THE PREPARATION AND PROPERTIES OF SOME PYRROLE ALDEHYDES

H. NAGY, A.R.I.C.

THE PREPARATION AND PROPERTIES OF SOME PYRROLE ALDEHYDES

A Thesis

by

H. Nagy, A.R.I.C.

Submitted in partial fulfillment of the requirements
for the degree of Master of Science.

November, 1970

Memorial University
of Newfoundland

ACKNOWLEDGEMENTS

The author wishes to express his sincere thanks to his Research Director, Dr. H. J. Anderson, for the guidance and encouragement he has given throughout the duration of this work. He would also like to thank Dr. C. E. Loader for the many helpful discussions and Dr. B. Gregory for obtaining the mass spectra. Financial assistance from Memorial University and the National Research Council are gratefully acknowledged.

ABSTRACT

The anomalous physical and chemical properties of 2-pyrrolecarbaldehyde are discussed. The preparation of 3-pyrrolecarbaldehyde was carried out on an increased scale, and the properties of this compound were investigated, especially in comparison to 2-pyrrolecarbaldehyde. The chemical properties of the two compounds were similar. 1-Methyl-3-pyrrolecarbaldehyde was prepared; in some reactions it resembled 3-pyrrolecarbaldehyde. The Wolff-Kishner reductions of the aldehydes gave good yields of the corresponding methyl compounds. Reactions were attempted using a protecting acetal group on some aldehydes, but these failed as the acetals were unstable.

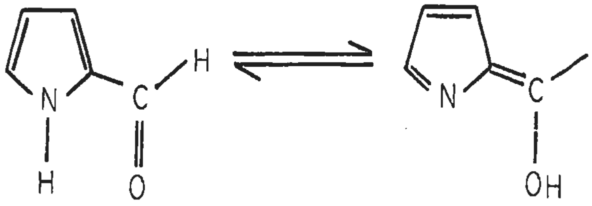
The ultraviolet spectra of 2- and 3-pyrrolecarbaldehydes obeyed the Beer-Lambert law and there was no evidence of association. The nuclear magnetic spectra, contrary to expectations, did not show long-range spin coupling to the aldehydic proton. The mass spectra of some new compounds are recorded. A suggested fragmentation pattern is given for 2-pyrrolecarbaldehyde, 3-pyrrolecarbaldehyde, 1-methylpyrrole-2-carbaldehyde and 1-methylpyrrole-3-carbaldehyde.

INDEX

INTRODUCTION

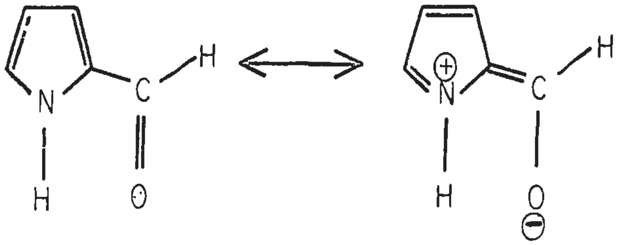
2-Pyrrolecarbaldehyde was prepared as early as 1900 by Bamberger and Djierdjian,[1] using the Reimer-Tiemann reaction, which gave a 13% yield. This method was improved,[2] and new methods[3-10] were also devised. The Gattermann reaction[7] gave excellent yields of α-formylpyrroles,[8] (or β-formylpyrroles, if the α-positions were blocked), but the reaction gave dyestuffs with unsubstituted pyrrole. A significant improvement was made in 1955 by Silverstein, Ryskiewicz and Willard,[9,10] who obtained a 79% yield of 2-pyrrolecarbaldehyde using the Vilsmeyer reaction.

2-Pyrrolecarbaldehyde was found to be unusual in its physical and chemical properties.[11-13] Angeli noted in 1909 that some aldehydes, including 2-pyrrolecarbaldehyde, did not undergo a reaction with "dioxyammonia", $NH(OH)_2$, to give hydroxamic acids,[11] and thus did not behave as a "true" aldehyde. This reference has been quoted more recently,[12] even though Angeli's hypothesis was dismissed by Oddo,[14] as there was no evidence for the existence of "dioxyammonia". Although fortuitously, Angeli was nevertheless correct, and 2-pyrrolecarbaldehyde fails to undergo many reactions typical of aldehydes. It forms such derivatives as the oxime, phenylhydrazone, and a bisulphite addition compound. It is oxidized by permanganate to the acid. The typical aldehyde tests with Schiff's and Fehling's solution are negative with 2-pyrrolecarbaldehyde, which also fails to undergo the Cannizarro, crossed-Cannizzaro, Perkin and benzoin condensations.[10,12] In its physical properties, it has a high molecular weight, indicating association, high solubility in polar solvents, and low infrared carbonyl frequency. Several explanations have been advanced to account for this behaviour, the first suggesting the predominant existence of the hydroxymethylene form, II:[11,13]



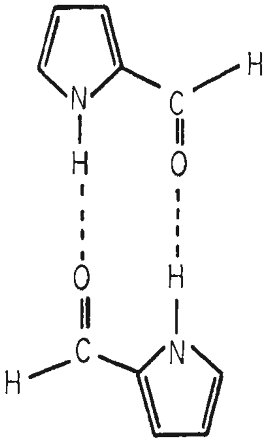
I II

Support for this hypothesis was given by the supposed isolation of the sodium salt of II, and by spectral evidence.[15] However, both of these results were erroneous.[16]



I III

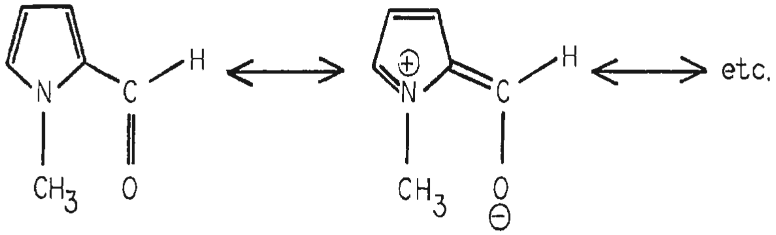
The contribution of III to the resonance hybrid has been suggested[17,18] to account for the anomalous physical and chemical properties. There is also a possibility, that a hydrogen-bonded dimer of the type IV may be formed:



IV

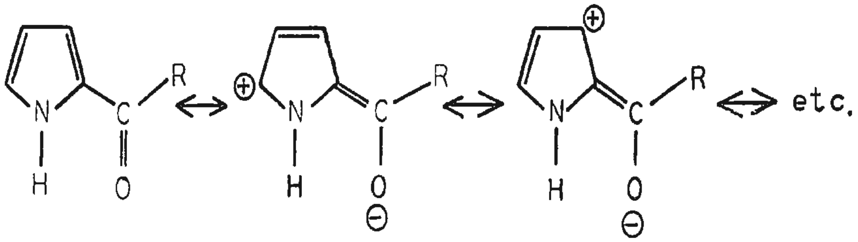
Such a dimer could also account for the unusual chemical properties and the high molecular weight. Evidence for association has been published and was found to be solvent,[19-22] concentration[12] and temperature[23] dependent. Methods used for investigating association include cryoscopic and ebullioscopic techniques,[19,23] dipole moment measurements[21] and spectroscopy.[12,24-31] Jones[31] envisages a dimer, IV, which exists in this state in the liquid phase, in concentrated solutions and perhaps also in the solid state. The monomeric species would only exist in very dilute solutions, below cca. 10^{-4} M.[31-34] Since 1-methyl-2-pyrrolecarbaldehyde cannot form a hydrogen-bonded dimer of the type IV, it should show no association.

This was borne out experimentally.[19] The existence of the hydroxymethylene form, II, is also precluded. Yet many of the anomalous chemical properties of 2-pyrrolecarbaldehyde are also common to 1-methyl-2-pyrrolecarbaldehyde. Neither forms a cyanohydrin, nor do they undergo the Cannizzaro or Perkin reactions or benzoin condensation, although the latter undergoes the crossed-Cannizzaro reaction.[10] Both compounds condense with compounds containing active methylene groups, such as diethyl malonate,[35,36] ethyl cyanoacetate or malononitrile,[35] but the 1-methyl compound gives generally better yields. This has been interpreted as supporting the greater resemblance of this compound to a true aldehyde.[12] As 1-substituted pyrrole compounds are generally more stable under a variety of reaction conditions, not necessarily with the aldehyde as the functional group, the higher yields may have been simply due to the greater stability of the pyrrole ring. In the infrared spectrum, the carbonyl absorptions of the two compounds are similar: in carbon tetrachloride solution these are at 1665 cm^{-1} for the 1-H and 1672 cm^{-1} [12] for the 1-methyl compound. Both of these absorptions are unusually low. Raman spectroscopy[9] and reduction potential measurements[37] also show similarity between the two aldehydes. Thus the anomalies of chemical and physical behaviour cannot be completely explained by either the hydroxymethylene structure, II, or by the existence of the dimer, IV. The resonance hybrid of the type I - III remains feasible for 1-methyl-2-pyrrolecarbaldehyde and could explain its anomalous properties:



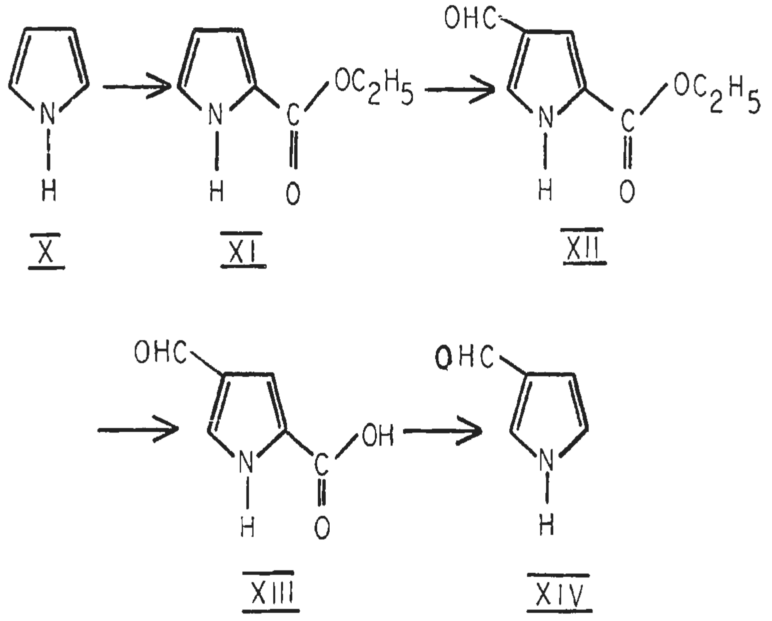
V VI

Pyrrole substitution occurs preferentially in the 2-position. Various methods have been used to obtain 3-substituted pyrroles, such as the use of 1-substituents[38,39] and 2-substituents[40-44] as directing groups, and ring closure.[45] With electron withdrawing 2-substituents, such as - COR, the resonance hybrid may be written as:

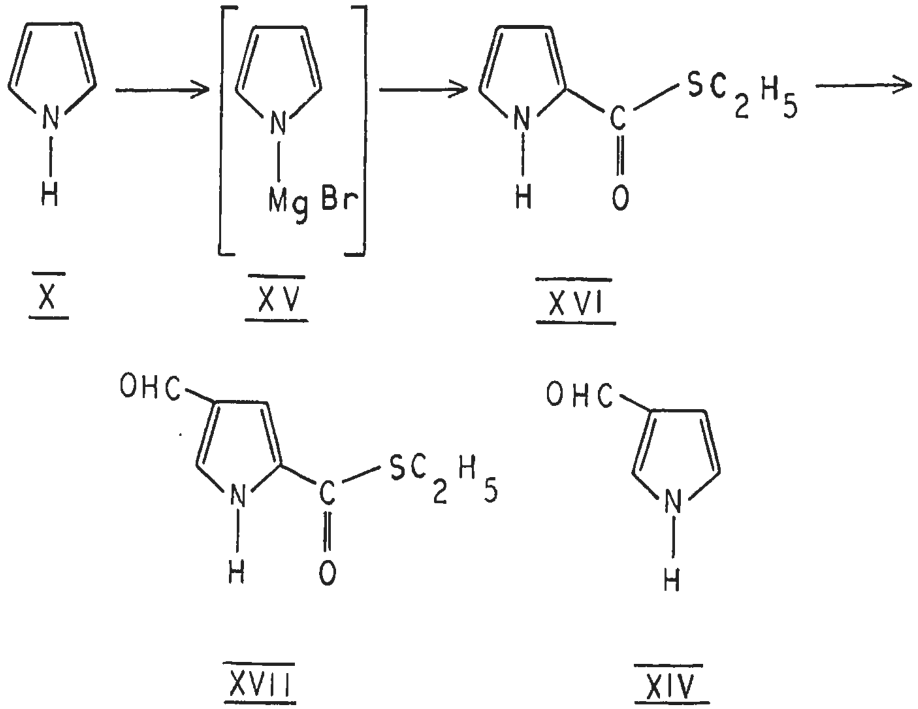


VII VIII IX

Such a substituent then deactivates the 3- and 5- positions towards electrophilic attack, relative to unsubstituted pyrrole. The degree of deactivation depends on the importance of the contributors VIII and IX. Usually substitution occurs at both the 4 and 5 positions, the relative amounts depend on the 2-substituent and other factors, e.g. the selectivity of the electrophile. An important consideration when choosing a directing group is the ease of subsequent removal of that group. 3-Pyrrolecarbaldehyde was first prepared in 1965,[45] using the following reaction sequence:



The overall yield was 0.05% from pyrrole. In the formylation stage, a 51% yield of the 5-formyl compound was obtained. The decarboxylation step, during the removal of the directing group, gave a poor yield. A new synthesis for 3-acylpyrroles was introduced by Loader and Anderson[46], who used a new directing group, ethyl thiolcarboxylate. This group was superior to ethyl carboxylate in both the directive properties and the ease of removal. 3-Pyrrolecarbaldehyde was prepared by the following sequence of reactions:



X

XV

XVI

XVII

XIV

The overall yield from pyrrole was reported to be 15.7%. This method was used to prepare the 3-pyrrolecarbaldehyde used in this work, the object of which was to scale up this reaction and to investigate the properties of 3-pyrrolecarbaldehyde, especially in comparison to 2-pyrrolecarbaldehyde, 1-methyl-2-pyrrolecarbaldehyde and 1-methyl-3-pyrrolecarbaldehyde.

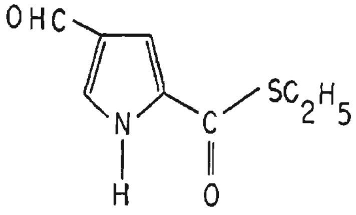
DISCUSSION

The preparation of 3-pyrrolecarbaldehyde

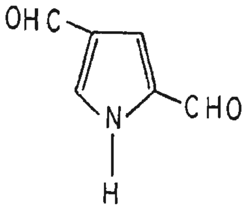
The method outlined in the introduction has been reported,[46] but increasing the reaction scale made modifications necessary.

In the preparation of ethyl 4-formyl-2-pyrrolethiolcarboxylate, it was found to be essential to use fractionally distilled dichloromethyl methyl ether. The method of isolating the ethyl 4-formyl-2-pyrrolethiolcarboxylate from the crude product was changed, Soxhlet extraction with petroleum ether gave an improved yield.

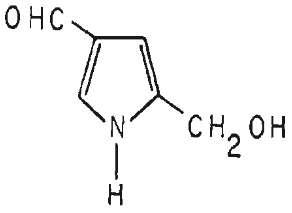
Difficulties were experienced with the removal of the thiolcarboxylate group using W5 Raney nickel. When the catalyst was not active enough, or insufficient amounts were used, apart from the starting material, XVII, 2,4-pyrroledicarbaldehyde, XVIII and 2-hydroxymethyl-4-formylpyrrole, XIX, were present, as well as 3-pyrrolecarbaldehyde, XIV. On the other hand, too much or too active catalyst reduced 3-pyrrolecarbaldehyde to pyrrole, X. Thus the following array of compounds could be expected:



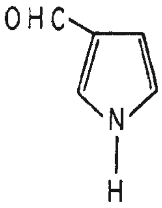
XVII



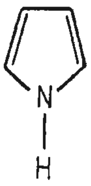
XVIII



XIX



XIV



X

Before the problems with the activity of the catalyst could be resolved, a method for following the reaction was required. Thin layer chromatography was attempted with a variety of substrates: "Woelm" Silica Gel H, Silica Gel G and Aluminium Oxide followed by iodine tank development, and "Woelm" Silica Gel GF-254 and Aluminium Oxide GF-254 for the ultraviolet fluorescence technique. A wide range of eluents was used. Unfortunately, in the iodine tank process, the colour of XIV was found to be much more intense, than the colour of XVII for similar concentrations. The use of ultraviolet fluorescence did not suffer from this disadvantage, but other difficulties arose - the R_f values of some components were very close and appeared to be concentration dependent. Thus thin layer chromatography was not a satisfactory method. Gas-liquid chromatography was also attempted using a "Carbowax" column, but the retention times were too long. The most satisfactory method was found to be taking aliquots and, after careful filtration and evaporation, determining the nuclear magnetic resonance spectrum in deuterochloroform. This gave a semi-quantitative assay of the compounds present. In those cases, where completion of the reaction was not achieved, more catalyst was added.

There is no standard method for estimating the activity of Raney nickel. The method for the preparation of W5 Raney nickel has been described,[47] but when different batches were prepared, their activity varied. The desulphurisation reaction required a large amount of catalyst, (8 g Raney nickel to 1 g XIX). Since the apparatus specified for this preparation was capable of handling only 50 - 60 g of catalyst, it usually meant, that by the time the catalyst was "standardized" by the desulphurisation reactions, there was little left of that batch of catalyst. Attempts were made to reduce the amount of catalyst necessary for this reaction. Three variables were altered: the time of deactivation of the catalyst in acetone; the time of reaction; and reaction temperature. It was found, that the most consistent results were obtained with the original method. The apparatus for the preparation of W5 Raney nickel was modified, to allow preparation of 200 - 240 g batches.

The isolation of 3-pyrrolecarbaldehyde was achieved either by chromatography,[46] or by distillation in vacuo. For larger scale preparations the latter was more convenient.

The Wolff-Kishner reaction on ethyl 4-formyl-2-pyrrolethiolcarboxylate (discussed later), gave 3-methylpyrrole in good yield in a single step. It was hoped, that under similar reaction conditions, but without any hydrazine present, hydrolysis followed by decarboxylation would occur. This alternative route to 3-pyrrolecarbaldehyde was unsuccessful, as tars were obtained. Reducing the reaction temperature to 20° prevented the hydrolysis of ethyl 4-formyl-2-pyrrolethiolcarboxylate.

Preparation of 1-methyl-3-pyrrolecarbaldehyde

When 2-pyrrolecarbaldehyde was prepared by the method of Silverstein, et al.,[9] the residue contained some 3-pyrrolecarbaldehyde,* XVI. The yield of XVI by this reaction was 0.4%, an eight-fold improvement on the method of Khan, et al..[45] Following a similar preparation of 1-methyl-2-pyrrolecarbaldehyde, the mother liquor was examined for the presence of 1-methyl-3-pyrrolecarbaldehyde. This component was isolated in a yield of 5.8%.

---

* The presence of this component in the residue was indicated by Dr. Loader in a personal communication.

Properties of the directing groups

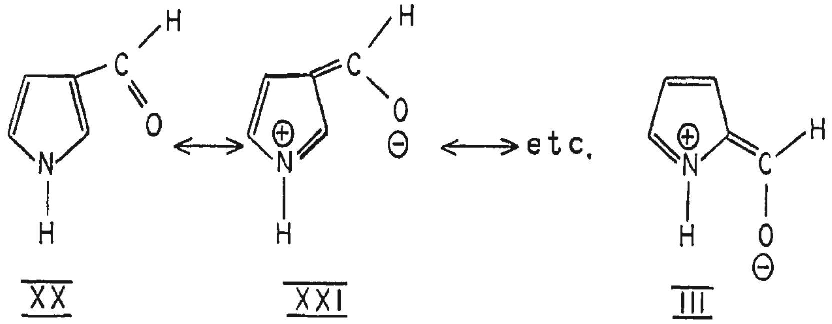
The methyl carboxylate and ethyl thiolcarboxylate groups in the 2-position of pyrrole have similar directing properties, leading to increased attack by electrophiles in the 4-position. Under different conditions, both groups have been used in the preparation of 3-pyrrolecarbaldehyde.[45,46] The behaviour of these groups in identical reactions was investigated. Benzoyl chloride, under Friedel-Crafts conditions, gave methyl 4-benzoyl-2-pyrrolecarboxylate (82%) and ethyl 4-benzoyl-2-pyrrolethiolcarboxylate (48%) respectively. A similar reaction with benzyl halides was expected to provide a route to 3-benzylpyrrole, but the reaction failed. 3-Benzylpyrrole was obtained by the Wolff-Kishner reaction on methyl 4-benzoyl-2-pyrrolecarboxylate. (Following the success of this reaction, it was applied to ethyl 4-formyl-2-pyrrolethiolcarboxylate, which gave a good yield of 3-methylpyrrole in a single step).

The effect of the aldehyde group in the 2-position of the pyrrole ring was similar to the two substituents above. 1-Methyl-2-pyrrolecarbaldehyde reacted with acetyl chloride under Friedel-Crafts conditions and gave 1-methyl-4-acetyl-2-pyrrolecarbaldehyde (83%).*

* Formylation of 1-methyl-2-pyrrolecarbaldehyde using dichloromethyl methyl ether, under Friedel-Crafts conditions, gave 1-methyl-2,4-pyrroledicarbaldehyde.

The chemical properties of 3-pyrrolecarbaldehyde

A resonance hybrid of the type I, III proposed for 2-pyrrolecarbaldehyde is also possible for 3-pyrrolecarbaldehyde:



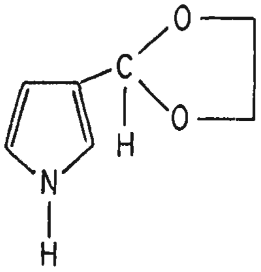
The contribution of XXI to the resonance hybrid is expected to be less, than the contribution of the corresponding canonical form, III, to the resonance hybrid of 2-pyrrolecarbaldehyde, because XXI requires a larger charge separation than III. For this reason, it was expected that 3-pyrrolecarbaldehyde would be less anomalous in its reactions, than 2-pyrrolecarboxaldehyde.

The standard tests for an aldehyde were carried out. 3-Pyrrolecarbaldehyde gave a negative Schiff's test. In the Tollens test a silver mirror was formed and a good yield of 3-pyrrolecarboxylic acid was isolated from the reaction. 2-Pyrrolecarbaldehyde has been reported as giving a negative Tollens test.[12] This appeared incongruous as a method describing the preparation of 2-pyrrolecarboxylic acid has also been published,[48] using silver oxide on the aldehyde. This test gave a good silver mirror, and

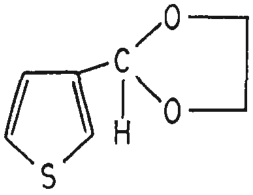
2-pyrrolecarboxylic acid was isolated from the reaction. In contrast, neither 1-methyl-2-pyrrolecarbaldehyde, nor 1-methyl-3-pyrrolecarbaldehyde gave a positive Tollens test.

