SYNTHETIC APPROACHES TO 6,9:19,22-DIIMINO-2,26:13,15-BIS(DIMETHYLETHENO)-10,12:23,25-BIS(TRIMETHYLENE)-3,7,8,18,20,21-HEXAMETHYL-1,14-DIAZA[26]ANNULENE

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This is to certify that the

thesis entitled

SYNTHETIC APPROACHES TO 6,9:19,22-DIIMINO-2,26:13,15-BIS(DIMETHYLETHENO)-10,12:23,25-BIS(TRIMETHYLENE)-3,7,8,18,20,21-HEXAMETHYL-1,14-DIAZA[26]ANNULENE

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ABSTRACT

SYNTHETIC APPROACHES TO 6,9:19,22-DIIMINO-2,26:13,15-BIS(DIMETHYLETHENE)-10,12:23,25-BIS(TRIMETHYLENE)-3,7,8,18,20,21-HEXAMETHYL-1,14-DIAZA[26]ANNULENE

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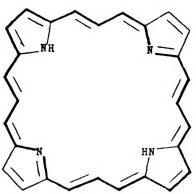
Several synthetic pathways to the preparation of a substituted 1,14-diaza[26]annulene, 78 -- a potentially aromatic macrocycle -- were investigated. The 1,14-diaza[26]annulene chosen was 79.



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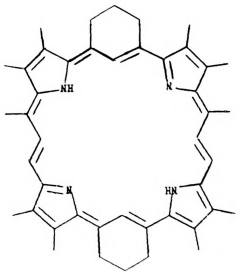

79

In the course of the investigation several tri- and tetra-substituted pyrroles were synthesized for the various pathways attempted. 2,5-Bis(3-oxobutenyl)-3,4-dimethylpyrrole, 91, was prepared by a Michael addition of one equivalent of 3,4-dimethylpyrrole, 80, with two equivalents of 3-butyn-2-one, 87. Reduction of 91 with $NaBH_4$ gave 2,5-bis(3-hydroxybutenyl)-3,4-dimethylpyrrole, 92.

2,5-Bis(3-oxobutyl)-3,4-dimethylpyrrole, 95, was also obtained by the Michael addition of 80 on methyl vinyl ketone as was 91 from 80 and 87. Ethyl 3-(3,4-dimethylpyrrol-2-yl)-propenoate, 99, was formed by another Michael reaction of 80 on ethyl propiolate. Reduction of 99 gave ethyl 3-(3,4-dimethylpyrrol-2-yl)propanoate, 100, which in turn reacted again with ethyl propiolate to give ethyl 3-(5-carbethoxyethyl-3,4-dimethylpyrrol-2-yl)propenoate, 101. Reduction of 101 gave diethyl 3,4-dimethylpyrrole-2,5-dipropanoate, 102. Compound 102 could be converted into the N,N-dimethylamide derivative, N,N,N',N',3,4-hexamethylpyrrole-2,5-dipropanamide, 105. The 3,4-dimethylpyrrole Grignard attack on 95 and 102 to give 97 and 103 was unsuccessful. The Vilsmeier acylation of 80 using 105 also failed to give 103.

Preparation of two new dipyrryltrimethine salts were successful. Reaction of dihydroresorcinol, 114, with 80 gave 3,4,3',4'-tetramethyl-dipyrryl-(2,2')-hexacyclotrimethine iodide, 115. Compound 108 was reduced to 1,3-bis-(3,4-dimethylpyrrol-2-yl)cyclohexane, 116. 5,5'-Bis(carbethoxyethyl)-3,4,3',4'-tetramethyl-dipyrryl-(2,2')-hexacyclotrimethine iodide, 120, was also prepared by the reaction of 114 with 100.

Spectral data for all the above compounds and other reactions of them are given.

SYNTHETIC APPROACHES TO 6,9:19,22-DIIMINO-2,26:13,15-BIS(DIMETHYLETHENO)-10,12:23,25-BIS(TRIMETHYLENE)-3,7,8,18,20,21-HEXAMETHYL-1,14-DIAZA[26]ANNULENE

By

Thomas Lee Bowman

A DISSERTATION

Submitted to
Michigan State University
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DOCTOR OF PHILOSOPHY

Department of Chemistry

1973

To my wife who has endured much over
the past five years and has been a
continuing source of encouragement;

To my parents who have given me so much.

ACKNOWLEDGMENTS

I would like to thank the Department of Chemistry at Michigan State University for providing financial support in the form of teaching assistantships for the past five years, which encouraged me to seek a teaching career. I would also like to acknowledge Dr. Eugene LeGoff for his interest in and the conception of the project. Thanks also goes to my fellow graduate students, Dean Ersfeld, Ara Yeramyan, Stamatios Mylanokis, Eugene Losey, and Thomas Kowar, who made life a little easier to bear during hard times. And above all, thanks to God, who controls the particles of this world and has allowed me to manipulate them in this synthesis.

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INTRODUCTION

One of the most actively investigated areas of organic chemistry over the past one hundred and eight years has been the concept of aromaticity. The metamorphosis of this concept is perhaps one of the best examples of the scientific method--the interaction of observable, experimental data with the theoretical explanations of that data. In 1865, Kekule proposed a cyclic array of six carbons involving three double bonds as the structure for benzene. Since then theoretical chemists have been trying to define and describe the factors in benzenoid compounds which give rise to the observations of substitution on rather than addition to the double bonds--a phenomenon which has been explained by the concept of aromaticity. In the twentieth century the concept of aromaticity has been extended to non-benzenoid compounds also. In addition to the works of the theoretician, many synthetic organic chemists have tried to synthesize a wide variety of cyclic, conjugated molecules in order to better define the aromatic concept. It is in this light that the present investigation was undertaken.

Prior to 1858 no clear theory of the molecular make-up of organic compounds existed. In the early 1800's the term "aromatic" had been applied to any isolated compound which

had an aromatic odor, whether or not it contained a benzene ring. After 1830, when good combustion analysis became available, aromatic compounds were categorized according to composition--relatively high carbon to hydrogen ratio. Around the middle of the nineteenth century it was recognized that there was a nucleus common to these aromatic compounds with high carbon to hydrogen ratio, which was benzene characterized in 1825 by Faraday.[1] Then in 1858 Couper[2] and Kekule[3] simultaneously proposed the tetravalent character of carbon and various molecular structures based on that idea. This was the beginning of structural organic chemistry.

The first attempt to provide a structure for these aromatic compounds was made in 1858 by Couper. In 1861 Loschmidt[4] put forth the idea of a cyclic structure for benzene but did not account for the tetravalency of carbon. He was the first to suggest that a six carbon nucleus was the basis for the aromatic compounds. Then in 1865 Kekule[5] set the groundwork for the structural definition of aromatic compounds. He felt that a series of aromatic compounds analogous to the then known aliphatic series existed; the simplest aromatic of this series had six carbons. It was in this 1865 paper that Kekule proposed the cyclic array of six carbons with alternating double and single bonds, 1, for benzene. The remaining valences were used for bonding to atoms external to the six-carbon nucleus. This structure accounted for the high carbon to hydrogen ratio but did not

satisfactorily explain the number of isomers for the substituted benzene compounds. This was to be clarified in a later paper by Kekule.

Erlenmeyer[6] agreed with this six carbon structure proposed by Kekule but disagreed that benzene was the basic unit of the aromatics. He felt that the basis for the aromatics should not be a core of six carbons but rather their chemical behavior--substitution rather than addition. Thus was born the criterion of chemical reactivity rather than structure for a description of aromatic compounds.

Because of the dissymmetry of structure 1, Kekule could not account in 1865 for the limited number of substitution isomers found for benzene. He clarified this point in a paper in 1872.[7] It was in this paper that Kekule suggested that due to interatomic collision of the carbons, the positions of the double bonds over a period of time change. At any particular time, benzene has the structure 1 but at another time has structure 2.

1

2

Therefore, whether benzene has the structure 1 or 2 depends on when the molecule is observed. In other words, at any particular point in time, benzene may be seen as 1 or 2 but over a short time period, benzene is neither 1 nor 2 but a

combination of 1 and 2. In this way all carbon-carbon bonds become equal, the molecule becomes symmetrical, and thus the limited number of substituted isomers is observed. Note that Kekule did not say that there is an equilibrium between the structures 1 and 2. Neither structure actually exists--only a combination of the two. This idea is very close to the concept of resonance which was formulated some sixty years later. The final structural definition of benzene by Kekule is that benzene is a planar structure consisting of a cyclic array of six carbons containing symmetrical bonds between carbons. However, Kekule's structure still did not explain why the aromatic ring reacted differently chemically from olefinic bonds.

Immediately following Kekule's proposal in 1865, a plethora of structural explanations of the structure of benzene were put forth by such noted men of science as Erlenmeyer, Claus, Ladenburg, Wichelhaus, Baeyer, and Meyer. The various proposed structures (3, 4, 5, 6, 7, and 8) did not enjoy a long life of acceptance. It was not until the 1890's

Claus[8]

3

Ladenburg[9]

4

Städeler,[10] Wichelhaus[11]

5

Meyer[12]

6

Armstrong[13]

7

Baeyer[14]

8

that a sound attempt was made to explain the unusual chemical reactivity of the aromatic compounds and relate this reactivity to the structure of the molecule and to the bonds involved. Bamberger[15] in 1890 attempted to make this relationship. He used the earlier proposed hexacentric structure 8 and stated that the hexacentric bonds had the potential for bonding. These centric bonds are held in an equilibrium state by some unknown force; this equilibrium is disrupted when the molecule reacts. Therefore, the molecule will rearrange or react in such a way upon disruption of this equilibrium as to restore the equilibrium position originally present. However, Bamberger's hypothesis lost favor because of the ill-defined forces which held the centric valencies in equilibrium, and there was nothing at that time to confirm the exclusive use of six valencies. These valencies can be equated to today's concept of the electron. Therefore, Bamberger had in a way anticipated the electronic theory of benzene by thirty-five years.

Finally in 1899 Thiele[16] introduced the ideas of partial bonds and conjugation to explain the reduced character of some olefinic bonds to addition--for example, 1,4-addition to conjugated dienes. Because of the reduced olefinic

character of the double bonds due to this "conjugation",[17] Thiele rationalized that the double bonds in Kekule's structure of benzene are not true double bonds and therefore should not react like olefinic bonds. The use of conjugation made all six carbon-carbon bonds equivalent and explained the symmetry of benzene and its reduced olefinic character. This idea is used quite extensively today but was rejected at the turn of the century because in addition to the conjugation concept, Thiele stated that the only criterion for an aromatic compound was that it have alternating single and double bonds in a cyclic array to allow for conjugation. This latter statement was disproved and as a result Thiele's conjugation theory rejected when Willstätter was unable to synthesize cyclobutadiene[18] and upon synthesizing cyclooctatetraene in 1913[19 a,b] showed that it did not possess aromatic properties. With these results it appeared at the beginning of the twentieth century that there was a uniqueness to the "aromatic sextet" that imparted the unique chemical reactivity to benzene.

No firm proposal existed as of 1915 which would enable the concept of aromaticity to be extended to compounds other than benzene. With the discovery of the atomic particles by Thompson, Townsend, and Millikan during the period of 1897 to 1908 and from these discoveries the development of the atomic theory by Rutherford, a new era opened up in which the concept of aromaticity was put on a broader and firmer base. With the rapid acceptance of the electronic theory

of valence proposed by G. N. Lewis and others, Armit and Robinson[20] in 1925 interpreted Bamberger's "potential valencies" as the idea of the "aromatic sextet". Robinson felt that the aromatic character and thus its chemical reactivity were due to the association of six valency electrons and these six electrons imparted properties to benzene much like the closed shell doublet of neon and the octet of the other inert gases. This "aromatic sextet" was symbolized by a circle and only meant the association of six electrons and not any particular linking of them. This concept of an "aromatic sextet" also afforded an explanation for the condensed benzenoid compounds. Thus, this was the first hypothesis that provided an explanation for the chemical reactivity and structure of aromatic compounds other than benzene.

Every theory put forward up to and including Robinson's "aromatic sextet" was formulated in order to explain the peculiar chemical reactivity (a property of the transition state) of a class of compounds called aromatic. This approach to the defining of aromatics was completely changed with the development of quantum mechanics in the 1920's and its initial use in the development of the valence bond theory by Heitler-London in 1927[21] and the molecular orbital theory by Hückel in 1931.[22] Both the valence bond and molecular orbital theories try to explain aromaticity on the basis of the ground state of the molecule rather than some transition state property. Both theories for the first

time enabled chemists to develop a theory of aromaticity to explain the basis for the chemical reactivity of aromatic compounds and also allowed them to predict aromatic character in yet unsynthesized compounds. The two theories accomplished these things with different degrees of success because they were based on different assumptions.

Valence bond theory regards a molecule as being composed of atoms which to a great extent retain their distinct character even when bonded. The complete atom is brought together with another atom, and in the process the orbitals overlap and the electrons interact to form the familiar two electron localized bond. In order to explain the bonding in the symmetrical benzene molecule, valence bond theory introduced the concept of "resonance" and "resonance energy".

The idea of resonance is based on a set of wave functions for a molecule, each of which may be regarded as a reasonable approximation to the true wave function for the ground state. A suitably-chosen combination of these wave functions will then be an even better approximation to the true wave function.[23] When this is done one obtains the wave functions which correspond to the two Kekule structures of benzene as the major contributing wave functions to the combination. Furthermore, an estimate of the energy based on the mixture of the functions will be lower than an estimate based on any of the individual functions making up the combination. This difference of energy between the mixture of functions and any individual function is called the

resonance energy. The reduced chemical reactivity of benzene as compared to three isolated olefinic bonds is a result of this resonance energy.

The problem with the valence bond theory is that it predicts a sizeable resonance energy per π-electron for such compounds as cyclobutadiene and cyclooctatetraene.[24] This has not been observed and therefore its use as a predictive tool has been diminished. However, Linus Pauling tries to justify its use by saying:

> I feel that the greatest advantage of the theory of resonance, as compared to other ways (such as molecular orbital theory) of discussing the structure of molecules for which a simple valence bond structure is not enough, is that it makes use of structural elements with which the chemist is familiar.[25]

Hückel developed the molecular orbital theory and reported it in 1931. In MO theory orbitals on atoms are initially brought together and a linear combination of these atomic orbitals produces a series of molecular orbitals of differing energy. The electrons are then placed into these molecular orbitals starting with the lowest energy orbital and filling each orbital of increasing energy according to Hund's Rule and the Pauli Exclusion Principle, until all the initially available electrons are used. Of course, this is not quite as easily visualized as the traditional idea of the two-electron localized bond. However, it provides better predictive ability than does the valence bond theory. As a consequence of Hückel's MO theory, he was able to make a general rule which became known as Hückel's Rule. It

states that "amongst fully conjugated, planar monocyclic polyolefins only those prossessing $(4n + 2)$ π-electrons, where n is an integer, will have special aromatic stability."[22] As a corollary, all similar systems with $4n$ π-electrons will not possess any special aromatic stability. This rule has been proven to work for many compounds with $n < 3$ and for some compounds where $n > 3$.

However, there are the larger monocyclic ring systems where Hückel's Rule and HMO theory begin to show inconsistencies. For example, in the larger annulenes, $n > 4$, according to HMO theory, the difference between localized (normal polyolefins) and delocalized ("aromatic" compounds) energy increases as ring size increases and the stability difference between $(4n + 2)$ and $4n$ π-electron systems goes to zero at higher n values (see Figure 1).[26] The latter statement has been shown to be true with the higher annulenes. Those compounds which should show aromaticity no longer do so but act like polyolefins. The former statement does not agree with the observed facts. The delocalization energy of the annulenes does not increase as the size of the ring system increases. In addition to this latter criticism, it is evident from Figure 1 that HMO theory predicts resonance stabilization for even the $4n$ series. This has been shown to be untrue. The lower members of the $4n$ series actually show a sizeable destabilization--a negative delocalization energy.[27] Thus Hückel's Rule does give a good qualitative or relative prediction of

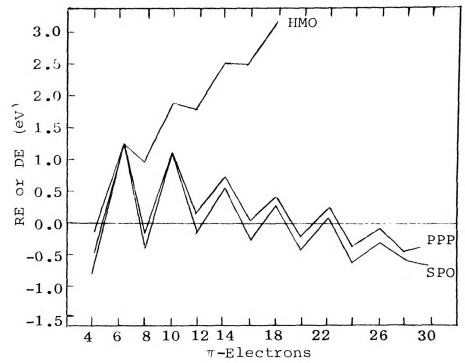


Figure 1

aromaticity to monocyclic ring systems, but gives very poor quantitative results for delocalization energies. As M. J. S. Dewar states: "The main value of the Hückel method lies in the facility with which it can be used to generalize chemical phenomena in a qualitative or even a semi-quantitative [for small values of n] manner."[28]

In order to remove the quantitative discrepancies of the HMO method, many theoreticians since 1931 have sought better quantum-mechanical methods, using fewer or more logical approximations in the calculations. M. J. S. Dewar published some of his work in 1965[26] in which he used three different methods to determine the delocalization energies of the monocyclic, conjugated ring system known as the

annulenes. The results of the three methods are shown in Figure 1. The three methods were the HMO method, PPP method which is a combination of Pople's method and Pariser, Parr values, and finally the SPO or split p-orbital method. The Hückel method, of course, assumes a planar polygon geometry, equal carbon-carbon bond lengths, and no electron-electron repulsions and because of these assumptions gives the results previously discussed. The latter two methods were developed so as to eliminate these assumptions. The results shown agree fairly well with the available experimental data. Thus it is seen that the relative aromatic stabilities of the $(4n + 2)$ π-electron and the $4n$ π-electron systems do approach a common value as predicted by HMO theory and Hückel's Rule; but contrary to HMO theory and consistent with experimental data, this value is not an ever-increasing delocalization energy but a value of zero delocalization energy. In addition, it accounts for the negative delocalization energies or antiaromaticity of the 4n series. The calculations also show at approximately what value of n the $(4n + 2)$ system becomes a simple polyolefin. This agrees with the observation that [22] annulene[29] is aromatic but that [30] annulene[29] is non-aromatic.

Based on these results Dewar proposed the following definition for aromaticity:[30] Cyclic conjugated systems are considered aromatic if cyclic delocalization of electrons makes a negative contribution to their heats of formation. It should be mentioned here that even Dewar's calculations

show too rapid a decrease in resonance energy for the $(4n + 2)$ π-electron system, but they have produced the closest agreement with experimental data for compounds having large n values. Figeys[31] in 1970 confirmed Dewar's results by another MO method.

Both Dewar's and Hückel's works were concerned with the resonance energy--the extra stabilization imparted to the aromatic molecule by the cyclic conjugated arrangement of the double bonds. Dewar's calculations can be and in most cases have been verified by experimentally determined heats of combustion and hydrogenation. However, there is another measurable physical property of the olefinic compounds which has been used to categorize the aromaticity of these cyclic conjugated systems. This physical property is the diamagnetic anisotropy[32,33,34] of the molecule, and the consequences of this property are the observed paramagnetic and diamagnetic chemical shifts in the NMR for the vinyl protons on the interior and exterior of the ring.[35] This is a criterion which is concerned with the ground state of the molecule which has been perturbed very slightly by the presence of a magnetic field.

If a closed conjugated path about which π-electrons can circulate exists in a molecule, then upon being placed in a magnetic field, the field will induce a flow of the π-electrons around that circular path. The circulating electrons will in turn produce their own small magnetic field. If the circular path is perpendicular to the applied

external magnetic field, H_0, then the induced magnetic field, H', of the circulating π-electrons will oppose the applied field (see Figure 2). This induced ring current and magnetic field can be observed and has been used as a criterion for aromaticity.[36] However, its direct measurement is difficult and can only be done on crystalline material.

As mentioned earlier, the effect of the induced ring current and magnetic field on the chemical shifts of protons in the NMR can be observed. This fact eliminates the problem of using only crystalline samples; both liquids and solids can be used. Figure 2 illustrates the effect of the magnetic field on a proton externally attached to the ring and also indicates what would happen to a proton within the ring for a diamagnetic ring current.

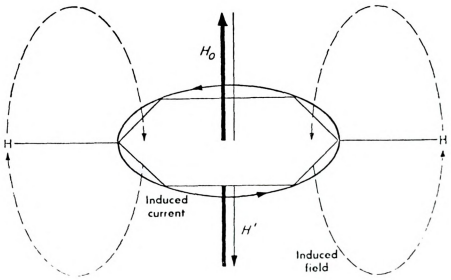


Figure 2

A proton external to the ring feels the positive enhancement of the applied magnetic field by the induced magnetic field. Therefore, an external field, H_0, smaller by the amount of the induced field, H', must be applied, and the resonance of that exterior proton will appear at a lower applied field value than for a linear olefinic proton. The reverse is true for a proton within the ring. The phenomenon just described is due to a diamagnetic ring current. The opposite effect, exterior protons shifted up-field and interior protons shifted down-field, is caused by a paramagnetic ring current. If there is no significant shift of the olefinic protons from their normal value of δ 4-6, then there is no induced ring current present and hence no extensive delocalization of π-electrons. It should be mentioned at this point that an observed paramagentic or diamagnetic ring current in a molecule can only give a qualitative statement of π-electron delocalization and no quantitative statement.

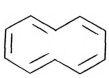
Sondheimer was the first to use this phenomenon extensively to determine the delocalization of π-electrons in the annulenes. These compounds are quite well suited for this technique because they possess both internal and external protons in different amount. So one can see both the up-field and down-field shift of the protons when the magnetic effect is present. It has been observed by Sondheimer that the [4n] annulenes give rise to a paramagnetic ring current and that [4n + 2] annulenes cause a diamagnetic ring current.

It has further been observed that some of the higher annulenes give only the chemical shifts of normal olefinic protons: in other words, no π-electron delocalization. So it appears that the use of the magnetic anisotropy and NMR chemical shifts of molecules allows one to determine the presence of π-electron delocalization and whether it is associated with a 4n or (4n + 2) π-electron system. Hence, one has available a qualitative criterion for aromaticity. The results of the application of this criterion and of Dewar's and Hückel's criteria to two series of monocyclic conjugated ring systems, the annulenes, and the hetero- annulenes will be presented in the next section.

From this brief discussion of the history of the concept of aromaticity, one can see a shift in emphasis from the use of odor and chemical reactivity in the 1800's to the use of ground state properties in the twentieth century as criteria for the definition of aromaticity; a broadening of the scope of aromaticity from benzene only to benzenoid compounds and finally to the non-benzenoid species; the use of MO theory with a variety of refinements to calculate and predict the ground state properties of the aromatic compounds; and the application of heats of combustion and hydrogenation and NMR chemical shifts to verify or nullify the calculations and predictions.

