This is to certify that the

thesis entitled

Part I The Synthesis of Porphyrins
Part II The Synthesis and Reactions
of Pyrroles

presented by

Kim Steven Chamberlin

has been accepted towards fulfillment
of the requirements for
Ph. D. degree in Organic Chemistry

Eugene LeGoff
Major professor

Date June 7, 1979

PART I

THE SYNTHESIS OF PORPHYRINS

PART II

THE SYNTHESIS AND REACTIONS OF PYRROLES

By

Kim Steven Chamberlin

A DISSERTATION

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

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1979

ABSTRACT

PART I

THE SYNTHESIS OF PORPHYRINS

PART II

THE SYNTHESIS AND REACTIONS OF PYRROLES

By

Kim S. Chamberlin

PART I

The most widely used models for the study of porphyrin chemistry is the sparingly soluble 2,3,7,8,12,13,17,18-octaethylporphyrin. Thus, a general synthetic route to more soluble higher homologues was developed. Condensation of 3,4-dialkylpyrroles with formaldehyde in the presence of hydrobromic acid in a large volume of ethanol gave 2,3,7,8,-12,13,17,18-octaalkylporphyrins.

Tetra(polymethylene)porphyrins were synthesized in one step from ethyl 2-methyl-3,4-polymethylenepyrrole-5-carboxylates. The 2-methylpyrroles were transformed into their monoacetoxymethyl derivatives when treated with one equivalent of lead tetraacetate in acetic acid. The resulting diesters were hydrolyzed with potassium hydroxide followed by cyclization to porphyrin in refluxing acetic acid.

PART II

Various acylmethylenetriphenylphosphoranes were synthesized by alkylation of lithiotriphenylphosphinioacetonide.

Kim S. Chamberlin

α,β-Unsaturated ketones were efficiently produced by refluxing these ylides with the appropriate aldehyde in methylene chloride. 3,4-Disubstituted pyrroles were prepared by the reaction of p-toluene-sulfonyl methyl isocyanide with the α,β-unsaturated ketones in the presence of base. Reduction of these acylpyrroles with lithium aluminum hydride led to six new 3,4-dialkylpyrroles.

Two pyrrole molecules were directly coupled or connected by one, three, or five carbon bridges to give bipyrroles, dipyrromethanes, dipyrrotrimethines, or dipyrropentadienones respectively.

To Marian

ACKNOWLEDGMENTS

I would like to thank the Department of Chemistry at Michigan State University for providing financial support in the form of teaching assistantship for the past five years. I would also like to express my appreciation to Professor Eugene LeGoff for his guidance, enthusiasm, and for arranging financial support.

"Like all young men I set out to be a genius, but mercifully laughter intervened."

Clea Lawrence Durrell

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PART I

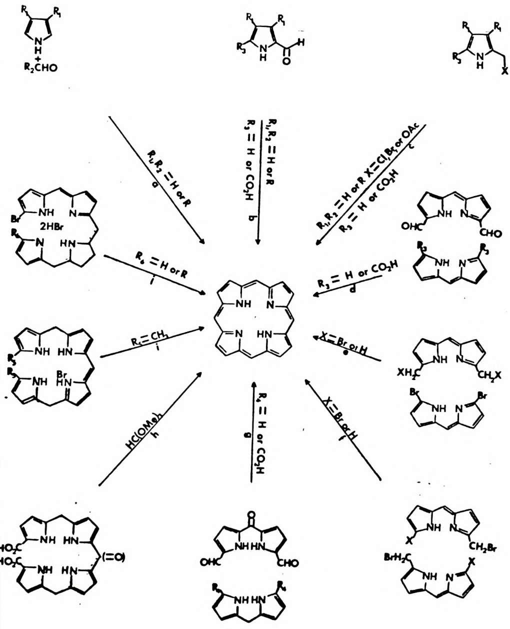
THE SYNTHESIS OF PORPHYRINS

INTRODUCTION

Porphyrins and their reduced derivatives are the primary ergy mediators of life. Chlorophylls a and b trap energy a reductive process while porphyrins release the energy the controlled oxidative processes of metabolism. Since e classic studies of Hans Fischer[1-3], culminating in the nthesis of chlorophyll[4], a great deal of knowledge of the emistry and structure of porphyrins has been accumulated.

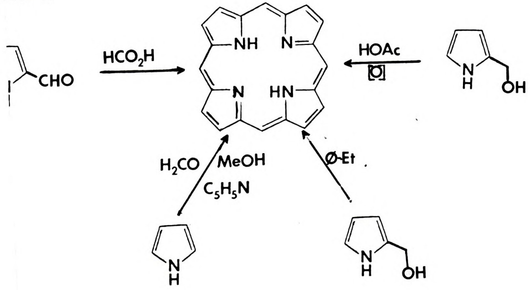
Various strategies for the synthesis of the pigments e been developed from pyrroles (a), pyrrole aldehyde (b), alomethylpyrrole (c), dipyrromethanes (d), dipyrro- nenes (e and f), dipyrroketones (g), (oxy-)bilanes (h), enes (i), or biladienes (j), Scheme 1. The relative t of each route, which is largely dependent on symmetry the nature of the substituent has been discussed in il previously[5].

The synthesis of porphyrins from pyrroles (routes a, d c) has often been used in the formation of symmetri- orphyrins. In 1935, Fischer[6] condensed pyrrole alde- in refluxing formic acid to yield the parent compound in. In the same year Rothemund[7] obtained porphin from aerobic reaction of pyrrole and formaldehyde. Neither ed yields of greater than 0.026%. A third approach eme 1

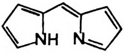

R₂CHO
R₁,R₂ = H or R
a
R₁,R₂ = H or R
R₃ = H or CO₂H
b
R₁,R₂ = H or R X=Cl,Br or OAc
R₃ = H or CO₂H
c
R₃ = H or CO₂H
d
X=Br or H
e
X=Br or H
f
R₄ = H or CO₂H
g
HC(OMe)₃
h
R₅ = CH₃
i
R₆ = H or R
j
2HBr

porphin was reported by Krol[8] who obtained a 5% yield
en 2-hydroxymethylpyrrole was refluxed in acetic acid
taining benzoyl peroxide as an oxidizing agent. The
zoyl peroxide irreversibly oxidized the porphyrinogens
ch formed as intermediates to porphyrins. Beitchman[9]
lified this procedure by using atmospheric oxygen as the
dizing agent. Although only a slightly higher yield of
phin was obtained, Beitchman found it considerably easier
purify his product. Longo and Adler[10] discovered that a
0% yield of porphin was formed when a total volume of
l of 2-hydroxymethylpyrrole was added to 3 liters of
acidified, chromatographed ethylbenzene at $100^{\circ}C$. They
orted that efforts to increase the reaction rate caused
ecrease in yield. The above reactions are shown in
eme 2.

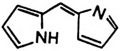
eme 2



β-Substituted porphyrins have also been synthesized many of the methods used in the preparation of porphin. e higher yields which are generally obtained are the re- lt of decreased side reactions involving electrophilic tack at the β positions and increased nucleophilicity the α position. Steric effects enhance the formation of yrryomethene (1) over its geometric isomer (2) which ld require isomerization before cyclization to porphyrin ld be possible.



1

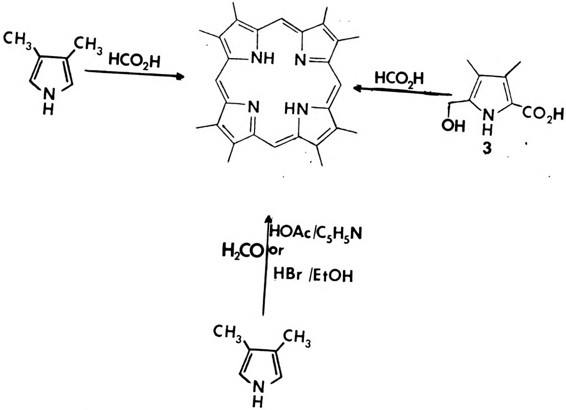


2

2,3,7,8,12,13,17,18-Octamethylporphyrin (OMP) was first rted by Fischer[11] who prepared it in 12% yield by heat- 3,4-dimethylpyrrole in formic acid. Siedel and ler[12] synthesized OMP in 47% yield by decarboxylation yrrole (3) in refluxing formic acid with concomitant ensation. An amazing 77% yield was obtained by Treibs laberele[13] when they refluxed 3,4-dimethylpyrrole with ldehyde in acetic acid and pyridine. A similar yield P was described by Cheng and LeGoff[14] using the same ants in acidified ethanol. The change of solvents rise to a far simpler work-up in the latter case, e 3.

Octaethylporphyrin (OEP) is one of the most widely used for the study of porphyrin chemistry. In addition to

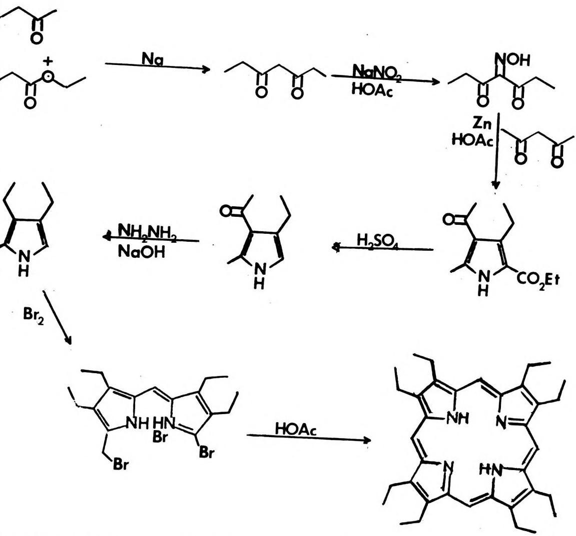
Scheme 3



ts "natural" substitution pattern, OEP is highly symmetri-
l, stable, and lacks extraneous functional groups. These
sirable properties have prompted numerous syntheses of
P. Any discussion of OEP must include the synthesis and
ansformations of its pyrrole precursors since these reac-
ons represent the major hurdle to its formation. Thus the
iginal preparation of OEP by Fischer and Bäumler (Scheme 4)
ve poor yields and the product was invariably contaminated
h bromine.

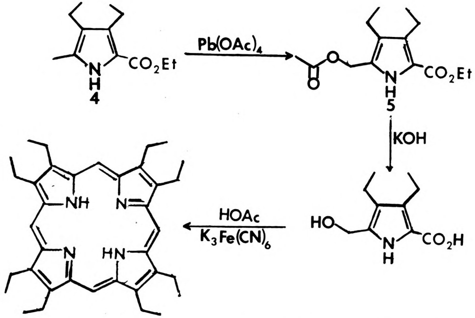
Modern routes to OEP take advantage of its symmetry by
ng condensations of monopyrroles. 2-Carboethoxy-3,4-
thyl-5-methyl pyrrole (4) is the usual intermediate in
se syntheses owing to its stability and well established

Scheme 4



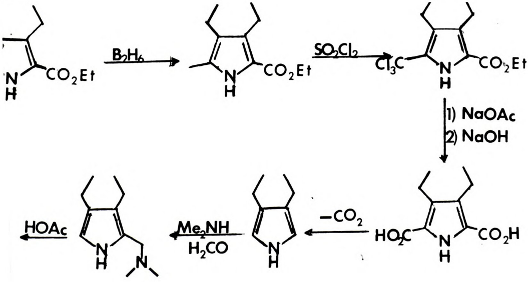
ansformations. Inhoffen, Furhop, Voight, and Brockman[16] ported the first high yield preparation of OEP, shown in heme 5. The acetoxymethylpyrrole (5) was isolated in % yield when 4 was treated with one equivalent of lead traacetate. This was then converted to the air-sensitive 4-diethyl-5-hydroxymethylpyrrole 2-carboxylic acid in 96% eld. Cyclization in the presence of potassium ferri-nide in hot acetic acid gave, after chromatography, 44% OEP. Unfortunately, this last step was reported to have en a disappointingly low yield when scaled up.

eme 5



Until recently the most widely used synthesis of OEP based on the improvements Whitlock and Hanauer[14] deped for the Eisner and Linstead[18] approach, Scheme 6. titative diborane reduction eliminated the need for pressure hydrogenation of 4-acetylpyrrole and subset chromatography of the product.

ne 6

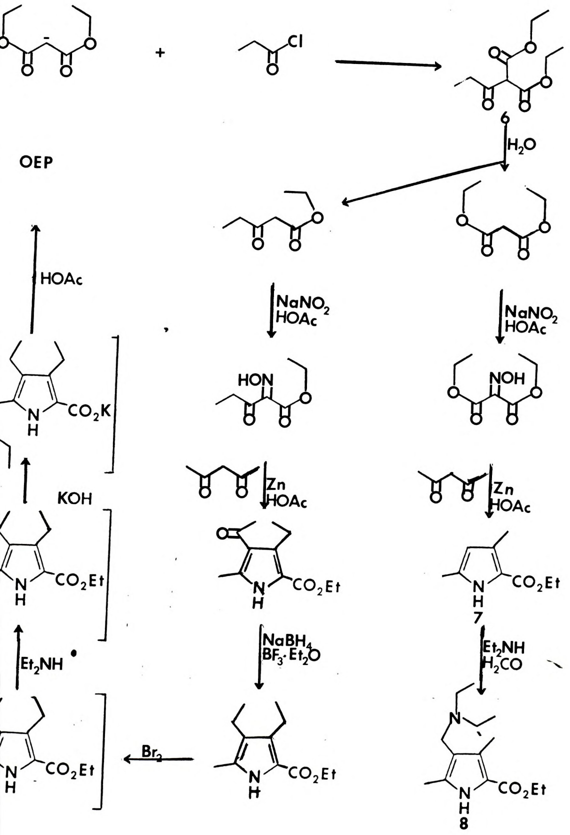


In 1976, Dolphin et al.[19] developed an efficient synthesis of OEP on a large scale, using inexpensive starting materials as shown in Scheme 7. Hydrolysis of (6) gave ethyl propionylacetate contaminated by regenerated starting material. This impurity was carried through the Knorr reaction, since even pure ethyl propionylacetate gives rise to some undesired ethyl-3,5-diethylpyrrole 2-carboxylate (7) <u>via</u> the Fischer-Fink side reaction. After reduction of the mixture, the undesired pyrrole (7) was easily removed y conversion to the Mannich base (8) followed by acid exraction. The large scale conversion of 4 to OEP owed its uccess to the avoidance of the often unreliable trichloriation of the α-methylpyrrole and lack of isolation of any ensitive intermediates.

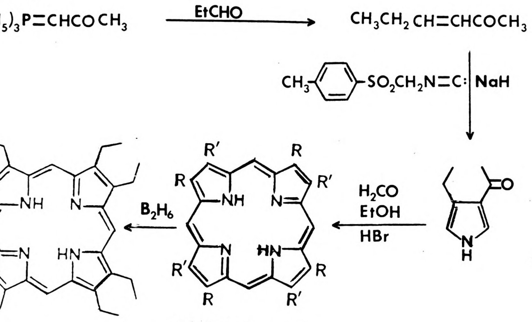
In the year following Dolphin's OEP synthesis, Cheng d LeGoff[14] published an even more efficient preparation the porphyrin, Scheme 8. Quantitative reduction of the omeric porphyrins led to a 55% overall yield for the fourep sequence in which no overly sensitive intermediates re formed.

Only two syntheses of octapropylporphyrin (OPP) have en reported. Both routes start from 2-methyl-3,4-dipropylrrole (9) which was prepared[20] by a long reaction sequence, gued by poor yields and sensitive intermediates, Scheme 9. cher[20] chose to make OPP through the dipyrromethene route le Siedel and Winkler[12] used the milder but longer method n monopyrrole (10), as shown in Scheme 10.

Scheme 7

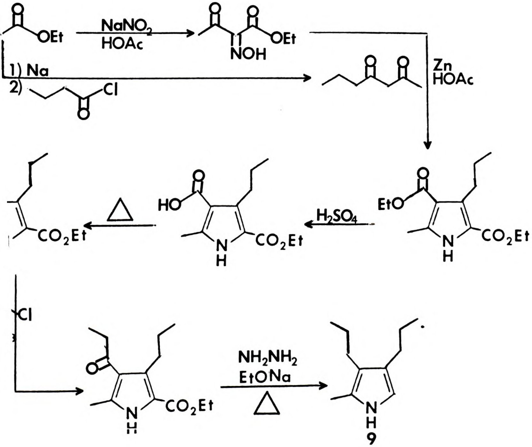

Cl
6
H_2O
OEP
HOAc
$NaNO_2$ HOAc
$NaNO_2$ HOAc
HON
NOH
Zn HOAc
Zn HOAc
CO_2K
KOH
CO_2Et
CO_2Et
CO_2Et
7
Et_2NH
$NaBH_4$ $BF_3 \cdot Et_2O$
Et_2NH H_2CO
CO_2Et
Br_2
CO_2Et
CO_2Et
8
N H

me 8

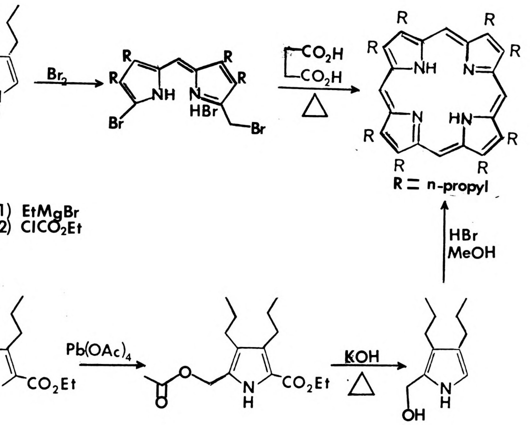


R≠R′=Et or CH$_3$CO

me 9

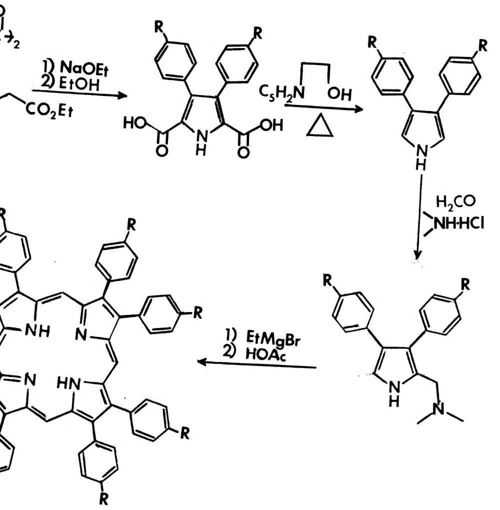


ne 10



ctaarylporphyrins[21] have been prepared as outlined in
11. This method worked well with benzil and its sub-
ed derivatives, but extension of this pyrrole synthe-
aliphatic α-diketones failed due to a facile self-
ondensation of these compounds under basic conditions.

e 11



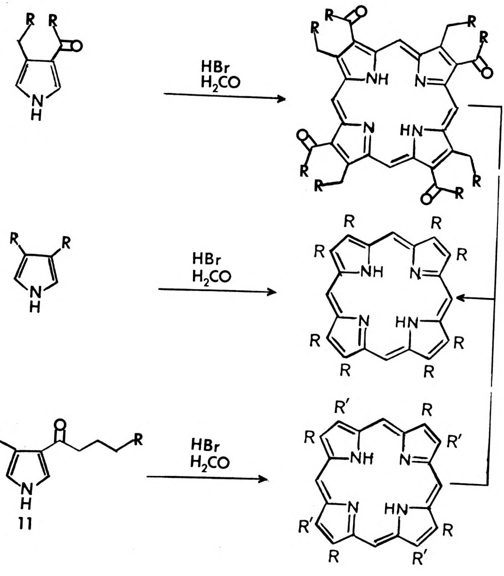
1) NaOEt
2) EtOH
CO₂Et
HO
OH
C₅H₂N OH
H₂CO
NH·HCl
1) EtMgBr
2) HOAc
NH
N
HN
R

RESULTS AND DISCUSSION

rder to provide a general synthetic route to meso-
metrical octasubstituted porphyrins a number of 3,4-
uted pyrroles (preparation in Part II) were required.
roles were effective intermediates, not only because
reactive α-positions but because the substituents in
ition prevent reaction at those sites. The relatively
nthesis of porphyrins devised by Cheng and LeGoff[14]
n because of the high yields and ease of work-up.
ategies to the target compounds (Scheme 12) seemed
y well suited. The most direct route to these por-
s by condensation of 3,4-dialkylpyrrole with formalde-
wever, 3,4-dialkylpyrroles must be synthesized from
roles and thus the number of steps in each path would
e. In addition the electron-rich 3,4-dialkylpyrroles
ir sensitive. Therefore, condensation of β-acyl-
ith formaldehyde to give acylporphyrins followed by
was attempted first.

