APPLICATIONS OF SPECTROSCOPIC METHODS TO PROBLEMS IN PYRROLE CHEMISTRY.

A THESIS PRESENTED
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

IN THE
UNIVERSITY OF ADELAIDE

by

Robert William GUY, B.Sc.(Hons.)
Department of Organic Chemistry

1965

CONTENTS

SUMMARY.

The infrared spectra of a number of acylpyrroles have been examined in the NH and carbonyl stretching region under high resolution in carbon tetrachloride. Analysis of the data show that the effect of each group on the NH stretching frequency is independent of other substituents and additive, and for pyrroles containing methyl and acyl groups the NH stretching frequencies may be obtained from the following equations:

Acetyl Pyrroles

$$\nu_{NH}\ (cm^{-1}) = 3496 - 9n_{\alpha}CH_3 + 2n_{\beta}CH_3 - 45n_{\alpha}COCH_3 - 18n_{\beta}COCH_3$$

Benzoyl Pyrroles

$$\nu_{NH}\ (cm^{-1}) = 3496 - 9n_{\alpha}CH_3 + 2n_{\beta}CH_3 - 42_{\alpha}COPh - 18n_{\beta}COPh$$

where n_{α} and n_{β} are the number of α and β substituents respectively. Pyrroles with β-acyl substituents show two concentration-independent bands and the weak lower frequency band is assumed to arise from interaction with the out-of-plane deformation of the NH group, producing a hot band. The carbonyl stretching frequency of an α-acylpyrrole is lower than the corresponding β-acylpyrrole and this is attributed to intramolecular hydrogen bonding with the NH group.

The NH stretching frequencies and electronic absorption spectra of pyrroles with phenyl substituents have also been examined, and the infrared data show that the NH stretching

frequency of a pyrrole with methyl and phenyl groups may be represented by the equation:

$$\nu_{NH}\ (cm^{-1}) = 3496 - 9n_{\alpha}CH_3 + 2n_{\beta}CH_3 - 12n_{\alpha}Ph - 7n_{\beta}Ph$$

In the NH stretching region a second band was observed for the majority of phenylpyrroles and is assumed to be a hot band by analogy with the β-acylpyrroles. Deviations from the calculated NH frequencies are small and suggest that steric interactions between adjacent phenyl groups are accommodated by slight deviation of the phenyl rings from coplanarity with the pyrrole ring, and the electronic spectra indicate that some rotation of adjacent phenyl groups occurs.

The NH stretching frequencies and electronic spectra of twenty-one alkyl- and ethoxycarbonyl-dipyrromethenes and twenty-two phenyldipyrromethenes have been measured and the results correlated with the electronic and steric effects of the substituents. It is suggested that there is some steric interaction between the two ethoxycarbonyl groups of 3,3'-diethoxycarbonyl-4,5,4',5'-tetramethyldipyrromethene, that interaction between two phenyl groups in the 3,3'-positions is accommodated by twisting of the phenyl rings with little or no distortion of the dipyrromethene skeleton. The effect of unsymmetrical substitution on the NH frequency is also discussed.

Twenty-one tetraarylazadipyrromethenes have been prepared and their electronic spectra measured. The spectra

indicate that protonation of the tetraarylazadipyrromethenes occurs on the heterocyclic nitrogen atom and not the meso-nitrogen atom. In addition, the spectra show that steric interaction of 3- and 3'-aryl substituents does not result in distortion of the azadipyrromethene skeleton, although this may occur when 3,3'-p-dimethylaminophenyl substituents are present.

Finally, a preliminary investigation of meso-substituted dipyrromethenes has been made. The spectra of the meso-phenyldipyrromethenes suggest that the protonated species is more crowded than the base, and it is postulated that the strain is relieved by reducing the central methine bond angle in the bases and twisting around the methine bridge bonds in the salts. The accurate measurement of the spectra of meso-alkyldipyrromethene bases is difficult due to the ease with which they tautomerize to the ethylenic form.

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STATEMENT.

The work described in this thesis incorporates no material previously submitted for a degree in any university, and to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference is made in the text.

(Robert W. Guy)

ACKNOWLEDGEMENTS

I would like to express my gratitude to my supervisor, Dr. R.A. Jones, for suggesting the subject of this investigation and for his guidance and encouragement throughout the course of the work.

My thanks are also due to other members of the staff and research students for many helpful discussions, particularly Dr. R.L.N. Harris, whose wide knowledge of pyrrole chemistry was of invaluable assistance.

I am also indebted to the Department of Physical and Inorganic Chemistry for the use of their Perkin-Elmer 21 infrared spectrophotometer.

This work was carried out during the tenure of a Commonwealth Post-Graduate Award, for which I am grateful.

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CHAPTER I

INTRODUCTION

1.1 General.

Absorption spectroscopy deals with interactions between matter and electromagnetic radiation in which energy is abstracted from the radiation field. Although the mechanism of absorption of energy by matter is different in the various regions of the electromagnetic spectrum, the energy required for a transition from a state of lower energy to a state of higher energy is directly related to the frequency of the radiation which causes the transition. The electronic, vibrational and rotational energies of molecules are quantized and the energy absorbed, E, is related to the frequency of the incident radiation, ν, by the equation $E=h\nu$, where h is Planck's constant. For a given excitation process, a molecule absorbs only one discrete amount of energy and hence absorbs radiation of only one frequency. However, as a group of molecules exists in a number of different vibrational and rotational states, each state differing by only a small amount of energy, a broad absorption band or "band-envelope" rather than a series of distinct absorption lines will normally be observed. Changes in electronic energy levels are generally observed in the ultraviolet and visible portion of the spectrum whereas energy changes involved in vibrational and rotational transitions are smaller and their spectral lines appear in the infrared

region. The effect on the absorption spectra of nuclear vibrations and electronic distribution within molecules can give information on the size and shape of the molecules and such factors as bond strengths and chemical reactivity. The present work describes the use of spectroscopy in investigating hydrogen bonding and the steric and electronic effects of substituents in a number of pyrrole derivatives.

1.2 Infrared spectroscopy and hydrogen bonding.

The source of infrared spectra of most interest to organic chemists is the interaction of electromagnetic energy with the usual vibrational modes of the molecules. The position of an absorption band depends on several factors, the most important being the masses of the atoms involved in the vibration and the bond forces between the masses. The frequency of the stretching vibration is given, to a first approximation, by the equation (1)

$$\nu = \frac{1}{2\pi c}\left(\frac{f}{\mu}\right)^{\frac{1}{2}} \qquad \ldots\ldots(1)$$

Where c is the velocity of light, f the force constant of the bond, and μ the reduced mass of the system.

A non-linear molecule that contains n atoms has 3n - 6 possible fundamental vibrations, which includes both longitudinal and bond-bending vibrations. However, not all the possible fundamental vibrations will give rise to absorption

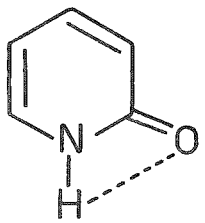
bands as absorption occurs only where a change of the dipolar character of the molecule takes place, and total symmetry about a bond will eliminate certain bands. Another simplifying factor which facilitates the interpretation of infrared spectra is the limited interaction between different vibrations. Certain groups of atoms give rise to absorption bands at, or near, the same frequency irrespective of the remainder of the molecule. These bands can be used to characterize the absorbing groups, and therefore the spectrum of a complex molecule may be divided into the absorption bands of various components of the molecule. The use of equation (1) for calculating vibration frequencies or force constants is of greatest value when the atoms joined by the bond have large mass differences and when the vibrations are mainly localized in the bond containing these atoms. This condition is met when one atom is hydrogen, and consequently stretching modes involving hydrogen atoms are among the most thoroughly studied and the most valuable bands for diagnostic purposes. The frequencies associated with the stretching vibrations of ordinary single bonds between hydrogen and fluorine, oxygen or nitrogen atoms are relatively high and occur in the frequency range 3800-3400 cm^{-1}. The hydrogen atoms of such bonds are sufficiently electropositive to form a weak attachment to a neighbouring electron donor atom or group. The effect of this attachment is to exert a

restraining influence on the restoring force of the normal bond and so to reduce the frequency of the stretching mode (but increase the frequencies of the deformation modes) relative to the frequency which is characteristic of the free unassociated mode. Consequently, the use of infrared spectroscopy has long been the method of choice for studying the phenomenon of hydrogen bonding.

Hydrogen bonding is an important form of molecular association and has probably been studied more intensively than any other types of association. Since the first suggestion of the existence of a hydrogen bond by Oddo and Puxeddu,[1] the exact nature of the bond has been the subject of much discussion. Today it is generally agreed that weak hydrogen bonds are entirely electrostatic in origin, but as the hydrogen bond becomes stronger and shorter the covalent contribution to bonding increases.[2]

Hydrogen bonds are favoured between an X-H bond and another atom Y, where X is highly electronegative and the Y atom possesses a lone pair of electrons. The electrostatic nature of the hydrogen bond has certain steric consequences, for significant hydrogen bonding can only occur if the two electronegative atoms are sufficiently close to one another.[2c] It is generally accepted that the strongest hydrogen bonds result when the X-H bond is collinear with the direction of the lone pair orbital on the Y atom.[3] However, with many

cases of intramolecular hydrogen bonding the X-H.....Y system must be non-linear and as the internuclear distance is governed by the size of the ring which is closed by the hydrogen bond, the most favourable geometry is provided if the ring is six-membered, although five-membered and seven-membered hydrogen bonded rings are known. The size of the ring closed by the hydrogen bond will determine whether the bonding is inter- or intra- molecular. For example, 2-pyridone (I) exists as the intermolecularly bound dimer (II) since the N-H.....O bond angle is unfavourable for intramolecular hydrogen bonding.[4] On the other hand, the five-membered ring closed by the hydrogen bond in 1-hydroxy-2-pyridone (III) allows intramolecular bonding and this exists as the monomer.[5]



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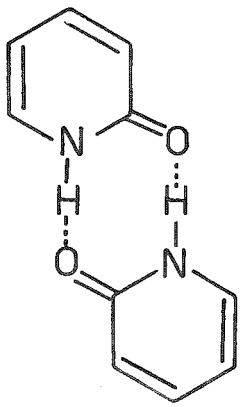

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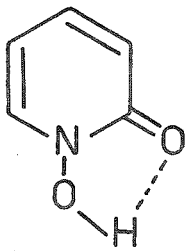


III

Inter- and intra- molecular hydrogen bonding can be differentiated by measuring the infrared spectrum of the compound at different dilutions. As dilution increases, the spectrum of an intermolecularly bonded compound approaches that of the non-bonded molecule; the intensity of the hydrogen-bonded vibration decreases and that of the non-bonded vibrational band increases. Under corresponding conditions the spectrum of the intramolecularly bonded compound remains unchanged.

Hydrogen bond energies are of the order of 3 to 5 Kcal $mole^{-1}$ [2b] and can therefore produce frequency shifts of the order of 100 cm^{-1}. The magnitude of the frequency shift depends on the strength of the hydrogen bond and there is evidence of an approximately linear relationship between the X-H.....Y distances and the stretching frequency of the X-H bond, although very short hydrogen bonds generally do not obey this relation.[6]

The hydrogen bond X-H.....Y not only alters the stretching and deformation frequencies of the X-H group, but also alters the intensities and the band widths. The latter phenomenon has posed one of the most interesting problems in the field of hydrogen bonding and several theories and approaches have been put forward to account for the considerable band widths.[7] Cannon[8] has proposed a mechanism involving an increased probability of proton transfer across

the hydrogen bond in the vibrationally excited state. The potential energy curve (Fig. 1) of the X-H.....Y system with respect to r_{XH} will show a double potential minimum. If it should so happen that the first excited state of the X-H vibration occurs above the level of the second minimum of the curve, the probability of proton transfer from one potential well to the other will be much increased. This would lead to a shortening of the lifetime of the excited state and so to a broadening of the absorption band.[9]

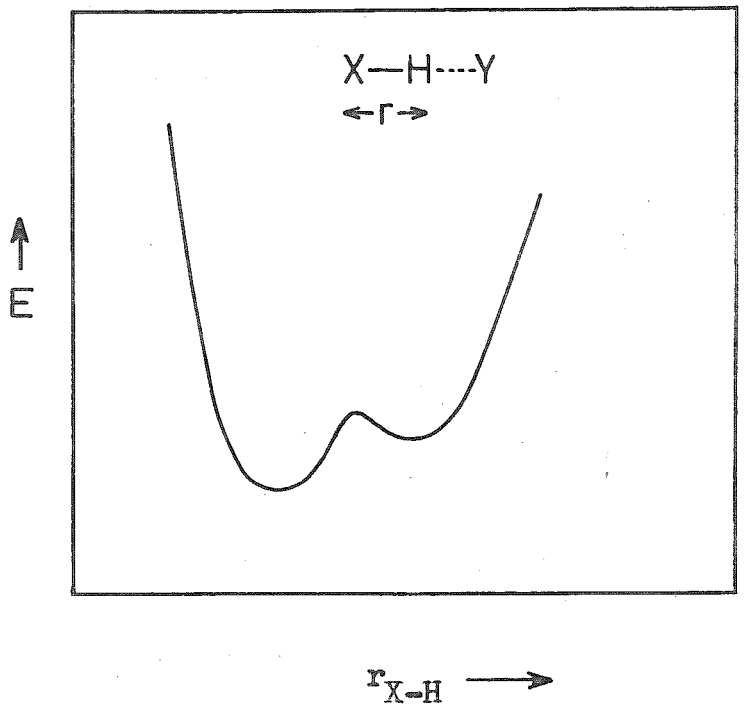
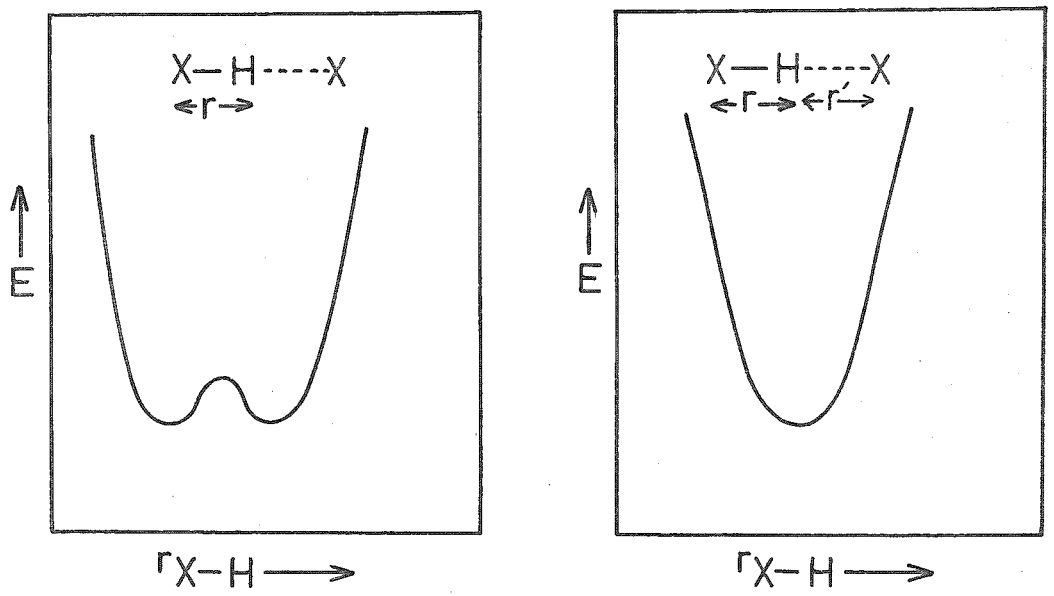


Fig. 1. - Potential energy curve for the X-H...Y system

If the system is symmetrical, i.e. X-H.....X, the potential energy curve will exhibit a symmetrical double minimum (Fig. 2 (a)) and with decreasing distance between the two minima (i.e. as the X.....X distance decreases) the limiting case is reached when the double minima disappear and the energy curve shows a single minimum. (Fig. 2 (b)).[9,10]



(a) Symmetrical system. (b) Symmetrical system where $r = r'$.

Fig. 2.

The great majority of hydrogen bonds are unsymmetrical[11] and only when the conditions are especially favourable and the hydrogen bond exceptionally strong is the hydrogen atom disposed symmetrically (e.g. nickel dimethylglyoxime).[12]

Generally, the intensity of an X-H band which is hydrogen bonded is increased relative to the unassociated band. Most of the detailed studies have been on intermolecularly bonded systems and, as the bond is usually unsymmetrical, resonance of a purely covalent character is not considered to play a part because this would require the hydrogen atom to be symmetrically placed between the two bonded atoms. However, it is likely that in intramolecular hydrogen bonded systems the covalent forces play a much larger part when the hydrogen bond could become part of an extended resonance system. Several examples of this type have been examined[13] and in these cases the intensity of the X-H band is greatly diminished. This has been attributed to the intramolecular hydrogen bonding becoming stabilized by considerable resonance contributions from covalent forms and facilitated by the cyclic nature of the system so that it is essentially a non-polar hydrogen bond. Due to the cyclic form of the hydrogen bonded system electron delocalization does not involve charge transfer and therefore the intensity of the X-H band is diminished. This is in contrast to the increase in intensity observed in intermolecular hydrogen bonds where transfer of charge does occur.

1.3 Electronic absorption spectra and steric effects.

The absorption of electromagnetic radiation by organic

compounds in the visible and ultraviolet regions involves promotion of electrons in σ-, π- and n-orbitals from the ground state to higher energy states. These higher energy states are described by molecular orbitals which are vacant in the ground state, and are often called antibonding orbitals and designated σ^* and π^*. As n-electrons do not form bonds they have no antibonding orbitals associated with them. The energy required for the transition of electrons varies widely, from high energies for $\sigma \longrightarrow \sigma^*$ transitions, intermediate energies for $\pi \longrightarrow \pi^*$ transitions (associated with unsaturated centres) and low energies for $n \longrightarrow \pi^*$ transitions.

All electronic transitions result in a redistribution of charge within the molecule but the exact electronic structures of the higher energy states are not completely understood. Some seem to have greater polar character than the ground state structure, others less polar character whilst others appear to be biradicals. The transitions $n \longrightarrow \pi^*$ and $n \longrightarrow \pi^*$ are very sensitive to solvent polarities, the energy of transition depending on whether the excited state of the molecule is more or less polar than the ground state. The n-electrons are stabilized by electrostatic attraction or hydrogen bonding with the solvent, and if the transition is from a less to a more polar structure, the n-electrons are stabilized in the excited state, and hence the energy of the transition is decreased. Conversely, when the transition is

from a more polar to a less polar structure the ground state is stabilized and hence more energy is required for the transition.[14] Polar solvents usually lower the energy of $\pi \longrightarrow \pi^*$ transitions.[14]

An isolated functional group, not in conjugation with any other groups, exhibiting absorption of a characteristic nature in the ultraviolet or visible region is termed a chromophore. When chromophoric groups are conjugated the lengthened π-electron system results in greater delocalization of the π-electrons and the energy required for the transition is lowered. Groups which do not in themselves show selective absorption above c.200 mμ but which, when attached to a chromophoric system, usually lower the energy of transition, are called auxochromes. Auxochromic groups contain non-bonding electrons and the transitions involving these electrons are responsible for this effect.

The intensity of absorption at any wavelength is related to the probability of the electronic transition which gives rise to the absorption. Thus maxima of absorption bands correspond to the most probable transitions in that region of absorption. The lengthened π-electron system resulting from conjugation of chromophoric groups results in a greater probability of the transition and hence increased intensity of the absorption band. Auxochromic groups also generally increase the intensity of absorption. According to the

Beer-Bouguer-Lambert law[15] the integrated fraction of light absorbed by a group of molecules is proportional to the number of absorbing systems in the light path, namely,

$$\log_{10}\left(\frac{Io}{I}\right) = \epsilon cl \qquad \ldots\ldots(2)$$

where Io and I are the intensities of the entrant and emergent light respectively, with a path length, l, of absorbing species at a concentration of c mole litre^{-1}. The constant ϵ is the decadic molar extinction coefficient in l.mole^{-1} cm^{-1}. The maximum extinction coefficient, ϵ, of an absorption band may be considerably affected by a change of solvent and has little theoretical significance, but the band area $A = \int \epsilon \, d\nu$ often remains constant and thus affords a better measure of absorption intensity and is the quantity of theoretical interest.

The effect of steric interactions within molecules on the electronic absorption spectra must be evaluated in terms of the effect on transition probability (intensity, ϵ) and the energy difference between ground and excited states (wavelength, λ). As the length of a conjugated system increases, the wavelength and intensity of the band associated with polarization along the lengthwise axis of the chromophore system both increase. In simple models the relationship can be expressed by $\lambda^2 \propto l$ and $\epsilon \propto l^2$. However, in

order for a conjugated system to be an effective chromophore it must be planar or nearly planar because maximum interaction between the chromophoric groups occurs in the planar arrangement.

In an analysis of the spectral effects of steric crowding the geometry of the excited state must be examined as well as that of the ground state.[16] In the ground state the sterically crowded molecule will assume a geometry of minimum potential energy; groups may be twisted, or bonds bent or stretched, or a combination of twisting, bending or stretching may most effectively relieve the steric strain. It is usually energetically more favourable to twist a bond than stretch it.[14]

The steric twisting or displacement of a bond which is part of a conjugated system almost invariably reduces the intensity of bands but the direction of the wavelength shift can be either to longer wavelengths (a bathochromic shift) or to lower wavelengths (a hypsochromic shift), the former being the more usual if the steric strain is distributed uniformly throughout the molecule and the latter usually occurring when one particular bond of a molecule is twisted. However, if only one bond in a conjugated system is twisted the wavelength displacement of the light absorption depends upon the sign and magnitude of the change in bond order of the bond on excitation.[17] Hypsochromic shifts arise if

the twisted bond has a greater bond order in the excited state than in the ground state and, conversely, bathochromic shifts result from a decrease in bond order during the transition. When resonance structures can be drawn for a molecule a bond which is single in all the principal canonical forms is termed an "essential" single bond, and a bond that is double in these forms is termed an "essential" double bond. Thus twisting about an essential single bond usually results in a hypsochromic shift but twisting about an essentially double bond results in a bathochromic shift.

1.4 Colour and constitution.

The correlation of the colour and chemical constitution of molecules has interested chemists for many years and many rules and theories, both empirical and theoretical, have been postulated to explain the electronic spectra. The molecular orbital approach to the problem is primarily physical and its application to complex systems presents difficulties. A simpler approach is the valence-bond method which can give a semi-quantitative account of the spectra and is much easier to apply to systems such as the dipyrromethenes with which this work is concerned. The assumptions underlying the concept of resonance in the valence-bond method account for the spectral anomalies observed in conjugated systems. The valence-bond approach indicates that a substance for which

two or more energetically similar resonance structures can be drawn will absorb at lower energies and higher intensities than a similar compound exhibiting less or no resonance. Any structural alteration which decreases the energy difference between canonical forms will cause absorption at lower energy and an increase in intensity, the greatest effect being observed when the change in structure results in the attainment of degeneracy.[18]

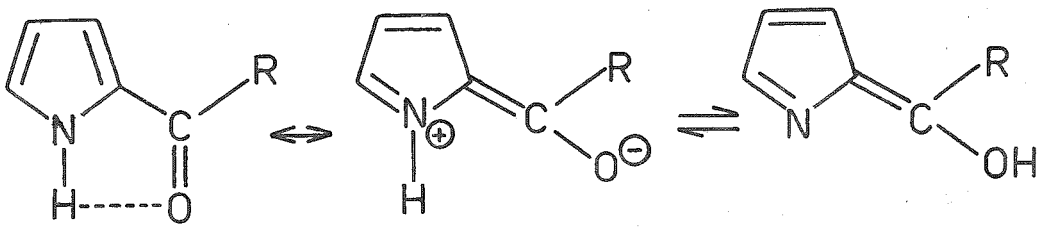
CHAPTER 2.

PYRROLES WITH ACYL SUBSTITUENTS.

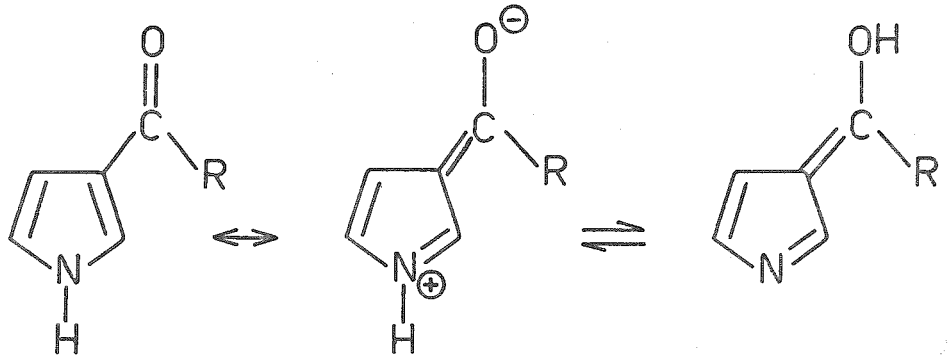
2.1 Introduction.

Although the infrared spectra of a variety of substituted pyrroles have been reported in the literature, very few systematic studies have been carried out and these have often been under low resolution. High resolution data are available for pyrroles containing methyl,[19] ethoxycarbonyl[20] and a limited number of other substituents.[21,22,23]

The unusual chemical reactivity of α-acylpyrroles[24,25] does not conform to the general pattern established for aromatic aldehydes and ketones and the carbonyl stretching frequencies are lower than those normally encountered with the latter.[26] Previous authors[21,26,27,28] who have studied the NH and carbonyl stretching frequencies of acylpyrroles have been particularly concerned with the possibility of keto-enol tautomerism in these compounds, which would explain their low reactivity with nucleophilic reagents. Both α- and β-acylpyrroles are potentially tautomeric (Scheme 2.1.), but infrared studies[26] indicate that they exist as the acyl compounds (Ia, IIIa) and not in the enol forms (II, IV).



Ia Ib Ic



IIIa IIIb IV

(R = H, CH_3, Ar)

Scheme 2.1.

Bond energy calculations indicate that the enol form (II, R = H) is destabilized by at least 7 Kcal $mole^{-1}$ relative to the keto form (Ia)[26] and this would suggest that the only species present under normal conditions would be the acyl pyrrole. The unusual reactivity and lowered carbonyl stretching frequency has been attributed to the contribution of the zwitterionic form (Ib, IIIb) to the resonance hybrid in the ground state,[26,29,30] i.e. the properties of the acyl-pyrroles are interpreted in terms of the ready polarizability of the pyrrole ring.

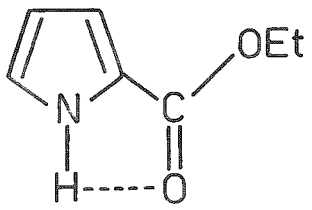
Earlier investigators[27,31] have also been concerned with the nature of the intermolecular bonding in ethoxycarbonyl- and acyl-pyrroles. Unfortunately much of the reported work has been carried out under low resolution and the results are

of doubtful significance. Most workers claim that there is no interaction between the NH and a carbonyl group in the α-position of the pyrrole. The main factors in this conclusion are the apparent independence of the NH and carbonyl stretching frequencies on the position of the substituent, and the similarity of the carbonyl frequency in the corresponding N-methylpyrroles.

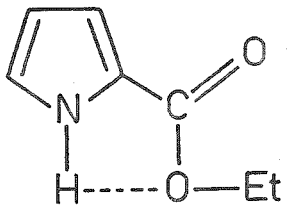
Intramolecular hydrogen bonding between α-ethoxycarbonyl groups and a pyrrole NH has been postulated by Badger et al.[32] to explain the NH stretching frequencies observed in dipyrromethanes containing an α-ethoxycarbonyl group. Kuhn and Kleinspehn[36] contend that only intermolecular hydrogen bonding occurs in these compounds, but they do suggest the possibility of a weak intramolecular hydrogen bond to account for the observed NH stretching frequencies in α-ethoxycarbonylpyrroles.

A systematic study of ethoxycarbonylpyrroles has been carried out by Jones and Moritz[20] as part of a detailed investigation of hydrogen bonding in dipyrromethanes and they interpret their results in terms of intramolecular association. They attribute the two NH bands observed for α-ethoxycarbonylpyrroles to the two rotational isomers V and VI.

They assign the lower frequency band to the isomer V and suggest that the small frequency shift between the two bands is due to the unfavourable hydrogen bond angle of 90°.



V



VI

The similar intensities of the two bands implies that the two isomers are equally preferred and thus the hydrogen bond energy differences must be very small (the frequency shift of 17 cm^{-1} would require a difference in bond energy of less than 1 Kcal $mole^{-1}$). It is also of interest that the frequency shift of the higher frequency band arising from the α-ethoxycarbonyl group is almost identical to the shift arising from the β-ethoxycarbonyl group. A second weak band observed in the case of pyrroles with no α-ethoxycarbonyl substituent is assumed by Jones and Moritz to be a hot band.

A hot band arises when there is a transition between adjacent states other than from the ground to the first excited state.[33] Such a transition occurs with low probability as the molecule must absorb a quantum of radiation while in an excited state and the proportion of molecules in an excited state at any one time is very small. The Boltzmann distribution law indicates that the number of excited molecules will be less than a few percent if the frequency of the first

transition is much over 600 cm^{-1}. Normally the hot bands can be neglected in spectroscopic work in condensed phases but hot bands have been detected in the spectra of acetylenes[34] and pyrrole itself.[35] In the latter case the band 18 cm^{-1} from the fundamental NH stretching band is assigned to a hot band which arises from strong interaction between the NH stretching vibration and the NH out-of-plane deformation vibration which occurs at 503 cm^{-1}.[35] This would also indicate substantial decoupling from other vibrations in the molecule.

It has been shown that for pyrroles with formyl, ethoxycarbonyl[20] and methyl[19] substituents the effect of each group on the NH stretching frequency is independent of the other groups and additive. The NH stretching frequencies can be represented by a single equation (3)[20]

$$\upsilon_{NH}(cm^{-1}) = 3496 - 9n_{\alpha}CH_3 + 2n_{\beta}CH_3 - 13n_{\beta}CO_2Et - \begin{cases} 14 \\ 31 \end{cases} n_{\alpha}CO_2Et \qquad \ldots\ldots(3)$$

where n_{α} and n_{β} are the number of α and β substituents respectively.

In this work the investigations discussed above have been extended to acetyl- and benzoyl-pyrroles. The carbonyl stretching frequencies of α-, β - and N-acylpyrroles have been measured to determine the effect of methyl groups on the conjugation of the ring and their effect on acyl sub-

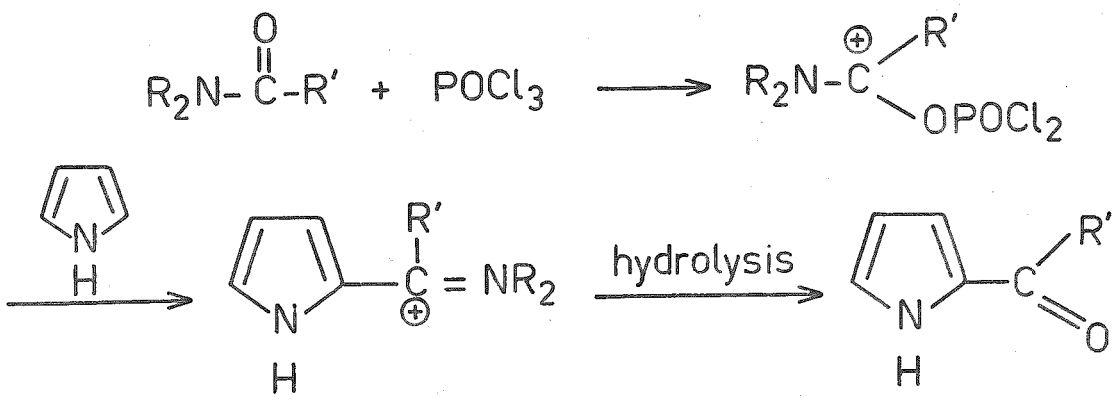
stituents in each of these positions.

2.2 Preparation of compounds.

Acylpyrroles can be prepared by either direct ring formation or acylation of an already formed pyrrole ring. Most of the common acylation procedures, such as the Grignard, Friedel-Crafts, Houben-Hoesch, Schotten-Baumann and Vilsmeier-Haack methods, were utilized in the synthesis of the acylpyrroles. All these methods preferentially acylate the pyrrole in the α-position, but if both α-positions are blocked may acylate the β- or N- position, the former usually occurring if the reaction is in acid media, and the latter under basic conditions.

The majority of α-benzoylpyrroles were prepared by the Schotten-Baumann procedure. There is some confusion in the literature as to whether this method gives α- or N- benzoylpyrroles but the results obtained in the present work are in agreement with the findings of Jones and Laslett[37] that benzoylation occurs in the α-position of alkylpyrroles.

The Vilsmeier-Haack synthesis (Scheme 22.) is probably the most generally applicable method for C-acylation of the pyrrole ring. Most of the formylpyrroles, several acetylpyrroles and one β-benzoylpyrrole were prepared in good yields by this route.



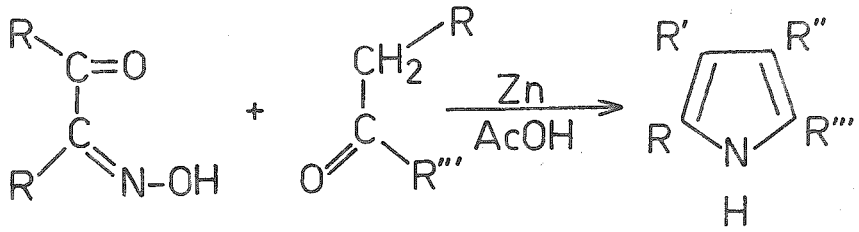
Scheme 2.2

The amides used for Vilsmeier-Haack formylation, acetylation and benzoylation were N,N-dimethylformamide, N,N-dimethylacetamide and N-benzoylmorpholine respectively. However, poor yields of 4-acetyl-2-formyl-3,5-dimethylpyrrole were obtained which was probably due to the simultaneous reaction of the acetyl group with the N,N-dimethylformamide-phosphorus oxychloride complex (c.f. Badger, Harris and Jones[38]). A more acceptable yield of the required formylpyrrole was obtained by the Gattermann reaction.[39]

Benzoylation of the highly reactive 2,5-dimethylpyrrole by the Friedel-Crafts reaction, using benzoyl chloride and zinc chloride, gave both 3-benzoyl-2,5-dimethylpyrrole and 3,4-dibenzoyl-2,5-dimethylpyrrole, the latter being the major product. (Similar diacylation of reactive pyrroles such as 2,5-dimethyl-1-phenylpyrrole under Friedel-Crafts

conditions has been reported by Rips and Buu-Hoi.[40])

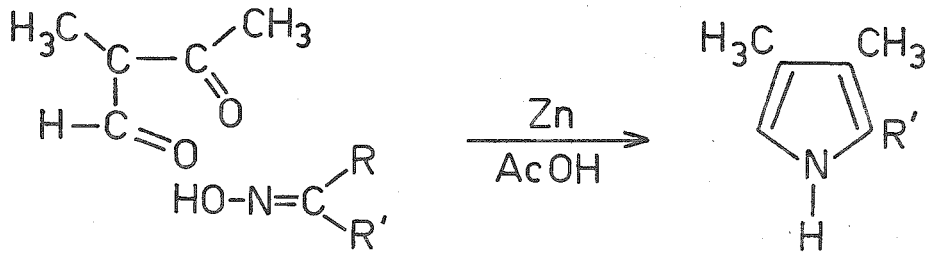
The pyrroles prepared by direct ring formation were nearly all made by the Knorr pyrrole synthesis (Scheme 2.3.) or a modification of this.



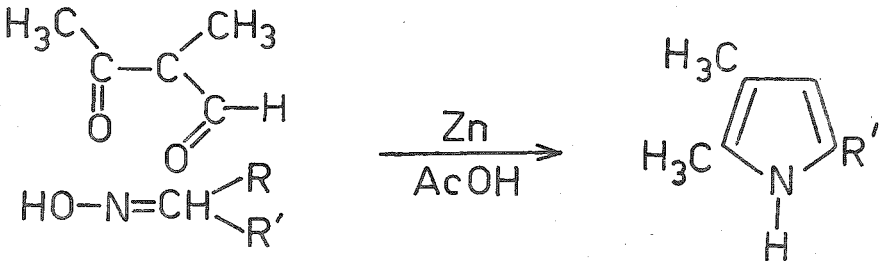
Scheme 2.3.

When an α-ketoester (R''' = CO_2Et) was used the hydroxyiminoketone was reduced to the amine prior to the condensation step. In the majority of cases the pyrroles were subsequently modified by saponification of the ethoxycarbonyl groups and decarboxylation by standard methods.[24,41]

Condensation of the sodium salt of 3-formylbutan-2-one and 3-hydroxyiminopentan-2,4-dione under the conditions of the Fischer-Fink synthesis[42] resulted in a small yield of 2-acetyl-4,5-dimethylpyrrole. The reactants can condense in two ways (Scheme 2.4) and both isomer (a) and isomer (b) have been obtained as the major products in analogous reactions.[42,43]



(a)



(b)

Scheme 2.4.