Aromaticity in the Annulenes

Benzene is the second member of a series of moncyclic, alternant hydrocarbons with alternating double and single bonds which have either 4n or (4n + 2) out-of-plane π-electrons. This series is called the annulene series and each member is designated as either a [4n] annulene or a [4n + 2] annulene.[37] Benzene is also the first member of the [4n + 2] annulenes, and cyclobutadiene is the first member of the [4n] annulene series. Cyclobutadiene has resisted isolation to date despite many attempts and the only other annulenes which were synthesized prior to 1959 are benzene and cyclooctatetraene. Since then Sondheimer and co-workers have synthesized approximately thirty-six annulenes ranging from [12] annulene to [30] annulene. Although the isomer 9a of [10] annulene has not been isolated, probably as a result of the non-bonded hydrogen-hydrogen interactions within the ring, two other isomers (9b and 9c) have been isolated and characterized by Masamune.[38]



9a

9b

9c

Because the heats of combustion and hydrogenation for only benzene, cyclooctatetraene, and [18] annulene have been determined, quantitative confirmation for Hückel's or Dewar's calculations can not be given, but the relative or

qualitative trends which their calculations predict can be observed by the NMR chemical shifts which arise as a result of the magnetic anisotropy of the molecules. This data for the annulenes and dehydroannulenes (annulenes with a triple bond) is given in Table I. It should be evident that the dehydroannulenes should still be able to sustain a ring current in a magnetic field just as the annulenes do because they still have a continuous, cyclic array of out-of-plane π-electrons.

It becomes apparent upon looking at the data that the [4n] annulenes show a paramagnetic ring current as evidenced by the up-field shift of the external protons and the down-field shift of the internal protons; the [4n + 2] annulenes show a diamagnetic ring current as shown by the opposite shift of the corresponding protons. This phenomenon can only exist if the molecule can be planar. Any deviation from planarity will reduce correspondingly the amount of ring current. When the molecule is quite non-planar, the olefinic protons resonate at the normal values of τ 4-6. This is evident for cyclooctatetraene and the lower members of the 4n and (4n + 2) series--compounds 9b, 9c, 11, 12, 13, 14, 15, and 18. As the ring size increases above [12] annulene, the rings can become planar or nearly so, and they exhibit the necessary chemical shifts for 4n paramagnetic and (4n + 2) diamagnetic molecules. The NMR spectra are very temperature-dependent. This temperature dependency is the result of the flexibility imparted to the large

rings by the energy present at room temperature. This flexibility of the molecule allows the protons to become equivalent or nearly equivalent. As the temperature is lowered, the molecule becomes less and less flexible until it finally is rigid enough for one to observe the absorptions of the unique inner and outer protons. It is the magnetic properties of the molecules at this inflexible stage (after removal of the external effects of temperature) which should allow one to determine the aromatic character of a molecule.

According to Dewar's calculations and Hückel's Rule, the $(4n + 2)$ π-electron system should be aromatic and the $4n$ π-electron systems should be antiaromatic, the two systems converging to nonaromaticity above 22 π-electrons. The NMR data verify these predictions. The [4n + 2] annulenes up to and including [22] annulene show aromaticity; the [4n] annulenes show antiaromaticity. As expected, [24] annulene is not aromatic, but there is some ambiguity as to the aromaticity of [26] annulene. Monodehydro[26]annulene, 42, shows a small diamagnetic ring current, but 1, 9, 17-tridehydro[26]annulene, 43, shows no ring current; in other words, it is polyolefinic in character. Although this ambiguity exists, the [26] annulenes appear to be almost, if not completely, polyene-like, because even though 42 shows a ring current, its effect is small. [28] Annulene has not been synthesized yet, although being a [4n] annulene it might have a paramagnetic ring current providing

it is planar. NMR data is not available for the three impure [30] annulenes that have been reported by Sondheimer. However, their extreme reactivity towards decomposition seems to indicate that they are not aromatic and act like normal polyenes. From this data that is presently available, it is still not certain that Dewar's prediction for disappearance of aromatic stability above 22 π-electrons is correct, at least for the annulenes. Further experimental data is needed. The hetero- annulenes discussed in the next section will provide some additional, but still inconclusive, evidence for Dewar's predictions.

Aromaticity in the Hetero-annulenes

The hetero-annulenes are species in which one or more of the carbon atoms in the annulene ring are replaced by a hetero-atom and/or the annulene ring is bridged by one or more hetero-atoms. The hetero-annulenes, porphyrins, corroles, and sapphyrins are examples of hetero-annulenes and are listed in Table II along with their NMR and UV spectral data. It has been shown that the perturbation of the annulene ring by the presence of the bridging nitrogen atoms and ethylenic bonds in the porphyrin ring system is quite small and these compounds do behave almost like the annulene hydrocarbons.[38] Many workers (references in Table II) have extended this fact to compounds with bridging atoms other than nitrogen; it appears that this extension is not unreasonable. Because of these facts, one might expect that

the hetero-annulenes would possess similar characteristics of aromaticity as do the annulenes corresponding to the presence of $(4n + 2)$ or $4n$ π-electrons, providing that the molecule is planar.

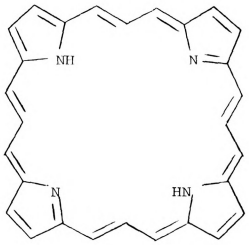
The effect of planarity on the aromaticity of $(4n + 2)$ π-electron systems is very well illustrated by the hetero-annulenes. The attainment of aromaticity by the hetero-bridged [10] annulenes as compared to [10] annulene itself and the loss of aromaticity in the sulfur-bridged [18] annulenes are good examples of the importance of planarity. Isomer 9a of [10] annulene is non-planar because of the hydrogen-hydrogen interaction as stated in the previous section. Upon removal of those hydrogens and their replacement by either a $-CH_2-$ group (10), an $-\ddot{O}-$ (47), or an $-\ddot{N}H-$ group (48), the molecule can become planar and the $(4n + 2)$ π-electron system exhibits aromatic character. In the 18 π-electron system, 53, the space requirement for the three sulfur atoms is too large for the center cavity and so the molecule is non-planar and non-aromatic. For those hetero-annulenes in Table II that can become planar or nearly planar, a paramagnetic ring current for $4n$ systems and a diamagnetic ring current for $(4n + 2)$ systems are observed. These observations are confirmed up to and including compound 76, a $4n$ π-electron system. No 26 or 28 π-electron system has been reported, so a gap in the critical area of Dewar's prediction exists. Finally, the 30 π-electron system, 77, shows no aromaticity and acts like separate furan rings and ethylenic bonds.

Purpose of Present Investigation

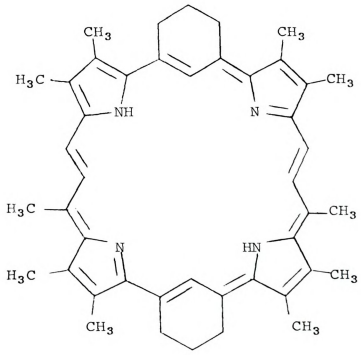
As stated in the previously presented history of aromaticity, Dewar predicted that the loss of aromaticity and antiaromaticity for the (4n + 2) and the 4n π-electronic systems respectively would occur above 22 π-electrons. Data from the annulenes of Sondheimer shows good agreement up to the cut-off point of 22, but there exists some ambiguity in the region of 26 π-electrons and higher. This ambiguity also exists in the hetero-annulenes because no 26 or 28 π-electron systems have been reported.

It is this gap in the experimental data in which a compound is needed to verify or refute Dewar's prediction that prompted the synthesis of a 26 π-electron system which possesses bridging groups that would be expected to reduce the flexibility of the molecule and thus enhance the chances of its being planar. A molecule that might satisfy these requirements is compound 78. It is a diaza [26] annulene which is bridged by two ethylenic groups and two imino groups. This molecule could conceivably be synthesized by starting with pyrrole and using reactions which have their precedence in porphyrin syntheses. Because both alpha and beta positions in pyrrole are reactive sites, it was desirable to block the beta positions; this was done by the use of methyl groups. A symmetrical substitution of two methyl groups was used to avoid the formation of structural isomers later in the synthesis. Upon introduction of two additional bridging groups into 78 later in the sequence,

the final 26 π-electron system sought was the title compound 79.



78



79

Table I. Annulenes.

NP = Nonplanar; D = diamagnetic; P = paramagnetic; + = Aromatic; 0 = Non-aromatic; sh = shoulder; m = multiplet; q = quartet; s = singlet; d = doublet; dd = double doublet.

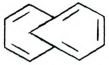
Aromatic	Structure	#πe^-	Name	U.V.	NMR	Ref
						(-40°)
0 (NP)	 9b	10	cis[5]-[10]annulene	~ 255 ~ 265	(THF-d_8) τ 4.34	38
				(MeOH)	(THF-d_8)	(-40°)
0 (NP)	 9c	10	trans-cis[4]-[10]-annulene	257 (29,000) 265 (20,000)	τ 4.16	38
					(CCl_4)	
+ (D)	 10	10	1,6-methano[10]-annulene	256 (68,000) 259 (63,000) 298 (6,200)	τ 2.7 τ 3.05 τ 10.5	4H 4H 40 2H

Table I. Continued.

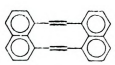
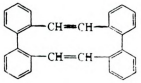
Aromatic	Structure	$\#\pi e^-$	Name	U.V.	NMR	Ref
0 (NP)	 11	10	Mono-trans-1,2:3,4:7, 8-tribenzo[10]annulene	242 (33,900) 286 (10,700)	(CCl_4) τ2.48-3.22 (m) 12H τ3.27-3.75 (m) 3H τ4.58 (d) 1H	41
0 (NP)	 12	10	Dinaphth[10]-annulene	log ε 218 (4.88) 244 (4.56) 274 (3.55) 289sh (3.48) 302sh (3.61) 341sh (4.18) 367 (4.34)	(CD_2Cl_2) τ 2.1-3.0 (m) 14H τ 6.51 (s) 1H τ 6.60 (d) 1H ($CDCl_3$) τ6.51→τ6.41 (s) 1H τ6.60→τ6.49 (d) 1H	42
0 (NP)	 13	12	Cis,cis-sym-tetra-benz[12]annulene	(cyclohexane) 240 (31,900)	(CCl_4) τ2.35-3.15 (m) 16H τ 4.18 (s) 4H	43

Table I. Continued.

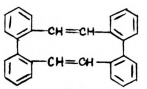
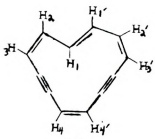
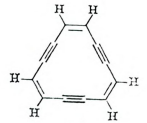
Aromatic	Structure	#πe⁻	Name	U.V.	NMR	Ref
0 (NP)	 14	12	trans,trans-sym-tetra-benz[12]-annulene	(cyclohexane) 226 (32,200) 248sh (24,100) 266 (34,100)	(CCl_4) τ 2.6-3.0 (m) 16H τ 3.82 (s) 4H	43
0 (NP)	 15	12	1,5-Bisdehydro[12]-annulene	(isooctane) 244 (51,900) 249 (54,800) 465 (183) >600	(CCl_4) τ5.47 (m) (H^4,$H^{4'}$)2H τ5.82 (d) (H^3,$H^{3'}$)2H τ4.97 (oct) (H^2,$H^{2'}$)2H τ-0.9 (q) (H',H'') 2H (acetone-d_6) (-80°) τ-1.55 (m) (H^4,$H^{4'}$)2H τ 4.82 (m) (H^3,H') 2H τ 5.24 (s) (H^2,$H^{2'}$)2H τ 2.69 (q) (H^1,$H^{1'}$)2H	44 53
0 (P)	 16	12	1,5,9-tridehydro[12]-annulene	(isooctane) 238 (36,200)	(CCl_4) τ 5.58 (s) 6H	45 59

Table I. Continued.

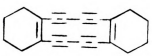
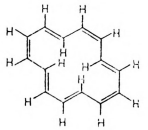
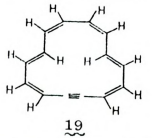
Aromatic	Structure	#π e⁻	Name	U.V.	NMR	Ref
0 (P)	 17	12	[5,6:11,12-bis(tetramethylene]-1,3,7,9-tetradehydro[12]-annulene	(ether) 234 (23,200) 242 (23,600) 247sh (21,700)	($CDCl_3$) (-20^0) τ 8.15-8.55 (m) 16H	46
0 (NP) + (D) (at low temp)	 18	14	[14]annulene	(isooctane) 314 (69,000) 374 (5,700)	($CDCl_3$) (R.T.) τ 4.42 (s) 14H τ 3.93 (s) (Peaks are in ratio 6:1 corresponding to two isomers) 4.42-sym; 3.93-antisym ($CDCl_3$) (-60^0) τ 2.4 10H τ 10.0 4H	47 48
+ (D)	 19	14	Monodehydro[14]-annulene	(isooctane) 312 (92,000) 365 (7,100) 392 (4,700)	($CDCl_3$) τ 1.2-2.7 (m) 10H τ 10.7 (dd) 2H	49 50

Table I. Continued.

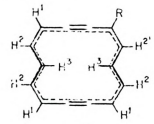
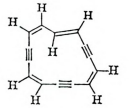
Aromatic	Structure	# πe^-	Name	U.V.	NMR	Ref
+ (D)	 20	14	1,8-Bisdehydro[14]-annulene	(isooctane) 309 (175,000) 402 (6,900) 410 (7,500) 424 (23,600) 586 (2,900)	($CDCl_3$) τ 15.54 (m) 2H τ 1.57 (m) 4H τ 0.45 (m) 4H	49 51
+ (D)	 21	14	1,5,9-tridehydro[14]-annulene	(pentane) 246 (5,380) 251 (5,860) 258 (6,120) 305 (137,000) 348 (3,180) 375 (5,370) 387 (8,200) 393 (8,500) 406 (26,600) 448 (150) 463 (370) 497 (320)	(CCl_4) τ 0.53-0.81 (m) 2H τ 1.46-1.92 (m) 5H τ 14.96 (t) 1H	52
0 (P)	 22	16	[16]Annulene	(isooctane) 284 (77,300) 430-450sh (700) >600	(CCl_4) (37^0) τ 3.27 (s) 16H (CS_2/CD_2Cl_2) (-110^0) τ -0.43 (t) 4H τ 4.60 (m) 12H	54 55

Table I. Continued.

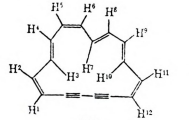
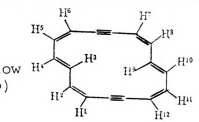
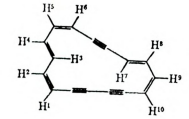
Aromatic	Structure	πe^-	Name	U.V.	NMR	Ref
0 (P)	 23	16	1,3-Bisdehydro[16]-annulene	281 (55,500) 291 (55,000) >600	(acetone-d_6) (0°) τ -3.05 (d) 1H τ -0.50 (q) 2H τ 1.85 (q) 2H τ 4.2-5.3 (m) 5H τ 5.5 (d) 2H at low temp (-80°), exists as 4 conformers	54 55
0 (P) (at low temp)	 24	16	1,9-Bisdehydro[16]-annulene	(isooctane) 270sh (40,300) 283 (54,200) 296 (38,500) >600	(acetone-d_6) (35°) τ 2.12 (q) 4H τ 4.12 (oct) 4H τ 4.73 (d) 4H (-80°) τ 0.2 2H τ 3.92 6H τ 4.5 4H	54 55
0 (P)	 25	16	1,3,9-tridehydro[16]-annulene	(isooctane) 279 (49,500) 290 (51,500) >600	(acetone-d_6) (35°) τ 0.8 (m) 2H τ 1.5 (m) 1H τ 2.65 (d) 1H τ3.8-4.7 (m) 3H τ5.0-5.4 (m) 3H at low temp. (-75°), exists as 4 conformers	54 55

Table I. Continued.

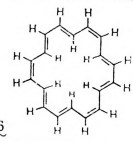
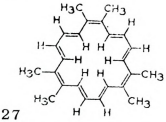
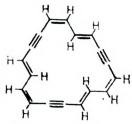
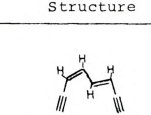
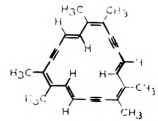
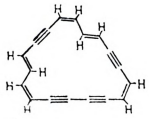
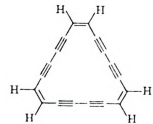
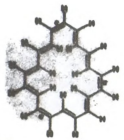
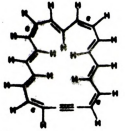
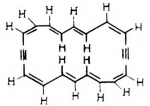
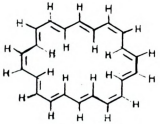
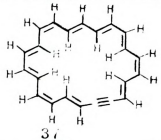
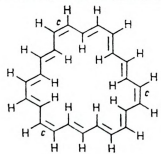
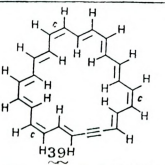
Aromatic	Structure	#πe^-	Name	U.V.	NMR		Ref
+ (D)	 26	18	[18]annulene	(isooctane) 278 (8,100) 369 (303,000) 408 (7,500) 448 (21,800)	(THF-d_8) τ 1.1 broad peak 12H τ 11.8 broad peak 6H (-60°) τ 0.72 (m) τ 12.99 (m)		48 50 56
?	 27	18	1,2,7,8,13,14-hexamethyl[18]annulene	(THF) 391 469	———		57
+ (D)	 28	18	1,7,13-Tridehydro-[18]annulene Isomer I	(isooctane) 233 (27,600) 237 (33,300) 244 (34,200) 252 (24,100) 295 (22,100) 313 (60,600) 322 (111,500) 335 (190,000) 364 (9,200) 368 (8,920) 378 (8,920) 385 (12,700) 395 (11,200) 399 (16,900) 433 (1,190)	($CDCl_3$) (60°) τ 1.7-3.1 (m) 9H τ 8.26 (dd) 3H		50 56

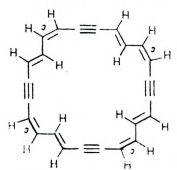
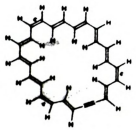
Table I. Continued

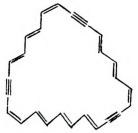
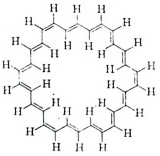
Aromatic	Structure	#πe⁻	Name	U.V.	NMR	Ref
+ (D)	 29	18	1,7,13-Tridehydro-[18]annulene Isomer II	(isooctane) 234 (30,800) 244 (26,300) 253 (22,800) 295 (22,500) 310 (58,300) 318 (93,000) 331 (166,000) 340 (90,500) 358 (8,100) 367 (8,050) 370 (8,200) 380 (8,600) 387 (12,600) 402 (16,800) 420 (12,860)	(CCl_4) (60°) τ 1.7-3.4 (m) 9H τ 7.8-8.6 (2q) 3H	58
+ (D)	 30	18	1,2,7,8,13,14-hexamethyl-5,11,17-tridehydro[18]annulene	(ΦH) 336 (93,700) 351 (146,000) 396 (14,900) 412 (15,200)	($CDCl_3$) τ 7.40 $-CH_3$ deshielded as compared to in-chain methyls in carotenoids	57

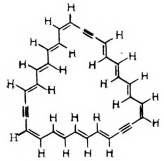
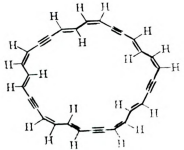
Aromatic	Structure	#πe⁻	Name	U.V.	NMR	Ref
+ (D)	 31	18	1,3,7,13-tetradehydro-[18]annulene	(isooctane) 228 (16,200) 297 (25,000) 316 (66,200) 327 (99,000) 338 (54,000) 354 (11,350) 363 (8,800) 374 (8,100) 383 (12,550) 395 (14,500) 414 (2,550)	(CCl_4) (60^0) τ 7.4-8.1 (m) 2H τ 1.8-3.5 (m) 8H	58
+ (D)	 32	18	1,3,7,9,13,15-hexadehydro[18]annulene	(cyclohexane) 227 (25,500) 236 (21,500) 260 (5,900) 315 (41,000) 317 (41,500) 333 (75,800) 357 (13,000) 366 (7,400) 378 (15,500) 388 (17,600) 405 (790)	(CCl_4) τ 2.98	59
0 (P)	 33	20	[20]annulene	(ether) 323 (146,000)	(THF-d_8) (-109^0) τ -3.9-(-)0.9 (m) 7H τ 3.4-5.9 (m) 13H	60

Aromatic	Structure	π-e$^-$	Name	U.V.	NMR	Ref
0 (P)	 34	20	mono-dehydro[20]-annulene	(ether) 308 (94,400) 322 (124,000)	(THF-d_8) (-90^0) τ-3.3-(-)0.1 (m) 5H τ 4.0-5.7 (m) 13H	60
0 (P)	 35	20	1,11-Bidehydro[20]-annulene	(isooctane) 319 (109,000) 336 (74,000)	THF-d_8) (-80^0) τ -1.6 broad peak 2H τ -0.45 broad peak 2H τ 4.4 4H τ 4.93 2H	53 61
+ (D)	 36	22	[22]annulene	(ether) 287 (18,300) 305sh (16,500) 383 (123,000) 400 (141,000) 450 (12,700) 483 (13,500)	(THF-d_8) (-90^0) τ 0.35-0.7 (m) 14H τ 0.9-1.5 (m) τ 10.4-11.2 (m) 8H	62

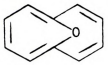
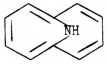
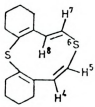
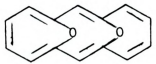
Aromatic	Structure	#πe^-	Name	U.V.	NMR	Ref
+ (D)	 37	22	monodehydro[22]-annulene	(ether) 280 (28,800) 372 (132,000) 438sh (11,900) 452 (12,200) 495sh (3,600)	CD_2Cl_2) τ 1.55-3.75 (m) 13H τ 6.55-9.30 (m) 7H	63
0 (P)	 38	24	[24]annulene	(ΦH) 360 (183,000) 375 (195,000)	(THF-d_8) (-80°) τ-2.9-(-)1.2 35 τ 5.27 65	50 64 67
0 (P)	 39H	24	monodehydro[24]-annulene	(ΦH) 356 (135,000) 370 (156,000) > 600	(THF-d_8) (-80°) τ-2.4-0.4 (m) 8H τ 4.3-6.0 (m) 14H	65

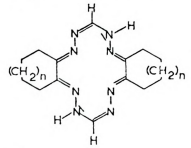
Aromatic	Structure	#π e⁻	Name	U.V.	NMR	Ref
0 (P)	 40	24	1,7,13,19-tetradehydro[24]annulene	(isooctane) 233 (23,300) 238 (23,000) 324 (122,000) 340 (255,000)	(toluene-d_8) (37°) τ 1.6 (dd) 4H τ 4.4-5.02 (m) 12H	50 66
0 (NP)	 41	24	1,3,7,9,13,15,19,21-octadehydro[24]-annulene	(ether) 243 (50,600) 248 (50,400) 307sh (27,400) 317sh (29,500) 329 (38,900) 341 (38,300) 352 (45,100)	($THF-d_8$) τ 3.85 (s)	68
+ (D) slightly	 42	26	monodehydro[26]-annulene	(ether) 291 (42,800) 370 (131,000) 386 (152,000) 439 (14,900) 460 (15,900)	(CD_2Cl_2) (-90°) τ 2.1-3.8 (m) 15H τ 5.2-6.0 (m) 9H	69

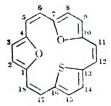
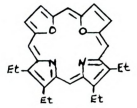
Aromatic	Structure	#πe^-	Name	U.V.	NMR	Ref
polyene		26	1,9,17-tridehydro-[26]annulene	(ether) 237 (23,000) 291 (33,700) 300 (33,400) 383 (119,000) 451 (12,300)	($CDCl_3$) τ 2.0-4.5 (m) (no change with temp.)	70
	43					
0 (based only on instability)		30	[30]annulene	(dioxane) 329 (44,000) 428 (144,000) (not pure)	Compound unstable--behaves as a polyene	61
	44					

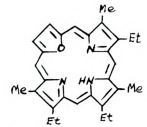
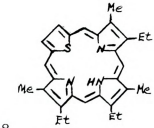
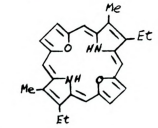
Aromatic	Structure	Name	U.V.	NMR	Ref
0 (based only on instability)	 45 (or isomer)	30 tridehydro[30]-annulene	(dioxane) 320 (47,000) 401 (108,000) (not pure)	———	61
?	 46 (or isomer)	30 Pentadehydro[30]-annulene	(dioxane) 307 (42,000) 318 (39,500) 378 (105,000) 396 (126,000) (not pure)	———	66 71

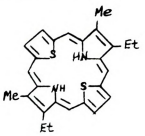
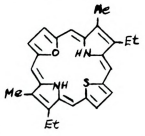
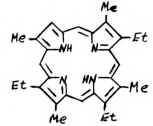
NP = non-planar; D = diamagnetic; P = paramagnetic; + = aromatic; 0 = non-aromatic; sh = shoulder; m = multiplet; q = quartet; s = singlet; d = doublet; dd = double doublet.

