3,4-Dihalopyrroles[1a,b]

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Eleven new 3,4-dichloro- and 3,4-dibromopyrroles were synthesized and studied. The chlorine atoms in the 3,4 positions were found to be unreactive to potassium fluoride in DMF, to hydrazine, and to lithium aluminum hydride. Further evidence is presented that halogenation with sulfuryl chloride proceeds by a free-radical mechanism. These compounds, together with those which had been prepared previously, form the basis of a representative spectral study of the 3,4-dihalopyrroles. Empirical band assignments were made for infrared spectra measured in both Nujol mulls and in carbon tetrachloride. The effect of halogen substitution on the ultraviolet spectra of pyrroles in ethanol was determined. The type of halogen present had no appreciable effect on the proton magnetic resonance (pmr) spectra of these compounds.

One of the objectives of the research program conducted in these laboratories is the study of the effects of electronegative substituents on the properties of porphyrins, dipyrromethenes, and their metal chelates. The halogens have been chosen as substituents to avoid the complications arising from the conjugative interactions of the pyrrole ring with unsaturated groups. The building blocks of these porphyrins and dipyrromethenes are the appropriately substituted 3,4-dihalopyrroles whose chemistry is described in this work.

Fischer synthesized several 3,4-dichloropyrroles,[2] including the parent 3,4-dichloropyrrole.[3] There are also some scattered reports[4,5] of other 3,4-dihalopyrroles in the literature. However, at present there are not enough data to draw conclusions concerning the attenuation of pyrrole reactivity caused by a 3,4-dihalo grouping, since previous studies[4,6–9] of reactivity were made exclusively with α- or β-monohalopyrroles.

Spectral studies of halopyrroles and in particular of 3,4-dihalopyrroles have not been reported previously. in an infrared study[10] only one halopyrrole was included. Work cited in the references of a recent review[8] and later ultraviolet studies[11–13] exclude all halopyrroles. In a study[5] of the halogenation of methyl pyrrole-2-carboxylate the ultraviolet and pmr spectra are reported for several halopyrroles including methyl 3,4-dichloropyrrole-2-carboxylate and methyl 3,4,5-trichloropyrrole-2-carboxylate. Although several other 3,4-dihalogen-substituted pyrroles are known,[2–4] spectral data are not available for these compounds.

Therefore, it is the purpose of this work to make available new intermediates for the synthesis of haloporphyrins and dipyrromethene chelates, to determine some basic rules of reactivity in this series, to measure the ultraviolet, infrared, and proton magnetic resonance spectra, and to set up spectra–structure correlations for this series of dihalopyrroles. Ultimately, it is hoped to obtain firm conclusions concerning the effects of electronegative substitution in porphyrins and dipyrromethene chelates.

Results

A terse summary of the reaction paths followed in the interconversion and preparation of the compounds utilized in this comprehensive study of 3,4-dihalopyrroles is displayed in Scheme I. Reference to the formulas in this scheme will be made in the following: Results, Discussion, and Experimental Section.

Infrared Spectra.—Table I contains a summary of the N—H, C=O, and C=C stretching frequencies of 3,4-dihalopyrroles. The solution spectra were useful in observing the unassociated N—H stretching vibration and the various C—H saturated modes. Since solid state and solution spectra were significantly the same, unless otherwise indicated, the Nujol mull spectra will be discussed.

The N—H stretching region in solution spectra contains a sharp peak in the range of 3448–3497 cm^{-1} characteristic of an unbonded or "free" N—H vibration. A broader absorption is also present in the range of 3215–3311 cm^{-1} for all compounds possessing either a carbonyl or a hydroxyl group, indicating some intermolecular association of the >C=O···H—N< or the >O···H—N< type. The mull spectra show the "associated" peak in the region of 3155–3378 cm^{-1} for most halopyrroles and sharp peaks at 3436 and 3460 cm^{-1} for **7** and **13**, respectively. The values at the extremes of this range occur with compounds whose structure possesses a hydroxy group depending on whether the halo substituents are chloro (**18**, **19**) or bromo (**27**). The esters absorb in a narrow region at about 3270, the aldehydes somewhat more variably at about 3230, and the dipyrrylmethanes at about 3220 cm^{-1}. The observed N—H stretching frequency of 3,4-dichloro-5-methylpyrrole-2-carboxylic acid (**10**) measured in Nujol is high at 3448 cm^{-1}, indicating that through carboxylate dimer formation the NH group becomes inaccessible to hydrogen bonding in the solid phase. As larger halogens are substituted in the series **2**, **25**, **30**, there is a gradual drop in the N—H absorption frequency contrary to the expectation based on electronegativity. This effect could be explained in terms of the considerable distortions in the pyrrole

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(2) H. Fischer and E. Elhardt, *Z. Physiol. Chem.*, **257**, 61 (1939).

(3) H. Fischer and K. Gangl, *ibid.*, **267**, 188 (1941).

(4) H. Fischer and H. Orth, "Die Chemie des Pyrrols," Vol. 1, Academische Verlags GmbH, Leipzig, 1934.

(5) P. Hodge and R. Rickards, *J. Chem. Soc.*, 459 (1965).

(6) A. H. Corwin and G. G. Kleinspehn, *J. Amer. Chem. Soc.*, **75**, 2089 (1953).

(7) A. Treibs and H. Kolm, *Justus Liebigs Ann. Chem.*, **614**, 176 (1958).

(8) E. Baltazzi and L. Krimmen, *Chem. Rev.*, **63**, 511 (1963).

(9) K. W. Doak and A. H. Corwin, *J. Amer. Chem. Soc.*, **71**, 159 (1949).