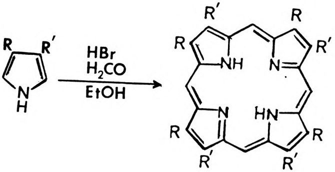
ituted thiophenes can be reduced to alkanes and
as a source of butyl or higher alkyl substituents.[22]
β-thienylpyrrole (11, R'=H) with formaldehyde and
nly trace amounts of the porphyrin. Indeed a pure
he product was never obtained. This is probably
tivation of the pyrrole by the electron withdrawing

e 12



tuent. Consequently, electrophilic attack occurs at the ositions on the thiophene moiety. Even if a modest yield phyrin could have been isolated from the resulting black r, nickel would probably have been incorporated into the from the reactions normally employed in reducing the -containing heterocycle. This would have required an nal step to obtain the metal-free product.

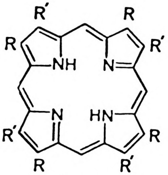
tention was next turned to porphyrin synthesis *via* the -4-acylpyrrole condensation with acidified formaldehyde. ults are tabulated in Table 1.



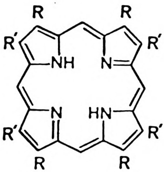
role	R	R'	% yield	porphyrin
2	$CH_3(CH_2)_2$	CH_3CH_2CO	17	12
3	$CH_3(CH_2)_3$	$CH_3(CH_2)_2CO$	57	13
	$CH_3(CH_2)_4$	$CH_3(CH_2)_3CO$	34	14
	$CH_3(CH_2)_5$	$CH_3(CH_2)_4CO$	42	15
	$CH_3(CH_2)_6$	$CH_3(CH_2)_5CO$	40	16
	$CH_3(CH_2)_7$	$CH_3(CH_2)_6CO$	36	17

isomeric porphyrins are possible in the condensation nsymmetrical pyrroles, Figure 1. Tetraacetyltetra- yrin, which had been separated by high pressure liquid

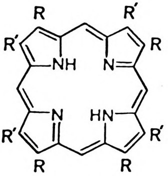
1



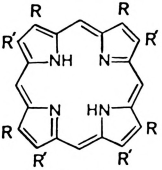
Type 1



Type 2



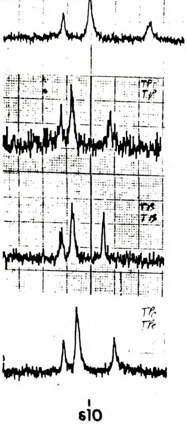
Type 3



Type 4

ɔgraphy, was obtained as a 2:4:1 mixture of Type II, ;, and Type IV isomers respectively[23]. Comparison of ı region in the PMR of the new porphyrins with the mixture of tetraacetyltetraethylporphyrin shows that probably a statistical 1:1:4:2 mixture of isomers gure 2. This is consistent with the distribution re- from the condensation of 3-tert-butylpyrrole with ıyde.

ıe results suggest that steric and electronic factors le effect on the formation of porphyrin isomers conditions used. A possible mechanism is shown in .



R,R' = CH_3CH_2-, or CH_3CO

R,R' = $CH_3(CH_2)_2$-, or CH_3CH_2CO

R,R' = $CH_3(CH_2)_3$-, or $CH_3(CH_2)_2CO$

R,R' = $CH_3(CH_2)_4$-, or $CH_3(CH_2)_3CO$

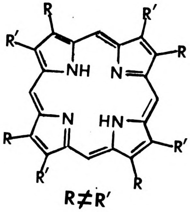
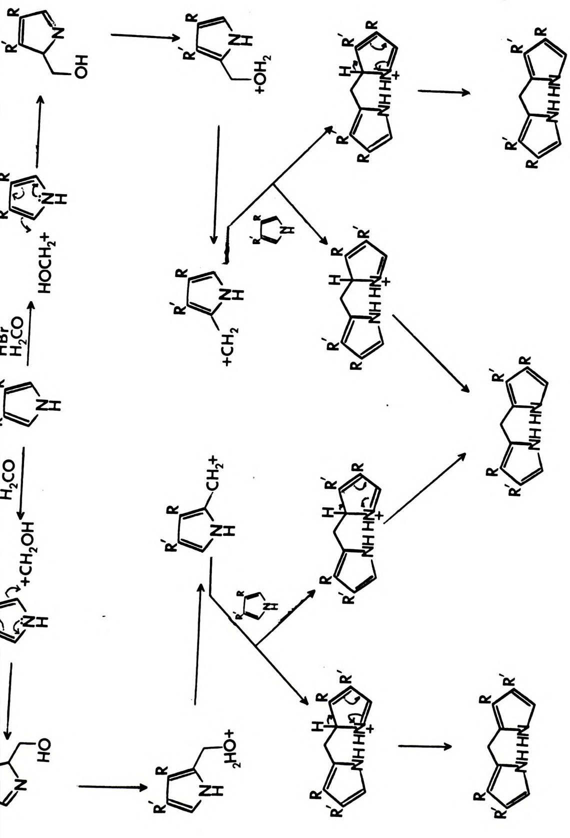
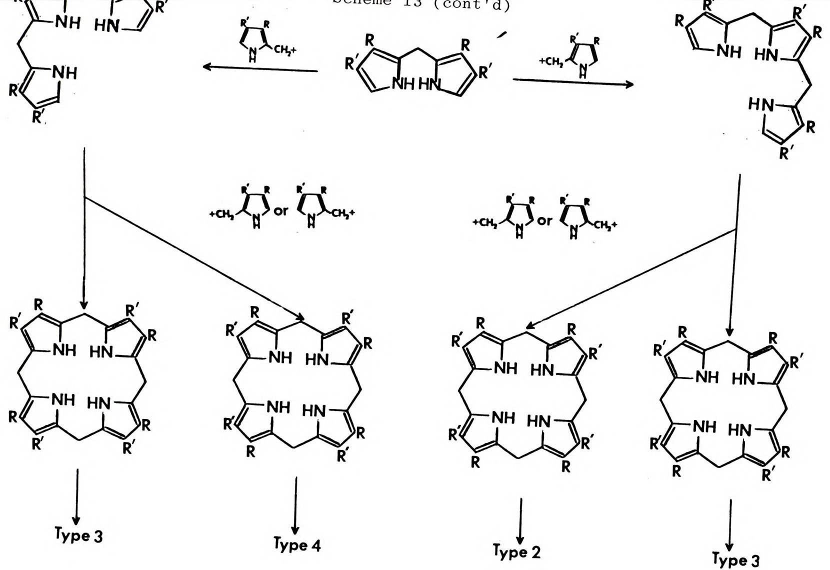


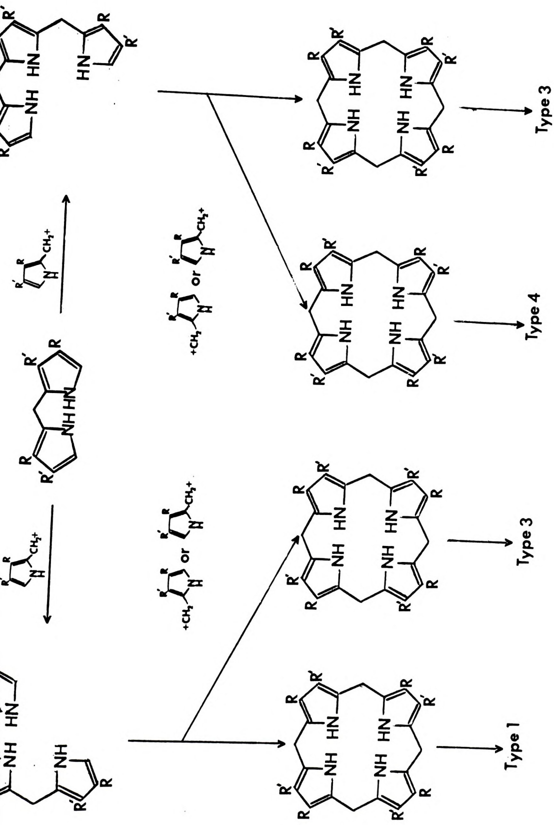
Figure 2. PMR of meso protons of porphyrin isomers.

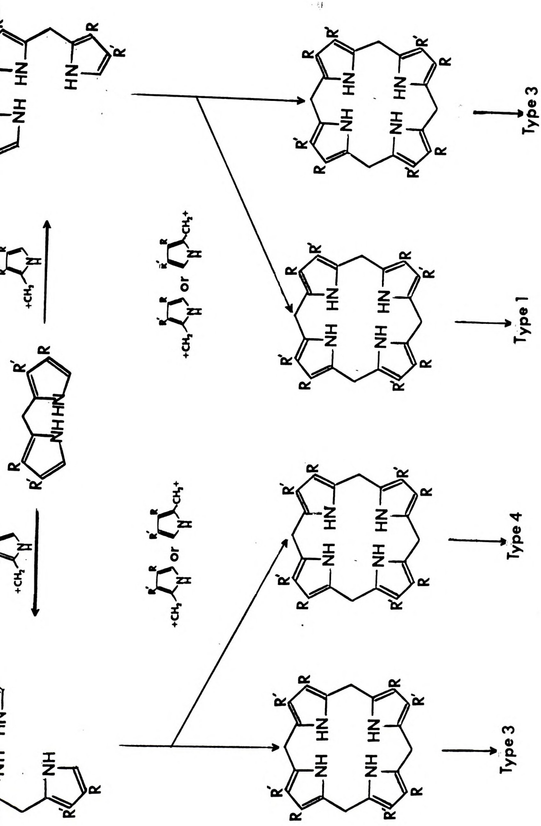


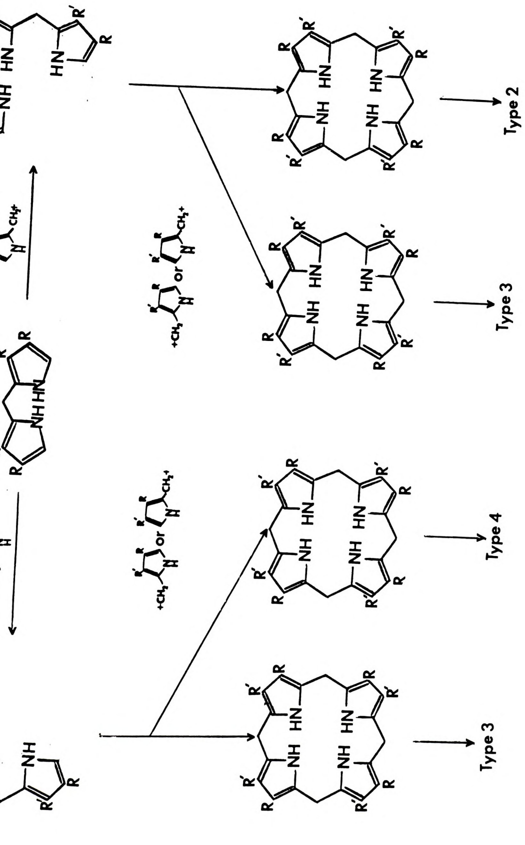
H_2CO
HBr
H_2CO
$HOCH_2^+$
$+CH_2OH$
$+OH_2$
$_2HO+$
$+CH_2$
CH_2^+

Scheme 13 (cont'd)

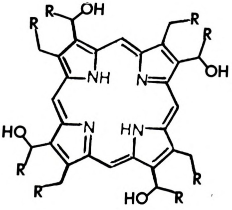



Type 3
Type 4
Type 3
Type 1
or
or
CH_2^+
NH
HN
R
R′


Type 3
Type 1
Type 4
Type 3
or
or


+CH₂
CH₂+
or
Type 2
Type 3
Type 4
Type 3

One possible route to symmetrical porphyrin was to
duce the tetraalkyltetraacylporphyrin to octaalkyl-
rphyrin. Diborane reduction resulted in a product which
ssessed a visible spectrum similar to OEP but required
re polar solvents to elute it from silica columns. The
ne result was obtained for 1) commercial diborane in
rahydrofuran, 2) freshly prepared diborane in tetrahydro-
an, 3) diborane in methylene chloride, 4) diborane gen-
ted *in situ*, 5) tetrabutylammonium borohydride, and
diborane stored over sodium borohydride. The major band
lated from chromatography was identical in every respect
he sole product obtained through the use of sodium
hydride. Infrared and mass spectroscopy confirmed that
product was a mixture of isomers of tetraalkyltetra-
oxyalkylporphyrins (18). More vigorous conditions gave
to visible spectra which indicated proportionately
er concentrations of chlorin, formed by hydroboration
ne porphyrin ring.

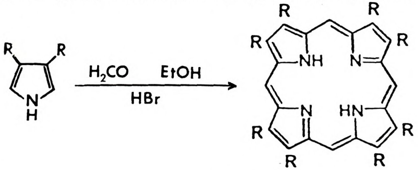


18

Reduction of acylporphyrins with lithium aluminum lride resulted in the formation of aluminum-containing phyrins. Aluminum can not be removed easily from the and and thus represents a poor route to the metal-free phyrins. Other reduction methods, such as Clemmensen Wolff-Kishner reactions, resulted in the destruction the porphyrin moiety.

Since the various methods of reducing ketones to hydro- bons proved to be unsuitable for ketoporphyrins 12-17, orts were directed to forming the target compounds from netrical pyrroles. The 3,4-dialkylpyrroles were con- ed with formaldehyde in acidified ethanol under nitrogen. r refluxing for one day, the cooled solution was exposed ir for one week to permit oxidation to the porphyrin. results of these reactions are shown in Table 2.

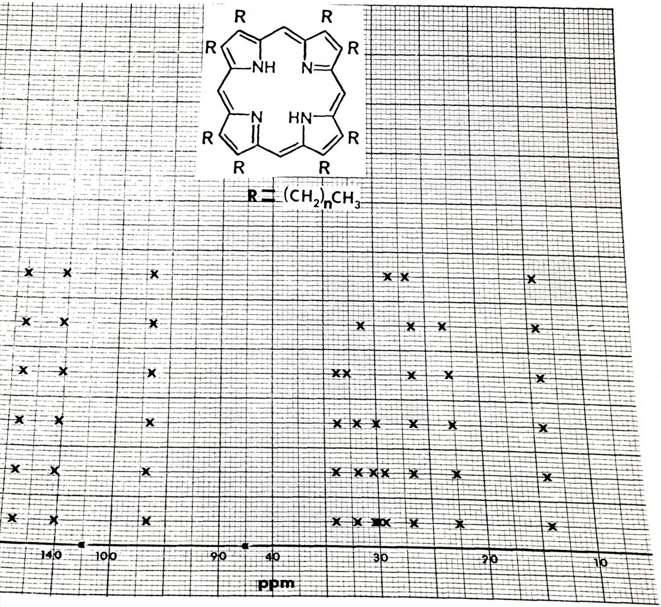
2



yrrole	R	% yield	porphyrin
60	$CH_3(CH_2)_2$-	32	19
61	$CH_3(CH_2)_3$-	33	20
62	$CH_3(CH_2)_4$-	40	21
63	$CH_3(CH_2)_5$-	11	22
64	$CH_3(CH_2)_6$-	11	23
65	$CH_3(CH_2)_7$-	22	24

The ^{13}CMR of these alkyl porphyrins are shown in able 3. As expected, the chemical shifts of the ring arbons are unaffected by different alkyl groups. The meso, β", and "α" carbons appear at 96.8, 140.2, and 144.1 ± .1 ppm respectively. The assignment of the alkyl carbons see experimental) is based on the Grant and Paul equation[25] sing a predetermined pentylporphyrin as the model[26]. The alculated chemical shifts are within ± 0.5 ppm of the tual values.

ble 3

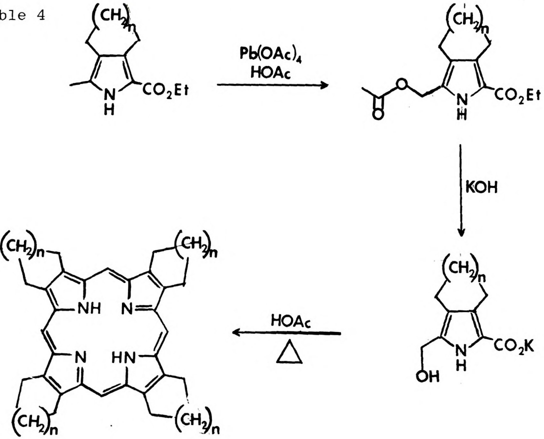


A new class of symmetrical porphyrins was synthesized
sing alkyl 2-methyl-3,4-polymethylenepyrrole 5-carboxylate
s an intermediate. This approach was preferable to the
se of 3,4-disubstituted pyrroles, since the tetrasubsti-
uted pyrroles are simpler to synthesize and less air
ensitive.

The usually near quantitative monohalogenation of the
rrole methyl group did not proceed as expected with these
rroles. When ethyl 2-methyl-3,4-trimethylenepyrrole
carboxylate (52) was treated with one equivalent of bromine,
greenish solution developed. This is in stark contrast to
e light orange to red hue normally obtained at the end of
e reaction. Upon treatment with diethylamine and work-up,
st of the starting pyrrole was recovered. The greenish
lution may have been a charge-transfer complex since
role-halogen complexes of this type are known[27]. Since
ochlorination of 52 with sulfuryl chloride also gave back
arge amount of starting material, monoacetoxymethyl-
roles were synthesized using one equivalent of lead
raacetate. Due to difficulties in the purification of
se diesters, they were often hydrolyzed to the corre-
ding hydroxy acids which were then transformed into
hyrins without isolation. The reactions and results
summarized in Table 4.

Another variation in the synthesis of 27 was to use
2-formyl-3,4-decamethylenepyrrole 5-carboxylate (69).
pyrrole, which was synthesized from 54 using two

ble 4

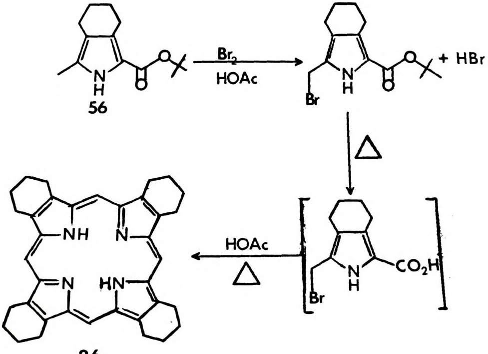


pyrrole	n	% yield from methylpyrrole	porphyrin
52	3	12	25
53	4	27	26
54	10	12	27

alents of lead tetraacetate, gave only a 1% yield of yrin when treated with potassium hydroxide followed fluxing in acetic acid. The addition of a second ron withdrawing group to the pyrrole ring apparently ises the acidity of the nitrogen hydrogen to such an that it is removed by base at a much faster rate he ester is hydrolyzed.