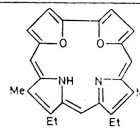
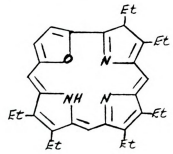
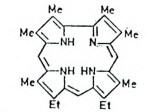
Aromatic	Structure	#πe⁻	Name	U.V.	NMR	Ref
+ (D)	 47	10	1,6-oxido[10]-annulene	255 (72,000) 299 (69,000) 392 (240)	(CDCl$_3$) τ 2.23-2.81 (A_2B_2) 4H centered at τ2.52	72
+ (D)	 48	10	1,6-imino[10]-annulene	~240 ~270 ~320 ~400	τ 2.8 (AA'BB') 4H τ 11.1 (s) 1H	73
0 (NP)	 49	12	mono-trans-dicyclo-hexeno[b,i]-1,6-dithia[10]annulene	(cyclohexane) 233 (9,500) 247.5 (9,000) 285 (6,400) 315sh (1,700)	(CCl_4) τ 3.17 (d) (H_4) 1H τ 3.72 (d) (H_8) 1H τ 3.92 (dd) (H_5) 1H τ 4.35 (dd) (H_7) 1H	74
+ (D)	 50	14	Syn-1,6:8,13-dioxido-[14]annulene	306 (169,000) 345 (144,000) 382 (8,500) 555 (775)	τ 2.06 (s) 2H τ 2.25 τ 2.40 (AA'BB') 8H	75

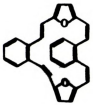
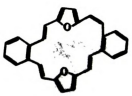
Aromatic	Structure	#π e⁻	Name	U.V.	NMR	Ref
0 (P)	 51	16	Dihydro-1,2,4,5,8,9,11,12-octaaza[14]annulene		($CDCl_3$) τ 2.68 (~1τ unit higher field than similar proton in linear species)	76
+ (D)	 52	18	1,4:7,10:13,16-trioxa[18]annulene	(EtOH) 220 (7,700) 239 (7,400) 309 (18,300) 323 (64,500) 332 (288,000) 370 (3,200) 391 (5,500) 405 (17,200)	(CCl_4) τ 1.32 6H τ 1.34 6H	77
0 (NP)	 53	18	1,4:7,10:13,16-trithia[18]annulene	(EtOH) 204 (18,000) 224 (16,800) 288 (17,300)	τ 3.27 τ 3.33	78

Aromatic	Structure	#π-e⁻	Name	U.V.	NMR	Ref
0 (ND)		18	1,4-oxa-7,10:13,16-dithia[18]annulene	(EtOH) 229 (15,400) 281 (28,900) 292 (29,300) 405 (9,850) 425 (9,500)	τ 2.9-3.58	79
	54					
+ (D)		18	1,4-thia-7,10:13,16-dioxa[18]annulene	(EtOH) 224 (14,400) 244 (11,700) 320 (18,200) 333 (43,000) 343 (45,000) 376 (5,100) 391 (7,100) 413 (16,600) 431 (2,100)	(CDCl$_3$) τ 1.0-1.72	80
	55					
+ (D)		18	12,13,17,18-tetraethyl-21,22-dioxaporphine	(TFA) 375.5 (212,000) 385.5 (229,000) 523 (10,500) 544.5 (10,790) 567 (5,320) 590 (1,350)	(CDCl$_3$/TFA) τ -1.71 1H τ -1.45 2H τ -1.31 1H τ -1.29 1H τ -0.79 2H τ -0.29 1H	81
	56					

Aromatic	Structure	πe^-	Name	U.V.	NMR	Ref
+ (D)	 57	18	7,12,18-trimethyl-8,13,17-triethyl-21-oxaporphine	(TFA) 385.5 (220,000) 389.5 (230,000) 523 (8,220) 552 (10,700) 602 (2,090)	τ -0.12 **2H** τ 0.02 2H τ 0.31 2H	81
+ (D)	 58	18	7,12,18-trimethyl-8,13,17-triethyl-21-thiaporphine	(TFA) 410 (175,000) 548 (6,800) 574.5 (7,970)	(CDCl$_3$) τ -0.06 2H τ 0.00 2H τ 0.02 2H	81
+ (D)	 59	18	7,18-dimethyl-8,17-diethyl-21,23-dioxaporphine	(TFA) 369.5sh (196,000) 376.5 (248,000) 493.5 (12,830) 531.5 (4,660) 556 (6,240) 613 (1,320)	(THF-d_8) as dihydrobromide τ -1.71 4H τ -0.98 4H	81

Aromatic	Structure	#πe^-	Name	U.V.	NMR	Ref
+ (D)	 60	18	7,18-dimethyl-8,17-diethyl-21,23-dithiaporphine	(TFA) 412 (156,000) 535.5 (6,800) 592.5 (4,470)	($CDCl_3$) τ -0.71 2H τ -0.68 2H τ -0.02 2H τ -0.02 2H	81
+ (D)	 61	18	7,18-dimethyl-8,17-diethyl-21-oxa-23-thiaporphine	(TFA) 398 (205,000) 517.5 (11,000) 581 (5,320)	($CDCl_3$) τ -0.59 2H τ -0.05 2H τ -0.02 2H τ -0.31 2H	81
+ (D)	 62	18	2,7,12,18-tetramethyl-8,13,18-triethylporphyrin	396 (144,500) 494 (12,180) 530 (8,410) 563 (5,960) 612 (3,480)	($CDCl_3$) τ -0.98 (m) 4H τ 0.4 (s) 1H τ 6.16 (s) Me τ 6.25 (s) τ 5.72 (q) Et τ 8.19 (t)	82

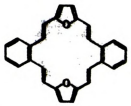
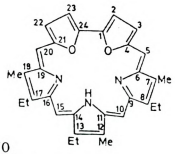
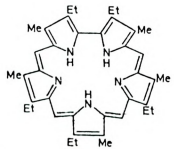
Aromatic	Structure	πe^-	Name	U.V.	NMR	Ref
+ (D)	 63	18	7,13-dimethyl-8,12-diethyl-21,24-dioxacorrole	(pyridine) 375 (147,900) 478.5 (10,300) 506.5 (23,560) 551 (8,660) 601.5 (17,320)	($CDCl_3$) τ 0.82 (s) 2H τ 0.96 (s) 1H τ 1.8 (AB) 4H τ 1.36	83
+ (D)	 64	18	7,8,12,13,17,18-hexaethyl-21-oxacorrole	(pyridine) 391 (186,000) 488.5 (8,060) 520 (22,410) 546.5 (10,670) 593.5 (27,420)	($CDCl_3$) τ 0.38 τ 0.54 (s) 3H τ 0.58 τ 0.66 τ 0.86 (AB) τ 13.6 (s) 2H	83
+ (D)	 65	18	2,3,8,12,17,18-hexamethyl-7,13-dimethyl-corrole	($CDCl_3$) 346 (16,200) 396 (115,000) 408 (99,300) 537 (17,400) 552 (18,300) 592 (23,000)	τ 0.88 (s) 2H τ 1.18 (s) 1H τ 13.48 (s) 3H	84

Aromatic	Structure	π-e$^-$	Name	U.V.	NMR	Ref
0 (NP)		20	1,4:11,14-dioxa-7,8:17,18-dibenzo-[20]annulene Isomer A	(EtOH) 206 (36,800) 333 (38,400)	(CCl_4) τ 2.77-3.32 (m) 8H τ 3.45 (ABq) 2H τ 3.71 (ABq) 2H τ 3.65 (s) 1H τ 3.85 (s) 2H τ 3.90 (s) 1H τ 3.56 (ABq) 2H τ 3.65 (ABq) 2H τ 3.97 (ABq) 2H τ 4.11 (ABq) 2H τ 4.19 (ABq) 2H τ 4.57 (ABq) 2H	85
0 (NP)		20	1,4,:11,14-dioxa-7,8:17,18-dibenzo-[20]annulene Isomer B	(EtOH) 208 (33,100 282 (28,900) 325 (45,300) 400 (13,000)	(CCl_4) τ 2.42-2.82 (m) 8H τ 2.69 (ABq) 2H τ 3.09 (ABq) 2H τ 3.10 (ABq) 2H τ 3.34 (ABq) 2H τ 3.48 (ABq) 2H τ 3.69 (ABq) 2H τ 3.98 (ABq) 2H τ 4.24 (ABq) 2H τ 3.40 (s) 1H τ 3.85 (s) 3H	85
0 (NP)		20	1,4:11,14-dioxa-7,8:17,18-dibenzo-[20]annulene Isomer C	($CHCl_3$) 208 (43,200) 264 (35,700) 289 (40,100) 353 (37,600)	(CCl_4) τ-2.52-2.66 (m) 4H τ 2.76-2.88 (m) 4H τ 2.97 (ABq) 2H τ 3.53 (ABq) 2H τ 3.26 (ABq) 2H τ 3.56 (ABq) 2H τ 3.70 (ABq) 2H τ 3.79 (ABq) 2H τ 3.76 (ABq) 2H τ 3.88 (ABq) 2H τ 3.16,3.69,3.86 (s) 1,2,1H	85

66

67

68

Aromatic	Structure	#πe⁻	Name	U.V.	NMR	Ref
0	 69	20	1,4:11,14-dioxa-7,8:17,18-dibenzo-[20] annulene Isomer D	(CHCl$_3$) 303 (45,100) 314sh (52,300) 358 (60,500) 375 (84,100)	(DMSO-d$_6$) τ 2.4-2.65 (m) 4H τ 2.7-2.95 (m) 4H τ 3.09 τ 3.49 (ABq) 8H 85 τ 3.72 (s) 4H	
+ (D)	 70	22	7,13,18-triethyl-8,12,17-trimethyl-dioxasapphyrin	(acetone/0.5% HClO$_4$) as perchlorate salt 435.5 (754,600) 592.5 (11,510) 622.5 (13,340) 648.5 (5,760) 686 (4,230)	(CDCl$_3$) τ -0.04 2H τ 0.28 2H τ -0.48 τ -0.45 τ -0.38 4H 86 -0.34 τ 16.55 1H	
+ (D)	 71	22	2,8,12,17,23-pentaethyl-3,7,13,18,22-pentamethylsapphyrin	(acetone/0.5% HClO$_4$) as perchlorate salt 450 (530,200) 579.5 (3,080) 629 (13,650) 688.5 (18,190)	(CDCl$_3$) τ -0.5 2H τ -0.32 2H 86 τ 13.9 4H	

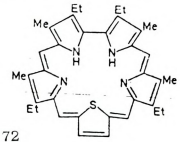
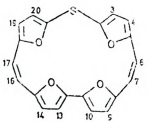
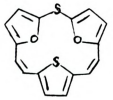
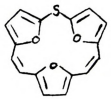
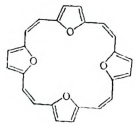
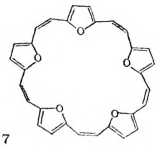
Aromatic	Structure	#πe^-	Name	U.V.	NMR	Ref
+ (D)	 72	22	2,8,17,23-tetra-ethyl-3,7,18,22-tetramethylthia-sapphyrin	285.5 (11,200) 331.5 (15,670) 468 (209,200) 594 (9,880) 645 (11,810) 752 (3,550)	(CDCl$_3$) τ -0.87 2H τ -0.31 2H τ -0.12 2H τ 12.2 2H	86
0	 73	22	2,5:8,11:12,15:18,21-tetraoxa-thia[20]-annulene	282 (44,500) 293sh (41,100) 322 (43,000) 460 (2,600)	τ 3.48 (ABq) 4H τ 3.70 τ 3.48 (ABq) 4H τ 3.88 τ 4.13 (ABq) 4H τ 4.19	87
0 (NP)	 74	22	2,5:14,17-dioxa-8,11-thio-thia[17]-annulene	(ether) 266 (25,200) 287 (25,600) 418 (2,700)	(CDCl$_3$) τ 3.22 (s) 2H τ 3.37 (ABq) 4H τ 4.02 τ 3.47 (ABq) 4H τ 4.04	87

Table II. Continued.

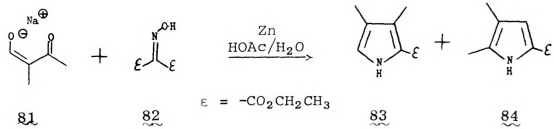
Aromatic	Structure	πe^-	Name	U.V.	NMR	Ref
				(ether)	($CDCl_3$)	
0		22	2,5:8,11:14,17-trioxythia[22]annulene	253 (19,600) 296sh (30,000) 305 (35,500) 417 (6,000)	τ 3.3 (ABq) 4H τ 3.95 2H τ 3.52(s) 4H τ 3.99(s)	87
	75					
0 (P)		24	1,4:7,10:13,16:19,22-tetraepoxy[24]annulene	(ether) isomer A 256 (12,100) 328sh (49,500) 343 (104,000) 360 (146,000) ($CHCl_3$) isomer B 260 (14,400) 335sh (52,200) 349 (108,000) 362 (156,000) 370sh (13,000)	τ 4.1-5.2 (higher than similar protons in linear species) τ 1.3-1.4	88
	76					
0		30	1,4:7,10:13,16:19,22:25,28-pentaepoxy[30]annulene	(ether) isomer A 234 (34,500) 299 (17,500) 319 (20,000) 410 (73,900) 480 (6,600) (ether) isomer B 298 (22,700) 313 (23,000) 400 (76,500) 412 (83,700) 465 (8,100) 500 (6,800)	τ 3.3-4.0 (same as similar protons in linear species)	88
	77					

DISCUSSION AND RESULTS

3,4-Dimethylpyrrole, 80, was chosen as the starting material for the construction of the ring system 78 because

80

it possesses only reactive α-positions, thus preventing reaction at the β-position, and it is symmetrical, eliminating structural isomers later in the synthesis. The precursor to 80 was ethyl 3,4-dimethylpyrrole-2-carboxylate, 83, which was prepared according to the procedure of Badger,[89] Scheme 1.



81 82 83 84

Scheme 1

The condensation of diethyl 2-aminomalonate, which results from the reduction of 82 in situ, can give either ethyl 3,4-dimethylpyrrole-2-carboxylate, 83, or ethyl 4,5-dimethylpyrrole-2-carboxylate, 84, depending on whether the

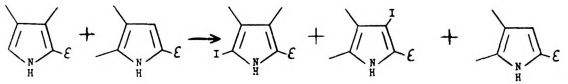
aldehyde or the ketone group in 3-formyl-butan-2-one, 81, is attacked. Since the aldehyde group is the more reactive, one would expect compound 83 to predominate. Badger reported that 83 was the only product isolated, even though he looked for the 4,5-isomer 84.

Upon repeating Badger's procedure, this author found, however, that there was approximately 20% of ethyl 4,5-dimethylpyrrole-2-carboxylate along with 80% of 83 in the product mixture. This was determined by integration of the peak areas of the 3-, 4-, and 5-methyl groups in the NMR spectrum of the mixture. The 3-methyl appeared at δ 2.28, the 4-methyl at δ 2.01, and the 5-methyl at δ 2.21. Recrystallization of the product mixture from isooctane as reported by Badger afforded a partial separation of the isomers but not a complete one. Pure 83 crystallized out of solution, but upon evaporation of the mother liquor, about one half of the initial amount of material remained. The NMR spectrum of this solid indicated approximately a 60:40 mixture of the 3,4- and the 4,5-isomers still remained.

Chromatography of the above mixture using a variety of solvents did not give a satisfactory separation of the two isomers, although with alumina and chloroform a small amount of the 4,5-isomer 84 was isolated and verified by comparison of its melting point with that reported in the literature.[90] With this result, it was decided to convert the mixture of pyrrolic esters into a compound which might have properties sufficiently different to affect a separation and yet be

convertible back into the pyrrolic esters after separation.

It has been reported by several people that halogenation of the pyrrole ring can be affected by reaction of pyrrole with halogen, and it has further been shown that the halogenated pyrroles can be reduced to the dehalogenated ring in several ways.[91] With this knowledge and the expectation that halogenation might take place preferentially at the more reactive and accessible α-position of 83 rather than at the β-position of 84, the iodination of the pyrrolic ester mixture was attempted using KI/H_2O_2 as the iodinating species.



83 84 85 86 84

The expected selectivity of reaction and the desired difference in adsorptivities on a chromatographic column were observed. Iodination of the mixture followed by separation on a silicic acid column eluted with benzene gave a 45% yield of ethyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate, 85, as the first fraction off the column. The melting point of 130.5-131.5° is in agreement with the literature value of 133-134°,[92] and the infrared spectrum[93] also agrees. Dehalogenation of 85 with zinc dust in acetic acid gave 83.

A second fraction yielded approximately 100 mg of ethyl 4,5-dimethyl-3-iodopyrrole-2-carboxylate, 86, as a

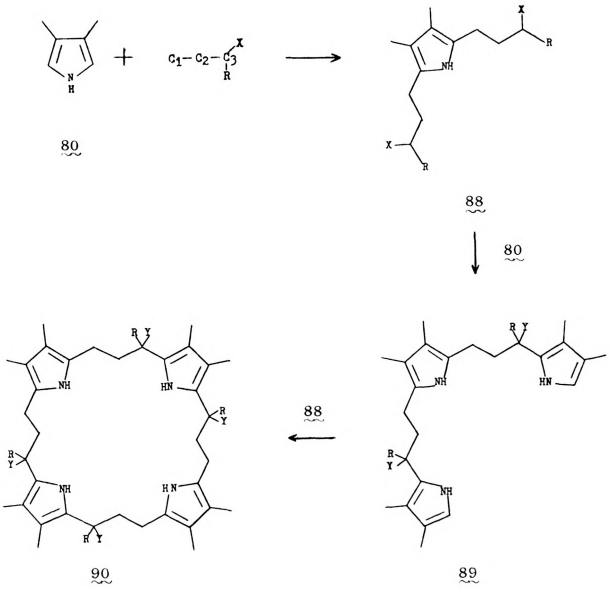
white crystalline solid whose melting point was 152.5-155°. The NMR of 86 shows a quartet (J = 7Hz, 2H) at δ 4.37 and a triplet (J = 7Hz, 3H) at δ 1.38 corresponding to the ethyl group in the ester, and two singlets, one at δ 2.28 (3H) and another at δ 2.0 (3H) which correspond to the 5-methyl and 4-methyl respectively. In addition there is a lack of absorption in the region δ 6.5-7.0 where the α- or β-pyrrolic hydrogens normally appear. The mass spectrum of 86 has a parent peak at 293 corresponding to a $C_9H_{12}NO_2I$ compound. Finally, reduction of 86 gave ethyl 4,5-dimethylpyrrole-2-carboxylate, 84, melting point 113-115° in agreement with the literature, 114-116°.[90]

The third fraction gave 300 mg of ethyl 4,5-dimethylpyrrole-2-carboxylate. Thus the results confirmed the expected selectivity of reaction at the α-position, and the iodinated products did allow a chromatographic separation.

Once the preparation and purification of ethyl 3,4-dimethylpyrrole-2-carboxylate, 83, was accomplished, 83 was hydrolyzed and decarboxylated according to the procedure of Badger[94] to give a 97% yield of 3,4-dimethylpyrrole, 80, and a 5% overall yield from the sodium salt of 3-formylbutan-2-one, 81.

There are several routes for the synthesis of the ring system 78 from 80. The first route attempted is that shown in Scheme 2. In the first step, 80 with its two free α-positions would react, possibly by a Michael-type reaction or Grignard reaction, at carbon 1 of a three-carbon unit

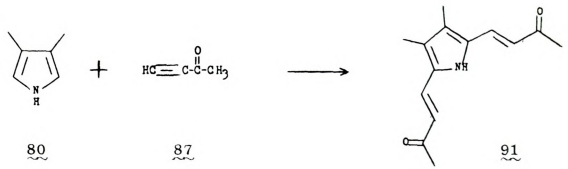
containing a functional group "X" on the third carbon to give 88.



Scheme 2

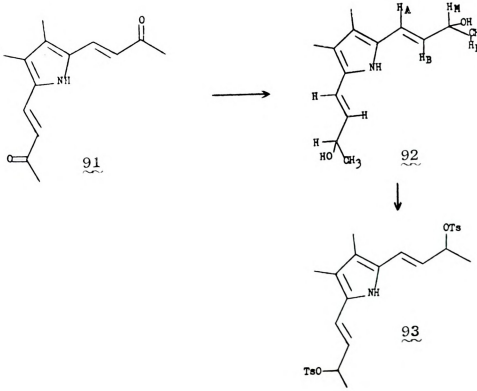
In the second step, 88 with the appropriate functional group "X" could react with an additional two molecules of 80 to give 89. Compound 89 in turn would react with a molecule of 88 to give 90, a derivative of 78.