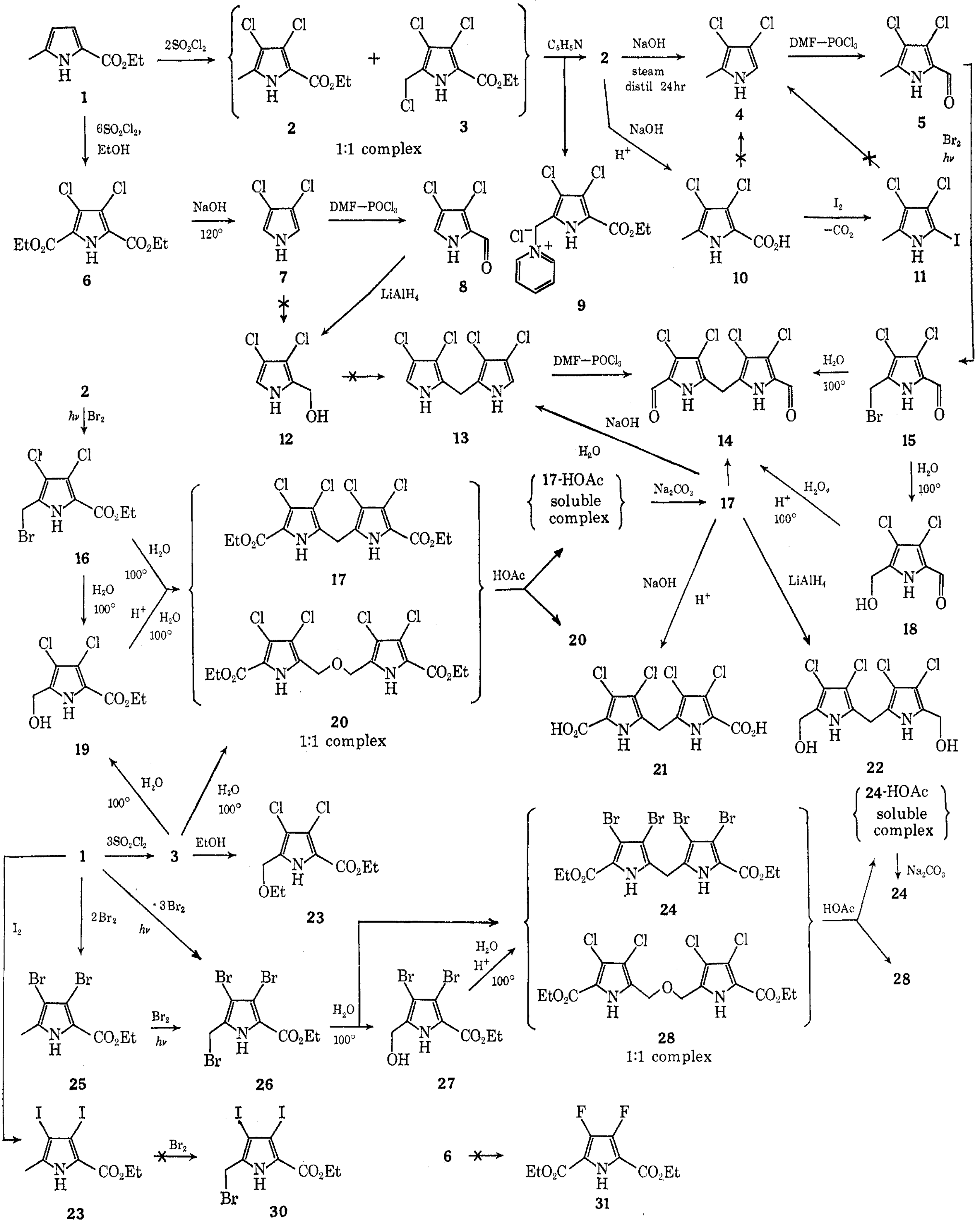
(10) U. Eisner, *J. Chem. Soc.*, 971 (1958).

(11) F. Erb-Debryne, *Ann. Chim.* (Paris), **9**, 73 (1964).

(12) R. Hinman and S. Theodoropulos, *J. Org. Chem.*, **28**, 3052 (1963),

(13) P. Chiorboli, A. Rastelli, and F. Nomichioli, *Theor. Chem. Acta*, **5**, 1 (1966).

Scheme I



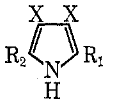
ring geometry caused by mutual repulsion between the halo groups in the 3,4 positions.

The ester carbonyl absorption frequency of 3,4-dihalopyrroles measured in Nujol is rather constant at 1667–1669 cm^{-1} unless either a hydroxy group (**19**, **27**) or another unsaturated substituent (**6**) is present. For compounds also measured in solution, this absorption is on the average about 3–5 cm^{-1} higher. The aldehyde carbonyl stretching frequencies are about 33–42 cm^{-1} lower than those of the analogous esters.

3,4-Dihalopyrroles possess two bands in the C=C stretch region of 1600–1470 cm^{-1}. The first band is weak and is ascribed to the asymmetrical stretch. The second band is somewhat stronger and is ascribed

TABLE I

INFRARED MAXIMA OF N—H, C═O, AND C═C STRETCHING MODES IN 3,4-DIHALOPYRROLES



Compd no.	X	R₁	R₂	Medium	cm⁻¹ N—H		C═O		C═C	
1	H	CO_2Et	Me	N[a]		3367	1681		1577	1497
				C[b]	3472	3311	1672		...[c]	1490
2	Cl	CO_2Et	Me	N		3300	1669		1563	1493
				C	3472	3311	1672			1490
3	Cl	CO_2Et	CH_2Cl	N		3279	1669		1560	1488
				C	3442	3268	1698	1673		1488
16	Cl	CO_2Et	CH_2Br	N		3279	1667		1558	1488
				C	3442	3268	1698	1672		1488
17	Cl	CO_2Et	PM[d]	N		3215	1669		1563	1484
				C		3215	1664			1488
19	Cl	CO_2Et	CH_2OH	N		3175	1681		1555	1493
23	Cl	CO_2Et	CH_2OEt	N		3279	1678		1563	1493
				C	3448	3268	1672			1486
20	Cl	CO_2Et	PMOM[e]	N		3268	1669		1560	1488
6	Cl	CO_2Et	CO_2Et	N		3279	1709		1531	
				C	3448	3268	1672			1486
9	Cl	CO_2Et	$CH_2Py^+Cl^-$	N		...[f]	1684		1555	1481
	Cl	CO_2Et	$CH_2Py^+Br^-$	N		...[f]	1686		1555	1481
8	Cl	CHO	H	N		3215	1642			1481
				C	3448	3247	1656			1481
5	Cl	CHO	Me	N		3215	1634		1558	1488
				C	3448	3236	1637			1493
15	Cl	CHO	CH_2Br	N		3185	1650		1553	1484
				C	3436	3236	1639			1488
14	Cl	CHO	PM	N		3226	1642		1553	1486
18	Cl	CHO	CH_2OH	N		3155	1639			1471
7	Cl	H	H	N	3436				1538	1513
				C	3497				1534	1493
13	Cl	H	PM	N	3460				1563	1493
				C	3472				1563	
10	Cl	CO_2H	Me	N	3448		1664		1570	1504
25	Br	CO_2Et	Me	N		3279	1669		1558	1488
				C	3448	3279	1667			1486
26	Br	CO_2Et	CH_2Br	N		3268	1667		1558	1488
24	Br	CO_2Et	PM	N		3205	1669		1563	1485
27	Br	CO_2Et	CH_2OH	N		3378	1658		1553	1484
29	I	CO_2Et	Me	N		3289	1669		1543	1475
				C	3448	3268	1667			1479

[a] Nujol mull. [b] Carbon tetrachloride solution. [c] Peaks in the 1550-cm⁻¹ region are obscured in the 0.2-mm cell by absorption due to solvent. [d] Pyrrylmethyl group with identical substituents on the pyrrole ring. [e] Pyrrylmethoxymethyl group with identical substituents on pyrrole ring. [f] Very broad absorption.

to the symmetrical mode.[14] In the ester series, the first band is fixed at 1558 ± 5 cm⁻¹ except for the diester **6** and for 3,4-dichloropyrrole **7** where it is low at 1531 and 1538 cm⁻¹. The values for the aldehydes are similar to those of the esters. The second band is more variable with most values falling around 1488 cm⁻¹, which is about 12 cm⁻¹ lower than the corresponding band in the unhalogenated[10] pyrrole compounds.