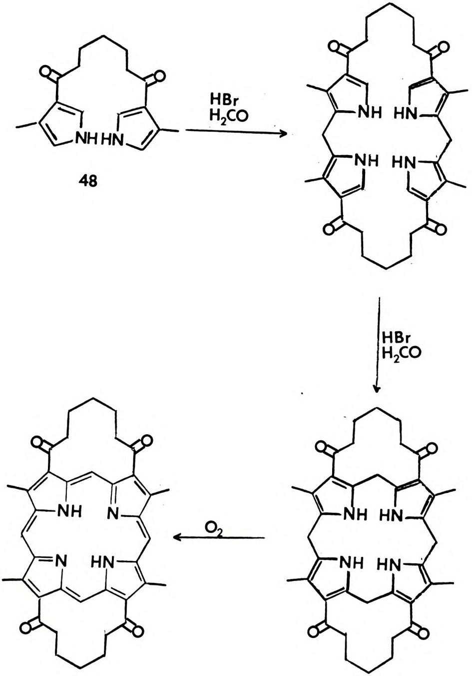
A third approach to these systems involved the "one-
ot" reaction of tert-butyl 2-methyl-3,4-trimethylenepyrrole
-carboxylate (56) with bromine. Tert-butylpyrrole esters
re rapidly hydrolyzed by acids. Addition of bromine to
rrole (56) in cold acetic acid under nitrogen gave an
ange solution which rapidly turned dark red when refluxed
d exposed to air. The bromine reacted to give 2-bromo-
thylpyrrole and hydrobromic acid. This acid hydrolyzed
e ester which decarboxylated to give 27% of porphyrin 26,
heme 14.

eme 14



In an attempt to synthesize an isomerically pure
II porphyrin, β-bridged pyrrole (48) was condensed
formaldehyde in acidified ethanol, Scheme 15. The

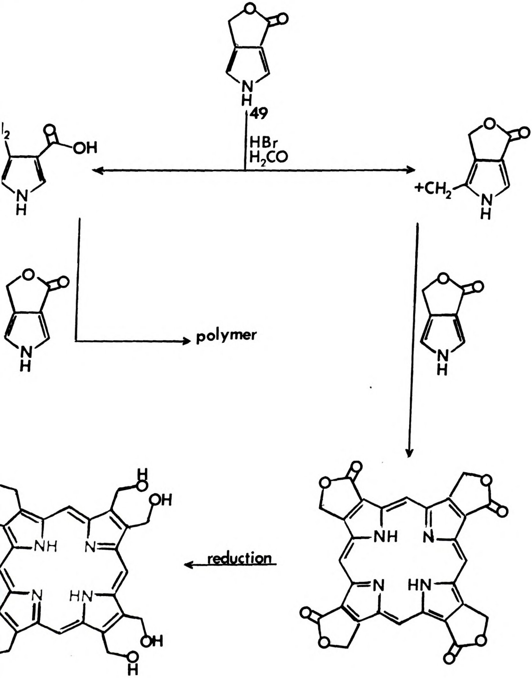
Scheme 15



sible spectrum showed that the reaction stopped at the pyrromethene or porphodimethene stage. This indicates at the reaction failed either because the formaldehyde uld not find its way inside the cavity of the initially rmed dipyrromethene, or more likely, the attack of the ectrophile was not selective. The α-position adjacent the methyl is more nucleophilic than α-position next the ketone. This should lead to the formation of the metrical dipyrromethene. If on the other hand the re- ion lacked sufficient regioselectivity, then formation the unsymmetrical dipyrromethene could occur and prevent hyrin formation due to steric strain.

It was envisioned that a symmetrical porphyrin bear- functionalized substituents could be formed via the ensation of pyrrole (49) by the usual conditions. Un- unately the lactone ring proved labile and provided an lly effective electrophile in the β-position. A red luble polymer was the sole product obtained. This is ned in Scheme 16.

heme 16



EXPERIMENTAL

neral Procedure

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

The infrared spectra were recorded on a Perkin-Elmer
del 237B or 137 spectrometer. The PMR spectra were ob-
ned on a Varian T-60 spectrometer with chemical shifts
orted in δ-units measured from tetramethylsilane as the
ernal standard. The ^{13}CMR were obtained on a Varian
-20 spectrometer with chemical shifts reported in δ-units
n $CDCl_3$ as the internal standard. The UV and visible
ctra were reporded on a Unicam SP-800 spectrometer using
n quartz cells. A Hitachi Perkin-Elmer RMU-6 mass
ctrometer was used to obtain the mass spectra.

Microanalyses were performed by Spang Microanalysis
ratory, Eagle Harbor, Michigan. Although not all of
analyses are within the generally accepted limits, they
included for completeness. The tendency of porphyrins
omplex metals and the difficulty in crystallizing these
cules frequently causes such deviations.

Tetrapropyltetrapropyrylporphyrin (12), tetrabutyltetrabutyryrlporphyrin (13), tetrapentyltetrapentyrylporphyrin (14), tetrahexyltetrahexyrylporphyrin (15), tetraheptyltetraheptyrylporphyrin (16), and tetraoctyltetraoctyrylporphyrin (17)

General Procedure:

A solution of pyrrole (42-47) (1.5 mmol), 37% aqueous formaldehyde (6 ml), 48% hydrobromic acid (1 ml), in absolute ethanol was refluxed for 24 hours. The reaction mixture was then allowed to stand at room temperature for one eek. The ethanol was removed under reduced pressure. fter neutralizing the residue with aqueous sodium carboate it was extracted with methylene chloride. The ethylene chloride was removed and the residue chromatoraphed on silica gel (methylene chloride/1% methanol luent). The yields are listed in Table 1 on page 16. ectral characteristics of 12, 13, 14, 15, 16, and 17 e summarized below.

traprool tetrapropyrylporphyrin (12)

λ_{max} (CHCl$_3$): 428 nm, 523, 555, 594, 648; IR (CHCl$_3$): 90 cm^{-1} (N-H), 1660 (C=O); PMR (CDCl$_3$): δ-3.44 (broad s, , N-$\underline{H}$), 1.25 (m, 12H, CH$_2$CH$_2$C$\underline{H}_3$), 1.52 (m, 12H, COCH$_2$C$\underline{H}_3$), 25 (m, 8H, CH$_2$C$\underline{H}_2$CH$_3$), 3.59 (m, 8H, COC$\underline{H}_2$), 4.12 (m, 8H, $_2$-porphyrin), 10.00 (s, 1H, meso-$\underline{H}$), 10.40 (s, 2H, meso-$\underline{H}$), 61 (s, 1H, meso-$\underline{H}$); MS (70 eV): m/e = 702 (parent).

Anal. Calcd for $C_{44}H_{54}N_4O_4$: C, 75.18; H, 7.79; N, 7.97
Found: C, 74.90; H, 7.58; N, 8.22.

Tetrabutyltetrabutyrylporphyrin (13)

λ_{max} ($CHCl_3$): 427 nm (ε = 240,000), 522 (16,000), 556 (8,900), 594 (7,100), 648 (3,100); IR ($CHCl_3$): 3400 cm^{-1} (N-H), 1655 (C=O); PMR ($CDCl_3$): δ-3.39 (broad s, 2H, N-$\underline{H}$), 1.03-1.07 (m, 24H, $C\underline{H}_3$), 1.75-2.25 (m, 24H, $CH_2C\underline{H}_2C\underline{H}_2CH_3$ and $COCH_2C\underline{H}_2CH_3$), 3.59 (m, 8H, $COC\underline{H}_2$), 4.20 (m, 8H, $C\underline{H}_2$-porphyrin), 10.09 (s, 1H, meso-$\underline{H}$), 10.45 (s, 2H, meso-$\underline{H}$), 10.60 (s, 1H, meso-$\underline{H}$); MS (70 eV): m/e = 814 (parent).

Anal. Calcd for $C_{52}H_{70}N_4O_4$: C, 76.62; H, 8.66; N, 6.87
Found: C, 76.28; H, 8.36; N, 6.93.

etrapentyltetrapentyrylporphyrin (14)

λ_{max} ($CHCl_3$): 427 nm, 521, 556, 593, 647; IR ($CHCl_3$): 300 cm^{-1} (N-H), 1665 (C=O); PMR ($CDCl_3$): δ-3.60 (broad s, H, N-$\underline{H}$), 0.98-1.20 (m, 24H, $C\underline{H}_3$), 1.43-2.34 (m, 40H, $H_2(C\underline{H}_2)_3CH_3$ and $COCH_2(C\underline{H}_2)_2CH_3$), 3.60 (m, 8H, $COC\underline{H}_2$), 4.05 n, 8H, $C\underline{H}_2$-porphyrin), 9.70 (s, 1H, meso-$\underline{H}$), 10.18 (s, 2H, eso-$\underline{H}$), 10.39 (s, 1H, meso-$\underline{H}$); MS (70 eV): m/e = 926 arent).

Anal. Calcd for $C_{60}H_{86}N_4O_4$: C, 77.71; H, 9.35; N, 6.04
Found: C, 77.05; H, 9.20; N, 6.36.

trahexyltetrahexyrylporphyrin (15)

λ_{max} ($CHCl_3$): 426 nm, 520, 556, 592, 647; IR ($CHCl_3$): 00 cm^{-1} (N-H), 1670 (C=O); PMR ($CDCl_3$): δ-3.34 (broad s, N-$\underline{H}$), 0.70-1.06 (m, 24H, $C\underline{H}_3$), 1.10-2.50 (m, 56H, $(C\underline{H}_2)_4CH_3$ and $COCH_2(C\underline{H}_2)_3CH_3$), 3.53 (m, 8H, $COC\underline{H}_2$), 4.10 8H, $C\underline{H}_2$-porphyrin), 10.00 (s, 1H, meso-$\underline{H}$), 10.30 (s,

2H, meso-H), 10.45 (s, 1H, meso-H); MS (70 eV): m/e = 1038 (parent).

Tetraheptyltetraheptyrylporphyrin (16)

λ_{max} ($CHCl_3$): 427 nm, 522, 558, 594, 650; IR ($CHCl_3$): 3300 cm^{-1} (N-H), 1665 (C=O); PMR ($CDCl_3$): δ-4.03 (broad s, 2H, N-H), 0.80-1.13 (m, 24H, CH_3), 1.15-2.50 (m, 72H, $CH_2(CH_2)_5CH_3$ and $COCH_2(CH_2)_4CH_3$), 3.57 (m, 8H, $COCH_2$), 4.08 (m, 8H, CH_2-porphyrin), 9.50 (s, 1H, meso-H), 10.15 (s, 2H, meso-H), 10.42 (s, 1H, meso-H); MS (70 eV): m/e = 1150 (parent).

Tetraoctyltetraoctyrylporphyrin (17)

λ_{max} ($CHCl_3$): 427 nm, 520, 555, 594, 650; IR ($CHCl_3$): 3290 cm^{-1} (N-H), 1665 (C=O); PMR ($CDCl_3$): δ-4.17 (broad s, 2H, N-H), 0.70-0.97 (m, 24H, CH_3), 1.00-2.44 (m, 88H, $H_2(CH_2)_6CH_3$ and $COCH_2(CH_2)_5CH_3$), 3.50 (m, 8H, $COCH_2$), 3.90 m, 8H, CH_2-porphyrin), 9.35 (s, 1H, meso-H), 10.10 (s, 2H, eso-H), 10.37 (s, 1H, meso-H); MS (70 eV): m/e = 1262 parent).

etrabutyltetra(α-hydroxy)butylporphyrin (18)

Tetrabutyltetrabutyrylporphyrin (0.32 mmol) was dis- olved in 150 ml of tetrahydrofuran and cooled in an ice ath under nitrogen. Diborane (4 ml of a 1N tetrahydrofuran olution) was added and the reaction mixture was stirred at for one hour and at room temperature for four hours. The action was quenched with hydrochloric acid (45 ml of a 5% ueous solution). The mixture was poured into 100 ml of an aqueous 1M sodium carbonate solution and the product extracted into methylene chloride. After removal of the solvent, the residue was chromatographed on alumina using 8% methanol in chloroform as eluent. Removal of the solvent yielded 0.278 mmol (87%) of 18: λ_{max} ($CHCl_3$): 408 nm, 508, 540, 575, 626; IR ($CHCl_3$): 3425 cm^{-1} (O-H), 3210 (N-H); MS (70 eV): m/e = 750 (parent - $4H_2O$).

Octapropylporphyrin (19), octabutylporphyrin (20), octapentylporphyrin (21), octahexylporphyrin (22), octaheptylporphyrin (23), and octaoctylporphyrin (24)

General Procedure:

A solution of pyrrole (60-65) (2.5 mmol), 37% aqueous formaldehyde (12 ml), and 48% hydrobromic acid (0.5 ml) in 100 ml of absolute alcohol was refluxed for 24 hours under nitrogen and for an additional 24 hours exposed to the atmosphere. The resulting solution was allowed to stand at room temperature for seven days. The ethanol was removed under reduced pressure. After neutralizing the residue with queous sodium carbonate, the organics were extracted into ethylene chloride. The methylene chloride was removed and he residue chromatographed on silica gel (1:1 hexane/toluene luent). The yields are listed in Table 2 on page 25. Spec-ral characteristics of 19, 20, 21, 22, 23, and 24 are ummarized below.

Octapropylporphyrin (19)

mp. sintered 275-278° (lit.[20,21] sintered 276°); λ_{max} ($CHCl_3$): 399 nm, 499, 535, 569, 622; IR ($CHCl_3$): 3310 cm^{-1} (N-H); PMR ($CDCl_3$): δ-3.44 (broad s, 2H, N-$\underline{H}$), 1.40 (t, 24H, $C\underline{H}_3$), 2.42 (hextet, 16H, $C\underline{H}_2CH_3$), 4.03 (t, 16H, $C\underline{H}_2$-porphyrin), 9.97 (s, 4H, meso-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ14.72 ($\underline{C}H_3$), 26.87 ($\underline{C}H_2CH_3$), 28.62 ($\underline{C}H_2$-porphyrin), 96.90 (meso carbons), 140.17 ("β" carbons), 144.35 ("α" carbons); MS (70 eV): m/e = 646 (parent).

Anal. Calcd for $C_{44}H_{62}N_4$: C, 81.68; H, 9.66; N, 8.66
Found: C, 81.35; H, 9.44; N, 8.53.

Octabutylporphyrin (20)

mp. sintered 266-267°; λ_{max} ($CHCl_3$): 400 nm, 500, 535, 569, 622; IR ($CHCl_3$): 3310 cm^{-1} (N-H); PMR ($CDCl_3$): δ-3.65 (broad s, 2H, N-$\underline{H}$), 1.12 (t, 24H, $C\underline{H}_3$), 1.77 (m, 16H, $C\underline{H}_2CH_3$), 2.20 (m, 16H, $C\underline{H}_2CH_2CH_3$), 3.95 (t, 16H, $C\underline{H}_2$-porphyrin), 9.85 s, 4H, meso-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ14.20 ($\underline{C}H_3$), 23.42 ($\underline{C}H_2CH_3$), 6.32 ($\underline{C}H_2$-porphyrin), 36.10 ($\underline{C}H_2$-CH_2CH_3), 96.70 (meso carbons), 40.17 ("β" carbons), 144.07 ("α" carbons); MS (70 eV): /e = 758 (parent).

Anal. Calcd for $C_{52}H_{78}N_4$: C, 82.26; H, 10.36; N, 7.38
Found: C, 82.93; H, 9.57; N, 7.18.

tapentylporphyrin (21)

mp. sintered 222-227°; λ_{max} ($CHCl_3$): 401 nm, 500, 535, 9, 594, 621; IR ($CHCl_3$): 3370 cm^{-1} (N-H); PMR ($CDCl_3$):

δ-3.58 (broad s, 2H, N-$\underline{H}$), 1.08 (t, 24H, $C\underline{H}_3$), 1.75 (m, 32H, $C\underline{H}_2C\underline{H}_2CH_3$), 2.36 (m, 16H, $C\underline{H}_2CH_2CH_2CH_3$), 4.03 (t, 16H, $C\underline{H}_2$-porphyrin), 10.00 (s, 4H, meso-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ14.06 ($\underline{C}H_3$), 22.74 ($\underline{C}H_2CH_3$), 26.61 ($\underline{C}H_2$-porphyrin), 32.56 ($\underline{C}H_2CH_2CH_3$), 33.56 ($\underline{C}H_2CH_2CH_2CH_3$), 96.79 (meso carbons), 40.22 ("β" carbons), 144.19 ("α" carbons); MS (70 eV): /e = 870 (parent).

<u>Anal</u>. Calcd for $C_{60}H_{94}N_4$: C, 82.70; H, 10.88; N, 6.43
Found: C, 82.88; H, 10.74; N, 6.40.

ctahexylporphyrin (**22**)

mp. sintered 173.5-175.5°; λ_{max} ($CHCl_3$): 399 nm, 500, 34, 569, 622; IR ($CHCl_3$): 3295 cm^{-1} (N-H); PMR ($CDCl_3$): -3.45 (broad s, 2H, N-$\underline{H}$), 1.08 (t, 24H, $C\underline{H}_3$), 1.70 (m, 48H, $_2C\underline{H}_2C\underline{H}_2CH_3$), 2.45 (m, 16H, $C\underline{H}_2CH_2CH_2CH_2CH_3$), 4.15 (t, 16H, $_2$-porphyrin), 10.08 (s, 4H, meso-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ14.03 H_3), 22.64 ($\underline{C}H_2CH_3$), 26.67 ($\underline{C}H_2$-porphyrin), 30.01 $H_2(CH_2)_2CH_3$), 31.90 ($\underline{C}H_2CH_2CH_3$), 33.80 ($\underline{C}H_2(CH_2)_3CH_3$), .78 (meso carbons), 140.31 ("β" carbons), 144.08 ("α" rbons); MS (70 eV): m/e = 982 (parent).

taheptylporphyrin (**23**)

mp. 151-152°; λ_{max} ($CHCl_3$); 400 nm, 501, 535, 569, 622; ($CHCl_3$): 3310 cm^{-1} (N-H); PMR ($CDCl_3$): δ1.05 (t, 24H,), 1.57 (m, 64H, $(C\underline{H}_2)_4CH_3$), 2.47 (m, 16H, $C\underline{H}_2(CH_2)_4CH_3$), 5 (t, 16H, $C\underline{H}_2$-porphyrin), 10.05 (s, 4H, meso-$\underline{H}$), N-H not erved; ^{13}CMR ($CDCl_3$): δ14.01 ($\underline{C}H_3$), 22.66 ($\underline{C}H_2CH_3$), 26.63 $_2$-porphyrin), 29.42 ($\underline{C}H_2CH_2CH_4CH_3$), 30.34 ($\underline{C}H_2(CH_2)_3CH_3$),

31.90 ($\underline{C}H_2CH_2CH_3$), 33.91 ($\underline{C}H_2(CH_2)_4CH_3$), 96.78 (meso carbons), 140.22 ("β" carbons), 144.08 ("α" carbons); MS (70 eV): m/e = 1094 (parent).

Anal. Calcd for $C_{76}H_{126}N_4$: C, 83.30; H, 11.59; N, 5.11
Found: C, 83.61; H, 11.48; N, 4.91.

ctaoctylporphyrin (24)

mp. 140.5-141°; λ_{max} ($CHCl_3$): 400 nm, 500, 536, 568,
21; IR ($CDCl_3$): 3310 cm^{-1} (N-H); PMR ($CDCl_3$): δ-3.53 (broad
, 2H, N-$\underline{H}$), 1.00 (t, 24H, $C\underline{H}_3$), 1.48 (m, 80H, $(C\underline{H}_2)_5CH_3$),
.42 (m, 16H, $C\underline{H}_2(CH_2)_5CH_3$), 4.10 (t, 16H, $C\underline{H}_2$-porphyrin),
0.03 (s, 4H, meso-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ14.01 ($\underline{C}H_3$), 22.63
H_2CH_3), 26.63 ($\underline{C}H_2$-porphyrin), 29.39 ($\underline{C}H_2(CH_2)_2CH_3$), 29.74
$H_2(CH_2)_3CH_3$), 30.41 ($\underline{C}H_2(CH_2)_4CH_3$), 31.93 ($\underline{C}H_2CH_2CH_3$),
3.93 ($\underline{C}H_2(CH_2)_5CH_3$), 96.79 (meso carbons), 140.21 ("β" car-
ns), 144.19 ("α" carbons); MS (70 eV): m/e = 1206 (parent).