Since the pyrrole ring is convertible into a Grignard species in which the α-position is the nucleophilic site, "X" could be either a halogen, tosylate, or a carbonyl group. These would permit carbon-carbon bond formation to take place by nucleophilic substitution in the second step of the sequence. The three-carbon unit chosen to meet the requirements was 3-butyn-2-one, 87; it has been shown that the α-position of the pyrrole ring adds across the acetylenic bond[95] of 3-butyn-2-one by a Michael reaction to give a monosubstituted pyrrole. Thus, 87 allows attachment of the three-carbon unit to 80. It also was anticipated that 87 might add to both sides of the more nucleophilic dialkylpyrrole, 80, to give a symmetrical tetraalkylpyrrole. In addition to the above features of disubstitution by the triple bond, 87 possesses the necessary electrophilic site (or the source for an alternative reactive site) at the third carbon for reaction with a Grignard species. Treatment of 3,4-dimethylpyrrole, 80, with two equivalents of 87 in refluxing methanol for 40 hours gave upon work-up a 54% yield of 2,5-bis(3-oxobutenyl)-3,4-dimethylpyrrole, 91, as golden crystals melting at 241-242°. The spectral data confirms the structure of 91.

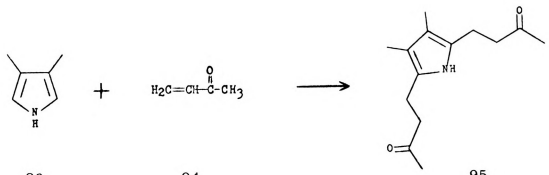


80 87 91

The N-H hydrogen in 91 is rather acidic as a result of the extended conjugation of the ring with the carbonyl groups. Because of this, compound 91 is not suited for reaction with a strong base like the Grignard species. Therefore, 91 was reduced with $NaBH_4$ in methanol to give a cream-colored solid. Its NMR spectrum in DMSO-d_6 indicated that the desired reduction product, 92, had been formed: an $ABMP_3$ pattern (δ 6.38, 6.05, and 4.33; J_{AB} = 15Hz, J_{BM} = 4Hz, $J_{AM} \simeq 0$, and J_{MP} = 6Hz) corresponding to 4H (δ 6.38 and 6.05) and 2H (δ 4.33) respectively, a doublet at δ 4.72 (J = 2Hz, 2H) for the hydroxyl hydrogen, a singlet at δ 1.91 (6H) for the 3,4-methyl groups, and a doublet at δ 1.2 (P of $ABMP_3$, J_{MP} = 6Hz, 6H) for the terminal methyl groups. Upon treatment of this compound with tosyl chloride in pyridine to form 93, only tarry solids were obtained which did not yield any identifiable products.



With these negative results for the conversion of 91 to 93, attention was directed toward the synthesis of the saturated diketone, 95. If the preparation of 95 could be accomplished, then direct nucleophilic attack on the carbonyl group could take place without the interference of the acidic N-H hydrogen. Treibs has reported the electrophilic substitution of acrylic esters on pyrrole and substituted pyrroles catalyzed by boron trifluoride etherate.[96] Application of

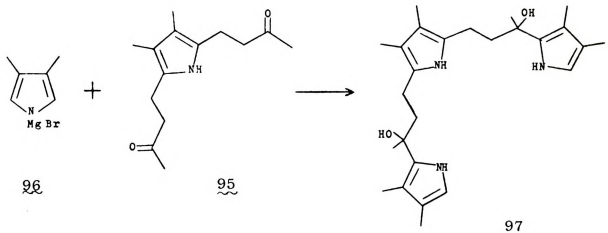


80 94 95

his procedure to the reaction of methyl vinyl ketone, 94, and 80 gave only a tar. Webb[97] was able to substitute pyrrole with 94 under mild acid conditions, and following his procedure with 80 this author obtained again a viscous liquid which could not be purified. Finally, it was found that 2,5-bis(3-oxobutyl)-3,4-dimethylpyrrole, 95, could be prepared in 87% yield by refluxing 80 and two equivalents of 94 in methanol for 4 hours. Compound 95 is a pale yellow viscous liquid boiling at 135-137°(0.15 mm). All spectral properties agree with the structure of 95.

Reaction of 95 with the 3,4-dimethylpyrrole Grignard, 96, gave only an impure solid which was very air sensitive

and unstable on either silicic acid or alumina columns.

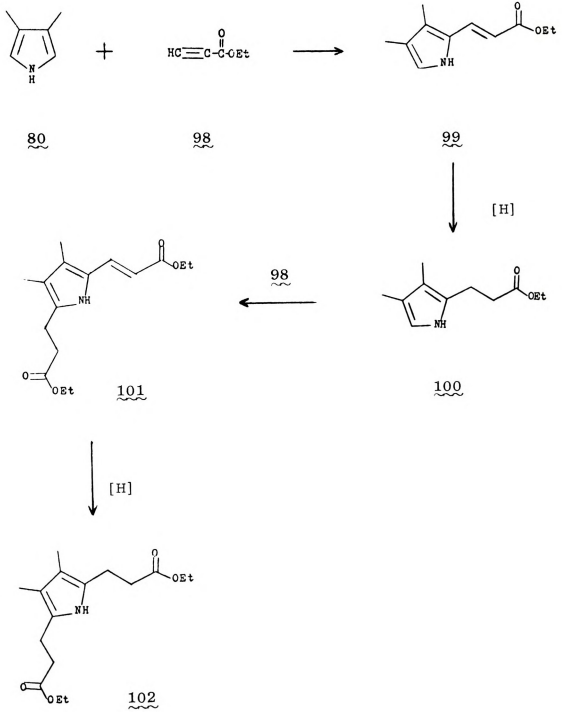


96 95 97

Efforts to convert the magnesium alkoxide from the Grignard reaction into the acetate of the alcohol were also unsuccessful. It appears that if alcohol 97 is formed, it is very unstable.

At this point, it did not seem that direct attack on the ketone carbonyl or conversion of that carbonyl to a good leaving group for participation in a nucleophilic substitution reaction was going to lead to success. It was thought that perhaps the reaction of the pyrrolic Grignard on an ester, where the product would be a pyrrolic ketone, might eliminate the experienced difficulties in the previous reactions. To this end, the sequence of reactions in Scheme 3 was carried out to prepare the diester 102.

The reaction of ethyl propiolate, 98, with 80 in refluxing ethanol was tried, using the previous reaction of 3-butyn-2-one, 87, with 80 as an example. A pale yellow solid melting at 50-51.5° was obtained in 76% yield. The

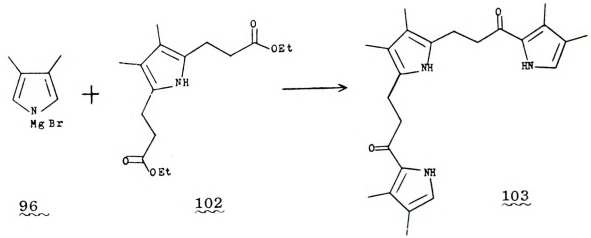


Scheme 3

spectral information and C, H analysis indicated that this compound was ethyl 3-(3,4-dimethylpyrrol-2-yl)propenoate, 99. Hydrogenation of 99 at 40-50 psi and room temperature with a Pd/C catalyst gave a quantitative yield of ethyl 3-(3,4-dimethylpyrrol-2-yl)propanoate, 100, in agreement with the spectra for 100. It is a pale yellow liquid boiling at 87-90°(0.2 mm) and is unstable on a silicic acid column.

A second molecule of 98 could be substituted on 100 to give ethyl 3-(5-carbethoxyethyl-3,4-dimethylpyrrol-2-yl)-propenoate, 101, in 47% yield as a pale yellow, waxy, crystalline solid recrystallizable from pentane and melting at 41.5-43.5°. The NMR, IR, mass spectrum, UV and C, H analysis confirmed its structure. Finally, 101 was reduced to give a quantitative yield of diethyl 3,4-dimethylpyrrole-2,5-dipropanoate, 102, as characterized by its spectral data.

Once 102 had been prepared, it was treated with the 3,4-dimethylpyrrole Grignard, 96, followed by the usual

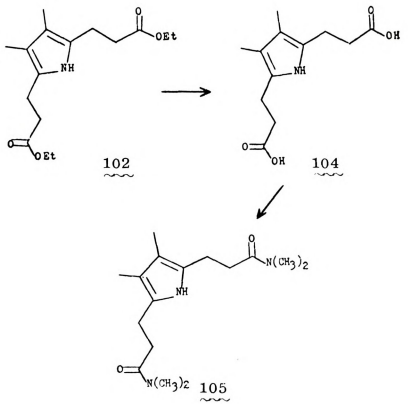


96 102 103

work-up, and a small amount (15%) of a white solid was

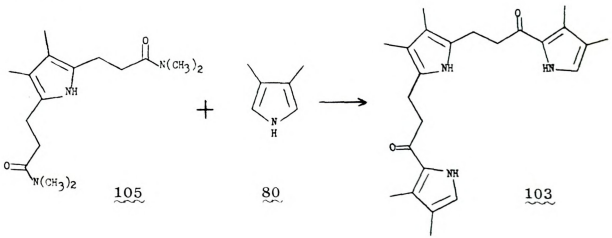
isolated which was recrystallized from chloroform/pentane and had a melting point of 148-150°. The NMR of the solid was inconsistent with either compound 103 or starting material, although it did indicate the presence of a free α-pyrrolic position. The mass of the largest ion in the mass spectrum was 293 rather than the expected parent ion of 393. Upon repeating the reaction three times, no solid product could be isolated.

Having had no success with the Grignard approach to the substitution of the two pyrrole rings at the ends of the three-carbon side chains, the author looked at the possible use of the Vilsmeier acylation reaction. Several groups[98,99] have demonstrated that pyrrole and various substituted pyrroles can be acylated in yields of 93% down to less than 5% by the Vilsmeier reaction. In order to utilize the Vilsmeier reaction in this synthesis, the N,N-dimethylamide derivative of 102 was prepared. Hydrolysis of 102 gave approximately a 94% yield of the dicarboxylic acid, 104. This green solid was then treated with triethylamine at 0-10° followed by ethyl chloroformate to give the mixed anhydride which was not isolated but reacted immediately with an excess of dimethylamine to give upon work-up a tan solid, recrystallizable from cyclohexane and melting at 101-102°. The NMR for 105 was consistent for N,N,N',N',3,4-hexamethylpyrrole-2,5-dipropanamide.

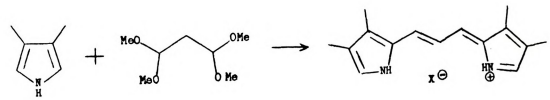


102 104 105

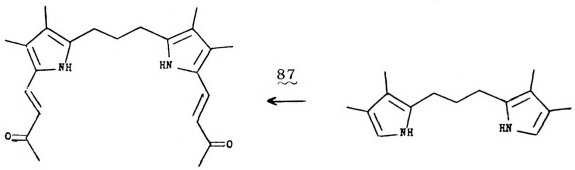
When 105 was treated with phosphorus oxychloride in the usual way[98,99] followed by two equivalents of 3,4-dimethylpyrrole, 80, and worked up, no compound corresponding to 103 except a small amount of starting material was isolated after chromatography of the reaction mixture. Similar results were obtained upon repetition of the reaction procedure.



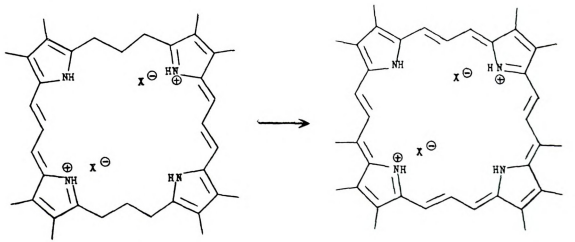
105 80 103



80 107 108



110 109



111 112

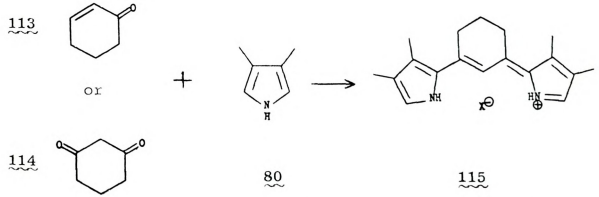
Scheme 4

Since the several attempts to synthesize that portion of compound 78, which possessed three of the four "corners" and two of the "sides" of the 26 π-electron ring, ended in dead ends, a new approach to the synthesis of the macrocyclic ring was sought. The approach taken was to synthesize compound 109, Scheme 4 -- a compound which incorporates two "corners" and one "side" of the macrocycle 78. If compound 109 could be made, then reaction of the trialkylpyrrole rings with their free α-positions with 87 should give 110. Once 110 was synthesized, 109 and 110 could undergo the typical condensation reaction of pyrroles with aldehydes or ketones to give a hexahydro-78, 111. Compound 111 could then be dehydrogenated with DDQ or possibly by just bubbling oxygen through a solution of 111 to give the decamethyl derivative of 78, 112.

The synthesis of 109 should be possible by preparing the dipyrryltrimethine salt, 108, followed by reduction. It has been shown that trisubstituted pyrroles (where one substituent is an ester group) and disubstituted pyrroles (where the substituents are phenyl groups) condense with 1,3-dicarbonyl compounds under acid conditions to give dipyrryltrimethine salts like 108.[100,101] This condensation has also been accomplished by LeGoff[102] using a trialkylpyrrole and 1,1,3,3-tetramethoxypropane, 107. The attempts to react 80 with 107 under hydrogen bromide catalysis proved unsuccessful. The only thing observed was the formation of a deep purple solution and isolation of a small

amount of a brownish-red solid which was insoluble in almost all solvents. Extraction in a Soxhlet with methylene chloride gave a purple solution which upon evaporation of solvent gave a deep maroon-colored solid, soluble in chloroform and methylene chloride. The NMR of this solid was incomprehensible. Upon repeating the reaction with variations in temperature, time of reaction, solvent, and mode of addition, the same results were obtained.

Assuming that possibly electrophilic attack on the trimethine bridge was taking place, a substituted bridging group was considered. This substituted bridging group would have to be a symmetrically-substituted one in order to eliminate the problems of structural isomers later in the synthesis. This could be accomplished by condensing 80 with either cyclohexen-2-one, 113, or dihydroresorcinol, 114, which would give the dipyrryltrimethine salt, 115.



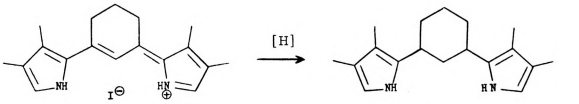
Treibs[103] had shown that reaction of either 113 or 114 with several substituted pyrroles gave (in varying yields) a trimethine salt analogous to 115. These salts all

absorbed at approximately 565-590 nm in the visible spectrum. Attempts at reacting 113 with 80 only led to an unpurifiable, deep maroon-colored solid which appeared as a glass on the walls of the flask upon removal of solvent.

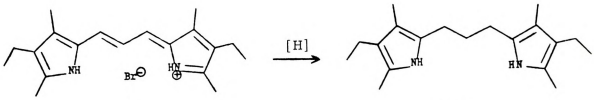
Synthesis of 115 (X = I) was successful from 114 and 80 according to all information except the NMR. A crystalline metallic-green solid precipitates out of the red-violet reaction mixture in 30% yield. After filtration, washing with ether, and drying, the compound had a melting point of 248-250° and had an absorption maximum in the visible range at 575 nm. The absorption maximum of analogous trimethine salts is at ~ 570 nm. The highest mass ion in the mass spectrum of 115 is m/e 266, which is the parent minus HI which is not to be unexpected. The infrared spectrum indicates extensive hydrogen bonding of the N-H hydrogens and a conjugated double bond system. The C, H analysis is in good agreement with a $C_{18}H_{23}N_2I$ molecular formula for 115. Because of the low solubility of 115 in the available NMR solvents, a 100 MHz spectrum accumulated on a time-averaging computer (CAT) was run. A satisfactory integration of the CAT spectrum could not be obtained because of a malfunction in the CAT integration capability, and there was too low a signal-to-noise ratio to allow a good integration of a single scan. The spectrum from the CAT and the available integration shows a singlet at δ 8.4 (1H) for the vinyl hydrogen, a doublet at δ 7.64 (J = 4Hz, 1H) for apparently only one α-pyrrolic hydrogen, a triplet at δ 3.1 (J = 7Hz, 4H) for

the allylic hydrogens, singlets at δ 2.42 (6H) and 2.13 (6H) for the 3- and 4-methyls respectively. The two large, broad singlets at δ 1.64 and 1.32 do not fit the structure of 115. These appear to be impurities.

The precedence for the reduction of 115 to 116 by catalytic hydrogenation with Pd/C in a Parr hydrogenator is found in the reduction of 117 to 118.



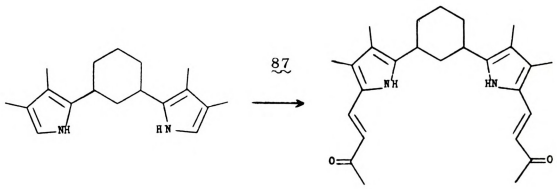
115 116



117 118

The NMR of 116 shows a broad singlet at δ 7.63 (2H) corresponding to the N-H hydrogens, a poorly-defined doublet at δ 6.43 (2H) for the α-pyrrolic hydrogens, a complex multiplet with two well-defined singlets from δ 3.03 to 1.36 (22H) corresponding to the 12 methyl hydrogens, the 8 methylene hydrogens, and the 2 methine hydrogens. From all the spectral data, except some parts of the NMR of 115, and the reduction product 116, it appears that the structure of 115 is that shown.

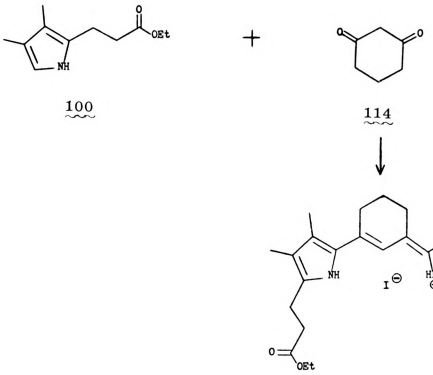
The next step in the sequence was to react 116 with 87 to give 119. The small amount of available 116 was reacted



116 119

with 87 and upon workup and chromatography on alumina with 10:2 benzene - methylene chloride, no identifiable product was isolated. Due to the lack of trimethine salt, 115, this reaction was not repeated.

The reaction leading to the trimethine salt, 120, was tried, using ethyl 3-(3,4-dimethylpyrrol-2-yl) propanoate, 100, as the pyrrole source. When 100 and 114 were refluxed for 3 1/2 hours with 51% HI and worked up, a green solid was obtained which was recrystallized from cyclohexane-methanol to give green needles melting at 136-138°. The NMR and the infrared spectra agree with structure 120. The NMR has a singlet at δ 8.05 (1H) for the vinyl hydrogen, a quartet at δ 4.13 (J = 7Hz, 4H), and a triplet at δ 1.25 (J = 7Hz, 6H) for the two ester ethyl groups, a complex multiplet at δ 3.4-2.83 (12H) for the side chain methylenes and the



100 114 120

allylic hydrogens, and then two singlets, one at δ 2.31 (6H) for the 3,3'-methyls and δ 2.01 (broad, 8H) for the 4,4'-methyls and the symmetrically-located methylene in the six-membered ring. Its UV maximum is at 597 nm.

It was with the synthesis of 120 which incorporates two "corners" and three "sides" of the 26-membered ring system that the synthesis of the title compound was terminated due to other commitments. However, it is evident from the last few reactions, that the synthetic approach most amenable to the successful synthesis of the title compound or a derivative is the path utilizing an appropriately substituted trimethine salt such as 120 or the saturated

derivative, 116, for the cyclization to the 26-membered ring. This cyclization step will probably be the poorest step in the sequence because of the large distances between the reacting ends of the linear tetrapyrrolic species. But if the reaction is done under high dilution, a respectable yield should result without much polymerization. The final step involving oxidation to give the completely conjugated system should be a facile one. It has been observed in the porphyrin syntheses from bilanes that the oxidation which gives the porphyrin ring is accomplished by aeration of the reaction mixture.[104]

Future work should include the preparation of 119 and then condensation of it with 116. Also the condensation of 120 with 116 should be attempted. If an alternative to these two sequences is needed, then preparation of some other appropriately substituted trimethine salt ought to be investigated.

EXPERIMENTAL

General Procedure

The melting points were determined on a Thomas Hoover Uni-melt melting point apparatus and are uncorrected.

The infrared spectra were recorded on a Perkin-Elmer Model 237B spectrophotometer. The NMR spectra were obtained on a Varian T-60 and HA-100 spectrometer with chemical shifts reported in δ-units measured from tetramethylsilane as the internal standard. The UV spectra were recorded using a Unicam Model SP-800 spectrophotometer using 1 cm quartz cells. Mass spectra were obtained with a Hitachi Perkin-Elmer RMU-6 mass spectrometer.

Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan.

Ethyl 3,4-dimethylpyrrole-2-carboxylate (83) and Ethyl 4,5-dimethylpyrrole-2-carboxylate (84)

A solution of 142,5 g (2.06 mole) of sodium nitrite in 210 ml of water was added dropwise over a 20 hour period (slowly enough to prevent evolution of nitrogen oxide gases) to a vigorously stirred solution of 120 g (0.75 mole) of diethyl malonate in 130 ml of glacial acetic acid. After 20 hours the solution was added to a separatory funnel and

allowed to separate into a lower aqueous layer and an upper organic layer for 3 hours. The layers were separated and the organic layer was added to a solution of 70 g (0.574 mole) of the sodium salt of 3-formylbutan-2-one in 250 ml of glacial acetic acid and 100 ml of water which was than heated to 95°. Upon reaching 95°, 75 g (1.15 mole) of zinc dust was added at such a rate as to maintain the temperature between 95-105°. When all the zinc had been added, the mixture was heated at 100-105° for one hour. The mixture was then slowly poured into approximately 2 liters of ice-water and chilled in the refrigerator overnight. The orange solid that precipitated was filtered, washed with water, and dried in vacuo over P_2O_5. The dry solid was sublimed at 78° (1 mm) to give approximately 9 g (10%) of a cream-colored solid melting at 84-90°. This solid was purified by recrystallization from isooctane yielding white needles of ethyl 3,4-dimethylpyrrole-2-carboxylate: mp 91-93° (lit. value 93°).[89]

Some of the sublimed material was chromatographed on alumina with chloroform giving ethyl 3,4-dimethylpyrrole-2-carboxylate as the first fraction. A second fraction provided a small amount of a cream-colored solid with mp 113-115°. The melting point and infrared spectrum are identical with the literature for ethyl 4,5-dimethyl-pyrrole-2-carboxylate.[90] The NMR spectrum of the sublimed material from subsequent runs indicated approximately 20% of the product mixture was the 4,5 isomer.