When R = R' = CO_2Et, (a) is the major product[43] and when R = $COCH_3$, R' = CO_2Et, (b) has been reported as the major product.[42] In the present case (R = R' = $COCH_3$), the product, which was obviously a mixture, showed two unassociated NH stretching bands at 3442 and 3430 cm^{-1}. The former band corresponds to the calculated value (3444 cm^{-1}) for isomer (b) (see the next section) and the latter to that of 2,4-diacetyl-3,5-dimethylpyrrole. The diacetyl compound probably arose by condensation of the hydroxyiminoketone with acetylacetone which was not completely removed in the initial preparation of the oxime. However, no band was observed near 3453 cm^{-1} which is the calculated value for isomer (a).

The convenient synthesis developed by Rainey and Adkins[44] was used in the synthesis of 1-acylpyrroles. The low yields often obtained by this method, which involves the treatment of potassium derivatives of pyrroles with acyl chlorides, has been attributed to the formation of the 2-isomers in the reaction and the isolation of both 1- and 2-isomers has been reported in the related alkylation reactions of alkali metal salts of pyrroles.[45] In this work a small amount of the 2-isomer was detected in the products from the preparation of 1-acetylpyrrole and 1-acetyl-3,4-dimethylpyrrole. However, whether the 2-isomers are present in the reaction product before the working up procedure is uncertain as the 1-acylpyrroles are known to rearrange thermally to the 2-isomers.[46] The 2,5-diacetylpyrrole was in fact prepared in this work by heating 1-acetylpyrrole in acetic anhydride at 300°;[24] the 1-acetylpyrrole evidently undergoes thermal isomerization as well as acetylation under these conditions.

2.3. Results and discussion.

The NH stretching frequencies observed are given in Table 2.1. Only one band was observed for compounds having the acyl substituent in the α-position, but the β-acylpyrroles showed two concentration-independent bands. In all cases the subsidiary band, which appears *c.* 17 cm^{-1}

Table 2.1. NH Stretching Frequencies of Acylpyrroles in dilute CCl_4.

Position of Substituents* 2	3	4	5	Observed ν cm^{-1}		Calculated ν cm^{-1}	$\triangle$ ≠ cm^{-1}
Ac	-	-	-	3453≠		3451	-2
Ac	-	-	Me	3445		3442	-3
Ac	Me	Me	-	3453		3455	2
Ac	Me	-	Me	3442		3444	2
Ac	-	Me	Me	3446		3444	-2
Ac	Me	Me	Me	3444		3446	2
Me	Ac	-	-	3468	3451 w	3469	1
-	Ac	Me	-	3482	3466 w	3480	-2
Me	Ac	Me	-	3472	3457 w	3471	-1
Me	Ac	-	Me	3457	3441 w	3460	3
-	Ac	Me	Me	3473	3457 w	3471	-2
Me	Ac	Me	Me	3463	3443 w	3462	-1
Bz	-	-	-	3454		3454	0
Bz	-	-	Me	3442		3445	3
Bz	Me	Me	-	3459		3458	-1
Bz	Me	-	Me	3447		3447	0
Bz	-	Me	Me	3442		3447	5
Bz	Me	Me	Me	3450		3449	-1
Me	Bz	Me	-	3476	3459 w	3471	-5
Me	Bz	-	Me	3457	3439 w	3460	3
-	Bz	Me	Me	3469	3452 w	3471	2
Me	Bz	Me	Me	3461	3442 w	3462	1

* Ac = $COCH_3$, Bz = COC_6H_5

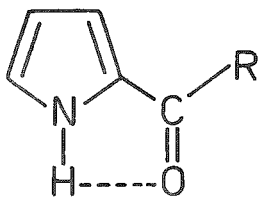
≠ $\triangle$ = calculated - observed

w weak

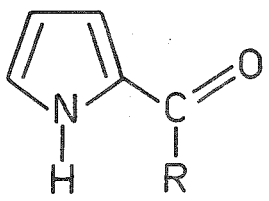
≠ Mirone and Lorenzelli[21] give 3457 cm^{-1}

lower than the major band, is comparatively weak and has a relative extinction coeffi cient of c. 1:15 and the position of the band was obtained by graphical resolution. The band can be attributed to a hot band resulting from a vibrational excited state near 500 cm^{-1}. The assignment of a band in this region to the out-of-plane NH deformation vi bration is consistent with the hot band explanation. The failure to observe this subsidiary band in the case of the α-acylpyrroles is also consistent with this assignment as the intramolecular hydrogen bonding of the NH would increase the frequency of the deformation mode and hence reduce the probability of a tran sition resulting in a hot band.

For pyrroles with an acyl substituent in the α-position two ro tational isomers are possible (VII and VIII).



VII



VIII

As only one band was observed for α-acylpyrroles and as the frequency shift arising from the acyl groups in the α-positi on is considerably greater than for the same group in the β-position, it is highly probable that the hydrogen bonded structure (VII) predominates to the exclusion of the

non-bonded structure (VIII). This is in agreement with dipole moment measurements made for 2-acetylpyrrole by Marinangeli.[47] Models* show that steric interaction between adjacent β-methyl and α-acetyl groups is small and it appears that, although the direction of the hydrogen bond is close to 90° to the NH bond axis, the stability of the hydrogen bonded structure is sufficient to overcome this steric interaction. Due to the partial π-character of the C-acyl bond (see Scheme 2.1) there will be restricted rotation about this bond. With α-benzoyl compounds the steric interaction is greater than in the α-acetyl case and this is probably relieved by rotation about the C-R bond (c.f. o-substituted benzoylpyrroles[26]). Out-of-plane deformation of the group R (Scheme 2.1) probably relieves any steric strain in the α-acetylpyrroles.

It has been shown previously that for methyl-, formyl- and ethoxycarbonyl-pyrroles[20] the effect of each substituent on the NH stretching frequency is additive and may be represented by a single equation. The results obtained in this investigation show that for acetyl- and benzoyl-pyrroles the NH stretching frequencies may be obtained from the following equations:-

Acetylpyrroles.

$$\nu_{NH}(cm^{-1}) = 3496 - 9n_{\alpha}CH_3 + 2n_{\beta}CH_3 - 45n_{\alpha}COCH_3 - 18n_{\beta}COCH_3 \quad .....(4)$$

* Dreiding Stereomodels

Benzoylpyrroles.

$$\nu_{NH}(cm^{-1}) = 3496 - 9n_{\alpha}CH_3 + 2n_{\beta}CH_3 - 42n_{\alpha}COPh - 18n_{\beta}COPh \quad .....(5)$$

Where n_{α} and n_{β} are the number of α and β substituents respectively. The error between the observed frequencies and those derived from the above equations are shown in the last column of the Tables.

The constants for the benzoyl substituents are slightly lower than for the acetyl substituents. This is to be expected as the carbonyl group of the benzoylpyrroles is conjugated with the phenyl ring and the overall electronic effect on the NH stretching frequency is therefore reduced.

Table 2.2 lists the NH stretching frequencies of acylpyrroles containing several other groups and the results are within the probable combined accuracy of the independent sets of data used. The discrepancy of $7cm^{-1}$ between the observed and calculated values for 3,4-dibenzoyl-2,5-dimethylpyrrole probably arises from a steric effect between the two adjacent benzoyl groups. A similar discrepancy was observed by Jones and Moritz[20] in the case of 3,4-diethoxycarbonyl-2,5-dimethylpyrrole.

This data should be useful in predicting the NH stretching frequencies of other substituted pyrroles or providing confirmatory evidence for the orientation of substituents in unknown compounds.

Table 2.2

NH Stretching Frequencies of Substituted Pyrroles in dilute CCl_4.

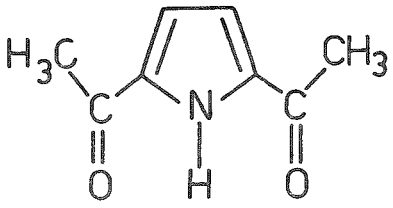
Position of Substituents * 2	3	4	5	Observed cm^{-1}	Calculated cm^{-1}	$\triangle$ cm^{-1}
Me	Bz	Bz	Me	3449	3442	-7
Me	Bz	Me	Cbe	3455 3438	3457 3440	2 2
Ac	Me	Ac	Me	3430	3426	-4
Ac	Me	Cbe	Me	3433	3431	-2
Me	Ac	Me	Cbe	3458 3440	3457 3440	-1 0
Me	Cbe	Me	X	3429	-	-

* Ac = $COCH_3$, Bz = COC_6H_5, Cbe = $CO_2C_2H_5$, X = $COCH_2CO_2C_2H_5$

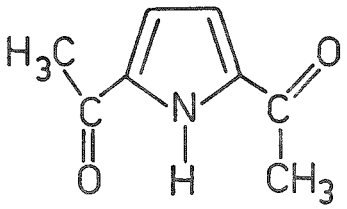
$\triangle$ = calculated - observed

Table 2.3 lists the NH stretching frequencies observed for pyrroles having acyl or ethoxycarbonyl substituents in both α-positions. The discrepancies in the observed frequencies probably arise from the stereochemistry of the compounds.

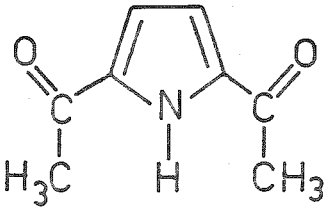
Three possible rotational isomers can be postulated for 2,5-diacetylpyrrole (IX, X and XI), the restricted rotation being due to the partial double-bond character of the C-acetyl bond.



IX



X

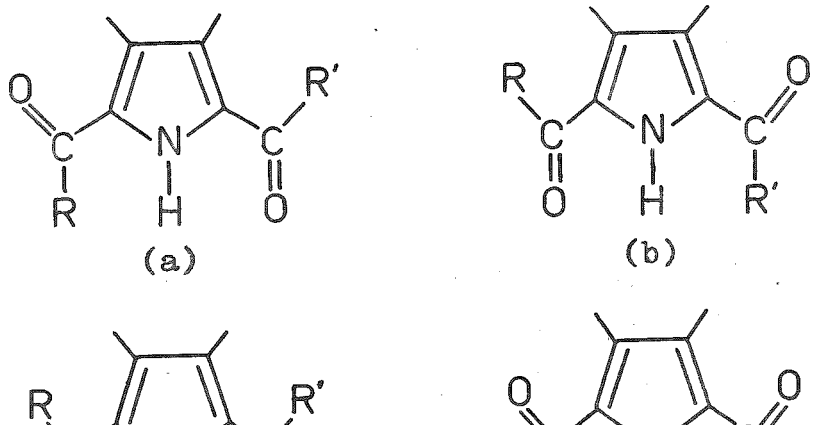


XI

Lorenzelli and Capellina[48] attribute the observed doubling of carbonyl frequencies in the infrared and Raman spectra and the presence of two polarographic reduction waves to the existence of the two isomers IX and X. Calculation of the NH frequency for X from equation (4) thus requires that a second constant for the α-acetyl group be obtained which is a measurement of the electronic effect only. In the case of ethoxycarboxylpyrroles the frequency shift of the higher frequency band arising from the α-ethoxycarbonyl group was approximately the same as the shift arising from the β-ethoxycarbonyl group. However, as both the rotational isomers (V and VI) in this instance are postulated as involving hydrogen bonding it cannot be assumed with certainty that the constant for the β-acetyl group can be used for the non-bonded α-acetyl group. The calculated NH frequency using the constant of -45 for both acetyl groups is 3406 cm^{-1}, and if the constant of -18 (corresponding to a β-acetyl group) is used for the second acetyl group the calculated value is 3433 cm^{-1}. The observed frequency of 3424 cm^{-1} (with a shoulder at 3435 cm^{-1}) is closer to the second of these

calculated values. These results indicate that X is the preferred isomer, which is in agreement with Marinangeli[47] who has shown by dipole measurements that X exists to the exclusion of IX and XI.

When the two ∝-substituents are different, four rotational isomers are possible (Scheme 2.5) and the calculated frequencies using the constants for the corresponding β-acyl substituent when the ∝-acyl group is in the anti-form (e.g. RCO- in (a)) are shown in Table 2.3.



Scheme 2.5

In all cases one of the ∝-groups is an ethoxycarbonyl group (R' = OEt) and as both rotational isomers are nearly equally preferred[20] it could be expected that (b) and (c) would be the preferred isomers of the compounds (2), (3), (4) and (6) in Table 2.3, and (5) would exist in all possible forms.

Table 2.3.

NH Stretching Frequencies of Pyrroles with Ethoxycarbonyl or Acyl Substituents in both α-positions.

	Substituents 2 (RCO)	3	4	5 (R'CO)	Observed cm^{-1}	Calculated cm^{-1}	Isomer (See Scheme 2.5)
1.	Ac	H	H	Ac	(3424 *	3433	a,b
					(3435 sh	3406	c
						3460	d
2.	Ac	Me	Me	Cbe	3447	3451	a
					3436	3441	b
						3424	c
						3468	d
3.	Bz	Me	Me	Cbe	3457 sh	3451	a
					3442	3444	b
						3427	c
						3468	d
4.	CHO	Me	Me	Cbe		3451	a
					3447	3450	b
					3436	3433	c
						3468	d
5.	Cbe	Me	Me	Cbe≠	3457	3455	a,b
					3438	3438	c
					3479	3472	d
6.	CHO	Cbe	Me	Cbe	3424 *	3436	a
						3435	b
						3418	c
						3453	d

* Mirone and Lorenzelli[21] gave 3430 cm^{-1} for (1), and 3431 cm^{-1} for (6).

≠ Jones and Moritz.[20]

The bands observed were very broad and obviously consisted of at least two superimposed bands and where possible graphical resolution was carried out. The majority of the results show marked discrepancies from the calculated values but no band that corresponded to (d) was observed except in the expected case of (5).

The NH stretching frequencies of the α-formylpyrroles prepared in the course of this work are given in Table 2.4. The constant of -36 for α-formyl groups derived by Jones and Moritz[20] was used to calculate the NH frequencies and these agree closely with the observed values.

Table 2.5 lists the carbonyl stretching frequencies for the 1-, 2- and 3- acylpyrroles. The carbonyl bands of the 2-acylpyrroles appear 30-40 cm^{-1} lower than the corresponding aromatic aldehydes and ketones (see Table 2.6). As expected, the benzoylpyrroles absorb 20 cm^{-1} lower than the acetylpyrroles due to conjugation of the carbonyl group with the phenyl ring as well as the pyrrole ring.

In an earlier study, Eisner and Erskine[27] reported that the carbonyl frequencies of 2- and 3-ethoxycarbonylpyrroles and 2- and 3-acetylpyrroles were independent of the position of substitution. However, the reinvestigation of these compounds and several others in dilute carbon tetrachloride solution has shown a definite dependence of the carbonyl frequency on the position of substitution (see Tables 2.5 and 26). The carbonyl frequency of corresponding isomers

Table 2.4

NH Stretching Frequencies of Formylpyrroles in dilute CCl_4.

Position of Substituents. 2	3	4	5	Observed cm^{-1}	Calculated * cm^{-1}	$\triangle$ cm^{-1}
H	H	H	CHO	3459	3460	1
Me	H	Me	CHO	3455	3453	-2
Me	Me	H	CHO	3451	3453	2
Me	Me	Me	CHO	3453	3455	2
Me	Et	Me	CHO	3450	-	-
Me	Cbe	Me	CHO	3442	3439	-3
Me	Me	Cbe	CHO	3436	3439	3
Me	Ac	Me	CHO	3438	3435	-3
Me	H	Ph	CHO	3442	3444	2
Ph	H	Ph	CHO	3443	3441	-2
Me	Ph	Ph	CHO	3438	3437	-1
Me	Cbe	Ph	CHO	3423	3421	-2

* Using the additional constants of -36 for the α-formyl group, and -12 and -7 for the α-phenyl and β-phenyl groups respectively (see Chapter 3).

Table 2.5. Carbonyl Stretching Frequencies (CM^{-1}) of Acylpyrroles in CCl_4.

Position of Me Groups	1-Ac	2-Ac	3-Ac	1-Bz	2-Bz	3-Bz
None	1734	1660	-	1706	1628	-
5	-	1652	-	1705	1626	-
4	-	-	1672	-	-	-
2	-	-	1663	-	-	-
4,5	1719	1647	1664	1702	1617	1647
3,5	1722	1637	1655	1700	1609	1617 ?
2,5	1721	-	1664	1704	-	1639
3,4	1719	1638	-	1701	1623	-
3,4,5	1718	1624	-	1699	1608	-
2,4,5	-	-	1657	-	-	1639
2,3,4,5	1709	-	-	-	-	-

(1-Benzoyl-2,3,4,5-tetraphenylpyrrole absorbs at 1710cm^{-1}).

Table 2.6

Carbonyl and NH Stretching Frequencies (cm^{-1}) of Acylpyrroles and Acylbenzenes

	$\nu_{C=O}$	ν_{NH}
1. Acetyl compounds.		
Acetophenone	1692	-
2-Acetylpyrrole	1660	3453
2-Acetyl-4,5-dimethylpyrrole	1647	3444
3-Acetyl-4,5-dimethylpyrrole	1664	3471
2. Benzoyl compounds.		
Benzophenone	1664	-
2-Benzoylpyrrole	1628	3454
2-Benzoyl-4,5-dimethylpyrrole	1617	3447
3-Benzoyl-4,5-dimethylpyrrole	1647	3471
3. Formyl compounds.		
Benzaldehyde	1708	-
2-Formylpyrrole	1665	3458
2-Formyl-3,5-dimethylpyrrole	1640	3455
3-Formyl-2,4-dimethylpyrrole	1674 *	3471 *
4. Ethoxycarbonyl compounds.		
Ethyl benzoate	1717	-
2-Ethoxycarbonylpyrrole	1699	3483, 3465
2-Ethoxycarbonyl-3,5-dimethylpyrrole	1682	3474, 3457
3-Ethoxycarbonyl-2,4-dimethylpyrrole	1711	3476

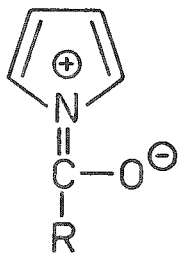
* Mirone and Lorenzelli[21]

is lower in all cases when the substituent is in the α-position as could be expected if the carbonyl group is intramolecularly hydrogen bonded. In many instances the carbonyl band is quite complex (particularly in ethoxycarbonylpyrroles) and it is probably easier to determine the orientation of substituents from the NH stretching frequencies.

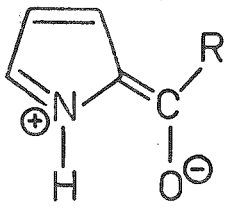
As the lowering of carbonyl frequency of acylpyrroles compared to acylbenzenes is attributed to the mesomeric release of electrons from the pyrrole ring to the carbonyl group it could be expected that an increase in the number of electron donating groups on the ring would further lower the carbonyl frequency. The effect of increased methylation does indeed show a general lowering of the carbonyl frequency but no uniform shift is apparent. The effect of increased methyl substitution when the acyl substituent is in the α-position is irregular but the effect on the carbonyl frequency of β-acylpyrroles is more consistent, each α- or β-methyl group lowering the carbonyl frequency by c. 7 cm^{-1}.

The carbonyl frequencies of N-acylpyrroles are 70-80 cm^{-1} higher than the corresponding 2-acylpyrroles, and the increase is nearly constant for corresponding isomers in the acetyl and benzoyl series. As in the C-acylpyrroles a shift to lower frequency is observed on the introduction of methyl substituents but is particularly small for N-benzoylpyrroles. The increased frequency of the carbonyl frequency in 1-acyl-

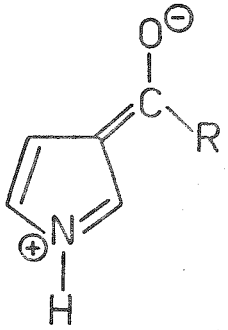
pyrroles compared with the 2- and 3-acylpyrroles shows that the degree of conjugation and the importance of the zwitterionic form is less for the 1-acylpyrroles (XII) than for the 2- and 3-acylpyrroles (XIII, XIV).



XII



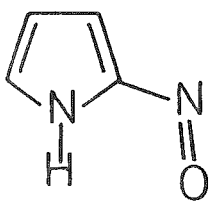
XIII



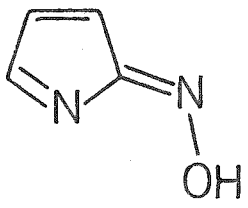
XIV

A direct comparison of the degree of conjugation of the ring with the acyl groups in the 2- and 3- positions is not possible. Intramolecular hydrogen bonding of the 2-acylpyrroles lowers the position of the carbonyl band and any difference due to the degree of conjugation is masked.

2-Nitroso-3,5-diphenylpyrrole was also examined in the course of this work. Previous investigators[24,49] have indicated that nitrosopyrroles exist in the hydroxyiminopyrrolenine form (XVI) and they have often been isolated as the sodium salts.



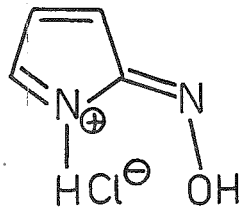
XV



XVI

2-Nitroso-3,5-diphenylpyrrole forms a stable hydrochloride salt and is also quite stable as the free base. The bright green colour of the latter indicates that it probably exists in the nitroso form and as the monomer. In dilute carbon tetrachloride solution a band at 3429 cm^{-1}, assigned to the unassociated NH stretching frequency, was observed. This corresponds to a shift of -48 cm^{-1} due to the nitroso group [compared to 2,4-diphenylpyrrole (see Chapter 3)] and this is close to the constants of -45 and -42 of α-acetyl and α-benzoyl groups. A comparison of the full infrared spectra of 2-nitroso-3,5-diphenylpyrrole and 2-formyl-3,5-diphenylpyrrole as mulls in nujol showed marked similarities, both exhibiting a broad unsymmetrical band at 3280 cm^{-1} (associated NH stretch) and strong bands near 820 and 1280 cm^{-1}. There is some controversy in the literature as to the region of the characteristic absorption of the nitroso group[50,51] and the wide differences in the frequency ranges quoted is probably due to dimerization and the geometrical isomerism of the dimers.[51b] Bellamy[51a] assigns the N=O stretching mode of the nitrosobenzene monomer to the band at 1513 cm^{-1}. The spectrum of 2-nitroso-3,5-diphenylpyrrole showed a band at 1550 cm^{-1} which was absent in the spectrum of the formyl analogue but this is much higher than would be expected for a pyrrole nitroso group if Bellamy's assignment for nitrosobenzene is correct. The spectrum of the nitroso-

pyrrole hydrochloride showed broad bands at 3350 cm^{-1} (OH stretch of N-OH ?) and near 2500 cm^{-1} (NH stretch of $C = \overset{+}{N} - H$?), but no strong bands near 820 and 1280 cm^{-1}. This suggests that the hydroxyiminopyrrolenine form (XVII) is the predominant contributing structure of the salt.



XVII.

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CHAPTER 3.

PYRROLES WITH PHENYL SUBSTITUENTS

3.1. Introduction.

As a preliminary study to a more detailed investigation of phenyldipyrromethenes (Chapter 5) a number of related phenylpyrroles were prepared and examined. The aims of the investigation were to determine the effect of phenyl substituents in the pyrrole ring on the NH stretching frequency and to estimate the magnitude of steric interaction between adjacent phenyl groups.

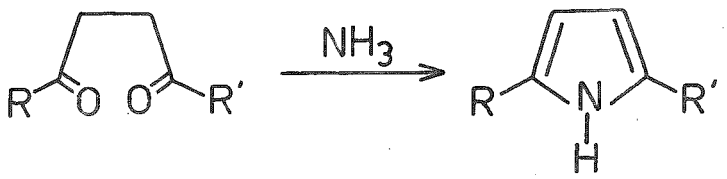
3.2. Preparation of compounds.

The majority of pyrroles with β-phenyl substituents were prepared by the Knorr synthesis. However, attempts to condense α-hydroxyiminoketones with phenylketones by this method (p.23, Scheme 2.3., R''' = Ph) usually resulted in poor yields of the desired α-phenylpyrroles. All the pyrroles prepared by the Knorr procedure, with the exception of 4-methyl-2-phenylpyrrole, contained ethoxycarbonyl groups and subsequent hydrolysis and decarboxylation was carried out by standard methods.[24,41] 3-Ethoxycarbonyl-2,4-dimethyl-5-phenylpyrrole and 3-ethoxycarbonyl-2,4,5-triphenylpyrrole were hydrolysed and decarboxylated in one step by heating with potassium hydroxide in diethylene glycol. The 2,4-dimethyl-5-phenylpyrrole obtained from the former pyrrole was a colourless solid, m.p. 71.5 - 72°, and showed an unassociated NH band at 3477 cm^{-1}. This compound

had previously been reported as a brown oil, b.p. 170°/12 mm, by Treibs and Ohorodnik[52] who prepared it by condensing benzylamine and acetylacetone.

2-Phenylpyrrole was prepared by the thermal isomerization of 1-phenylpyrrole.[24] Several attempts were made to prepare it from 2-phenyl-2-pyrroline, which can be obtained in good yield by the reductive cyclization of β-benzoylpropionitrile.[53] Dehydrogenation of the pyrroline using silver oxide, dibenzoyl peroxide, 2,3,4,5-tetrachloro-1,4-benzoquinone (chloranil) and 10% palladium-carbon were tried but all resulted in very low yields of the pyrrole under the conditions employed. (Selenium dehydrogenation of 2,4-diphenyl-2-pyrroline gives acceptable yields of 2,4-diphenylpyrrole[54] but Knott[53] has reported that 2-phenyl-2-pyrroline gives no 2-phenylpyrrole under the same conditions.)

The Paal-Knorr synthesis (Scheme 3.1.) was utilized in the preparation of 2,5-diphenylpyrrole[55] and 2-methyl-5-phenylpyrrole.[55,56] It is of interest to note that more vigorous conditions are necessary when α-phenyl substituents are present than in the corresponding preparation of α-alkyl-pyrroles.

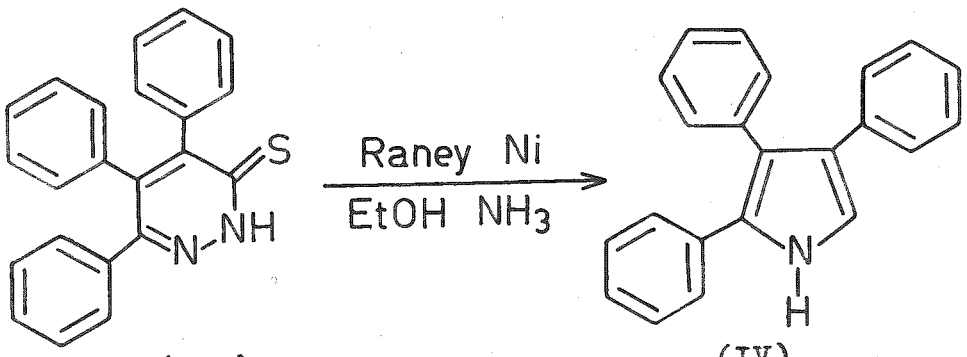


Scheme 3.1.

Heating the diketone(I, R = R' = Ph) with ammonium carbonate is ineffective,[57] and refluxing with ammonium acetate in acetic acid, or alternatively, heating with ethanolic ammonia in an autoclave, is necessary for pyrrole formation. This observation is consistent with the low yields of ∝-phenylpyrroles obtained from the related Knorr synthesis.

The 2,3-diphenylpyrroles were prepared in good yields by the method described by Davidson,[58] which involves condensation of benzoin and the appropriate ∝-methylene ketone in ammonium acetate and acetic acid.

2,3,4-Triphenylpyrrole (IV) was prepared by Raney nickel desulphurization of 4,5,6-triphenyl-3(2H)-pyridazine-thione (III) according to the method outlined by Pollack and Tišler.[59]



(III) (IV)

3.3. Results and discussion.

The NH stretching frequencies of the pyrroles containing phenyl and methyl substituents are given in Table 3.1. As

Table 3.1.

NH STRETCHING FREQUENCIES OF PHENYLPYRROLES IN CCl_4.

Substituents 2	3	4	5	Observed* cm^{-1}	Calculated cm^{-1}	△ cm^{-1}
				△ = calculated-observed		
Ph	H	H	H	3486 (3466)	3484	-2
Ph	H	H	CH_3	3470 (3452)	3475	+5
Ph	CH_3	H	CH_3	3469 (3447)	3477	+8
H	Ph	H	CH_3	3480 (3460)	3480	0
H	CH_3	H	Ph	3484 (3467)	3486	-2
CH_3	Ph	CH_3	H	3482 (3463)	3482	0
H	Ph	C_2H_5	CH_3	3480 (3458)	-	-
Ph	Ph	H	CH_3	3463 (3443)	3468	+5
Ph	H	Ph	H	3478 -	3477	-1
Ph	H	H	Ph	3472 (3451)	3472	0
CH_3	Ph	Ph	H	3474 (3452)	3473	-1
Ph	Ph	Ph	H	3470	3470	0
Ph	Ph	Ph	CH_3	3462	3461	-1
Ph	Ph	H	Ph	3463	3465	+2
Ph	Ph	Ph	Ph	3459	3458	-1

* Bands quoted in brackets were, in the majority of cases, obtained by graphical resolution and are considered to be hot bands.

The half-band widths were c. 20 cm^{-1}.

has been previously observed for acyl, ethoxycarbonyl and methyl substituents, the effect of phenyl substituents on the NH stretching frequency of the pyrroles is independent of other groups and additive and may be represented by the single equation -

$$\upsilon_{NH}\ (cm^{-1}) = 3496 - 9n_{\alpha}CH_3 + 2n_{\beta}CH_3 - 12n_{\alpha}Ph - 7n_{\beta}Ph \quad \ldots\ldots(6)$$

where n_{α} and n_{β} are the number of substituents in the α and β positions.

Models* show that steric interaction between adjacent phenyl groups is greater for $\alpha\beta$ substituents than for $\beta\beta'$ substituents. Nevertheless, the deviations from the calculated NH stretching frequencies are small, even for tetraphenylpyrrole, and suggest that the steric interactions are slight and are readily accommodated by a small deviation of the phenyl groups from coplanarity omit with the pyrrole ring.

In the spectra of a number of the pyrroles examined a second band, which is approximately one-twentieth the intensity of the major band, is observed. The position of this band is c. 20 cm^{-1} lower than that of the main band and by analogy with the methyl-, ethoxycarbonyl- and acyl-

---

* Dreiding Stereomodels

pyrroles it is assumed to be a hot band arising from the NH out-of-plane deformation near 500 cm^{-1}. The major absorption band of several of the pyrroles, particularly those having more than one phenyl group, appeared to be asymmetric but it was not possible to determine the precise position of the hot band.

Table 3.2. lists the NH stretching frequencies for phenylpyrroles having several different substituents and agree well with those calculated using the equation:-

$$\upsilon_{NH}\ (cm^{-1}) = 3496 - 9n_{\alpha}CH_3 + 2n_{\beta}CH_3 - 12n_{\alpha}Ph - 7n_{\beta}Ph - 13n_{\beta}CO_2Et - \begin{Bmatrix}14\\31\end{Bmatrix}n_{\alpha}CO_2Et - 18n_{\beta}Ac \qquad \ldots\ldots(7)$$

The ultraviolet absorption spectra of a variety of substituted pyrroles have been reported[60,61] but no general agreement seems to have been reached on the nature of the spectra and no really systematic studies have been carried out. However, the ultraviolet absorption spectra of the phenylpyrroles provides further information on the steric interaction of adjacent substituents. As other groups, particularly ethoxycarbonyl and acyl substituents, complicate the spectra and sometimes produce new absorption bands,[61] the pyrroles containing only phenyl groups were examined and the spectra are recorded in Table 3.3.

Table 3.2.

NH STRETCHING FREQUENCIES OF ETHOXYCARBONYLPHENYLPYRROLES IN CCl_4.

$\triangle$ = calculated-observed

Substituents 2	3	4	5	Observed* cm^{-1}	Calculated cm^{-1}	$\triangle$ cm^{-1}
CH_3	CO_2Et	Ph	H	3469 (3452)	3467	-2
CH_3	CO_2Et	Ph	Ph	3456 (3437)	3455	-1
CH_3	CO_2Et	CH_3	Ph	3458 (3440)	3464	+6
Ph	CO_2Et	Ph	Ph	3450 (3425)	3452	+2
CO_2Et	CH_3	Ph	CH_3	3467 3451	3468 3451	+1 0
CO_2Et	Ph	Ph	CH_3	3461 3444	3459 3442	-2 -2
CO_2Et	Ph	CO_2Et	CH_3	- 3436	3453 3436	- 0
CO_2Et	Ph	CO_2Et	Ph	- 3430	3450 3433	- +3
CO_2Et	Ph	Ac	CH_3	3448 3432	3448 3431	0 +1

* Bands quoted in brackets were, in the majority of cases, obtained by graphical resolution and are considered to be hot bands.

King, Bauer and Lutz[62] have examined several phenylfurans together with some of the corresponding thiophens and pyrroles and note the similarity of the spectra of these compounds with butadiene derivatives. The spectra of the corresponding phenyl substituted furans, thiophens and pyrroles are very similar, the 2,5-disubstituted compounds, which are linearly conjugated, resembling 1,4-diphenylbutadiene and the 2,4-disubstituted compounds, which are cross-conjugated, resembling 1-phenylbutadiene and styrene.

An examination of Table 3.3. shows that the absorption bands occur in three main regions, 230-240mμ, 250-265mμ, and near 300mμ. The 250-265mμ region appears to be characteristic of substitution in the β-position (c.f. King, Bauer and Lutz[62]). In all cases, the compounds with phenyl substituents in both α-positions absorb at longer wavelengths and higher intensities than those with only one α-phenyl substituent. The addition of a phenyl substituent in a β-position adjacent to another phenyl group results in a hypsochromic shift and/or a decrease in intensity of the long wavelength band (c.f. (3) and (5), (2) and (4), (5) and (6)) which would indicate that there is some degree of steric interaction between adjacent phenyl groups.

Table 3.3.

ULTRAVIOLET SPECTRA OF PHENYLPYRROLES AND PHENYLFURANS IN 95% EtOH

	Substituents				Pyrroles		Furans*	
	2	3	4	5	$\lambda_{m}\mu$	$\epsilon \times 10^{-3}$	$\lambda_{m}\mu$	$\epsilon \times 10^{-3}$
1.	Ph	H	H	H	230 sh 287	8.0 20.3	-	-≠
2.	Ph	H	H	Ph	230 322 sh 329	12.0 26.2 26.5	226 324	16.2 29.2
3.	Ph	H	Ph	H	236 249 284 sh 305	17.7 19.2 18.7 19.6	230 242 277	17.8 19.4 20.0
4.	Ph	H	Ph	Ph	238 257 300 sh 320	15.5 14.2 20.6 25.6	231 255 315sh 320 325sh	20.7 14.8 24.3 25.0 24.5
5.	Ph	Ph	Ph	H	254 303 sh	24.0 16.0	-	-≠
6.	Ph	Ph	Ph	Ph	233 263 304 sh 319	-≠ - - -	232 260 314sh 320 325sh	23.9 16.8 21.6 22.3 21.9

* King, Bauer and Lutz[62]

≠ not sufficiently soluble for accurate intensity measurements.

≠ unreported.

CHAPTER 4.

THE NH STRETCHING FREQUENCIES AND ELECTRONIC SPECTRA OF ALKYL- AND ETHOXYCARBONYL-DIPYRROMETHENES.

4.1 INTRODUCTION.

Several investigators[32,36,63] have examined the infrared absorption spectra of dipyrromethenes* but they have not attempted to correlate the results of their studies with the electronic absorption spectra. The majority of spectra reported have been of dipyrromethenes prepared as intermediates in the synthesis of naturally occurring porphyrins or their analogues. This work describes a more systematic study of the spectra of alkyl- and ethoxycarbonyl-dipyrromethenes.