Anal. Calcd for $C_{84}H_{142}N_4$: C, 83.51; H, 11.85; N, 4.64
Found: C, 83.25; H, 11.71; N, 4.70.

2-3,4-5,6-7,8-Tetra(trimethylene)porphyrin (25)

Ethyl 2-methyl-3,4-trimethylenepyrrole 5-carboxylate
3) (0.24, 1.3 mmol) was dissolved in 10 ml of acetic acid.
ad tetraacetate (0.6g) was added and the mixture was
rred at room temperature for 10 min. Water (50 ml) was
ed and the product was extracted into methylene chloride.
er removal of the methylene chloride, 0.25 g of potassium
roxide in 5 ml of water and 5 ml of ethanol was added to
residual oil. This solution was refluxed for 2 hours,

cooled, and diluted with 20 ml of acetic acid. This acidic solution was refluxed for 1 hour while air was blown over the surface. After sitting one day, the black solution was poured into water and extracted into methylene chloride. The methylene chloride was removed under reduced pressure and the residue chromatographed on alumina using 1% methanol n methylene chloride as the eluent. Removal of the solvent ave 0.017 g (12%) of 25: λ_{max} ($CHCl_3$): 419 nm, 516, 552, 88, 638; MS (70 eV): m/e = 470 (parent).

,2-3,4-5,6-7,8-Tetra(tetramethylene)porphyrin (26)

) Ethyl 2-methyl-3,4-tetramethylenepyrrole 5-carboxylate 1.78 g, 8.6 mmol) was dissolved in 10 ml of acetic acid. ead tetraacetate (4.2 g) was added over a 15 min period. ter (100 ml) was added and the product extracted into thylene chloride. The methylene chloride was removed der reduced pressure and 2 g of potassium hydroxide in ml of water and 10 ml of ethanol was added to the residual oil. This solution was refluxed for 2 hours, cooled, d diluted with 20 ml of acetic acid. The acidic solution s refluxed for one hour while air was blown over the surce. After evaporation of the solvent, the porphyrin was omatographed on alumina using 1% methanol in methylene oride as an eluent to yield 0.3 g (27%) of 26.

2-Carbo-t-butoxy-3,4-tetramethylene-5-methylpyrrole) (1.17 g, 5 mmol) was dissolved in 10 ml of acetic acid cooled to 0^{o} under nitrogen. Sulfuryl chloride (5 mmol)

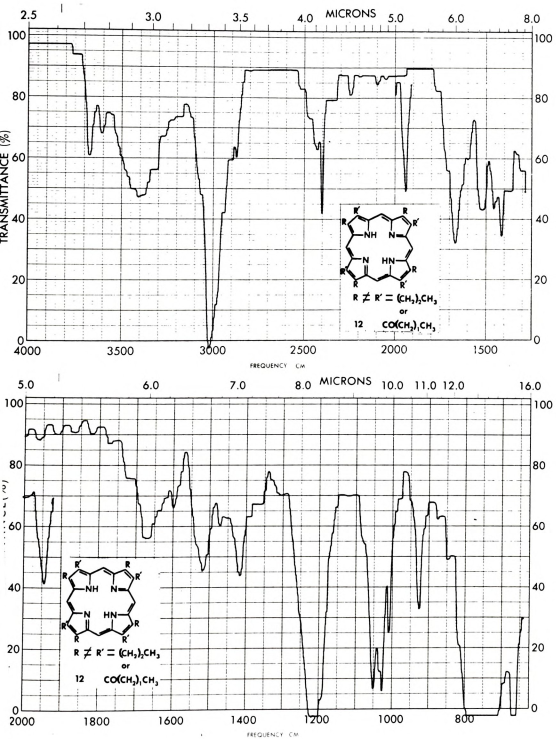
in 20 ml of acetic acid was added dropwise to the pyrrole solution over 15 min. The initially light yellow solution turned green. After stirring for one hour at room temperature, the nitrogen was removed and the solution was refluxed. Heating was continued for three hours and the solution was allowed to sit for a week at room temperature. After removal of the solvent the residue was chromatographed on silica gel using 1% methanol in methylene chloride as eluent to yield 0.02 g (1%) of 26: λ_{max} ($CHCl_3$): 419 nm, 518 nm, 553, 589, 638; PMR ($CDCl_3$): δ2.58 (m, 16H, porphyrin-$CH_2C\underline{H}_2C\underline{H}_2CH_2$-porphyrin), 4.17 (m, 16H, porphyrin-$C\underline{H}_2CH_2CH_2C\underline{H}_2$-orphyrin), 10.00 (s, 4H, meso-$\underline{H}$); MS (70 eV): m/e = 526 (parent).

,2-3,4-5,6-7,8-Tetra(decamethylene)porphyrin (27)

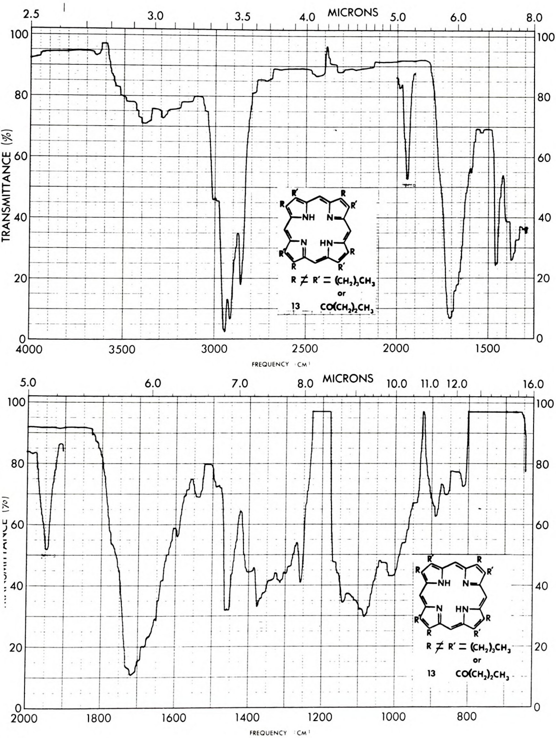
) 2-Carbethoxy-5-formyl-3,4-decamethylenepyrrole (2.95, .7 mmol) and 3 g of potassium hydroxide were refluxed for hours in 80 ml of 50% aqueous ethanol. After cooling to oom temperature, the solution was neutralized with acetic cid. The solvent was removed under reduced pressure. etic acid (60 ml) was added to the residue and the soluon was refluxed for 3 hours while air was blown over the rface. After sitting one week, the solvent was removed d the mixture was chromatographed on silica gel using thylene chloride as the eluent. The product was recryslized from toluene to yield 0.02 g (1%) of 27.

B) 2-Carbethoxy-5-acetoxymethyl-3,4-decamethylene-pyrrole (1.0 g, 2.9 mmol) was dissolved in 20 ml of 50% aqueous ethanol. Potassium hydroxide (1 g) was added and the solution was refluxed for two hours. Acetic acid (50 ml) was added to the cooled solution and this was refluxed for one hour while air was passed over the surface. After sitting one week, the solvent was removed and the residue was hromatographed on silica gel using 1:1 toluene/methylene hloride as eluent. Recrystalization from toluene yielded .07 (12%) of 27: λ_{max} ($CHCl_3$): 400 nm, 502, 535, 520, 622; MR ($CDCl_3$/DMSO-d_6): δ1.3-2.0 (m, 48H, $-CH_2CH_2(C\underline{H}_2)_6CH_2CH_2-$), .43 (m, 16H, $-CH_2C\underline{H}_2(CH_2)_6C\underline{H}_2CH_2-$), 4.13 (m, 16H, $-C\underline{H}_2CH_2-$ $CH_2)_6CH_2C\underline{H}_2-$), 10.42 (m, 4H, meso-$\underline{H}$); MS (70 eV): m/e = 2 (parent).

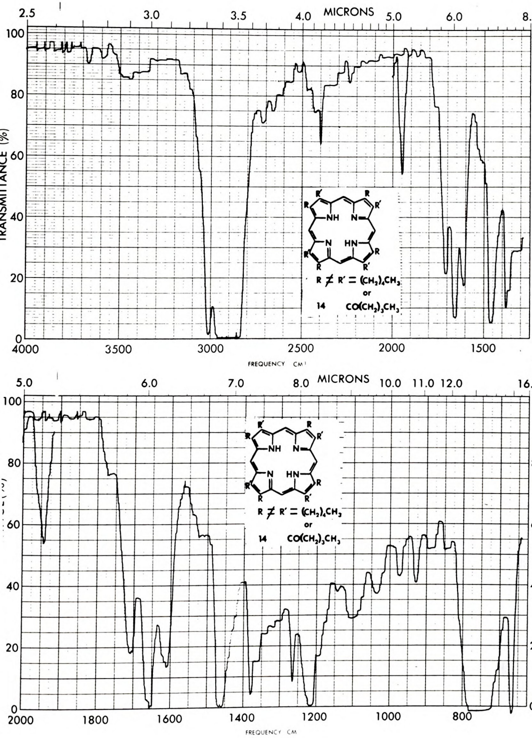
APPENDIX



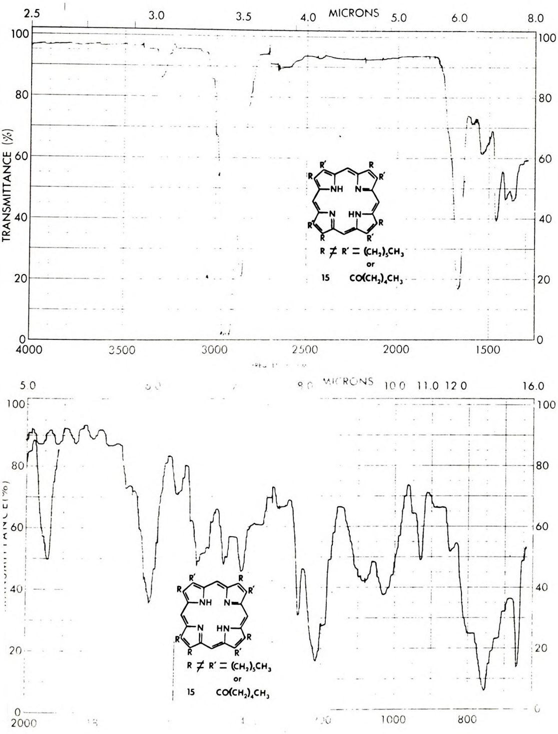
igure 3. Infrared spectrum of tetrapropyltetrapropyrylporphyrin (12).



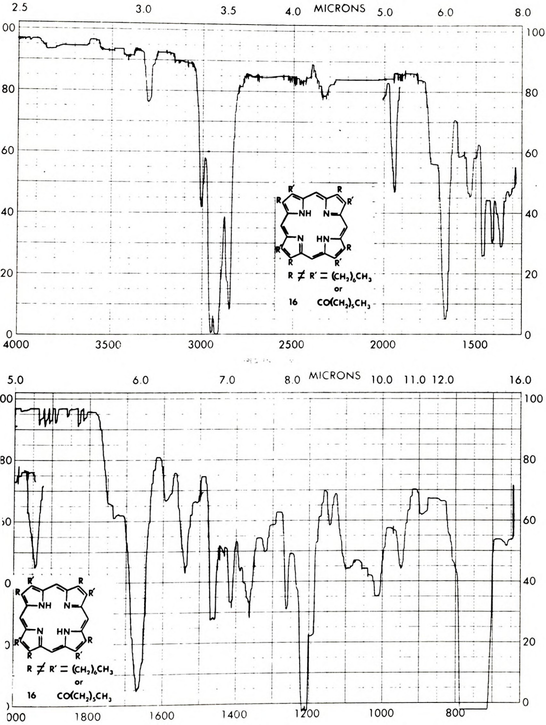
gure 4. Infrared spectrum of tetrabutyltetrabutyrylporphyrin (13).



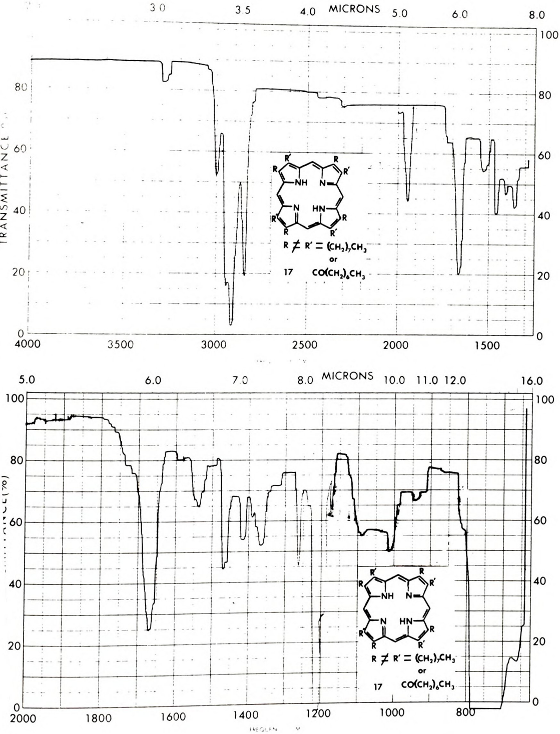
ure 5. Infrared spectrum of tetrapentyltetrapentyrylporphyrin (14).



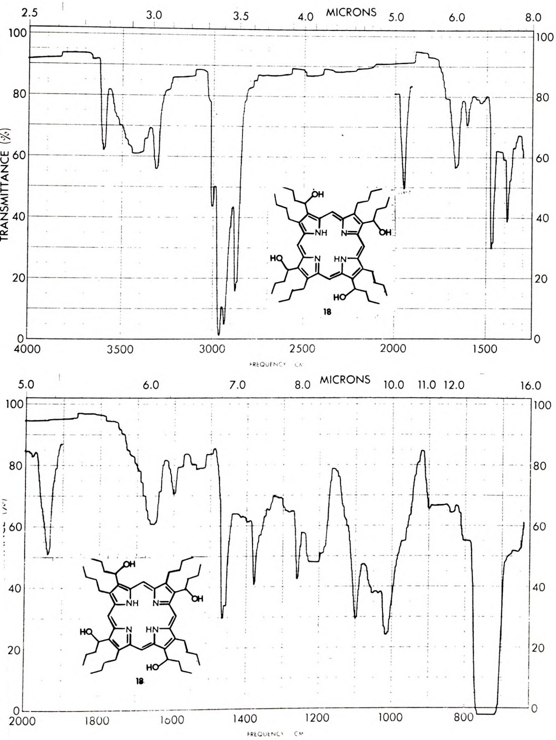
igure 6. Infrared spectrum of tetrahexyltetrahexyrylporphyrin (15).



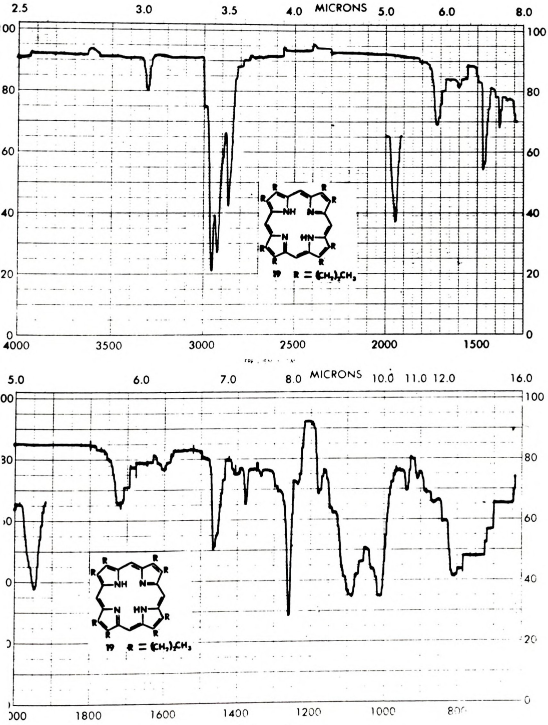
ure 7. Infrared spectrum of tetraheptyltetraheptyrylporphyrin (16).



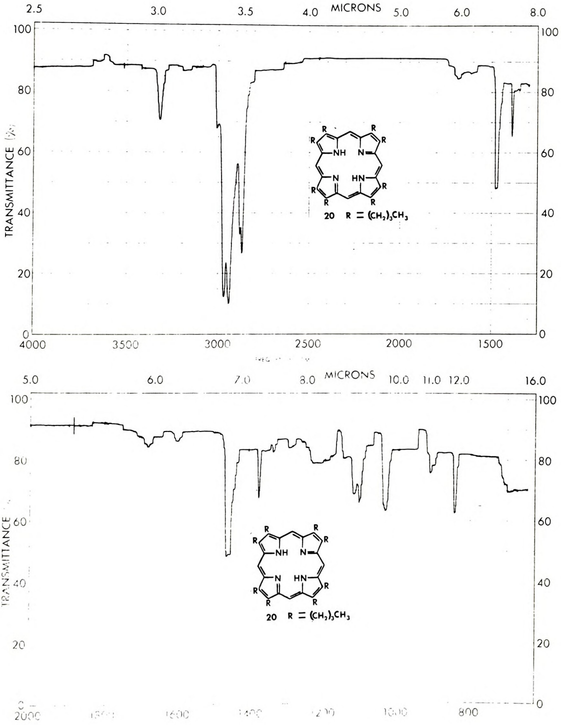
gure 8. Infrared spectrum of tetraoctyltetra-octyrylporphyrin (17).



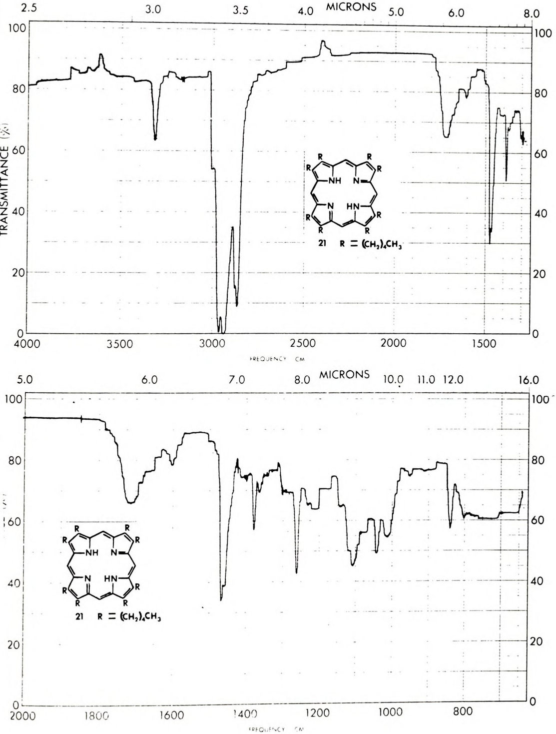
gure 9. Infrared spectrum of tetrabutyltetra(α-hydroxy)butylporphyrin (18).



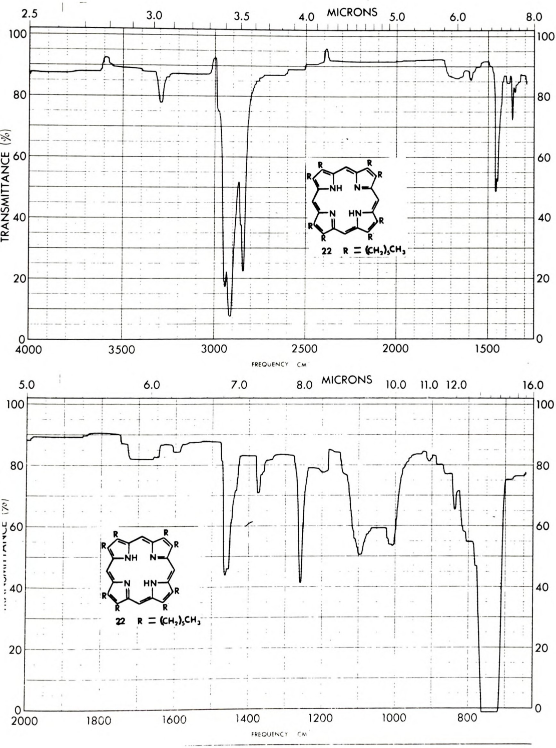
gure 10. Infrared spectrum of octapropylporphyrin (19).