3-Pyrrolecarbaldehyde also gave standard derivatives, such as the oxime and the 2,4-dinitrophenylhydrazone. The direct formation of the ethylene acetal, XXII, was not successful. This may have been due to either the decomposition of 3-pyrrolecarbaldehyde in the presence of the acid catalyst, or to the reactivity of the acetal, or both. 2-Pyrrolecarbaldehyde also failed to give an acetal directly with a variety of acid catalysts. Both aldehydes, when in solution with acid catalysts but no glycol, darkened rapidly and produced a tar in normal reaction times. Other π-excessive heterocyclic aldehydes form acetals directly: 3-thiophenecarbaldehyde[49] and 3-furancarbaldehyde[50] both give good yields of the corresponding ethylene acetals, XXIII, XXIV. 1-Methyl-2-pyrrolecarbaldehyde and ethyl 4-formyl-2-pyrrolethiolcarboxylate formed the ethylene acetal directly. The latter, XXV, was reacted with Raney nickel, which removed the thiolcarboxylate group, leaving the 3-(1,3-dioxolan-2-yl)-pyrrole XXII.*

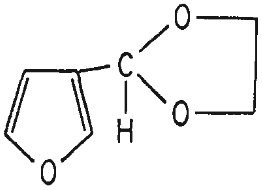
* The preparation of 3-pyrrolecarbaldehyde diethyl acetal was unsuccessful by this method.



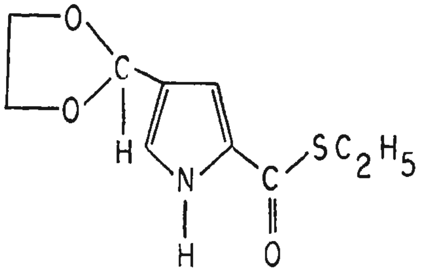
XXII



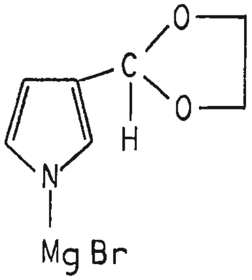
XXIII



XXIV



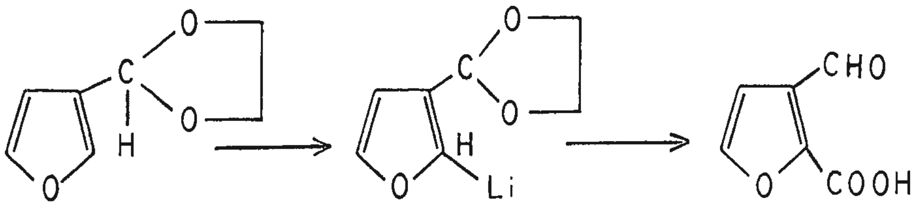
XXV



XXVI

The ethylene acetals of ethyl 4-formyl-2-pyrrolethiolcarboxylate and of 3-pyrrolecarbaldehyde were unstable to air and light. Dilute acid at pH 6 was capable of hydrolyzing both compounds to the aldehydes.*

3-(1,3-Dioxolan-2-yl)-furan, XXIV, has been used to obtain 2,3-disubstituted furans by the following reaction:[50b]

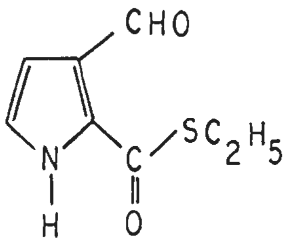


XXIV

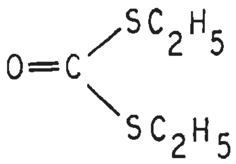
* The diethylene acetal of methyl 4-acetyl-2-pyrrolecarboxylate has also been described as "tres fragile".[50a]

3-(1,3-Dioxolan-2-yl)-thiophene also undergoes a similar sequence of reactions.[49] It was hoped that a comparable reaction scheme could be applied to 3-(1,3-dioxolan-2-yl)-pyrrole. With 1-H pyrroles, n-butyllithium would probably give the 1-carboxylic acid, when the lithiopyrrole reacts with carbon dioxide. The pyrrole Grignard reagent, formed by the reaction of ethylmagnesium bromide and the acetal, was expected to give the 3-formyl-2-pyrrolecarboxylic acid with carbon dioxide. This reaction was unsuccessful.

An attempt was made to prepare 3-formyl-2-pyrrolethiolcarboxylate, XXVII, by the action of S-diethyl dithiocarbonate, XXVIII, on the Grignard reagent, XXVI.



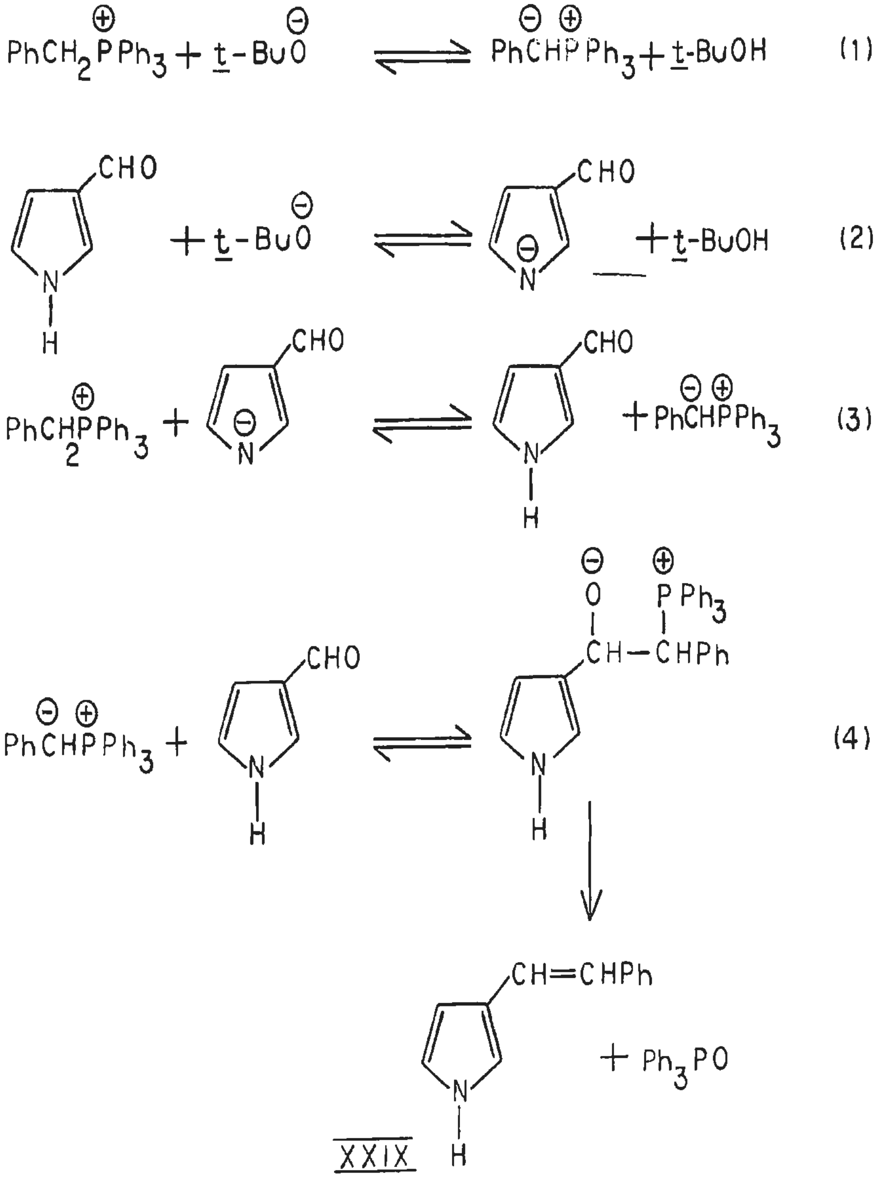
XXVII



XXVIII

With the view of obtaining 3,4-pyrroledicarbaldehyde by the formylation of XXVII followed by the removal of the thiolcarboxylate group, the preparation of XXVII was attempted, but was unsuccessful. The formylation of ethyl 4-(1,3-dioxolan-2-yl)-pyrrolethiolcarboxylate, XXV, using the Vilsmeyer reaction, failed. The evolution of hydrochloric acid may have hydrolyzed the acetal.

The Wittig reaction with triphenylbenzylphosphonium chloride gave the expected product with 3-pyrrolecarbaldehyde and 1-methyl-3-pyrrolecarbaldehyde. Potassium tertiary-butoxide was used as the base, but the yield from the 1-H compound was very poor and was not repeatable. The following equilibria may exist (cf. ref. 51):



To obtain the styrylpyrrole, XXIX, the equilibria (3) and (4) must lie to the right. In the case of the 1-methyl compound, the equilibria (2) and (3) do not exist and better yields are obtained. This parallels the behaviour of 1-H and 1-methyl-2-pyrrolecarbaldehydes.[51] The use of sodium hydride instead of sodium ethoxide eliminated the side reactions and gave good yields. However, in the Wittig reaction of 3-pyrrolecarbaldehyde, the replacement of potassium tertiary-butoxide by sodium hydride did not improve the yield.

The condensation reaction of 3-pyrrolecarbaldehyde with diethyl malonate gave oils. Chromatographic methods and different solvent combinations failed to crystallize the oil. It was only after several months' standing that the oil solidified. This reaction was repeated on 2-pyrrolecarbaldehyde, when an oil was obtained. The nuclear magnetic spectrum indicated the expected material, but the oil did not crystallize. (Lit. m.p.:[35] 132°)

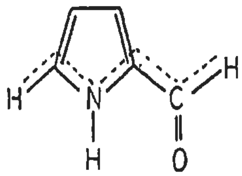
The benzoin condensation did not take place with 3-pyrrolecarbaldehyde. The Perkin reaction was attempted with 2-pyrrolecarbaldehyde, but it failed, confirming earlier results. 3-Pyrrolecarbaldehyde did not undergo this reaction.

The reduction of 3-pyrrolecarbaldehyde was attempted with lithium aluminium hydride. The reaction was unsuccessful. The Wolff-Kishner reaction on 3-pyrrolecarbaldehyde gave a good yield of 3-methylpyrrole. This reaction was also attempted on ethyl 4-formyl-2-pyrrolethiolcarboxylate, when 3-methylpyrrole was formed directly. This synthesis appears to be the most satisfactory method for the preparation of 3-methylpyrrole.[72-74]

Physical properties

Nuclear magnetic resonance (NMR) spectra

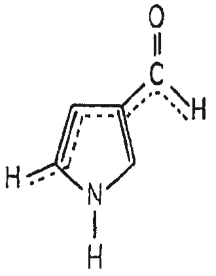
In the case of 2-pyrrolecarbaldehyde, coupling occurs between the aldehydic proton and the 5-hydrogen.[45,52] This long-range coupling is claimed to be stereospecific, with the aldehyde group in the following conformation:



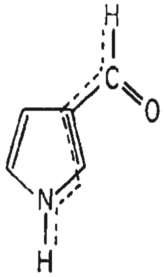
I

The "straightest zig-zag path" rule[53-55] is observed. Similar coupling occurs in 1-methyl-2-pyrrolecarbaldehyde. The aldehydic proton in liquid furfural also couples with the 5-hydrogen,[53,56,57] but in addition, stereospecific long-range spin coupling to the 4-hydrogen is observed,[58,59] which is solvent dependent.[59] This observation contradicts the "zig-zag" rule, therefore conclusions about conformation based on long-range coupling should be made with caution.

In 3-furancarbaldehyde and 3-thiophenecarbaldehyde coupling to the 5-hydrogen occurs,[57,60] and the latter also shows coupling of the aldehydic proton to the 4-hydrogen.[59]
In 3-pyrrolecarbaldehyde, long-range splitting was expected between the aldehydic proton and the 5-proton in the conformation XXX, or between the aldehydic proton and the 1-proton in the conformation XXXI, observing the "zig-zag" rule in both cases:



XXX



XXXI

In 1-methyl-3-pyrrolecarbaldehyde, coupling analogous to XXX was expected. In addition, "anomalous" long-range coupling to the 4-proton, as in 3-thiophenecarbaldehyde, was a possibility. In this work, the 100 mHz spectra of 3-pyrrolecarbaldehyde and 1-methyl-3-pyrrolecarbaldehyde did not show any measurable long-range spin coupling to the aldehydic proton.