All the ethyl esters show a band at 1285 cm⁻¹ and one at about 1115 cm⁻¹, indicative of the C—O stretch which is absent in the aldehyde spectra. Another group of bands present are at about 1440, 1365, 1150, 1050, 875, and 775 cm⁻¹, all of which are assigned to the presence of the ethyl group. The bands at 1390 cm⁻¹ are due to a methylene group adjacent to a double bond and the bands at 1220 cm⁻¹ are the C—O stretching vibrations on the ethyl side of the oxygen. All of the above bands are within about 5 cm⁻¹ except for the hydroxymethyl compounds. Three aldehydes (**5**, **15**, **18**) show the CH deformation vibration at 840 and dipyrrylmethane **14** at 853 while that of 3,4-dichloropyrrole-2-aldehyde occurs at 785 cm⁻¹. All aldehydes studied show bands at 1360 and 1260 cm⁻¹ and in the region of 1230–1160 cm⁻¹.[15] The four tetrasubstituted pyrrolealdehydes (**5**, **15**, **18**, **14**) possess a band at 1410 cm⁻¹ which can be ascribed to a methylene vibration. All aldehydes show a band at 1059, but only the tetrasubstituted aldehydes show, in addition, an absorption at 1107 cm⁻¹. This band is ascribed to a C—C stretch involving the exocyclic carbon of the substituent while the former is probably due to a C—C stretch involving the formyl groups.

The two characteristic aldehyde CH stretch and combination[15] modes appear in the expected range

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(14) Assignments are made by analogy to the study described in ref 10.

(15) L. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley & Sons, Inc., New York, N. Y., 1962.

TABLE II

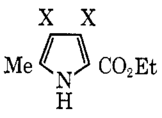
ULTRAVIOLET SPECTRA OF SUBSTITUTED 3,4-DIHALOPYRROLES

Compd	Substituents					Band I		Band II	
no.	2	3	4	5	Medium	λ, mμ	ϵ	λ, mμ	ϵ
. . .^{a}	H	H	H	H	E^b	183		211	15,000
7	H	Cl	Cl	H	E	208	5,240		
1	CO_2Et	H	H	Me	E	231	3,320	277	18,690
2	CO_2Et	Cl	Cl	Me	E	245	6,950^c	275	15,440
25	CO_2Et	Br	Br	Me	E	255	8,440^c	278	15,350
29	CO_2Et	I	I	Me	E	265	11,700^c	277	15,560
. . .^{a}	CHO	H	H	H	E	252	5,000	290	16,600
8	CHO	Cl	Cl	H	E	265	7,860^c	290	13,440
5	CHO	Cl	Cl	Me	E	270	6,310^c	304	17,080
13	H	Cl	Cl	PM^d	C^e	250	5,700^f		
17	CO_2Et	Cl	Cl	PM	C	247	14,700^c	270	23,800
14	CHO	Cl	Cl	PM	C	270	5,300	294 309	8,300 7,900

[a] Reference 16. [b] Absolute ethanol. [c] The extinction coefficient reflects only the intensity measured with no correction made for overlapping peaks. [d] PM, pyrrylmethyl group with identical substituents on the pyrrole ring. [e] Spectro-Grade chloroform. [f] Very sharp peak.

but higher than average. The first band is somewhat variable between 2874 and 2857, while the second is stationary at 2833 cm^{-1}. The pyrrole CH nuclear vibrations are constant at 3160 cm^{-1} irrespective of the other α substituent.

Ultraviolet Spectra.—The ultraviolet spectra of representative 3,4-dihalopyrroles measured in solution are summarized in Table II. Since there is no general agreement on the theoretical interpretation of the spectrum of pyrrole,[16] only the observed effects of substituents can be presented for 3,4-dihalopyrroles. The substitution of two chlorine atoms into the β positions of pyrrole produces a new band at 208 mμ (ϵ 5240). For the corresponding dimethyl compound this band occurs at 205 mμ (ϵ 4400).[17] Similar substitution of chlorine atoms into β positions of pyrrole-2-aldehyde shifts band I toward band II but has no effect on the position of band II and lowers its intensity by 20%. In the series X = H, Cl, Br, and I for structure **32**, band I, a shoulder, increases by about 10 mμ for each successive derivative with its intensity also increasing in steps of 3000 units. Band II remains stationary at about 277 mμ (ϵ 15,500) after an initial drop of 20% in intensity upon halogenation. The introduction of a methyl group into 3,4-dichloropyrrole-2-aldehyde **8** causes a small bathochromic shift in band I and a large one in band II going from 290 mμ (ϵ 13,400) to 304 (17,100). Substitution of a formyl group for a carbethoxy group shifts both band I and band II to longer wavelength.



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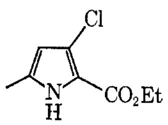
An exceptionally large difference in absorption becomes apparent in comparing the dipyrrylmethane **13** with the pyrrole **7**. A part of this shift may be explained by changing of solvents and another part by the introduction of a methylene group, but the bulk of the shift represents evidence for possible electronic interaction between the two π systems within the dipyrrylmethane molecule. A similar conclusion could be reached on comparing the pairs of spectra of **17** and **2** and of **14** and **5**, although in these cases the spectrum of each dipyrrylmethane is not so dramatically different from the spectrum of its corresponding monopyrrole.

Proton Magnetic Resonance.—The proton magnetic resonance spectra of 3,4-dihalopyrroles and the corresponding dipyrrylmethanes are summarized in Tables III and IV. The resonance signal of the ethyl group in carbethoxy compounds is generally unaffected by substituents to about 0.1 ppm and occurs as a triplet and a quartet at τ 8.65 and 5.75, respectively. The ring methyl gives rise to a sharp singlet at 7.72 ± 0.06 and the methylene gives a sharp singlet at τ 5.48 ± 0.10. The methylene joining two pyrryl groups in dipyrrylmethanes occurs as a sharp singlet at τ 6.0 in deuteriochloroform and 0.25 ppm lower in pyridine. This value drops to τ 3.5 upon substitution of bromine (see Table IV). In general, the proton resonance signal for NH could not be detected. The pmr spectra of 3,4-dihalogenated pyrroles are thus found to be relatively simple and therefore provide a valuable diagnostic check for the characterization of new as well as of old pyrrole compounds.

Discussion

The 1:1 compound adducts isolated in this work are the following pairs: **2** and **3**, **33** and **34**, **17** and **20**, and **24** and **28**. Each pair possesses a sharp melting point and with the exception of **33** and **34** can be separated chemically into its individual components.