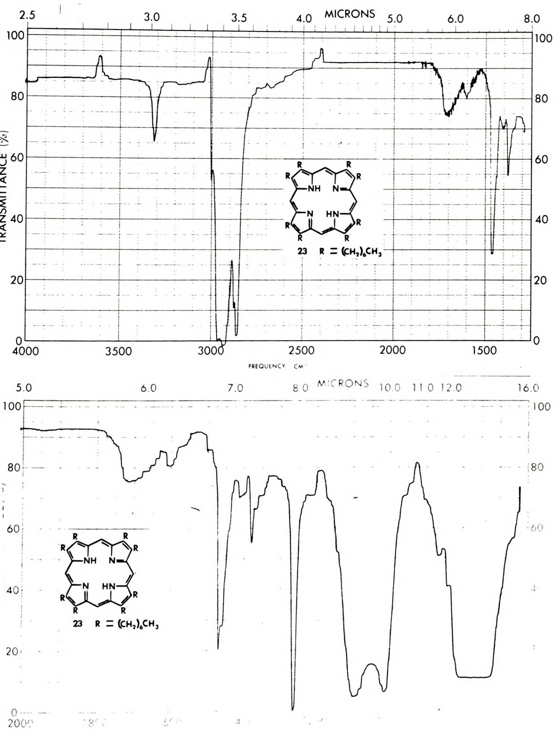
gure 11. Infrared spectrum of octabutylporphyrin (20).



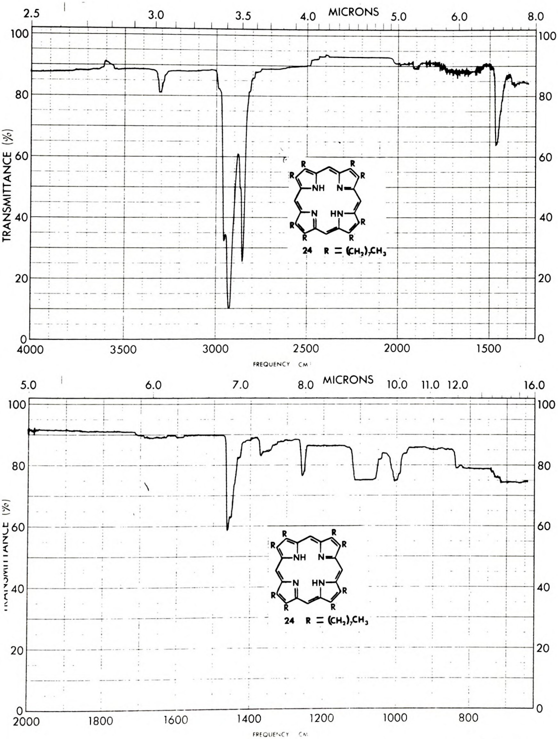
gure 12. Infrared spectrum of octapentylporphyrin ($\underset{\sim}{21}$).



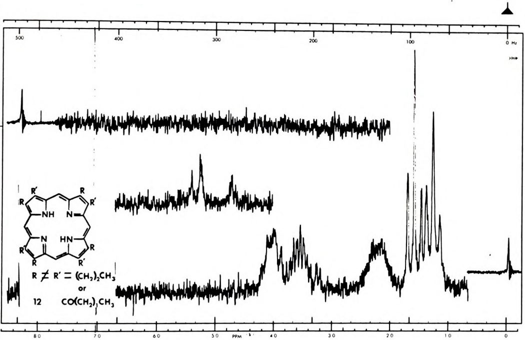
igure 13. Infrared spectrum of octahexylporphyrin (22).



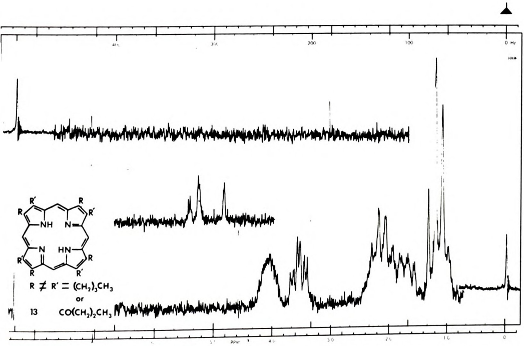
ure 14. Infrared spectrum of octaheptylporphyrin (23).



gure 15. Infrared spectrum of octaoctylporphyrin (24).



gure 16. PMR spectrum of tetrapropyltetrapropyryl-porphyrin (12).



ure 17. PMR spectrum of tetrabutyltetrabutyryl-porphyrin (13).

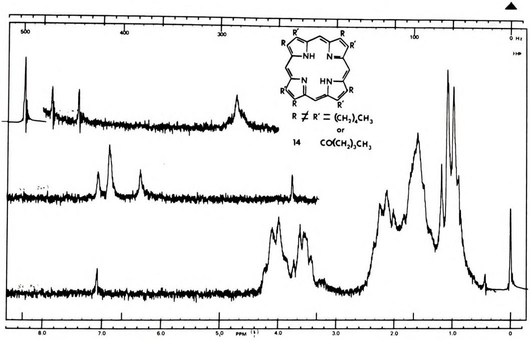


Figure 18. PMR spectrum of tetrapentyltetrapentyryl-porphyrin (14).

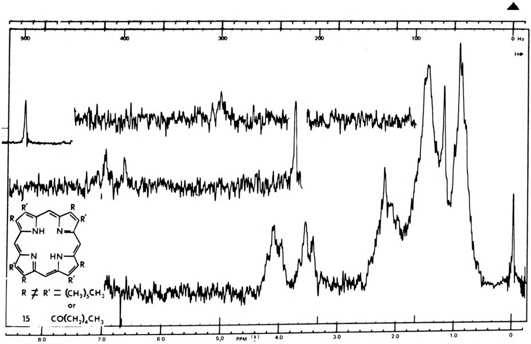


Figure 19. PMR spectrum of tetrahexyltetrahexyryl-porphyrin (15).

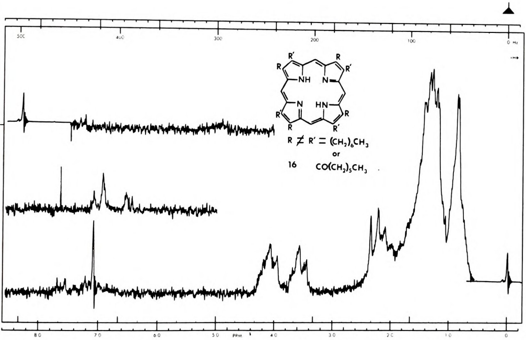
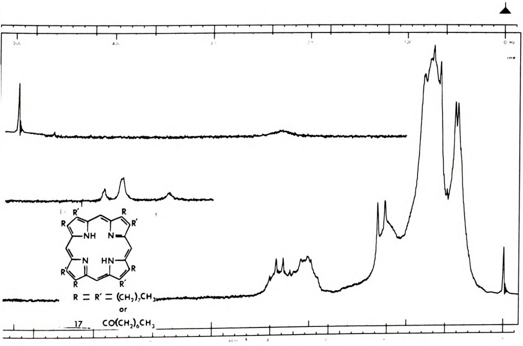


Figure 20. PMR spectrum of tetraheptyltetraheptyryl-porphyrin (16).



'igure 21. PMR spectrum of tetraoctyltetraoctyryl-porphyrin (17).

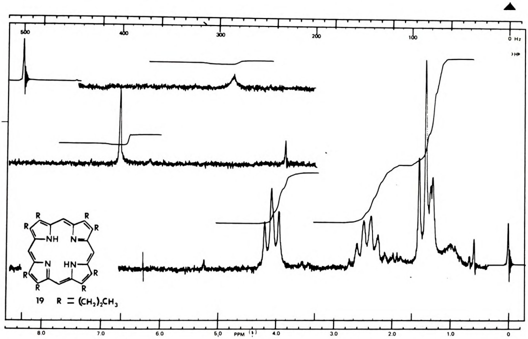
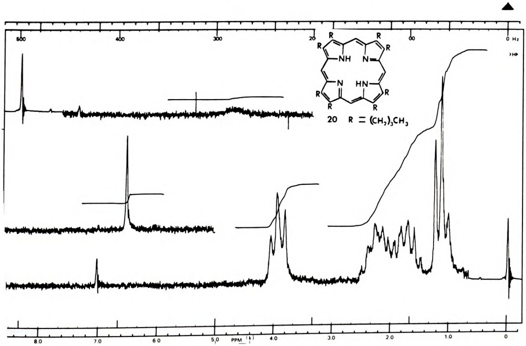


Figure 22. PMR spectrum of octapropylporphyrin (19).



igure 23. PMR spectrum of octabutylporphyrin (20).

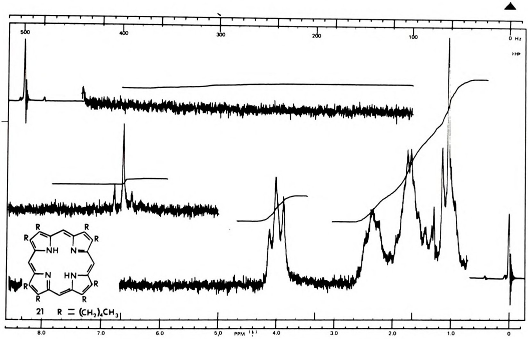
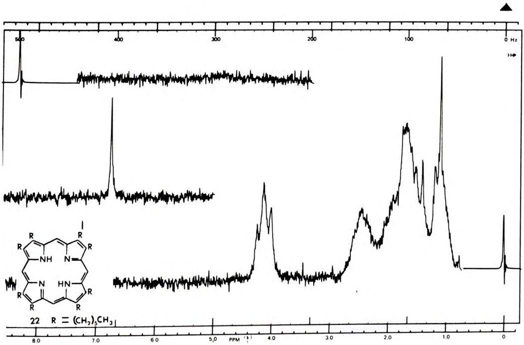


Figure 24. PMR spectrum of octapentylporphyrin (21).



igure 25. PMR spectrum of octahexylporphyrin (22).

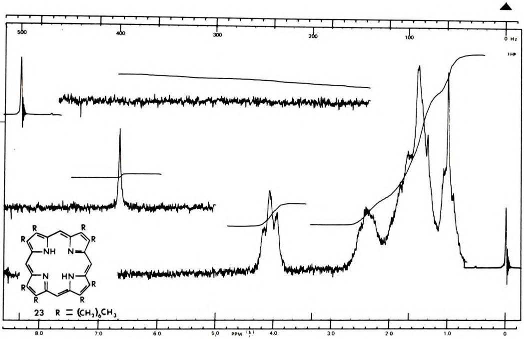
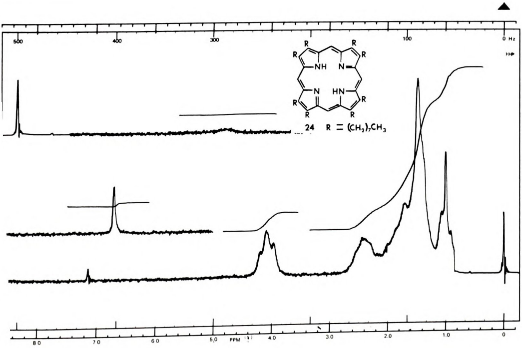


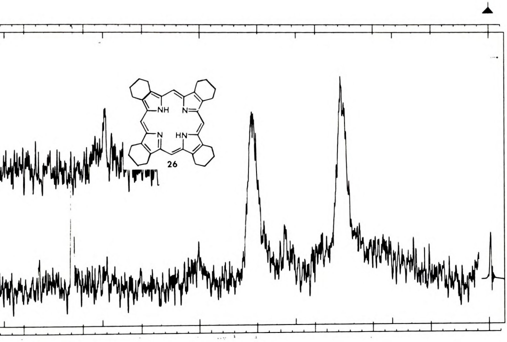
Figure 26. PMR spectrum of octaheptylporphyrin (23).



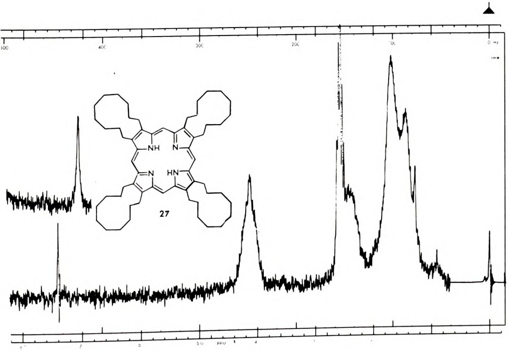
igure 27. PMR spectrum of octaoctylporphyrin (24).

Porphyrin	m/e	I
19	707	100
	693	36
	679	10
	646	4
	354	18
20	818	100
	812	74
	758	59
	409	17
	406	15
21	932	100
	871	9
	465	19
22	1044	100
	984	14
	962	19
	522	28
23	1155	100
	1150	43
	1096	100
	577	39
	548	38
24	1269	20
	1208	100
	1166	19
	604	36

Figure 28. Mass spectra of octaalkylporphyrins.



igure 29. PMR spectrum of 1,2-3,4-5,6-7,8-tetra-(tetramethylene)porphyrin (26).



gure 30. PMR spectrum of 1,2-3,4-5,6-7,8-tetra-(decamethylene)porphyrin (27).

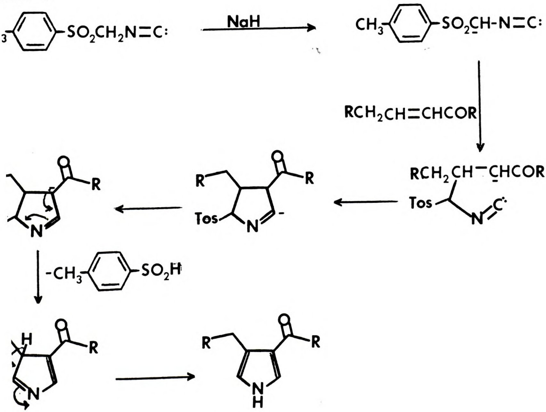
PART II

THE SYNTHESIS AND REACTIONS OF PYRROLES

INTRODUCTION

The introduction of a new synthetic route to 3,4-substituted pyrroles by van Leusen et al.[28] in 1972 has rmitted the direct synthesis of many pyrroles which had eviously been available only through multistep reac- ons[1,29,30,31]. In this procedure the acidic proton $_a = 11$) of p-toluenesulfonylmethyl isocyanide (TosMIC) readily removed by base, and the resulting nucleophile en adds to Michael acceptors followed by closure of the g. Loss of p-toluenesulfinic acid and tautomerization pletes the reaction, Scheme 1.

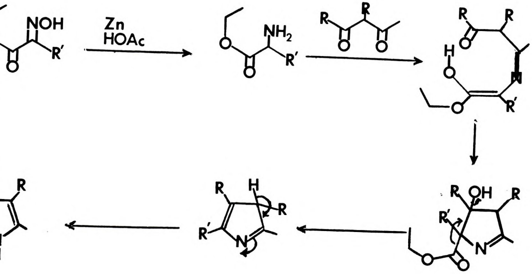
eme 1



Ten new pyrroles were prepared by this reaction and erved as precursors to the porphyrins described in Part I.

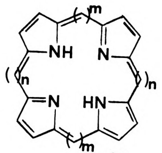
The reductive condensation of oximes with β-diketones s reported by Kleinspehn[32] in 1955. The oxime is reduced *situ* and always condenses with the least hindered carnyl function. An internal aldol condensation then forms five-membered ring, which after ester cleavage and tautorization gives the pyrrole (Scheme 2). This modified orr reaction led to the synthesis of several novel pyrroles l several well-known, synthetically useful pyrroles.

eme 2



O₂Et or CN

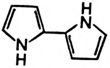
Several potentially useful dipyrrolic intermediates synthesized for use in the synthesis of ring expanded yrins (28)[33,34,35]. These included dipyrroles of the wing kind:



28

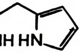
$m + n \geq 2$
$m = n = 1 =$ porphyrin

1) Two pyrrole units are directly connected to form
yrrole (29).

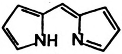


29

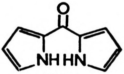
2) Two pyrrole units are connected by a one carbon
dge to form dipyrromethane (30), dipyrromethene (31),
dipyrroketone (32).



30

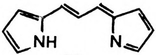


31



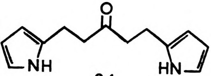
32

3) Two pyrrole units are connected by a three carbon
ge to form dipyrrotrimethine (33).

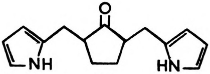


33

4) Two pyrrole units are connected by a five carbon
ge to form dipyrropentadienones (34, 35).



34



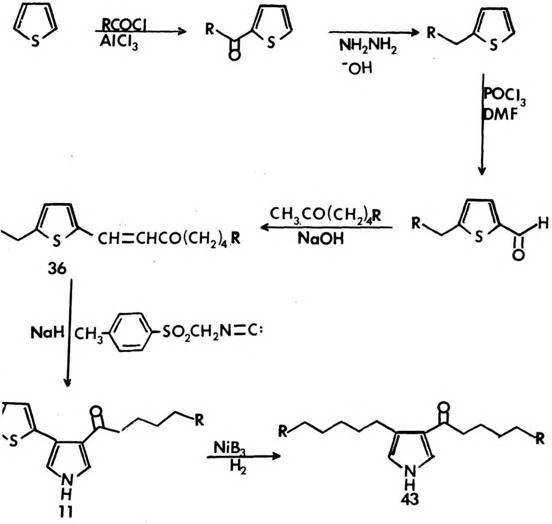
35

RESULTS AND DISCUSSION

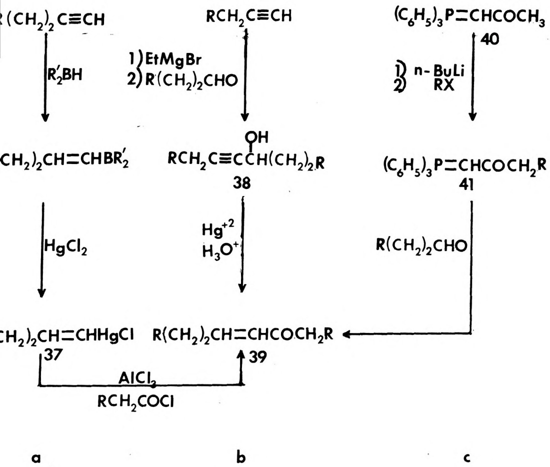
nthesis of pyrroles

In order to prepare the 3,4-disubstituted pyrroles ed in Part I, a general synthesis of α,β-unsaturated ones was required. Four possible routes were explored shown in Schemes 3 and 4.

eme 3



cheme 4



Thiophene-2-carboxaldehyde was condensed with 2-
tanone in the presence of base to give 1-(2-thienyl)-
-1-ene (36). Unlike furfural, which is known to give
l amounts of the wrong isomer[36], no competing condensa-
at the methylene group was observed. This α,β-
turated ketone reacted with TosMIC under basic condi-
s to give 3-butyryl-4-(2-thienyl)pyrrole (11). At-
ted reduction of the thiophene moiety using Raney nickel
ed unpromising, but nickel boride was effective under
conditions described by C. A. Brown[37], giving pyrrole
which was contaminated with small amounts of 3-(2-
yl)-4-butyrylpyrrole. This route to the target compound

as discontinued for the following reasons: 1) It is not
ıitable for preparing octapropylporphyrin; 2) 5-alkyl thio-
ıene-2-carboxaldehyde would have to be prepared in three
:eps—Friedel-Crafts acylation of thiophene followed by
olff-Kishner reduction of the ketone and formylation—for
is route to be applicable to the higher homologues;
high regioselectivity of the aldol condensation is re-
ired; 4) better routes to pyrrole (39) were found.