Vestling and Downing[64] appear to have been the first to determine the NH stretching frequency of a dipyrromethene and subsequent investigators[32,36,63] have shown that these compounds exhibit very strong intramolecular hydrogen bonding. The NH stretching frequencies are considerably lower than those of dipyrromethanes[32,36] or pure liquid pyrrole despite the unfavourable N-H...N bond angle of *c.* 120° (calculated using accepted bond lengths and angles for porphyrins[65,66] and phthalocyanins[67]). The strength of the hydrogen bond has been attributed to the fact that the potential energy curve for the NH stretch has a symmetrical double minimum,

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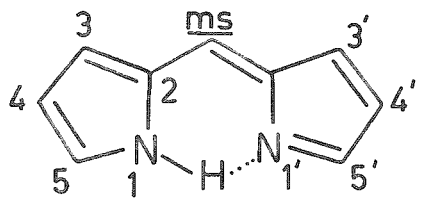
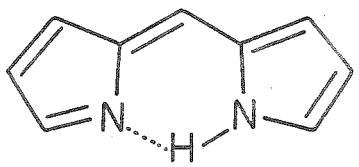
* The names dipyrromethine, dipyrrylmethene, and dipyrrylmethine have also been commonly used in the literature. Chemical Abstracts uses the more systematic (but more cumbersome) name 2-(2-pyrrolylmethylene)-2H-pyrrolenine.

each minimum corresponding to one of the tautomers I and II.[36]



I



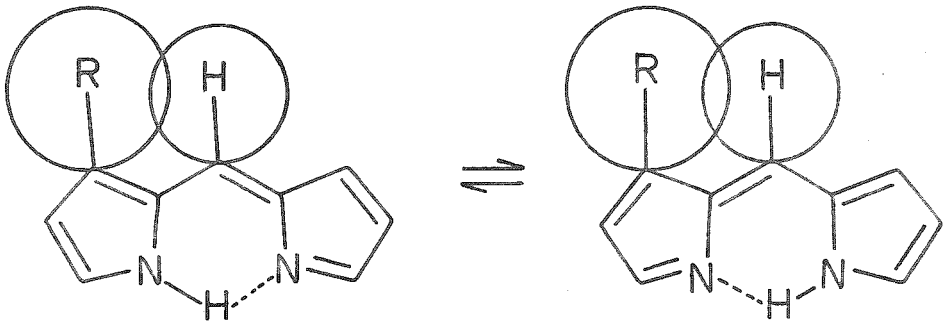
II

Badger et al.[32] recorded the NH stretching frequency of several dipyrromethenes and showed that the position of the band moved to higher frequencies when the substituent in the 3- and/or 3'-position (see (I) for the numbering of dipyrromethene rings) was large and that it moved to a lower frequency when electron- withdrawing substituents (CO_2Et) were present. It was suggested that these shifts were due, respectively, to a loss of coplanarity of the dipyrromethene skeleton, resulting in a weakening of the hydrogen bond, and to an increase in the acidity of the pyrrolyl NH with a consequent increase in the NH bond length and a resultant more symmetrical hydrogen bond. Kuhn and Kleinspehn[36] in a similar study interpreted the effect of ethoxycarbonyl groups in the 3(3')- and 4(4')- positions in terms of resonance interaction with the system (the effect of which depends on the position of the substituents) and the symmetry of the system.

The electronic absorption spectra can give valuable information on steric interactions within dipyrromethene

systems. The dipyrromethenes are coloured compounds and their more stable and intensely coloured salts are classified as cyanine dyes. Brunings and Corwin[68] first reported the effect of steric crowding on the electronic absorption spectra of dipyrromethene systems and Brooker[69] extended the study to a wide variety of cyanine dyes. In addition, the spectra of a small number of sterically crowded dipyrromethene salts and their free bases have been examined by Knott.[70] In almost all cases studied by these workers the absorption maximum shifted bathochromically as a result of crowding the two heterocyclic nuclei out of a common plane (or increasing the crowding in an already distorted molecule) and all showed a marked decrease in intensity compared to the related uncrowded dyes. Brooker[69] and Knott[70] interpreted their results in terms of the resonance treatment proposed by Förster,[71] and Dewar[72] has discussed the results in terms of molecular-orbital theory. The majority of dipyrromethenes considered by these workers were distorted by crowding substituents on the nitrogen atoms whereas this work is concerned with the possibility of steric crowding by groups in the 3- and 3'- positions. In this case the interpretation of the results is complicated by the fact that these substituents may interact with the meso hydrogen atom and not necessarily with each other. The electronic spectra might be expected to be of some value in deciding which tautomer is more stable

in the ground state in the case of unsymmetrical sterically crowded systems of the type shown in Scheme 4.1., as the effect of crowding on the spectra will depend on whether an essential double or single bond is twisted to relieve the strain (see Chapter 1).



III IV

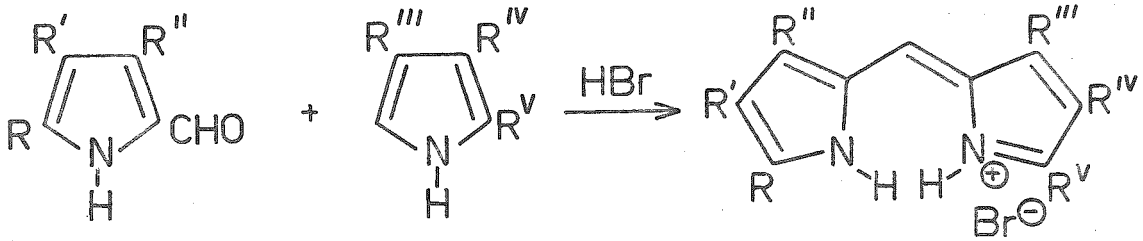
Scheme 4.1.

In the present work the NH stretching frequency of twenty-one alkyl- and ethoxycarbonyl-dipyrromethenes and the electronic spectra of both the free bases and protonated forms have been examined and the spectral data have been interpreted empirically in terms of the steric and electronic effects of the substituents. A completed examination of this series of dipyrromethenes is prevented by the instability of the simpler members, many of which have never been isolated.

4.2 Synthesis of compounds.

Most of the dipyrromethenes were prepared by condensing

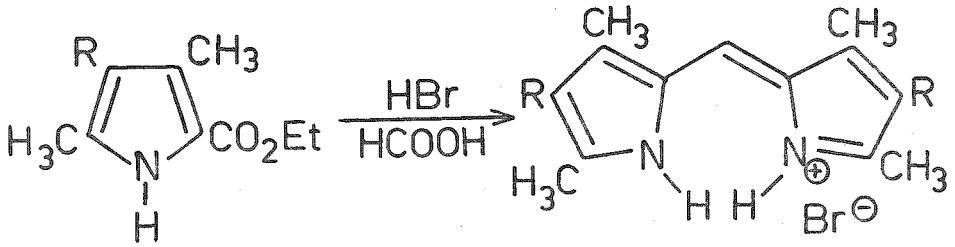
an ∝-formylpyrrole with an ∝-unsubstituted pyrrole in the presence of hydrobromic acid (Scheme 4.2.). This method gave nearly quantitative yields of the dipyrromethene hydrobromide in most cases.



V VI VII

Scheme 4.2

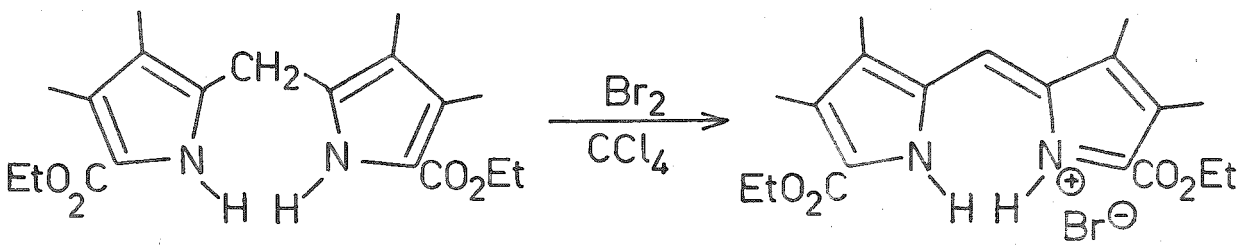
The coupling of ∝-unsubstituted pyrroles with formic acid and hydrobromic acid was also utilized; this is probably a special case of the above method, since formylpyrrole may be an intermediate in the condensation.[73] The symmetrical dipyromethenes (VIII, R=Me, Et) were prepared by heating the ∝-ethoxycarbonylpyrroles (IX, R=Me, Et) in formic acid and hydrobromic acid.



VIII IX

Treatment of the dipyrromethene salts in ethanol with aqueous ammonia, or shaking a chloroform solution with calcium hydroxide, sodium acetate or barium hydroxide gave the free bases.

The dipyrromethenes with 5- and 5'-ethoxycarbonyl substituents were prepared by the brominative oxidation of the corresponding dipyrromethanes (Scheme 4.3.). The synthesis of these compounds by coupling of α-formylpyrroles and α-unsubstituted pyrroles is usually unsatisfactory as the presence of the α-ethoxycarbonyl groups slows down the condensation and leads to the formation of abnormal products.[73]

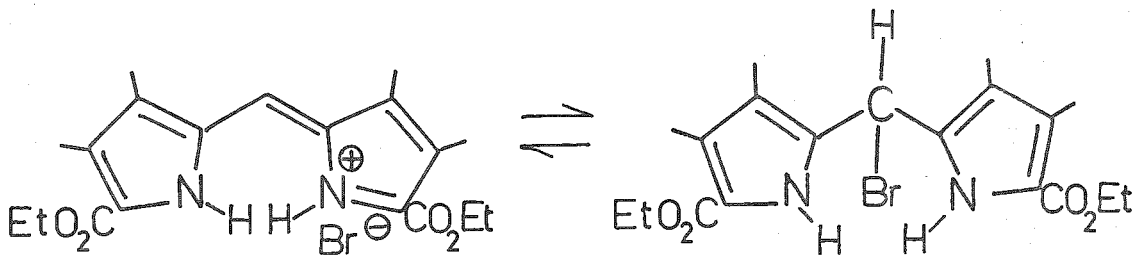


X XI

Scheme 4.3.

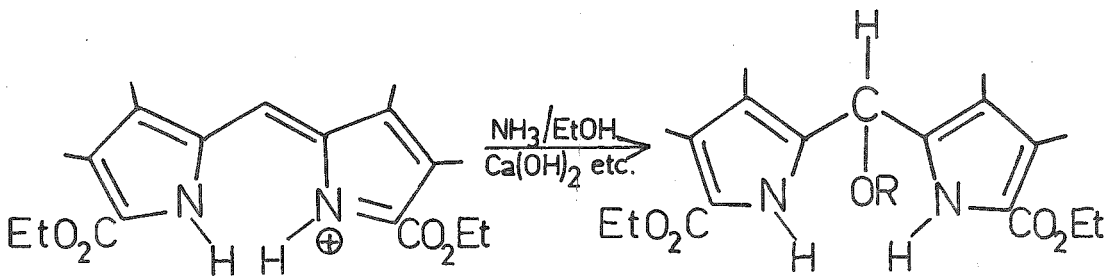
The presence of 5- or 5'-ethoxycarbonyl substituents in dipyrromethenes has a marked effect on the stability of the system. These substituents exert a more powerful

electron-withdrawing effect than when they are in the 3,3',4 or 4' positions[74] and enhance the positive character of the meso carbon atom. This increases the tendency of the dipyrromethene to form a covalent structure (XIII) instead of the usual ionic dye (XII).[73,74]



XII XIII

This is reflected in the preferential formation of dipyrrocarbinols and dipyrromethane ethers (Scheme 4.4.) when the usual methods of conversion to the free base are used.[73,74]



XIV XV

Scheme 4.4.

The bases were accordingly prepared by treating a solution of the salt in dry chloroform with triethylamine.

4.3. Measurement of the Spectra.

The NH stretching frequencies of the dipyrromethenes, measured in carbon tetrachloride solution, were very broad and the frequencies quoted have an accuracy of measurement of c. $\pm$ 3cm^{-1}. A decrease in NH frequency was accompanied by an increase in the half-band width which is characteristic of hydrogen bonded systems. The half-band widths were 100-200 cm^{-1}.

The electronic spectra were measured in ethanol, carbon tetrachloride and 1N ethanolic hydrogen chloride. The insolubility of the dipyrromethene salts in carbon tetrachloride prevented their measurement in this solvent. The spectra of the free bases showed broad, symmetrical long wavelength bands and the hydrochlorides showed much sharper, more intense and slightly asymmetric long wavelength bands (see Fig. 4.1.). In the following discussion only these long wavelength absorption bands are considered. The full spectra of the dipyrromethenes and their hydrochlorides are recorded in the Experimental section (Chapter 8.).

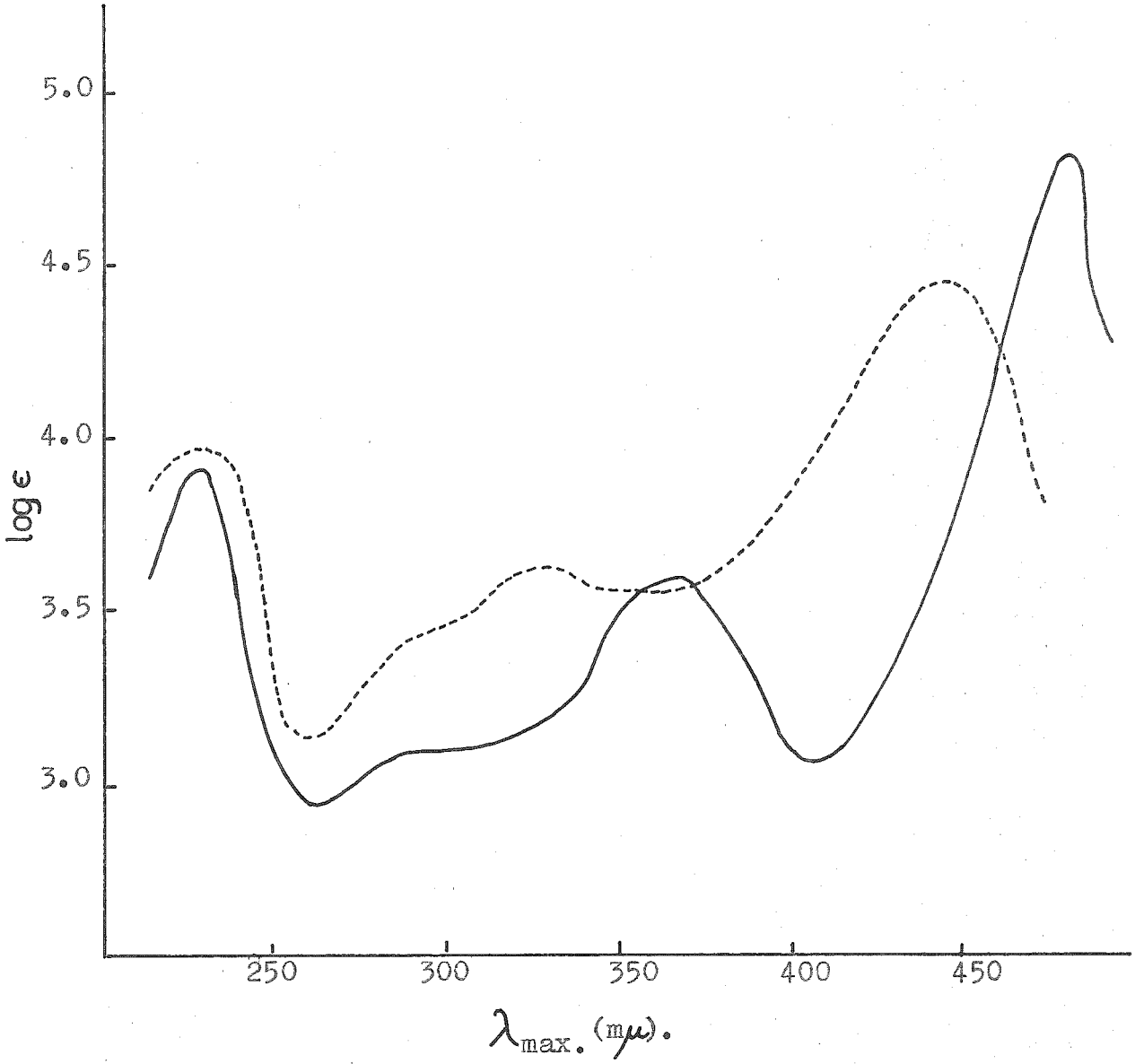


Fig. 4.1. The Electronic Absorption Spectrum of 3,4,5,3',4',5'-Hexamethyldipyrromethene in 95% EtOH (--------) and 1N HCl/EtOH (———).

4.4. Results and Discussion.

(a) Alkyl-Substituted Dipyrromethenes.

Calculations, using accepted bond lengths and angles for porphyrins[65,66] and phthalocyanins,[67] show that for 3,3'-dimethyldipyrromethenes there is little overlap of the van der Waals radii of the methyl groups either with each other or with the meso hydrogen atom (c.f. Brooker[69]). Consequently any effect that these methyl groups may have will be predominantly electronic.

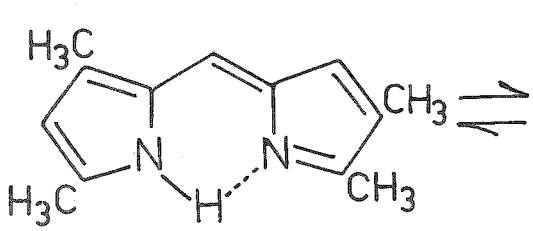
The electron-donating effect of the methyl groups would be expected to increase the basicity of the pyrrolyl nitrogen and reduce the NH bond length. Examination of Table 4.1. shows that the NH stretching frequency increases as the number of methyl groups increases. It has been shown that for methylpyrroles an α-methyl group causes a decrease in the NH stretching frequency of 9cm^{-1} and that a β-methyl group increases the frequency by 2cm^{-1} (see Chapters 2 and 3). A similar situation may exist in the case of methyldipyrromethenes. A comparison of the NH stretching frequency of 4,4'-diethoxycarbonyl-3,5,3',5'-tetramethyldipyrromethene and 4,4'-diethoxycarbonyl-3,3'-dimethyldipyrromethene (Table 4.2., Nos. 7 and 11) shows that the α-methyl groups in the 5,5'-positions decrease the NH stretching frequency by 15 cm^{-1}. Also, although the replacement of the α-methyl groups by ethyl groups causes negligible change in the NH

Table 4.1. Long Wavelength Electronic Absorption Maxima and NH Stretching Frequency of Alkyl Dipyrromethenes.

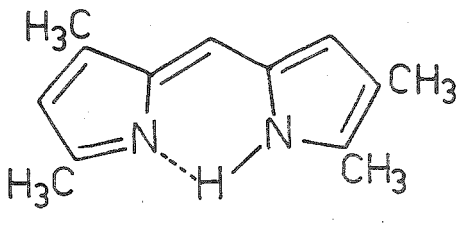
	Substituent 5	4	3	3'	4'	5'	Solvent*	λ max. mμ	λ max. log ε	ν NH cm.$^{-1}$
1.	Me	H	Me	Me	H	Me	C	437	4.47	3260
							E	435	4.52	
							H	463	5.03	
2.	Me	H	Me	H	Me	Me	C	439	4.40	3273
							E	439	4.40	
							H	476	4.80	
3.	Me	Me	H	H	Me	Me	C	442	4.38	3260
							E	441	4.36	
							H	472	4.77	
4.	Me	Me	Me	Me	H	Me	C	434	4.41	3266
							E	433	4.39	
							H	474	4.84	
5.	Me	Me	Me	Me	Me	Me	C	444	4.42	3281
							E	442	4.48	
							H	480	4.80	
6.	Me	Me	Et	Et	Me	Me	C	454	4.50	3270
							E	443	4.59	
							H	478	4.90	
7.	Me	Et	Me	Me	Et	Me	C	451	4.40	3279
							E	447	4.53	
							H	483	4.86	
8.	Et	Me	Me	Me	Me	Et	C	449	4.42	3250
							E	448	4.43	
							H	484	4.80	

* C, carbon tetrachloride E, ethanol H, 1N ethanolic hydrochloric acid

stretching frequency (Table 4.1, Nos. 5,6, and 7), the frequency of the band is decreased by 31cm^{-1} on replacing the α-methyl groups by ethyl groups (Table 4.1, No. 8). The abnormally high value for 3,5,4',5'-tetramethyldipyrromethene (Table 4.1., No. 2) could be due to the asymmetry of the system, as there may not be a symmetrical double minimum of potential energy for the NH stretching mode (this implies that one of the two possible tautomeric forms (XVI and XVII) of the dipyrromethene predominates in the ground state).



XVI



XVII

In the electronic spectra of the alkyldipyrromethenes there is little or no shift in the position of the long wavelength band for carbon tetrachloride and ethanol solutions, showing that the polarity of the solvent has little effect upon the system. Protonation of the dipyrromethenes produces a bathochromic shift of the long wavelength band of 30-40mμ and is accompanied by a marked increase in intensity. This effect is normal for conjugated systems when they acquire a charge, and in this case it is also

enhanced by the increase in the symmetry of the dipyrromethene skeleton on protonation. The replacement of a methyl group in any position by an ethyl group (Table 4.1., Nos. 5,6,7 and 8) has little effect on the electronic spectra of the hexa-alkyldipyrromethenes. Hence, the steric requirement of an ethyl group in the 3(or 3') position is comparable with that of a methyl group.

(b) Ethoxycarbonyl-Substituted Dipyrromethenes.

Table 4.2. records the spectral data for four classes of dipyrromethenes: (a) with one ethoxycarbonyl group, (b) with two ethoxycarbonyl groups in a symmetrical arrangement, (c) with two ethoxycarbonyl groups in an asymmetrical arrangement and (d) with three ethoxycarbonyl groups.

In general, the replacement of an alkyl group or hydrogen by an ethoxycarbonyl group produces a decrease in the NH stretching frequency. The electron-withdrawing ability of the ethoxycarbonyl group increases the acidity of the NH group and consequently increases the NH bond length. The replacement of hydrogen in the 4-position by an ethoxycarbonyl group decreases the NH stretching frequency by c. 20cm^{-1} and in the 3-position by c. 10cm^{-1}. The introduction of an ethoxycarbonyl group in the place of a methyl group in the 5-position increases the NH stretching frequency by 4cm^{-1}. This may be explained in terms of a

Table 4.2. Long Wavelength Electronic Absorption Maxima and NH Stretching Frequency of Ethoxycarbonyl Dipyrromethenes.

	Substituent						Sol-	λ max.		ν_{NH}
	5	4	3	3'	4'	5'	vent*	mμ	log ε	cm.$^{-1}$
1.	Me	Me	Me	Me	Me	Cbe	C	417	4.40	3285
							E	410	4.35	
							H	467	4.60	
2.	Me	Me	Me	Me	Cbe	Me	C	420	4.52	3246
							E	409	4.47	
							H	470	4.86	
3.	Me	Et	Me	Me	Cbe	Me	C	420	4.48	3248
							E	410	4.44	
							H	471	4.88	
4.	Me	Me	Me	Cbe	Me	Me	C	416	4.46	3239
							E	407	4.48	
							H	470	4.91	
5.	Cbe	Me	Me	Me	Me	Cbe	C	458	4.40	3280
							E	453	**	
							H	500	**	
6.	Cbe	Me	Et	Et	Me	Cbe	C	462	4.30	3289
							E	458	**	
							H	505	**	
7.	Me	Cbe	Me	Me	Cbe	Me	C	451	4.63	3280
							E	452	4.55	
							H	465	5.06	

(Table 4.2. Cont'd)

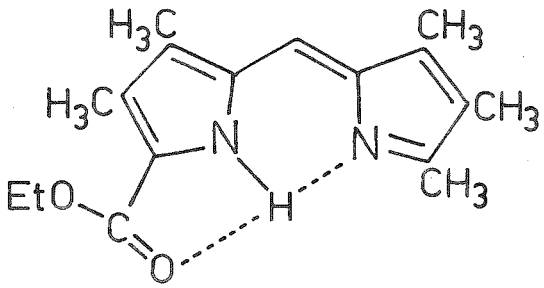
	Substituent 5	4	3	3'	4'	5	Solvent*	λ max. mμ	λ max. log ε	ν NH cm.$^{-1}$
8.	Me	Cbe	Me	Cbe	Me	Me	C	459	4.57	3250
							E	453	4.45	
							H	480	4.50	
9.	Me	Me	Cbe	Cbe	Me	Me	C	485	4.50	3239
							E	479	4.41	
							H	526	4.92	
10.	H	Cbe	Me	Me	Cbe	Me	C	440	4.52	3234
							E	433	4.44	
							H	459	5.04	
11.	H	Cbe	Me	Me	Cbe	H	C	437	4.51	3235
							E	434	4.38	
							H	444	4.81	
12.	Me	Cbe	Me	Cbe	Me	Cbe	C	438	4.40	3226
							E	442	4.30	
							H	≠	--	

* C carbon tetrachloride, E ethanol, H 1N ethanolic hydrochloric acid.

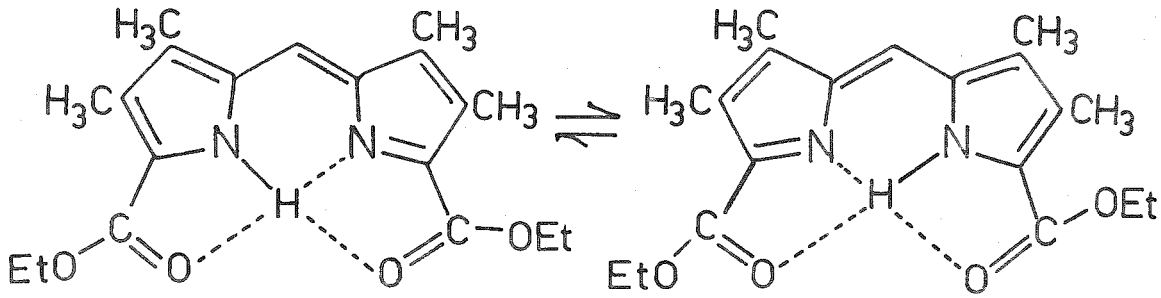
** dipyrromethenes not sufficiently stable in ethanol to allow for accurate intensity measurements.

≠ not stable in ethanolic hydrochloric acid.

competing C=O....H-N hydrogen bond (XVIII) which will weaken the N....H-N hydrogen bond. Also, the C=O....H-N bond may stabilize the tautomeric form shown (XVIII) and hence increase the asymmetry of the N....H-N bond such that the vibration will no longer have a symmetrical double minimum of potential energy. In the case of 5,5'-diethoxy-carbonyldipyrromethene (XIX) the N-H....N bond would be expected to be completely symmetrical and the degree of C=O....H-N bonding greater than for XVIII.



XVIII



XIX

The carbonyl stretching frequencies of the diethoxycarbonyldipyrromethenes (Table 4.2., Nos. 5,7,8 and 9) measured in dilute carbon tetrachloride solution all occurred near 1710cm^{-1} but the 5,5'-diethoxycarbonyldipyrromethene (5) showed a strong shoulder at 1699cm^{-1} and this lower frequency band is probably due to hydrogen bonding. The dipyrromethene with one α-ethoxycarbonyl group (XVIII) showed two carbonyl bands at 1707 and 1699cm^{-1}.

Kuhn and Kleinspehn[36] based their arguments for the difference in the degree of hydrogen bonding of the 3(3')-ethoxycarbonyl- and 4(4')-ethoxycarbonyldipyrromethenes on the relative stabilities of the charged canonical forms of the resonance hybrids, and they did not consider any possible steric interactions involving the ethoxycarbonyl group in the 3-position. An examination of the spectral data for the dipyrromethenes with ethoxycarbonyl groups in the 3'-, 4'-, 3,3'-, 4,3'-, and 4,4'-positions (Table 4.2., Nos. 4,2,9,8 and 7) shows that as well as the difference in the electronic effects in the 3- and 4-positions there appears to be a steric effect due to the ethoxycarbonyl group in the 3-position.

Considering first the NH stretching frequencies, the difference in the position of the band for the 4,3'- and 4,4'-diethoxycarbonyl compounds could be due partly to the asymmetry of the 4,3'-compound (c.f. the shift of 13cm^{-1}

for the corresponding alkyldipyrromethenes) and partly due to a difference in the electronic effects of the ester groups (c.f. Kuhn and Kleinspehn[36]). However, it is also consistent with the twisting of the two pyrrole rings out of coplanarity due to interaction between the 3-methyl and 3'-ethoxycarbonyl groups. Similarly, the position of the NH stretching frequency of the 3,3'-diethoxycarbonyldipyrromethene compared with the 4,4'-compound may be explained in terms of either an electronic or steric effect.

Table 4.3. records the effect on the spectra of substituents in the 4- and 4'-positions. The most significant feature is that, when the dipyromethenes are protonated, the resultant bathochromic shift of the long wavelength electronic absorption band decreases as the electron-withdrawing power of the 4,4'-substituent increases. If it is assumed that the electronic spectra of the corresponding 3,3'-substituted compounds will show similar behaviour then the long wavelength band of 3,3'-diethoxycarbonyldipyrromethene should undergo a comparatively small bathochromic shift when the compound is protonated. However, a much larger shift than normal is observed and in fact the electronic absorption bands of both the base and the protonated species are at much longer wavelengths (and are slightly less intense) than the bands of the corresponding 4,4'-diethoxycarbonyl compound. It is therefore probable that there is some

Table 4.3. Electronic Effect of Substituents in the 4,4'-Positions of 3,3',5,5'-Tetramethyldipyrromethene.

	4,4'-Substituent	Solvent	υ_{NH} ($cm.^{-1}$)	Base		Protonated Species	
				λmax. ($m\mu$)	logϵ	λmax ($m\mu$)	logϵ
1.	Methoxycarbonylethyl	CCl_4	3281	450	4.53		
		EtOH		445	4.58	482	4.98
2.	Ethyl	CCl_4	3279	451	4.40		
		EtOH		447	4.53	483	4.86
3.	Methyl	CCl_4	3281	444	4.42		
		EtOH		442	4.48	480	4.80
4.	Hydrogen	CCl_4	3260	437	4.47		
		EtOH		435	4.52	463	5.03
5.	Acetyl	CCl_4	3240	446	*		
		EtOH		424	*	472	*
7.	Cyano	CCl_4	3220	448	*		
		EtOH		446	*	470	*
8.	Ethoxycarbonyl	CCl_4	3220	451	4.63		
		EtOH		452	4.55	465	5.06

* dipyrromethenes not sufficiently soluble for an accurate measurement of intensity.

steric interaction between the ethoxycarbonyl groups in the 3- and 3'-positions. As the similarity of the data for the 3'- and 4'-ethoxycarbonyldipyrromethenes (Table 4.2., Nos. 2 and 4) show that there is little or no steric interaction between the 3-methyl and 3'-ethoxycarbonyl groups and that the electronic effect of the ester group in the 3(3')- and 4(4')-position are similar, the spectral shifts for the 4,3'-diethoxycarbonyl compound are probably due to the asymmetry of the system.

The dipyrromethenes which have no substituent in the 5- and/or 5'- positions (Table 4.2., Nos. 10 and 11) both have the NH stretching frequency at about 3235 cm^{-1}. The electronic effect of the ester groups in the 4,4'-position is constant and it therefore appears that the electronic effect of a methyl group in the 5'-position compensates for the asymmetry of 4,4'-diethoxycarbonyl-3,3',5'-trimethyl-dipyrromethene. The electronic absorption moves progressively to longer wavelengths (437 → 440 → 451 mμ) on the insertion of methyl groups in the 5,5'-positions (Table 4.2., Nos. 10,11 and 7) and this effect is consistent with the usual effect of alkyl substitution on a conjugated system (c.f. Woodward's rule[75]).

The NH stretching frequency of the unsymmetrical 4,3',5'-triethoxycarbonyldipyrromethene (Table 4.2., No. 12) is lower than expected. Replacement of a 5(5')-methyl substituent by an ethoxycarbonyl group usually has little effect

on the NH frequency (the electron-withdrawing effect is counteracted by the competing hydrogen bonding). The NH frequency would hence be expected to be similar to the NH frequency of the 3,4'-diethoxycarbonyl compound (Table 4.2., No. 8). The reason for the increased hydrogen bond strength is obscure but may be due to a symmetry factor.

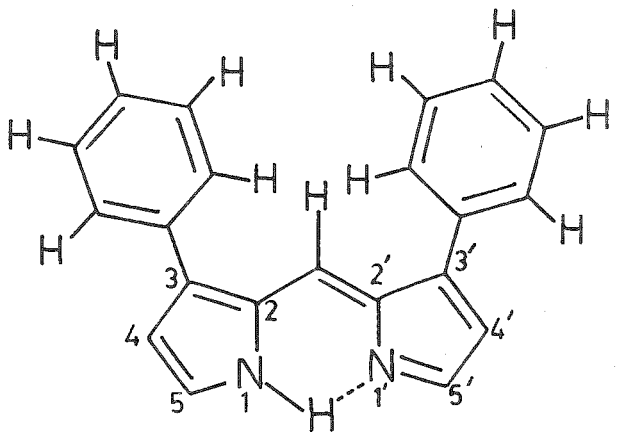
The effect of unsymmetrical arrangement of substituents on the spectra of dipyrromethenes is discussed further in the next chapter.

CHAPTER 5.

THE NH STRETCHING FREQUENCIES AND ELECTRONIC SPECTRA OF PHENYLDIPYRROMETHENES.

5.1 Introduction.

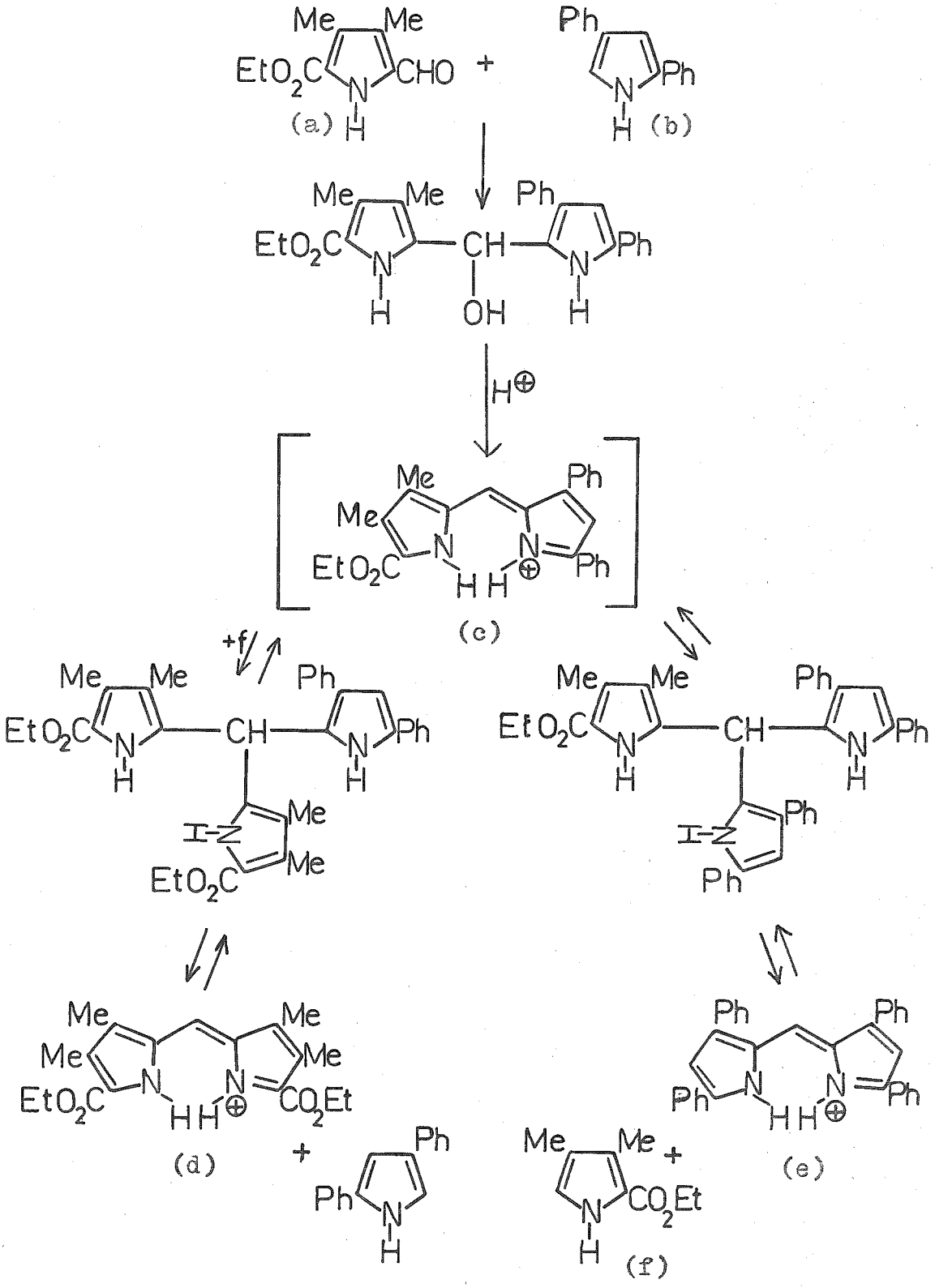
Comparatively few investigations of phenyl substituted pyrroles, porphyrins or polypyrrole pigments (excluding the benzo derivatives) have been reported in the literature. In fact, only two dipyrromethene bases with phenyl substituents on the heterocylic rings have been described[76] although a small number of dipyrromethene hydrobromides and hydrochlorides are known. In this work the investigation of the spectra of alkyl- and ethoxycarbonyl-dipyrromethenes described in the previous chapter has been extended to twenty-two phenyl substituted compounds. The purpose of the investigation was to study the steric interaction between phenyl substituents in the 3,3'-positions of the dipyrromethene system.