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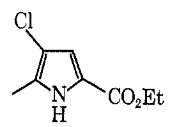

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Elemental analyses and pmr spectra are also in accord with the 1:1 compound structures. Two modes of binding can be considered: charge transfer and hydrogen bonding. It is probable that the pyrrole ring can function as a π acid when it possesses electronega-

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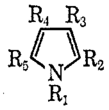
(16) H. Jaffee and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," John Wiley & Sons, Inc., New York, N. Y., 1962, p 351.

(17) R. Hinman and S. Theodoropulos, *J. Org. Chem.*, **28**, 3052 (1963).

TABLE III

PROTON MAGNETIC RESONANCE SPECTRA[a] OF 3,4-DIHALOPYRROLES

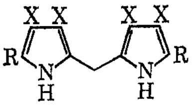


Substituents, [chemical shifts[b] (multiplicity)]					Compd
R_1	R_2	R_3	R_4	R_5	no.
H	CO_2Et [8.73 (3),[c] 5.82 (4)]	H [4.25 (3) (J = 3.9[d])]	H [3.38 (3) J = 3.9)]	Me [7.77]	1
H	CO_2Et [8.65 (3), 5.75 (4)]	Cl	Cl	Me [7.78]	2
H	CO_2Et [8.65 (3), 5.77 (4)]	Br	Br	Me [7.75]	25
H	CO_2Et [8.65 (3), 5.78 (4)]	I	I	Me [7.66]	29
H	CO_2Et [8.63 (3), 5.73 (4)]	Cl	Cl	CO_2Et [8.63 (3), 5.73 (4)]	6
H	CO_2Et [8.63 (3), 5.73 (4)]	Cl	Cl	CH_2Cl [5.55]	3
H	CO_2Et [8.62 (3), 5.67 (4)]	Cl	Cl	CH_2Br [5.58]	16
H	CO_2Et [8.67 (3), 5.77 (4)]	Cl	Cl	CH_2OH [5.43]	19
H	CO_2Et [8.56 (3), 5.63 (4)]	Br	Br	CH_2Br [5.53]	26
H	CO_2Et [8.61 (3), 5.73 (4)]	Br	Br	CH_2OH [5.38]	27
H	CHO [0.36 (2) (J = 1.1)]	Cl	Cl	H [2.91 (2) (J = 1.1)]	8
H	CHO [0.86]	Cl	Cl	Me [7.69]	5
H	H [3.38 (2) (J = 3.1)]	Cl	Cl	H [3.38 (2) (J = 3.1)]	7
H [6.07]	Cl	Cl	Cl	Cl	
H	CO_2Et [8.70 (3), 8.65 (3), 5.85 (4), 5.68 (4)]	H (Cl) [3.50]	Cl (H) [3.45]	Me [7.78[e]]	33, 34

[a] Measured in deuteriochloroform at ~37°. [b] Relative to internal TMS, given in τ units. [c] Multiplicity of band if split. [d] J is given in hertz. [e] Could not be resolved.

TABLE IV

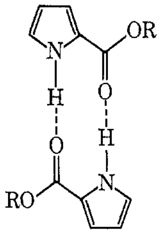
PROTON MAGNETIC RESONANCE SPECTRA OF DIPYRRYLMETHANES



	Bridge	Substituents [chemical shifts[a] (multiplicity)]				Compd
Solvent	[chemical shifts[a]]	R	X	Other		no.
$CDCl_3$	CH_2 [5.93]	CO_2Et [8.61 (3),[b] 5.78 (4)]	Cl	NH [−0.88]		17
$CDCl_3$	CH_2 [6.04]	CO_2Et [8.63 (3), 5.92 (4)]	Cl	CH_3CO_2H[c] [7.96]		
$CDCl_3$	CHBr [3.52]	CO_2Et [8.66 (3), 5.67 (4)]	Cl			
$CDCl_3$	CH_2 [6.09]	H [3.46 (2) (J = 2.9[d])]	Cl			13
$CDCl_3$	CH_2 [5.57]	CH_2OH [6.23, 6.8[f]]	Cl	Et_2O[e] [8.92 (3), 6.54 (4)]	NH [1.90 (2)]	22
Pyridine	CH_2 [5.75]	CO_2Et [8.98 (3), 5.85 (4)]	Br	$C_2H_4Cl_2$[c] [6.28]		24
DMSO	CH_2 [6.07]	$CONHNH_2$ [4.02]	Cl			
DMSO	CH_2 [6.05]	$CONHNHSO_2Ph$ [2.42 (2), 1.92 (3), 0.38, 0.08, −1.90]	Cl			
DMSO	CH_2 [5.93]	CHO [0.47]	Cl	NH [6.4[f]]		14

[a] Relative to internal TMS, given in τ units. [b] Multiplicity of split band. [c] Solvent cocrystallized. [d] J is given in hertz. [e] Residual ether from reaction solvent. [f] Very broad band.

tive chlorine or bromine and carbethoxy substituents. However, charge transfer complexes can form only between two dissimilar molecules, *i.e.*, between pairs of either strong donor and good to moderate acceptor molecules or strong acceptors and moderate to good donors.[18] *A priori*, it then becomes unlikely that pairs of such similar molecules as **2** and **3**, **33** and **34**, **17** and **20**, and **24** and **28**, or the case cited in the literature,[19] would form stable π complexes. Additional evidence was obtained to rule out charge-transfer interactions and to help support the more reasonable hydrogen-bonding mechanism **35**. The ultraviolet and the infrared spectra of **2**, **3**, and of equimolar solutions of **2** and **3** were measured. It was found that both electronic and vibrational spectra of the 1:1 solutions were composites of their corresponding individual spectra. These results help further to substantiate the lack of electronic interactions and therefore support the hydrogen bonding dimer **35**. This tendency to dimerize in dihalopyrrole esters and aldehydes is additionally evidenced by the considerably smaller "free" NH peak, the very large, broad "bonded" NH vibration, and the total absence of any free NH peak in the solution infrared spectrum of the dipyrrylmethane **17**. A molecular model of a strainless, totally hydrogen-bonded dimer of **17** was constructed as a verification of the interpretation of the above infrared results. Unfortunately, the solubility was too low for the determination of the molecular weight.



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The isolation of the pair **33** and **34** offers an interesting observation. The fact that these intermediates were formed in equal amounts suggests that the sulfuryl chloride reaction in ether can proceed at least in part through a free-radical mechanism. Substitution into the 3 position, which has been deactivated by the adjacent carbethoxy group, can occur only by a homolytic attack,[5] whereas substitution into the 4 position can, in addition, occur also by electrophilic attack. Of course, further chlorination with sulfuryl chloride of the methyl side chain must occur by a free-radical mechanism.