Another synthesis of α,β-unsaturated ketones involved
e use of vinyl mercuric chloride (37), as shown in
ıeme 4 path a. This reagent was prepared in the manner
scribed by H. C. Brown[38]. Thus treatment of vinyl boranes
:h mercuric acetate gave 37, along with large quantities
elemental mercury. This mixture defied purification de-
te repeated washing of the precipitate. Although crude
reacted smoothly with acid chlorides to give 39, the
te was marred by modest yields, toxic compounds, and a
iously unpleasant odor associated with the vinyl mercuric
oride.

A different approach to α,β-unsaturated ketones was de-
ıed to use the Meyer-Schuster rearrangement of acetylenic
ɔinols prepared by addition of acetylenic Grignard re-
ts to appropriate aldehydes, as shown in Scheme 4 path b.
e a large number of terminal alkynes and aldehydes can
btained from chemical supply houses, path b would pro-
an easy access to the α,β-unsaturated ketones. How-
, yields of the isomerized product were only modest,

nd the development of an improved synthesis led to discontinuation of this route.

The best synthesis of α,β-unsaturated ketones proved o be *via* a Wittig reaction. Alkylation of the deep red ithiotriphenylphosphinoacetonide[40] gave the substituted -ketophosphorane (41) as shown in Scheme 4 path c. The esired α,β-unsaturated ketone (39) was efficiently produced refluxing the new ylide with a suitable aldehyde in thylene chloride (Table 1).

ble 1. $$\underset{40}{(C_6H_5)_3P = CHCOCH_3} \xrightarrow[2)\ RX]{1)\ n\text{-}BuLi} \underset{41}{(C_6H_5)_3P = CHCOCH_2R}$$

$$\xrightarrow{R(CH_2)_2CHO} R(CH_2)_2CH = CHCOCH_2R$$

R	α,β-unsaturated ketone	% yield from 40	39
$_3$-	$CH_3(CH_2)_2CH{=}CHCOCH_2CH_3$	85	a
$_3CH_2$-	$CH_3(CH_2)_3CH{=}CHCO(CH_2)_2CH_3$	92	b
$(CH_2)_2$-	$CH_3(CH_2)_4CH{=}CHCO(CH_2)_3CH_3$	64	c
$(CH_2)_3$-	$CH_3(CH_2)_5CH{=}CHCO(CH_2)_4CH_3$	56	d
$(CH_2)_4$-	$CH_3(CH_2)_6CH{=}CHCO(CH_2)_5CH_3$	62	e
$(CH_2)_5$-	$CH_3(CH_2)_7CH{=}CHCO(CH_2)_6CH_3$	62	f
$_2CH_2CH_2$-	$CH_3CH{=}CHCO(CH_2)_5COCH{=}CHCH_3$	68	g

It was found that removal of lithium salts from the methylenetriphenylphosphorane prior to its reaction with aldehyde resulted in higher yields. Apparently the ium cation complexes the ylide and decreases the charge arbon by creating a more enolate-like species, which is

ss likely to react with aldehydes to form a betaine interliate. The alkylated Wittig reagents were invariably coninated with starting material. Separation at this stage not possible, so the impurity was carried through the ction and the resulting methyl ketone separated from the ger chain ketone by distillation.

3,4-Disubstituted pyrroles were synthesized by reacting MIC under basic conditions with α,β-unsaturated carbonyls shown in Scheme 1. Results are summarized in Table 2.

le 2

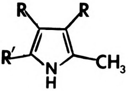
R	R'	% yield	pyrrole
$COCH_2CH_3$	$CH_2CH_2CH_3$	74	42
$CO(CH_2)_2CH_3$	$CH_2(CH_2)_2CH_3$	69	43
$CO(CH_2)_3CH_3$	$CH_2(CH_2)_3CH_3$	34	44
$CO(CH_2)_4CH_3$	$CH_2(CH_2)_4CH_3$	28	45
$CO(CH_2)_5CH_3$	$CH_2(CH_2)_5CH_3$	31	46
$CO(CH_2)_6CH_3$	$CH_2(CH_2)_6CH_3$	42	47
$-CO(CH_2)_5CO-$	2 CH_3	53	48
$-COOCH_2CH_2-$		11	49
$CO(CH_2)_2CH_3$	2-thienyl	35	11

This provides a simple method for preparing 2,5-stituted pyrroles which were previously inaccessible. the C_2, C_5, and nitrogen atoms of the pyrrole ring erived from TosMIC, a large variety of pyrroles can

obtained by varying the structure of the Michael ceptor.

A different pyrrole synthesis gave various 2,3,4,5-trasubstituted pyrroles by reductive condensation of imes with β-diketones, Scheme 2. Results are summarized Table 3.

le 3

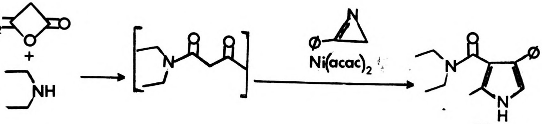


R	R'	pyrrole	% yield	ref
CH_3	CO_2Et	50	65	32
CH_2CH_3	CO_2Et	51	64	43
$-CH_2CH_2CH_2-$	CO_2Et	52	7	--
$-CH_2(CH_2)_2CH_2-$	CO_2Et	53	56	--
$-CH_2(CH_2)_8CH_2-$	CO_2Et	54	50	--
CH_3	$CO_2C(CH_3)_3$	55	50	43
$-CH_2(CH_2)_2CH_2-$	$CO_2C(CH_3)_3$	56	43	--
CH_3	$CO_2CH_2C_6H_5$	57	76	43
CH_3	CN	58	46	32

This modified Knorr synthesis led to extremely useful ole intermediates since mono-, di- or trihalogenation he α-methyl group yielded reactive alkyl halides, alde- s, or carboxylic acids respectively.

A convenient one pot synthesis of a β-pyrrole car- nide (59) was conducted as shown in Scheme 5. Reaction iethylamine with diketene gave N,N-diethyl acetoacetamide

heme 5



59

ich was reacted without isolation with 2-phenylazirine give 59 in 61% yield. Variation of the nucleophile ld lead to different acetoacetic acid derivatives which ld also be converted to pyrroles. The functionalized roles could serve as useful intermediates in the synsis of porphyrins and other pyrrolic annulenes.

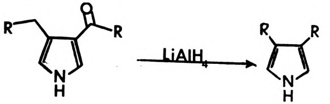
ctions of pyrroles

Transformation of functional groups:

Following a reported synthesis of 3,4-dipropylpyrrole[41], reduction of β-ketopyrroles with lithium aluminum hyle was investigated. The reduction of amides to amines lithium aluminum hydride is well known and extension his reaction to these vinylogous amides proved to be an edingly clean, high-yield method for reducing the nes (Table 4). The crude, spectroscopically pure oles, were extremely air sensitive. It proved necessary onvert them to the octaalkylporphyrins, as shown in I.

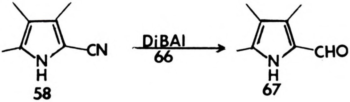
Another useful reduction procedure for the transformaof functional groups on pyrroles utilizes the relay recent discovery that reduction of nitriles can be

le 4



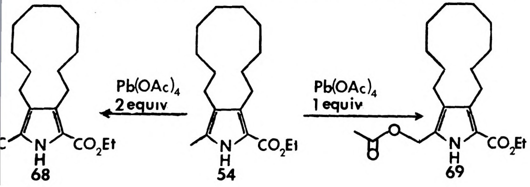
R	% yield	pyrrole
$CH_3(CH_2)_2$-	70	60
$CH_3(CH_2)_3$-	76	61
$CH_3(CH_2)_4$-	86	62
$CH_3(CH_2)_5$-	87	63
$CH_3(CH_2)_6$-	89	64
$CH_3(CH_2)_7$-	85	65

ped at aldehydes using one equivalent of diisobutyl inum hydride (66)[42]. Cyanopyrrole (58) was reduced dehyde (67) using DiBAl in 66% yield. This reagent ly simplifies the lengthy procedure[43] previously used eparing 67.



Oxidation of α-alkylpyrroles can also be used to pro- he necessary functionalization for synthetic inter- es. Thus when ethyl 2-methyl-3,4-decamethylenepyrrole oxylate (54) was treated with one equivalent of lead cetate, it yielded 82% of monoacetoxymethylpyrrole (68).

equivalents of lead tetraacetate gave α-formylpyrrole
) in 55% yield. These new functionalized pyrroles were
d in the preparation of porphyrins described in Part I.



Preparation and derivatization of dipyrrolic intermediates:

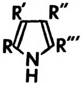
Much of the synthetic effort in this part of the re-
ch was directed toward the preparation of dipyrrolic
rmediates (29)-(35). They are divided into four
gories.

(i) Zero carbon bridge:

Bipyrroles have been prepared by the Ullman reaction
odopyrroles. In an earlier study[44] of bipyrroles, it
oted that the iodopyrroles must contain at least one
for the coupling to succeed. Various new iodopyrroles
synthesized to test this statement and to provide syn-
cally useful intermediates (Table 5).

It was found that the Ullman coupling succeeded only
the 2-iodopyrrole bore an ester function at the 5-
ion and that yields improved if an ester was also
ed at the 3-position. Other electron-withdrawing
onality in 70, 72, and 78 failed to activate the

le 5



R	R'	R"	R'''	% yield	pyrrole	method	ref
	CH_3CO	CH_2CH_3	I	71	70	A	--
	CO_2Et	CH_3	I	54	71	A	--
	CH_3CO	C_6H_5	I	84	72	A	--
	CH_3	CH_3	I	21	73	A	--
	CH_3	CH_3	I	95	74	B	44
	CH_3	CO_2Et	I	88	75	B	44
C_6H_5	CH_3	CO_2Et	I	78	76	B	44
	I	I	CH_3	99	77	A	--
	H	H	CO	15	78	A	--

A = pyrrole-H + KI + H_2O_2. Method B = pyrrole-CO_2H + I_2.

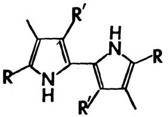
and an ester at the 4-position proved equally

though no new bipyrroles resulted from this study, a
of improvements were found. Iodopyrrole (74) led to
pected product when the reaction was run in dimethyl-
de as described[44], see page 84. However, bipyrrole
s formed in 38% yield when dimethylacetamide was used
ent.

new method of coupling iodopyrroles gave improved
Bis(triphenylphosphine)nickel(II) dichloride was
with zinc in the presence of triphenylphosphine to
tris(triphenylphosphine)nickel(0) *in situ*. Yields

inging from 50-100% were obtained when this homogeneous
ckel reagent[45] was used in place of copper as the coupling
agent. The lower yields occurred when the extremely air-
nsitive nickel coupling reaction was scaled-up. The
oduct had to be isolated as the bipyrrole diacid (80) due
difficulty in separating the very insoluble bipyrrole
om the triphenylphosphine used in the reaction. Hydrolysis
the esters gave a base soluble product which could be
sily isolated by basic extraction of the reaction mixture
llowed by neutralization.

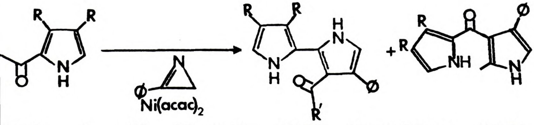
Synthetically useful bipyrroles could be produced by
lification of the functionality on the existing bi-
roles. Since difficulties were encountered in the pref-
ntial hydrolysis of tetraester (81), mixed bipyrrole
raester (82) was synthesized by coupling iodopyrrole (76),
lowed by removal of the benzyl groups by catalytic hy-
genation[43]. In contradiction to an earlier report[46]
ch claimed "benzilic compounds are not significantly
ogenolyzed" by nickel boride, it was found that diacid
could be conveniently produced by nickel boride reduc-
of the mixed tetraester (82). The reagent is readily
ared by the reduction of nickel(II) dichloride hexa-
ate with sodium borohydride while hydrogen is provided
ugh the reaction of water with the reducing reagent.
method of reducing pyrrole benzyl esters eliminates
need for an external hydrogen source and specialized
pment.



R	R'	bipyrrole
CO_2Et	CH_3	79
CO_2H	CH_3	80
CO_2Et	CO_2Et	81
$CO_2CH_2C_6H_5$	CO_2Et	82
CO_2H	CO_2Et	83

A new method for synthesizing bipyrroles was developed zing pyrroles (80), (81), and (82) bearing substitu- which are suitable for pyrrole syntheses. These pyr- were synthesized by known methods[47,48]. Thus a ate conversion to bipyrroles 87 and 88 was obtained 2-phenylazirine was stirred with pyrroles 84 and 85 ight in acetone. Two isomeric products were isolated, own in Table 6.

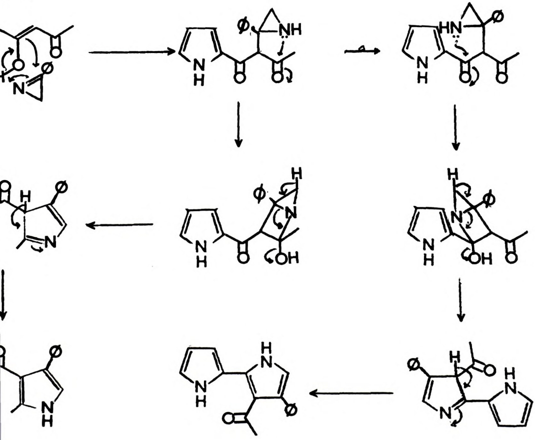
6



rrole	R	R'	bipyrrole	yield	dipyrroketone	yield
84	H	CH_3	87	17.4	90	40.0
85	CH_3	CH_3	88	37.4	91	59.3
86	CH_3	OEt	89	0	92	0

The minor component, which eluted first during chroma-
raphy, was tentatively assigned the bipyrrole structure.
extreme insolubility of both isomers made spectroscopic
surements difficult. Supportive evidence for the assign-
was found in the beautiful blue fluorescence of the
r component, which is characteristic of bipyrroles, and
xtreme air-sensitivity which would be expected of its
tron-rich half. A possible mechanism is shown in
me 6. Dipyrroketone is formed predominantly in this
tion because it results from the kinetically preferred
eophilic attack at the ketone rather than the vinylogous
e.

ne 6

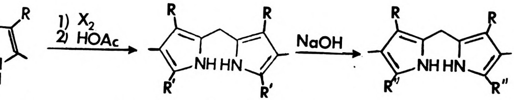


A small amount of uncharacterized solid was obtained n a corresponding reaction of β-ketoester (86). No yrrole could be isolated from the modified Knorr reac- n with any of these pyrroles.

(ii) Single carbon bridge:

As possible precursors to porphyrins and platyrins[35], mber of dipyrromethanes were prepared in the manner ribed by Paine[43], Table 7.

e 7 .

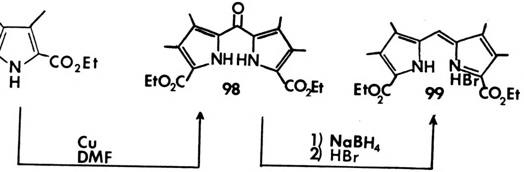


R	R'	R''	% yield	dipyrromethane
CH_3	CO_2Et	--	40	93
CO_2Et	CO_2Et	--	54	94
CH_3	$CO_2CH_2C_6H_5$	--	42	95
CH_3	--	CO_2H	55	96
CO_2Et	--	CO_2H	84	97

In contrast to Paine's report, the α-ethyl esters be preferentially hydrolyzed when treated with base, g it unnecessary to synthesize the mixed tetraesters, ved by catalytic reduction of the benzyl esters.

s mentioned on page 79, ethyl 2-iodo-3,4-dimethyl- .e-5-carboxylate led to an unexpected product when lman reaction was run in dimethylformamide. Although

product had a PMR spectrum identical to that expected bipyrrole, it was identified as dipyrroketone (98) on basis of its melting point[49,50] and mass spectrum. Re- tion with sodium borohydride yielded dipyrromethene (99) ch verified the existence of the inserted carbon.

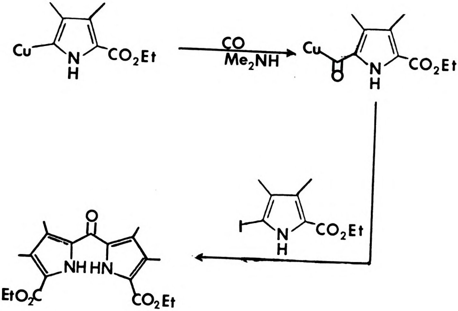


Since the product might have incorporated carbon ide, formed by decomposition of dimethylformamide, as in Scheme 7, the reaction was repeated under a carbon ide atmosphere. The resulting product was bipyrrole and these proved to be the only conditions under which ole was formed using dimethylformamide as the solvent. er investigation is necessary to provide a plausible nism and explain the change of products under carbon ide.

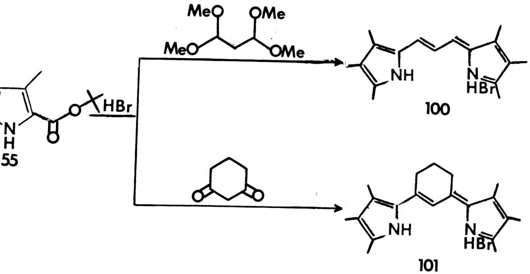
(iii) Three carbon bridge:

ipyrrotrimethine has proven useful in the synthesis anded porphyrin systems[35]. Dipyrrotrimethines (100) 01) were synthesized by reacting tert-butyl ester ith the appropriate β-dicarbonyl compound under acidic ions, Scheme 8.

cheme 7


Cu
CO₂Et
CO
Me₂NH
Cu
CO₂Et
I
CO₂Et
EtO₂C
CO₂Et

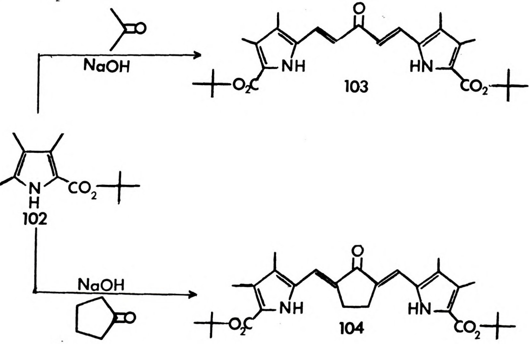
eme 8


55
HBr
MeO
OMe
MeO
OMe
100
101
HBr
HBr

(iv) Five carbon bridge:

As a possible precursor to a 26 pi annulene, both 1,5-
(5-carbo-*t*-butoxy-3,4-dimethyl-2-pyrro)-1,4-pentadiene-
ne (103) and 2,5-di-(5-carbo-*t*-butoxy-3,4-dimethyl-pyrr-
lmethylene)-cyclopentanone (104) were synthesized by
cting pyrrole aldehyde (102) under aldol condensation
litions with acetone and cyclopentanone respectively
ieme 9).

eme 9



EXPERIMENTAL

neral

Instruments used are described in Part I.