5.2. Synthesis of Compounds.

The majority of compounds were prepared by condensing an α-formylpyrrole with an α-unsubstituted pyrrole (see Scheme 4.2.). However, the attempted synthesis of 5-ethoxycarbonyl-3,4-dimethyl-3',5'-diphenyldipyrromethene (Scheme 5.1., (c)) by condensing 2,4-diphenylpyrrole (b) with 2-ethoxycarbonyl-5-formyl-3,4-dimethylpyrrole (a) resulted in the formation of 3,5,3',5'-tetraphenyldipyrromethene (e). Several mechanisms for the aldehyde synthesis of dipyrromethenes have been suggested[77,78,79,80] and Scheme 5.1. shows a possible reaction route, based on the mechanism proposed by Treibs *et al.*,[80] which accounts for the formation of the symmetrical product. The presence of an α-ethoxycarbonyl substituent has a marked effect on the reactivities of pyrroles and dipyrromethenes, and alters the relative reaction rates of the various steps (see the kinetic studies of Corwin[77,78]). Dipyrromethenes with ethoxycarbonyl groups in the 5- and 5'- positions are very unstable in acid and the much greater stability of the tetraphenyldipyrromethene (e) would account for the preferential formation of the latter. The condensation of 2-formyl-3,5-diphenylpyrrole with 2-ethoxycarbonyl-3,4-dimethylpyrrole also resulted in the formation of the tetraphenyl compound.

The 3,4,5,3',4',5'-hexaphenyldipyrromethene was prepared by treating a solution of 2-methyl-3,4,5-triphenylpyrrole in acetic acid with sulphuryl chloride. It is



Scheme 5.1.

probable that 3,4,5-triphenylpyrrole-2-carboxylic acid and 2-formyl-3,4,5-triphenylpyrrole were also formed in the reaction but no attempt was made to isolate them.

5.3. Results and Discussion.

Steric interaction between substituents in the 3- and 3'- positions of dipyrromethenes may be accommodated in several ways: (a) by deviation of the two heterocyclic rings from coplanarity, (b) by changes in bond angles in the coplanar system, and (c) by the twisting or bending out of plane of one or both of the 3,3'-substituents. Each of these modifications requires energy which must be subtracted from the resonance energy of the system and the relative energies required has been discussed briefly by Brunings and Corwin,[68] who were concerned with steric interactions between methyl substituents on the nitrogen atoms. They suggested that the bending of the N-methyl substituents out of plane would require less energy than the alteration of bond angles and is therefore more likely, although all the possible modifications may occur to some extent in practice. In the present investigation it would be expected that steric interaction between phenyl groups and other substituents in the 3,3'-positions would be most readily relieved by rotation of the phenyl ring from the plane of the dipyrromethene skeleton. Scale drawings (c.f. Knott[70])

show that 3- and 3'- phenyl substituents interact with each other (and also the meso-hydrogen atom) to some extent, but the degree of the overcrowding is not sufficiently large to suggested that distortion of the dipyrromethene skeleton will occur.

Table 5.1. records the spectral data for dipyrromethenes with phenyl and methyl substituents. In general, the replacement of any alkyl group by a phenyl group decreases the NH stretching frequency by c.16 cm^{-1}. (In pyrroles, replacement of any methyl group by a phenyl substituent decreases the NH frequency by c.4 cm^{-1}). The phenyl group must therefore act as an electron-withdrawing group and hence increases the NH bond length. However, when the replacement results in phenyl substituents in both the 3- and 3'- positions, or in adjacent positions on one of the heterocyclic rings, the NH frequencies vary considerably. The NH frequencies of the 3,5,4',5'-tetrasubstituted dipyrromethenes also show variations from the expected values and these anomalies may be due to symmetry factors. The interpretation of the NH frequencies of unsymmetrically substituted dipyrromethenes is made difficult by the necessity to consider the influence of such substitution on the shape of the potential energy curve of the NH stretching mode. If the arrangement of substituents results in one of the tautomeric forms being more stable than the other (see

Table 5.1. Long Wavelength Electronic Absorption Maxima and NH Stretching Frequency of Phenyl Dipyrromethenes.

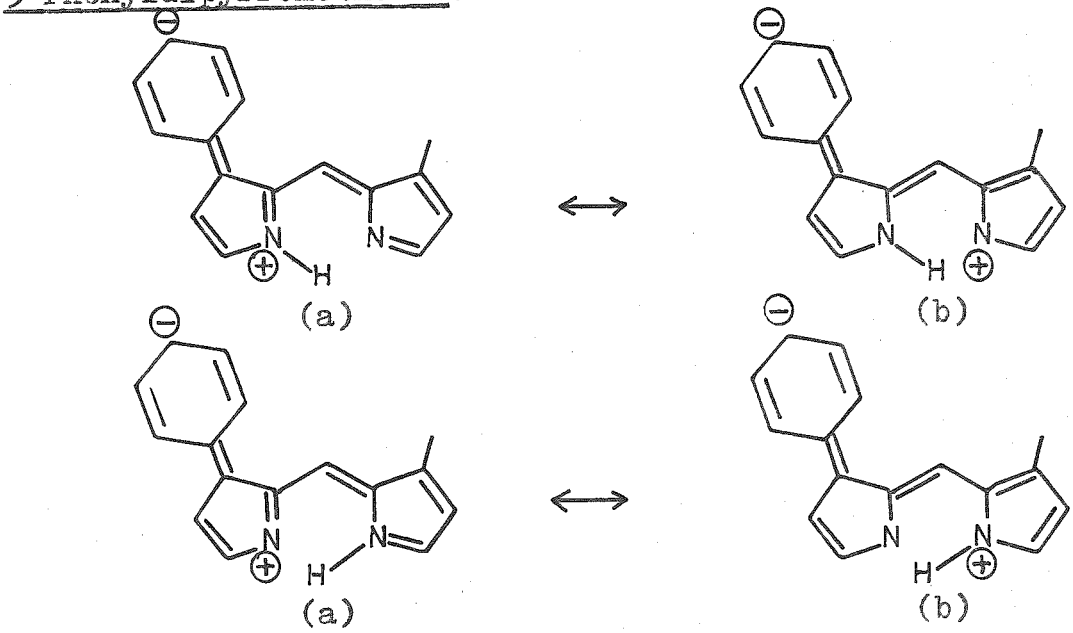
No	Substituent 5	4	3	3'	4'	5'	Solvent*	λ max. mμ	log ε	ν_{NH} cm.$^{-1}$
I	Me	H	Me	Me	H	Me	C	437	4.47	3260
							E	435	4.52	
							H	465	5.03	
II	Me	H	Me	Ph	H	Me	C	448	4.47	3245
							E	443	4.45	
							H	474	4.92	
III	Me	H	Me	Ph	H	Ph	C	474	4.51	3227
							E	467	4.52	
							H	505	4.98	
IV	Me	H	Ph	Ph	H	Me	C	465	4.57	3247
							E	457	4.52	
							H	485	4.90	
V	Me	H	Ph	Ph	H	Ph	C	495	4.51	3232
							E	489	4.53	
							H	521	4.89	
VI	Ph	H	Ph	Ph	H	Ph	C	540	4.60	c. 3200
							E	523	4.64	
							H	561	5.19	
VII	Me	Me	H	Me	H	Me	C	439	4.40	3273
							E	439	4.40	
							H	476	4.80	
VIII	Me	Me	H	Ph	H	Me	C	444	4.41	3280
							E	439	4.40	
							H	489	4.80	
IX	Me	Me	H	Ph	H	Ph	C	474	4.45	3240
							E	470	4.40	
							H	521	4.87	

No.	Substituent 5	4	3	3'	4'	5'	Solvent*	$\lambda_{max.}$ mμ	log ε	ν_{NH} cm.$^{-1}$
X	Me	Me	Me	Me	H	Me	C	434	4.41	3266
							E	433	4.39	
							H	474	4.84	
XI	Me	Me	Me	Ph	H	Ph	C	469	4.46	3226
							E	466	4.44	
							H	513	4.93	
XII	Me	Et	Me	Ph	H	Ph	C	467	4.48	3222
							E	465	4.46	
							H	514	4.91	
XIII	Me	Me	Me	Me	Me	Me	C	444	4.42	3281
							E	442	4.48	
							H	480	4.80	
XIV	Me	Ph	Me	Me	Me	Me	C	448	4.40	3266
							E	444	4.40	
							H	485	4.85	
XV	Me	Ph	Me	Me	Ph	Me	C	453	4.40	3249
							E	446	4.38	
							H	470	4.83	
XVI	Me	Et	Me	Me	Et	Me	C	451	4.40	3279
							E	447	4.53	
							H	483	4.86	
XVII	Me	Et	Ph	Ph	Et	Me	C	463	4.55	3262
							E	457	4.56	
							H	490	5.04	
XVIII	Me	Ph	Me	Ph	Ph	Me	C	476	4.42	3248
							E	470	4.46	
							H	504	4.82	
XIX	Me	Ph	Ph	Ph	Ph	Me	C	479	4.59	3238
							E	476	4.53	
							H	509	4.79	

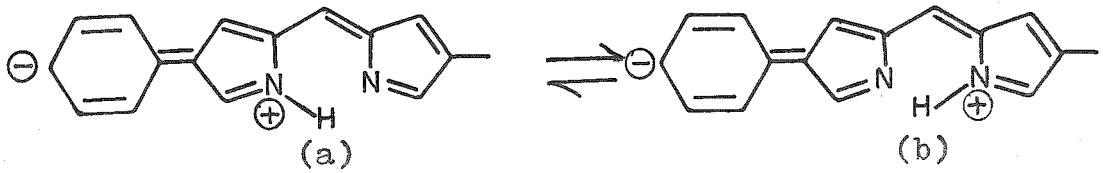
No.	Substituent 5	4	3	3'	4'	5'	Solvent*	λ max. mμ	λ max. log ε	ν NH cm.$^{-1}$
XX	Ph	Ph	Ph	Ph	Ph	Ph	C	535	4.51	c.3190
							E	524	4.50	
							H	561	4.86	

* C, Carbon tetrachloride;
E Ethanol;
H 1N ethanolic hydrogen chloride.

3-Phenyldipyrromethenes.



4-Phenyldipyrromethenes.



5-Phenyldipyrromethenes.

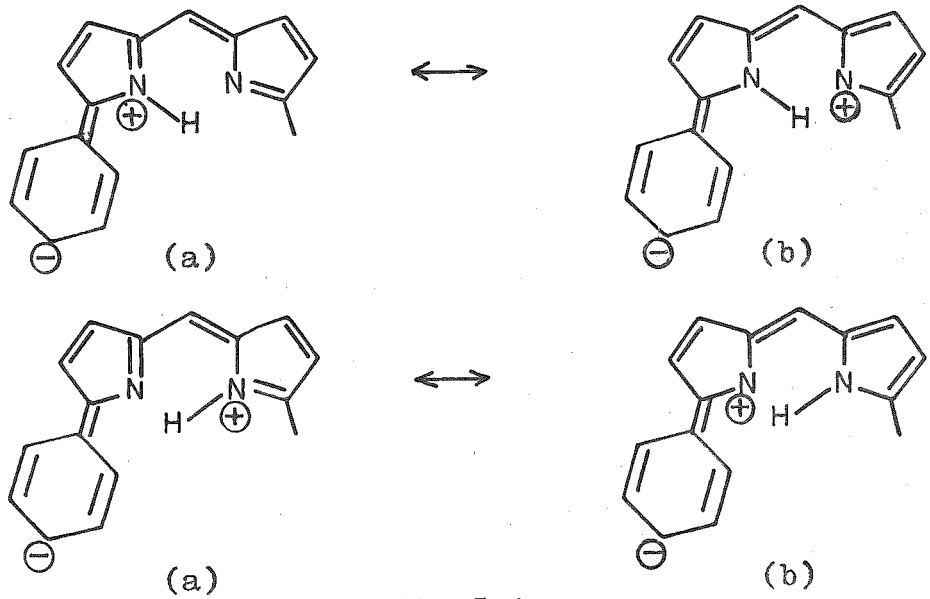


Fig.5.1.

page 44), then the potential energy curve will not have a symmetrical double minimum and hence the strength of the hydrogen bond will be decreased.

The infrared data indicate that some unsymmetrically substituted compounds do have a symmetrical double minimum but others do not (c.f. Kuhn and Kleinspehn[36]). This can be explained by considering the contributing resonance structures with charges on the nitrogen atoms of dipyrromethenes with phenyl substituents in the 3-, 4- and 5-positions. A phenyl group in the 4- or 4'- position increases the acidity of the NH group, but no resonance structure with the positive charge on the other nitrogen atom can be drawn. In contrast, a phenyl group in the 3-, 3'-, 5- or 5'- position reduces the basicity of the nitrogen which acts as the hydrogen acceptor as well. However, as the resonance structures (b) with the positive charge on this nitrogen would contribute less to the actual resonance structure than the other canonical forms,[36] the electron-withdrawing effect on each nitrogen will not be equal. Nevertheless, unsymmetrical substitution of the 4- and 4'-positions would be expected to reduce the symmetry of the potential energy curve for the NH stretching mode more than unsymmetrical substitution in the 3- and 3'- or 5- and 5'-positions. The same approach can be applied to dipyrromethenes with electron-donating substituents except in

this case the resonance structures have negative charges on the nitrogen atoms, and 4(4')-substitution will weaken the hydrogen bond by reducing the acidity of the NH group as well as by reducing the symmetry of the potential energy curve (c.f. the opposing effects of an electron-withdrawing substituent). This would explain the high NH stretching frequencies of the 4,5,3',5'-tetrasubstituted dipyrromethenes compared with the corresponding 3,5,3',5'-tetrasubstituted compounds (Table 5.1., I and VII, II and VIII, III and IX). If only compounds with symmetrical arrangement of substituents are considered, the difficulties of assessing the influence of asymmetry on the spectra can be avoided.

The replacement of both 3- and 3'- methyl groups by phenyl groups generally results in a decreased NH frequency of c. 12 cm^{-1} (Table 5.1., I and IV, XV and XIX, XVII and XVII, and Table 5.2. VII and IX). The insertion of phenyl substituents in the 4- and 4'- positions of symmetrical 3,5,3',5'-tetrasubstituted dipyrromethenes results in a decrease in NH frequency of c. 10 cm^{-1} (Table 5.1., I and XV, IV and XIX, VI and XX) and insertion of alkyl substituents increases the frequency by c. 20 cm^{-1} (Table 5.1., I and XIII, I and XVI, IV and XVII). It follows, therefore, that the decrease of 10 cm^{-1} is equivalent to a decrease of c. 30cm^{-1} if methyl groups had been replaced (c.f. the actual case

of XIII and XV where the observed shift is 32 cm^{-1}). This greater decrease in NH frequency caused by 4,4'-phenyl groups compared to 3,3'-phenyl groups can be explained by considering the resonance structures shown in Fig. 5.1 (each tautomer will contribute equally to the resonance hybrid in the case of symmetrical diphenyl compounds) but is also consistent with the twisting of the 3,3'-phenyl groups from coplanarity.

The resonance structures depicted in Fig. 5.1. suggest that 3(3')- and 5(5')-phenyl substituents will effect the NH frequency to a similar extent. However, phenyl substitution in the 5- and 5'-positions is observed to decrease the NH frequency much more than substitution in the 3- and 3'- positions (c.f. IV and VI, XIX and XX). This also suggests that the 3(3')- phenyl groups are twisted. (The NH bands of the 5,5'-diphenyldipyrromethenes are very broad and of low intensity and these features are characteristic of strong intramolecular hydrogen bonds which can become part of an extended resonance system.[13])

The electronic spectra of phenyl pyrroles (Table 3.3.) show that phenyl substituents in the α-position conjugate strongly with the pyrrole ring and produce large bathochromic shifts. On the other hand, β-phenyl substituents have smaller effects on the electronic spectra, particularly

when they are adjacent to other phenyl groups (c.f. 2,5-diphenylpyrrole, 2,3,5-triphenylpyrrole and 2,3,4,5-tetraphenylpyrrole). The dipyrromethene spectra show similar characteristics. Replacement of 5- and/or 5'- methyl substituents by phenyl groups causes large bathochromic shifts of the long wavelength absorption band (c. 30 mμ) whereas replacement in the 3,3'-positions generally causes much smaller shifts which vary in both direction and magnitude. Whether the shift is bathochromic or hypsochromic seems to depend on whether the phenyl groups are adjacent (either on the pyrrole rings or in the 3- and 3'- positions) and this type of dependence would be expected if the phenyl groups twist out of plane. The identical band positions observed for 3,5,3',5'-tetraphenyldipyrromethene and 3,4,5,3',4',5'-hexaphenyldipyrromethene and the lower band intensities of the latter also indicate that adjacent phenyl groups are twisted.

The effect on the electronic spectra caused by the replacement of the 4- and/or 4'- methyl groups in 3,4,5,3',4',5'-hexamethyldipyrromethene by phenyl groups is very similar to that observed when the methyl groups are replaced by ethoxycarbonyl substituents. In particular, the small bathochromic shift of the long wavelength band on protonation of the 4,4'-diphenyl compound is as expected for electron-withdrawing groups in the 4,4'-positions (c.f.

Tables 5.3. and 4.3.).

Table 5.2. records the spectral data for dipyrromethenes with phenyl, methyl and ethoxycarbonyl substituents. The spectral data are difficult to interpret as most of the compounds have an unsymmetrical arrangement of substituents but some information on the effect of adjacent phenyl and ethoxycarbonyl substituents can be obtained. The NH stretching frequencies and electronic spectra of XXI, XXII and XXIII show the normal shifts observed for substitution of phenyl groups in the 3- and 5- positions. The spectral data of XXIV, XXV, and XXVI show no features which suggest that the dipyrromethene skeleton is distorted and any interaction between the phenyl and ethoxycarbonyl groups is probably relieved by twisting one or both groups out of plane. The reason for the greatly increased NH frequency of XXIV is not clear but appears to be characteristic for dipyrromethenes with this arrangement of methyl and phenyl substituents (c.f. VIII). However, the reduction in NH frequency caused by the 3-ethoxycarbonyl group in XXIV is normal (c.f. VIII and XXIV, IX and XXV).

An examination of Tables 5.3. and 5.4. shows that there is little interaction between 3(3')- phenyl and 4(4')-ethoxycarbonyl groups. Ethoxycarbonyl groups in the 4- and 4'- positions of both 5,5'-dimethyl-3,3'-diphenyldipyrromethene (I) and 3,5,3',5'-tetramethyldipyrromethene

Table 5.2. Long Wavelength Electronic Absorption Maxima and NH Stretching Frequency of Ethoxycarbonyl Phenyl Dipyrromethenes.

No.	Substituent 5	4	3	3'	4'	5'	Solvent*	$\lambda_{max.}$ mμ	log ε	ν_{NH} cm.$^{-1}$
XXI	Me	H	Me	Me	Cbe	Me	C	427	4.47	3243
							E	415	4.46	
							H	461	4.99	
XXII	Me	H	Ph	Me	Cbe	Me	C	450	4.54	3225
							E	448	4.40	
							H	472	4.72	
XXIII	Ph	H	Ph	Me	Cbe	Me	C	487	4.64	3211
							E	475	4.43	
							H	513	5.04	
XXIV	Me	H	Ph	Cbe	Me	Me	C	463	4.51	3264
							E	459	4.56	
							H	483	4.90	
XXV	Ph	H	Ph	Cbe	Me	Me	C	508	4.49	3215
							E	508	4.49	
							H	544	4.98	
XXVI	Ph	H	Ph	Cbe	Me	Cbe	C	463	4.38	3216
							E	453	**	
							H	516	**	
XXVII	Me	Cbe	Me	Me	Cbe	Me	C	451	4.63	3220
							E	452	4.55	
							H	465	5.06	
XXVIII	Me	Cbe	Ph	Me	Cbe	Me	C	459	4.61	3214
							E	463	4.48	
							H	474	5.03	

No.	Substituent 5	4	3	3'	4'	5'	Solvent*	λ_{max} mμ	log ε	ν_{NH} cm.$^{-1}$
XXIX	Me	Cbe	Ph	Ph	Cbe	Me	C	467	4.51	3210
							E	472	4.56	
							H	483	5.01	

* C, Carbon tetrachloride;
E, ethanol;
H, 1N ethanolic hydrogen chloride

** Not stable in ethanol.

Table 5.3. Electronic Effect of Substituents in the 4,4'-Positions of 3,5,3',5'-Tetramethyldipyrromethene.

4,4'-Substituent	ν_{NH} cm.$^{-1}$	$\lambda_{max.}$ (Base) (mμ)	$\lambda_{max.}$ (Protonated Species) (mμ)	Δ^*
Ethyl	3279	447	483	36
Hydrogen	3260	435	463	28
Phenyl	3249	446	470	24
Ethoxycarbonyl †	3220	452	465	13

Table 5.4. Electronic Effect of Substituents in the 4,4'-Positions of 5,5'-dimethyl-3,3'-diphenyldipyrromethene.

4,4'-Substituent	ν_{NH} cm.$^{-1}$	λ_{max} (Base) (mμ)	λ_{max} (Protonated Species) (mμ)	Δ^*
Ethyl	3262	457	490	43
Hydrogen	3247	457	485	28
Phenyl	3239	476	509	23
Ethoxycarbonyl †	3210	472	483	11

*$\Delta = \lambda_{max.}$ (Protonated Species) - $\lambda_{max.}$ (Base)

† (C=O (cm.$^{-1}$) = 1710 cm.$^{-1}$)

(IV) decrease the NH frequency by c. 40 cm^{-1} and have the same carbonyl stretching frequency (1710 cm^{-1}). Protonation of both diethoxycarbonyldipyrromethenes also results in unusually small bathochromic shifts of the long wavelength electronic absorption bands.

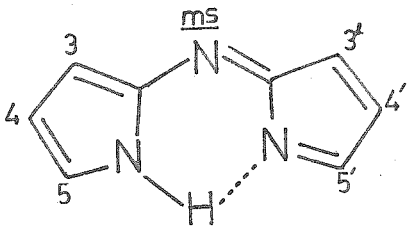
It is clear from the present study that steric interaction between phenyl substituents in the 3- and 3'- positions is relieved by rotation of the phenyl rings and not by distortion of the dipyrromethene skeleton, but no detailed analysis of the spectra of phenyldipyrromethenes is possible from the data available. In the foregoing discussion only the general features of the spectra have been considered and there are several anomalies which are difficult to understand. The examination of more compounds is necessary before these could be explained but it is doubtful if many of the more simply substituted dipyrromethenes, particularly the mono-substituted compounds, could be prepared and hence a complete interpretation of the effect of phenyl substituents on the spectra would still be difficult.

CHAPTER 6.

3,5,3',5'-TETRAARYLAZADIPYRROMETHENES.

6.1. Introduction.

The azadipyrromethenes* (a) are closely related to the dipyrromethenes, the meso CH group of the latter having been replaced by a nitrogen atom.



(a)

Only 3,5,3',5'-tetraaryl and 5,5'-diaryl derivatives of azadipyrromethene have been prepared and their properties differ markedly from those of the corresponding dipyrromethenes.[54,81] It was hoped that a comparison of the spectra of the tetraaryl- and diaryl- azadipyrromethenes would provide information on the steric effects of 3,3'-substituents but the anomalous behaviour of the latter compounds prevented this approach.

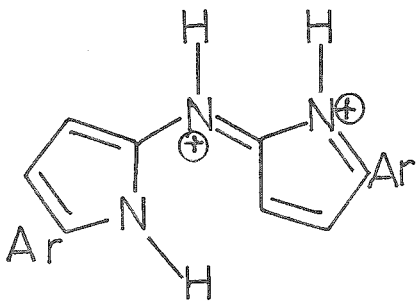
Replacement of the methine carbon (-CH=) by the more electronegative imino nitrogen (-N=) in the dipyrromethene system would be expected to reduce the basicity, and in fact 3,5,3',5'-tetraphenylazadipyrromethene hydrochloride is unstable and rapidly converts to the base in air, whereas the corresponding dipyrromethene is stable both as the base

---

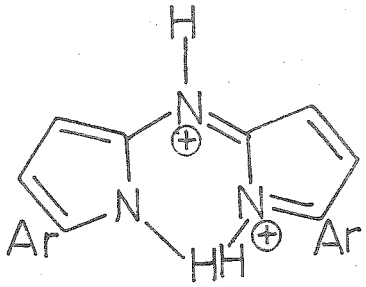
* 2-(2-pyrrolylimino)-2H-pyrrolenines

and the salt. (Most dipyrromethenes are more stable as the salt than the free base.) On the other hand, the 5,5'-diarylazadipyrromethenes exist only in the mono- or di-protonated forms and the bases have never been isolated.

In a previous investigation[82] it was suggested that the diarylazadipyrromethene salts exist in the trans-configuration (b) which would have less steric interaction than the normal "cis" arrangement (c). (Models indicate that the tetraaryl compounds would be more crowded in the "trans" configuration.)



(b)



(c)

Further work is necessary to determine the exact structures of the 5,5'-diaryldipyrromethenes and only the tetraaryl compounds are considered in the present discussion.

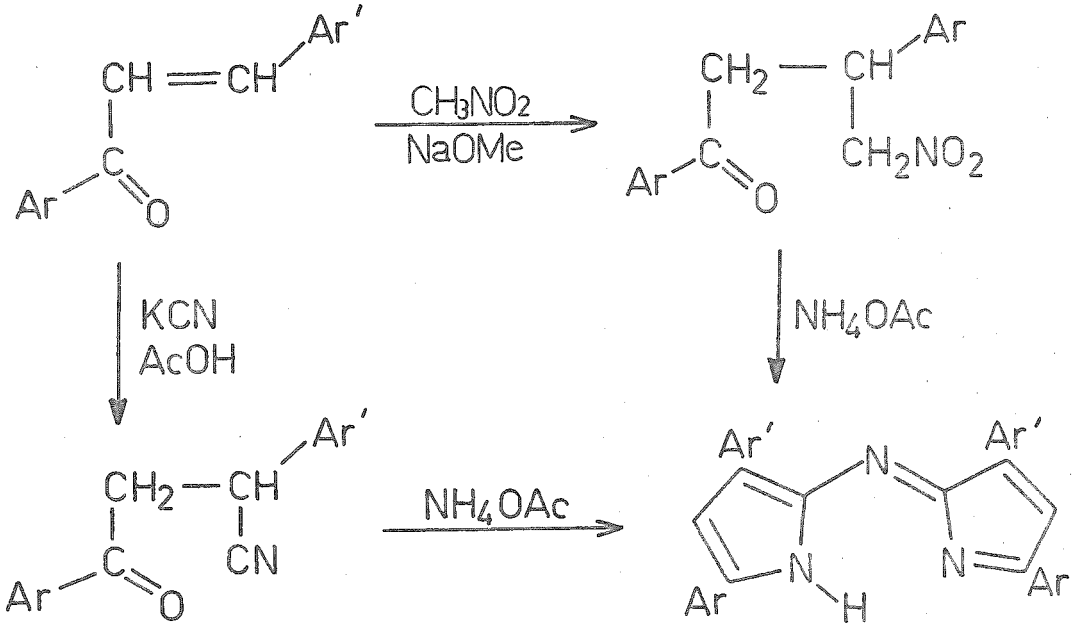
6.2. Preparation of Compounds.

Nitroketones of the type $ArCOCH_2CH(CH_2NO_2)Ar'$, and cyanoketones of the type $ArCOCH_2CH(CN)Ar'$, when fused with ammonium acetate readily give 3,5,3',5'-tetraarylazadipyrro-

methenes. The cyanoketones, but not the nitroketones, can also be converted to azadipyrromethenes by heating with hydroxylamine hydrochloride in a suitable solvent[81] and this method is used to prepare the 5,5'-diaryl compounds (from $ArCOCH_2CH_2CN$). The mechanisms and the scope of these unusual reactions have been discussed by Rogers[54,83] and Knott,[81] Further investigations[82] have confirmed that azadipyrromethenes with alkyl substituents in the 5,5'-positions cannot be prepared by either method, and that only tetraarylazadipyrromethenes can be prepared by the ammonium acetate reaction.

Tetraarylazadipyrromethenes can also be synthesized by condensing a 2-nitroso-3,5-diarylpyrrole with a 2,4-diarylpyrrole (c.f. the aldehyde synthesis of dipyrromethenes) but all attempts to condense the nitrosopyrrole with more reactive pyrroles, such as 2,3,4-trimethylpyrrole and 3-ethoxycarbonyl-2,4-dimethylpyrrole, failed.[82] The failure to isolate any alkylazadipyrromethenes is probably due to the extreme instability of these compounds.

The 3,5,3',5'-tetraarylazadipyrromethenes described in the present work were prepared by fusion of a cyanoketone or nitroketone (prepared from the appropriate chalcone) with an excess of ammonium acetate (Scheme 6.1). All the compounds obtained were very stable and many sublimed at atmospheric pressure with little decomposition.



Scheme 6.1.

6.3. Results and Discussion.

Scale drawings and molecular models of 3,5,3',5'-tetraphenyldipyrromethene indicate that the 3,3'-phenyl substituents interact with each other and the meso hydrogen atom. The replacement of the meso CH group by a nitrogen atom should result in shorter bridge bonds[84] (c.f. the bridge bond lengths of porphyrins[65,66] and phthalocyanins[67]) and hence increased steric interaction of the 3,3'-phenyl groups. The relative size of the nitrogen lone-pair may also affect the amount of interaction in the 3,3'-positions. There is some disagreement in the literature as to the

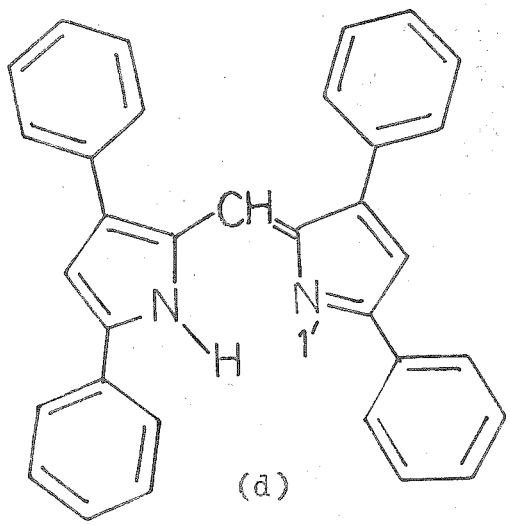
steric requirements of the nitrogen electron-pair (in sp^3 hybridization), and the volume occupied by these electrons has been estimated as both greater[85,86] and less[87] than the volume occupied by the electrons of a CH bond. However, most of the evidence indicates that the nitrogen lone-pair and the electrons of the CH bond have somewhat similar steric requirements. If it can be assumed that the same size relationships apply in the case of sp^2 hybridization, then the replacement of the methine group by an imino nitrogen in the dipyrromethene system should not alter the steric interaction of the 3,3'-substituents to any great extent.

Table 6.1. The Spectra of 3,5,3',5'-Tetraphenyldipyrromethene and 3,5,3',5'-Tetraphenylazadipyrromethene.

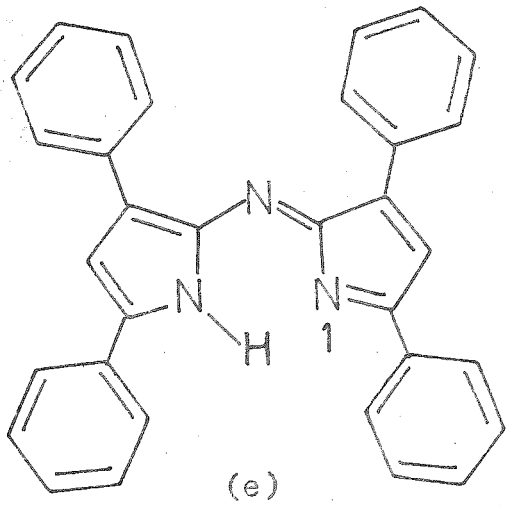
Compound	$CHCl_3$		$CHCl_3$/HCl		ν_{NH} (cm^{-1})
	λ(mμ)	logϵ	λ(mμ)	logϵ	
Dipyrromethene (d)	298 533	4.70 4.62	296 561	4.69 5.10	3200
Azadipyrromethene (e)	304 600	4.68 4.73	310 631	4.60 5.05	3240

Table 6.1. records the spectral data for 3,5,3',5'-tetraphenyldipyrromethene (d) and 3,5,3',5'-tetraphenylaza-

dipyrromethene (e).



(d)



(e)

The strength of the N-H....N hydrogen bond in the aza-dipyrromethene (as shown by the NH stretching frequency) is less than in the dipyrromethene. This may be due to the reduced basicity of the 1'-nitrogen atom caused by the imino nitrogen atom (this will be counteracted to some extent by the increased acidity of the NH group) but is also consistent with increased rotation of the 3,3'-phenyl groups (see Chapter 5).

The effect on the electronic spectra of dye systems when methine groups are replaced by imino nitrogen atoms has been examined by Knott[88] who developed a general rule, based on Förster's colour rule,[71] covering structural changes of this type. This rule can be easily applied in the case where nitrogen replaces a methine carbon as, if the carbon atom at which replacement takes place is separated from the

active $\pm$M centres of the auxochromes (the heterocyclic nitrogen atoms in azadipyrromethenes) by an odd number of conjugated atoms, a hypsochromic shift of the long wavelength band results, while separation by an even number of atoms results in a bathochromic shift.[88] The observed bathochromic shift of the long wavelength band of the azadipyrromethene compared to the corresponding band of the dipyrromethene is hence as predicted.

When a chloroform solution of compound (d) or (e) is saturated with hydrogen chloride, the long wavelength band moves c. 30 mμ bathochromically suggesting that both compounds protonate in the same position (the 1'-nitrogen), and that the meso-nitrogen is not protonated under these conditions. This apparent low basicity may be due to steric hindrance by the 3,3'-phenyl groups to a solvated proton approaching the meso-nitrogen, or alternatively, if protonation does occur, the stability of the resulting cation is reduced because solvation is sterically hindered.

Table 6.2. records the electronic spectra of the tetraarylazadipyrromethenes measured in chloroform and chloroform saturated with hydrogen chloride. The majority of compounds were insoluble in the common organic solvents, and chloroform was found to be the most suitable solvent for the spectral measurements although several compounds were only sparingly soluble. The azadipyrromethenes were not very stable in

Table 6.2a. Electronic Absorption Spectra of 5,5'-Diaryl-3,3'-diphenyldipyrromethenes in chloroform.

	Substituents*		$CHCl_3$		$CHCl_3$/HCl	
	3,3'-	5,5'-	λ(mμ)	log ε	λ(mμ)	△**
I	Ph	Ph	305	4.68		
			600	4.73	631	31
II	Ph	C_6H_4Cl-p	311	4.71		
			602	4.67	639	37
III	Ph	C_6H_4Br-p	313	4.76		
			609	4.70	641	31
IV	Ph	C_6H_4Me-p	314	4.63		
			612	4.67	646	34
V	Ph	C_6H_4NHAc-p	328	†		
			617	†	(627)††	(10)
VI	Ph	BiPh	338	4.55		
			621	4.58	672	51
VII	Ph	Naphth.	308	4.42		
			340	4.49		
			350	4.48		
			621	4.59	672	51
VIII	Ph	C_6H_4OMe-p	320	4.59		
			623	4.68	678	55

* Ph = phenyl, BiPh= 4-biphenylyl, Naphth= 2-naphthyl.

** $\triangle = \lambda(CHCl_3/HCl) - \lambda(CHCl_3)$

† Compound not sufficiently soluble for accurate intensity measurements.

†† The acetamido group is possibly hydrolysed under these conditions. (EtOH present in $CHCl_3$).

Table 6.2b. Electronic Absorption Spectra of 3,5,3',5'-Tetraarylazadipyrromethenes in chloroform.

	Substituents		$CHCl_3$		$CHCl_3/HCl$	
	3,3'-	5,5'-	λ(mμ)	log ε	λ(mμ)	△
IX	C_6H_4Cl-p	Ph	306	4.61		
			604	4.66	636	32
X	C_6H_4Me-p	Ph	306	4.62		
			602	4.71	634	32
XI	Naphth	Ph	300	4.62		
			333sh	4.32		
			610	4.60	645	35
XII	C_6H_4OMe-p	Ph	306	4.61		
			608	4.75	642	34
XIII	$C_6H_4NO_2$-m	Ph	302	4.61		
			608	4.67	632	24
XIV	C_6H_4Cl-p	C_6H_4Me-p	314	4.71		
			610	4.77	644	34
XV	C_6H_4Me-p	C_6H_4Me-p	314	4.67		
			612	4.68	648	36
XVI	C_6H_4Cl-p	C_6H_4Ome-p	324	4.63		
			626	4.74	680	54
XVII	C_6H_4OMe-p	C_6H_4Ome-p	324	4.59		
			626	4.70	680	54

Table 6.2c. Electronic Absorption Spectra of Azadipyrromethenes with 3,3'-p-Dimethylaminophenyl Substituents.

