 g.) was dissolved in the minimum volume of boiling methanol (1 l.), and sodium

hydroxide (0.67 g., 1 mol.) in water (20 ml.) was added. The solution was heated under reflux for 30 min. and methanol allowed to distil off (approx. 175 ml.) until solid started to precipitate. The solution was heated under reflux for a further 30 min. and the precipitated solid separated, washed with methanol, and dried at 100° (5 g.), m. p. 211—215°. The product was crystallised to constant melting point from chloroform-ethanol (13 crystallisations), to yield the *tetramethyl ester*, m. p. 250—251° (Found: C, 54.8; H, 5.0; N, 6.8%; *M*, 347. C₁₈H₂₀N₂O₈ requires C, 55.1; H, 5.1; N, 7.15%; *M*, 392.4) (light absorption, see Table 3).

Triethyl 4,4'-Dimethyl-5-iododipyrromethane-3,3',5'-tricarboxylate (III).—3,3',5'-Triethoxycarbonyl-4,4'-dimethyldipyrromethane-5'-carboxylic acid¹⁴ (13.25 g.) and sodium hydrogen carbonate (8.9 g.) in ethanol (150 ml.) and water (110 ml.) were stirred at 40—50°. A solution of iodine (7.8 g.) and potassium iodide (8 g.) in water (150 ml.) was added during ½ hr. The mixture was stirred for a further 1½ hr. and the precipitate was separated, to give the *iodo-compound*, feathery needles (7.0 g., 44.5%), m. p. 164.5—166° (from ethanol) (Found: C, 46.4; H, 4.85; I, 25.0; N, 5.45%; *M*, 504. C₂₀H₂₅I N₂O₆ requires C, 46.5; H, 4.9; I, 24.6; N, 5.4%; *M*, 516.3).

Attempted Ullmann Condensation of Triethyl 4,4'-Dimethyl-5-iododipyrromethane-3,3',5'-tricarboxylate.—*Triethyl 4,4'-dimethyldipyrromethane-3,3',5'-tricarboxylate*. The foregoing iododipyrromethane (5 g.) and copper-bronze (7.5 g.) were ground together in a mortar, transferred to a 100 ml. flask, and heated on an oil-bath until the temperature of the mixture was 180°. The mixture was heated at 175—180° for 5 min., cooled to room temperature, transferred to an extraction thimble and extracted with two portions of boiling ethanol. Both extracts yielded solids which gave the triethyl ester, needles, m. p. 189—190° (from ethanol) (lit.,¹⁴ 187°) (Found: C, 61.7; H, 6.8; N, 7.2%; *M*, 394. Calc. for C₂₀H₂₆N₂O₆: C, 61.5; H, 6.7; N, 7.2%; *M*, 390.4), ν_{\max} . (P.E.) 3410 (NH) and 1675 cm.⁻¹ (ester carbonyl).

When the reaction was carried out in *NN*-dimethylformamide by stirring at 100° for ½ hr., the only product isolated was triethyl 4,4'-dimethyldipyrromethane-3,3',5'-tricarboxylate (1.22 g.), m. p. 189—190°.

Diethyl 3-Ethyl-5-(4''-ethylpyrrol-2''-yl)-3'-methyl-5'-(4''-methylpyrrol-2''-yl)dipyrromethane-3''-4'-dicarboxylate hydrobromide (IX; R = Et).—Diethyl 5-formyl-4,4'-dimethyl-2,2'-bipyrrole-3,3'-dicarboxylate² (533 mg., 1 mol.) was dissolved in warm methanol (55 ml.) and oxygen-free nitrogen bubbled through the solution for 5 min. 4,4'-Diethyl-2,2'-bipyrrole¹ (300 mg., 1 mol.) was added to the solution, which was warmed to dissolve the bipyrrole and then cooled to room temperature, the nitrogen atmosphere being maintained. Hydrogen bromide (0.6 ml. of a 48% w/v solution in glacial acetic acid) was added. The solution immediately became blue and, after 15 hr. at room temperature, the hydrobromide was separated, washed with methanol, and dried at 80° (853 mg., 92%). It crystallised from chloroform-methanol as green needles. (Found: C, 59.9; H, 5.75; Br, 14.3; N, 9.4. C₂₂H₃₅BrN₄O₄ requires C, 59.7; H, 6.05; Br, 13.7; N, 9.6%), λ_{\max} . (CHCl₃) 290, 359, 380, 425, 590, and 635 m μ (ϵ 13,100, 26,800, 18,400, 9350, 50,500, and 99,000), ν_{\max} . (P.E.) 3200 (bonded NH), 1690 (ester carbonyl), 1620sh, 1603, 1585sh, 1270, and 975 cm.⁻¹.

Ethyl 3,3'-Dimethyl-5-(4''-methylpyrrol-2''-yl)-5'-(4''-methylpyrrol-2''-yl)-3''-4'-dicarboxylate hydrobromide (IX; R = Me).—This was prepared similarly from diethyl 5-formyl-4,4'-dimethyl-2,2'-bipyrrole-3,3'-dicarboxylate² (760 mg., 1 mol.) and 4,4'-dimethyl-2,2'-bipyrrole¹ (364 mg., 1 mol) in methanol (75 ml.) with the addition of 48% w/v hydrogen bromide in acetic acid (0.8 ml.). The mixture was stored in an atmosphere of nitrogen for 15 hr., and the hydrobromide was separated, washed with methanol, and dried at 80° (967 mg., 77%). It crystallised from chloroform as green rods (Found: C, 58.1; H, 5.4; Br, 14.3; N, 9.8. C₂₇H₃₁BrN₄O₄ requires C, 58.4; H, 5.6; Br, 14.4; N, 10.1%), λ_{\max} . (CHCl₃) 291, 359, 377, 425, 590, and 635 m μ (ϵ 13,150, 26,400, 19,000, 9350, 44,800, and 92,000) ν_{\max} . (P.E.) 3200 (bonded NH), 1690 (ester carbonyl), 1620sh, 1605, 1590sh, 1270, and 975 cm.⁻¹.

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