(2-Thienyl)-hex-1-ene (36)

Thiophene 2-carboxaldehyde (7 g, 62.5 mmol) and 2-
ntanone (13 g, 150 mmol) was stirred in 150 ml of water
70° for four hours along with 1 g of sodium hydroxide.
e resulting oil was separated and the aqueous layer was
racted twice with ether (50 ml). The organic layers
e combined and dried over magnesium sulfate. The vola-
es were removed under reduced pressure to yield 9.7 g
%) of 36: IR (Neat): 1670 cm^{-1} (C=O); PMR ($CDCl_3$): δ0.97
3H, $C\underline{H}_3$), 1.67 (hextet, 2H, $C\underline{H}_2CH_3$), 2.54 (t, 2H,
$\underline{H}_2$), 6.43 (d, 1H, C$\underline{H}$=CHCO), 6.85-7.33 (m, 3H, thiophene-
7.50 (d, 1H, CH=C$\underline{H}$CO); MS (70 eV): m/e = 180 (parent).

droxy-4-decyne (38)

Magnesium turnings (1.2 g, 49.3 mmol) was added to
l of tetrahydrofuran under nitrogen along with a crystal
odine. Bromoethane (6 g, 54.9 mmol) was added at such
te that the exothermic reaction remained mildly vigor-
After one hour no more magnesium was visible. 1-
yne (25 mmol) in 20 ml of tetrahydrofuran was added
wise over three hours, followed by the dropwise addi-
of n-pentanal (25 mmol). After sitting overnight the

ution was added to 500 ml of saturated ammonium chloride water. This was extracted with ether (2 X 100 ml) and ed over magnesium sulfate. The volatiles were removed er reduced pressure to yield 3.6 g (93%) of **38**: IR at): 3400 cm^{-1} (N-H), 2375 (C≡C); PMR ($CDCl_3$): δ0.93 erlapping t, 6H, $C\underline{H}_3$), 1.43 (m, 6H, $CH_3C\underline{H}_2CH_2C{\equiv}CCH(OH)$- $C\underline{H}_2CH_3$), 2.20 (t, 2H, $C\underline{H}_2C{\equiv}C$), 3.47 (broad s, 1H, $O\underline{H}$); (70 eV): m/e = 154 (parent).

yrylmethylenetriphenylphosphorane (**41a**), butyrylmethyl- riphenylphosphorane (**41b**), pentyrylmethylenetriphenyl- phorane (**41c**), hexyrylmethylenetriphenylphosphorane), heptyrylmethylenetriphenylphosphorane (**41e**), and rylmethylenetriphenylphosphorane (**41f**)

ral Procedure:

To a solution of acetylmethylenetriphenylphosphorane g, 85 mmol) in dry tetrahydrofuran (700 ml) was added ution of n-butyllithium (40 ml of a 2.2 N hexane solu- 85 mmol) was added. After stirring the dark red ion for 15 min at -78° alkyl halide (85 mmol) was . The solution was stirred overnight at room tempera- (red color of ylide anion was discharged). The tetra- furan was removed under reduced pressure. The residual as dissolved in methylene chloride. This solution was d with water followed by removal of the methylene de. Yields, spectral characteristics, and purifica- ethods (if any) are summarized below.

pyrylmethylenetriphenylphosphorane (41a)

The residual oil was taken up into 50 ml of methylene oride and filtered into 400 ml of ether. The white solid collected by filtration and vacuum dried to give 27.8 g 95% pure 41a: mp 193-195°; IR (Nujol): 1535 cm^{-1} (C=O); (CDCl$_3$): δ1.17 (t, 3H, $C\underline{H}_3$), 2.30 (q, 2H, $C\underline{H}_2CH_3$), 3.64 1H, P=C$\underline{H}$), 7.0-7.7 (m, 15H, $C_6\underline{H}_5$); ^{13}CMR (CDCl$_3$): .79 ($\underline{C}H_3$), 35.84 (d, CO$\underline{C}H_2$, J_{P-C} 15.6 Hz), 51.09 (d, I, J_{P-C} 106 Hz), 126.50-134.57 (seven signals, $\underline{C}_6H_5$), 23 (C=O).

rylmethylenetriphenylphosphorane (41b)

The residual oil was taken up into 50 ml of methylene ride and filtered into 400 ml of ether. The white solid collected by filtration and vacuum dried to give 29.4 g 0% pure 41b: mp 132-134°; IR (Nujol): 1535 cm^{-1} (C=O); (CDCl$_3$): δ0.95 (t, 3H, $C\underline{H}_3$), 1.58 (sextet, 2H, $C\underline{H}_2CH_3$), (m, 2H, CO$C\underline{H}_2$), 3.57 (d, 1H, P=C$\underline{H}$), 7.0-7.7 (m, 15H,); ^{13}CMR (CDCl$_3$): δ13.40 ($\underline{C}H_3$), 19.60 ($\underline{C}H_2CH_3$), 42.45 OC$\underline{H}_2$, J_{P-C} 15.6 Hz), 50.22 (d, P=$\underline{C}$H, J_{P-C} 106 Hz), 5-132.32 (seven signals, $\underline{C}_6H_5$), 192.76 (C=O).

rylmethylenetriphenylphosphorane (41c)

The resulting ylide was 89% pure and was used without er purification. IR (Nujol): 1535 cm^{-1} (C=O); PMR $_3$): δ0.90 (t, 3H, $C\underline{H}_3$), 1.50 (m, 4H, $C\underline{H}_2C\underline{H}_2CH_3$), 2.27 H, CO$C\underline{H}_2$), 3.66 (d, 1H, P=C$\underline{H}$), 7.0-7.7 (m, 15H, $C_6\underline{H}_5$); (CDCl$_3$): δ13.38 ($\underline{C}H_3$), 22.05 ($\underline{C}H_2CH_3$), 28.05

$\mathrm{_2CH_2CH_3}$), 40.66 (d, $\mathrm{COC\underline{H}_2}$, $\mathrm{J_{P-C}}$ 15.4 Hz), 50.16 (d, H, $\mathrm{J_{P-C}}$ 108 Hz), 124.43-132.50 (seven signals, $\mathrm{\underline{C}_6H_5}$), .16 ($\mathrm{\underline{C}}$=O).

yrylmethylenetriphenylphosphorane (41d)

The resulting ylide which was 88% pure was used without her purification. IR ($\mathrm{CHCl_3}$): 1535 $\mathrm{cm^{-1}}$ (C=O); PMR $\mathrm{l_3}$): δ0.85 (t, 3H, $\mathrm{C\underline{H}_3}$), 1.0-1.8 (m, 6H, $\mathrm{C\underline{H}_2C\underline{H}_2C\underline{H}_2CH_3}$), (m, 2H, $\mathrm{COC\underline{H}_2}$), 3.60 (d, 1H, P=C$\underline{\mathrm{H}}$), 7.0-7.7 (m, 15H,); $\mathrm{^{13}CMR}$ ($\mathrm{CDCl_3}$): δ12.86 ($\mathrm{\underline{C}H_3}$), 21.31 ($\mathrm{\underline{C}H_2CH_3}$), 25.58 $\mathrm{(CH_2)_2CH_3}$), 30.65 ($\mathrm{\underline{C}H_2CH_2CH_3}$), 40.35 (d, $\mathrm{CO\underline{C}H_2}$, $\mathrm{J_{P-C}}$ Hz), 50.29 (d, P=$\underline{\mathrm{C}}$H, $\mathrm{J_{P-C}}$ 107 Hz), 124.46-132.54 en signals, $\mathrm{\underline{C}_6H_5}$), 192.45 ($\mathrm{\underline{C}}$=O).

yrylmethylenetriphenylphosphorane (41e)

The resulting ylide which was 73% pure was used without her purification. IR (Nujol): 1535 $\mathrm{cm^{-1}}$ (C=O); PMR $\mathrm{_3}$): δ0.83 (t, 3H, $\mathrm{C\underline{H}_3}$), 1.1-1.8 (m, 8H, $\mathrm{(C\underline{H}_2)_4CH_3}$), (q, 2H, $\mathrm{COC\underline{H}_2}$), 3.61 (d, 1H, P=C$\underline{\mathrm{H}}$), 7.0-7.7 (m, 15H, ; $\mathrm{^{13}CMR}$ ($\mathrm{CDCl_3}$): δ13.52 ($\mathrm{\underline{C}H_3}$), 22.05 ($\mathrm{\underline{C}H_2CH_3}$), 26.60 $\mathrm{CH_2)_3CH_3}$), 28.76 ($\mathrm{\underline{C}H_2(CH_2)_2CH_3}$), 31.24 ($\mathrm{\underline{C}H_2CH_2CH_3}$), (d, $\mathrm{CO\underline{C}H_2}$, $\mathrm{J_{P-C}}$ 14.6 Hz), 50.33 (d, P=$\underline{\mathrm{C}}$H, $\mathrm{J_{P-C}}$ 107 124.63-132.66 (seven signals, $\mathrm{\underline{C}_6H_5}$), 193.45 ($\mathrm{\underline{C}}$=O).

ylmethylenetriphenylphosphorane (41f)

The resulting ylide was 73% pure and was used without er purification. IR (Nujol): 1535 $\mathrm{cm^{-1}}$ (C=O); PMR): δ0.83 (t, 3H, $\mathrm{C\underline{H}_3}$), 1.1-1.8 (m, 10H, $\mathrm{(C\underline{H}_2)_5CH_3}$), q, 2H, $\mathrm{COC\underline{H}_2}$), 3.63 (d, 1H, P=C$\underline{\mathrm{H}}$), 7.0-7.7 (m, 15H,

; ^{13}CMR ($CDCl_3$): δ11.76 ($\underline{C}H_3$), 20.13 ($\underline{C}H_2CH_3$), 24.70
$CH_2)_4CH_3$), 26.76 ($\underline{C}H_2(CH_2)_2CH_3$), 27.13 ($\underline{C}H_2(CH_2)_3CH_3$),
($\underline{C}H_2CH_2CH_3$), 39.12 (d, $CO\underline{C}H_2$, J_{P-C} 15.2 Hz), 49.21 (d,
J_{P-C} 108 Hz, 122.86-132.04 (seven signals, $\underline{C}_6H_5$),
6 ($\underline{C}$=O).

iacetylmethylenetriphenylphosphorylpropane (41g)

To a solution of acetylmethylenetriphenylphosphorane
g, 21.3 mmol) in dry tetrahydrofuran (150 ml) was added
ution of n-butyllithium (10 ml of a 2.2 N hexane solu-
21.3 mmol). After stirring the solution for 15 min at
1,3-diiodopropane (1.23 ml, 10.7 mmol) was added. The
ion was stirred overnight at room temperature (red
of ylide anion was discharged). The tetrahydrofuran
emoved under reduced pressure. The resulting solid was
lved in methylene chloride and filtered into 100 ml
her. The white solid which precipitated was collected
tration and vacuum dried to yield 7.2 g (100% yield)
bis-Wittig reagent: IR (Nujol): 1535 cm^{-1} (C=O);
DCl_3): δ1.50 (m, 6H, $COCH_2(C\underline{H}_2)_3CH_2CO$), 2.21 (m, 4H,
, 3.59 (d, 2H, P=C$\underline{H}$), 7.0-7.7 (m, 30H, $C_6\underline{H}_5$); ^{13}CMR
): δ26.08 ($CH_2\underline{C}H_2CH_2\underline{C}H_2CH_2$), 27.34 ($CH_2CH_2\underline{C}H_2CH_2CH_2$),
(d, $CO\underline{C}H_2$, J_{P-C} 14.8 Hz), 49.78 (d, P=$\underline{C}$H, J_{P-C} 107
23.68-132.00 (seven signals, $\underline{C}_6H_5$), 192.59 ($\underline{C}$=O).

tene-3-one (39a), 5-decene-4-one (39b), 6-dodecene-5- (39c), 7-tetradecene-6-one (39d), 8-hexadecene-7-one), and 9-octadecene-8-one (39f)

ral Procedure:

A solution of ylide (41a-f) (60 mmol) and the appro- :e aldehyde (12 mmol) in 250 ml of methylene chloride efluxed under nitrogen for 24 hours. Pentane was added he precipitate of triphenylphosphine oxide filtered the solution. Distillation gave the α,β-unsaturated e. The yields are listed in Table 1 on page 73. Spec- characteristics of 39a, 39b, 39c, 39d, 39e, and 39f are rized below.

ene-3-one (39a)

IR (Neat): 1685 cm^{-1} (C=O); PMR ($CDCl_3$): δ0.8-1.1 lapping t, 6H, $C\underline{H}_3$), 1.47 (hextet, 2H, $C\underline{H}_2CH_3$), 2.0-2.7 apping t, 4H, $C\underline{H}_2CH{=}CH$ and $COC\underline{H}_2$), 5.8-7.0 (AB quartet, =C$\underline{H}$); MS (70 eV): m/e = 126 (parent).

ne-4-one (39b)

6-Hydroxy-4-decyne (1 g, 6.5 mmol) and mercuric oxide , 0.48 mmol) were refluxed in 25 ml of 85% formic acid e hour. The cooled solution was diluted with 200 ml sodium carbonate in water. The product was extracted ther (3 X 50 ml). The ether was removed under reduced e and the brownish liquid (60%) was suitable for con- to pyrrole (43).

b) From Wittig reaction: IR (Neat): 1680 cm^{-1} (C=O);
R ($CDCl_3$): δ0.93 (t, 6H, $C\underline{H}_3$), 1.2-1.7 (m, 6H, $CH_3C\underline{H}_2C\underline{H}_2$
d $COCH_2C\underline{H}_2CH_3$), 2.0-2.6 (overlapping t, 4H, $C\underline{H}_2CH=CH$ and
$C\underline{H}_2$), 5.7-6.9 (AB quartet, 2H, $C\underline{H}=C\underline{H}$); MS (70 eV): m/e =
4 (parent).

Dodecene-5-one (39c)

IR (Neat): 1700 cm^{-1} (C=O); PMR ($CDCl_3$): δ0.90 (t, 6H,
$_3$), 1.1-1.8 (m, 10H, $CH_3(C\underline{H}_2)_3$ and $COCH_2(C\underline{H}_2)_2CH_3$), 2.0-
6 (m, 4H, $C\underline{H}_2CH=CH$ and $COC\underline{H}_2$), 5.7-7.0 (AB quartet, 2H,
=$C\underline{H}$); MS (70 eV): m/e = 182 (parent).

Tetradecene-6-one (39d)

IR (Neat): 1710 cm^{-1} (C=O); PMR ($CDCl_3$): δ0.90 (t, 6H,
), 1.1-1.8 (m, 14H, $CH_3(C\underline{H}_2)_4$ and $COCH_2(C\underline{H}_2)_3CH_3$), 2.0-2.6
4H, $C\underline{H}_2CH=CH$ and $COC\underline{H}_2$), 5.8-7.0 (AB quartet, 2H, $C\underline{H}=C\underline{H}$);
(70 eV): m/e = 210 (parent).

exadecene-7-one (39e)

IR (Neat): 1710 cm^{-1} (C=O); PMR ($CDCl_3$): δ0.87 (t, 6H,
, 1.0-1.5 (m, 18H, $CH_3(C\underline{H}_2)_5$ and $COCH_2(C\underline{H}_2)_4CH_3$), 2.1-2.6
4H, $C\underline{H}_2CH=CH$ and $COC\underline{H}_2$), 5.8-7.0 (AB quartet, 2H, $C\underline{H}=C\underline{H}$):
70 eV): m/e = 238 (parent).

tadecene-8-one (39f)

IR (Neat): 1700 cm^{-1} (C=O); PMR ($CDCl_3$): δ0.90 (t, 6H,
, 1.1-1.5 (m, 22H, $CH_3(C\underline{H}_2)_6$ and $COCH_2(C\underline{H}_2)_5CH_3$), 2.1-2.6
4H, $C\underline{H}_2CH=CH$ and $COC\underline{H}_2$), 5.8-7.0 (AB quartet, 2H, $C\underline{H}=C\underline{H}$);
70 eV): m/e = 266 (parent).

11-Tridecadiene-4,10-dione (39g)

A solution of ylide (41g) (7.4 g, 11 mmol) and acetal-hyde (44 mmol) in 50 ml of methylene chloride was stirred room temperature for 84 hours. The solvent and remaining dehyde was removed under reduced pressure. Pentane was ded and the precipitate of triphenylphosphine oxide ltered from the solution. The pentane was removed under duced pressure to give 1.7 g (68%) of 39g : IR (Neat): 0 and 1640 cm^{-1} (C=O); PMR ($CDCl_3$): δ1.43 (m, 6H, $COCH_2$-$_2)_3CH_2CO$), 1.82 (two s, 6H, $C\underline{H}_3$), 2.50 (overlapping t, $COC\underline{H}_2$), 5.8-7.0 (AB quartet, 2H, $C\underline{H}$=$C\underline{H}$).

ropyl-4-propyrylpyrrole (42), 3-butyl-4-butyrylpyrrole), 3-pentyl-4-pentyrylpyrrole (44), 3-hexyl-4-hexyryl-role (45), 3-heptyl-4-heptyrylpyrrole (46), 3-octyl-4-rylpyrrole (47), 1.7-bis[-3-(4-methylpyrro)]-1,7-heptane-e(48), 1H-pyrro-[3,4,a]- butyrolactone (49), and 3-ryl-4-(2-thienyl)-pyrrole (11)

ral Procedure:

A solution of p-toluenesulfonyl methyl isocyanide (20) and α,β-unsaturated ketone (39) (20 mmol) in 100 ml ther-dimethyl sulfoxide (2:1) was added dropwise to a red solution of sodium hydride (40 mmol) in 40 ml of r. The mixture was stirred for 15-30 min after comple- of addition. Water (100 ml) was added to the stirred ure and the product was extracted with ether (3 X 100 ml). ether was removed under reduced pressure and the product

ecrystalized from methylene chloride/pentane. Yields are isted in Table 2 on page 75. Spectral characteristics of 2, 43, 44, 45, 46, 47, 48, 49, and 50.

-Propyl-4-propyrylpyrrole (42)

mp. 96-98°; IR (Nujol): 3200 cm^{-1} (N-H), 1535 (C=O); IR ($CDCl_3$): δ1.13 (overlapping t, 6H, $C\underline{H}_3$), 1.58 (hextet, , $CH_3C\underline{H}_2CH_2$), 2.72 (m, 4H, $COC\underline{H}_2$ and $C\underline{H}_2$-pyrrole), 6.45 , 1H, 2-pyrrole-$\underline{H}$), 7.23 (m, 1H, 5-pyrrole-$\underline{H}$), 9.22 road s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ7.85 ($\underline{C}H_3CH_2CO$), 13.00 $H_3CH_2CH_2$), 22.11 ($CH_3\underline{C}H_2CH_2$), 27.55 ($CH_3CH_2\underline{C}H_2$), 31.40 H_2CO), 116.39 (C_5-pyrrole carbon), 121.09 (C_3-pyrrole rbon), 123.81 (C_2-pyrrole carbon), 124.01 (C_4-pyrrole rbon), 195.85 ($\underline{C}$=O); MS (70 eV): m/e = 164 (parent).

utyl-4-butyrylpyrrole (43)

a) 3-Butyryl-4-(2-thienyl)-pyrrole (0.6 g, 2.7 mmol) nickel (II) dichloride hexahydrate (6.45 g, 27 mmol) e dissolved in 300 ml of ethanol. The solution was led to 0° and refluxed under nitrogen while sodium borohride (81.5 mmol) in 80 ml of water was added dropwise. er completion of addition the solution was refluxed for hour. The precipitated nickel was filtered from the led solution and the solvent removed under reduced pres-e. The crude product was eluted from an alumina column ield 80% of 43 after removal of the solvent.

) From TosMIC reaction: mp. 70-72°; IR (Nujol): 3200 (N-H), 1665 (C=O); PMR ($CDCl_3$): δ0.97 (overlapping t,

H, $C\underline{H}_3$), 1.2-1.9 (m, 6H, $CH_3C\underline{H}_2C\underline{H}_2CH_2$ and $COCH_2C\underline{H}_2CH_3$), .70 (overlapping t, 4H, $COC\underline{H}_2$ and $C\underline{H}_2$-pyrrol), 6.48 (m, H, C_2-pyrrole-$\underline{H}$), 7.27 (m, 1H, C_5-pyrrole-$\underline{H}$), 9.28 (broad , 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ12.93 ($\underline{C}H_3$'s), 17.41 ($CH_3\underline{C}H_2$-H_2CO), 21.50 ($CH_3\underline{C}H_2(CH_2)_2$), 25.18 ($CH_3(CH_2)_2\underline{C}H_2$), 31.28 $CH_3CH_2\underline{C}H_2CH_2$), 40.58 ($\underline{C}H_2CO$), 116.39 ($C_5$-pyrrole carbon-$\underline{H}$), 21.67 ($C_3$-pyrrole carbon-$\underline{H}$), 124.03 ($C_2$-pyrrole carbon-$\underline{H}$), 24.39 ($C_4$-pyrrole carbon-$\underline{H}$), 195.51 ($\underline{C}$=O); MS (70 eV): /e = 192 (parent).