Experimental Section

Materials and Apparatus.—The organic starting materials were Eastman Kodak practical grade and were used without further purification. The inorganic reagents were gererally of analytical grade. Solvents used were analytical grade except where large-scale recrystallizations were involved. The elemental analyses were determined by Alfred Bernhardt, Germany. Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. Solution infrared spectra were measured on a Beckman Model IR-8 spectrophotometer; Nujol mull spectra were obtained using a Perkin-Elmer Infracord. The proton magnetic resonance spectra were recorded on a Varian Associates Model A-60 spectrometer with readings relative to internal tertramethylsilane in τ units.[20] The ultraviolet specta were measured on an Applied Physics Corp. Cary Model 14 spectrophotometer.

Ethyl 5-Methylpyrrole-2-carboxylate (1).—The literature procedure[21,22] was found unsuitable for large-scale preparation. A solution of 332 g (4.8 mol) sodium nitrite in 500 ml of water was added dropwise to a cooled (below 20°) solution of 520 g (4.0 mol) of ethyl acetoacetate in 1560 g of glacial acetic acid. After 12 hr, the reaction mixture was divided into three equal parts, and each part in turn was treated with 176 g (1.33 mol) of 4,4-dimethoxy-2-butanone and 191 g (2.9 g-atoms) of zinc dust which was added portionwise to the well-stirred solution as rapidly as foaming permitted. The mixture was heated at 120° for 10 min and after slow cooling to 50° was poured into ice water and stirred for 1 hr. The orange solid was washed well with ice water, dried in air, and distilled *in vacuo* (short air condenser), bp 110–120° (0.1 mm), 130–160° (0.3 mm), until the pressure started rising. The distillate was recrystallized from Skellysolve B, yield 135 g (22%), mp 98–100° (lit.[22] mp 100°).

A by-product was isolated and recrystallized from hexane which is identical with the product obtained in 12.6% yield by omitting 4,4-dimethoxy-2-butanone from the above procedure: mp 83°; pmr ($CDCl_3$) τ 8.54 (t, 3), 5.50 (q, 2), 7.72 (s, 3); ir (Nujol) 1706 cm^{-1} (C=O).

Anal. Calcd for 2,5-dicarbethoxy-3,6-dimethylpyrazine, $C_{12}H_{16}N_2O_4$: C, 57.13; H, 6.39; N, 11.11. Found: C, 57.36; H, 6.44; N, 11.26.

Ethyl 3,4-Dichloro-5-methylpyrrole-2-carboxylate (2).—An ice-cooled solution of 7.6 g (0.050 mol) of **1** in 100 ml of absolute ether was treated dropwise with 13.5 g (0.100 mol) of sulfuryl chloride over a 15-min period. The solvent was removed and the residue was dissolved in 50 ml of ethanol. This solution was poured into ice water, collected, and recrystallized three times from carbon tetrachloride, yield 1.5 g (13%), mp 158–160°.

When the residue was not treated with ethanol but recrystallized directly from either chloroform or carbon tetrachloride, a compound mixture resulted, mp 134–136°.

Anal. Calcd for 1:1 **2**-**3**, $C_{16}H_{17}N_2Cl_5O_4$: C, 40.15; H, 3.58; N, 5.85; Cl, 37.04. Found: C, 40.15; H, 3.60; N, 5.62; Cl, 36.96.

This compound mixture was broken up by treating its chloroform solution with a few milliliters of pyridine to obtain **9**, the insoluble pyridinium salt of the chloromethyl compound, mp 230–235° dec. Pure **2** was then obtained by recrystallization from a small amount of chloroform, mp 161–162°.

Anal. Calcd for $C_8H_9NCl_2O_2$: C, 43.26; H, 4.08; N, 6.31; Cl, 31.93. Found: C, 43.31; H, 4.24; N, 6.30; Cl, 31.86.

3,4-Dichloro-2-methylpyrrole (4).—Into a 250-ml three-necked flask equipped with a graduated Dean-Stark trap, nitrogen inlet, and stirrer were placed 3.3 g (0.015 mol) of ester **2** and 5 g (0.125 mol) of sodium hydroxide in 175 ml of water. The reaction was boiled under nitrogen for 20 hr. The product appeared after 1 hr and the reaction was about 80% complete after 8 hr. The liquid product was drawn off from the top and weighed, yield 2.0 g (89%), mp 16.0–16.5°, d^{23} 1.27 g/ml.

Pure **4** is a colorless, highly refractive, syrupy liquid possessing a strong characteristic odor somewhat similar to 3,4-dichloropyrrole **7**. Upon brief exposure to atmospheric oxygen, the clear liquid turns brown and then to a black solid. Its dichloromethane solution was stable enough to enter it into the next reaction.

3,4-Dichloro-5-methylpyrrole-2-aldehyde (5).—A formylating mixture was prepared by slowly adding 2.5 g (0.0165 mol) of phosphorus oxychloride into 1.2 g (0.0165 mol) of chilled dimethylformamide,[23] and then quickly diluting with 15 ml of methylene chloride. To this well-stirred solution, 2.0 g (0.0135 mol) of **4** in 15 ml of methylene chloride was added at 0° during 15 min. A bright yellow solid separated. The mixture was diluted with 15 ml of methylene chloride, heated for 30 min (hydrogen chloride was evolved), and neutralized with a 20-ml

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[18] L. J. Andrews and R. M. Keefer, "Molecular Complexes in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964.

[19] G. Mazzara and A. Borgo, *Gazz. Chim. Ital.*, **35**, 104 (1905). The isolated "compound" methyl 3,4-dichloropyrrole-2-carboxylate was later[5] shown to be a 1:1 mixture of the 3,4-dichloro and 4,5-dichloro isomers.

[20] G. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

[21] H. Fischer and E. Fink, *Z. Physiol. Chem.*, **283**, 152 (1948).

[22] H. Fischer and E. Fink, *ibid.*, **280**, 123 (1944).

[23] "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., John Wiley & Sons, Inc., New York, N. Y., 1963, p 831.

solution of 8.2 g (0.1 mol) of sodium acetate. The mixture was brought to a boil and upon cooling the product separated. It was recrystallized from Skellysolve B containing 5% carbon tetrachloride, yield 2.3 g (96%), mp 169–170°, semicarbazone mp 258° dec.

Anal. Calcd for $C_6H_5NCl_2O$: C, 40.48; H, 2.83; N, 7.87; Cl, 39.83. Found: C, 40.65; H, 2.78; N, 8.02; Cl, 40.14.

5-Bromomethyl-3,4-dichloropyrrole-2-aldehyde (**15**).—Under illumination from a 150-W frosted lamp, 3.2 g (0.020 mol) of bromine in 5 ml of carbon tetrachloride was added in 15 min to a solution of 3.6 g (0.020 mol) of aldehyde **5** in 120 ml of dry carbon tetrachloride. After refluxing for 15 min, the solvent was removed under vacuum and the residue was recrystallized twice from carbon tetrachloride, yield 1.5 g (29%), mp 147–150° dec with evolution of gas.