A barrier to internal rotation has been shown by N.M.R. measurements in 1-methyl-2-pyrrolecarbaldehyde,[61*] 2-furancarbaldehyde,[62] and 2-acetylfuran.[62]
These studies were carried out over a temperature range between +30° to -115°C. 3-Pyrrolecarbaldehyde and

---

* See footnote in Appendix I.

1-methyl-3-pyrrolecarbaldehyde do not show evidence for the existence of such an energy barrier at normal operating temperature.

The imino proton always appeared as a broad band, as expected, due to the quadrupole induced relaxation of 14_{N}. The ring protons were well defined and N.M.R. afforded a convenient method for following most reactions. This was particularly true for preparations of acetals, where both the disappearing aldehyde proton and the corresponding proton in the acetals appeared as sharp singlets. In the Wittig reactions, N.M.R. spectra gave unambiguous evidence of the stereochemistry of the products.

Virtually all the compounds in this study were affected by the catalytic amounts of acid present in deuterochloroform. To avoid the formation of tars, it was necessary to filter the solvent through basic alumina, particularly when recovery of the material was contemplated.

Ultraviolet spectra

Pyrrole-2-carbaldehyde has been reported as not obeying the Beer-Lambert law,[12] which was used as evidence for association at higher concentrations. The work was repeated but it was found that the compound obeyed this law in 95% ethanol between the concentrations of 0.03 - 0.00001 moles per litre. The use of a non-polar solvent, methylcyclohexane, was attempted over the range of concentrations 0.06 - 0.0001 mole l^{-1}, there was no evidence for a concentration dependent change in the species in solution, (i.e. either fully dissociated or associated species exist throughout this range of dilutions).

Pyrrole-3-carbaldehyde was also found to obey the Beer-Lambert law in the concentration range 0.03 - 0.00002 moles l^{-1}, with 95% ethanol as solvent. The ultraviolet spectra of some new compounds were recorded. They follow the general pattern of two or three bands, in common with the spectra of the majority of pyrroles.[71] Four bands were observed in the case of an acetal and a styrylpyrrole. The absorption data are shown in Table 4.

Infrared spectra

The carbonyl and NH frequencies were recorded for some new compounds. Generally, both non-bonded and bonded NH peaks were observed; the former were sharp, and the latter broad, bands. The absorption data are shown in Table 5.

Mass spectra

In the field of pyrrole derivatives, there is a marked lack of systematic studies. There have been publications on the diagnostic use of mass spectral data of nitrogen heterocycles[65] and some pyrrole fragmentation patterns were investigated.[66-68] Jones[31] recently reviewed the mass spectral data of pyrrole, alkyl pyrroles, acyl pyrroles and pyrrolecarboxylic esters.

In this study, the fragmentation modes of 2-pyrrolecarbaldehyde, 3-pyrrolecarbaldehyde, 1-methyl-2-pyrrolecarbaldehyde and 1-methyl-3-pyrrolecarbaldehyde were investigated. These compounds all gave a strong parent peak, P, and a strong P-1 peak. The aldehyde groups followed the normal fragmentation pattern. The fragmentation of the 1-methyl compounds was similar to the pattern of 1-alkyl pyrroles.[31]

Since a low resolution instrument was used, differentiation between isobaric fragments was not possible. Thus the peak at 28, could be due to N_2^+, $C_2H_4^+$, CH_2N^+ or CO^+. Similarly, the peak at 39, common to all three compounds, could be C_2HN^+ or $C_3H_3^+$. High resolution studies[65] on pyrroles showed mainly $C_3H_3^+$, with about 1% C_2HN^+. The $C_3H_3^+$ ion is probably present as the cyclopropenyl ion.[31]

The spectra of some new compounds were normalized.

EXPERIMENTAL

Melting points (uncorrected) were determined in a Fisher-Johns melting point apparatus. Infrared spectra were recorded by a Perkin Elmer 237 grating spectrophotometer as chloroform solutions. Ultraviolet spectra were obtained on a Unicam SP 800 spectrophotometer, using 95% ethanol as solvent. Nuclear magnetic resonance spectra were recorded on a Varian A-60 analytical spectrometer. (Some spectra were obtained on a Varian HA-100 nuclear magnetic resonance spectrometer). The solvent used was deuterochloroform using tetramethylsilane as internal standard. Mass spectra were determined on a Hitachi-Perkin Elmer RMU-6E (low resolution) mass spectrometer.

Ethyl 4-formyl-2-pyrrolethiolcarboxylate

The preparation has been described.[46] The following modifications improved the yield: (a) The dichloromethyl methyl ether was fractionated through a Widmer column. (b) The crude product, which was an oily solid, was extracted with a Soxhlet apparatus, using petroleum ether (b.p. 80 - 100°C). The extraction time was up to 3 days. Consistent yields of 88% were obtained. (c) The required material could also be isolated from the crude product by sublimation, which gave slightly lower yields than the Soxhlet extraction.

W5 Raney Ni catalyst

The method described[47] was modified to allow preparation of this catalyst on a larger scale. The washing chamber diameter was increased from 5 cm to 10 cm, all other dimensions remained unchanged. A fourfold increase in all the reagents was used, but the catalyst was washed with 40 litres of deionized water instead of 60 litres. The steel stirrer was replaced by a teflon stirrer which gave better agitation on this scale. The yield of catalyst was 200 - 220 g per batch.

3-Pyrrolecarbaldehyde

The preparation has been described.[46] In preparations involving 10 g or more of ethyl 4-formyl-2-pyrrolethiolcarboxylate, the final isolation of 3-pyrrolecarbaldehyde was accomplished more conveniently by distillation, than by chromatography. The distillation was carried out *in vacuo*. using a short-path distillation apparatus. The required product distilled at 132 - 142°, (1 mm), as a colourless oil which later solidified. When stored in sample tubes over sodium hydroxide pellets, 3-pyrrolecarbaldehyde was stable over long periods.

Attempted hydrolysis and decarboxylation of ethyl 4-formyl-2-pyrrolethiolcarboxylate to 3-pyrrolecarbaldehyde

Ethyl 4-formyl-2-pyrrolethiolcarboxylate (366 mg, 2 mmole) and potassium hydroxide (448 mg, 8 mmole) were mixed in triethylene glycol (4 ml). The solution was kept below 100°C for 30 mins, water (1 ml) was added and the temperature was slowly raised. The solution was kept at 190°C for 8 hours, even though the solution darkened considerably even below 100°C, and it was soon black. After cooling, extraction with ether was attempted. The ether extracts gave < 10 mg oil, the rest of the product was a black amorphous solid which was insoluble in ether and chloroform.

1-Methyl-3-pyrrolecarbaldehyde

1-Methyl-2-pyrrolecarbaldehyde was prepared by the Vilsmeyer reaction.[9] The mother liquor was fractionally distilled, the fraction boiling at 75°, 0.1 mm, was almost completely 1-methyl-3-pyrrolecarbaldehyde. The fraction collected at 40 - 70°, (0.1 mm), was redistilled, which gave more of the required product. The combined distillate was diluted with ether, when the solution was cooled in solid carbon dioxide-ethanol bath, a colourless solid crystallized. This was centrifuged rapidly. The solvent was decanted and the solids melted on approaching room temperature. The residual solvents were removed by leaving the oil in a vacuum desiccator for 48 hrs. Yield: 10.4 g, 5.8%. Anal. Calcd. for C_6H_7NO: C, 66.03; H, 6.47. Found: C, 65.72; H, 6.42. PMR spectrum: 0.25 τ, (1H, singlet); 2.72 τ, (1H, complex); 3.37 τ, (2H, complex); 6.32 τ, (3H, singlet).

The fractions were conveniently assayed by either gas liquid chromatography, using a Beckman "Carbowax-4000 dioleate, No. 70-008" column at 220°, 30 p.s.i. pressure; or by PMR spectroscopy.

Attempted preparation of methyl 4-benzyl-2-pyrrolecarboxylate

(a) Directly from methyl 2-pyrrolecarboxylate

The method used was similar to the preparation of methyl 4-benzoyl-2-pyrrolecarboxylate. Benzyl bromide and benzyl chloride were used as alkylating agents in carbon disulphide or dichloromethane as solvents. Reaction mixtures were refluxed for 1 - 4 hrs. Only starting material was isolated from these reactions.

(b) By reduction of methyl 4-benzoyl-2-pyrrolecarboxylate

Reduction by diborane in tetrahydrofuran, hydrogenation with 5% Pd charcoal catalyst in ethanol for 15 hrs at room temperature, hydrogenation with Pd black catalyst for 48 hrs at room temperature and reduction by refluxing zinc and acetic acid over 48 hrs, all failed.

Methyl 4-benzoyl-2-pyrrolecarboxylate

Methyl 2-pyrrolecarboxylate (500 mg, 4 mmole) was dissolved in methylene chloride (20 ml). Aluminium chloride (1.680 g, 12.6 mmole) was added, followed by dropwise addition of benzoyl chloride (843 mg, 6 mmole) in methylene chloride (6 ml). The mixture was stirred and refluxed for 2½ hours, it was cooled and poured on a mixture of dilute hydrochloric acid and ice. The mixture was stirred for 25 mins, and extracted with chloroform. The organic phase was washed with dilute hydrochloric acid, saturated potassium bicarbonate solution and water until neutral. The organic phase was dried (Na_2SO_4), filtered and evaporated to an oily solid. Recrystallization from aqueous 2-propanol (12 : 5 mixture) gave a colourless solid, (0.760 g, 82%), m.p. 145 - 146°. Anal. Calcd. for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.80. Found: C, 68.48; H, 4.74. Proton Magnetic Resonance (PMR) spectrum: - 0.17 τ (1H, broad); 2.05 - 2.73 τ (7H, complex); 6.14 τ, (3H, singlet).

Hydrolysis in methanolic potassium hydroxide, followed by acidification gave the corresponding acid, m.p. 223.5 - 224°C, dec. (Lit.[69] 224-225°, dec.). Thermal decarboxylation of the acid gave 3-benzoylpyrrole, m.p. 96 - 97°C (lit. m.p. 96 - 97°C).

Ethyl 4-benzoyl-2-pyrrolethiolcarboxylate

Ethyl 2-pyrrolethiolcarboxylate (465 mg, 3 mmole) was dissolved in methylene chloride (20 ml). Aluminium chloride (1.00 g, 7.5 mmole) was added and the mixture was stirred at room temperature for 20 minutes. Benzoyl chloride (512 mg, 3.6 mmole) in methylene chloride (5 ml) was added dropwise and the reaction mixture was stirred and refluxed for 3 hours. The mixture was cooled and poured into dilute HCl solution. After ½ hour stirring, the organic phase was separated, washed with dilute HCl, water, saturated sodium bicarbonate solution, and finally dried (Na_2SO_4). Evaporation gave an oil, which crystallized when triturated with petroleum ether (b.p. 40 - 60°). Recrystallization from benzene gave a colourless solid, (352 mg, 48%), m.p. 103.5°. Anal. Calcd. for $C_{14}H_{13}O_2NS$: C, 64.86; H, 5.05. Found: C, 65.14; H, 5.25. PMR spectrum: 1.97 - 2.69 τ, (7H, complex); 6.89 τ, (2H, quartet); 8.65 τ, (3H, triplet).