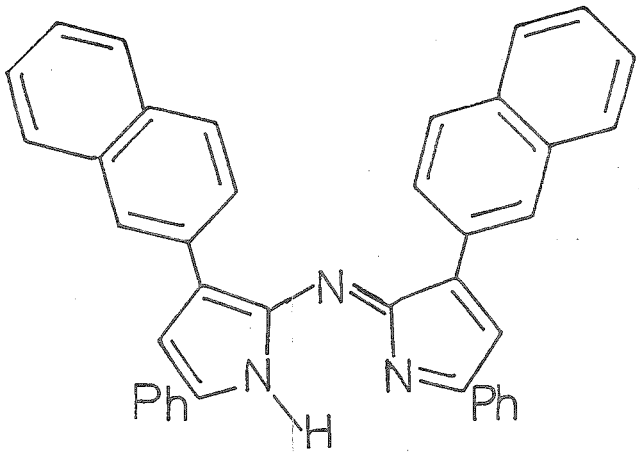
	Substituents		$CHCl_3$ ≠		$CHCl_3/HCl$ ≠	△
	3,3'-	5,5'-	λ(mμ)	log ε	λ(mμ)	
XVIII	$C_6H_4NMe_2$-p	Ph	303	4.70		
			532	4.38	600	-
			625	4.52	638	-
XIX	$C_6H_4\overset{+}{N}Me_3I^-$-p	Ph	305	≠		
			609	≠	643	34
XX	$C_6H_4NMe_2$-p	C_6H_4OMe-p	324	4.65		
			540	4.42	623	-
			643	4.57	697	-
XXI	$C_6H_4\overset{+}{N}Me_3I^-$-p	C_6H_4OMe-p	322	≠		
			635	≠	699	64

≠ Compound not sufficiently soluble for accurate intensity measurements.

≠ Ethanol added for solubility in XIX and XXI.

ethanolic hydrogen chloride (and several were not soluble in this solvent) and the spectra in acid solution were determined by saturating the chloroform solutions with dry hydrogen chloride. These solutions were slightly more stable but were not completely satisfactory as decomposition still occurred, and the spectra could not be measured in different acid concentrations. The azadipyrromethenes showed two bands of similar intensity near 300 and 600 mμ, and in chloroform-hydrogen chloride the long wavelength band increased in intensity and shifted bathochromically, but was much broader and more symmetrical than the corresponding band of the protonated dipyrromethenes.

The introduction of substituents into the 3(3')-phenyl rings of 3,5,3',5'-tetraphenylazadipyrromethene has little effect on the spectra (Table 6.2b) and the small shifts observed show no obvious relationship to the type of substituent. None of the substituents in the 3,3'-phenyl rings would have any steric effect and the 2-naphthyl groups (XI) should also have the same steric requirements as phenyl substituents, and any spectral shifts due to the substituents will be caused by electronic factors.



XI

If the 3,3'-phenyl substituents in the azadipyrromethenes are twisted out of plane (c.f. the phenyldipyrromethenes) then substitution in these phenyl groups would not be expected to cause any large changes in the visible region of the spectra. The data recorded in Table 6.2b are hence consistent with the twisting of the phenyl groups from planarity.

The introduction of p-substituents into the 5,5'-phenyl rings (Table 6.2a) causes both bands to shift bathochromically. As these aryl groups are conjugated strongly with the azadipyrromethene system some correlation between the spectral shifts ($\Delta\lambda_{max.}$) and the electronic effect of the substituents could be expected. An approximate relationship between $\Delta\lambda_{max.}$ of the x-band and the appropriate Hammett σ constants of substituents in the phenyl group of malachite green has been established,[89] and a similar correlation of the displacement of the

primary (203.5 mμ) band of monosubstituted benzenes with the $\Delta\sigma$ values of the substituents has also been shown.[90] ($\Delta\sigma = \sigma p - \sigma m$ and is an approximate measure of the resonance effect of the substituent.[14]) As the long wavelength band of the tetraarylazadipyrromethenes shifts bathochromically for both electron-withdrawing and electron-donating substituents it is likely that the shift is related to the resonance effect (given by $\Delta\sigma$) of the substituents. The displacement of the long wavelength band plotted against the $\Delta\sigma$ value of the substituent (Fig. 6.1.) shows an approximate relationship, $\Delta\lambda$ increasing with $\Delta\sigma$, but data for more compounds are necessary before any definite relationship could be established.

The long wavelength band generally shifts c.30 mμ bathochromically when the azadipyrromethenes are measured in acid solution ($CHCl_3$/HCl). However, compounds VIII, XVI, XVII, VI and VII (Table 6.2.) show larger shifts (c.55 mμ) and this may be due to the greater conjugating effect of these substituents resulting in a more stable azadipyrromethene salt. (These compounds decomposed relatively slowly in acid solution.)

The introduction of p-dimethylamino substituents into the 3,3'-phenyl rings (Table 6.2c.) does not alter the band near 300 mμ but causes a bathochromic shift and decreases the intensity of the long wavelength band, and an additional

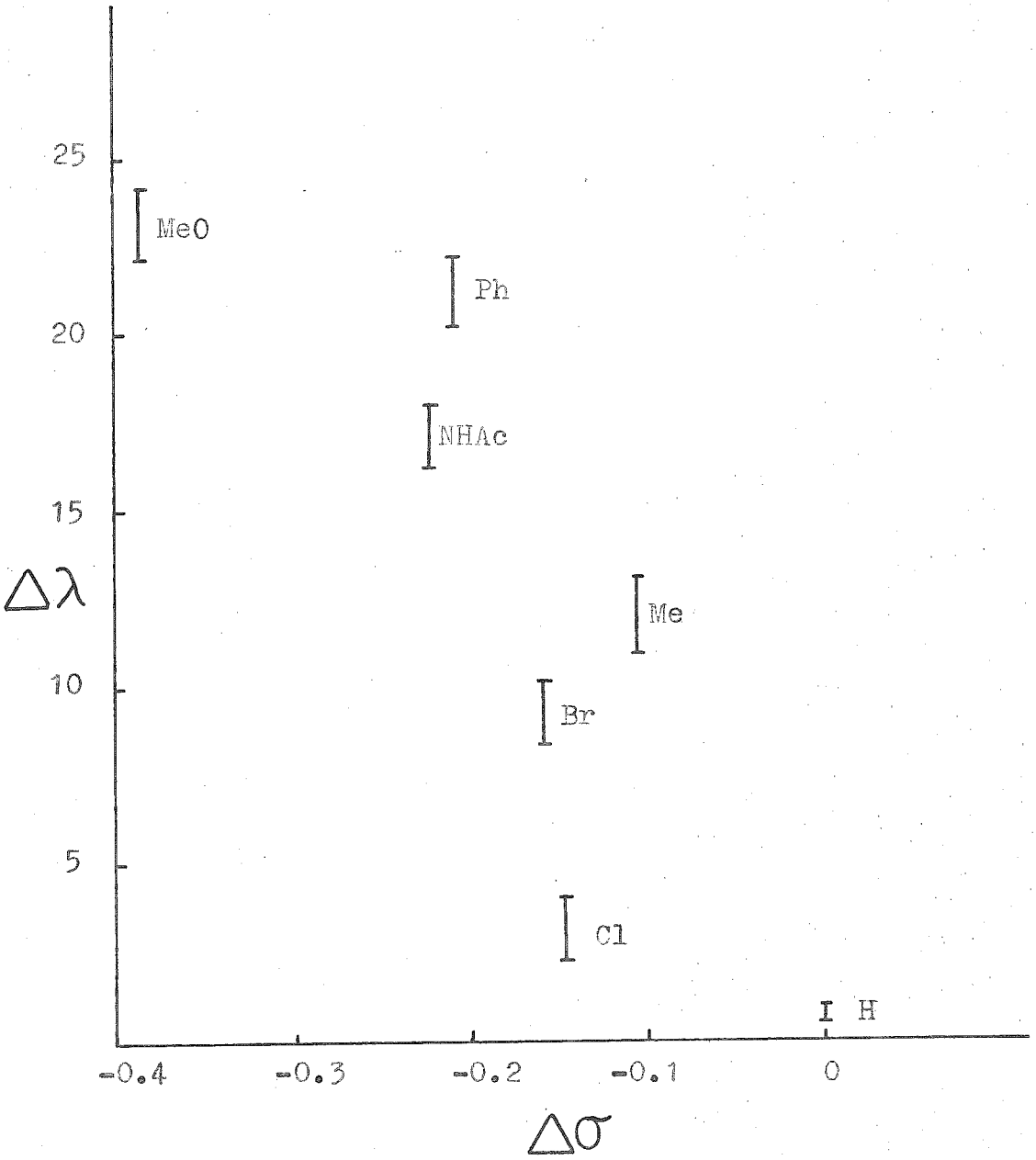
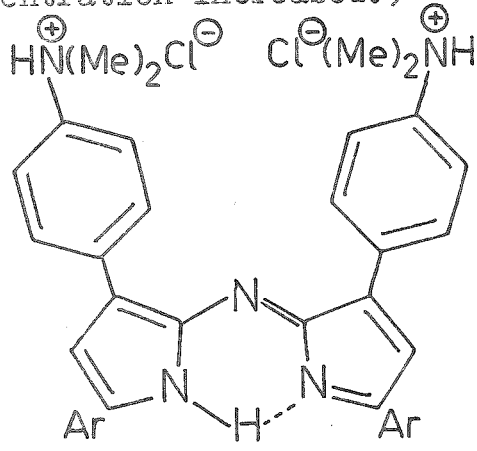
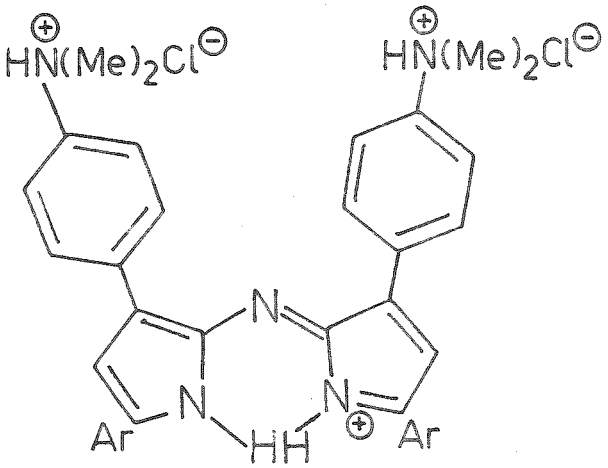


Fig. 6.1. The displacement of the long wavelength band of tetraarylazadipyrromethenes plotted against the $\Delta\sigma$ values of the p-substituents in the 5,5'-phenyl rings.

band near 530 mμ is observed. The spectra of the dimethiodides XIX and XX, however, closely resemble the corresponding 3,3'-diphenyl compounds (the slight spectral differences are probably due to the ethanol added for solubility). The spectra of XVIII and XX measured in chloroform-hydrogen chloride solution suggest that a mixture of the two protonated forms XXII and XXIII is present under these conditions. (Compound XVIII was also measured in ethanolic hydrogen chloride and the band at 600 mμ disappeared as the acid concentration increased.)



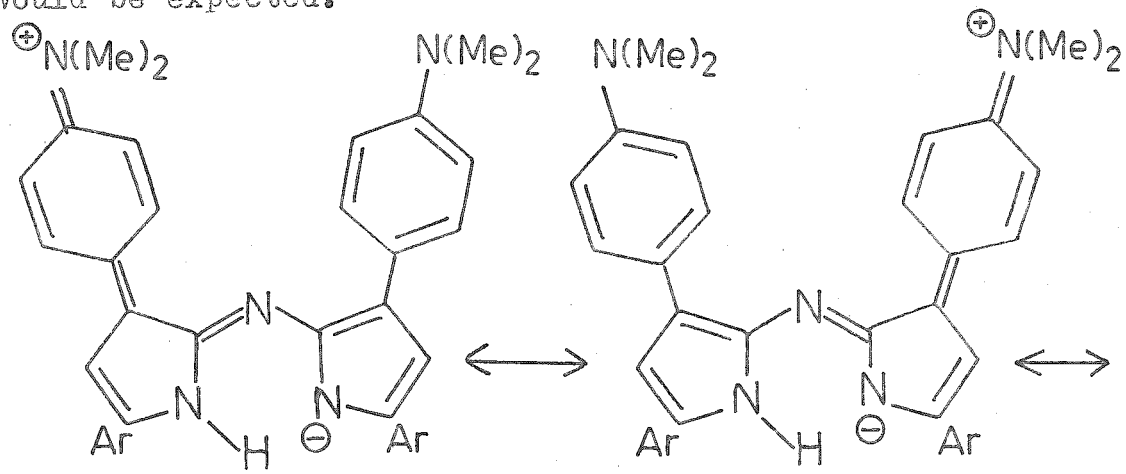
XXII



XXIII

These results show that the anomalous effect of the 3(3')-p-dimethylaminophenyl group is due to strong conjugation with the azadipyrromethene system, as the anomalies disappear when the lone-pair of the amino group is involved in bond formation. Strong conjugation of the 3,3'-aryl group would increase the double-bond character of the bond between the pyrrole ring and the aryl group (see Scheme 6.2.) and

hence increase the energy required to twist the aryl groups from planarity. If, as a consequence, the steric strain in the molecule was relieved by twisting the heterocyclic nuclei from coplanarity, a bathochromic shift and decrease in intensity of the long wavelength band similar to that observed would be expected.



Scheme 6.2.

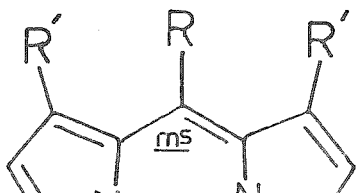
Little information on the effect of the aryl substituents could be obtained from the infrared data. The NH stretching frequencies of the tetraarylazadipyrromethenes all occurred near 3240 cm^{-1} but the breadth and low intensities of the bands prevented any assessment of the shifts caused by the substituents.

CHAPTER 7.

A PRELIMINARY STUDY OF DIPYRROMETHENES WITH *meso*-SUBSTITUENTS.

7.1. Introduction.

In order to obtain further information on the way in which dipyrromethenes accommodate steric crowding, the spectra of a number of meso-substituted compounds were examined. In the preceeding chapters steric interaction between 3- and 3'- substituents was considered and the spectral data showed that little if any distortion of the dipyrromethene skeleton occurred and the strain was usually relieved by bending or twisting the 3,3'-substituents. The introduction of meso-substituents causes much greater steric crowding and it is unlikely that the strain could be taken up by distorting the 3-, 3'- or meso- groups alone, and other modifications such as the alteration of bond angles and twisting of the central methine bonds should result.



I

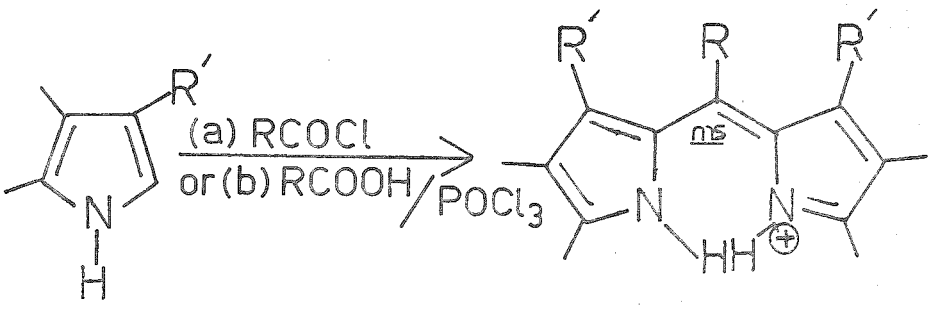
Interaction of the meso- group (R) with the 3,3'-substituents (R') will cause both the bridge bonds to twist i.e. distortion of both an essential single bond and an

essential double bond occurs and the spectral shifts will be the result of opposing hypsochromic and bathochromic effects.[70] On the other hand, twisting of adjacent bonds in a degenerate system, such as a symmetrically substituted dipyrromethene salt, results only in bathochromic shifts.[69] Thus the interpretation of the spectra of the dipyrromethene bases is more difficult, but any distortion of the bridge bonds should be apparent from the decreased intensity of the long wavelength band. In addition, the infrared spectra should show increased NH stretching frequencies due to the weakened N-H....N hydrogen bond.

In this preliminary investigation the spectra of symmetrically substituted dipyrromethenes with phenyl, methyl and ethyl groups in the meso-position were examined.

7.2. Synthesis of meso-substituted dipyrromethenes.

The compounds were prepared by methods analogous to the usual dipyrromethene syntheses. The symmetrical dipyrromethenes were synthesized by heating an α-unsubstituted pyrrole with the appropriate acyl chloride, and in some cases the acyl chloride was prepared *in situ* by heating the pyrrole with a carboxylic acid in the presence of phosphorus oxychloride (Scheme 7.1).

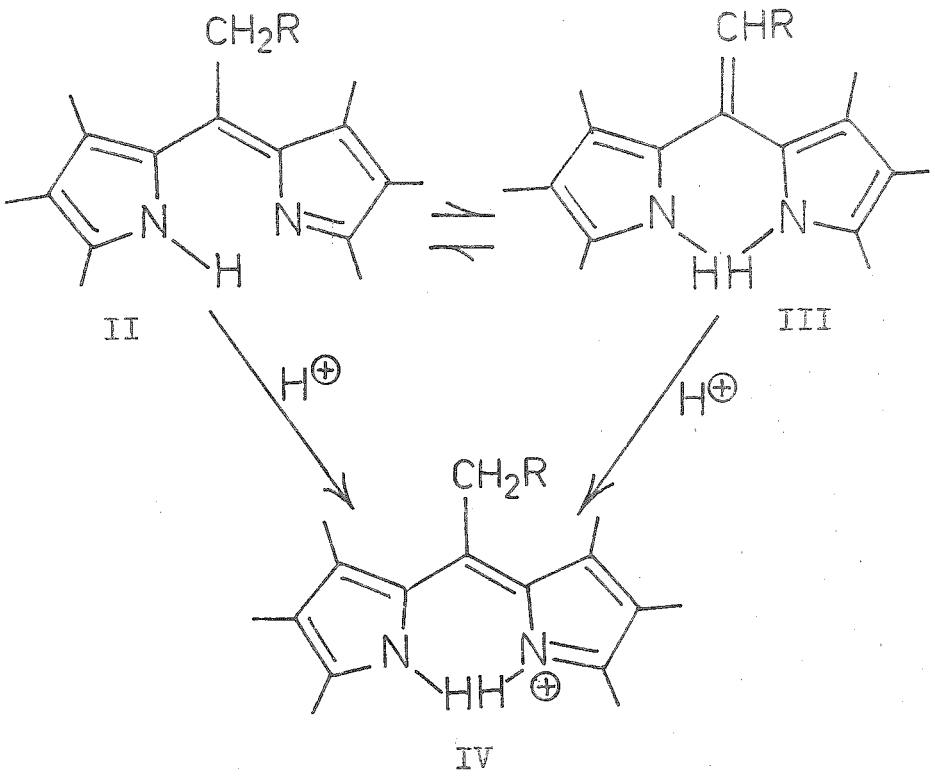


Scheme 7.1.

The unsymmetrical compounds were made by condensing an α-acylpyrrole with an α-unsubstituted pyrrole using phosphorus pentoxide (Scheme 7.2).

Dipyrromethenes with meso-alkyl substituents (II) exhibit tautomerism and can rearrange to the ethylenic structure (III), the relative stabilities of the two tautomers depending on the substituents in the heterocyclic rings and also the meso-substituent.[91,92a] In acid the ethylenic form (III) is converted to the dipyrromethene salt (IV).

The compounds with meso-alkyl substituents prepared in the present work were isolated in the ethylenic form or as the hydrochloride salts. The dipyrromethene hydrochloride obtained from the reaction of 2,4-diphenylpyrrole with acetyl chloride had m.p. 173-175° and thus was the monohydrochloride salt (m.p. 176°) described by Treibs and Hintermeier,[98] and not the dihydrochloride (m.p. 202°) reported by Jeffreys and Knott.[70]



The syntheses of the highly crowded unsymmetrical dipyrromethenes with meso-ethoxycarbonylmethyl ($-CH_2CO_2Et$) groups reported by Filippovich et al.[92] were re-examined in the course of this work. These workers reported that two different dipyrromethenes were obtained from the condensation (using phosphorus pentoxide) of pyrroles V and VI (Scheme 7.2.), and of VII and VIII and inferred that they were the N-isomers* IX and X.

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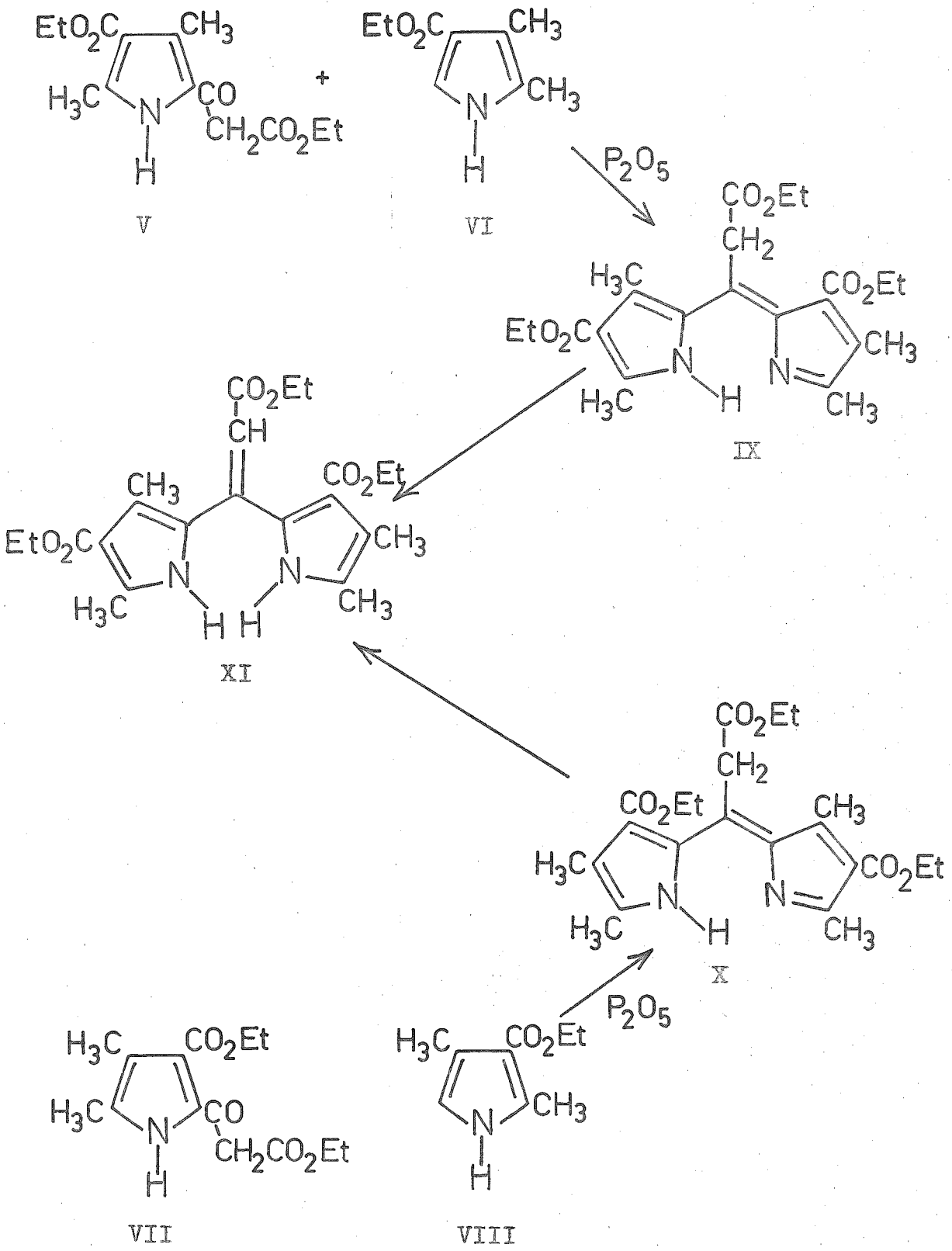
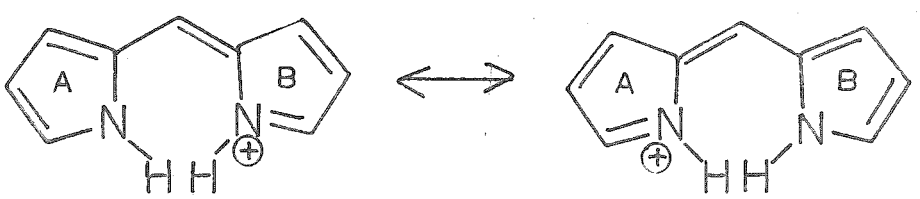
* The term "N-isomers" is used[64] for the two tautomeric forms of a dipyrromethene base (e.g. Scheme 7.2., IX and X).


EtO2C
CH3
H3C
N
H
CO
CH2CO2Et
+
V
VI
P2O5
CO2Et
CH2
IX
X
XI
CH
CH3
CO2Et
CH3
H3C
H H
VII
VIII

Scheme 7.2.

Similar results to those reported by Filippovich[92] were obtained. Small amounts of the dipyrromethenes IX and X were isolated (the structures shown in Scheme 7.3. are those postulated by Filippovich) but were difficult to purify as both tended to rearrange to the ethylenic form in solution. When ammonium hydroxide was added to the reaction mixtures the dipyrrolylethylene XI was isolated and this apparently exists in two forms (m.p. 184-185° from the condensation of V and VI, and m.p. 193-194° from VII and VIII) which may be rotational isomers.

Fischer[93] has suggested the possibility of N-isomerism in dipyrromethenes and reported the isolation of a hydroxy-dipyrromethene in two different forms which may have been N-isomers.[94] However, it is unlikely that N-isomers would normally be obtained as most dipyrromethene syntheses involve initial formation of the salt, and the resonance hybrid of the salt would be the same regardless of the mode of formation (Scheme 7.3.).



Scheme 7.3.

The meso-ethoxycarbonylmethyl compounds under consideration showed several unusual features. Firstly, the free base was isolated directly from the reaction even though phosphoric acid was present, and the colour change from purple to red if ammonium hydroxide was added to the reaction mixture suggested that the dipyrromethene salt was indeed formed. Moreover, the hydrochloride salt (formed from X) was unstable and converted to the ethylenic form XI in air with the loss of hydrogen chloride. The unusual instability of the dipyrromethene salt may be due to severe steric interaction of the 3(3')-ethoxycarbonyl group and the meso-substituent, which inhibits the formation of a planar resonance stabilized cation. Finally, several rotational isomers of the dipyrromethene can be envisaged which are no more strained than the "cis-structures" shown in Scheme 7.2. Thus IX and X might not be N-isomers, but rotational isomers, or possibly both. The structures are discussed further in the next section in the light of their infrared spectra.

7.3. Results and Discussion.

It has been estimated[95,96] that the meso-phenyl substituents of meso-tetraphenylporphin cannot be within 50-60° of being coplanar with the porphin skeleton and X-ray analysis of the copper complex[65] has shown that the phenyl residues are at right angles to the system. The small change in

the NH stretching frequency when meso-phenyl groups are introduced into the porphin molecule[32,97] also indicates that the phenyl rings are twisted. By analogy, meso-phenyl substituents in dipyrromethenes should be twisted out of plane and if the dipyrromethene is substituted in the 3- and 3'-positions the phenyl group could be rotated as much as 90°. In this case the phenyl substituent is electronically isolated from the dipyrromethene system and any spectral shifts will be due solely to its steric effect.

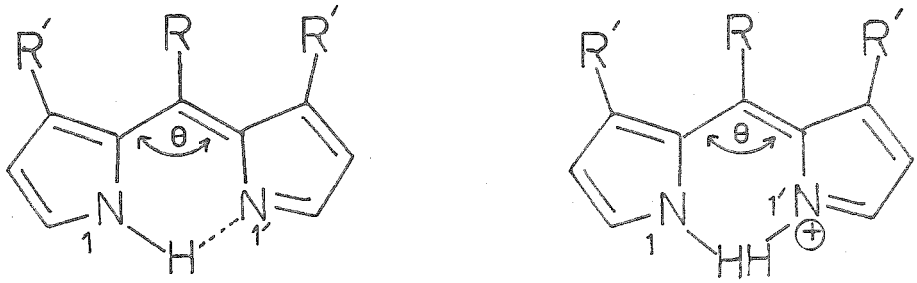
The long wavelength absorption bands of three meso-phenyldipyrromethenes are recorded in Table 7.1. These compounds cannot rearrange to the "ethylenic" form and both the free bases and the salts are stable. Molecular models and scale drawings show that there is significant steric interaction of the meso-phenyl ring with the 3,3'-methyl groups (XIII, XV) even when the phenyl ring is at right angles to the plane of the heterocyclic nuclei. The overcrowding could be relieved in several ways (c.f. page 63); twisting around the central methine bonds, closure of the methine bond angle, (θ) (see Scheme 7.4.), or bending the 3,3'-methyl groups outwards are all possible modifications.

Table 7.1. Long Wavelength Absorption Maxima of meso-Substituted Dipyrromethenes.

	Substituents *							Sol-vent **	$\lambda_{max.}$	
	5	4	3	ms	3'	4'	5'		(mμ)	(log ε)
XII	Me	Me	Me	H	Me	Me	Me	C	444	4.42
								E	442	4.48
								H	480	4.80
XIII	Me	Me	Me	Ph	Me	Me	Me	C	461	4.40
								E	461	4.46
								H	515	4.58
XIV	Me	Cbe	Me	H	Me	Cbe	Me	C	451	4.63
								E	452	4.55
								H	465	5.06
XV	Me	Cbe	Me	Ph	Me	Cbe	Me	C	476	4.62
								E	474	4.60
								H	510	4.78
XVI	Ph	H	Ph	H	Ph	H	Ph	C	540	4.60
								E	523	4.64
								H	561	5.19
XVII	Ph	H	Ph	Ph	Ph	H	Ph	C	550	4.53
								E	543	- ≠
								H	617	4.60
XVIII	Ph	H	Ph	Me	Ph	H	Ph	C	530	4.20
								E	526	- ≠
								H	596	4.62
XIX	Ph	H	Ph	Et	Ph	H	Ph	C	540	4.18
								E	533	- ≠
								H	602	4.47

* Cbe, ethoxycarbonyl ** C, CCl_4; E, 95% EtOH; H, 1N HCl/EtOH

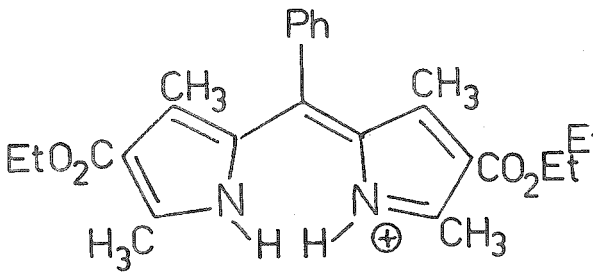
≠ Not sufficiently soluble for accurate intensity measurement.
≠ decomposes.



Scheme 7.4.

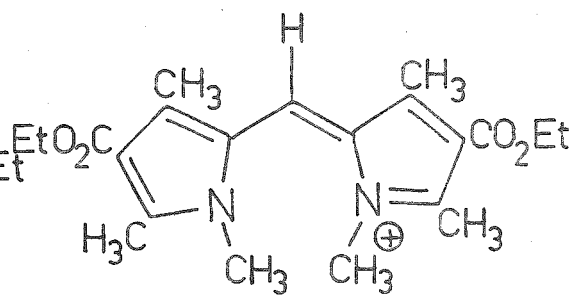
The long wavelength band of XII and XIV shifts c. 20 mμ bathochromically when a meso-phenyl group is introduced. However, the intensity is not significantly altered and this indicates that any distortion of the central methine bonds is slight. On the other hand, the long wavelength band of the protonated compounds shifts c. 50 mμ bathochromically and shows a marked decrease in intensity. Thus the salts appear to be more crowded than the bases and this might be explained as follows. - If the steric strain in the base could be accommodated by closure of the bridge bond angle, (θ), the N-H....N distance would be decreased and the increased symmetry of the molecule would result in a bathochromic shift of the absorption band. An increase in intensity would also be expected but could be counteracted by the hypochromic effect of altering the bridge bond angle. On proton addition, the steric interaction of the 1- and 1'- protons would oppose the closure of the bridge bond angle and force the molecule to relieve the

strain by twisting the bridge bonds resulting in the large bathochromic shift and decrease in intensity observed. Interestingly, the position and intensity of the long wavelength band of XVa and XX[68] are almost identical. As the spectral shifts caused by the N-methyl substituents in XX are mainly due to their steric effect,[69] and the meso-phenyl substituent in XVa is probably electronically isolated from the system, the amount of crowding in these two compounds must be similar and the strain relieved by twisting around the bridge bonds (c.f. Dewar[72]).



XVa.

$\lambda_{max.}$ 510 mμ
log ε 4.78
} EtOH



XX.

$\lambda_{max.}$ 515 mμ
log ε 4.76
} $CHCl_3$

The meso-phenyldipyrromethenes XIII and XV showed complex absorption in the 3400-3000 cm^{-1} region of the infrared spectrum. A broad band with several inflections extended into the CH stretching region and is consistent

with a strengthened and more symmetrical N-H....N hydrogen bond resulting from the closure of the bridge bond angle.

The 3-, 3'- and meso-phenyl substituents of XVII interact even when all the phenyl rings are at right angles to the dipyrromethene system. The large bathochromic shift observed on protonation suggests that XVII is more distorted than XIII or XV, but any comparison with the corresponding meso-hydrogen compound XVI is difficult as the increased rotation of the 3,3'-phenyl rings must be considered. The infrared spectrum of XVII showed a broad very weak band with several inflections in the 3250-3100 cm^{-1} which might be due to strengthened hydrogen bonding, but XVI also showed a broad weak band in this region.

Accurate measurement of the spectra of the meso-alkyldipyrromethene bases was complicated by the ease with which they rearranged to the ethylenic form. Jeffreys and Knott[70] reported that stable solutions of meso-alkyl - 3,5,3',5'-tetraphenyldipyrromethenes could be prepared by adding triethylamine to a solution of the hydrochloride salt in carbon tetrachloride. However, in the present work these dipyrromethenes were found to tautomerize under these conditions and this might explain the very low extinction coefficients reported by the above workers. The intensities recorded in Table 7.1. for XVIII and IX measured in carbon tetrachloride are extrapolated values, zero time being taken as the time of addition of the triethylamine, but are probably

still slightly low. However, it appears that these compounds are more strained than XVII and the small wavelength shifts of the bases may result from the opposing hypsochromic and bathochromic effects of twisting adjacent bonds in a non-degenerate system.[70]

Table 7.2. Long Wavelength Electronic Absorption Band of meso-Substituted Dipyrromethene Hydrochlorides.

Substituents.							$\lambda_{max.}$	
5	4	3	ms	3'	4'	5'	($m\mu$)	(log ϵ)
Me	Cbe	Me	H	Me	Cbe	Me	465	5.06
Me	Cbe	Me	Ph	Me	Cbe	Me	510	4.78
Me	Cbe	Me	Me	Me	Cbe	Me *	483	4.79
Me	Cbe	Me	Et	Me	Cbe	Me *	492	4.68
Ph	H	Ph	H	Ph	H	Ph	561	5.19
Ph	H	Ph	Ph	Ph	H	Ph	617	4.60
Ph	H	Ph	Me	Ph	H	Ph	596	4.62
Ph	H	Ph	Et	Ph	H	Ph	602	4.47

* Prepared *in situ* from the ethylenic form by the addition of acid.

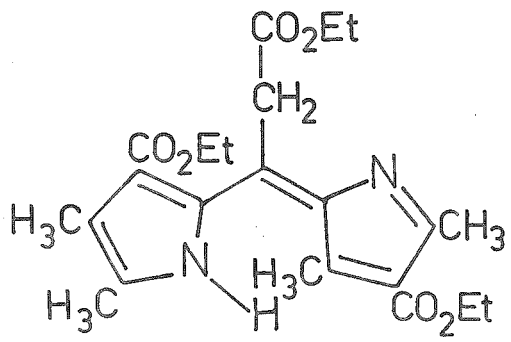
The long wavelength bands of several meso-substituted dipyrromethenes are compared in Table 7.2. The intensities

indicate that a meso- ethyl group has a larger steric requirement than a methyl or phenyl substituent. The greater bathochromic shift caused by the meso-phenyl substituent may be due to the fact that the meso-methyl and ethyl substituents cannot be electronically isolated from the dipyrromethene system to the same extent as the phenyl ring.