Anal. Calcd for $C_6H_4Cl_2BrNO$: C, 28.05; H, 1.57; N, 5.45; Br, 31.11; Cl, 27.60. Found: C, 27.87; H, 1.80; N, 5.34; Br, 30.83; Cl, 27.50.

Ethyl 5-Bromomethyl-3,4-dichloropyrrole-2-carboxylate (**16**).—A refluxing and illuminated solution of 11.0 g (0.0500 mol) of **2** in 475 ml of dry carbon tetrachloride was treated dropwise with 8.0 g (0.050 mol) of bromine in 10 ml of carbon tetrachloride. The solvent was removed (*in vacuo*) and the residue was recrystallized from carbon tetrachloride, yield 8.3 g (55%), mp 173–174° dec.

Anal. Calcd for $C_8H_8NCl_2BrO_2$: C, 31.92; H, 2.68; N, 4.65; Cl, 23.56; Br, 26.55. Found: C, 31.90; H, 2.93; N, 4.48; Cl, 23.39; Br, 26.39.

Ethyl 3,4-Dichloro-5-chloromethylpyrrole-2-carboxylate (**3**).—A 400-ml dry ether solution containing 40.0 g (0.261 mol) of **1** was treated dropwise under nitrogen with 110 g (0.811 mol) of sulfuryl chloride. The crystals which separated upon cooling were recrystallized from chloroform, yield 50.5 g (74.8%), mp 158–159° (lit.[2] mp 160–161° with browning).

Ethyl 3,4-Dibromo-5-methylpyrrole-2-carboxylate (**25**).—To 1.5 g (0.010 mol) of **1** in 80 ml of ether at 3–4° was added dropwise 3.3 g (0.020 mol) of bromine in 10 ml of carbon tetrachloride. The solvents were removed *in vacuo* and the product was recrystallized from 80 ml of carbon tetrachloride, yield 2.5 g (81%), mp 172–174°, (lit.[4] mp 176°).

Anal. Calcd for $C_8H_9NBr_2O_2$: C, 30.89; H, 2.92; N, 4.50; Br, 51.39. Found: C, 30.97; H, 2.99; N, 4.29; Br, 51.31.

Ethyl 3,4-Dibromo-5-bromomethylpyrrole-2-carboxylate (**26**).—Under illumination, 9.4 g (0.030 mol) of **25** in 250 ml of boiling carbon tetrachloride was treated dropwise with 4.8 g (0.030 mol) of bromine in 20 ml of carbon tetrachloride. White crystals separated upon cooling, yield 8.2 g (69.5%), mp 190–192° dec.

Anal. Calcd for $C_8H_8NBr_3O_2$: C, 24.64; H, 2.07; N, 3.59; Br, 61.49. Found: C, 24.51; H, 2.43; N, 3.51; Br, 60.62.

Compound **26** was also prepared directly from **1** in illuminated and refluxing carbon tetrachloride in 60.8% yield.

Ethyl 3,4-Diiodo-5-methylpyrrole-2-carboxylate (**29**).—Into an open flask were placed 153 g (0.100 mol) of **1** and a 500-ml solution containing 100 g (1.00 mol) of potassium bicarbonate. The mixture was heated to near boiling and gradually a solution of 76.0 g (0.30 mol) of iodine and 250 g (1.5 mol) of potassium iodide in water was added. Heating was continued for 30 min. The crude product was recrystallized several times from carbon tetrachloride, yield 21.0 g (53%), mp 193–195° and 220° dec.

Anal. Calcd for $C_8H_9NI_2O_2$: C, 23.72; H, 2.24; N, 3.46; I, 62.67. Found: C, 24.57; H, 2.46; N, 3.73; I, 65.16.

Compund **29** was treated with bromine in carbon tetrachloride in an attempt to produce **30**. An immediate violet coloration, indicative of iodine liberation, was observed. No product could be isolated.

Ethyl 3,4-Dichloro-5-hydroxymethylpyrrole-2-carboxylate (**19**).—A suspension of 6.0 g (0.020 mol) of **16** was refluxed 4 hr in 750 ml of water containing 5 ml of 48% hydrobromic acid. The suspension was filtered hot through a preheated sintered-glass funnel to remove the brownish solids. The clear filtrate yielded 2.3 g (49%) of a lustrous product after recrystallization from chloroform, mp 144–145° (lit.[2] mp 144° obtained from hydrolysis of **3**).

Anal. Calcd for $C_8H_9NCl_2O_3$: C, 40.35; H, 3.81; N, 5.88; Cl, 29.78. Found: C, 40.30; H, 3.88; N, 5.82; Cl, 29.70.

Diethyl 3,3′,4,4′-Tetrachloro-2,2′-dipyrrylmethane-5,5′-dicarboxylate (**17**). **A. From 16.**—The dark residue from the above reaction was air-dried and recrystallized from ethylene chloride, chloroform, and again from ethylene chloride. Fine white crystals of **17** containing *ca.* one molecule of solvent were obtained, 2.6 g (53%), mp 212–214° (lit.[2] mp 211°); at 120° a phase change occurs with loss of solvent.

Anal. Calcd for $C_{15}H_{14}N_2Cl_4O_4 \cdot C_2H_4Cl_2$: C, 38.74; H, 3.44; N, 5.32; Cl, 40.36. Found: C, 37.60; H, 3.06; N, 5.28; Cl, 39.26.

A sample of this transparent crystalline compound was heated at 125° for 18 hr and was allowed to cool in air. The resulting free-flowing powder was analyzed.

Anal. Calcd for $C_{15}H_{14}N_2Cl_4O_4 \cdot H_2O$: C, 40.38; H, 3.62; N, 6.28; Cl, 31.79. Found: C, 40.62; H, 3.38; N, 6.35; Cl, 31.84.

When **17** was recrystallized from glacial acetic acid, very fine wooly crystals were obtained containing one molecule of solvent. They are extremely soluble in carbon tetrachloride, chloroform, dichloroethane, and similar solvents.

Anal. Calcd for $C_{15}H_{14}N_2Cl_4O_4 \cdot C_2H_4O_2$: C, 41.82; H, 3.72; N, 5.74; Cl, 29.73. Found: C, 41.96; H, 3.93; N, 5.92; Cl, 29.05.

When 1.0 g (0.0030 mol) of **16** was refluxed 18 hr in glacial acetic acid, 0.60 g of starting material was isolated. Attempted synthesis of **17** in ethanol resulted in an 83% yield of **23**, mp 104–105° (lit.[2] mp 105°).