3-Benzylpyrrole

Methyl 4-benzoyl-2-pyrrolecarboxylate (425 mg, 1.85 mmole), potassium hydroxide (350 mg, 6.25 mmole) and hydrazine (64%, in water, 332 mg, 6.65 mmole) were added to triethylene glycol (3 ml). The solution was kept at 100°C for 90 mins while the water present distilled off. Then the solution was gradually heated to 190°C, and kept at that temperature for 5 hrs, during which time decarboxylation occurred. The solution was cooled and water (5 ml) was added. The solution was poured on excess acetic acid (1 ml, glacial) and it was extracted with ether. The ether extract was washed with water, satd. $NaHCO_3$ soln., and water. It was dried ($MgSO_4$), and was evaporated to a light yellow oil, (270 mg, 92%). PMR indicated the expected product. The oil was redistilled under vacuum and gave a colourless oil, (180 mg, 61%). Anal. Calcd. for $C_{11}H_{11}N$:

C, 84.04; H, 7.05. Found: C, 84.07; H, 7.22. PMR spectrum: 2.78 τ, (5H, singlet); 3.51 τ, (1H, complex); 3.70 τ, (1H, complex); 3.96 τ, (1H, complex); 6.20 τ, (2H, singlet).

1-Methyl-4-acetyl-2-pyrrolecarbaldehyde

Aluminium chloride (56 g, 0.42 mole) was suspended in methylene chloride (200 ml). Acetyl chloride (12.0 g, 0.153 mole) was dissolved in methylene chloride (50 ml) and the solution was added to the suspension, followed by dropwise addition of 1-methyl-2-pyrrolecarbaldehyde (8.8 g, 0.08 mole) in methylene chloride (50 ml). The mixture was refluxed for 2 hrs. It was poured on ice and the mixture was stirred overnight. The organic phase was separated and the aqueous phase was reextracted with chloroform. The combined organic phase was washed with water, dried ($MgSO_4$), evaporated *in vacuo* to an oily solid. On recrystallization from benzene and petroleum ether (b.p. 60 - 80°), a light fawn solid was obtained, (8.7 g, m.p. 105°). The mother liquor was chromatographed on neutral alumina, using chloroform-benzene (1 : 3) as eluent. This gave additional solids (1.2 g, m.p. 105°). Total yield: 9.9 g, 83%. Sublimation gave a colourless solid, m.p. 105.5°. Anal. Calcd. for $C_8H_9O_2N$: C, 63.56; H, 6.00. Found: C, 63.79; H, 6.13. PMR spectrum: 0.25 τ, (1H, doublet); 2.43 τ, (1H, complex); 2.60 τ, (1H, complex); 5.95 τ, (3H, doublet); 7.53 τ, (3H, singlet).

1-Methyl-2,4-pyrroledicarbaldehyde

1-Methyl-2-pyrrolecarbaldehyde (2.75 g, 25 mmole) was dissolved in methylene chloride (25 ml). Nitromethane (3 ml) in methylene chloride (25 ml) was added, with stirring, followed by aluminium chloride (15.6 g, 117 mmole) and dichloromethyl methyl ether (7.6 g, 66 mmole) in methylene chloride (25 ml). The mixture was stirred at room temperature for 1 hr and refluxed for 10 mins. The mixture was cooled and poured on ice. The organic phase was separated and the aqueous phase was extracted with $CHCl_3$. The combined organic phase was washed with water, dried ($MgSO_4$), and passed through a very short neutral alumina column. Evaporation *in vacuo* gave a colourless oil and some solids. Distillation at 0.5 mm, from an oil bath at 52°C, removed 680 mg oil which was identified as starting meterial using gas liquid chromatography (GLC). The remaining black solid was chromatographed using neutral alumina and chloroform as eluent. Evaporation gave a brown oil, which was extracted with petroleum ether (b.p. 80 - 100°C). This gave light yellow crystals, (980 mg, 26%), m.p. 95°. Anal. Calcd. for $C_7H_7NO_2$: C, 61.31; H, 5.15. Found: C, 61.30; H, 5.20. PMR spectrum: 0.18 τ, (1H, singlet; 4-CHO); 0.33 τ, (1H, singlet; 2-CHO); 2.50 τ, (1H, complex); 2.67 τ, (1H, complex); 5.99 τ, (3H, singlet).

3-Pyrrolecarboxylic acid

Silver nitrate (276 g, 1.6 mmole) in water (2.7 ml) was added to sodium hydroxide (1N, 55 ml), with stirring. 3-Pyrrolecarbaldehyde (50 mg, 0.53 mmole), dissolved in ethanol (4 ml), was added and the mixture was stirred at room temperature for 1 hr. The mixture was extracted with ether, the aqueous phase was acidified with 6N hydrochloric acid (~ 18 ml) and extracted with ether. The ether phase was dried ($MgSO_4$) and evaporated to a fawn solid, (42 mg, 76%), m.p. 144 - 144.5°. A small portion was recrystallized from water, m.p. 144.5 - 145.5°C, dec. (Lit. m.p. 144.5 - 145.5°C).

3-Pyrrolecarbaldoxime

Hydroxylamine hydrochloride (416 mg, 7 mmole) and sodium acetate trihydrate (900 mg, 6.6 mmole) were ground up in a mortar and hydroxylamine was extracted into ethanol. 3-Pyrrolecarbaldehyde (285 mg, 3 mmole) was added to the extract, which was refluxed for 15 mins. Evaporation *in vacuo* gave an oil. Crystallization from water (4 ml) gave a fawn solid, which was recrystallized from benzene to colourless crystals, (194 mg, 59%), m.p. 133.5°. Anal. Calcd. for $C_5H_6N_2O$: C, 54.54; H, 5.49. Found: C, 54.56; H, 5.51.

Ethyl 4-(1,3-dioxolan-2-yl)-2-pyrrolethiolcarboxylate

Ethyl 4-formyl-2-pyrrolethiolcarboxylate (11.68 g, 0.075 mole) and ethylene glycol (192 ml) were added to benzene (940 ml) containing p-toluenesulphonic acid (768 mg). Molecular sieves (10 g) were added. The mixture was refluxed using a Dean and Stark separator for 72 hours on a steam bath. The benzene phase was washed with $NaHCO_3$ solution and dried ($MgSO_4$). Evaporation gave a yellow solid, which was recrystallized from ether-petroleum ether (b.p. 40 - 60°C) to light yellow needles, (12 g, 83.5%), m.p. 60.5 - 61°. Second recrystallization gave a solid, m.p. 61.5°C. Anal. Calcd. for $C_{10}H_{13}NO_3S$: C, 52.86; H, 5.77. Found: C, 52.68; H, 5.77. PMR spectrum: 2.76 τ, (1H, complex); 2.81 τ, (1H, complex); 4.04 τ, (1H, singlet); 5.88 τ, (4H, complex); 6.91 τ, (2H, quartet); 8.68 τ, (3H, triplet).

3-(1,3-dioxolan-2-yl)-pyrrole

W5 Raney nickel (32 g) was washed with acetone (3×100 ml). Ethyl 4-formyl-2-pyrrolethiolcarboxylate, ethylene acetal (2.0 g, 8.8 mmole) in acetone (125 ml) was added and the mixture was stirred for 70 minutes. The mixture was filtered and the Raney nickel was washed well with acetone. Evaporation gave 950 mg oil. This was dissolved in ether, and the solution cooled in solid CO_2, when colourless crystals separated, (650 mg, 53%), m.p. 63°.

Anal. Calcd. for $C_7H_9NO_2$: C, 60.42; H, 6.52. Found: C, 60.41; H, 6.64. PMR spectrum: 3.28 τ, (1H, complex); 3.44 τ, (1H, complex); 3.71 τ, (1H, complex); 4.18 τ, (1H, singlet); 6.03 τ, (4H, complex).

Attempted preparation of 3-pyrrolecarbaldehyde diethyl acetal

3-Pyrrolecarbaldehyde (285 mg, 3 mmole) was dissolved in absolute ethanol (5 ml). Ethyl orthoformate (477 mg, 3.2 mmole) and powdered ammonium chloride (4.2 mg) were added and the mixture was refluxed for 30 minutes. The solvent was removed *in vacuo*, ether and water were added. The organic phase was separated, washed with water, dried (K_2CO_3). Evaporation gave an oil, the PMR spectrum showed only the presence of the starting materials.

Attempted preparation of 3-formyl-2-pyrrolecarboxylic acid

3-(1,3-Dioxolan-2-yl)-pyrrole (80 mg, 0.57 mmole) was dissolved in ether (18 ml, anh.), under nitrogen. Ethyl magnesium bromide (0.8 ml of 1.5 M solution in ether, 1.2 mmole) was added through a septum. The solution was stirred for 15 minutes. Solid carbon dioxide was added, after 10 mins the solution was made alkaline with potassium hydroxide (6N). The alkaline aqueous phase was washed well with ether and it was then acidified with hydrochloric acid (6N). Extraction of the acid phase with ether, followed by washing and drying over anh. magnesium sulphate gave, on evaporation, less than 3 mg oil.

Attempted preparation of ethyl 3-formyl-2-pyrrolethiolcarboxylate

3-(1,3-Dioxolan-2-yl)-pyrrole (100 mg, 0.72 mmole) in ether (5 ml, anh.) was cooled in ice under dry nitrogen atmosphere. Ethylmagnesium bromide (1 ml, 1.5 mmole in ether) was added and the solution was stirred for 30 mins. Di-S-ethyl dithiocarbonate, (150 mg, 1 mmole) in ether (1 ml, anh.) was added. The solution was stirred overnight, it was poured on ammonium chloride solution (aqueous, 10%). The mixture was extracted with ether. The ether phase was washed with water, dried ($MgSO_4$), and was evaporated to 114 mg dark brown oil. The PMR spectrum showed a mixture of 3-pyrrolecarbaldehyde and di-S-ethyl dithiocarbonate.

Attempted preparation of ethyl 2,3-diformyl-5-pyrrolethiolcarboxylate

Phosphorus oxychloride (153 mg, 1 mmole) was added to dimethyl formamide (2 ml, excess) and dichloromethane (3 ml). The solution was cooled and stirred. A solution of ethyl 4-(1,3-dioxolan-2-yl)-2-pyrrolethiolcarboxylate (90 mg, 0.4 mmole) in dichloromethane (5 ml) was added. The solution was refluxed for 30 mins. When cool, it was poured on saturated sodium acetate solution (750 mg sodium acetate trihydrate in 1 ml water). The solution was refluxed for 15 mins. The organic layer was separated, washed with water and dried ($MgSO_4$). Evaporation gave an oil, the PMR spectrum indicated ethyl 4-formyl-2-pyrrolethiolcarboxylate only.

1-Methyl-3-styrylpyrrole

Potassium (234 mg, 6 mmole) was dissolved in tert.-butyl alcohol (7 ml) under nitrogen. Ether (anh., 5 ml) was added followed by benzyltriphenylphosphonium chloride (1.94 g, 5 mmole). The mixture was stirred and cooled. 1-Methylpyrrole-3-carbaldehyde (444 mg, 4 mmole) was dissolved in ether (anh., 5 ml) and was added dropwise to the mixture. Stirring at room temperature was continued for 3 hours. The mixture was poured on water (30 ml), and it was extracted with ether. The organic phase was washed with water and dried ($MgSO_4$). On evaporation, a yellow oily solid was obtained. This was chromatographed on silica gel (BDH), using benzene as eluent. The early fractions were evaporated to an oil which crystallized from petroleum ether (b.p. 80 - 100°C). The crude product was sublimed to colourless crystals, (130 mg, 16%), m.p. 95°. Anal. Calcd. for $C_{13}H_{13}N$: C, 85.20; H, 7.15. Found: C, 85.01; H, 7.12. PMR spectrum: 2.5 - 2.8 τ, (5H, complex); 3.09 τ, (2H, doublet); 3.27 τ, (1H, complex); 3.41 τ, (1H, complex); 3.51 τ, (1H, complex); 6.39 τ, (3H, singlet).

Attempted preparation of 3-styrylpyrrole

Potassium (234 mg, 6 mmole) was dissolved in tert.-butyl alcohol under a nitrogen atmosphere. Ether (5 ml, anh.) was added, with stirring, followed by benzyltriphenylphosphonium chloride (1.94 g, 5 mmole).