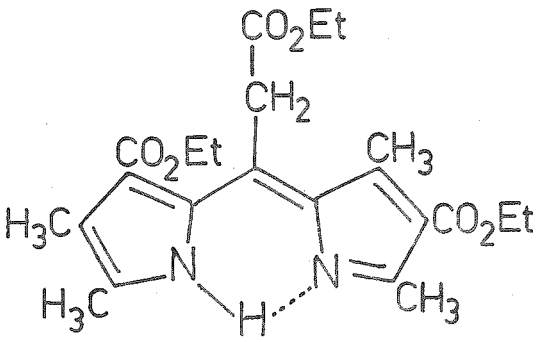
The infrared spectra of the meso-ethoxycarbonylmethyldipyrromethenes (Scheme 7.2., IX and X) showed marked differences in the NH stretching region (c.f. Filippovich[92d]). In dilute carbon tetrachloride IX showed a broad NH band at c. 3240 cm^{-1} characteristic of dipyrromethenes, whereas X showed a sharp band at 3452 cm^{-1}. Filippovich suggested that the NH group of IX was intramolecularly hydrogen bonded to the carbonyl group of the meso-substituent, but as this would involve the formation of a seven-membered hydrogen bonded ring it is doubtful in the NH frequency would be as low as 3240 cm^{-1}. In addition, the carbonyl stretching frequencies of IX and X are the same, and hence a normal dipyrromethene N-H....N hydrogen bond appears more likely. The infrared data indicate that IX and X are rotational isomers, but not necessarily N-isomers, and two possible structures which are not N-isomers are shown below.

The structure of these compounds could be clarified by a more thorough study, but as their anomalous behaviour made them of little value in the present study these compounds

were not investigated further.



IX



X

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CHAPTER 8

EXPERIMENTAL

EXPERIMENTAL

8.1. Physical Measurements.

(1) Melting Points.

Melting points were determined using a Gallenkamp melting point apparatus or a Kofler hot-stage melting point apparatus, and are uncorrected.

(2) Infrared spectra.

The full infrared spectra in the region 4000-800 cm^{-1} were measured for 0.208M solutions in chloroform in matched 0.096mm cells using a Perkin-Elmer model 21 spectrophotometer with sodium chloride optics. The carbonyl stretching frequencies were determined for c. 10^{-4} M solutions in carbon tetrachloride in matched 3mm cells using a Grubb-Parsons S4 double-beam spectrophotometer with a calcium fluoride prism. All measurements were calibrated against polystyrene[99] at 1601, 1028, and 907 cm^{-1}.

The NH stretching frequencies were determined for c.10^{-4} M solutions in carbon tetrachloride in 100 mm cells with a double-beam Unicam SP700 spectrometer equipped with a 7,500 1/in grating, Ge filter and PbS detector. The instrument was calibrated against ammonia.

(3) Electronic Absorption Spectra.

The electronic absorption spectra were measured for c. 5 x 10^{-5} M solutions (in solvents as given in the tables) in 10 mm cells using a Unicam SP700 spectrometer.

8.2. General.

(1) Analyses.

The microanalyses were carried out by the Australian Microanalytical Service, Melbourne (Dr. K.W. Zimmermann).

(2) Chromatography.

The alumina used for chromatography of dipyrromethenes was "grade IV alumina, acid washed." B.D.H. "alumina for chromatography" was washed with 1% hydrochloric acid until the eluate was acidic, then washed with water until the eluate was neutral, dried in an oven at 160° for 12-20 hr and finally deactivated by the addition of 10% by weight of water, distributed evenly by mechanical shaking.

(3) Solvents.

The spectroscopic grade chloroform and carbon tetrachloride used as solvents in the measurement of the electronic absorption spectra were shaken thoroughly with calcium hydroxide and filtered immediately before use.

These solvents when used for infrared measurements were purified by washing twice with concentrated sulphuric acid, then with 10% sodium carbonate solution and finally with water. After drying over magnesium sulphate they were filtered and stored at 0°.

8.3. Pyrroles.

2,4-Diethoxycarbonyl-3,5-dimethylpyrrole. -

The diester was prepared by the method of MacDonald,[100] and was obtained as pale yellow needles, m.p. 136° (lit.[100] m.p. 136°).

3-Ethoxycarbonyl-2,4-dimethylpyrrole-5-carboxylic acid. -

The pyrrole carboxylic acid was obtained as colourless needles, m.p. 202° (lit.[101] m.p. 202°) by the method of Knorr.[101]

3-Ethoxycarbonyl-2,4-dimethylpyrrole. -

The pyrrole was prepared from 3-ethoxycarbonyl-2,4-dimethylpyrrole-5-carboxylic acid by the method of Badger, Harris and Jones,[102] and crystallized from hexane as colourless needles, m.p. 78° (lit.[102] m.p. 75-76°).

4-Ethoxycarbonyl-2-formyl-3,5-dimethylpyrrole. -

A mixture of phosphorus oxychloride (9 ml) in N,N-dimethylformamide (20 ml) was added dropwise with stirring

to a cooled (0°) solution of 3-ethoxycarbonyl-2,4,-dimethylpyrrole (5 g) in N,N-dimethylformamide (40 ml). The mixture was heated on a steam-bath for 1 hr, poured into water (150 ml) and solid sodium acetate added until the solution was neutral to Congo Red. The solution was allowed to stand at 0° overnight, the product collected and recrystallized from ethanol to give 4-ethoxycarbonyl-2-formyl-3,5-dimethylpyrrole (5 g, 86%) as colourless needles, m.p. 165° (lit.[24] m.p. 165°).

2,4-Dimethylpyrrole. -

This compound was prepared by the method of Corwin and Krieble,[103] and was obtained as a colourless oil, b.p. 162-164° (lit.[103] b.p. 72°/25 mm).

2-Formyl-3,5-dimethylpyrrole. -

Phosphorus oxychloride (2 g) in N,N-dimethylformamide (5 ml) was added dropwise with stirring to 2,4-dimethylpyrrole (1 g) in N,N-dimethylformamide (6 ml). The temperature of the reaction mixture was maintained at 0° during the addition. The mixture was allowed to warm to room temperature, then poured into a hot saturated solution of sodium acetate in water and the solution left overnight. The mixture was extracted with ether and evaporation of the extracts gave the aldehyde (1 g, 80%) which was recrystallized from water to yield colourless needles, m.p. 89-90° (lit.[103] m.p. 91°).

4-Ethoxycarbonyl-2,3-dimethylpyrrole-5-carboxylic acid. -

The pyrrole carboxylic acid was prepared by the method of Corwin[103] and formed colourless needles, m.p. 201° (lit.[103] m.p. 201°).

4-Ethoxycarbonyl-2,3-dimethylpyrrole. -

A mixture of 4-ethoxycarbonyl-2,3-dimethylpyrrole-5-carboxylic acid (8 g) and ethanolamine (8 ml) was refluxed under nitrogen for 2 hr and then poured into water. The resulting solid was recrystallized from aqueous ethanol to give 4-ethoxycarbonyl-2,3-dimethylpyrrole (5 g, 80%) as colourless needles, m.p. 110-111° (lit.[24] m.p. 110-111°).

3-Ethoxycarbonyl-2-formyl-4,5-dimethylpyrrole. -

Phosphorus oxychloride (9 g) in dimethylformamide (20 ml) was added dropwise to a cold stirred solution of 4-ethoxycarbonyl-2,3-dimethylpyrrole (5 g) in dimethylformamide (40 ml). The mixture was heated on a steam-bath for 2 hr and then poured into a hot saturated solution of sodium acetate in water. The formylpyrrole (5.5 g, 91%) separated from the cold mixture and was recrystallized from ethanol to give colourless needles, m.p. 129° (lit.[24] m.p. 129°).

2,3-Dimethylpyrrole. -

The pyrrole was prepared by the method of Corwin and Krieble[103] and was obtained as a colourless oil, b.p.65°/14mm.

(lit.[103] b.p. 72°/25 mm).

2-Formyl-4,5-dimethylpyrrole. -

Phosphorus oxychloride (2 ml) in dimethylformamide (5 ml) was added dropwise to a cold stirred solution of 2,3-dimethylpyrrole (1 g) in dimethylformamide (6 ml), allowed to warm to room temperature, then poured into a hot, saturated solution of sodium acetate in water and the solution left at 0° overnight. The solution was extracted with ether. Evaporation of the dried ether extracts and crystallization of the residue from water gave 2-formyl-4,5-dimethylpyrrole (0.9 g, 75%) as colourless needles, m.p. 126-127° (lit.[103] m.p. 127.5-128°).

2-Ethoxycarbonyl-3,4,5-trimethylpyrrole. -

This compound was prepared by the method of Badger, Harris and Jones[38] and was obtained as colourless needles, m.p. 128° (lit.[38] m.p. 127-128°).

Potassium 3,4,5-trimethylpyrrole-2-carboxylate. -

The potassium salt was prepared from 2-ethoxycarbonyl-3,4,5-trimethylpyrrole by the method of Badger *et al.*[32]

2,3,4-Trimethylpyrrole. -

This compound was prepared by the method of Treibs and Zinsmeister,[104] and obtained as colourless plates, m.p. 38-39°

(lit.[104] m.p. 39°). It was stored at -10° under nitrogen to avoid decomposition.

3,4,5-Trimethylpyrrole-2-carboxylic acid. -

Acidification of a cold aqueous solution of potassium 3,4,5-trimethylpyrrole-2-carboxylate with acetic acid gave the acid as a colourless precipitate. The acid, m.p. 122-125° (lit.[24] m.p. 126°) was washed with water and dried *in vacuo* over potassium hydroxide.

2-Formyl-3,4,5-trimethylpyrrole. -

Phosphorus oxychloride (9 ml) in dimethylformamide (20 ml) was added dropwise to a cold stirred solution of 3,4,5-trimethylpyrrole-2-carboxylic acid (5 g) in dimethylformamide (40 ml). The mixture was then heated on a steam-bath for 2 hr and poured into a hot saturated solution of sodium acetate in water. The product separated from the solution on standing at 0° overnight and was recrystallized from aqueous ethanol to give 2-formyl-3,4,5-trimethylpyrrole (3.8 g, 86%) as colourless needles, m.p. 146-147° (lit.[24] m.p. 147°).

4-Acetyl-2,3-dimethylpyrrole. -

The sodium salt of ethyl acetopyruvate[105] (41 g) in water (220 ml) was heated to 85° and the pH adjusted to 6.0 with dilute hydrochloric acid. 3-Aminobutanone hydrochloride (prepared from the tin complex[103] (42 g)) was added to this

solution over a period of 1 hr. The mixture was kept at pH 6.0 by the addition of aqueous sodium hydroxide (10%). The mixture was stirred for 1 hr and 4-acetyl-2,3,-dimethylpyrrole-5-carboxylic acid (7 g, 17%) collected. Decarboxylation[24] of the acid (0.5 g) gave 4-acetyl-2,3-dimethylpyrrole (0.28 g, 75%), which crystallized from water as colourless prisms, m.p. 137° (lit.[24] m.p. 137°).

4-Ethyl-2,3-dimethylpyrrole. -

A solution of 4-acetyl-2,3,-dimethylpyrrole (0.5 g) in ether (10 ml) was added to a suspension of lithium aluminium hydride (0.1 g) in ether (50 ml). The mixture was refluxed for 12 hr and then slowly hydrolysed with water. The ether layer was separated and the aqueous solution extracted several times with ether. Evaporation of the dried ether extracts and distillation of the residue gave 4-ethyl-2,3-dimethylpyrrole (0.4 g, 85%) as a colourless oil, b.p. 89°/12 mm (lit.[24] b.p. 113°/26 mm).

2-Ethoxycarbonyl-4-ethyl-3,5-dimethylpyrrole. -

The pyrrole was prepared by the method of Bullock et al.,[106] and was obtained from ethanol as colourless needles, m.p. 92-93° (lit.[106] m.p. 94°).

Potassium 4-ethyl-3,5-dimethylpyrrole-2-carboxylate. -

2-Ethoxycarbonyl-4-ethyl-3,5-dimethylpyrrole (20 g)

was refluxed for 3 hr with potassium hydroxide (20 g) in absolute ethanol (200 ml). The volume of the solution was reduced to 100 ml, dry ether (600 ml) added, and the mixture left at 0^{o} overnight. The potassium salt was collected and washed with ether.

3-Ethyl-2,4-dimethylpyrrole.-

A mixture of 3-acetyl-5-ethoxycarbonyl-2,4-dimethylpyrrole (10 g), diethylene glycol (50 ml), hydrazine hydrate (90%, 5 ml) and potassium hydroxide (7 g) was warmed on steam-bath until the potassium hydroxide had dissolved and then refluxed for 1 hr. The mixture was distilled until the temperature of the mixture reached 175^{o} and refluxed for a further 3 hr. The mixture was poured into water, extracted with ether, and the dried extracts evaporated under nitrogen. The residue was distilled to give 3-ethyl-2,4-dimethylpyrrole (2.4 g, 40%) as a colourless oil, b.p. 96^{o}/16 mm. (lit.[24] b.p. $77-78^{o}$/10 mm).

4-Ethyl-2-formyl-3,5-dimethylpyrrole. -

To 3-ethyl-2,4-dimethylpyrrole (5.5 g) in dimethylformamide (40 ml) was added, dropwise with stirring, phosphorus oxychloride (9 ml) in dimethylformamide (20 ml). The temperature during the reaction was maintained at $0-5^{o}$C. The mixture was then heated on a steam-bath for 1 hr and poured into saturated aqueous sodium acetate (600 ml). The aldehyde

(4 g, 90%) precipitated on standing at 0° overnight and was obtained from water as colourless needles, m.p. 104-105° (lit.[24] m.p. 105-106°).

2-Ethoxycarbonyl-3,4-dimethylpyrrole. -

This compound was prepared as described by Badger, Jones and Laslett.[107] It had m.p. 93-94° (lit.[107] m.p. 93-95°).

3,4-Dimethylpyrrole. -

2-Ethoxycarbonyl-3,4,-dimethylpyrrole was hydrolysed and decarboxylated as described by Badger, Harris and Jones.[108] It was obtained as a colourless oil, b.p. 164-166° (lit.[108] b.p. 164-166°/760 mm), and solidified on cooling to give colourless plates, m.p. 33° (lit.[108] m.p. 32-33°).

2-Ethoxycarbonyl-5-formyl-3,4-dimethylpyrrole. -

This compound was prepared by the method of Badger and Ward.[109] Recrystallization from aqueous ethanol gave 2-ethoxycarbonyl-5-formyl-3,4-dimethylpyrrole as colourless needles, m.p. 108° (lit.[110] m.p. 108°).

2-Acetyl-5-ethoxycarbonyl-3,4-dimethylpyrrole. -

Phosphorus oxychloride (1.2 g) was slowly added to a mixture of 2-ethoxycarbonyl-3,4-dimethylpyrrole (1 g) and N,N-dimethylacetamide (0.7 g) at 0°. After the initial reaction

the mixture was heated on a steam-bath for 2 hr and then poured into water. The solution was neutralized (to Congo Red) with sodium acetate and allowed to stand for 5 hr at 0°. The 2-acetyl-5-ethoxycarbonyl-3,4-dimethylpyrrole (0.8 g, 66%) separated, and crystallized from 2,2,4-trimethylpentane as buff-coloured needles, m.p. 106° (lit.[111] m.p. 106°).

2-Ethyl-3,4-dimethylpyrrole. -

A mixture of 2-acetyl-5-ethoxycarbonyl-3,4-dimethylpyrrole (2 g), diethylene glycol (10 ml), hydrazine hydrate (90%, 1 ml) and potassium hydroxide (2 g) was warmed on a steam-bath until most of the potassium hydroxide had dissolved. The solution was refluxed for 1 hr and then distilled until the temperature of the mixture reached 175°. The solution was refluxed for a further 3 hr after which it was poured into water and extracted with ether. Evaporation of the dried ether extracts and distillation of the residue gave 2-ethyl-3,4-dimethylpyrrole (0.4 g, 37%) as a colourless oil, b.p. 122-123° (lit.[24] b.p. 77-78°/10 mm).

2-Bromomethyl-5-ethoxycarbonyl-3,4-dimethylpyrrole. -

This compound was prepared by the method of Fischer and Walach[112] and crystallized from acetic acid as colourless needles, m.p. 128° (lit.[112] m.p. 128°).

2-Bromomethyl-5-ethoxycarbonyl-3-ethyl-4-methylpyrrole. -

The bromomethyl pyrrole was prepared in 80% yield by the method of Fischer and Ernst.[79] It was obtained from acetic acid as colourless needles, m.p. 133-134° (lit.[79] m.p. 128-132°).

2-Chloromethyl-3,5-diethoxycarbonyl-4-methylpyrrole. -

The chloromethylpyrrole was prepared by the method of Corwin et al.,[113] and was obtained as colourless needles, m.p. 154-155° (lit.[113] m.p. 156°).

2,3,4,5-Tetramethylpyrrole. -

This compound was prepared by the method of Johnson et al.,[114] and was obtained as colourless plates, m.p. 108-110° (lit.[114] m.p. 109-110°).

3,5-Diethoxycarbonyl-2-formyl-4-methylpyrrole. -

Oxidation of 2,4-diethoxycarbonyl-3,5-dimethylpyrrole was carried out by the method described by Corwin et al.[113] to give the formyl pyrrole. Recrystallization of the product from toluene gave colourless needles, m.p. 122-124° (lit.[113] m.p. 124°).

3-Acetyl-5-ethoxycarbonyl-2,4-dimethylpyrrole. -

This compound was prepared by the method described by Fischer.[115] The pyrrole was obtained as colourless needles,

m.p. 143-144° (lit.[115] m.p. 143-144°).

3-Acetyl-2,4-dimethylpyrrole-5-carboxylic acid. -

Hydrolysis of 3-acetyl-5-ethoxycarbonyl-2,4-dimethylpyrrole was effected by refluxing for 1 hr with 10% aqueous potassium hydroxide. The mixture was filtered, cooled to 0°, and the acid precipitated with acetic acid. Recrystallization from aqueous ethanol yielded colourless prisms, m.p. 230° (lit.[116] m.p. 231°).

3-Acetyl-2,4-dimethylpyrrole. -

This pyrrole was prepared by the method of Badger, Harris and Jones,[117] and was obtained as colourless needles, m.p. 139-140° (lit.[116] m.p. 139°).

4-Acetyl-2-formyl-3,5-dimethylpyrrole. -

This compound was prepared by the method described by Fischer and Amann.[39] The formyl pyrrole (55%) was obtained from water as colourless needles, m.p. 164° (lit.[39] m.p.166°).

2-Methyl-5-phenylpyrrole. -

This compound was prepared by the method of Tedder and Webster.[55] Recrystallization from aqueous ethanol gave colourless prisms, m.p. 98-98.5° (lit.[55] m.p. 96-98°).

2,5-Diphenylpyrrole. -

This compound was prepared from dibenzoylethane by the

method described by Tedder and Webster[55] and crystallized from aqueous ethanol as pale yellow needles, m.p. 142-143° (lit.[55] m.p. 143-145°).

2,4-Diphenylpyrrole. -

This compound was prepared by the method of Rogers,[54] using a W7 Raney nickel catalyst, and crystallized from toluene as long colourless needles, m.p. 178° (lit.[54] m.p. 178°).

2-Formyl-3,5-diphenylpyrrole. -

To a cooled solution of 2,4-diphenylpyrrole (9 g) in dimethylformamide (40 ml) was added, dropwise with stirring, phosphorus oxychloride (9 ml) in dimethylformamide (20 ml). The mixture was heated on a steam-bath for 1 hr and then poured into water (500 ml) containing sodium acetate (20 g). The solution was warmed to 50° for 30 min and then cooled to 0°. The formylpyrrole (11 g, 97%) separated, and repeated recrystallizations from toluene gave colourless needles, m.p. 190-191° (lit.[76] m.p. 187-188°).

2,3,4,5-Tetraphenylpyrrole. -

This compound, m.p. 214° (lit.[58] m.p. 214°) was prepared by the method of Davidson.[58]

2-Methyl-3,4,5-triphenylpyrrole. -

This compound was prepared by the method of Davidson,[58]

and was obtained as colourless needles, m.p. 164° (lit.[58] m.p. 164°).

3-Ethoxycarbonyl-2,4-dimethyl-5-phenylpyrrole. -

Zinc dust (50 g) was added to a vigorously stirred solution of 1-hydroxyimino-1-phenylacetone[132] (27 g) and ethyl acetoacetate (26 g) in acetic acid (100 ml) at such a rate that the temperature remained at 60-65°. The mixture was heated on a steam-bath for 2 hr and then poured into an ice-water mixture. The precipitated product was collected and recrystallized from aqueous methanol to yield 3-ethoxycarbonyl-2,4-dimethyl-5-phenylpyrrole as colourless plates, m.p. 120-121.5°.

(Found: C,74.0; H,7.0; N,5.6. $C_{15}H_{17}NO_2$ requires C,74.0; H,7.0; N,5.8%.)

2,4-Dimethyl-5-phenylpyrrole. -

3-Ethoxycarbonyl-2,4-dimethyl-5-phenylpyrrole (10 g) was added to a hot solution of potassium hydroxide (7 g) in diethylene glycol (50 ml) and refluxed for 2 hr. The mixture was distilled until the temperature reached 175° and then refluxed for a further 6 hr. The solution was poured into water and the precipitated solid collected. Recrystallization from aqueous ethanol gave colourless needles of 2,4-dimethyl-5-phenylpyrrole (3 g, 60%), m.p. 71.5-72°.

(Found: C,84.1; H,7.8; N,8.1. $C_{12}H_{13}N$ requires C, 84.2; H, 7.7; N, 8.2%.)

Treibs and Ohorodnik[52] reported this compound as a brown oil, b.p. 170°/12 mm.

4-Ethoxycarbonyl-5-methyl-2,3-diphenylpyrrole. -

This compound was prepared by the method of Davidson,[58] and was obtained as yellow needles, m.p. 203° (lit.[58] m.p. 203°).

5-Methyl-2,3-diphenylpyrrole. -

4-Ethoxycarbonyl-5-methyl-2,3-diphenylpyrrole (5 g) was refluxed in 60% sulphuric acid (50 ml) for 3 hr. The mixture was poured into water and the precipitated solid collected and dried. Ethanolamine (4 ml) was added to the solid and the mixture refluxed for 1 hr and then poured into water. The solid was collected and distilled (b.p. 174°/1 mm) and the distillate solidified on cooling. Recrystallization from hexane gave 5-methyl-2,3-diphenylpyrrole (2.8 g, 71%) as colourless needles, m.p. 80°.

(Found: C, 87.1; H, 6.5; N, 5.7. $C_{17}H_{15}N$ requires C,87.5; H, 6.5; N, 6.0%)

5-Ethoxycarbonyl-2,4-dimethyl-3-phenylpyrrole. -

Sodium nitrite (17 g) in water (20 ml) was added slowly to a cold (5-10°), stirred solution of ethyl acetoacetate (34 g) in acetic acid (100 ml). The mixture was stirred for

a further hour and allowed to stand overnight. The mixture was then added to a solution of benzyl methyl ketone (32 g) in acetic acid (150 ml) and zinc dust (50 g) was added at a rate which kept the reaction mixture at a temperature of 60-70°. The mixture was heated on a steam-bath for 2 hr and poured into an ice-water mixture. The colourless solid which separated at 0° was collected and crystallized from ethanol to give 5-ethoxycarbonyl-2,4-dimethyl-3-phenylpyrrole (11 g, 17%) as colourless prisms, m.p. 143-144°.

(Found: C, 74.2; H, 7.1; N, 5.9. $C_{15}H_{17}NO_2$ requires C, 74.1; H, 7.0; N, 5.8%.)

2,4-Dimethyl-3-phenylpyrrole. -

5-Ethoxycarbonyl-2,4-dimethyl-3-phenylpyrrole (10 g) was hydrolysed by refluxing with 10% aqueous potassium hydroxide for 2 hr. The mixture was filtered, cooled, acidified with acetic acid and extracted with ether. The dried ether extracts were evaporated under reduced pressure. The residue was refluxed with ethanolamine (8 ml) under nitrogen for 1 hr and poured into water. The aqueous solution was extracted with ether, the dried extracts evaporated and the residue distilled to give a colourless oil, b.p. 120°/0.7 mm. The oil solidified to give 2,4-dimethyl-3-phenylpyrrole (6 g, 85%) which on recrystallization from hexane yielded colourless plates, m.p. 65-66°.

(Found: C, 84.0; H, 7.7; N, 7.9. $C_{12}H_{13}N$ requires C, 84.2; H, 7.7; N, 8.2%)

2,4-Diethoxycarbonyl-5-methyl-3-phenylpyrrole. -

A vigorously stirred suspension of ethyl benzoylacetate (36 g) in acetic acid (90 ml) was treated slowly with sodium nitrite (22 g) in water (30 ml) at 5-10°. The mixture was stirred for a further hour and allowed to stand at room temperature for 2 hr. Ethyl acetoacetate (26 g) in acetic acid (100 ml) was then added followed by zinc dust (39 g) at a rate which kept the mixture at 70-80°. The mixture was refluxed for 2 hr and poured into an ice-water mixture with vigorous agitation. The pyrrole separated as a yellow oil which crystallized at 0°. 2,4-Diethoxycarbonyl-5-methyl-3-phenylpyrrole (36 g, 80%) crystallized from ethanol as colourless prisms, m.p. 124-125° (lit.[41] m.p. 125°).

Potassium 4-ethoxycarbonyl-5-methyl-3-phenylpyrrole-2-carboxylate. -

2,4-Diethoxycarbonyl-5-methyl-3-phenylpyrrole (10 g) was refluxed for 3 hr with potassium hydroxide (10 g) in absolute ethanol (100 ml). The volume of the solution was reduced to 40 ml and the potassium salt which separated on cooling collected and washed with ether.

4-Ethoxycarbonyl-5-methyl-3-phenylpyrrole-2-carboxylic acid. -

The potassium salt was dissolved in water and the solution acidified with acetic acid. The pyrrole acid was collected and dried. Recrystallization from alcohol yielded colourless needles, m.p. 207° (lit.[118] m.p. 209°).

3-Ethoxycarbonyl-2-methyl-4-phenylpyrrole. -

4-Ethoxycarbonyl-5-methyl-3-phenylpyrrole-2-carboxylic acid (23 g) was refluxed with ethanolamine (12 ml) for 1 hr under nitrogen. The mixture was poured into water and the solid collected. Recrystallization from ethanol yielded 3-ethoxycarbonyl-2-methyl-4-phenylpyrrole as pale yellow needles, m.p. 103-104° (lit.[118] m.p. 105°).

2-Methyl-4-phenylpyrrole. -

2,4-Diethoxycarbonyl-5-methyl-3-phenylpyrrole (30 g) and potassium hydroxide (45 g) were finely ground in a mortar and placed in a stainless steel autoclave (capacity 100 ml). Water (15 ml) was added and the mixture stirred into a paste. The autoclave was heated in an oven at 160° for 4 hr, and the cooled mixture poured into water and extracted with ether. The extracts were dried and evaporated to give 2-methyl-4-phenylpyrrole (10 g, 80%), a colourless oil, b.p. 175°/25 mm (lit.[118] b.p. 166-169°/20 mm).

2-Formyl-5-methyl-3-phenylpyrrole. -

A solution of 2-methyl-4-phenylpyrrole (2.5 g) in dimethylformamide (10 ml) was cooled in ice, and a solution of phosphorus oxychloride (3 ml) in dimethylformamide (10 ml) added dropwise with stirring during 30 min. The pH of the solution was adjusted to 10 with sodium hydroxide and the precipitated solid collected. Recrystallization of the crude solid from ethanol gave 2-formyl-5-methyl-3-phenylpyrrole as colourless needles (3.2 g, 84%), m.p. 169°.

(Found: C, 78.1; H, 6.0; N, 7.6. $C_{12}H_{11}NO$ requires C, 77.8; H, 6.0; N, 7.6%.)

4-Ethoxycarbonyl-2-formyl-5-methyl-3-phenylpyrrole. -

This compound was prepared by the method of Cook and Majer[119] and was obtained from aqueous ethanol as colourless needles, m.p. 149° (lit.[119] m.p. 149°).

4-Methyl-2-phenylpyrrole. -

This compound was prepared by the method of Haines and Eisner[120] and crystallized from aqueous ethanol as colourless plates, m.p. 152° (lit.[24] m.p. 152°).

2-Ethoxycarbonyl-5-methyl-3,4-diphenylpyrrole. -

Ethyl benzoylacetate (51 g) in acetic acid (120 ml) at 0-5° was treated with sodium nitrite (17 g) in water (20 ml)

with vigorous stirring. The mixture was stirred for a further hour and allowed to stand overnight at room temperature. After the addition of benzyl methyl ketone (32 g) in acetic acid (150 ml), zinc dust (60 g) was added slowly so that the temperature remained between 70-90°. The mixture was refluxed for 2 hr, poured into water, and allowed to stand at 0° overnight during which time the pyrrole crystallized. Recrystallization from ethanol gave 2-ethoxycarbonyl-5-methyl-3,4-diphenylpyrrole as colourless needles, (15 g, 20%), m.p. 168°.

(Found: C, 79.1; H, 6.4; N, 4.5. $C_{20}H_{19}NO_2$ requires C, 78.7; H, 6.3; N, 4.6%.)

Potassium 5-methyl-3,4-diphenylpyrrole-2-carboxylate. -

2-Ethoxycarbonyl-5-methyl-3,4-diphenylpyrrole (10 g) was refluxed in ethanol (100 ml) containing potassium hydroxide (10 g) until a sample removed from the mixture gave no turbidity with water (about 4 hr). The volume of the solution was reduced to 40 ml and cooled to 0°. The potassium salt crystallized as colourless plates which were washed with ether and dried.

5-Methyl-3,4-diphenylpyrrole. -

Potassium 5-methyl-3,4-diphenyl-2-carboxylate was dissolved in water and the solution acidified with acetic

acid. The precipitated acid was collected, washed with water, dissolved in ether and dried over magnesium sulphate. (The acid was too unstable to be dried in a desiccator.) The ether was removed under reduced pressure and ethanolamine (8 ml) added to the residue. The mixture was refluxed for 1 hr and then poured into water. The pyrrole crystallized on cooling to 0°. Recrystallization from hexane (charcoal) gave 5-methyl-3,4-diphenylpyrrole (7 g, 91%) as colourless prisms, m.p. 78°, which decomposed on standing.

(Found: C, 87.6; H, 6.2; N, 6.0. $C_{17}H_{15}N$ requires C, 87.5; H, 6.5; N, 6.0%.)

2-Formyl-5-methyl-3,4-diphenylpyrrole. -

Potassium 5-methyl-3,4-diphenylpyrrole-2-carboxylate (7 g) was dissolved in dimethylformamide (30 ml) and cooled at 0°. A solution of phosphorus oxychloride (10 ml) in dimethylformamide (20 ml) was added dropwise with stirring at a rate which kept the temperature of the mixture below 5°. The mixture was heated on a steam bath for 3 hr, and poured into a saturated solution of sodium acetate in water (300 ml). The solid which separated was collected and recrystallized from benzene to give 2-formyl-5-methyl-3,4-diphenylpyrrole (4 g, 70%) as colourless prisms, m.p. 230°.

(Found: C, 82.5; H, 5.8; N, 5.2. $C_{18}H_{15}NO$ requires C, 82.7; H, 5.8; N, 5.4%.)

3-Ethoxycarbonyl-2,4,5-triphenylpyrrole. -

Benzoin (10 g), ethyl benzoylacetate (14 g), acetic acid (500 ml) and ammonium acetate (60 g) were refluxed for 2 hr. The solution was cooled and water added to precipitate the pyrrole. The solid was collected and recrystallized from methanol to give 3-ethoxycarbonyl-2,4,5-triphenylpyrrole (6.5 g, 74%) as colourless needles, m.p. 145° (lit.[121] m.p. 145°).

2,4,5-Triphenylpyrrole. -

3-Ethoxycarbonyl-2,4,5-triphenylpyrrole (5 g) was added to a hot solution of potassium hydroxide (7 g) in diethylene glycol (50 ml) and refluxed for 2 hr. The mixture was distilled until the temperature reached 180° and then refluxed for a further 3 hr. The solution was poured into water and the solid collected. Recrystallization from methanol gave 2,3,5-triphenylpyrrole (3.5 g, 74%) as colourless prisms, m.p. 142° (lit.[55] m.p. 142°).

2,4-Diethoxycarbonyl-3,5-diphenylpyrrole. -

Sodium nitrite (7 g) in water (10 ml) was added to a stirred suspension of ethyl benzoylacetate (36 g) in acetic acid (113 ml) and the temperature maintained at 5-7° during the addition. The mixture was kept at room temperature for 4 hr and then zinc dust (25 g) was added at a rate which kept the mixture boiling gently. Refluxing was continued for a further 2 hr and the hot mixture poured into ice-water.

The pyrrole separated as an oil and was extracted with benzene. The dried extracts were evaporated to give an oil which on crystallization from aqueous ethanol yielded 2,4-diethoxycarbonyl-3,5-diphenylpyrrole (12 g, 43%) as colourless prisms, m.p. 121-122°.

(Found: C, 72.5; H, 5.9; N, 4.1. $C_{22}H_{21}NO_4$ requires C, 72.7; H, 5.9; N, 3.9%.)

3-Acetyl-5-ethoxycarbonyl-2-methyl-4-phenylpyrrole. -

A vigorously stirred solution of ethyl benzoylacetate (51 g) in acetic acid (120 ml) was treated with sodium nitrite (17 g) in water (20 ml) at a rate which maintained the temperature of the mixture at 5-7°. The mixture was stirred for a further hour and allowed to stand overnight. Acetylacetone (25 g), in acetic acid (150 ml) was added and zinc dust (50 g) added gradually so that the temperature remained at 60-70°. When the addition of zinc was complete, the mixture was heated for 1 hr and then poured into ice-water. Recrystallization of the product from aqueous ethanol gave 3-acetyl-5-ethoxycarbonyl-2-methyl-4-phenylpyrrole, (51 g, 67%) as large colourless prisms, m.p. 128°.

(Found: C, 70.9; H, 6.3; N, 5.2. $C_{16}H_{17}NO_3$ requires C, 70.8; H, 6.3; N, 5.2%.)

3-Ethyl-2-methyl-4-phenylpyrrole. -

A mixture of 3-acetyl-5-ethoxycarbonyl-2-methyl-4-phenylpyrrole (36 g), diethylene glycol (150 ml), hydrazine hydrate (90%, 15 ml) and potassium hydroxide (20 g) was warmed until most of the potassium hydroxide had dissolved and then refluxed for 1 hr. The mixture was distilled until the temperature reached 175°, refluxed for 3 hr, and poured into water. Extraction of the aqueous solution with ether, and evaporation of the solvent gave 3-ethyl-2-methyl-4-phenylpyrrole (12 g, 48%) as a colourless oil, b.p. 116°/ 4mm.

(Found: C, 84.5; H, 8.0; N, 7.5. $C_{13}H_{15}N$ requires C, 84.3; H, 8.2; N, 7.6%.

2,3,4-Triphenylpyrrole. -

This was prepared essentially by the method of Pollack and Tišler.[59] 3,4,5-Triphenyl-3(2H)-pyridazinone[122] (32 g) in toluene (250 ml) was refluxed with phosphorus pentasulphide (4.5 g) for 12 hr. The mixture was filtered and the toluene removed from the filtrate under reduced pressure. The residue was extracted with hot ethanol and 4,5,6-triphenyl-3(2H)-pyridazinethione (4.5 g, 15%) crystallized from the cooled solution as yellow needles, m.p. 300-303° (lit.[59] m.p. 303-304°). The pyridazinethione (4.5 g) and Raney nickel W6 [123] were refluxed in ethanol saturated with ammonia for 4 hr. The mixture was filtered and 2,3,4,-triphenylpyrrole (0.7 g,

19%) crystallized from the filtrate as colourless needles, m.p. 168° (lit.[59] m.p. 168°).

2-Formylpyrrole. -

This compound was prepared by the method of Silverstein et al.[124] and obtained as colourless needles, m.p. 42-44° (lit.[124] m.p. 42-44°).

2-Methylpyrrole. -

The method described by Cantor, Lancaster and Vander Werf[125] gave 2-methylpyrrole as an oil, b.p. 148-150°/760 mm, (lit.[125] b.p. 147-148°/740 mm).

2-Acetylpyrrole. -

2-Acetylpyrrole was obtained as colourless needles, m.p. 89° (lit.[126] m.p. 90°) by the method of Adkins et al.[126]

2-Acetyl-3,5-dimethylpyrrole. -

Phosphorus oxychloride (1.2 g) was gradually added to a mixture of 2,4-dimethylpyrrole (1 g) and N,N-dimethylacetamide (0.7 g) with stirring, the temperature being maintained below 5° with ice-cooling. After the initial reaction had subsided, the mixture was heated at 100° for 2 hr and then cooled. A saturated solution of sodium acetate in water (250 ml) was added, cautiously at first and then as rapidly as possible. The mixture was heated at 100° for 30 min, cooled, and

extracted with ether. Removal of the ether from the dried extracts and recrystallization of the residue from hexane gave 2-acetyl-3,5-dimethylpyrrole (0.6 g, 60%), m.p. 121° (lit.[24] m.p. 121°) as pale yellow needles.