Ethyl 3,4-dimethylpyrrole-2-carboxylate -- mp 91-93°; ir ($CHCl_3$) 3440 and 3275 cm^{-1} (N-H), 2950, 2900, and 2840 cm^{-1} (C-H), 1670 cm^{-1} (C=O), 1575 cm^{-1} (C=C), and 1260, 1140 cm^{-1} (C-O); nmr ($CDCl_3$) δ 6.7 (d, J = 2Hz, 1H, α-H), δ 4.35 (q, J = 7Hz, 2H, $-O-CH_2CH_3$), δ 2.28 (s, 3H, $3-CH_3$), δ 2.01 (s, 3H, $4-CH_3$), and δ 1.35 (t, J = 7Hz, 3H, $-O-CH_2CH_3$).

Ethyl 4,5-dimethylpyrrole-2-carboxylate -- mp 113-115°; ir ($CHCl_3$) 3440 and 3280 cm^{-1} (N-H), 2960, 2900, and 2840 cm^{-1} (C-H), 1675 cm^{-1} (C=O), 1575 cm^{-1} (C=C), and 1225 cm^{-1} (C-O); nmr ($CDCl_3$) δ 6.72 (s, 1H, β-H), δ 4.32 (q, J = 7Hz, 2H, $-O-CH_2CH_3$), δ 2.21 (s, 3H, $5-CH_3$), δ 2.01 (s, 3H, $4-CH_3$), δ 1.33 (t, J = 7Hz, 3H, $-O-CH_2-CH_3$).

Separation of ethyl 3,4-dimethylpyrrole-2-carboxylate (83) and ethyl 4,5-dimethylpyrrole-2-carboxylate (84) -- ethyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate (85) and ethyl 4,5-dimethyl-3-iodopyrrole-2-carboxylate (86)

To a solution of 17.0 g (102 mmole) of the pyrrolic ester mixture (83) and (84) recovered after recrystallization from isooctane, 6 g (100 mmole) acetic acid, and 11.4 g (100 mmole) of 30% H_2O_2 in 150 ml of ethanol at 80° was added dropwise a solution of 17 g (100 mmole) potassium iodide in 75 ml of water. The solution was heated at 80° overnight, at which time the red color of the iodine had disappeared. The solution was cooled and crystallized in the refrigerator. A cream-colored solid (15.4 g) was collected upon filtration. The filtrant was diluted with its volume of water and again cooled. An additional 4 g was

obtained. The crystals were dried over P_2O_5 in vacuo. One gram of the dried material was chromatographed on silicic acid with benzene. The first fraction gave 800 mg of a white crystalline solid whose melting point corresponds to the literature value for ethyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate: mp 130.5-131.5° (lit. value 133-134°);[92] ir ($CHCl_3$) 3440 and 3225 cm^{-1} (N-H), 2975 and 2900 cm^{-1} (C-H), 1710, 1690, 1680 cm^{-1} (C=O), 1560 cm^{-1} (C=C), 1225 and 1140 cm^{-1} (C-O); nmr ($CDCl_3$) δ 4.37 (q, J = 7Hz, 2H, $-O-CH_2-CH_3$), δ 2.3 (s, 3H, $3-CH_3$), δ 1.97 (s, 3H, $4-CH_3$), δ 1.35 (t, J = 7Hz, 3H, $-O-CH_2CH_3$); mass spectrum (70 eV) m/e 293 (parent).

Anal. Calc'd for $C_9H_{12}NO_2I$: C, 36.89; H, 4.13.

Found : C, 36.81; H, 4.12.

The second fraction gave 100 mg of a white crystalline solid which is ethyl 4,5-dimethyl-3-iodopyrrole-2-carboxylate: mp 152.5-155°; ir ($CHCl_3$) 3440 and 3275 cm^{-1} (N-H), 2950, 2900, and 2850 cm^{-1} (C-H), 1700, 1680 sh, 1660 cm^{-1} (C=O), 1565 cm^{-1} (C=C), 1240 cm^{-1} (C-O); nmr ($CDCl_3$) δ 4.37 (q, J = 7Hz, 2H, $-O-CH_2CH_3$), δ 2.28 (s, 3H, $5-CH_3$), δ 2.0 (s, 3H, $4-CH_3$), δ 1.38 (t, J = 7Hz, 3H, $-O-CH_2CH_3$); mass spectrum (70 eV) m/e 293 (parent).

Anal. Calc'd for $C_9H_{12}NO_2I$: C, 36.89; H, 4.13; I, 43.32.

Found : C, 36.81; H, 4.03; I, 43.28.

The third fraction gave 300 mg of ethyl 4,5-dimethyl-pyrrole-2-carboxylate.

Reduction of ethyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate (85) and ethyl 4,5-dimethyl-3-iodopyrrole-2-carboxylate (86) to ethyl 3,4-dimethylpyrrole-2-carboxylate (83) and ethyl 4,5-dimethylpyrrole-2-carboxylate (84)

To a solution of 300 mg (1.02 mmole) of the corresponding iodopyrrole in 5 ml of acetic acid heated to reflux was added in small portions 268 mg (4.1 mmole) of zinc dust. The mixture was refluxed for 30 minutes after addition of the zinc, cooled, and poured into 50 ml of water. The precipitated solid was filtered, washed with water, and dried. Recrystallization from ethanol gave 152 mg (90%) of the respective dehalogenated pyrrole identified by its melting point and NMR spectrum.

2,5-Bis(3-oxobutenyl)-3,4-dimethylpyrrole (91)

A mixture of 3.5 g (36.9 mmole) of 3,4-dimethylpyrrole and 5.1 g (75 mmole) of 3-butyn-2-one in 125 ml of oxygen-purged methanol was refluxed in a nitrogen atmosphere for 40 hours. Precipitation of the diketone began after approximately 5 hours. The mixture was cooled in an ice-bath and the solid filtered. The golden crystalline material was recrystallized from 95% ethanol to yield 4.6 g (54%) of product: mp 241-242°; ir (KBr) 3300 cm^{-1} (N-H), 2900 cm^{-1} (C-H), 1675 cm^{-1} (C=O, and 1630, 1615, and 1580 cm^{-1} (C=C); nmr ($(CF_3)_2CO \cdot 1.5\ H_2O$) δ 7.71 and 6.55 (ABq, J = 16Hz, 4H, vinyl hydrogens), δ 2.46 (s, 6H, $-CH_3$ α to C=O), and δ 2.18 (s, 6H, 3,4-CH_3's): uv max ($CHCl_3$) 283 (11,700), 317 (6350), and 425 (23,500); mass spectrum (70 eV) m/e 231 (parent).

Anal. Calc'd for $C_{14}H_{17}NO_2$: C, 72.79; H, 7.42.
Found : C, 72.83; H, 7.42.

2,5-Bis(3-hydroxybutenyl)-3,4-dimethylpyrrole (92)

To a stirred solution of 0.25 g (8.06 mmole) of 2,5-bis-(3-oxobutenyl)-3,4-dimethylpyrrole in 25 ml of methanol cooled at 10^0 was added in small portions a two-fold excess of $NaBH_4$, allowing consumption of the portion before further addition. The initially orange solution changed to a pale yellow color indicating that reduction had taken place. The mixture was poured into cold water and the product was extracted with ether. The ether layer was separated and dried over K_2CO_3. The ether was removed and the resulting yellow oil was dissolved in a minimum amount of chloroform, and pentane was added until turbidity. The solution was cooled and the solid filtered, washed with pentane, and then the cream-colored solid was dried in a drying pistol. The compound turns green upon exposure to air and silicic acid and alumina columns. The NMR shows an $ABMP_3$ pattern (δ 6.38, 6.05, and 4.33; J_{AB} = 15Hz, J_{BM} = 4Hz, $J_{AM} \simeq 0$, and J_{MP} = 6Hz), corresponding to 4H (δ 6.38 and 6.05) and 2H (δ 4.33) respectively, a doublet at δ 4.72 (J = 2Hz, 2H) for the hydroxyl hydrogen, a singlet at δ 1.91 (6H) for the 3,4-methyl groups, and a doublet at δ 1.2 (P of $ABMP_3$, J_{MP} = 6Hz, 6H) for the terminal methyl groups; ir (KBr) 3300 cm^{-1} broad (N-H, O-H), 2950, 2900, and 2840 cm^{-1} (C-H), 1700 and 1570 cm^{-1} (C=C).

2,5-Bis(3-oxobutyl)-3,4-dimethylpyrrole (95).

Two grams (21.05 mmole) of 3,4-dimethylpyrrole, 3.242 g (46.31 mmole) of methyl vinyl ketone, and a trace of hydroquinone were dissolved in 75 ml of methanol which had been purged of oxygen in a flask equipped with a reflux condensor, nitrogen bubbler, and a magnetic stirrer. The mixture was refluxed under a nitrogen atmosphere for 4 hours. The methanol was then removed on a rotary evaporator and the oily residue was distilled under vacuum to yield 4.3 g (87%) of a yellow oil: bp 135-37° (0.15 mm); ir (liquid film) 3375 cm^{-1} (N-H), 2940, 2900, 2850 cm^{-1} (C-H), 1720 cm^{-1} (C=O), 1620 cm^{-1} (C=C); nmr ($CDCl_3$) δ 8.23 (s, 1H, N-H), δ 2.71 (s, 8H, methylenes), δ 2.13 (s, 6H, 3,4-CH_3's), δ 1.9 (s, 6H, CH_3 α to C=O); mass spectrum (70 eV) m/e 235 (parent).

Anal. Calc'd for $C_{14}H_{21}NO_2$: C, 71.55; H, 9.01.

Found : C, 70.15; H, 8.68.

Ethyl 3-(3,4-dimethylpyrrol-2-yl)propenoate (99)

Three grams (31.5 mmole) of 3,4-dimethylpyrrole and 4.5 g (46 mmole) of ethyl propiolate were added to 50 ml of oxygen-purged dry ethanol and refluxed under a nitrogen atmosphere for 15 hours. After removal of ethanol on a rotary evaporator, the yellow residue was chromatographed on alumina with 10:3 carbon tetrachloride-methylene chloride. The first fraction yielded 4.62 g (76%) of a pale yellow solid. This solid was sublimed at 40-45° (0.2 mm):

mp 50-51.5°; ir ($CHCl_3$) 3260 cm^{-1} (N-H), 3025 cm^{-1} (olefinic C-H), 2975, 2905, and 2850 cm^{-1} (C-H), 1675 cm^{-1} (C=O), 1590 and 1550 cm^{-1} (C=C), and 1160 cm^{-1} (C-O); nmr ($CDCl_3$) δ 6.8 and 5.47 (ABq, J = 12Hz, 2H, vinyl hydrogens), δ 6.76 (d, 1H, α-pyrrolic hydrogens), δ 4.2 (q, J = 7Hz, 2H, $-O-CH_2CH_3$), δ 2.11 (s, 3H, $3-CH_3$), δ 2.03 (s, 3H, $4-CH_3$), and δ 1.3 (t, J = 7Hz, 3H, $-O-CH_2CH_3$); uv (95% EtOH) 206 (11,980, 287 (3467), 349 (22,300); mass spectrum (70 eV) m/e 193 (parent).

Anal. Calc'd for $C_{11}H_{15}NO_2$: C, 68.45; H, 7.83.
Found : C, 68.45; H, 7.87.

Ethyl 3-(3,4-dimethylpyrrol-2-yl) propanoate (10Q).

A solution of 1.0 g (5.18 mmole) of ethyl 3-(3,4-dimethylpyrrol-2-yl)propenoate in 200 ml of 95% ethanol containing 0.3 g Pd/C was hydrogenated at 40-50 psi for 60 minutes at room temperature on a Parr hydrogenator. After filtration of the catalyst and removal of solvent on a rotary evaporator, a pale yellow liquid was obtained. This was distilled at 87-90° (0.2 mm) to give almost a quantitative yield of the desired product. The pyrrolic ester was unstable on a silicic acid column. Ir (liquid film) 3375 cm^{-1} (N-H), 2975, 2940, 2900, and 2850 cm^{-1} (C-H), 1720 cm^{-1} (C=O), 1595 cm^{-1} (C=C), 1210 and 1180 cm^{-1} (C-O); nmr ($CDCl_3$) δ 8.16 (d, J = 2Hz, 1H, N-H), δ 6.36 (d, J = 1Hz, 1H, α-pyrrolic hydrogen), δ 4.15 (q, J = 7Hz, 2H, $-O-CH_2CH_3$), δ 2.66 (A_2B_2 multiplet, 4H, methylenes), δ 2.0 (s, 3H, $4-CH_3$),

δ 1.93 (s, 3H, 3-CH_3), and δ 1.2 (t, J = 7Hz, 3H, -O-CH_2CH_3); mass spectrum (70 eV) m/e 195 (parent).

Anal. Calc'd for $C_{11}H_{17}NO_2$: C, 67.75; H, 8.79.
Found : C, 67.81; H, 8.77.

Ethyl 3-(5-carbethoxyethyl-3,4-dimethylpyrrol-2-yl)-propenoate (101).

A solution of 3.9 g (20 mmole) of ethyl 3-(3,4-dimethylpyrrol-2-yl)propanoate and 2.94 g (30 mmole) of ethyl propiolate in 50 ml of oxygen-purged ethanol was refluxed under a nitrogen atmosphere for 4 hours. The orange solution that resulted was concentrated on a rotary evaporator and the residue chromatographed on alumina with 5:6 benzene-methylene chloride. The first fraction gave 2.74 g (47%) of a pale yellow, waxy solid which was recrystallized from pentane to yield pale yellow needles: mp 41.5-43.5°; ir ($CHCl_3$) 3240 cm^{-1} (N-H), 2960, 2900, and 2840 cm^{-1} (C-H), 1720 and 1670 cm^{-1} (C=O), 1580 and 1550 cm^{-1} (C=C), and 1160 cm^{-1} (C-O); nmr ($CDCl_3$) δ 6.73 and 5.37 (ABq, J = 12Hz, 2H, vinyl hydrogens), δ 4.2 (q, J = 7Hz, 2H, -O-CH_2CH_3 on unsaturated ester), δ 4.16 (q, J = 7Hz, 2H, -O-CH_2CH_3 on saturated ester), δ 2.77 (A_2B_2 multiplet, 4H, methylenes), δ 2.05 (s, 3H, 4-CH_3), δ 1.95 (s, 3H, 3-CH_3), δ 1.28 (t, J = 7Hz, 3H, -O-CH_2CH_3 on unsaturated ester), and δ 1.23 (t, J = 7 Hz, 3H, -O-CH_2CH_3 on saturated ester; uv (95% EtOH) 202 (12,260), 292 (2420), 356 (21,900); mass spectrum (70 eV) m/e 293 (parent).

Anal. Calc'd for $C_{16}H_{23}NO_4$: C, 65.58; H, 7.91.
Found : C, 65.41; H, 7.83.

Diethyl 3,4-dimethylpyrrole-2,5-dipropanoate (102)

One gram (3.51 mmole) of ethyl 3-(5-carbethoxyethyl-3,4-dimethylpyrrol-2-yl)propenoate was dissolved in 200 ml of 95% ethanol and 0.3 g Pd/C added. The mixture was hydrogenated at 40-50 psi for 60 minutes at room temperature on a Parr hydrogenator. After filtration of the catalyst and removal of solvent on a rotary evaporator, a yellow liquid remained. This was distilled at 144-145° (0.2 mm) to yield almost a quantitative amount of the desired reduction product. The compound was slightly air sensitive, turning an orange-yellow. Ir ($CHCl_3$) 3410 cm^{-1} (N-H), 3015 cm^{-1} (olefinic C-H), 2960, 2900, and 2840 cm^{-1} (C-H), 1720 and 1675 cm^{-1} (C=O), 1600 and 1580 sh cm^{-1} (C=C), and 1240 and 1160 cm^{-1} (C-O); nmr ($CDCl_3$) δ 8.38 (s, 1H, N-H), δ 4.2 (q, J = 7Hz, 4H, $-O-CH_2CH_3$), δ 2.67 (A_2B_2 multiplet, 8H, methylenes), δ 1.95 (s, 6H, 3,4-CH_3's), and δ 1.28 (t, J = 7Hz, 6H, $-O-CH_2CH_3$); mass spectrum (70 eV) m/e 295 (parent.

Anal. Calc'd for $C_{16}H_{25}NO_4$: C, 65.14; H, 8.54.
Found : C, 65.03; H, 8.51.

N,N,N',N',3,4-hexamethylpyrrole-2,5-dipropanamide (105)

A solution of 0.5 g (1.7 mmole) of diethyl 3,4-dimethylpyrrole-2,5-dipropanoate, 10 ml ethanol, and 15 ml of 5% aqueous KOH was refluxed for 5 hours. The ethanol was

removed on a rotary evaporator and the aqueous solution acidified to pH 5 with 2M HCl. The aqueous solution was extracted with ether and dried over Na_2SO_4. Upon removal of the ether, a green solid was obtained. An aqueous solution of this solid was acidic and the NMR of the solid showed: δ 8.43 (s, 1H, N-H), δ 2.68 (A_2B_2 multiplet, 8H, methylene hydrogens), and δ 1.9 (s, 6H, 3,4-CH_3's), consistent with 3,4-dimethylpyrrole-2,5-dipropanoic acid (104)

Approximately 0.5 g (2.09 mmole) of the above acid was dissolved in 15 ml of chloroform and cooled to 0-10°. To this stirred solution was added 0.4 g (3.9 mmole) of triethylamine followed by 0.5 g (4.6 mmole) of ethyl chloroformate and then stirred for 15-20 minutes at 0-10°. The solution was saturated with excess dimethylamine at 0-10° and then stirred at this temperature for 15 minutes followed by 30 minutes at room temperature. The chloroform solution was washed twice with 10% aqueous Na_2CO_3 solution and then dried over Na_2SO_4. The chloroform was removed and the brownish solid recrystallized from cyclohexane giving 0.5 g (96%) of a tan-colored crystalline solid: mp 101-102°; nmr ($CDCl_3$) δ 2.97 (s, 12H, all N-CH_3), δ 2.77 (A_2B_2 multiplet, 8H, methylene hydrogens), and δ 1.93 (s, 6H, 3,4-CH_3's).

Attempted synthesis of 3,4,3',4'-tetramethyl-dipyrryl-(2,2')-hexacyclotrimethine bromide (108)

To a solution of 0.2 g (2.1 mmole) of 3,4-dimethylpyrrole and 0.3 ml of 50% HBr in 4 ml ethanol heated at 50° was added dropwise 0.1 g (1.05 mmole) of cyclohexenone. The

solution slowly turned blue. The heat was removed and the mixture stirred for 6 hours. The solid which had formed was filtered and washed with 1:1 ethanol-water. A deep maroon, insoluble, rubbery solid remained. The blue filtrant was evaporated to give a red-violet solid as a film on the flask. The solid was extracted with methylene chloride (Soxhlet) giving a red-violet solution. Removal of the solvent gave a red-violet solid as a film on the flask. The NMR indicated impure material. Purification of this solid could not be accomplished.

3,4,3',4'-Tetramethyl-dipyrryl-(2,2')-hexacyclotrimethine iodide (115)

A mixture of 0.25 g (2.63 mmole) of 3,4-dimethylpyrrole, 0.1467 g (1.31 mmole) of dihydroresorcinol, and 0.6 g (2.39 mmole) of 51% HI in 7 ml of ethanol was heated at 92° for 2 hours. The solution turned from a yellow to a red-violet color. The solution was cooled in the freezer for 5 hours and then filtered. The deep metallic green crystals were washed repeatedly with ether to yield, upon drying in a drying pistol over P_2O_5, 162 mg (30%) of product recrystallizable from methanol: mp 248-50°; ir ($CHCl_3$) 3150 cm^{-1} (N-H), 2900 cm^{-1} (C-H), 1600, 1555, and 1520 cm^{-1} (C=C); nmr ($CDCl_3$) δ 8.4 (s, 1H, vinyl hydrogen), δ 7.64 (d, J = 4Hz, 1H, α-pyrrolic hydrogen), δ 3.1 (t, 4H, allylic hydrogens), δ 2.42 (s, 6H, 4,4'-methyls), and δ 2.13 (s, 6H, 3,3'-methyls); uv ($CHCl_3$) 282 sh (4140), 291 (8270), 368 (2960),

538 sh (14,200), and 575 (88,600); mass spectrum (70 eV) m/e 266 (parent - HI).

Anal. Calc'd for $C_{18}H_{23}N_2I$: C, 54.87; H, 5.88.
Found : C, 54.88; H, 5.82.

1,3-Bis(3,5-dimethyl-4-ethylpyrrol-2-yl)propane (118)

A solution of 0.363 g (1.0 mmole) of bis-2-(3,5-dimethyl-4-ethylpyrrole)trimethine bromide (117) and 0.136 g (1.0 mmole) of sodium acetate in 100 ml of 95% ethanol containing 0.1 g Pd/C was hydrogenated at 40-50 psi for 3 hours at room temperature on a Parr hydrogenator. The solution was filtered through K_2CO_3 and the ethanol removed on a rotary evaporator. The residue was dissolved in ether and filtered to remove sodium acetate. Upon removal of the ether, a greenish viscous oil remained. After further removal of solvent at 0.2 mm Hg pressure, the viscous liquid gave an NMR spectrum devoid of olefinic hydrogens and the appearance of additional alkyl hydrogens. NMR ($CDCl_3$) δ 7.1 (s, 2H, N-H), δ 2.8 - 1.5 (complex multiplet), δ 2.08 (s, 5-CH_3), δ 1.95 (s, 3-CH_3), and δ 1.07 (t, J = 8Hz, 6H, -CH_2CH_3). Peaks between δ 2.8 - 1.5 correspond to 22H.

1,3-Bis 3,4-dimethylpyrrol-2-yl)cyclohexane (116)

A solution of 100 mg (0.5 mmole) of the corresponding trimethine iodide and 150 mg (1.83 mmole) of sodium acetate in 100 ml of ethanol containing 0.1 g Pd/C was hydrogenated at 40-50 psi at room temperature for 2 hours in a Parr

hydrogenator. After filtration of the catalyst over K_2CO_3, the solvent was removed on a rotary evaporator. The residue was dissolved in a water-ether mixture and the ether separated and dried over K_2CO_3. Upon removal of the ether, a yellowish-orange viscous liquid was obtained. Any residual solvent was removed under 0.2 mm Hg pressure. The liquid was very air sensitive, turning green in the air. It was distilled at 185-190° (0.18 mm) to give a glassy syrup. The NMR spectrum indicates that the liquid is the desired product: nmr ($CDCl_3$) δ 7.6 (s, 2H, N-H), δ 6.43 (d, J = 2.5Hz, 2H, α-pyrrolic hydrogens), δ 3.47 - 1.2 (complex multiplet), δ 2.03 (s), δ 2.00 (s). Peaks between) 3.47 - 1.2 correspond to 22H.