3-Pyrrolecarbaldehyde (380 mg, 4 mmole) in ether (5 ml) was added and the mixture was stirred for 5 hrs at room temperature. The reaction mixture was poured on water (30 ml) and was extracted with ether. The organic phase was washed with water and was dried ($MgSO_4$). Evaporation gave an oil, which was chromatographed on a 1.2 cm × 30 cm silica gel column using benzene as eluent. From the first 200 ml extract, an oily solid (522 mg) was obtained by evaporation. This product was sublimed, and gave two bands of crystals (38 mg), m.p. 113 - 114° and 121 - 121.5°. The PMR spectrum indicated, that both were the *trans* isomer. The mass spectrum of the crystals m.p. 121 - 121.5° was as expected. Repeating the experiment was unsuccessful.

The replacement of potassium *t*-butoxide as the base by sodium hydride was attempted. The solvent used was dry dimethyl sulphoxide. Otherwise the reaction conditions were similar to the previous method. Chromatography gave only starting material and triphenylphosphine oxide.

Ethyl 1-carbethoxy-3-(3-pyrrolyl)acrylate

3-Pyrrolecarbaldehyde (200 mg, 2.1 mmole) was dissolved in a few drops of ethanol. Diethyl malonate (600 mg, 3.7 mmole), methylamine hydrochloride (100 mg, 1.3 mmole) and anh. K_2CO_3 (200 mg, 1.5 mmole) were added. The mixture was kept at room temperature for 4 days, then poured into water and extracted with ether. The ether phase was washed with water and dried ($MgSO_4$). Evaporation gave 190 mg yellow oil, which was chromatographed on neutral alumina, using benzene as eluent. The different fractions were kept, and one crystallized after 3 months. This was recrystallized from ether-petroleum ether (b.p. 60 - 80°C), and gave a light yellow solid, (89 mg, 18%). M.p. 62 - 63°. Anal. Calcd. for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37. Found: C, 60.56; H, 6.29. PMR spectrum: 2.22 τ, (1H, singlet); 2.85 τ, (1H, complex); 3.18 τ, (1H, complex); 3.58 τ, (1H, complex); 5.70 τ, (4H, multiplet); 8.68 τ, (6H, multiplet).

Attempted benzoin condensation of 3-pyrrolecarbaldehyde

3-Pyrrolecarbaldehyde (380 mg, 4 mmole) was dissolved in absolute ethanol (5 ml). Sodium cyanide (40 mg), dissolved in water (5 ml), was added and the solution was refluxed for 5 hrs. The ethanol was removed *in vacuo,* 10 ml water was added and the aqueous phase was extracted with ether. The ether extracts were washed with water, dried ($MgSO_4$). Evaporation gave an oil which slowly solidified. The PMR spectrum indicated starting material only.

Attempted Perkin reaction of 3-pyrrolecarbaldehyde

3-Pyrrolecarbaldehyde (285 mg, 3 mmole), acetic anhydride (425 mg, 4.5 mmole) and potassium acetate (294 mg, 3 mmole, freshly fused) were mixed well. The mixture was kept at 150° for 4 hrs, (the colour turned black within

10 mins. of heating). Cooled, extracted with ether and water - the extraction failed, a lump of solidified polymer did not dissolve in either solvent.

3-Methylpyrrole

(a) From 3-pyrrolecarbaldehyde

3-Pyrrolecarbaldehyde (352 mg, 3.7 mmole), KOH (700 mg, 12.5 mmole) and hydrazine hydrate (64%, 664 mg, 13.3 mmole) were mixed with triethylene glycol (6 ml). The temperature of the mixture was kept just below 100°C for 90 minutes. The water was distilled off and the temperature was gradually raised to 190°C. An oil gradually distilled over at approximately 143°C (lit. b.p. of 3-methylpyrrole: 143°[36]). After 8 hours, no more distillate was collected. The oil was dissolved in ether, the ether phase was washed and was dried over anh. $MgSO_4$. Evaporation gave a colourless oil, (200 mg, 67%), which gave the expected PMR spectrum. PMR spectrum: 3.31 τ, (1H, complex); 3.44 τ, (1H, complex); 3.89 τ, (1H, complex); 7.85 τ, (3H, singlet).

(b) From ethyl 4-formyl-2-pyrrolethiolcarboxylate

Ethyl 4-formyl-2-pyrrolethiolcarboxylate (338 mg, 1.85 mmole), KOH (350 mg, 6.25 mmole) and hydrazine hydrate (64%, 332 mg, 6.6 mmole) were mixed in triethylene glycol (3 ml). The reaction mixture was kept at 90° for 90 minutes and water (2 ml) was added. After 15 minutes water was distilled off. The temperature of the mixture was gradually raised to 190 , when decarboxylation occurred. An oil distilled gradually over a period of about 6 hours. The oil was dissolved in ether, the ether phase was washed with water, dried over anh. magnesium sulphate and was evaporated to an oil, (73 mg, 49%). The PMR spectrum was similar to the 3-methylpyrrole obtained in the previous preparation.

Ultraviolet studies on 2-pyrrolecarbaldehyde

From 40 mm to 1 mm, fixed path length "Spectrosil" silica cells were used. Below 1 mm, fixed path length fused silica cells in demountable stainless steel mounts were used. The path lengths of the 0.00317 cm and 0.0102 cm cells were measured by their diffraction pattern and are accurate to within 5%. The path lengths of the "Spectrosil" cells were accurate to within 0.1%.

The cells and volumetric flasks were cleaned by the following method:

(a) Washed well with hot water.

(b) Rinsed well with freshly prepared chromic acid, using concentrated nitric acid.

(c) Rinsed with hot water (13 times).

(d) Rinsed with distilled water (4 times).

(e) Rinsed twice with freshly distilled, boiling ethanol (95%).

(f) Rinsed twice with freshly distilled, cold ethanol (95%).

(g) Dried in a vacuum desiccator.

The spectra were run progressing from the weakest to the stronger solution. Whenever it was necessary to use the same set of cells for spectra of different solutions, the new solution was used to rinse the cell at least 4 times. The demountable cells were washed well with freshly distilled ethanol and were dried by passing dry nitrogen through them.

To avoid instrumental errors, wherever possible, concentrations and path lengths were chosen so that the absorbance values fell between 0.7 and 1.3.

The solvent used was freshly distilled ethanol (95%). The use of a non-polar solvent, methylcyclohexane, was also attempted. The absorption data are shown in Tables 1 and 2.

TABLE 1. 2-Pyrrolecarbaldehyde in 95% ethanol

Concentration (moles ℓ^{-1})	Path length (cm)	Absorbance	ε_{max} (at ν_{max} = 34,500 cm^{-1})
0.03289	0.00317	1.575	16,100(a)
0.008222	0.0102	1.325	16,100
0.001117	0.050	0.922	16,500
0.0008377	0.10	1.355	16,200
0.0005585	0.10	0.933	16,700
0.0002792	0.20	0.910	16,300
0.0001117	0.20	0.365	16,300
	0.50	0.905	16,200
	0.50	0.910	16,100
0.00008377	0.50	0.675	16,100
	0.50	0.675	16,100
	1.00	1.360	16,200
0.00005585	1.00	0.940	16,800
0.00002792	2.00	0.925	16,500
0.00001117	4.00	0.750	16,800

(a) A correction factor was applied for stray light effect. (Original value of ε_{max} = 15110).

The extinction coefficient at 34,500 cm^{-1} is 16500 ± 2.5%. (There was a broad inflexion at ν_{max} 39,000 - 40,000 cm^{-1}, ε_{max} 5,200, which was not examined).

TABLE 2. 2-Pyrrolecarbaldehyde in methylcyclohexane

Concentration (moles ℓ^{-1})	Path length (cm)	Absorbance	ε_{max}	ν_{max} (a) (cm^{-1})
0.05835	0.0102	0.985	16,600	35,300
0.05710	0.0102	0.990	16,900	35,300
0.01167	0.050	0.910	15,600	35,400
0.005835	0.10	0.910	15,600	35,600
0.005710	0.10	0.897	15,700	35,600
0.001167	0.50	0.900	15,400	35,700
0.0001167	4.00	0.705	15,100	35,800

The extinction coefficient at 35,500 ± 300 cm^{-1} is 16,000 ± 6%.

Ultraviolet studies on 3-pyrrolecarbaldehyde

The experimental details and precautions taken were similar to those used in the ultraviolet studies of 2-pyrrolecarbaldehyde. There were two main absorption bands, each preceeded by an inflexion. The main bands were investigated. The absorption data are shown in Table 3.

TABLE 3. 3-Pyrrolecarbaldehyde in 95% ethanol

Concentration (moles ℓ^{-1})	Path length (cm)	Absorbance	ε_{max}	ν_{max} (cm^{-1})
0.03334	0.00317	1.185	11,200	49,500
"	"	1.105	10,700	40,600
0.010002	0.0102	1.170	11,500	49,500
"	"	1.100	10,800	40,600
0.0020004	0.050	1.130	11,300	49,400
"	"	1.090	10,900	40,600
0.0010002	0.100	1.140	11,400	49,300
"	"	1.110	11,100	40,600
0.00040008	0.200	0.865	10,800	49,300
"	"	0.850	10,600	40,600
0.00010002	1.000	0.995	10,000	49,000
"	"	1.090	10,900	40,500
0.000040008	2.000	0.630	7,900	48,300
"	"	0.840	10,500	40,600
0.000020004	4.000	0.510	6,400	47,900
"	"	0.865	10,800	40,600

The absorption band in the vicinity of 49,500 cm^{-1} was unreal, due to rising end absorption and solvent cut off. This resulted in the variation of ν_{max} and ε_{max}. The absorption at 40,550 cm^{-1} gave ε_{max} = 10,800 ± 3%. An attempt to change to a non-polar solvent, methylcyclohexane, failed, as 3-pyrrolecarbaldehyde was not sufficiently soluble to permit preparations of solutions of 0.03 molar strength.

TABLE 4. Ultraviolet spectra of some new compounds

Solvent: 95% ethanol

Compound	ν_{max} (cm^{-1})	ε_{max}
Methyl 4-benzoyl-2-pyrrolecarboxylate	34,850	10,700
	39,700*	16,200
	41,850	20,800
Ethyl 4-benzoyl-2-pyrrolethiolcarboxylate	32,900	17,600
	36,200	12,000
	40,600	19,500
3-Benzylpyrrole	37,120	1,000
	38,080	1,000
	48,500 (a)	16,000 (a)
1-Methyl-4-acetyl-2-pyrrolecarbaldehyde	34,450	15,200
	38,500*	9,500*
	42,200	22,700
1-Methyl-2,4-pyrroledicarbaldehyde	34,410	15,380
	38,500*	9,600*
	42,200	24,700
Ethyl 4-(1,3-dioxolan-2-yl)-2-pyrrolethiolcarboxylate	33,550	20,600
	37,100	10,800
	38,500*	9,900*
	44,000	25,500
1-Methyl-3-styrylpyrrole	31,830	28,300
	33,000*	26,600*
	42,400*	12,700*
	43,570	13,300
Ethyl 1-carbethoxy-3-(3-pyrrolyl)-acrylate	31,830 (b)	15,100

Notes: * Denotes an inflexion.

(a) This absorption is in the vicinity of the solvent cut-off region. The ν_{max} and ε_{max} values are only approximate.

(b) There is an inflexion between 33,000 - 36,000 cm^{-1} but ν_{max} and ε_{max} for this absorption could not be determined.

TABLE 5. Infrared spectra of some new compounds

Solvent: Chloroform

Compound	C=O (cm^{-1})	N-H (cm^{-1})	
		Non-bonded	Bonded
Methyl 4-benzoyl-2-pyrrolecarboxylate	1620 1700	3420	3240
Ethyl 4-benzoyl-2-pyrrolethiolcarboxylate	1635 (broad)	3420	3243
1-Methyl-2,4-pyrroledicarbaldehyde	1672	-	-
1-Methyl-4-acetyl-2-pyrrolecarbaldehyde	1657(a)	-	-
Ethyl 4-(1,3-dioxolan-2-yl)-2-pyrrolethiolcarboxylate	1630 (broad)	3420	3200
Ethyl-1-carbethoxy-3-(3-pyrrolyl)-acrylate	1720	3460	3195
3-Benzylpyrrole	-	3470	-
(3-Pyrrolecarbaldehyde(b)	1676	3460	3230(c))

(a) Broad band with inflexion on both sides.