2-Acetyl-5-methylpyrrole, m.p. 88-89° (lit.[24] m.p. 89°) and 2-acetyl-4,5-dimethylpyrrole, m.p. 113° (lit.[24] m.p. 112.5°) were prepared from the corresponding methylpyrroles by methods similar to that described for 2-acetyl-3,5-dimethylpyrrole.

3-Acetyl-2,5-dimethylpyrrole. -

This compound was prepared by the method of Kleinspehn and Briod[127] and was obtained from hexane as colourless needles, m.p. 94° (lit.[127] m.p. 94.5-95°).

3-Acetyl-2-methylpyrrole. -

This compound was prepared according to the method of Cornforth and Firth[128] and crystallized from aqueous ethanol as pale yellow needles, m.p. 93-94° (lit.[128] m.p. 94-95°).

3-Acetyl-4-methylpyrrole. -

A sample of 3-acetyl-4-methylpyrrole kindly provided by Dr. R.L.N. Harris was recrystallized from hexane to yield colourless needles, m.p. 117° (lit.[38] m.p. 117°).

2-Acetyl-3,4,5-trimethylpyrrole. -

Potassium 3,4,5-trimethylpyrrole-2-carboxylate (2.5 g), glacial acetic acid (2 ml) and redistilled acetyl chloride (2 ml) were heated under reflux for 30 min. The mixture was cooled, poured into water and extracted with chloroform. Evaporation of the dried extracts gave a solid residue which was recrystallized from 2,2,4-trimethylpentane and then aqueous ethanol to yield pale yellow needles, (0.6 g, 30%) m.p. 138° (lit.[24] m.p. 137°).

2,5-Diacetylpyrrole. -

This compound was prepared by heating 1-acetylpyrrole with acetic anhydride at 300° in a sealed tube for 3 hr. The mixture was poured into cold water and the precipitate collected. The diacetylpyrrole was recrystallized from hot water to yield colourless needles, m.p. 161-162° (lit.[24] m.p. 161-162°).

3-Acetyl-2,4,5-trimethylpyrrole. -

This compound was prepared by the method of Fischer and Bartholomäus[162] and was obtained from ethanol as colourless needles, m.p. 207-208° (lit.[24] m.p. 207-209°).

2,4-Diacetyl-3,5-dimethylpyrrole. -

Preparation of this compound according to the method described by Fischer and Orth[24] gave colourless needles, m.p. 132-133° (lit.[24] m.p. 136°).

2-Acetyl-4-ethoxycarbonyl-3,5-dimethylpyrrole. -

This compound was prepared by the method of Zanetti and Levi,[129] and was obtained from ethanol as colourless needles, m.p. 138° (lit.[129] m.p. 139°).

2-Benzoylpyrrole, m.p. 78-79° (lit.[37] m.p. 78-79°); 2-benzoyl-5-methylpyrrole, m.p. 142° (lit.[37] m.p. 142°); 2-benzoyl-3,4-dimethylpyrrole, m.p. 76-77° (lit.[37] m.p. 76-77°); 2-benzoyl-3,5-dimethylpyrrole, m.p. 118.5-119° (lit.[37] m.p. 118.5-119°); 2-benzoyl-3,4,5-trimethylpyrrole, m.p. 136-137° (lit.[37] m.p. 136-137°); 1-benzoylpyrrole, b.p. 94-96°/0.2 mm (lit.[37] b.p. 94-96°/0.2 mm); 1-benzoylpyrrole-2-methylpyrrole, b.p. 160-162°/23 mm (lit.[37] b.p. 160-162°/23 mm); 1-benzoyl-2,4-dimethylpyrrole, b.p. 126-128°/0.5 mm (lit.[37] b.p. 126-128°/0.5 mm); 1-benzoylpyrrole-2,5-dimethylpyrrole, m.p. 38° (lit.[37] m.p. 38°); 1-benzoyl-2,3,4-trimethylpyrrole, b.p. 110-114°/0.02 mm (lit.[37] b.p. 110-114°/0.02 mm) were either gifts from, or prepared by the method of, Jones and Laslett.[37]

3-Benzoyl-5-ethoxycarbonyl-2,4-dimethylpyrrole. -

This compound was prepared by the method of Fischer and Hansen [130] and was obtained from ethanol as pale yellow needles, m.p. 117.5° (lit.[130] m.p. 118°).

3-Benzoyl-2,4-dimethylpyrrole-5-carboxylic acid. -

3-Benzoyl-5-ethoxycarbonyl-2,4-dimethylpyrrole (10 g) was refluxed for 4 hr with potassium hydroxide (10 g) in absolute ethanol (100 ml). The volume of the solution was reduced to 50 ml and dry ether (400 ml) added. The mixture was left at 0° overnight and the potassium salt collected and dissolved in water. Acidification of the solution with acetic acid precipitated the pyrrole acid as a buff-coloured solid, m.p. 189-192° (lit.[130] m.p. 194°) which was dried in a desiccator.

3-Benzoyl-2,4-dimethylpyrrole. -

3-Benzoyl-2,4-dimethylpyrrole-5-carboxylic acid (5 g) was refluxed with ethanolamine (8 ml) for 2 hr. The mixture was poured into water and the collected solid recrystallized from aqueous ethanol to yield pale yellow plates, m.p. 130° (lit.[130] m.p. 130°).

2-Acetyl-3,4-dimethylpyrrole. -

2-Acetyl-5-ethoxycarbonyl-3,4-dimethylpyrrole was refluxed with ethanolic potassium hydroxide (10%) for 2 hr.

The solution was cooled and the potassium salt collected and dissolved in water. Acidification with dilute hydrochloride acid gave the pyrrole carboxylic acid.

The dried acid was refluxed with an equimolar quantity of ethanolamine for 1 hr and the mixture poured into water. The aqueous mixture was extracted with ether and removal of the ether from the dried extracts gave 2-acetyl-3,4-dimethylpyrrole (74%) which crystallized as pale yellow needles, m.p. 135° (lit.[24] m.p. 135°) from aqueous ethanol.

2-Benzoyl-4,5-dimethylpyrrole. -

2,3-Dimethylpyrrole was shaken with excess benzoyl chloride and aqueous sodium hydroxide to give 2-benzoyl-4,5-dimethylpyrrole, m.p. 156-157° (needles from hexane).

(Found: C, 78.2; H, 6.6. $C_{13}H_{13}NO$ requires C, 78.4; H, 6.5%.)

3-Benzoyl-2,5-dimethylpyrrole. -

N-benzoylmorpholine (9.5 g) was added slowly to cold phosphorus oxychloride (3 g) with stirring. 2,5-Dimethylpyrrole (3 g) was added dropwise to the cooled solution which was then heated at 100° for 2 hr. Saturated aqueous sodium acetate (300 ml) was added and the mixture refluxed for 1 hr. The mixture was then cooled and extracted with ether (3 x 100 ml). The extracts were dried and the ether removed. The residual oil was distilled (182°/2 mm) to give 3-benzoyl-2,5-dimethyl-

pyrrole, m.p. 129-130° (lit.[131] m.p. 129-130°).

3-Benzoyl-4,5-dimethylpyrrole. -

The sodium salt of ethylbenzoylpyruvate[135] (25 g) in water (110 ml) was heated to 85° and the pH adjusted to 6.0 with hydrochloric acid. 3-Aminobutanone hydrochloride (prepared from the tin complex[103] (21 g)) was added to the solution over a period of 1 hr. The mixture was kept at pH 6.0 by the addition of aqueous sodium hydroxide. The mixture was stirred for 1 hr and 3-benzoyl-4,5-dimethylpyrrole-2-carboxylic acid (1 g) separated. The acid (1 g) was heated at 220° in an atmosphere of nitrogen and the cooled residue extracted with ethyl acetate. Removal of the solvent gave 3-benzoyl-4,5-dimethylpyrrole, (0.5 g, 61%) m.p. 190° (lit.[133] m.p. 192°), (needles from aqueous ethanol).

3-Benzoyl-2,4,5-trimethylpyrrole. -

Zinc dust (30 g) was added slowly to benzoylacetone (32 g) and biacetylmonoxime (20 g) in acetic acid (200 ml) with stirring while keeping the temperature below 80°. The mixture was then refluxed for 1 hr and poured into water (1 l.). 3-Benzoyl-2,4,5-trimethylpyrrole (18 g, 47%) separated, which crystallized from ethanol as colourless needles, m.p. 172.5-173.5° (lit.[24] m.p. 174°).

2-Benzoyl-5-ethoxycarbonyl-3,4-dimethylpyrrole. -

A sample of 2-benzoyl-3,4-dimethyl-5-ethoxycarbonyl-pyrrole, m.p. 120° (colourless needles) was kindly supplied by Mr. R.L. Laslett.

2,5-Dimethylpyrrole. -

This was prepared by the method described by Vogel [134] and was obtained as a colourless oil, b.p. 165-167° (lit.[134] b.p. 78-80°/25 mm).

1-Acetyl-2,5-dimethylpyrrole. -

2,5-Dimethylpyrrole (3.5 g) in toluene (75 ml) was added to potassium sand (4 g) under dry toluene (25 ml). The mixture was refluxed with stirring for 3 hr and then acetyl chloride (11.5 g) was added dropwise to the cold stirred solution over a period of 10 min. The mixture was heated on a steam-bath for 5 hr and filtered hot. The toluene was removed from the filtrate under reduced pressure and the residual oil distilled to give 1-acetyl-2,5-dimethylpyrrole (2.6 g, 52%) as a colourless oil, b.p. 122-125°/27 mm.

(Found: C, 69.7; H, 8.05; N, 10.5. $C_8H_{11}NO$ requires C, 70.0; H, 8.1; N, 10.2%.)

The following compounds were prepared by methods analogous to that used for 1-acetyl-2,5-dimethylpyrrole:-

1-Acetylpyrrole, was obtained as a pale yellow oil, b.p. 181° (lit.[24] b.p. 180-181°).

1-Acetyl-2,4-dimethylpyrrole, was obtained as a colourless oil, b.p. 105-108°/3 mm.

(Found: C, 70.4; H, 7.8; N, 10.2. $C_8H_{11}NO$ requires C, 70.0; H, 8.1; N, 10.2%.)

1-Acetyl-2,3-dimethylpyrrole, was obtained as a colourless oil, b.p. 107°/2 mm.

(Found: C, 69.9; H, 8.3; N, 9.9%.)

1-Acetyl-3,4-dimethylpyrrole, was obtained as a pale yellow oil, b.p. 88°/4.5 mm.

(Found: C, 69.9; H, 7.9; N, 10.1%.)

1-Acetyl-2,3,4-trimethylpyrrole, was obtained as a pale yellow oil, b.p. 162°/2 mm.

(Found: C, 71.2; H, 8.8; N, 9.0. $C_9H_{13}NO$ requires C, 71.5; H, 8.7; N, 9.3%.)

1-Benzoyl-2,3,-dimethylpyrrole, prepared from potassium 2,3-dimethylpyrrole and benzoyl chloride was obtained as a

colourless oil, b.p. 116°/3 mm.

(Found: C, 78.2; H, 6.7; N, 7.2. $C_{13}H_{13}NO$ requires C, 78.4; H, 6.6; N, 7.0%.)

1-Benzoyl-3,4-dimethylpyrrole, was obtained as a colourless oil, b.p. 114°/1 mm.

(Found: C, 78.3; H, 6.5%.)

2-Nitroso-3,5-diphenylpyrrole. -

The nitrosopyrrole, m.p. 137-139° (lit.[54] m.p. 139-140°) and the hydrochloride salt, m.p. 188-190° decomp. (lit.[54] m.p. 190° decomp.) were prepared by the method of Rogers.[54]

3-Ethoxycarbonyl-2,4-dimethylpyrrole-5-(ethyl β-keto-propionate) m.p. 141-142° (lit.[92a] 140,5-142°) and 4-ethoxycarbonyl-2,3-dimethylpyrrole-5-(ethyl β-ketopropionate) m.p. 57° (lit.[92a] m.p. 56-57°) were prepared by the method of Filippovich et al.[92a]

2-Phenylpyrrole. -

This compound was prepared by the thermal isomerization of 1-phenylpyrrole.[24] Recrystallization from aqueous ethanol gave colourless plates, m.p. 129° (lit.[24] m.p. 129°).

2-Phenyl-2-pyrroline. -

The pyrroline was prepared from β-benzoylpropionitrile by the method of Knott,[53] and was obtained as an oil, b.p. 122-125°/15 mm (lit.[53] b.p. 252°/760 mm), which solidified on cooling to give colourless plates, m.p. 44-45° (lit.[53] m.p. 46°). The picrate had m.p. 198° (lit.[53] m.p. 198°). Attempts to dehydrogenate the pyrroline by heating with silver oxide, heating with 2,3,5,6-tetrachloro-1,4-benzoquinone in cumene, treating with dibenzoylperoxide in benzene at 45°, and heating with 10% palladium-carbon at 260° in a sealed tube, all resulted in small yields of 2-phenylpyrrole.

8.4. Alkyl- and ethoxycarbonyl-dipyrromethenes.

The following dipyrromethenes were prepared by procedures previously reported in the literature.

3,5,3',5'-Tetramethyldipyrromethene, m.p. 117-119° (lit.[103] m.p. 116-118°), λ* max. EtOH 289 (3.66), 435 (4.52). 1N HCl/EtOH 226 (3.94), 463 (5.03).

4,5,4',5'-Tetramethyldipyrromethene, m.p. 116° (lit.[103] m.p. 116°), λ max. EtOH 233 (3.81), 441 (4.36). 1N HCl/EtOH 357 (3.73), 472 (4.77).

3,5,4',5'-Tetramethyldipyrromethene, m.p. 81-82° (lit.[103] m.p. 82-83°), λ max. EtOH 295 (3.57), 439 (4.40). 1N HCl/EtOH 238 (3.72), 476 (4.80).

* Maxima in mμ, log ε in parentheses.

3,4,5,3',4',5'-Hexamethyldipyrromethene, m.p. 169.6-170° (lit.[112] m.p. 168°), λmax. EtOH 224 (4.08), 280 sh (3.39), 325 (3.63), 442 (4.48). 1N HCl/EtOH 229 (3.89), 362 (3.59), 480 (4.80).

4'-Ethoxycarbonyl-3,4,5,3',5'-pentamethyldipyrromethene, m.p. 126° (lit.[112] m.p. 127°), λmax. EtOH 225 (4.01), 262 (3.73), 409 (4.47). 1N HCl/EtOH 226 (4.04), 263 (3.68), 470 (4.86).

3,3'-Diethoxycarbonyl-4,5,4',5'-tetramethyldipyrromethene, m.p. 163-164° (lit.[136] m.p. 164°), λmax. EtOH 209 (4.34), 224 sh (3.98), 479 (4.41). 1N/HCl EtOH 227 (3.93), 362 (3.78), 526 (4.92).

4,4'-Diethoxycarbonyl-3,5,3',5'-tetramethyldipyrromethene, m.p. 190° (lit.[137] m.p. 190°), λmax. EtOH 220 (4.38), 261 (3.89), 452 (4.55). 1N HCl/EtOH 212 (4.43), 247 (3.89), 344 (3.54), 465 (5.06).

4-Ethoxycarbonyl-3,5,3',5'-tetramethyldipyrromethene, m.p. 120° (lit.[138] m.p. 120°), λmax. EtOH 213 (4.15), 226 sh (4.08), 254 (3.78), 415 (4.46), 467 sh (4.13). 1N HCl/EtOH 210 (4.27), 223 sh (4.10), 260 (3.66), 351 (3.69), 461 (4.99).

4'-Ethoxycarbonyl-4-ethyl-3,5,3',5'-tetramethyldipyrromethene, m.p. 131-132° (lit.[139] 132°), λ max. EtOH 214 (4.28), 259 (3.85), 410 (4.44). 1N HCl/EtOH 223 sh (4.07), 262 (3.70), 471 (4.88).

3,4,5,3',5'-Pentamethyldipyrromethene. -

Dry hydrogen chloride was passed through a cooled solution of 2-formyl-3,5-dimethylpyrrole (1.2 g) and 2,3,4-trimethylpyrrole (1.0 g) in anhydrous ethanol (15 ml). The dipyrromethene hydrochloride which separated was collected, washed with ether, and dissolved in chloroform. The chloroform solution was shaken with aqueous ammonia, dried, and evaporated. Recrystallization of the residue from acetone (cooled in dry ice-ethanol) gave the dipyrromethene base as orange needles, m.p. 93-94° (lit.[112] m.p. 89-99°).

λ max. EtOH 222 (3.97), 270 (3.41), 433 (4.39). 1N HCl/EtOH 232 (3.84), 357 (3.59), 474 (4.84).

4,4'-Diethyl-3,5,3',5'-tetramethyldipyrromethene. -

A mixture of 2-ethoxycarbonyl-4-ethyl-3,5-dimethylpyrrole (2 g), formic acid (98%, 2 ml) and hydrobromic acid (48%, 2 ml) was heated at 100° for 4 hr and then allowed to cool. The product was collected and washed with ether. The dipyrromethene hydrobromide was dissolved in chloroform, washed with aqueous ammonia, dried and evaporated to give 3,3'-

diethyl-4,5,4',5'-tetramethyldipyrromethene (1.0 g, 83%), which crystallized from acetone as red plates, m.p. 151° (lit.[140] m.p. 151°), λmax. EtOH 225 (3.80), 286 sh (3.28), 322 (3.50), 447 (4.53). 1N HCl/EtOH 229 (4.04), 280 (3.33), 360 (3.82), 483 (4.86).

3,3'-Diethyl-3,5,3',5'-tetramethyldipyrromethene. -

4-Ethyl-2,3-dimethylpyrrole (1 g) in formic acid (5 ml) was heated at 100° for 3 min. Perchloric acid (60%, 0.5 ml) was added and the mixture heated for a further 10 min. and then cooled to 0°. The perchlorate salt which separated was collected, washed with ether, and dissolved in hot ethanol. A few drops of aqueous ammonia (d. 0,88) were added and the dipyrromethene base (0.4 g, 67%) crystallized from the cooled solution as red needles, m.p. 106° (lit.[141] m.p. 108°), λ max. EtOH 226 (3.80), 320 (3.52), 443 (4.59). 1N HCl/EtOH 230 (3.92), 280 (3.40), 363 (3.79), 478 (4.90).

4,4'-Diacetyl-3,5,3',5'-tetramethyldipyrromethene. -

A solution of the dipyrromethene hydrochloride, m.p. 197-199° (lit.[93] m.p. 200°), in chloroform was washed with aqueous ammonia, dried and evaporated. Recrystallization of the residue from ethanol yielded the dipyrromethene base as orange prisms, m.p. 217° (lit.[142] m.p. 219°), λ**max. EtOH

** Compound not sufficiently soluble for accurate intensity measurements.

248, 280, 424 mμ. 1N HCl/EtOH 232, 284, 472 mμ.

5,5'-Diethoxycarbonyl-3,4,3',4'-tetramethyldipyrromethane. - This compound was prepared from 2-bromomethyl-5-ethoxycarbonyl-3,4-dimethylpyrrole by the method of Fischer and Walach[112] and was obtained from ethanol as colourless needles, m.p. 198° (lit.[112] 198°).

5,5'-Diethoxycarbonyl-3,4,3',4'-tetramethyldipyrromethene. - The dipyrromethene hydrobromide, m.p. 163-165° (lit.[74] 160-165°) was prepared by the brominative oxidation of the corresponding methane according to the method of Brunings and Corwin.[74] A few drops of triethylamine were added to a chloroform solution of the hydrobromide, the solution washed rapidly with water and dried. Evaporation of the solvent gave 5,5'-diethoxycarbonyl-3,4,3',4'-tetramethyldipyrromethene which crystallized from hexane as orange plates, m.p. 174°.

(Found: C, 66.1; H, 7.0; N, 8.4. $C_{19}H_{24}N_2O_4$ requires, C, 66.3; H, 7.0; N, 8.1%). $\lambda_{max.}$ EtOH 260, 289, 453 mμ. 1N HCl/EtOH 500 mμ.

5,5'-Diethoxycarbonyl-3,3'-diethyl-4,4'-dimethyldipyrromethane.- This compound was prepared by the method of Fischer

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≠ Unstable in ethanol and ethanolic hydrochloric acid.

and Halbig[143] and was obtained from ethanol as colourless needles, m.p. 126° (lit.[143] 126°).

5,5'-Diethoxycarbonyl-3,3'-diethyl-4,4'-dimethyldipyrromethene.-

To a stirred solution of 5,5'-diethoxycarbonyl-3,3'-diethyl-4,4'-dimethyldipyrromethane (1 g) in dry carbon tetrachloride (100 ml) was added bromine (0.4 g) in carbon tetrachloride (5 cc). The solution was cooled to 0° and the pyrromethene hydrobromide separated as red needles. The hydrobromide was dissolved in dry chloroform and a few drops of triethylamine added. The solvent was evaporated and the residue extracted with hot hexane. The dipyrromethene base crystallized from the cooled solution as orange-red plates, m.p. 111-112° (lit.[36] m.p. 112.5°). λ_{max} EtOH 259, 292 sh, 458 mμ. 1N HCl/EtOH 505 mμ.

4,3',5'-Triethoxycarbonyl-3,5,4'-trimethyldipyrromethane. -

A mixture of 2-chloromethyl-3,5-diethoxycarbonyl-4-methylpyrrole (5 g), 3-ethoxycarbonyl-2,4-dimethylpyrrole (4 g), ethanol (40 ml) and 2N hydrochloric acid (1 ml) was heated under reflux for 2 hr, then diluted with water (50 ml). The dipyrromethane (5 g, 56%) separated from the cooled solution and recrystallization from ethanol yielded colourless needles, m.p. 157-158° (lit.[143] 157-158°).

ǂ Unstable in ethanol and ethanolic hydrochloric acid.

4,3',5'-Triethoxycarbonyl-3,5,4'-trimethyldipyrromethene. -

The dipyrromethene hydrobromide, prepared from 4,3',5'-triethoxycarbonyl-3,5,4'-trimethyldipyrromethane by the method of Brunings and Corwin,[74] was dissolved in chloroform and a few drops of triethylamine added. The solvent was removed *in vacuo* and the solid residue extracted with benzene. Most of the solvent was removed and the dipyrromethene precipitated by the addition of hexane. Recrystallization from anhydrous acetone yielded orange needles, m.p. 126° (lit.[74] m.p. 125-126°).

5,5'-Diethyl-3,4,3',4'-tetramethyldipyrromethene. -

2-Ethyl-3,4-dimethylpyrrole (1 g) in formic acid (98%, 6 ml) was heated at 100° for 3 min. Perchloric acid (60%, 0.5 ml) was added and the mixture heated at 100° for a further 10 min. Red needles (0.6 g), m.p. 212-213° separated from the cooled solution. (This compound is probably the perchlorate but no satisfactory analysis was obtained.) Treatment of the perchlorate in hot ethanol with ammonia gave 5,5'-diethyl-3,4,3',4'-tetramethyldipyrromethene and recrystallization from acetone yielded orange plates, m.p. 128-129°.

(Found: C, 79.5; H, 9.4; N, 10.7. $C_{17}H_{24}N_2$ requires C, 79.6; H, 9.4; N, 10.9%). λmax. EtOH 225 (3.94), 448 (4.43). 1N HCl/EtOH 227 sh (4.10), 278 (3.56), 366 (3.81), 484 (4.80).

3',4-Diethoxycarbonyl-3,5,4',5'-tetramethyldipyrromethene. - 4-Ethoxycarbonyl-2-formyl-3,5-dimethylpyrrole (0.98 g) and 3-ethoxycarbonyl-2,4-dimethylpyrrole (0.84 g) were heated at 100° for 3 min in hydrobromic acid (48%, 5 ml) and then cooled. Water was added and the mixture extracted with chloroform (3 x 25 ml). The chloroform extracts were washed with dilute ammonia, dried, and evaporated. Recrystallization of the residue from acetone gave 3',4-diethoxycarbonyl-3,5,4',5'-tetramethyldipyrromethene (1.3 g, 75%) as orange needles, m.p. 175-177°.
(Found: C, 66.2; H, 6.9; N, 8.1. $C_{19}H_{24}N_2O_4$ requires C, 66.3; H, 7.0; N, 8.1%). λmax. EtOH 222 (4.37), 256 (3.91), 453 (4.45). 1N HCl/EtOH 210 (4.49), 243 (3.99), 480 (4.50).

5'-Ethoxycarbonyl-3,4,5,3',4'-pentamethyldipyrromethene. - The dipyrromethene hydrobromide, m.p. 201° (lit.[110] 202°) in chloroform was shaken with barium hydroxide. The chloroform solution was filtered and evaporated to give the dipyrromethene m.p. 125-126°, orange-red plates from hexane.
(Found: C, 71.7; H, 8.0%. $C_{17}H_{22}N_2O_2$ requires C, 71.3; H, 7.7%). λmax. EtOH 253 (3.93), 410 (4.35). 1N HCl/EtOH 251 (4.12), 467 (4.60).

3-Ethoxycarbonyl-4,5,3',4',5'-pentamethyldipyrromethene. - 4-Ethoxycarbonyl-2-formyl-3,5-dimethylpyrrole (0.98 g) and potassium 3,4,5-trimethylpyrrole-2-carboxylate (1.5 g) were

heated at 100° for 3 min. in hydrobromic acid (48%, 5 ml). The cooled mixture was diluted with water (25 ml) and extracted with chloroform (3 x 25 ml). The chloroform extracts were washed with dilute ammonia, dried, and evaporated to give 3-ethoxycarbonyl-4,5,3',4',5'-pentamethyldipyrromethene (0.88 g, 70%), m.p. 124-125.5°, orange plates from acetone.

(Found: C, 71.1; H, 7.7; N, 9.5%. $C_{17}H_{22}N_2O_2$ requires C, 71.3; H, 7.7; N, 9.8%). λmax. EtOH 212 (4.32), 226 sh (4.23), 260 sh (3.99), 407 (4.48). 1N HCl/EtOH 263 (3.83), 370 sh (3.89), 470 (4.91).

4,4'-Dicyano-3,5,3',5'-tetramethyldipyrromethene. - This compound was prepared from the hydrobromide, m.p. 242° (lit.[144] 242°) by the method described by Fischer and Rothemund[144] and had m.p. 256° (lit.[144] 280°).

(Found: C, 72.6, 72.55; H, 6.0, 5.9; N, 21.2. $C_{15}H_{14}N_4$ requires C, 72.0; H, 5.6; N, 22.4%). λmax.** EtOH 238, 446 mμ. 1N HCl/EtOH 238, 345, 470 mμ.

4,4'-Diethoxycarbonyl-3,3',5'-trimethyldipyrromethene, m.p. 147-148°, λmax. EtOH 219 (4.43), 338 sh (3.82), 433 (4.44). 1N HCl/EtOH 242 (3.97), 351 (3.65), 459 (5.04), and 4,4'-

** Compound not sufficiently soluble for an accurate intensity measurement.

-diethoxycarbonyl-3,3'-dimethyldipyrromethene, m.p. 129-130° (lit.[145] 129°) λmax. EtOH 219 (4.44), 263 (3.84), 434 (4.38). 1N HCl/EtOH 221 (4.43), 286 (3.70), 353 (3.47), 444 (4.81), were kindly donated by Dr. J. Ferguson.

4,4'-Di(2-methoxycarbonylethyl)-3,5,3',5'-tetramethyldipyrromethene, m.p. 133-134°, (Found: C, 67.5; H, 7.6; N, 7.4%. $C_{21}H_{28}N_2O_4$ requires C, 67.7; H, 7.6; N, 7.5%) λmax. EtOH 300 (3.40), 320 (3.51), 445 (4.58). 1N HCl/EtOH 228 (3.99), 288 (3.13), 362 (3.77), 482 (4.98), was kindly provided by Dr. R.L.N. Harris.

8.5. Phenyldipyrromethenes.

3,5,5'-Trimethyl-3'-phenyldipyrromethene. -

Hydrobromic acid (48%, 0.5 ml) was added to 2-formyl-5-methyl-3-phenylpyrrole (1.9 g) and 2,4-dimethylpyrrole (1.0 g) in ethanol (5 ml). The solution was heated at 80° for 5 min and cooled to give the dipyrromethene hydrobromide. The crude hydrobromide was dissolved in chloroform and shaken with aqueous ammonia. The chloroform solution was dried and evaporated to give 3,5,5'-trimethyl-3'-phenyldipyrromethene (2.2 g, 85%), m.p. 104° (orange plates from ethanol).

(Found: C, 82.7; H, 6.8; N, 10.5. $C_{18}H_{18}N_2$ requires C, 82.4; H, 6.9; N, 10.7%). $\lambda_{max.}$ * EtOH 219 (4.16), 277 (3.63), 443 (4.45). 1N HCl/EtOH 222 (4.26), 260 (3.53), 365 (3.68), 474 (4.92).

The following dipyrromethenes were prepared by methods analogous to that described for 3,5,5'-trimethyl-3'-phenyldipyrromethene:-

5,5'-Dimethyl-3,3'-diphenyldipyrromethene. -
2-Formyl-5-methyl-3-phenylpyrrole (1.9 g) and 2-methyl-4-phenylpyrrole (1.6g) gave 5,5'-dimethyl-3,3'-diphenyldipyrromethene (2.5 g, 75%), m.p. 178° (orange plates from acetone).

(Found: C, 85.4; H, 6.4; N, 8.4. $C_{23}H_{20}N_2$ requires C, 85.2; H, 6.2; N, 8.6%). $\lambda_{max.}$ EtOH 220 (4.34), 258 sh (3.95),

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* Maxima in mμ, log ε in parentheses.

276 sh (3.80), 457 (4.52). 1N HCl/EtOH 222 (4.41), 263 (3.79), 380 (3.82), 485 (4.90).

4'-Ethoxycarbonyl-5,3',5'-trimethyl-3-phenyldipyrromethene. - 2-Formyl-5-methyl-3-phenylpyrrole (0.9 g) and 3-ethoxycarbonyl-2,4-dimethylpyrrole (0.8 g) gave 4'-ethoxycarbonyl-5,3',5'-trimethyl-3-phenyldipyrromethene (1.2 g, 70%), m.p. 114-115° (orange prisms from ethanol),

(Found: C, 75.0; H, 6.5; N, 8.5. $C_{21}H_{22}N_2O_2$ requires C, 75.4; H, 6.6; N, 8.4%). $\lambda_{max.}$ EtOH 217 sh (4.42), 263 sh (4.04), 448 (4.40), 483 sh (4.35). 1N HCl/EtOH 222 (4.33), 260 (3.91), 472 (4.88).

3'-Ethoxycarbonyl-5,4',5'-trimethyl-3-phenyldipyrromethene. - 3-Ethoxycarbonyl-2-formyl-4,5-dimethylpyrrole (1.0 g) and 2-methyl-4-phenylpyrrole (0.8 g) gave 3'-ethoxycarbonyl-5,4',5'-trimethyl-3-phenyldipyrromethene (1.4 g, 67%), m.p. 149° (red needles from ethanol).

(Found: C, 75.6; H, 6.6; N, 7.9. $C_{21}H_{22}N_2O_2$ requires C, 75.4; H, 6.6; N, 8.4%). $\lambda_{max.}$ EtOH 220 (4.24), 459 (4.51). 1N HCl/EtOH 222 (4.44), 263 (3.80), 379 (3.87), 483 (4.90).

3,5-Dimethyl-3',5'-diphenyldipyrromethene. - Hydrobromic acid (48%, 0.5 ml) was added to 2-formyl-3,5-diphenylpyrrole (0.6 g) and 2,4-dimethylpyrrole (0.2 g) in acetic acid (1.5 ml) at 100°. After 10 min the solution was

cooled to 0° and ether (5 ml) added. The dipyrromethene hydrobromide, which separated from the solution, was re-dissolved in chloroform and the solution shaken with barium hydroxide for 30 min. Removal of the solvent under vacuum gave 3,5-dimethyl-3',5'-diphenyldipyrromethene (0.6 g, 75%), m.p. 154° (red needles from ethanol).

(Found: C, 84.7; H, 6.2; N, 8.4%. $C_{23}H_{20}N_2$ requires C, 85.1; H, 6.2; N, 8.6%). $\lambda_{max.}$ EtOH 225 (4.20), 285 (4.35), 467 (4.52). 1N HCl/EtOH 221 (4.27), 273 (4.33), 377 (3.95), 505 (4.98).

The following dipyrromethenes were prepared by an analogous method to that used for 3,5-dimethyl-3',5'-diphenyldipyrromethene. -

5-Methyl-3,3',5'-triphenyldipyrromethene. - 2-Formyl-3,5-diphenylpyrrole (1.2 g) and 2-methyl-4-phenylpyrrole (0.8 g) gave 5-methyl-3,3',5'-triphenyldipyrromethene (1.4 g, 70%), m.p. 190° (red prisms from chloroform: ethanol).

(Found: C, 87.4; H, 5.4; N, 6.6. $C_{29}H_{22}N_2$ requires C, 87.4; H, 5.6; N, 7.0%). $\lambda_{max.}$ EtOH* 287 (3.55), 489 (4.53). 1N HCl/EtOH* 283 (4.15), 388 (3.81), 521 (4.89).

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* Contains 1% carbon tetrachloride.

4,5,5'-Trimethyl-3'-phenyldipyrromethene. -
2-Formyl-5-methyl-3-phenylpyrrole (0.9 g) and 2,3-dimethylpyrrole (0.5 g) gave 4,5,5'-trimethyl-3'-phenyldipyrromethene (1.1 g, 78%), m.p. 116-118° (orange plates from ethanol).

(Found: C, 82.6; H, 7.0; N, 10.6. $C_{18}H_{18}N_2$ requires C, 82.4; H, 6.9; N, 10.7%). $\lambda_{max.}$ EtOH 225 (3.80), 439 (4.40). 1N HCl/EtOH 227 (3.82), 489 (4.80).

4,5-Dimethyl-3'-5'-diphenyldipyrromethene. -
2-Formyl-3,5-diphenylpyrrole (1.2 g) and 2,3-dimethylpyrrole (0.4 g) gave 4,5-dimethyl-3',5'-diphenyldipyrromethene (1,0 g, 63%), m.p. 114-114,5° (red needles from ethanol).

(Found: C, 84.8; H, 6.1; N, 8.5. $C_{23}H_{20}N_2$ requires C, 85.1; H, 6.2; N, 8.6%). $\lambda_{max.}$ EtOH 238 (4.01), 290(4.22), 470 (4.40). 1N HCl/EtOH 220 (4.24), 284 (4.27), 391 (3.85), 521 (4.87).

4,4'-Diethoxycarbonyl-5,3',5'-trimethyl-3-phenyldipyrromethene. -
4-Ethoxycarbonyl-2-formyl-3,5-dimethylpyrrole (1.0 g) and 3-ethoxycarbonyl-2-methyl-4-phenylpyrrole (1.1 g) gave 4,4'-diethoxycarbonyl-5,3',5'-trimethyl-3-phenyldipyrromethene (1.4 g, 66%), m.p. 164° (orange needles from acetone).

(Found: C, 70.7; H, 6.2; N, 6.9. $C_{24}H_{26}N_2O_4$ requires C, 70.9; H, 6.5; N, 6.9%). $\lambda_{max.}$ EtOH 216 sh (4.54), 262 (4.10), 463 (4.48). 1N HCl/EtOH 249 (4.00), 370 (3.54), 474 (5.03).

4,4'-Diethoxycarbonyl-5,5'-dimethyl-3,3'-diphenyldipyrromethene. -

3-Ethoxycarbonyl-5-formyl-2-methyl-4-phenylpyrrole (1.3 g) and 3-ethoxycarbonyl-2-methyl-4-phenylpyrrole (1.1 g) gave 4,4'-diethoxycarbonyl-5,5'-dimethyl-3,3'-diphenyldipyrromethene (1.7 g, 71%), m.p. 188-189° (orange plates from acetone).

(Found: C, 74.1; H, 6.0; N, 6.0. $C_{29}H_{28}N_4O_2$ requires C, 74.3; H, 6.1; N, 5.9%). $\lambda_{max.}$ EtOH 215 (4.32), 266 (4.03), 472 (4.56). 1N HCl/EtOH 220 sh (4.45), 251 (4.01), 388 (3.76), 483 (5.01).

3,5,3',5'-Tetraphenyldipyrromethene. -

This compound, m.p. 286-287° (lit.[76] m.p. 284-286°) was prepared by method described by Rogers.[76] The hydrobromide m.p. 263-264° (lit.,[119] m.p. 262°) was prepared by shaking the dipyrromethene in chloroform with hydrobromic acid (48%). $\lambda_{max.}$ EtOH* 292 (4.70), 360 (3.68), 523 (4.64). 1N HCl/EtOH* 296 (4.68), 396 (4.19), 561 (5.19).

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* Contains 1% carbon tetrachloride.