Reaction of 1,3-bis(3,4-dimethylpyrrol-2-yl)cyclohexane (116) with 3-butyn-2-one (87), the attempted synthesis of 119

A solution of ~ 0.5 mmole of 116 and 103 mg (1.5 mmole) of 3-butyn-2-one in 7 ml of methanol was refluxed for 4 hours. The solvent was then removed and the reddish-brown viscous liquid was chromatographed on alumina with 10:2 benzene-methylene chloride. No identifiable product could be isolated.

5,5'-Bis(carbethoxyethyl)-3,4,3',4'-tetramethyl-dipyrryl-(2,2')-hexacyclotrimethine iodide 120

A mixture of 0.5 g (2.56 mmole) of ethyl 3-(3,4-dimethylpyrrol-2-yl)propanoate, 0.1434 g (1.28 mmole) of dihydroresorcinol, and 0.6 g (~ 2.25 mmole) of 51% HI in 7 ml

of ethanol was heated at 60-80° for 3 1/2 hours. The solution turned from a yellow to a deep blue color. The mixture was cooled in the refrigerator and then filtered to give a mat of green crystals. This solid was recrystallized from cyclohexane-methanol to give green needles: mp 136-138°; ir ($CHCl_3$) 3150 cm^{-1} (N-H), 2925 cm^{-1} (C-H), 1720 cm^{-1} (C=O), 1610, 1550, 1500 cm^{-1} (C=C), and 1290 cm^{-1} (C-O); nmr ($CDCl_3$) δ 8.05 (s, 1H, vinyl hydrogen), δ 4.13 (q, 4H, $-O-CH_2CH_3$), δ 3.4-2.83 (complex multiplet, 12H, methylenes in side chain, and allylic hydrogens), δ 2.31 (s, 6H, 3,3'-methyls), δ 2.01 (s, 8H, methylene in six-member ring and 4,4'-methyls), and δ 1.25 (t, 6H, $-O-CH_2CH_3$); uv maximum ($CHCl_3$) 597, 552 sh, 375, 297, and 282 sh.

APPENDIX

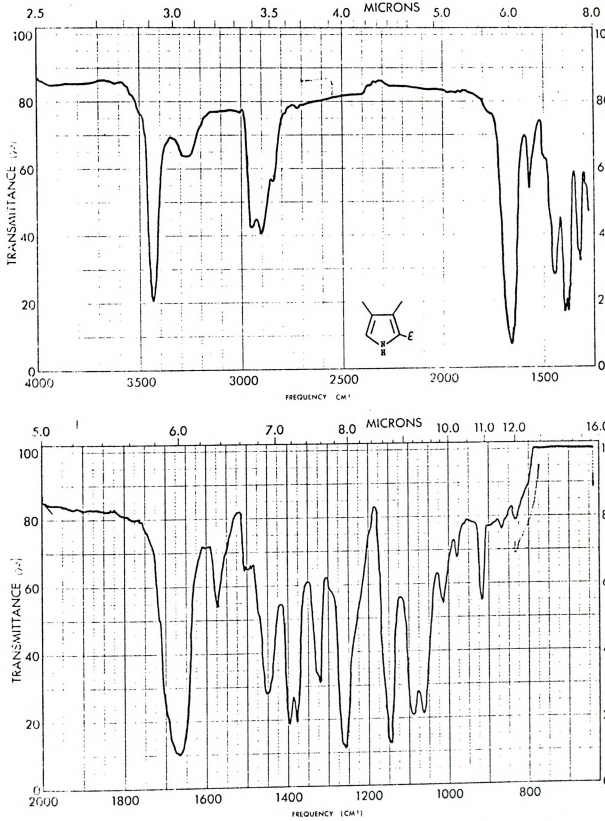


Figure 3. Infrared spectrum of ethyl 3,4-dimethylpyrrole-2-carboxylate, 83 ($CHCl_3$).

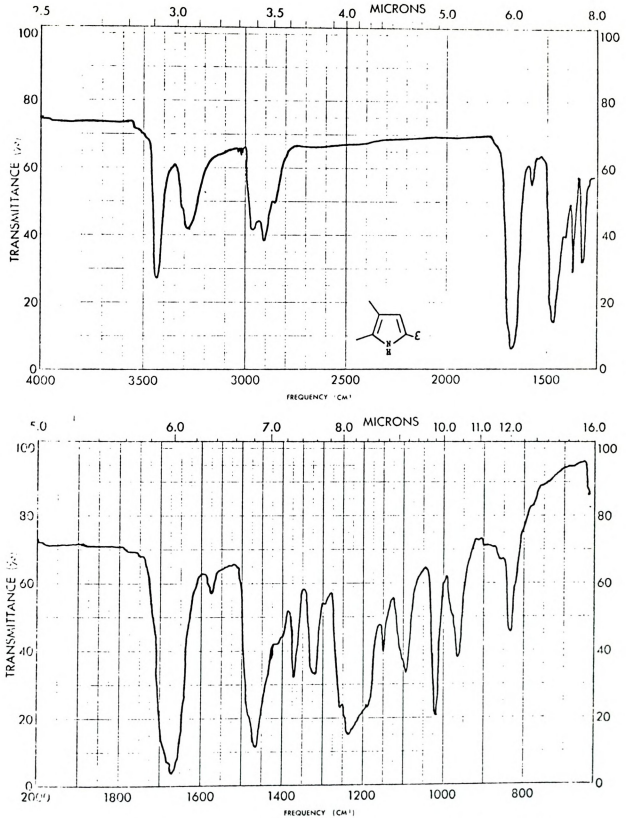


Figure 4. Infrared spectrum of ethyl 4,5-dimethylpyrrole-2-carboxylate, 84 ($CHCl_3$).

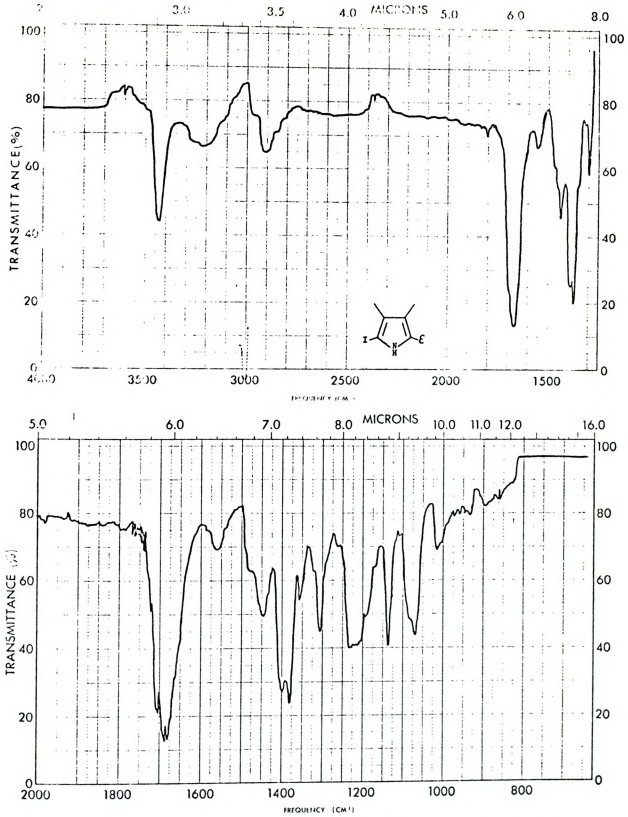


Figure 5. Infrared spectrum of ethyl 3,4-dimethyl-5-iodo-pyrrole-2-carboxylate, 85 ($CHCl_3$).

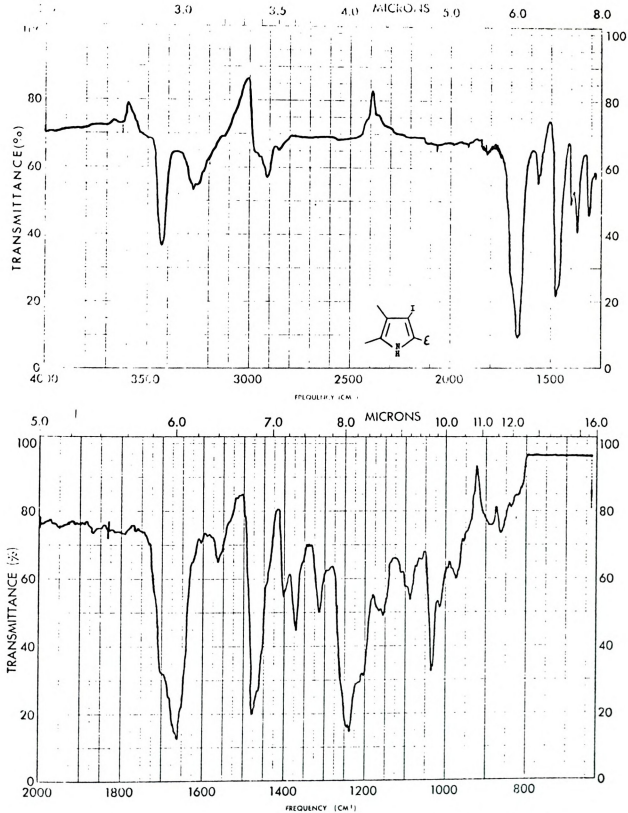


Figure 6. Infrared spectrum of ethyl 4,5-dimethyl-3-iodopyrrole-2-carboxylate, 86 ($CHCl_3$).

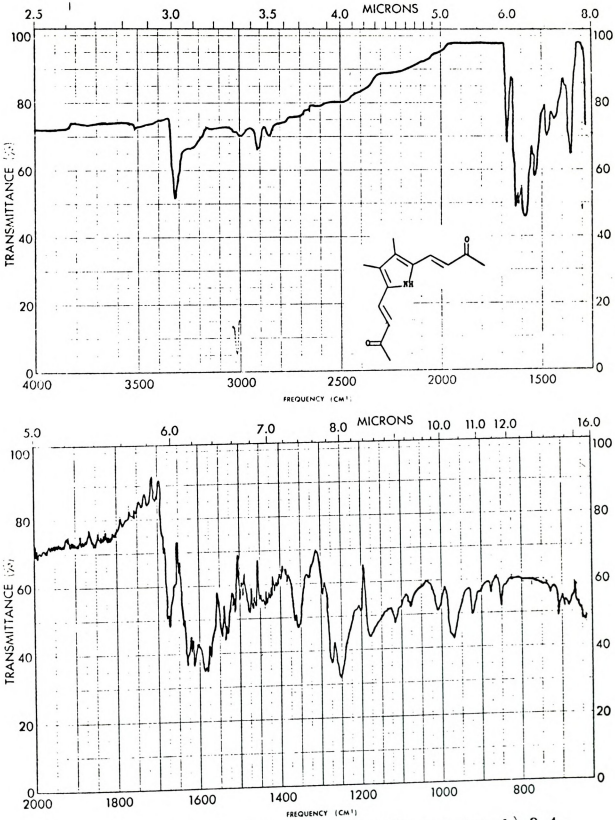


Figure 7. Infrared spectrum of 2,5-bis(3-oxobutenyl)-3,4-dimethylpyrrole, 91 (KBr).

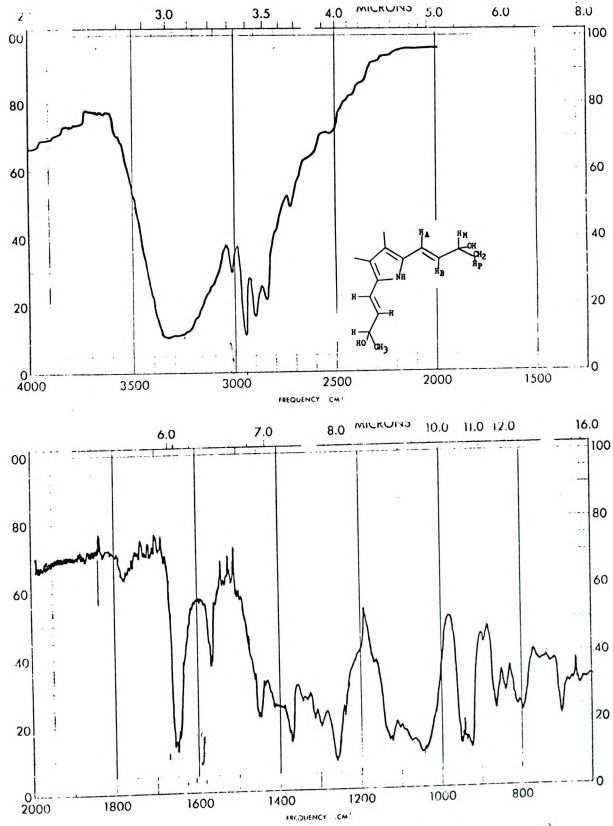


Figure 8. Infrared spectrum of 2,5-bis(3-hydroxybutenyl)-3,4-dimethylpyrrole, 92 (KBr).

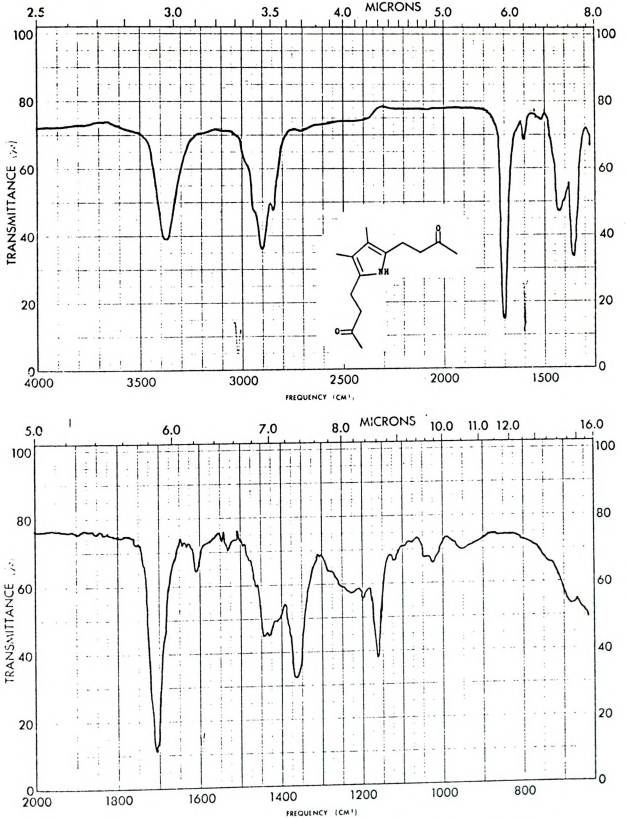


Figure 9. Infrared spectrum of 2,5-bis(3-oxobutyl)-3,4-dimethylpyrrole, 95 (liquid film).

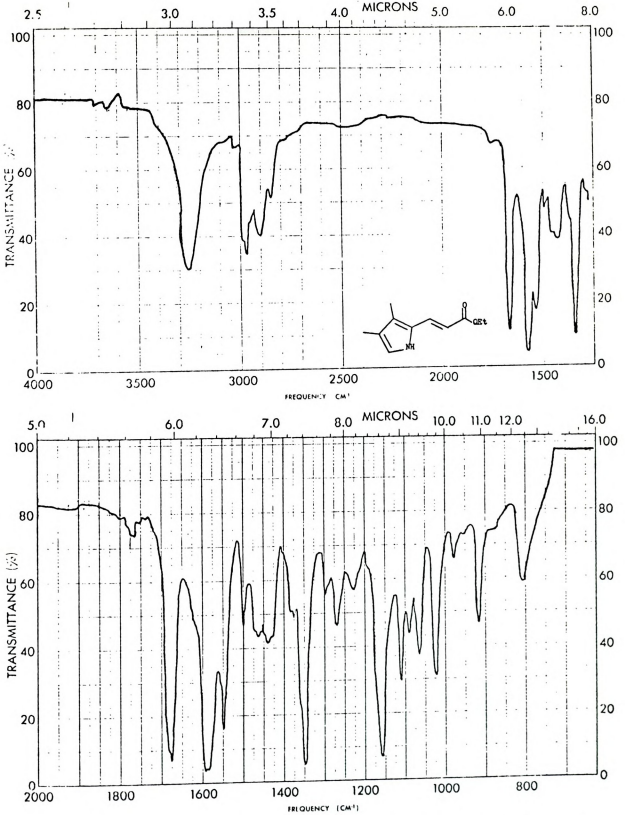


Figure 10. Infrared spectrum of ethyl 3-(3,4-dimethylpyrrol-2-yl)propenoate, 99 ($CHCl_3$).

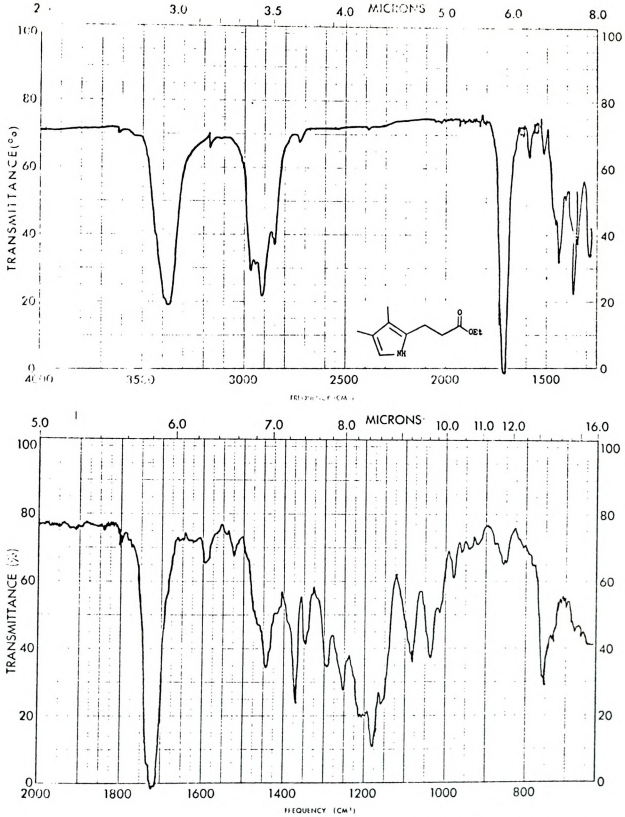


Figure 11. Infrared spectrum of ethyl 3-(3,4-dimethylpyrrol-2-yl)propanoate, 100 ($CHCl_3$)

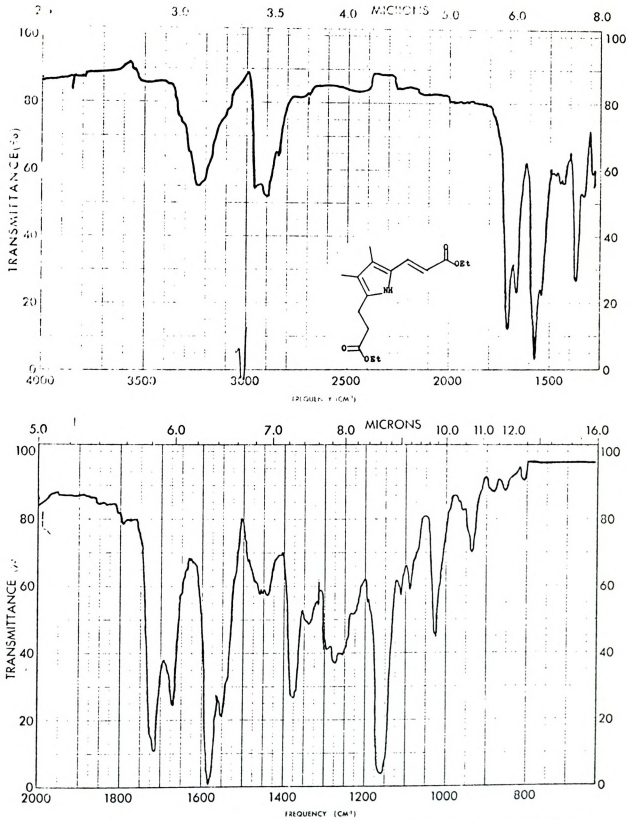


Figure 12. Infrared spectrum of ethyl 3-(5-carbethoxyethyl-3,4-dimethylpyrrol-2-yl)propenoate, 101 ($CHCl_3$).

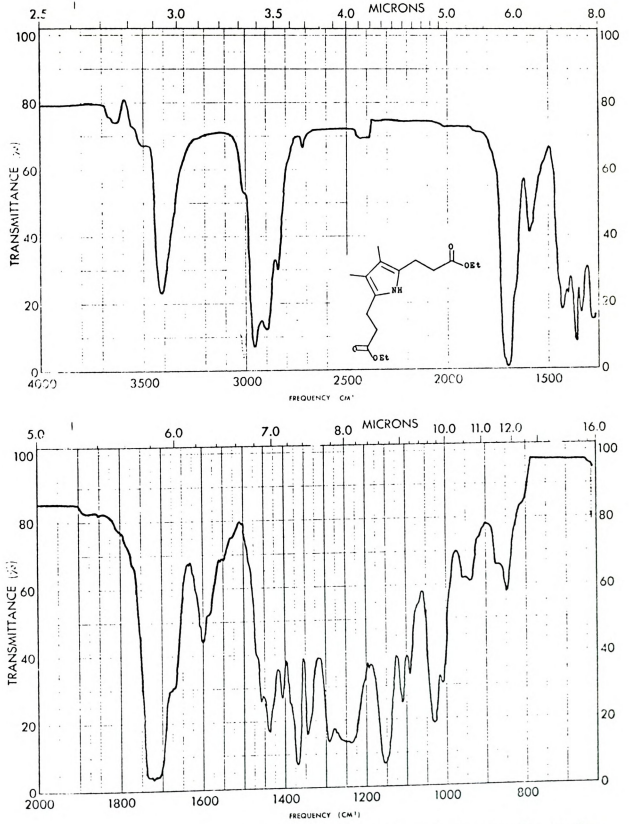


Figure 13. Infrared spectrum of diethyl 3,4-dimethylpyrrole-2,5-dipropanoate, 102 ($CHCl_3$).