(b) The spectrum of this known compound was recorded in carbon tetrachloride. The non-bonded N-H frequency was calculated to 3478 cm^{-1}, using Jones's rules[32-34]. The observed wavenumber is low.

(c) The compound was only sparingly soluble in carbon tetrachloride, which resulted in a weak spectrum. The bonded N-H wavenumber is approximate.

Mass Spectra

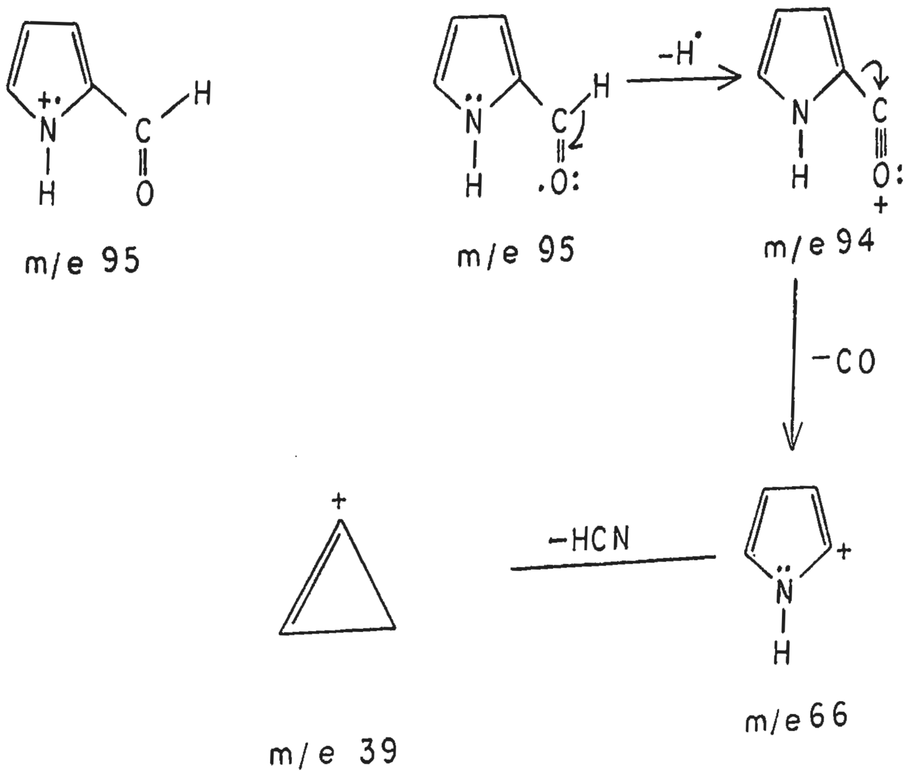
The instrument used was a Hitachi-Perkin Elmer RMU-6E. Unless otherwise stated, the direct inlet system was used. The acceptable total ion current variation level was 6%. Peaks of intensity below 5% were not included in the normalized spectra.

2-Pyrrolecarbaldehyde

Indirect inlet system was used.

m/e	%	m/e	%	m/e	%
96	7	94	63	39	16
95	100	66	43		

Suggested fragmentation pattern:



The structure of the ion at m/e 39 is uncertain; it may be acyclic.

3-Pyrrolecarbaldehyde

Indirect inlet system was used.

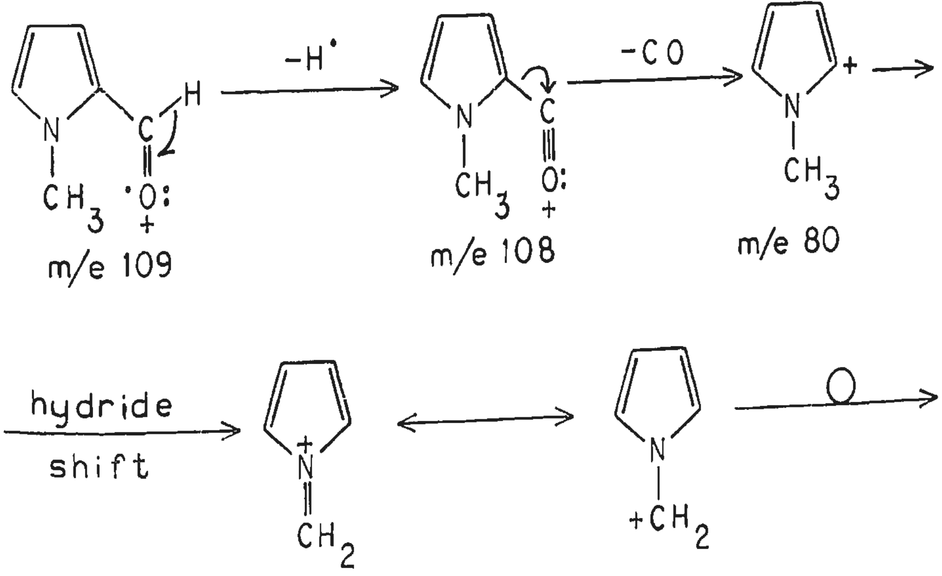
m/e	%	m/e	%	m/e	%
96	6.5	66	43	38	8
95	100	44	14	34	10
94	72	39	24		

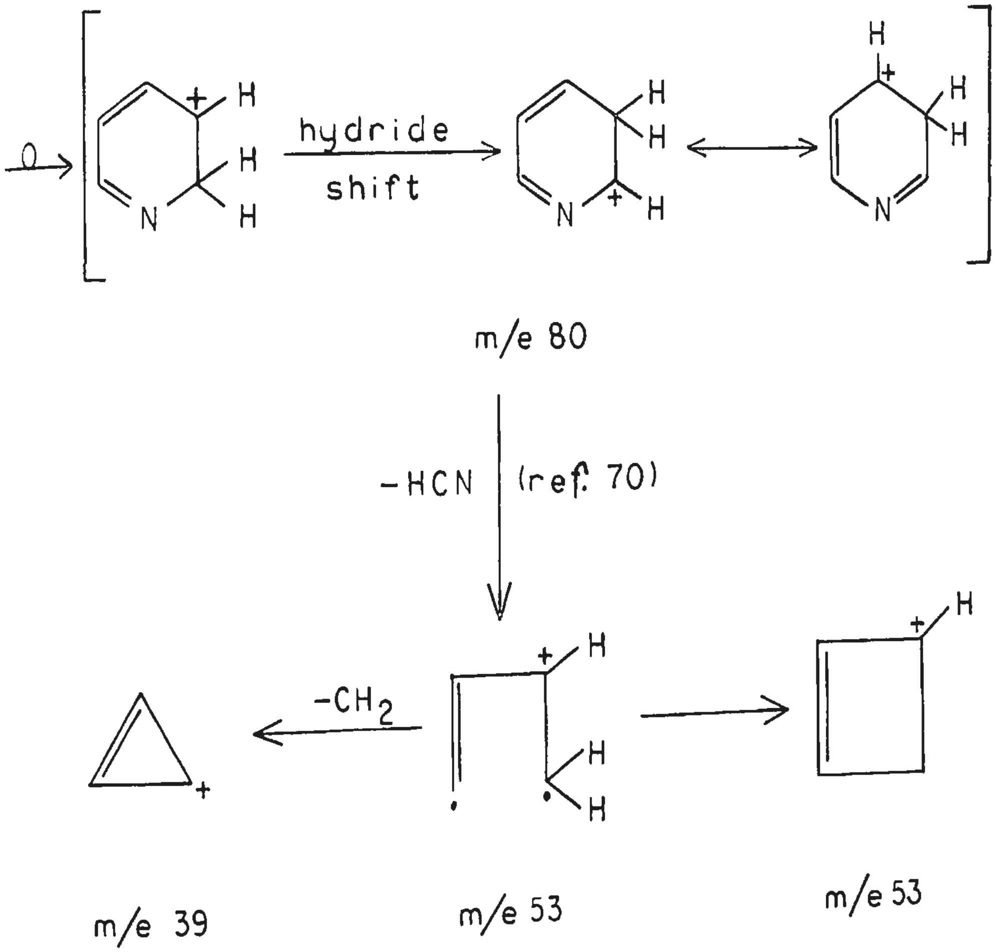
The fragmentation appears to be similar to 2-pyrrolecarbaldehyde. The peak at m/e 44 and m/e 34 are due to CO_2 and $O^{16}O^{18}$ and do not arise from the compound. The m/e 38 peak was not identified.

1-Methyl-2-pyrrolecarbaldehyde

m/e	%	m/e	%	m/e	%
110	7	80	23	39	16
109	100	78	6		
108	76	53	28		

Suggested fragmentation scheme:





The peak at 78 was not identified.

1-Methyl-3-pyrrolecarbaldehyde

m/e	%	m/e	%	m/e	%
110	9	80	16	42	6
109	100	53	22	39	18
108	99				

The fragmentation scheme seems similar to 1-methyl-2-pyrrolecarbaldehyde. The peak at m/e 78 does not appear, and there is a peak at m/e 42. In 1-methylpyrroles, the fragment m/e 42 has been attributed to $CH_3\overset{+}{N}{\equiv}CH$.[70]

Methyl 4-benzoyl-2-pyrrolecarboxylate

m/e	%	m/e	%	m/e	%
230	12	153	9	92	6
229	83	152	98	77	14
198	8	121	8	51	5
170	11	120	100		
169	5	105	9		

Ethyl 4-benzoyl-2-pyrrolethiolcarboxylate

m/e	%	m/e	%	m/e	%
260	6	198	100	120	12
259	30	151	6	105	20
199	16	149	8	77	10
		136	14	44	6

1-Methyl-4-acetyl-2-pyrrolecarbaldehyde

m/e	%	m/e	%	m/e	%
152	6	136	100	53	8
151	63	108	5	43	5
137	10	80	7	39	8

1-Methyl-2,4-pyrroledicarbaldehyde

m/e	%	m/e	%	m/e	%
138	92	108	6	39	8
137	100	80	7		
136	89	53	11		

2-(3-Pyrrolyl)-1,3-dioxolane

m/e	%	m/e	%	m/e	%
139	6	80	50	52	28
138	54	79	46	51	11
137	100	73	16	50	6
109	19	68	8	45	10
108	11	67	21	41	8
95	11	66	14	39	30
94	95	53	8	38	9

Ethyl 1-carbethoxy-3-(3-pyrrolyl)-acrylate

m/e	%	m/e	%	m/e	%
238	15	147	53	91	46
237	100	137	8	80	6
193	14	124	21	69	5
192	88	120	33	68	10
191	15	119	42	67	6
173	7	118	7	65	22
165	22	96	14	64	9
164	24	95	5	63	9
163	18	94	6	44	8
162	11	93	16	41	7
148	26	92	22	39	8

3-Styrylpyrrole (Not confirmed by analysis)

m/e	%	m/e	%	m/e	%
170	12	141	19	67	7
169	88	140	6	63	6
168	100	139	10	51	6
167	48	136	6	44	8
166	17	115	10	39	6
154	6	84	6		

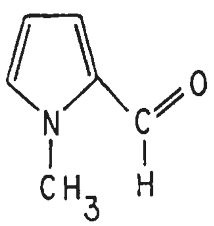
1-Methyl-3-styrylpyrrole

m/e	%	m/e	%	m/e	%
184	15	168	34	91	7
183	100	167	6	90.5	13
182	75	141	11	83.5	7
181	11	139	6	81	6
180	6	115	7	42	10
169	9	91	11		

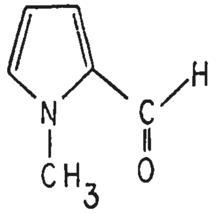
APPENDIX I.