B. From 3.—A suspension of 85.6 g (0.341 mol) of **3** in 650 ml of water was refluxed for 4 hr. The gray powder obtained was recrystallized once from glacial acetic acid to form the molecular compound of **17** with acetic acid. This solid was extracted with five 100-ml portions of boiling carbon tetrachloride. The insoluble residue was a white powder, 13.7 g (18%), mp 195–197°.

Anal. Calcd for **20**, $C_{16}H_{16}N_2Cl_4O_5$: C, 41.94; H, 3.52; N, 6.12; Cl, 30.96. Found: C, 41.72; H, 3.54; N, 6.13; Cl, 31.15.

Work-up of the combined extractates yielded 18.0 g (25%) of pure **17** complexes with acetic acid. This complex was broken up with solid sodium carbonate.

C. From 19.—When the alcohol **19** was refluxed for 12 hr in water, the starting material was recovered. However, acidification with hydrobromic acid followed by 4 hr of reflux afforded **17** in 40% yield.

3,3′,4,4′-Tetrachloro-2,2′-dipyrrylmethane (**13**).—After repeated unsuccessful trials it was found that standard decarboxylation procedures including that of Chu and Chu[24] are too extreme because product **13** is too sensitive. A suspension of 2.1 g (0.0050 mol) of diester **17** in a solution of 5.0 g (0.125 mol) of sodium hydroxide in 175 ml of water was refluxed under rigorous exclusion of oxygen and light for 20 hr. The brownish solution was cooled slowly and after 1 hr the powdery product was collected, washed with water, and dried in a stream of nitrogen, yield 1.2 g (86%), mp 111–113°, light sensitive and unstable to storage; **13** is very soluble in halocarbon solvents forming solutions unstable to oxygen.

Anal. Calcd for $C_9H_6N_2Cl_4$: C, 38.06; H, 2.13; N, 9.87; Cl, 49.94. Found: C, 38.22; H, 2.30; N, 10.01; Cl, 49.47.

3,3′,4,4′-Tetrachloro-2,2′-dipyrrylmethane-5,5′-dialdehyde (**14**). **A. From 17 by the McFayden–Stevens Method.**[25]—The bishydrazide was prepared by refluxing the diester **17** with a 50–100-fold excess of **85**% hydrazine hydrate solution in ethanol for several hours. The yield was about 96%. The bisbenzenesulfonylhydrazide was prepared by treating the bishydrazide with 2 mol of benzenesulfonyl chloride in pyridine overnight.[26] The milky suspension obtained by dilution of the reaction mixture with water was coagulated for filtration by addition of acetic acid. The dried bissulfonylhydrazide was recrystallized from a large volume of 95% ethanol, yield 61%, mp 164–170° (resinifies).

Anal. Calcd for $C_{23}H_{18}N_6Cl_4S_2O_6 \cdot {}^1/_2C_2H_5OH$: C, 40.98; H, 3.01; N, 11.95; S, 9.12. Found: C, 41.22; H, 3.13; N, 12.04; S, 9.13.

A suspension of this bisbenzenesulfonylhydrazide, 17.0 g (0.025 mol), was heated in 300 ml of ethylene glycol to 160°. To this was added at once 30 g (0.27 mol) of sodium carbonate. Brisk evolution of nitrogen accompanied the reaction. After 75 sec, the reaction mixture was quenched with 400 ml of hot water.[26] The aldehyde separated as a nearly colorless powder, yield 4.5 g (53%), darkens at 235° without melting and melts at 300° dec.

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(24) T. Chu and E. Chu, *J. Org. Chem.*, **19**, 266 (1954).

(25) E. Mosettig, *Org. React.*, **8**, 232 (1954).

(26) D. Price, E. May, and F. Pickel, *J. Amer. Chem. Soc.*, **62**, 2818 (1939).

Anal. Calcd for $C_{11}H_6N_2Cl_4O_2$: C, 38.85; H, 1.78; N, 8.25; Cl, 41.71. Found: C, 38.99; H, 1.92; N, 8.44; Cl, 41.59.

B. From 13.—In an attempted monoformylation by the Villsmeier method[23] employing 1 mol of dimethylformamide–phosphorus oxychloride complex a nearly quantitative yield of the diformylated product **14** resulted.

C. From 15.—The bromomethylaldehyde **15**, 0.5 g (0.002 mol), was refluxed in water for 17 hr. The products isolated follow: **18**, mp 145–147°, ir 3413 cm^{-1} (OH str, in Nujol); **5**, mp 167–170°, ir identical with ir of authentic sample; impure **14**, melting point and ir spectrum identical with those of compounds prepared above.

Diethyl 3,3′,4,4′-Tetrabromo-2,2′-dipyrrylmethane-5,5′-dicarboxylate (24).—Compound **26** (5 g, 0.0128 mol) was suspended in 600 ml of water; the mixture was refluxed for 2.5 hr. White crystalline material was separated mechanically from the brown lumps and was recrystallized from chloroform, mp 139–141°.

Anal. Calcd for $C_8H_9NBr_2O_3$: C, 29.38; H, 2.77; N, 4.28; Br, 48.87. Found: C, 30.10; H, 2.76; N, 4.29; Br, 50.12.

The brown lumps were recrystallized from glacial acetic acid twice to obtain an analytical sample of **24**, mp 223–225°; solvent evolved at 120°.

Anal. Calcd for $C_{15}H_{14}N_2Br_4O_4 \cdot C_2H_4O_2$: C, 30.66; H, 2.72; N, 4.21; Br, 48.00. Found: C, 30.64; H, 2.52; N, 4.08; Br, 48.62.

In a larger run (4 hr) the ether by-product **28** was isolated and recrystallized from acetic acid, mp 219–221°.

Anal. Calcd for $C_{16}H_{16}N_2Br_4O_5$: C, 30.21; H, 2.54; N, 4.40; Br, 50.26. Found: C, 30.73; H, 3.22; N, 4.32; Br, 49.70.

As in the preparation of **17** the carbon tetrachloride extracts were worked up into ethylene chloride and the acetic acid complex was broken down with solid sodium bicarbonate. The dipyrrylmethane **24** crystallized rapidly from the filtrate, 120° transition, mp 219–221°.

Anal. Calcd for $C_{15}H_{14}N_2Br_4O_4 \cdot {}^1/_2C_2H_4Cl_2$: C, 29.32; H, 2.46; N, 4.27; Br, 48.77; Cl, 5.41. Found: C, 29.37; H, 2.53; N, 4.07; Br, 48.91; Cl, 5.28.

Diethyl 3,4-Dichloropyrrole-2,5-dicarboxylate (6).—An ether solution of 30.6 g (0.200 mol) of **1** was treated dropwise with cooling with 162 g (1.20 mol) of sulfuryl chloride. After 3 hr at room temperature the volatile materials were removed *in vacuo* and the residual oil was refluxed with 400 ml of 95% ethanol for 2 hr. The product **6** was recrystallized once from Skellysolve B, 27.5 g (51.9%), mp 98–106°, which was of sufficient purity for the next step. Repeated recrystallizations from Skellysolve B lowered the yield to 24% and raised the melting point to 112–114° (lit.[2] mp 116°).