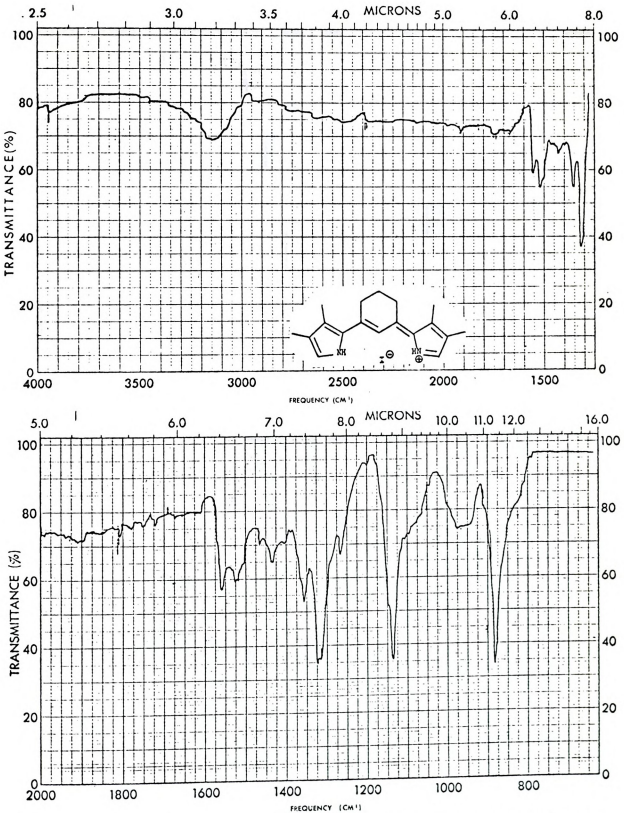


Figure 14. Infrared spectrum of 3,4,3',4'-tetramethyl-dipyr-ryl-(2,2')-hexacyclotrimethine iodide, 115 ($CHCl_3$).

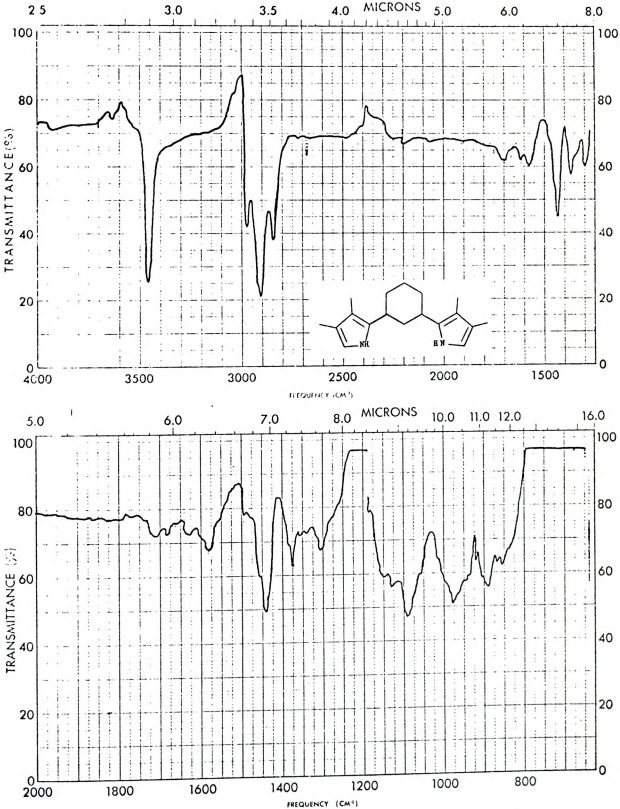


Figure 15. Infrared spectrum of 1,3-bis(3,4-dimethylpyrrol-2-yl)cyclohexane, 116 ($CHCl_3$).

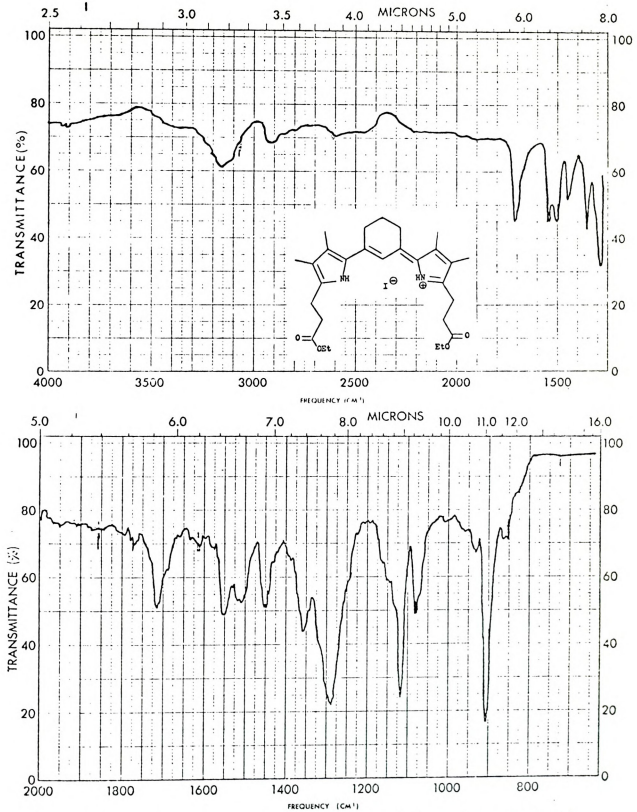


Figure 16. Infrared spectrum of 5,5'-bis(carbethoxyethyl)-3,4,3',4'-tetramethyl-dipyrryl-(2,2')-hexacyclotrimethine iodide, 120 ($CHCl_3$).

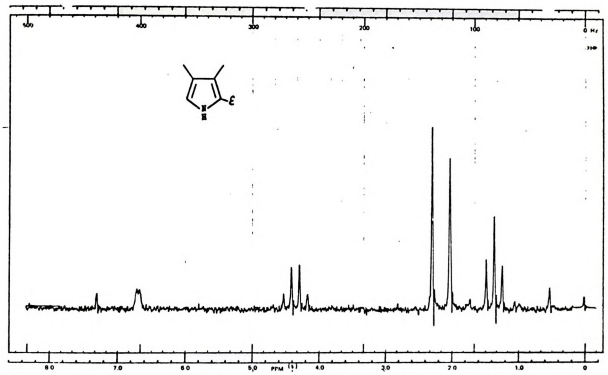


Figure 17. NMR spectrum of ethyl 3,4-dimethylpyrrole-2-carboxylate, 83 ($CDCl_3$).

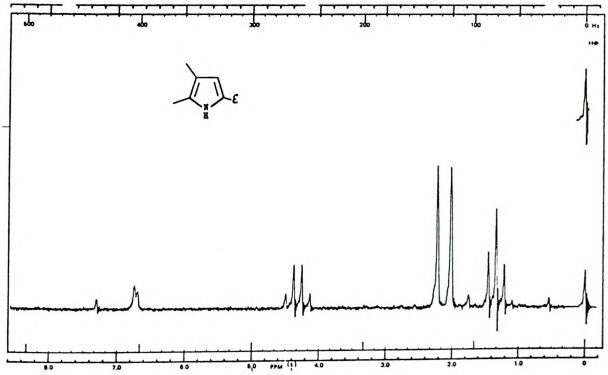


Figure 18. NMR spectrum of ethyl 4,5-dimethylpyrrole-2-carboxylate, 84 ($CDCl_3$).

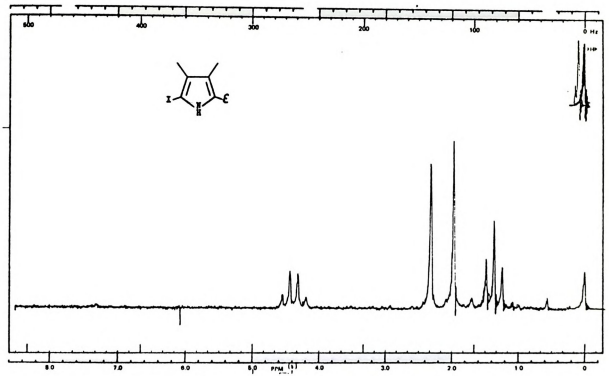


Figure 19. NMR spectrum of ethyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate, 85 ($CDCl_3$).

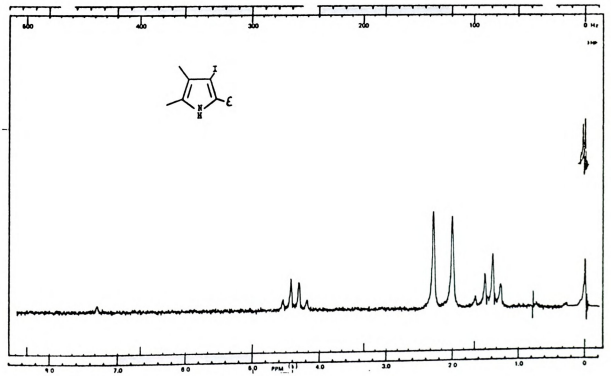


Figure 20. NMR spectrum of ethyl 4,5-dimethyl-3-iodopyrrole-2-carboxylate, 86 ($CDCl_3$).

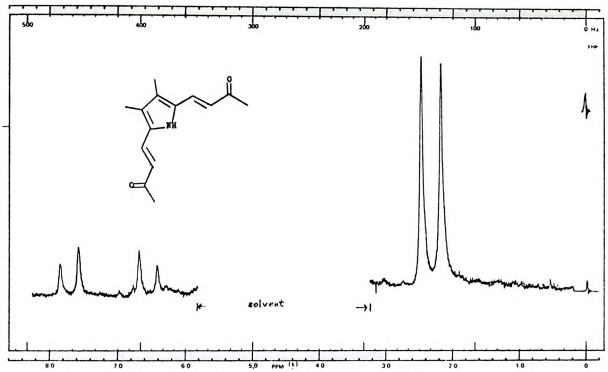


Figure 21. NMR spectrum of 2,5-bis(3-oxobutenyl)-3,4-dimethylpyrrole, 91 ($(CF_3)_2C{=}O{\cdot}1.5\ H_2O$).

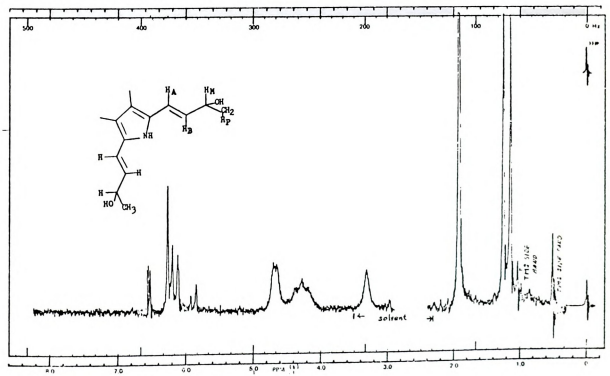


Figure 22. NMR spectrum of 2,5-bis(3-hydroxybutenyl)-3,4-dimethylpyrrol, 92 ($CDCl_3$).

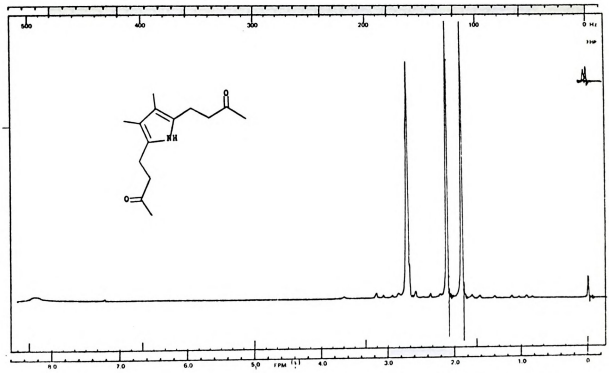


Figure 23. NMR spectrum of 2,5-bis(3-oxobutyl)-3,4-dimethylpyrrole, 95 ($CDCl_3$)

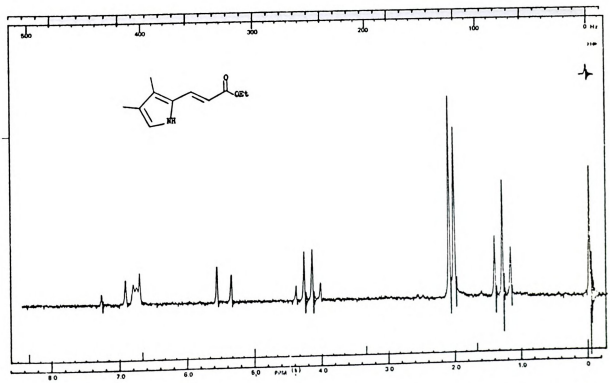


Figure 24. NMR spectrum of ethyl 3-(3,4-dimethylpyrrol-2-yl)-propenoate, 99 ($CDCl_3$).

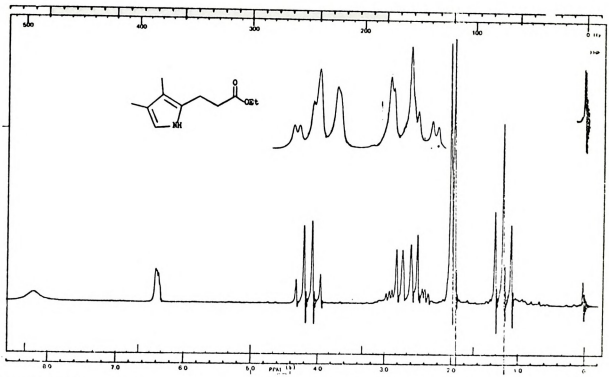


Figure 25. NMR spectrum of ethyl 3-(3,4-dimethylpyrrol-2-yl)-propanoate, 100 ($CDCl_3$). Insert: 100 MHz spectrum of A_2B_2 pattern at δ 2.55.

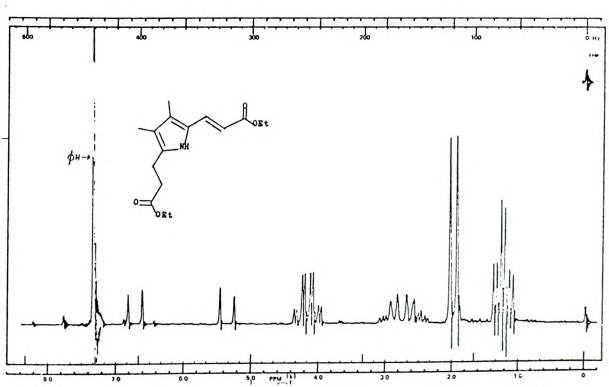


Figure 26. NMR spectrum of ethyl 3-(5-carbethoxyethyl-3,4-dimethylpyrrol-2-yl)propenoate, 101 ($CDCl_3$).

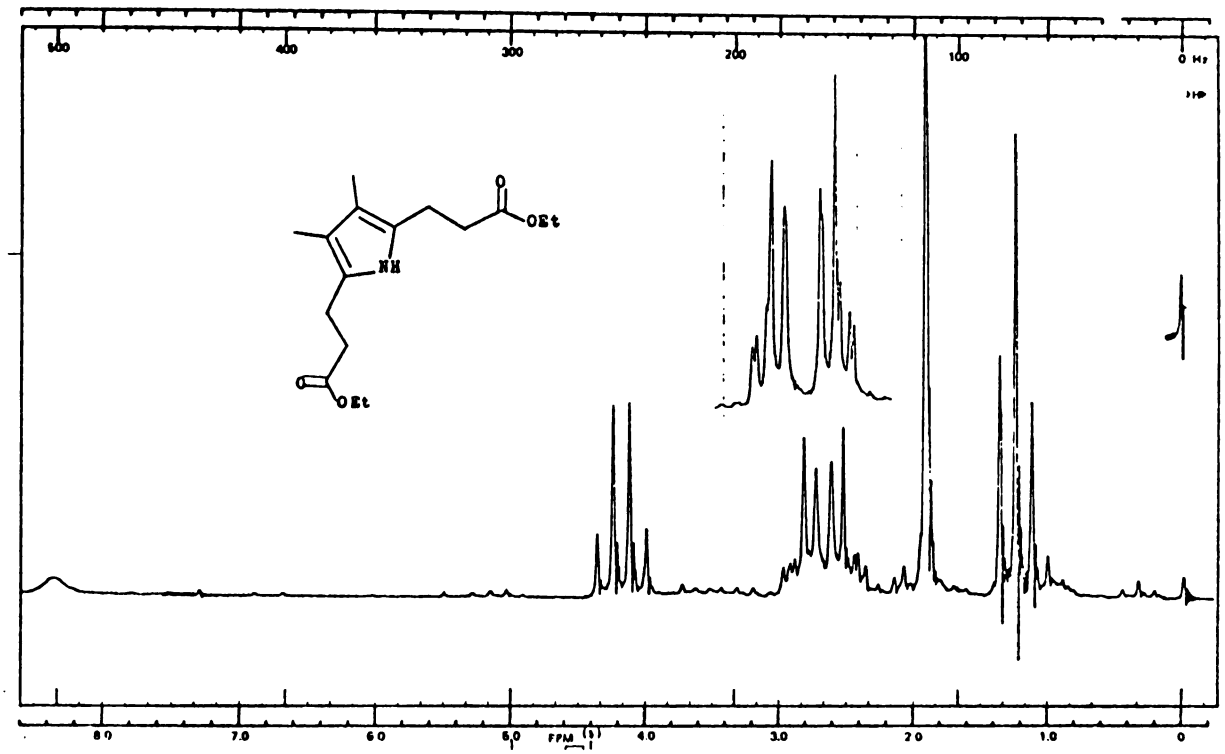


Figure 27. NMR spectrum of diethyl 3,4-dimethylpyrrole-2,5-dipropanoate, 102 ($CDCl_3$). Insert: 100 MHz spectrum of A_2B_2 pattern at δ 2.67.

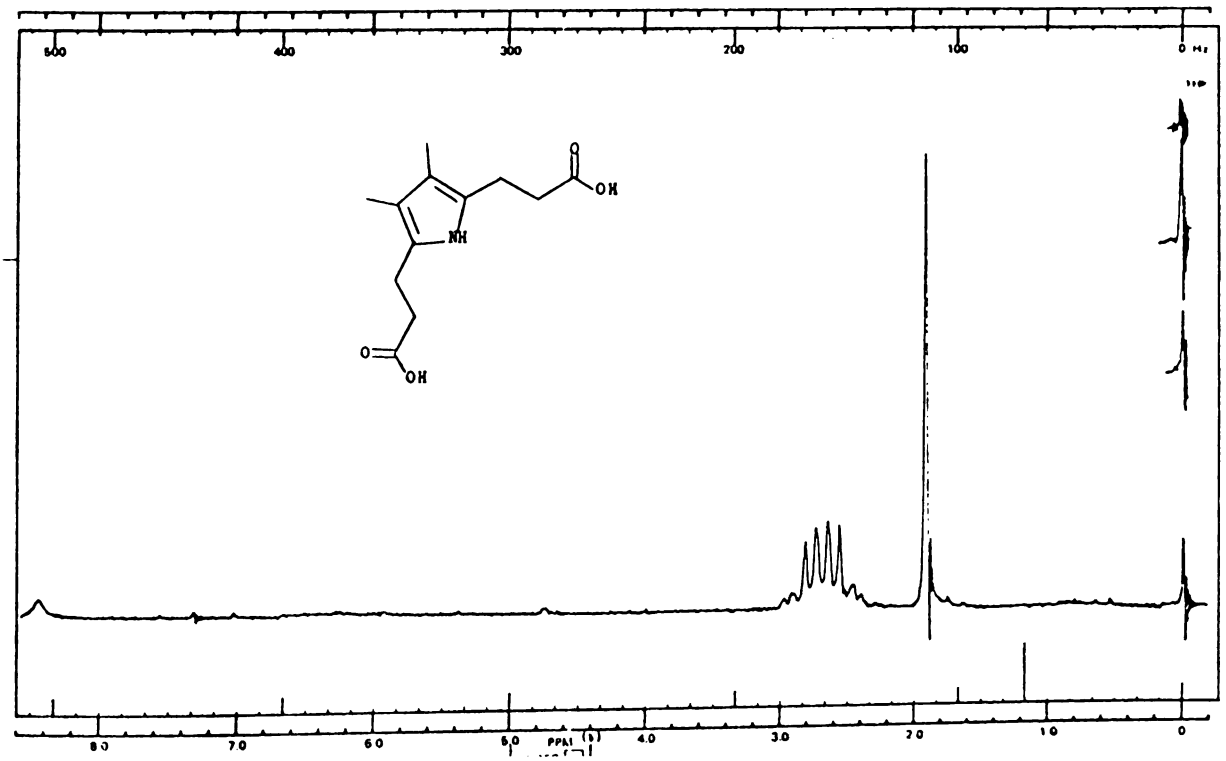


Figure 28. NMR spectrum of 3,4-dimethylpyrrole-2,5-dipropanoic acid, 104 ($CDCl_3$)

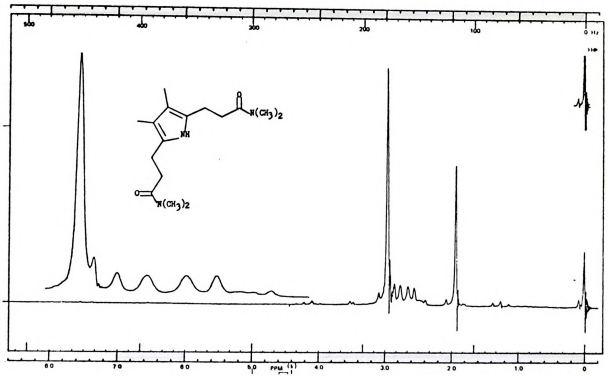


Figure 29. NMR spectrum of N,N,N',N',3,4-hexamethylpyrrole-2,5-dipropanamide, 105 ($CDCl_3$). Insert: 100 **Hz** sweep width of spectrum at δ 2.77.

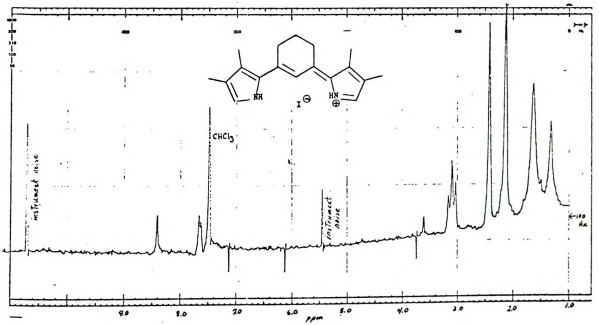


Figure 30. NMR spectrum of 3,4,3',4'-tetramethyl-dipyrryl-(2,2')-hexacyclotrimethine iodide, 115 ($CDCl_3$).

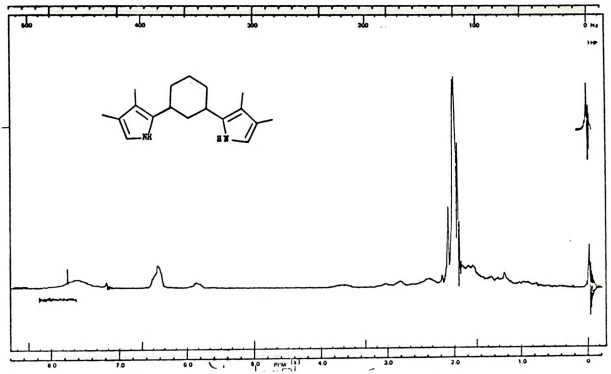


Figure 31. NMR spectrum of 1,3-bis(3,4-dimethylpyrrol-2-yl)-cyclohexane, 116 ($CDCl_3$).