Footnote from page 20

This publication appeared, when most of this work had been completed. The authors, Arlinger, Dahlqvist, Forsen, propcsed that 1-methyl-2-pyrrolecarbaldehyde exists in the two planar rotational isomers:

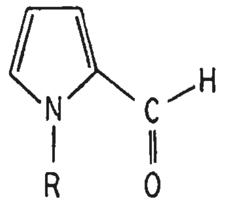


XXXII



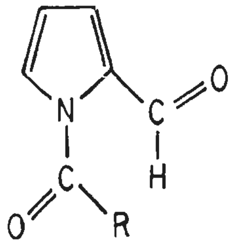
V

Their evidence showed that the isomer XXXII was the predominant form at -60°, and that the ratio between the isomers was 22 : 1. The authors also report, that a preliminary examination of 2-pyrrolecarbaldehyde showed a similar isomer ratio. This is in contrast with the hitherto generally accepted predominant conformations of 2-pyrrolecarbaldehyde and 1-alkyl-2-formylpyrroles. Jones[63] used dipole moment, infrared, ultraviolet and nuclear magnetic resonance studies as evidence for the predominant existence of the conformer XXXIII:

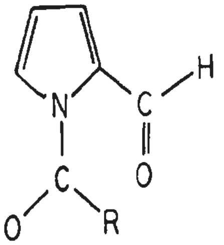


XXXIII

Jones reiterated his evidence and conclusions more recently,[64] but he also added that in 1-ethoxycarbonyl-2-formylpyrrole and 1-acetyl-2-formylpyrrole, the conformer XXXIV accounts for 70% of the mixture:



XXXIV



XXXV

If the results and conclusions of Arlinger et al. are confirmed, a critical review of intramolecular and intermolecular hydrogen bonding in 2-pyrrolecarbaldehyde is necessary. Since nuclear magnetic resonance spectra were produced as evidence both for and against the existence of the same conformer, the validity of this method for conformational analysis has to be examined. The empirical "zig-zag path rule" would lose its validity.

REFERENCES

1. E. Bamberger, G. Djierdjian, Chem. Ber. 33, 536 (1900).

2. H. Fischer, H. Beller, A. Stern. Chem. Ber. 61, 1074 (1928).

3. T. Reichstein, Helv. Chim. Acta. 13, 349 (1930). Chem. Abstr. 24, 3782 (1930).

4. L. Alessandri. Atti. Accad. Lincei, (Firenze), 23, II, 65-70, Chem. Abstr. 9, 1044 (1915).

5. L. Alessandri, M. Passerini. Gazz. Chim. Ital. 51, I, 1262-85 (1921). Chem. Abstr. 16, 94 (1922).

6. a. W. Tschelinzew, A. Terentjew. Chem. Ber. 47, 2652 (1914). Chem. Abstr. 9, 88 (1915).

   b. N. Putochin. Chem. Ber. 59, 1993 (1926).

7. H. Fischer, W. Zerweck. Chem. Ber. 55, 1942 (1922).

8. A. H. Corwin, "Heterocyclic Compounds", Volume I. Editor: R. C. Elderfield. J. Wiley & Sons, (1950). Page 310.

9. R. M. Silverstein, E. E. Ryskiewicz, C. Willard. "Organic Syntheses, Collective Volume 4", Editor: N. Rabjohn. J. Wiley & Sons, (1963). Page 881.

10. R. M. Silverstein, E. E. Ryskiewicz, C. Willard, R. C. Koehler. J. Org. Chem. 20, 669 (1955).

11.a. A. Angeli, G. Marchetti. Atti. Accad. Lincei (Firenze) {5}, 17, II. 360-66. Chem. Abstr. 3, 2938 (1909).

b. A. Angeli, L. Alessandri. Atti. Accad. Lincei (Firenze) {5}, 23, II, 94 (1914). Chem. Abstr. 9, 1321 (1915).

12. W. Herz, J. Brasch. J. Org. Chem. 23, 1513 (1958).

13. H. Fischer, H. Orth. "Die Chemie des Pyrrols". Akademische Verlag, Leipzig, 1934.

14. G. Oddo, E. Deleo. Chem. Ber. 69, 294-8 (1936). Chem. Abstr. 30, 3407 (1936).

15. G. Rastelli, A. Mingozzi. Gazz. Chim. Ital. 55, 549 (1925). Chem. Abstr. 20, 597 (1926).

16. R. Andrisano, G. Pappalardo, L. Bolognari. Gazz. Chim. Ital. 85, 1430 (1955). Chem. Abstr. 50, 3896 (1956).

G. B. Bonino, A. M. Marinangeli. Atti. Accad. Naz. Lincei, Rend., Classe Sci. Fis. Mat. Nat. 19, 222-9 (1955). Chem. Abstr. 50, 11111 (1956).

17. U. Eisner, R. L. Erskine. J. Chem. Soc. 971 (1958).

18. P. Pratesi, V. Berti. Boll. Sci. Fac. Chim. Ind. Bologna. 188-99 (1940). Chem. Abstr. 37, 639 (1943).

19. B. Emmert, K. Diehl, F. Gollwitzer. Chem. Ber. 62, 1733 (1929). Chem. Abstr. 23, 4698 (1929).

B. Emmert, K. Diehl. Chem. Ber. 64, 130 (1931). Chem. Abstr. 25, 2997 (1931).

20. M. T. Sardina, C. Bonino. Boll. Sci. Fac. Chim. Ind. Bologna. 12, 155 (1954). Chem. Abstr. 49, 10709 (1955). A. Marinangeli, C. Bonino. Ann. Chim. (Rome) 44, 949-55 (1954). Chem. Abstr. 50, 303 (1956).

21. P. Chiorboli. Gazz. Chim. Ital. 81, 906 (1951).

22. P. Pratesi, V. Berti. Atti. Congr. Intern, Chim. 10°, Rome, 1938. 3, 313-17 (1939). Chem. Abstr. 33, 9320 (1939).

23. A. M. Buswell, J. R. Downing, W. H. Rodebush. J. Amer. Chem. Soc. 62, 2759 (1940).

24. G. B. Bonino, P. Chiorboli. Atti. Accad. Naz. Lincei, Rend., Classe Sci. Fis., Mat. Nat. 10, 104-8 (1951). Chem. Abstr. 46, 494 (1952).

25. P. Mirone, V, Lorenzelli. Ann. Chim.(Rome) 48, 881 (1958).

26. P. Mirone, V. Lorenzelli. Ann. Chim.(Rome) 49, 59 (1959).

27. L. D. Miroshnichenko, R. P. Evstigneeva, N. A. Preobrazhenskii, Zh. Obshchei Khim. 33, 2885 (1963). Chem. Abstr. 60, 2451 (1964).

28. M. K. A. Khan, K. J. Morgan. J. Chem. Soc. 2579 (1964).

29. R. Grigg. J. Chem. Soc. 5149 (1965).

30 31. "Advances in Heterocyclic Chemistry", Vol. II. Editors: A. R. Katritzky, A. J. Boulton. Academic Press (1970). Page 383-472.

32. R. A. Jones, A. G. Moritz. Spectrochim. Acta. 21, 295 (1965).

33. R. W. Guy, R. A. Jones. Aust. J. Chem. 19, 107 (1966).

34. R. W. Guy, R. A. Jones, Spectrochim. Acta. 21, 1011 (1965).

35. H. Fischer, F. Schubert. Physiol, Chem. 575, II, 1926.

36. W. Kutscher, O. Klamerth. Physiol Chem. 289, 229-33 (1952). Chem. Abstr. 49, 5433 (1955).

37. G. B. Bonino, G. Scaramelli. Chem. Ber. 75, 1948 (1942).

38. H. J. Anderson, S. J. Griffiths. Can. J. Chem. 45, 2227 (1967).

39. H. J. Anderson. Can. J. Chem. 35, 21 (1957).

40. H. J. Anderson, C. W. Huang. Can. J. Chem. 45, 897 (1967).

41. H. J. Anderson, L. C. Hopkins. Can. J. Chem. 44, 1831 (1966).

42. H. J. Anderson, S. F. Lee. Can. J. Chem. 43, 409 (1965).

43. H. J. Anderson, L. C. Hopkins. Can. J. Chem. 42, 1279 (1964).

44. H. J. Anderson, C. W. Huang. Can. J. Chem. 48, 1550 (1970).

45. M. K. A. Khan, K. J. Morgan, D. P. Morrey. Tetrahedron. 22, 2095 (1966).

46. C. E. Loader, H. J. Anderson. Tetrahedron. 25, 3879 (1969).

47. R. Mozingo. "Organic Syntheses" (Edited by E. C. Horning), coll. vol. III, 176-80. Wiley, New York, (1947).

48. P. Hodge, R. W. Rickards. J. Chem. Soc. 2543 (1963).

49. S. Gronowitz, B. Gestblom, B. Mathiasson. Arkiv Kem. 20, 407 (1963).

50a. J. Elguero, R. Jacquier, B. Shimizu. Bull. Soc. Chim. 1585 (1970).

b. M. C. Zaluski, M. Robba, M. Bonhomme. Bull. Soc. Chim. 1838 (1970).

51. R. A. Jones, T. Pojarlieva, R. J. Head. Tetrahedron, 24, 2013 (1968).

52. S. Gronowitz, A. B. Hornfeldt, B. Gestblom, R. A. Hoffman. Arkiv Kem. 18, 151 (1961).

53. R. J. Abraham, J. J. Bernstein. Can. J. Chem. 39, 905 (1961).

54. C. N. Banwell, N. Sheppard. Discussions Faraday Soc. 34, 115 (1962).

55. G. J. Karabatsos, F. M. Vane. J. Amer. Chem. Soc. 85, 3886 (1963).

56. J. B. Leane, R. E. Richards. Trans. Faraday Soc. 55, 518 (1959).

57. S. Gronowitz, R. A. Hoffman. Acta Chem. Scand. 13, 1687 (1959).

58. K. I. Dahlqvist, S. Forsen. J. Phys. Chem. 69, 4062 (1969).

59. S. Gronowitz, G. Sörlin, B. Gestblom, R. A. Hoffman. Arkiv Kem. 19, 483 (1962).

60. R. A. Hoffman, S. Gronowitz. Arkiv. Kem. 16, 515 (1962).

61. L. Arlinger, K. I. Dahlqvist, S. Forsen. Acta. Chem. Scand. 24, 672 (1970).

62. L. Arlinger, K. I. Dahlqvist, S. Forsen. Acta. Chem. Scand. 24, 662 (1970).

63. R. A. Jones, P. H. Wright. Tetrahedron Letters. 53, 5495 (1968).

64. R. A. Jones. Angew. Chem. Internat. Ed. 8, 993 (1969).

65. A. L. Jennings, J. E. Boggs. J. Org. Chem. 29, 2065 (1964).

66. A. M. Duffield, R. Bengelmans, H, Budzikiewicz, D. A. Lighter, D. H. Williams, C. Djerassi. J. Amer. Chem. Soc. 87, 805 (1965).

67. H. Budzikiewicz, C. Djerassi, A. H. Jackson, G. W. Kenner, D. J. Newman, J. M. Wilson. J. Chem. Soc. 1949 (1964).

68. A. H. Jackson, G. W. Kenner, H. Budzikiewicz, C. Djerassi, J. M. Wilson. Tetrahedron. 23, 603 (1967).

69. A. Gomez Sanchez, M. Gomez Guillen, U. Scheidegger. Carbohydrate Res. 3, 486 (1967).

70. M. Marx, C. Djerassi. J. Amer. Chem. Soc. 90, 678 (1968).

71. U. Eisner, P. H. Gore. J. Chem. Soc. 922 (1958).

72. R. L. Hinman, S. Theodoropulos. J. Org. Chem. 28, 3052 (1963).

73. P. S. Skell, G. P. Bean. J. Amer. Chem. Soc. 84, 4655 (1962).

74. J. Elguero, R. Jacquier, B. Shimizu. Bull. Soc. Chim. 2996 (1967).