3,4,5-Trimethyl-3',5'-diphenyldipyrromethene. - Potassium 3,4,5-trimethylpyrrole-2-carboxylate (1.2 g) in acetic acid (2 ml) was added to 2-formyl-3,5-diphenylpyrrole (1.4 g) in acetic acid (10 ml) followed by hydrobromic acid (48%, 2 ml). Ether (10 ml) was added and the solution kept at 0° for 3 hr to give 3,4,5-trimethyl-3',5'-diphenyldipyrromethene hydrobromide (1.2 g, 80%), m.p. 196-197° (red needles from 5% ethanolic hydrogen bromide).

(Found: C, 68.7; H, 5.5; N, 6.7. $C_{24}H_{23}BrN_2$ requires C, 68.8; H, 5.6; N, 6.4%). The hydrobromide was dissolved in chloroform and shaken with anhydrous sodium acetate for 30 min. The chloroform solution was filtered, run on to a short column of alumina, and the free base eluted with benzene. The eluate was evaporated under nitrogen to give 3,4,5-trimethyl-3',5'-diphenyldipyrromethene, m.p. 150-151° (red needles from ethanol).

(Found: C, 85.0; H, 6.3; N, 8.0. $C_{24}H_{22}N_2$ requires C, 85.2; H, 6.6; N, 8.3%). $\lambda_{max.}$ EtOH 226 sh (4.17), 290 (4.29), 466 (4.44). 1N HCl/EtOH 224 (4.30), 283 (4.42), 384 (3.88), 513 (4.93).

4-Ethyl-3,5-dimethyl-3',5'-diphenyldipyrromethene. - Potassium 4-ethyl-3,5-dimethylpyrrole-2-carboxylate (0.6 g) in acetic acid (5 ml) and hydrobromic acid (48%, 2 ml) was

added to 2-formyl-3,5-diphenylpyrrole (0.7 g) in hot acetic acid (10 ml). Ether (10 ml) was added and the solution kept at 0° for 3 hr. 4-Ethyl-3,5-dimethyl-3',5'-diphenyldipyrromethene hydrobromide (1.1 g, 84%) separated and was recrystallized from 5% ethanolic hydrogen bromide to yield red needles, m.p. 211-213°.

(Found: C, 68.9; H, 5.7; N, 6.5. $C_{25}H_{25}BrN_2$ requires C, 69.3; H, 5.8; N, 6.5%). The hydrobromide was suspended in hot ethanol and ammonia (d 0.88, 0.5 ml) added. The dipyrromethene, m.p. 127-128°, crystallized from the cooled solution as red needles.

(Found: C, 84.8; H, 6.5; N, 7.9. $C_{25}H_{24}N_2$ requires C, 85.2; H, 6.9; N, 7.95%). $\lambda_{max.}$ EtOH 224 sh (4.19), 289 (4.34), 465 (4.46). 1N HCl/EtOH 222 (4.41), 283 (4.34), 379 (3.91), 514 (4.91).

The following dipyrromethenes were prepared by methods analogous to that described for 4-ethyl-3,5-dimethyl-3',5'-diphenyldipyrromethene. -

4'-Ethoxycarbonyl-3',5'-dimethyl-3,5-diphenyldipyrromethene.- 3-Ethoxycarbonyl-2,4-dimethylpyrrole (0.4 g) and 2-formyl-3,5-diphenylpyrrole (0.6 g) gave 4-ethoxycarbonyl-3',5'-dimethyl-3,5-diphenyldipyrromethene, (0.6 g, 60%), m.p. 154°

(red needles from ethanol).

(Found: C, 78.4; H, 6.3; N, 6.7. $C_{26}H_{24}N_2O$ requires C, 78.8; H, 6.1; N, 7.1%). $\lambda_{max.}$ EtOH 229 (4.32), 280 (4.35), 475 (4.43). 1$\underline{N}$ HCl/EtOH 278 (4.23), 338 (3.68), 389 (3.75), 513 (5.04).

3'-Ethoxycarbonyl-4',5'-dimethyl-3,5-diphenyldipyrromethene.- 2,4-Diphenylpyrrole (0.2 g) and 3-ethoxycarbonyl-2-formyl-4,5-dimethylpyrrole (0.3 g) gave 3'-ethoxycarbonyl-4',5'-dimethyl-3,5-diphenyldipyrromethene (0.28 g, 56%), m.p. 127° (red needles from cyclohexane).

(Found: C, 78.6; H, 6.4; N, 6.9. $C_{26}H_{24}N_2O_2$ requires C, 78.8; H, 6.1; N, 7.1%). $\lambda_{max.}$ EtOH 223 (4.37), 289 (4.33), 355 (3.81), 508 (4.49). 1$\underline{N}$ HCl/EtOH 223 (4.32), 283 sh (4.21), 291 sh (4.26), 382 (4.01) 544 (4.98).

3,5,3',4',5'-Pentamethyl-4-phenyldipyrromethene. -

An intimate mixture of 2-formyl-3,4,5-trimethylpyrrole (0.3 g) and potassium 2,4-dimethyl-3-phenylpyrrole-5-carboxylate (0.6 g) in hydrobromic acid (48%, 3 ml) was heated at 100° for 5 min. The solid product was dissolved in chloroform and shaken with aqueous ammonia. The dried chloroform solution was evaporated to give 3,5,3',4',5'-pentamethyl-4-phenyldipyrromethene (0.38 g, 61%), m.p. 123° (orange prisms from ethanol).

(Found: C, 82.3; H, 7.9; N, 9.6. $C_{20}H_{22}N_2$ requires C, 82.7; H, 7.6; N, 9.65%). $\lambda_{max.}$ EtOH 444 (4.40). 1N HCl/EtOH 216 (4.60), 364 (3.82), 485 (4.85).

The following dipyrromethenes were synthesised by an analogous method to that used for 3,5,3',4',5'-pentamethyl-4-phenyldipyrromethene. -

3,5,5'-Trimethyl-4,3',4'-triphenyldipyrromethene. - 2-Formyl-5-methyl-3,4-diphenylpyrrole (0.6 g) and potassium 2,4-dimethyl-3-phenylpyrrole-5-carboxylate (0.5 g) gave 3,5,5'-trimethyl-4,3',4'-triphenyldipyrromethene (0.6 g, 60%), m.p. 205° (red needles from ethanol).

(Found: C, 86.7; H, 6.2; N, 6.5. $C_{30}H_{26}N_2$ requires C, 86.9; H, 6.3; N, 6.8%). $\lambda_{max.}$ EtOH 470 (4.46). 1N HCl/EtOH 221 (4.30), 413 (3.93), 504 (4.82).

3,5,3',5'-Tetramethyl-4,4'-diphenyldipyrromethene. - A solution of 5-ethoxycarbonyl-2,4,-dimethyl-3-phenylpyrrole (2 g) in formic acid (98%, 2 ml) and hydrobromic acid (48%, 2 ml) was heated at 100° for 6 hr. The solution was cooled and ether (5 ml) added to give 3,5,3',5'-tetramethyl-4,4'-diphenyldipyrromethene hydrobromide (0.8 g, 90%), m.p. 240-243° (red needles from chloroform:hexane).

(Found: C, 69.2; H, 6.1; N, 6.3. $C_{25}H_{25}BrN_2$ requires C, 69.3; H, 5.8; N, 6.5%). The hydrobromide was dissolved in chloroform and shaken with aqueous ammonia. Evaporation of the dried chloroform extract gave the dipyrromethene base, m.p. 223° (orange needles from ethanol).

(Found: C, 84.8; H, 6.8; N, 7.8. $C_{25}H_{24}N_2$ requires C, 85.2; H, 6.7; N, 7.9%). $\lambda_{max.}$ EtOH 225 (4.15), 279 (3.65), 446 (4.38). 1N HCl/EtOH 226 (4.64), 249 (3.94), 365 (3.85), 470 (4.83).

4,4'-Diethyl-5,5'-dimethyl-3,3'-diphenyldipyrromethene. - 3-Ethyl-2-methyl-4-phenylpyrrole (1.0 g) in formic acid (98%, 5 ml) was heated at 100° for 5 min. Perchloric acid (60%, 0.5 ml) was added and the mixture heated at 100° for a further 15 min. The dipyrromethe perchlorate separated from the cooled solution. The perchlorate was dissolved in chloroform and shaken with aqueous ammonia. Evaporation of the dried chloroform extract gave 4,4'-diethyl-5,5'-dimethyl-3,3'-diphenyldipyrromethene (1.5 g, 70%), m.p. 147° (with decomp.),(orange needles from acetone).

(Found: C, 85.0; H, 7.1; H, 7.2. $C_{27}H_{28}N_2$ requires C, 85.2; H, 7.4; N, 7.4%). $\lambda_{max.}$ EtOH 223 (4.36), 236 (4.20), 457 (4.56). 1N HCl/EtOH 225 (4.38), 261 (3.57), 385 (3.86), 490 (5.04).

5,5'-Dimethyl-3,4,3',4'-tetraphenyldipyrromethene. - 2-Ethoxycarbonyl-5-methyl-3,4-diphenylpyrrole (5 g) in formic acid (98%, 5 ml) and hydrobromic acid (48%, 5 ml) was heated at 100° for 4 hr and then allowed to stand at 0° for 12 hr. The product was collected, washed with ether, and recrystallized from 5% ethanolic hydrogen bromide to give 5,5'-dimethyl-3,4,3',4'-tetraphenyldipyrromethene hydrobromide (3 g,75%) as red needles, m.p. 280° (decomp.).

(Found: C, 74.9; H, 5.4; N, 5.0. $C_{35}H_{29}BrN_2$ requires C, 75.4; H, 5.2; N, 5.0%). The hydrobromide was dissolved in chloroform and shaken with aqueous ammonia. Evaporation of the dried chloroform extract gave the dipyrromethene, m.p. 211-212° (orange needles from chloroform: hexane).

(Found: C, 88.4; H, 6.0; N, 5.8. $C_{35}H_{28}N_2$ requires C, 88.2; H, 5.9; H, 5.9%). $\lambda_{max.}$ EtOH 222 sh (4.36), 241 sh (4.26), 262 sh (4.13), 476 (4.53). 1N HCl/EtOH 239 (4.68), 315 (4.10), 365 (4.28), 509 (4.79).

3,4,5,3',4',5'-Hexaphenyldipyrromethene. -

Sulphuryl chloride (3.5 ml) in acetic acid (7 ml) was added to a stirred solution of 2-methyl-3,4,5-triphenylpyrrole (5 g) in acetic acid (50 ml) at 50-60°. The solution was heated at 100° for 1 hr and then poured into water. The mixture was made basic with sodium hydroxide and the red solid collected. Repeated recrystallizations from

nitrobenzene:methanol gave 3,4,5,3',4',5'-hexaphenyldipyrromethene (1g, 33%) as red needles, m.p. >360°.

(Found: C, 89.8; H, 5.5; N, 4.7. $C_{45}H_{32}N_2$ requires C, 90.0; H, 5.4; N, 4.7%). $\lambda_{max.}$ EtOH* 299 (4.39), 524 (4.50). 1N HCl/EtOH 305 (4.27), 415 (3.99), 561 (4.86).

3',5'-Diethoxycarbonyl-4'-methyl-3,5-diphenyldipyrromethene.-

Dry hydrogen chloride was passed into a solution of 2,4-diphenylpyrrole (1.2 g) and 2,4-diethoxycarbonyl-5-formyl-3-methylpyrrole (1.3 g) in ether (30 ml) at 0°. The dipyrromethene hydrochloride was dissolved in chloroform and triethylamine (0.5 ml) added. The solution was rapidly washed with water, dried, and evaporated to give 3',5'-diethoxycarbonyl-4'-methyl-3,5-diphenyldipyrromethene (1.8 g, 72%), m.p. 181-182° (orange needles from acetone).

(Found: C, 74.3; H, 5.6; N, 5.9. $C_{28}H_{26}N_2O_4$ requires C, 74.0; H, 5.8; N, 6.2%). $\lambda_{max.}$ EtOH 453. 1N HCl/EtOH 516. This compound is not sufficiently stable in ethanol for accurate measurements.

Attempted preparation of 5-ethoxycarbonyl-3,4-dimethyl-3',5'-diphenyldipyrromethene. -

2,4-Diphenylpyrrole (0.4 g) in hot acetic acid (8 ml)

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* Contains 1% carbon tetrachloride

was added to a solution of 2-ethoxycarbonyl-5-formyl-3,4-dimethylpyrrole (0.6 g) in acetic acid (5 ml) immediately followed by hydrobromic acid (48%, 2 ml). The mixture was heated at 100° for 5 min and then left at 0° for 12 hr. Chloroform (50 ml) was added and the solution washed several times with water and finally with aqueous ammonia. Evaporation of the dried chloroform extract and recrystallization of the residue from nitrobenzene gave 3,5,3',5'-tetraphenyldipyrromethene (0.3 g, 30%). It had m.p. 285-287°, not depressed by admixture with an authentic specimen, and the electronic absorption spectra in ethanol and 1$\underline{\underline{N}}$ ethanolic hydrobromic acid were identical. 2-Formyl-3,5-diphenylpyrrole and 2-ethoxycarbonyl-3,4-dimethylpyrrole under the same conditions also gave 3,5,3',5'-tetraphenyldipyrromethene.

8.6. 3,5,3',5'-Tetraarylazadipyrromethenes.

The following chalcones were prepared by the literature methods:-

Chalcone (benzylideneacetophenone), m.p. 53-56° (lit.[146] m.p. 55-57°); 4'-methylchalcone, m.p. 95° (lit.[147] m.p. 96,5°); 4-methylchalcone, m.p. 72° (lit.[148] m.p. 74.5°); 4,4'-dimethylchalcone, m.p. 128° (lit.[149] m.p. 128-129°); 4'-chlorochalcone, m.p. 100° (lit.[150] m.p. 101° (with decomp.)); 4-chlorochalcone, m.p. 116° (lit.[151] m.p. 115-116°); 4'-bromochalcone, m.p. 105.5° (lit.[150] m.p. 104-105°); 4'-methoxychalcone, m.p. 107° (lit.[152] m.p. 106-107°); 4-methoxychalcone, m.p. 76-78° (lit.[153] m.p. 77-78°); 4,4'-dimethoxychalcone, m.p. 101-102° (lit.[154] m.p. 101-102°); 4'-acetamidochalcone, m.p. 168° (lit.[151] m.p. 168°); 4-dimethylaminochalcone, m.p. 115° (lit.[155] m.p. 113-114°); 3-nitrochalcone, m.p. 145° (lit.[156] m.p. 145-146°); 4'-phenylchalcone, m.p. 154° (lit.[150] m.p. 156°); 3',4'-benzochalcone, m.p. 104° (lit.[157] m.p. 105°); 3,4-benzochalcone, m.p. 157-158° (lit.[158] m.p. 157-158°); 4-dimethylamino-4'-methoxychalcone, m.p. 127° (lit.[159] m.p. 127°); 4-chloro-4'-methoxychalcone, m.p. 129-131° (lit.[160] m.p. 130-131°).

4-Chloro-4'-methylchalcone. -

Sodium methoxide (from 0.5 g sodium) in methanol (15 ml) was added to a solution of p-methylacetophenone (13 g) and p-chlorobenzaldehyde (14 g) in methanol (50 ml). The

solution was allowed to stand at room temperature for 15 min and then cooled to 0° and stirred vigorously to give 4-Chloro-4'-methoxychalcone (22 g, 88%). Recrystallization from ethanol gave pale yellow needles, m.p. 148-149°.

(Found: C, 74.4; H, 4.9. $C_{16}H_{13}C_{10}$ requires C, 74.8; H, 5.1%).

The following azadipyrromethenes were prepared by the method described by Rogers.[54]

3,3'-di-p-dimethylaminophenyl-5,5'-diphenylazadipyrromethene, m.p. 275-278° (lit.[54] m.p. 276-278°) (the dimethiodide[54] had m.p. >350°); 3,3-di-p-anisyl-5,5'-diphenylazadipyrromethene, m.p. 289-290° (lit.[54] m.p. 228-290°); 3,3'-di-m-nitrophenyl-5,5'-diphenylazadipyrromethene, m.p. 320° (lit.[54] m.p. 330°); 5,5'-di-p-anisyl-3,3'-diphenylazadipyrromethene, m.p. 239-241° (lit.[54] m.p. 239-242°); 3,5,3',5'-tetra-p-anisylazadipyrromethene, m.p. 282-283° (lit.[54] m.p. 281-282°).

3,5,3',5'-Tetraphenylazadipyrromethene. -

β-Benzoyl-α-phenylpropionitrile[161] (5 g) and ammonium acetate (25 g) were heated in a stainless steel autoclave (capacity, 100 ml) at 200° for 30 min to give the azadipyrromethene (2.8 g, 100%) which was recrystallized from nitrobenzene to yield blue needles with a metallic lustre, m.p. 286° (lit.[54] m.p. 287-288°).

3,3'-Diphenyl-5,5'-di-p-tolylazadipyrromethene. -

Sodium methoxide (from 1.5 g sodium) in methanol (50 ml) was added to 4'-methylchalcone (12 g) and nitromethane (4 ml) in methanol (100 ml) at 25°. The mixture was refluxed for 1 hr and then cooled to 0° and acidified with acetic acid. On the addition of water (200 ml) to the alcoholic solution, a brown oil separated. The aqueous layer was decanted and the oil heated with ammonium acetate (50 g) at 190° until the azadipyrromethene formed. The solid was collected and any unreacted nitroketone and ammonium acetate removed by washing with hot acetone and hot water. Recrystallization of the residue from nitrobenzene gave 3,3'-diphenyl-5,5'-di-p-tolylazadipyrromethene (11 g, 86%), m.p. 282-283° as long needles with a golden metallic lustre.

(Found: C, 85.8; H, 5.5; N, 8.9. $C_{34}H_{27}N_3$ requires C, 85.5; H, 5.7; N, 8.8%).

The following azadipyrromethenes were prepared in yields of 80-100% by methods analogous to that used for the synthesis of 3,3'-diphenyl-5,5'-di-p-tolylazadipyrromethene. All were recrystallized from nitrobenzene.

5,5'-Diphenyl-3,3'-di-p-tolylazadipyrromethene, prepared from 4-methylchalcone, was obtained as fine needles with a coppery metallic lustre, m.p. 284-285°.

(Found: C, 85.4; H, 5.8; N, 8.8. $C_{34}H_{27}N_3$ requires C, 85.5; H, 5.7; N, 8.8%).

3,5,3',5'-Tetra-p-tolylazadipyrromethene, prepared from 4,4'-dimethylchalcone, was obtained as gold prisms with a green sheen, m.p. 292-293°.

(Found: C, 85.4; H, 6.1; N, 8.1. $C_{36}H_{31}N_3$ requires C, 85.5; H, 6.2; N, 8.3%).

5,5'-Di-p-chlorophenyl-3,3'-diphenylazadipyrromethene, prepared from 4'-chlorochalcone, was obtained as needles with a coppery sheen, m.p. 307-308°.

(Found: C, 74.3; H, 4.3; N, 7.8. $C_{32}H_{21}Cl_2N_3$ requires C, 74.1; H, 4.1; N, 8.1%).

3,3'-Di-p-chlorophenyl-5,5'-diphenylazadipyrromethene, prepared from 4-chlorochalcone, was obtained as blue needles with a metallic lustre, m.p. 321-324°.

(Found: C, 74.0; H, 4.15; N, 7.8. $C_{32}H_{21}Cl_2N_3$ requires C, 74.1; H, 4.1; N, 8.1%).

5,5'-Di-p-bromophenyl-3,3'-diphenylazadipyrromethene, prepared from 4'-bromochalcone, was obtained as purple plates with a metallic sheen, m.p. 308-309°.

(Found: C, 63.4; H, 3.7; N, 6.7. $C_{32}H_{21}Br_2N_3$ requires C, 63.3; H, 3.5; N, 6.9%).

5,5'-Di(2-naphthyl)-3,3'-diphenylazadipyrromethene, prepared from 3',4'-benzochalcone, was obtained as purple needles with a gold lustre, m.p. 306-307°.

(Found: C, 87.0; H, 5.0; N, 7.5. $C_{40}H_{27}N_3$ requires C, 87.4; H, 5.0; N, 7.7%).

3,3'-Di(2-naphthyl)-5,5'-diphenylazadipyrromethene, prepared from 3,4-benzochalcone, was obtained as purple prisms, m.p. 298-299°.

(Found: C, 87.2; H, 5.1; N, 7.6. $C_{40}H_{27}N_3$ requires C, 87.4; H, 5.0; N, 7.7%).

5,5'-Di-p-anisyl-3,3'-di-p-dimethylaminophenylazadipyrromethene, prepared from 4-dimethylamino-4'-methoxychalcone, was obtained as small copper-coloured prisms, m.p. 273-274°.

(Found: C, 76.7; H, 6.3; N, 12.0. $C_{38}H_{37}N_5O_2$ requires C, 76.6; H, 6.3; N, 11.8%). The dimethiodide was prepared by adding iodomethane to a solution of the azadipyrromethene in nitrobenzene. The methiodide which separated from the solution was collected and purified by dissolving in methanol, filtering the solution, and precipitating the product with ether. The dimethiodide was obtained as small purple prisms, m.p. $>350°$.

(Found: N, 8.0. $C_{40}H_{43}I_2N_5O_2$ requires N, 8.0%).

5,5'-Di-p-anisyl-3,3'-di-p-chlorophenylazadipyrromethene, prepared from 4-chloro-4'-methoxychalcone, was obtained as long needles with a bronze lustre, m.p. 314-318°.

(Found: C, 70.5; H, 4.3; N, 7.0. $C_{34}H_{25}Cl_2O_2N_3$ requires C, 70.6; H, 4.4; N, 7.3%).

3,3'-Di-p-chlorophenyl-5,5'-di-p-tolylazadipyrromethene, prepared from 4-chloro-4'-methylchalcone, was obtained as short needles with a golden metallic sheen, m.p. 313-315°.

(Found: C, 74.5; H, 4.7; N, 7.5. $C_{34}H_{25}Cl_2N_3$ requires C, 74.7; H, 4.6; N, 7.7%).

5,5'-Di-p-biphenylyl-3,3'-diphenylazadipyrromethene. -

In this preparation the intermediate nitroketone was isolated and characterized. A solution of sodium (1.5 g) in methanol (50 ml) was run into a mixture of 4'-phenylchalcone (12.5 g) and nitromethane (4 ml) in methanol (100 ml) at 25°. The mixture was heated on a steam-bath for 1 hr, cooled to 0° and acidified with acetic acid. The nitroketone (11 g, 73%) separated on addition of water (200 ml) to the solution. The product was collected, washed with water and recrystallized from methanol to give 1-biphenylyl-4- nitro-3-phenylbutan-1-one as colourless plates, m.p. 137°.

(Found: C, 76.3; H, 5.6; N, 4.0. $C_{22}H_{19}NO_3$ requires C, 76.5;

H, 4.6; N, 4.1%). Heating the nitroketone (10 g) with ammonium acetate at 190° gave 5,5'-di-p-biphenylyl-3,3'-diphenylazadipyrromethene (8.1 g, 92%) which crystallized from nitrobenzene as blue needles with a golden sheen, m.p. 320°.

(Found: C, 87.5; H, 5.4; N, 6.7. $C_{44}H_{31}N_3$ requires C, 87.7; H, 5.2; N, 7.0%).

5,5'-Di-p-acetamidophenyl-3,3'-diphenylazadipyrromethene. - 4'-Acetamidochalcone (18 g) and potassium cyanide (16.2 g) in methanol (250 ml) were refluxed for 20 min during which time a mixture of acetic acid (12 ml) and water (33 ml) was slowly added. After refluxing the mixture for a further 20 min the mixture was cooled and poured onto ice. The precipitated solid (17 g, 85%) was collected and washed with water until free of cyanide ions. Recrystallization of the product from aqueous methanol gave 1-p-acetamidophenyl-3-cyano-3-phenylpropan-1-one as colourless needles, m.p. 153-154°.

(Found: C, 74.0; H, 5.5; N, 9.4. $C_{18}H_{16}N_2O_2$ requires C, 74.0; H, 5.5; N, 9.6%). The cyanoketone (10 g) was heated with an excess of ammonium acetate to give 5,5'-di-p-acetamidophenyl-3,3'-diphenylazadipyrromethene (7 g, 72%) which crystallized from nitrobenzene as dull purple prisms, m.p. 360°.

(Found: C, 76.5; H, 5.5; N, 12.1. $C_{36}H_{29}N_5O_2$ requires C, 76.7; H, 5.2; N, 12.4%).

8.7. Dipyrromethenes with meso-Substituents.

3,4,5,3',4',5'-Hexamethyl-ms-phenyldipyrromethene. -

This compound was prepared by the method of Jones and Laslett[37] and was obtained as red plates with a green reflex, m.p. 194-195° (lit.[37] m.p. 193-195°).

3,5,3',5'-Tetramethyl-4,4'-diethoxycarbonyl-ms-phenyldipyrromethene. -

A chloroform solution of the dipyrromethene hydrochloride, m.p. 203-205° (lit.[98] m.p. 204°), was washed with ammonium hydroxide and then with water. Evaporation of the dried chloroform extract and recrystallization of the residue from ethanol gave the dipyrromethene base as orange prisms, m.p. 160-161° (lit.[98] m.p. 159°). $\lambda_{max.}$ EtOH 219 (4.48), 262 (4.00), 325 (3.79), 457 sh (4.54), 474 (4.60). 1N HCl/EtOH 216 (4.48), 249 (4.04), 377 (4.21), 510 (4.78).

ms,3,5,3',5'-Pentaphenyldipyrromethene. -

This compound was prepared by the method of Rogers[76] and was obtained from nitrobenzene as red needles, m.p.

269-271° (lit.[76] m.p. 268-270°). $\lambda_{max.}$ EtOH 296, 543. 1N HCl/EtOH 238 (4.38), 294 (4.30), 413 (4.10), 617 (4.60).

ms-Methyl-3,5,3',5'-tetraphenyldipyrromethene hydrochloride.-

The monohydrochloride was prepared by the method of Treibs and Hintermeier[98] and was obtained from chloroform: hexane as purple plates with a metallic lustre, m.p. 173-175° (lit.[98] m.p. 176°; Jeffreys and Knott[70] reported the dihydrochloride, m.p. 202°). $\lambda_{max.}$ 1N HCl/EtOH 234 (4.29), 291 (4.24), 386 sh (3.72), 420 (3.77), 596 (4.62).

ms-Ethyl-3,5,3',5'-tetraphenyldipyrromethene hydrochloride.-

The hydrochloride salt was prepared by the method described by Jeffreys and Knott[70] and was obtained from chloroform: hexane as blue needles with a metallic lustre, m.p. 189-190° (lit.[70] m.p. 190°). $\lambda_{max.}$ 1N HCl/EtOH 234 (4.33), 293 (4.34), 424 (3.75), 600 (4.47).

1,1-Bis(3-ethoxycarbonyl-2,4-dimethylpyrrolyl-(5)-)-ethylene. -

This compound was prepared by the method described by Treibs and Hintermeier[98] and was obtained from aqueous ethanol as yellow needles, m.p. 208° (lit.[98] m.p. 208°).

1,1-Bis(3-ethoxycarbonyl-2,4-dimethylpyrrolyl-(5)-)-2-methylethylene. -

This compound was prepared by the method of Treibs and Hintermeier[98] and crystallized from ethanol as pale yellow needles, m.p. 232-233° (lit.[98] m.p. 229°).

3',4-Diethoxycarbonyl-ms-ethoxycarbonylmethyl-3,5,4',5'-tetramethyldipyrromethene. -

The following experiments were carried out under identical conditions to those described by Filippovich et al.[92]

(a) 3-Ethoxycarbonyl-2,4-dimethylpyrrole-5-(ethyl β-ketoproprionate) and 4-ethoxycarbonyl-2,3-dimethylpyrrole in anhydrous chloroform treated with phosphorus pentoxide gave a dipyrromethene, m.p. 115-119° (lit.[92c] m.p. 118-120°). When ammonium hydroxide was added to the reaction mixture, the ethylenic form was obtained as yellow needles, m.p. 191-192° (lit.[92c] 192-194.5°).

(b) 4-Ethoxycarbonyl-2,3-dimethylpyrrole-5-(ethyl β-ketopropionate) and 3-ethoxycarbonyl-2,4-dimethylpyrrole in anhydrous chloroform treated with phosphorus pentoxide gave a dipyrromethene, m.p. 142-146° (lit.[92c] m.p. 147-148°). Addition of ammonium hydroxide to the reaction mixture gave the ethylenic form as yellow prisms, m.p. 184-185° (lit.[92b,c] m.p. 184-185.5°).

8.8. Miscellaneous.

1-Benzoyl-2,3,4,5-tetraphenylpyrrole. -

2,3,4,5-Tetraphenylpyrrole (12 g) in toluene (100 ml) was added to potassium sand (4 g) under dry toluene (50 ml). The mixture was refluxed with stirring for 5 hr and then benzoyl chloride (25 g) was added dropwise to the cold stirred solution over a period of 20 min. The mixture was heated on a steam-bath for 6 hr and filtered hot. Evaporation of the toluene under reduced pressure and recrystallization of the residue from benzene-hexane gave 1-benzoyl-2,3,4,5-tetraphenylpyrrole (9.5 g, 62%) as pale yellow plates, m.p. 246.5°.

(Found: C, 88.75; H, 5.5; N, 2.9. $C_{35}H_{25}NO$ requires C, 88.4; H, 5.3; N, 2.95%.)

3,4-Dibenzoyl-2,5-dimethylpyrrole. -

2,5-Dimethylpyrrole (2 g) was dissolved in carbon disulphide (30 ml) and benzoyl chloride (2 g) and anhydrous zinc chloride (4 g) added. The mixture was heated (steam-bath) under reflux for 6 hr and allowed to stand at room temperature overnight. The solvent was removed and water added to the residue. The solid was collected, washed with 10% sodium hydroxide, and recrystallized from methanol to yield 3,4-dibenzoyl-2,5-dimethylpyrrole (2.9 g, 45%) as

colourless needles, m.p. 227°. (Found: C, 79.1; H, 5.6; N, 4.5. $C_{20}H_{17}NO_2$ requires C, 79.2; H, 5.65; N, 4.6%.) Evaporation of the mother liquors gave a small amount of 3-benzoyl-2,5-dimethylpyrrole, m.p. 127-129° (lit.[131] m.p. 129-130°). Its infrared spectrum was identical with that of an authentic specimen.

Condensation of 3-formyl-butan-2-one and 3-aminopentan-2,4-dione. -

Zinc dust (6 g) was slowly added to a mixture of 3-formyl-butan-2-one (sodium salt, 4.7 g) and 3-hydroxyimino-pentan-2,4-dione[163] (4 g) in aqueous acetic acid (50%, 200 ml) so that the temperature remained at 70-80°. The mixture was heated on a steam-bath for 15 min and poured into an ice-water mixture, the solid (0.7 g, 15%) collected and recrystallized from ethanol. The yellow product, m.p. 107-118°, was a mixture of pyrroles and the infrared spectrum (in dilute CCl_4) showed bands at 3430 and 3442 cm^{-1}, which correspond to the NH frequencies of 2-acetyl-4,5-dimethyl-pyrrole and 2,4-diacetyl-3,5-dimethylpyrrole respectively. No attempt was made to separate the pyrroles.

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Guy, R., & Jones, R. (1965). Pyrrole studies. IV. The electronic spectra of alkyl- and ethoxycarbonyldipyrromethenes. *Australian Journal of Chemistry, 18*(3), 363-371.

Spectrochimica Acta, 1965, Vol. 21, pp. 1011 to 1013. Pergamon Press Ltd. Printed in Northern Ireland

Pyrrole studies—VII.* The NH stretching frequencies of substituted pyrroles. Phenyl substituents

(*Received* 29 *September* 1964)

Abstract—Data for pyrroles containing methyl and phenyl groups show that the NH stretching frequency may be represented by the equation:

$$\nu_{NH}(cm^{-1}) = 3496 - 9n_{\alpha}CH_3 + 2n_{\beta}CH_3 - 12n_{\alpha}\phi - 7n_{\beta}\phi$$

where n_{α} and n_{β} are the number of substituents in the α and β positions respectively.

As a preliminary study of a more detailed investigation of intramolecular hydrogen bonding in phenyldipyrromethenes [1, 2], the NH stretching frequency of a number of related pyrroles has been examined.

It has already been shown [3, 4] that for methyl pyrroles and ethoxycarbonylpyrroles the effect of each substituent on the NH group is independent of the other groups and additive. The results obtained in this investigation show that the NH stretching frequencies of phenylpyrroles (Table 1) may also be represented by a single equation.

$$\nu_{NH}(cm^{-1}) = 3496 - 9n_{\alpha}CH_3 + 2n_{\beta}CH_3 - 12n_{\alpha}\phi - 7n_{\beta}\phi$$

where n_{α} and n_{β} are the number of substituents in the α and β positions respectively.

Models† show that steric interaction between adjacent phenyl groups is greater for $\alpha\beta$ substituents than for $\beta\beta'$ substituents. However, deviations from the calculated NH stretching frequency are small, even for tetraphenylpyrrole, and suggest that the steric interactions are small and are readily accommodated by a slight deviation of the phenyl groups from coplanarity with the pyrrole ring.

In the spectra of a majority of the compounds examined a second band, which is approximately one-twentieth the intensity of the major band, is observed. The position of this band is *ca.* 20 cm^{-1} lower than that of the major band and by analogy with the methyl and ethoxycarbonyl compounds [4] it is assumed to be a hot band arising from the NH out-of-plane de-

Table 1. NH stretching frequencies of phenylpyrroles in CCl_4

Substituents				$\Delta\nu$ = calculated–observed		
2	3	4	5	Observed* (cm^{-1})	Calculated (cm^{-1})	$\Delta\nu$ (cm^{-1})
ϕ	H	H	H	3486 (3466)	3484	−2
ϕ	H	H	CH_3	3470 (3452)	3475	+5
ϕ	CH_3	H	CH_3	3469 (3447)	3477	+8
H	ϕ	H	CH_3	3480 (3460)	3480	0
CH_3	ϕ	CH_3	H	3482 (3463)	3482	0
H	ϕ	C_2H_5	CH_3	3480 (3458)	—	—
ϕ	ϕ	H	CH_3	3463 (3443)	3468	+5
ϕ	H	ϕ	H	3478	3477	−1
ϕ	H	H	ϕ	3472 (3451)	3472	0
CH_3	ϕ	ϕ	H	3474 (3452)	3473	−1
ϕ	ϕ	ϕ	H	3470	3470	0
ϕ	ϕ	ϕ	CH_3	3462	3461	−1
ϕ	ϕ	H	ϕ	3463	3465	+2
ϕ	ϕ	ϕ	ϕ	3459	3458	−1

* Bands quoted in brackets were, in the majority of cases, obtained by graphical resolution and are considered to be hot bands.

Table 2. NH stretching frequencies of ethoxycarbonylphenylpyrroles in CCl_4

Substituents 2	3	4	5	$\Delta\nu$ = calculated-observed Observed* (cm^{-1})	Calculated (cm^{-1})	$\Delta\nu$ (cm^{-1})
CH_3	CO_2Et	ϕ	H	3469 (3452)	3467	−2
CH_3	CO_2Et	ϕ	ϕ	3456 (3437)	3455	−1
CH_3	CO_2Et	CH_3	ϕ	3458 (3440)	3464	+6
ϕ	CO_2Et	ϕ	ϕ	3450 (3425)	3452	+2
CO_2Et	CH_3	ϕ	CH_3	3467 3451	3468 3451	+1 0
CO_2Et	ϕ	ϕ	CH_3†	3461 3444	3459 3442	−2 −2
CO_2Et	ϕ	CO_2Et	CH_3	— 3436	3453 3436	— 0
CO_2Et	ϕ	CO_2Et	ϕ	— 3430	3450 3433	— +3

* Bands quoted in brackets were, in the majority of cases, obtained by graphical resolution and are considered to be hot bands.

formation at *ca.* 600 cm^{-1}. In several spectra, particularly those of pyrroles having more than one phenyl group, the main absorption band appeared to be asymmetric but it was not possible to determine the precise position of the hot band.

Table 2 lists the NH stretching frequencies for pyrroles having methyl, phenyl and ethoxycarbonyl groups. The observed frequencies agree well with those calculated from the constants for the three groups.

$$\nu_{NH}(cm^{-1}) = 3496 - 9n_\alpha CH_3 + 2n\beta CH_3 - 12n_\alpha\phi - 7n_\beta\phi - 13n_\beta CO_2Et - \begin{Bmatrix}41\\31\end{Bmatrix} n_\alpha\ CO_2Et.$$

Experimental

Pyrroles: All the compounds were prepared by known methods and were recrystallized or distilled immediately before measurement.

Spectra: The NH stretching frequencies were determined for *ca.* $10^{-4}M$ solutions in carbon tetrachloride in 100 mm cells with a Unicam SP 700 spectrometer. All measurements were calibrated against ammonia [5].

Acknowledgement—We acknowledge the award of a Commonwealth Post-graduate Grant (to R. W. G.).

R. W. Guy
R. Alan Jones

Department of Organic Chemistry
University of Adelaide
Adelaide, South Australia

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