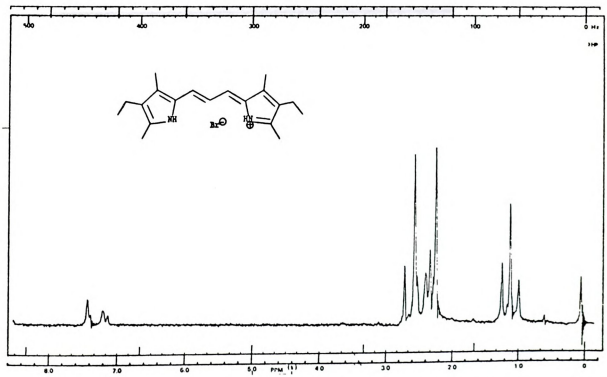


Figure 32. NMR spectrum of bis-2-(3,5-dimethyl-4-ethylpyrrole)-trimethine bromide, 117 ($CDCl_3$).

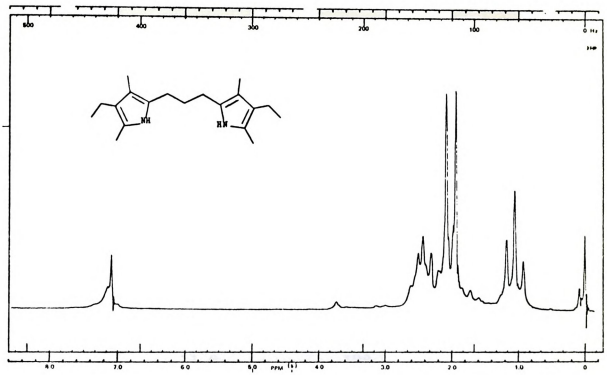


Figure 33. NMR spectrum of 1,3-bis(3,5-dimethyl-4-ethylpyrrol-2-yl)propane, 118 ($CDCl_3$).

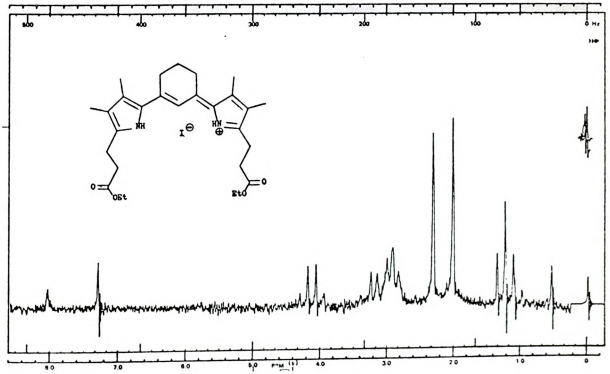


Figure 34. NMR spectrum of 5,5'-bis(carbethoxyethyl)-3,4,3',4'-tetramethyl-dipyrryl-(2,2')-hexacyclotrimethine iodide, 120 ($CDCl_3$).

Table III. Mass spectrum of ethyl 3,4-dimethyl-5-iodo-pyrrole-2-carboxylate, 85.

m/e	Relative Intensity	m/e	Relative Intensity
28	100.0	94	9.1
29	18.7	95	4.5
32	57.1	111	7.1
36	14.2	120	8.1
38	8.9	121	11.6
39	32.1	122	6.2
40	11.6	127	6.2
41	11.6	128	6.2
43	7.1	139	8.1
44	10.7	167	6.2
51	7.1	193	8.9
52	8.9	219	5.4
53	6.2	220	8.1
63	7.1	221	10.7
64	8.9	232	7.1
65	36.6	246	18.7
66	28.6	247	78.6
67	11.6	248	26.8
90	6.2	264	12.5
91	12.5	265	8.9
92	53.6	293	92.9
93	17.8	294	10.7

Table IV. Mass spectrum of ethyl 4,5-dimethyl-3-iodopyrrole-2-carboxylate, 86.

m/e	Relative Intensity	m/e	Relative Intensity
50	17.8	84	12.2
51	27.8	91	18.9
52	24.4	92	64.4
53	16.7	93	36.7
54	10.0	94	26.7
55	17.8	95	11.1
56	22.2	98	15.6
57	11.1	119	8.9
63	13.3	120	20.0
64	13.3	121	27.8
65	42.2	122	33.3
66	34.4	123	8.9
67	35.6	138	8.9
68	7.8	149	8.9
69	16.7	167	18.9
71	8.9	220	10.0
76	10.0	221	14.4
77	18.9	246	11.1
78	13.3	247	81.1
79	11.1	248	30.0
80	8.9	293	100.0
81	8.9	294	13.3

Table V. Mass spectrum of 2,5-bis(3-oxobutenyl)-3,4-dimethylpyrrole, 91.

m/e	Relative Intensity	m/e	Relative Intensity
28	100.0	130	7.1
29	7.9	131	4.8
31	7.9	143	5.6
32	80.1	144	21.4
39	11.9	145	13.5
40	9.5	146	13.5
41	10.3	158	4.8
42	4.8	159	6.3
44	3.9	160	10.3
45	6.3	170	9.5
51	6.3	172	9.5
52	4.8	173	6.3
53	6.3	174	73.0
54	3.9	175	10.3
56	5.6	186	6.3
58	3.2	188	32.5
63	5.6	216	38.1
65	11.1	217	6.3
77	10.3	230	6.3
91	11.9	231	71.4
115	6.3	232	11.9
117	5.6	233	3.2

Table VI. Mass spectrum of 2,5-bis(3-oxobutyl)-3,4-dimethylpyrrole, 95.

m/e	Relative Intensity	m/e	Relative Intensity
43	62.8	132	14.7
51	7.8	133	6.7
53	11.8	134	73.5
55	11.8	135	17.6
65	8.8	144	10.8
77	19.6	145	17.6
79	10.8	146	17.6
91	11.8	147	7.8
93	6.7	148	5.9
106	7.8	158	8.8
107	5.9	159	12.7
108	17.6	160	37.3
117	5.9	161	7.8
118	5.9	176	6.7
119	8.8	177	9.8
120	22.5	178	100.0
121	38.2	179	35.3
122	9.8	192	8.8
130	6.7	217	9.8
131	6.7	235	45.0
		236	9.8

Table VII. Mass spectrum of ethyl 3-(3,4-dimethylpyrrol-2-yl)propenoate, 99.

m/e	Relative Intensity	m/e	Relative Intensity
32	100.0	78	7.1
38	3.9	79	7.1
39	23.0	80	4.8
40	7.9	91	19.9
41	14.3	92	6.3
42	7.9	93	10.3
43	4.8	94	5.6
44	3.9	105	7.1
45	4.8	117	7.9
50	4.8	118	51.5
51	9.5	119	34.9
52	8.9	120	46.0
53	8.9	121	38.1
54	4.8	132	7.1
63	7.9	146	21.4
64	3.9	147	45.2
65	17.5	148	29.3
66	6.3	164	11.1
67	5.6	165	3.9
77	16.6	193	54.8
		194	7.9

Table VIII. Mass spectrum of ethyl 3-(3,4-dimethylpyrrol-2-yl)propanoate, 100.

m/e	Relative Intensity	m/e	Relative Intensity
27	18.2	80	6.1
28	47.9	91	7.0
29	14.6	92	5.1
31	5.6	93	18.2
32	9.6	94	13.6
39	19.7	95	9.6
41	20.7	97	7.1
42	19.7	106	19.9
51	6.1	107	24.7
52	6.1	108	100.0
53	11.6	109	30.8
54	5.6	120	30.8
55	6.1	121	23.7
65	10.1	122	25.3
66	6.1	148	17.2
67	7.6	149	12.1
77	14.6	195	68.7
79	11.1	196	9.0

Table IX. Mass spectrum of ethyl 3-(5-carbethoxyethyl-3,4-dimethylpyrrol-2-yl)propenoate, 101.

m/e	Relative Intensity	m/e	Relative Intensity
28	74.5	161	7.0
29	17.5	172	5.3
31	9.6	173	27.2
32	100.0	174	14.0
40	21.9	178	7.9
44	14.0	202	12.3
69	13.2	206	70.1
77	6.1	207	10.7
91	6.1	218	5.3
117	5.3	219	7.0
130	6.1	220	5.3
131	7.0	221	4.4
132	13.2	247	6.1
134	5.3	248	7.0
144	6.1	264	19.3
146	10.7	293	51.8
160	44.7	294	10.7

Table X. Mass spectrum of diethyl 3,4-dimethylpyrrole-2,5-dipropanoate, 102.

m/e	Relative Intensity	m/e	Relative Intensity
41	5.5	135	4.8
43	4.2	148	3.9
55	4.5	152	3.2
57	3.2	160	3.9
67	2.3	162	44.8
69	2.6	163	7.1
77	4.2	176	3.9
79	3.2	194	3.2
91	4.8	204	3.5
108	3.2	208	100.0
119	2.9	209	14.8
120	4.2	222	3.2
121	2.6	250	4.2
132	4.5	295	25.8
134	25.1	296	5.2

Table XI. Mass spectrum of 3,4,3',4'-tetramethyl-dipyrryl-(2,2')-hexacyclotrimethine iodide, 115.

m/e	Relative Intensity	m/e	Relative Intensity
39	33.3	115	7.8
40	27.7	117	7.1
41	73.8	118	7.1
42	23.4	124	7.1
43	38.3	127	17.0
44	27.7	128	32.6
45	7.1	130	6.4
50	22.7	131	14.9
51	9.2	132	12.0
53	7.1	133	7.1
55	11.3	141	5.0
56	53.9	142	5.0
57	17.0	149	51.8
65	10.6	150	7.1
67	6.4	151	2.8
74	7.8	152	3.5
75	7.1	153	3.5
76	32.6	154	7.1
77	14.2	155	5.0
91	7.1	156	7.1
92	4.3	157	3.5
93	5.0	158	4.3
94	14.2	159	3.5
95	7.1	165	4.3
104	35.5	166	3.5
105	9.9	167	5.0
108	7.1	168	7.1

(continued)

Table XI. Continued.

m/e	Relative Intensity	m/e	Relative Intensity
169	3.5	222	5.0
170	8.5	223	11.3
171	7.1	224	4.3
172	9.9	225	5.7
173	4.3	231	4.3
178	3.5	232	7.8
179	2.8	233	8.5
180	4.3	234	12.0
181	5.0	235	7.8
191	3.5	236	11.3
192	3.5	237	5.7
193	3.5	238	4.3
194	4.3	239	4.3
195	5.7	246	6.4
196	3.5	247	9.2
204	5.0	248	11.3
205	7.8	249	22.5
206	5.7	250	8.5
207	5.0	251	34.8
208	5.0	252	7.1
209	4.3	253	4.3
210	3.5	263	46.1
217	3.5	264	100.0
218	5.0	265	34.0
219	7.1	266	56.7
220	7.1	267	14.2
221	6.4	268	7.1

BIBLIOGRAPHY

BIBLIOGRAPHY

1. M. Faraday, Phil. Trans. Roy. Soc. London, p. 440 (1825).
2. A. S. Couper, Compt. Rend. Acad. Sci., 46, 1107 (1858).
3. F. A. Kekule, Ann., 106, 132 (1858).
4. J. Loschmidt, Ostwalds Klassiker Exakten Wiss., 190, 58-60 (1913).
5. F. A. Kekule, Bull. Soc. Chim. France, 3, 98 (1865).
6. E. Erlenmeyer, Ann., 137, 327 (1866).
7. F. A. Kekule, Ann., 162, 77 (1872).
8. A. Claus, "Theoretische Betrachtungen und deren Anwendung zur Systematik der organische Chemie," p. 208 (O. Hollander, Freiberg, 1867).
9. A. Ladenburg, Ann., 140, 272 (1869).
10. G. Städeler, J. Prakt. Chem., 103, 106 (1868).
11. H. Wichelhaus, Ber., 2, 197 (1869).
12. L. Meyer, "Modern Theorien in der Chemie," 2nd ed., 1872.
13. H. Armstrong, J. Chem. Soc., 51, 258 (1887).
14. A. Baeyer, Ann., 245, 106 (1888).
15. E. Bamberger, Ann., 257, 1, 47-48 (1890).
16. J. Thiele, Ann., 306, 87 (1899).
17. J. Thiele coined the word "conjugation" in Ann., 306, 87 (1899).
18. R. Willstätter and W. van Schmaedel, Ber., 39, 1892 (1905).

19. a) R. Willstätter and E. Waser, Ber., 44, 3423 (1911).

b) R. Willstätter and M. Heidelberger, Ber., 46, 517 (1913).

20. J. W. Armit and R. Robinson, J. Chem. Soc., 127, 1604 (1925).

21. H. Heitler and F. London, Z. Phys., 44, 455 (1927).

22. E. Hückel, Z. Physik, 70, 204 (1931); 72, 310 (1931).

23. H. C. Longuet-Higgins, in Theoretical Organic Chemistry: Kekule Symposium, (London: Butterworth's Scientific Publ., 1959), p. 9.

24. D. P. Craig, Non-Benzenoid Aromatic Compounds, D. Ginsberg, ed., (New York: Interscience Publishers, Inc., 1959), p. 14.

25. Linus Pauling, Perspectives in Organic Chemistry, Alexander R. Todd, ed., (New York: Interscience Publishers, Inc., 1956), p. 6.

26. M. J. S. Dewar and G. J. Gleicher, J. Amer. Chem. Soc., 87, 685 (1965); A. L. H. Chung and M. J. S. Dewar, J. Chem. Phys., 42, 756 (1965).

27. M. J. S. Dewar, J. Amer. Chem. Soc., 74, 3353 (1952).

28. M. J. S. Dewar, The Molecular Orbital Theory of Organic Chemistry, (New York: McGraw-Hill, 1969), p. 98.

29. F. Sondheimer, et al., J. Amer. Chem. Soc., 84, 4307 (1962).

30. M. J. S. Dewar, in Aromaticity Special Publication no. 21 of the Chemical Society, London, pp. 177-198, (1967).

31. H. P. Figeys, Tet., 26, 5225 (1970).

32. L. Pauling, J. Chem. Phys., 4, 673 (1936).

33. F. London, J. Phys. Radium., 8, 397 (1937).

34. E. D. Bergman, J. Horau, A. Pacault, A. Pullman, and B. Pullman, J. Chim. Phys., 49, 474 (1952).

35. J. A. Pople, J. Chem. Phys., 24, 1111 (1956).

36. H. Watanabe, K. Ito, and M. Kubu, J. Amer. Chem. Soc., 82, 3294 (1960); Y. Matsunaga, Bull. Chem. Soc. Japan, 30, 227 (1957).

37. Franz Sondheimer and Reuven Wolovsky, J. Amer. Chem. Soc., 84, 260 (1962).

38. M. Zeruer and M. Gouterman, Theor. Chim. Acta, 4, 44 (1966).

39. S. Masamune and N. Darby, Accts. Chem. Res., 5, 272 (1972).

40. E. Vogel and H. D. Roth, Angew. Chem. Intern. Ed. Eng., 3, 228 (1964).

41. Klaus Grohmann and F. Sondheimer, J. Amer. Chem. Soc., 98, 7119 (1967).

42. R. H. Mitchell and F. Sondheimer, J. Amer. Chem. Soc., 90, 530 (1968).

43. K. Grohmann, P.D. Howes, R. H. Mitchell, A. Monahan, and Franz Sondheimer, J. Org. Chem., 38, 808 (1973).

44. R. Wolovsky and Franz Sondheimer, J. Amer. Chem. Soc., 87, 5720 (1965).

45. F. Sondheimer, R. Wolovsky, P. J. Garratt, and I. C. Calder, J. Amer. Chem. Soc., 88, 2610 (1966).

46. G. M. Pilling and Franz Sondheimer, J. Amer. Chem. Soc., 93, 1970 (1971).

47. Franz Sondheimer and Y. Gaoni, J. Amer. Chem. Soc., 82, 5766 (1960).

48. Y. Gaoni and F. Sondheimer, Proc. Chem. Soc., 1964, 299; Y. Gaoni, A. Melera, Franz Sondheimer, and R. Wolovsky, Proc. Chem. Soc., 1964, 397.

49. Franz Sondheimer and Y. Gaoni, J. Amer. Chem. Soc., 82, 5765 (1960).

50. L. M. Jackman, F. Sondheimer, Y. Amiel, D. A. Ben-Efraim, Y. Gaoni, R. Wolovsky, and A. A. Bother-By, J. Amer. Chem. Soc., 84, 4307 (1962).

51. F. Sondheimer, Y. Gaoni, L. M. Jackman, N. A. Bailey, and R. Mason, J. Amer. Chem. Soc., 84, 4595 (1962).

52. J. Mayer and Franz Sondheimer, J. Amer. Chem. Soc., 88, 602 (1966).

53. Franz Sondheimer in Aromaticity Special Publication no. 21 of the Chemical Society, London, pp.75-108 (1967).

54. I. C. Calder, Y. Gaoni, and F. Sondheimer, J. Amer. Chem. Soc., 90, 4946 (1968).

55. I. C. Calder, Y. Gaoni, P. J. Garratt, and F. Sondheimer, J. Amer. Chem. Soc., 90, 4954 (1968).

56. Franz Sondheimer and R. Wolovsky, Tet. Letters, 1959, 3.

57. Franz Sondheimer and D. A. Ben-Efraim, J. Amer. Chem. Soc., 85, 52 (1963).

58. R. Wolovsky, J. Amer. Chem. Soc., 87, 3638 (1965).

59. W. H. Okamura, Franz Sondheimer, J. Amer. Chem. Soc., 89, 5991 (1967).

60. B. W. Metcalf, F. Sondheimer, J. Amer. Chem. Soc., 93, 6675 (1971).

61. Franz Sondheimer and Y. Gaoni, J. Amer. Chem. Soc., 84, 3520 (1962).

62. R. M. McQuilkin, B. W. Metcalf, and Franz Sondheimer, Chem. Comm., 1971, 338.

63. R. M. McQuilkin and Franz Sondheimer, J. Amer. Chem. Soc., 92, 6341 (1970).

64. Franz Sondheimer and R. Wolovsky, J. Amer. Chem. Soc., 81, 4755 (1959).

65. K. Stöckel and Franz Sondheimer, J. Chem. Soc. - Perkin I, 1972, 355.

66. Franz Sondheimer and R. Wolovsky, J. Amer. Chem. Soc., 84, 260 (1962).

67. I. C. Calder and F. Sondheimer, Chem. Comm., 1966, 904

68. R. M. McQuilkin, P. J. Garratt, and F. Sondheimer, J. Amer. Chem. Soc., 92, 6682 (1970).

69. B. W. Metcalf and F. Sondheimer, J. Amer. Chem. Soc., 93, 5271 (1971).

70. C. C. Leznoff and Franz Sondheimer, J. Amer. Chem. Soc., 89, 4247 (1967).

71. Franz Sondheimer, R. Wolovsky, and D. A. Ben-Efraim, J. Amer. Chem. Soc., 83, 1686 (1961).

72. Franz Sondheimer and Arnon Shani, J. Amer. Chem. Soc., 86, 3168 (1964).

73. E. Vogel, W. Pretzer, and W. A. Böll, Tet. Letters, 1965, 3613.

74. P. J. Garratt, A. B. Holmes, F. Sondheimer, and K. P. C. Vollhardt, Chem. Comm., 1971, 947.

75. E. Vogel, M. Biskup, A. Vogel, and H. Günther, Angew. Chem. Intern. Ed. Eng., 5, 734 (1966).

76. H. Neunhoeffer and Lothar Matitschke, Tet. Letters, 1970, 655.

77. G. M. Badger, J. A. Elix, G. E. Lewis, U. P. Singh, and T. M. Spotswood, Chem. Comm., 1965, 269.

78. G. M. Badger, J. A. Elix, and G. E. Lewis, Aust. J. Chem., 18, 70 (1965).

79. G. M. Badger, G. E. Lewis, and U. P. Singh, Aust. J. Chem., 19, 257 (1966).

80. G. M. Badger, G. E. Lewis, U. P. Singh, and T. M. Spotswood, Chem. Comm., 1965, 492.

81. M. J. Broadhurst, R. Grigg, and A. W. Johnson, J. Chem. Soc. - C., 1971, 3681.

82. P. Bamfield, R. Grigg, A. W. Johnson, R. W. Kenyon, J. Chem. Soc. - C., 1968, 1259.

83. M. J. Broadhurst, R. Grigg, and A. W. Johnson, J. Chem. Soc. - Perkin I., 1972, 1124.

84. A. W. Johnson and I. T. Kay, J. Chem. Soc., 1965, 1620.

85. J. A. Elix and M. V. Sargent, J. Amer. Chem. Soc., 90, 1631 (1968).

86. M. J. Broadhurst, R. Grigg, and A. W. Johnson, J. Chem. Soc. - Perkin I., 1972, 2111.

87. T. M. Cresp and M. V. Sargent, Chem. Comm., 1971, 1458.

88. J. A. Elix, Chem. Comm., 1968, 343.

89. G. M. Badger, R. A. Jones, and R. L. Laslett, Aust. J. Chem., 17, 1157 (1964).

90. G. M. Badger, Aust. J. Chem., 18, 1977 (1965).

91. A. Treibs and H. G. Kolm, Ann., 614, 176 (1958).

92. R. Grigg, A. W. Johnson, and J. W. F. Walsey, J. Chem. Soc., 1963, 359.

93. R. Grigg, J. Chem. Soc., 1965, 5149.

94. G. M. Badger, R. L. N. Harris, and R. A. Jones, Aust. J. Chem., 17, 1022 (1964).

95. A. W. Johnson, J. Chem. Soc., 1947, 1629.

96. A. Treibs, Karl-Heinz Michel, Ann., 589, 163 (1954).

97. I. D. Webb and G. T. Borcherdt, J. Amer. Chem. Soc., 73, 752 (1951).

98. A. Ermili, A. J. Castro, and P. A. Westfall, J. Org. Chem., 30, 339 (1965).

99. R. M. Silverstein, E. E. Ryskiewicz, C. Willard, R. C. Koehler, J. Org. Chem., 20, 668 (1954).

100. A. H. Cook and J. R. Majer, J. Chem. Soc., 1944, 482.

101. P. Bamfield, A. W. Johnson, and J. Leng, J. Chem. Soc., 1965, 7001.

102. E. LeGoff, unpublished work.

103. A. Treibs and E. Herrmann, Ann., 589, 207 (1954).

104. P. J. Crook, A. H. Jackson, and G. W. Kenner, J. Chem. Soc. - C., 1971, 474.