3,4-Dichloropyrrole (7).—A silver-lined autoclave[3] was not available and a glass-lined autoclave was found unsuitable. Therefore, a reflux method was developed. Into a 250-ml flask fitted with a stirrer, condenser, and a nitrogen inlet were placed 5.6 g (0.020 mol) of diester **6**, 120 ml of diethylene glycol, and 5.0 g (0.125 mol) of sodium hydroxide in 15 ml of water. The resulting solution was refluxed for 5 hr, cooled, poured into ice, filtered, and extracted with ether. The residue from ether was sublimed, yield 1.20 g (44.1%), mp 73.5–74° (lit.[3] mp 74°).

Anal. Calcd for $C_4H_3NCl_2$: C, 35.33; H, 2.22; N, 10.30; Cl, 52.15. Found: C, 35.22; H, 2.22; N, 10.25; Cl, 52.06.

2,3,4,5-Tetrachloropyrrole.—A solution of 1.36 g (0.0100 mol) of 3,4-dichloropyrrole **7** in 125 ml of ether was treated dropwise (3–5°) with 2.70 g (0.0200 mol) of sulfuryl chloride, and the product was isolated by sublimation at 50° bath temperature, yield 1.85 g (90.2%), mp 107–108° (lit.[4] mp 108°), decomposes on standing.

Anal. Calcd for C_4HNCl_4: C, 23.45; H, 0.49; N, 6.84; Cl, 69.22. Found: C, 23.58; H, 0.56; N, 6.80; Cl, 69.23.

3,4-Dichloropyrrole-2-aldehyde (8).—A methylene chloride solution of 3.4 g (0.025 mol) of 3,4-dichloropyrrole **7** was formylated ($POCl_3$ + DMF) and worked up as described under the preparation of **5**. The essentially pure aldehyde was recrystallized from chloroform, yield 2.8 g (68%), mp 170–172°. The semicarbazone had mp 251° dec; the 2,4-dinitrophenylhydrazone did not melt below 285°.

Anal. Calcd for $C_5H_3NCl_2O$: C, 36.62; H, 1.84; N, 8.54; Cl, 43.24. Found: C, 36.44; H, 2.27; N, 8.40; Cl, 43.30.

3,4-Dichloro-2-iodo-5-methylpyrrole (11).—To a warmed solution of 0.90 g (0.0050 mol) of 3,4-dichloro-5-methylpyrrole-2-carboxylic acid (obtained by alkaline hydrolysis) of **2**) containing 2.0 g (0.020 mol) of potassium bicarbonate in 40 ml of water was added a solution of 2.5 g (0.010 mol) of iodine and 6.12 g (0.039 mol) of potassium iodide in 40 ml of water. Addition was stopped when decolorization of iodine ceased. The flask was cooled and the precipitate was sublimed at 50°, yield 1.2 g (86%), mp 81–82° unstable, slightly yellow compound possessing a characteristic odor. This compound decomposes spontaneously to black polymers.

Reduction with Lithium Aluminum Hydride. A. Reduction of 3,4-Dichloropyrrole-2-aldehyde (8).—To a well-stirred, nitrogen-protected mixture of 5.7 g (0.15 mol) of $LiAlH_4$ in 150 ml of absolute ether was added a solution of 16.4 g (0.10 mol) of aldehyde **8** in 1.5 hr. After a 2-hr reflux, water (100 ml) was added cautiously followed by dilute sulfuric acid. The ether layer was separated, washed well (H_2O, $NaHCO_3$ solution, H_2O), and dried over solid sodium sulfate overnight. The ether was removed *in vacuo* and upon warming to room temperature the red oil decomposed to a dark solid and water.

B. Reduction of Diethyl 3,3′,4,4′-Tetrachloridipyrrylmethane-2,2′-dicarboxylate (17).—To a suspension of 1.5 g (0.040 mol) of $LiAlH_4$ in 150 ml of ether was added portionwise 4.28 g g (0.0100 mol) of powdered diester **17**. After 1 hr of reflux, the product was worked up as in method A. The product **22** was a reactive, nearly colorless liquid which could not be distilled or chromatogaphically purified without decomposition.

Fluorination of Diethyl 3,4-dichloropyrrole-2,5-dicarboxylate (6). A. Potassium Fluoride.—A solution of 5 g (0.018 mol) of dihalide **6** and 3.0 g (0.05 mol) of anhydrous KF in 50 ml of DMF was refluxed with exclusion of moisture overnight. The solid obtained upon evaporation was recrystallized twice from ethanol, mp 114–116°; mixture melting point with **6** undepressed.

A similar reaction mixture with 1-methyl-2-pyrrolidinone substituted for the solvent was refluxed 36 hr and, after recrystallization from ethanol, the melting point was 115–116°, mixture melting point with **6** undepressed.

B. Arsenic(III) Fluoride.—A 50-ml ethanol solution containing 1.0 g (0.004 mol) of **6** and 0.80 g (0.006 mol) of AsF_3 was refluxed for 3 days. The product was recrystallized from 95% EtOH and melting points and mixture melting points were found undepressed.

C. Antimony(III) Fluoride.—Two days of reflux of **6** with SbF_3 also yielded starting material.

D. Silver(I) Fluoride.—A 50-ml absolute EtOH solution of 6.3 g (0.022 mol) of **6** and 10 g (0.079 mol) of AgF was similarly refluxed, and, upon vacuum sublimation of the precipitate, starting material was formed.

Registry No.—**1**, 3284-51-3; **2**, 24691-21-2; **3**, 24691-22-3; **4**, 24691-23-4; **5**, 24691-24-5; **6**, 24728-04-9; **7**, 1192-19-4; **8**, 24691-26-7; **8** simicarbazone, 24691-27-8; **8** 2,4-dinitrophenylhydrazone, 24691-28-9; **9** Cl, 24691-29-0; **9** Br, 24699-64-7; **10**, 24691-30-3; **11**, 24691-31-4; **13**, 24691-32-5; **14**, 24728-05-0; **15**, 24691-33-6; **16**, 24691-34-7; **17**, 24691-35-8; **17** bisbenzenesulfonylhydrazide, 24691 36-9; **18**, 24691-37-0; **19**, 24691-38-1; **20**, 24728-06-1; **22**, 24691-39-2; **23**, 24691-40-5; **24**, 24691-41-6; **25**, 24728-07-2; **26**, 24691-42-7; **27**, 24691-43-8; **28**, 24691-48-3; **29**, 24691-44-9; **33**, 24691-45-0; **34**, 24691-46-1; 2,5-dicarbethoxy-3,6-dimethylpyrazine, 24691-47-2; 2,3,4,5-tetrachloropyrrole, 24691-49-4.