-Pentyl-4-pentyrylpyrrole (**44**)

mp. 63-65°; IR (Nujol): 3210 cm^{-1} (N-H), 1640 cm^{-1} =O); PMR ($CDCl_3$): δ0.88 (overlapping t, 6H, $C\underline{H}_3$), 1.1-9 (m, 10H, $CH_3(C\underline{H}_2)_3CH_2$ and $COCH_2(C\underline{H}_2)_2CH_3$), 2.70 (overlapping t, 4H, $C\underline{H}_2$-pyrrole and $COC\underline{H}_2$), 6.45 (m, 1H, C_2-rrole-$\underline{H}$), 7.25 (m, 1H, C_5-pyrrole-$\underline{H}$), 9.00 (broad s, 1H, $\underline{H}$); ^{13}CMR ($CDCl_3$): δ13.81 and 13.93 ($\underline{C}H_3$'s), 22.46 (CH_3-$_2$'s), 26.43 ($CH_3(CH_2)_3\underline{C}H_2$), 27.24 ($CH_3CH_2\underline{C}H_2CH_2CO$), 29.66 $H_3(CH_2)_2\underline{C}H_2CH_2$), 31.75 ($CH_3CH_2\underline{C}H_2CH_2CH_2$), 39.63 ($\underline{C}H_2CO$), 7.33 ($C_5$-pyrrole carbon), 123.04 (C_3-pyrrole carbon), .87 (C_2-pyrrole carbon), 126.23 (C_4-pyrrole carbon), .44 (C=O); MS (70 eV): m/e = 220 (parent).

exyl-4-hexyrylpyrrole (**45**)

mp. 65.5-67°; IR (Nujol): 3200 cm^{-1} (N-H), 1625 (C=O); ($CDCl_3$): δ0.90 (overlapping t, 6H, $C\underline{H}_3$), 1.1-1.9 (m, 14H, $(C\underline{H}_2)_4CH_2$ and $COCH_2(C\underline{H}_2)_3CH_3$), 2.70 (overlapping t, 4H,

-pyrrole and COC$\underline{H}_2$), 6.42 (m, 1H, C_2-pyrrole-$\underline{H}$), 7.23
1H, C_5-pyrrole-$\underline{H}$), 8.32 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$):
.82 and 14.19 ($\underline{C}H_3$'s), 22.48 ($CH_3\underline{C}H_2$'s), 24.79 ($CH_3(CH_2)_2$-
CH_2CO), 26.46 ($CH_3(CH_2)_4\underline{C}H_2$), 29.19 ($CH_3(CH_2)_2\underline{C}H_2(CH_2)_2$),
96 ($CH_3(CH_2)_3\underline{C}H_2CH_2$), 31.65 ($CH_3CH_2\underline{C}H_2(CH_2)_3$ and CH_3CH_2-
$(CH_2)_2CO$), 39.90 ($CH_3(CH_2)_3\underline{C}H_2CO$), 117.33 ($C_5$-pyrrole
bon), 123.08 (C_3-pyrrole carbon), 124.84 (C_2-pyrrole
on), 126.23 (C_4-pyrrole carbon), 197.47 ($\underline{C}$=O); MS (70
: m/e = 248 (parent).

eptyl-4-heptyrylpyrrole (46)

mp. 64.5-67°; IR (Nujol): 3195 cm^{-1} (N-H), 1610 (C=O);
($CDCl_3$): δ0.85 (overlapping t, 6H, $C\underline{H}_3$), 1.34 (m, 18H,
$C\underline{H}_2)_2CH_2$ and $COCH_2(C\underline{H}_2)_4CH_3$), 2.71 (overlapping t, 4H,
pyrrole and COC$\underline{H}_2$), 6.45 (m, 1H, C_2-pyrrole-$\underline{H}$), 7.27
1H, C_5-pyrrole-$\underline{H}$), 9.13 (broad s, 1H, N-$\underline{H}$); ^{13}CMR
l_3): δ13.84 ($\underline{C}H_3$'s), 22.37 and 22.48 ($CH_3\underline{C}H_2$'s), 25.20
$(CH_2)_3\underline{C}H_2CH_2CO$), 26.53 ($CH_3(CH_2)_5\underline{C}H_2$), 29.06 and 29.49
$(CH_2)_2\underline{C}H_2(CH_2)_2CO$ and $CH_3(CH_2)_3\underline{C}H_2(CH_2)_2$), 31.56 and
5 ($CH_3CH_2\underline{C}H_2(CH_2)_4$ and $CH_3CH_2\underline{C}H_2(CH_2)_3CO$), 39.96 ($CH_3$-
$)_4\underline{C}H_2CO$), 117.49 (C_5-pyrrole carbon), 122.79 (C_3-pyrrole
n), 125.20 (C_2-pyrrole carbon), 126.02 (C_4-pyrrole car-
197.80 ($\underline{C}$=O); MS (70 eV): m/e = 266 (parent).

yl-4-octyrylpyrrole (47)

mp. 42-44°; IR (Nujol): 3200 cm^{-1} (N-H), 1620 (C=O);
$CDCl_3$): δ0.90 (overlapping t, 6H, $C\underline{H}_3$), 1.27 (m, 22H,
$\underline{H}_2)_6CH_2$ and $COCH_2(C\underline{H}_2)_5CH_3$), 2.67 (overlapping t, 4H,

$\mathrm{\underline{H}_2}$-pyrrole and $\mathrm{COC\underline{H}_2}$), 6.42 ($\mathrm{C_2}$-pyrrole-$\mathrm{\underline{H}}$), 7.25 (m, 1H, $_5$-pyrrole-$\mathrm{\underline{H}}$), 9.73 (broad s, 1H, N-$\mathrm{\underline{H}}$); MS (70 eV): m/e = 94 (parent).

,7-Bis[-3-(4-methylpyrro)]-1,7-heptanedione (48)

Same procedure as other 3,4-disubstituted pyrroles exept two equivalents of p-toluenesulfonyl methyl isocyanide nd four equivalents of sodium hydride were used to give a 3% yield of 48: mp. 78-80°; IR (Nujol): 3290 cm^{-1} (N-H), 50 cm^{-1} (C=O); PMR ($\mathrm{CDCl_3/DMSO\text{-}d_6}$): δ1.53 (m, 6H, $\mathrm{COCH_2}$-$\mathrm{\underline{H}_2)_3CH_2CO}$), 2.23 (s, 6H, $\mathrm{C\underline{H}_3}$), 2.65 (t, 4H, $\mathrm{COC\underline{H}_2}$), 6.40 , 1H, $\mathrm{C_2}$-pyrrole-$\mathrm{\underline{H}}$), 7.22 (m, 1H, $\mathrm{C_5}$-pyrrole-$\mathrm{\underline{H}}$), 10.04 road s, 1H, N-$\mathrm{\underline{H}}$), ^{13}CMR ($\mathrm{DMSO\text{-}d_6}$): δ12.81 ($\mathrm{\underline{C}H_3}$), 25.32 $\mathrm{OCH_2\underline{C}H_2CH_2\underline{C}H_2CH_2CO}$), 29.53 ($\mathrm{COCH_2CH_2\underline{C}H_2CH_2CH_2CO}$), 39.49 $\mathrm{O\underline{C}H_2}$), 118.94 ($\mathrm{C_2}$-pyrrole carbon), 119.35 ($\mathrm{C_4}$-pyrrole rbon), 123.46 ($\mathrm{C_3}$-pyrrole carbon), 126.03 ($\mathrm{C_5}$-pyrrole rbon), 196.52 ($\mathrm{\underline{C}}$=O); MS (70 eV): m/e = 286 (parent).

-pyrro-[3,4,a]-γ-butyrolactone (49)

mp. 163-166° (decomp.); IR (Nujol): 3300 cm^{-1} (N-H), 0 (C=O); PMR ($\mathrm{CDCl_3}$): δ5.15 (s, 2H, $\mathrm{C\underline{H}_2}$), 6.60 (m, 1H, pyrrole-$\mathrm{\underline{H}}$), 7.10 (m, 1H, $\mathrm{C_5}$-pyrrole-$\mathrm{\underline{H}}$), 9.83 (broad s, N-$\mathrm{\underline{H}}$); MS (70 eV): m/e = 123 (parent).

utyryl-4-(2-thienyl)-pyrrole (11)

mp. 136-137°; PMR ($\mathrm{CDCl_3}$): δ0.95 (5, 3H, $\mathrm{C\underline{H}_3}$), 1.70 tet, 2H, $\mathrm{C\underline{H}_2CH_3}$), 2.67 (t, 2H, $\mathrm{COC\underline{H}_2}$), 6.8-7.4 (m, 5H, ole and thiophene protons), 10.07 (broad s, 1H, N-$\mathrm{\underline{H}}$); R ($\mathrm{CDCl_3}$): δ12.91 ($\mathrm{\underline{C}H_3}$), 17.34 ($\mathrm{\underline{C}H_2CH_3}$), 40.95 ($\mathrm{CO\underline{C}H_2}$),

116.61, 118.88, 121.01, 122.34, 124.77, 125.23, 125.81, and 136.17 (eight signals, pyrrole and thiophene carbons), 195.08 ($\underline{C}$=O); MS (70 eV): m/e = 219 (parent).

2-Carbethoxy-3,4,5-trimethylpyrrole (50), 2-carbethoxy-3,4-diethyl-5-methylpyrrole (51), 2-carbethoxy-3,4-trimethylene-5-methylpyrrole (52), 2-carbethoxy-3,4-tetramethylene-5-methylpyrrole (53), 2-carbethoxy-3,4-decamethylene-5-methylpyrrole (54), 2-carbo-t-butoxy-3,4,5-trimethylpyrrole (55), 2-carbo-t-butoxy-3,4-trimethylene-5-methylpyrrole (56), 2-carbobenzyloxyl-3,4,5-trimethylpyrrole (57), and 3,4,5-trimethyl-2-pyrrole carbonitrile (58)

General Procedure:

The appropriate β-diketone (1 mole) and zinc dust (265 g) in 500 ml of acetic acid were stirred rapidly while diethyl oximinomalonate (or ethyl oximinocyanoacetate) (1 mole) in 250 ml of acetic acid was added dropwise. The exothermic reaction was kept at 95° by adjusting the rate of addition. Towards the end of the addition a steam bath was required to maintain the temperature. After being tirred and heated for an additional hour, the solution was oured into 2 kg of ice. The product was collected by filration and recrystalized from 95% ethanol. Yields and pectral characteristics are summarized below.

2-Carbethoxy-3,4,5-trimethylpyrrole (50)

IR (Nujol): 3380 cm^{-1} (N-H), 1665 (C=O); PMR ($CDCl_3$): δ1.40 (t, 3H, $CH_2C\underline{H}_3$), 1.92, 2.18, and 2.28 (three s, 9H, $C\underline{H}_3$), 4.28 (q, 2H, $C\underline{H}_2CH_3$), 8.97 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ8.50 (C_4-$\underline{C}H_3$), 10.50 (C_3-$\underline{C}H_3$), 11.10 (C_5-$\underline{C}H_3$), 14.38 ($OCH_2\underline{C}H_3$), 59.38 ($O\underline{C}H_2CH_3$), 116.45 and 116.79 (C_2 and C_4 pyrrole carbons), 127.18 and 129.66 (C_3 and C_5 pyrrole carbons), 161.91 ($\underline{C}$=O); MO (70 eV): m/e = 181 (parent).

2-Carbethoxy-3,4-diethyl-5-methylpyrrole (51)

IR (Nujol): 3280 cm^{-1} (N-H), 1650 (C=O); PMR ($CDCl_3$): δ0.9-1.4 (overlapping t, 9H, $CH_2C\underline{H}_3$), 1.95 (s, 3H, $C\underline{H}_3$), 2.28 (q, 2H, C_3-$C\underline{H}_2CH_3$), 2.61 (q, 2H, C_4-$C\underline{H}_2CH_3$), 4.17 (q, 2H, $OC\underline{H}_2CH_3$), 8.83 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ11.11 (C_5-$\underline{C}H_3$), 14.32 ($OCH_2\underline{C}H_3$), 15.78 (C_3 and C_4-$\underline{C}H_3$), 16.90 (C_4-$\underline{C}H_2CH_3$), 18.24 (C_3-$\underline{C}H_2CH_3$), 59.36 ($O\underline{C}H_2CH_3$), 116.50 (C_2-pyrrole carbon), 122.89 (C_4-pyrrole carbon), 129.46 (C_5-pyrrole carbon), 133.34 (C_3-pyrrole carbon), 161.56 ($\underline{C}$=O); MS (70 eV): m/e = 209 (parent).

2-Carbethoxy-3,4-trimethylene-5-methylpyrrole (52)

mp. 139-141°; IR (Nujol): 3270 cm^{-1} (N-H), 1645 (C=O); MR ($CDCl_3$): δ1.33 (t, 3H, $CH_2C\underline{H}_3$), 2.13 (s, 3H, $C\underline{H}_3$), 2.0-.9 (m, 6H, -$C\underline{H}_2C\underline{H}_2C\underline{H}_2$-), 4.23 (q, 2H, $OC\underline{H}_2CH_3$), 8.67 (broad , 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ11.89 (C_5-$\underline{C}H_3$), 14.38 ($OCH_2\underline{C}H_3$), 4.10 (-$CH_2\underline{C}H_2CH_2$-), 26.50 (C_4-$\underline{C}H_2$), 30.74 (C_3-$\underline{C}H_2$), 59.38 $O\underline{C}H_2CH_3$), 112.54 (C_2-pyrrole carbon), 125.53 (C_4-pyrrole

carbon), 129.36 (C_5-pyrrole carbon), 138.95 (C_3-pyrrole carbon), 161.56 ($\underline{C}$=O); MS (70 eV): m/e = 193 (parent).

2-Carbethoxy-3,4-tetramethylene-5-methylpyrrole (53)

mp. 132-133°; IR (Nujol): 3290 cm^{-1} (N-H), 1635 (C=O); PMR ($CDCl_3$): δ1.30 (t, 3H, $CH_2C\underline{H}_3$), 1.72 (overlapping p, 4H, $-CH_2C\underline{H}_2C\underline{H}_2CH_2-$), 2.12-2.67 (m, 4H, $-C\underline{H}_2CH_2CH_2C\underline{H}_2-$), 2.20 (s, 3H, $C\underline{H}_3$), 4.18 (q, 2H, $C\underline{H}_2CH_3$), 8.83 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ10.01 (C_5-$\underline{C}H_3$), 14.27 ($OCH_2\underline{C}H_3$), 20.81 (C_3-$\underline{C}H_2$), 22.66 ($-CH_2\underline{C}H_2\underline{C}H_2CH_2-$), 23.06 ($C_4$-$\underline{C}H_2$), 59.30 ($O\underline{C}H_2CH_3$), 116.83 ($C_2$-pyrrole carbon), 119.21 (C_4-pyrrole carbon), 125.54 (C_5-pyrrole carbon), 132.50 (C_3-pyrrole carbon), 162.14 ($\underline{C}$=O); MS (70 eV): m/e = 207 (parent).

2-Carbethoxy-3,4-decamethylene-5-methylpyrrole (54)

mp. 142-143°; IR (Nujol): 3275 cm^{-1} (N-H), 1630 (C=O); PMR ($CDCl_3$): δ1.30 (t, 3H, $CH_2C\underline{H}_3$), 1.42 (m, 16H, $-CH_2(C\underline{H}_2)-CH_2-$), 2.17 (s, 3H, $C\underline{H}_3$), 2.27 (q, 2H, C_4-CH_2), 2.73 (q, 2H, C_3-CH_2), 4.23 (q, 2H, $C\underline{H}_2CH_3$), 8.83 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ11.47 (C_5-$\underline{C}H_3$), 14.27 (OCH_2-$\underline{C}H_3$), 21.10, 2.58, 25.52, 25.63, 26.13, 26.44, 28.50 ($-(\underline{C}H_2)_{10}-$), 59.25 ($O\underline{C}H_2CH_3$), 116.21 ($C_2$-pyrrole carbon), 122.02 (C_4-pyrrole arbon), 130.03 (C_5-pyrrole carbon), 132.49 (C_3-pyrrole arbon), 161.43 (C=O); MS (70 eV): m/e = 291 (parent).

-Carbo-t-butoxy-3,4,5-trimethylpyrrole (55)

IR (Nujol): 3310 cm^{-1} (N-H), 1660 (C=O); PMR ($CDCl_3$): 1.57 (s, 9H, $C(C\underline{H}_3)_3$), 1.87, 2.13, 2.20 (three s, 9H, $C\underline{H}_3$), .07 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ8.51 (C_4-$\underline{C}H_3$), 0.59 (C_3-$\underline{C}H_3$), 11.12 (C_5-$\underline{C}H_3$), 28.36 ($C(\underline{C}H_3)_3$), 79.67

($\underline{C}(CH_3)_3$), 116.49 (C_2-pyrrole carbon), 117.76 (C_4-pyrrole carbon), 126.18 (C_3-pyrrole carbon), 129.05 (C_5-pyrrole carbon), 161.60 ($\underline{C}$=O); MS (70 eV): m/e = 209 (parent).

2-Carbo-t-butoxy-3,4-tetramethylene-5-methylpyrrole (56)

IR (Nujol): 3310 cm^{-1} (N-H), 1650 (C=O); PMR ($CDCl_3$): δ1.57 (s, 9H, $C(C\underline{H}_3)_3$), 1.73 (m, 4H, $-CH_2(C\underline{H}_2)_2CH_2-$), 2.18 (s, 3H, $C\underline{H}_3$), 2.53 (m, 4H, $-C\underline{H}_2(CH_2)C\underline{H}_2-$), 9.20 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ10.17 (C_5-$\underline{C}H_3$), 20.92, 22.85, 23.15, 26.59 ($-(\underline{C}H_2)_4-$), 28.32 ($C(\underline{C}H_3)_3$), 79.59 ($\underline{C}(CH_3)_3$), 118.26 (C_2-pyrrole carbon), 119.00 (C_4-pyrrole carbon), 124.55 (C_5-pyrrole carbon), 132.28, (C_3-pyrrole carbon), 161.77 (C=O); MS (70 eV): m/e = 235 (parent).

2-Carbobenzyloxyl-3,4,5-trimethylpyrrole (57)

IR (Nujol): 3300 cm^{-1} (N-H), 1655 (C=O): PMR ($CDCl_3$):
δ1.83, 2.12, 2.20 (three s, 9H, $C\underline{H}_3$), 5.15 (s, 2H, $OC\underline{H}_2$),
7.15 (s, 5H, $C_6\underline{H}_5$), 8.92 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$):
δ8.52 (C_4-$\underline{C}H_3$), 10.62 (C_3-$\underline{C}H_3$), 11.18 (C_5-$\underline{C}H_3$), 65.16
$O\underline{C}H_2$), 116.08, (C_2-pyrrole carbon), 117.06 (C_4-pyrrole
arbon), 127.77 (ortho and para phenyl carbons), 128.33
C_3-pyrrole carbon), 129.76 (meta phenyl carbons), 130.01
C_5-pyrrole carbon), 136.62 (quaternary phenyl carbon),
61.41 ($\underline{C}$=O); MS (70 eV): m/e = 243 (parent).

,4,5-Trimethyl-2-pyrrole carbonitrile (58)

IR (Nujol): 3265 cm^{-1} (N-H), 2210 (CN); PMR ($CDCl_3$):
.83, 2.05, 2.10 (three s, 9H, $C\underline{H}_3$), 8.60 (broad s, 1H,
$\underline{H}$); ^{13}CMR ($CDCl_3$): δ8.41 (C_4-$\underline{C}H_3$), 9.88 (C_3-$\underline{C}H_3$), 11.17

(C_5-$\underline{C}H_3$), 96.06 ($\underline{C}N$), 115.63, 130.83, 131.36 (pyrrole carbons); MS (70 eV): m/e = 134 (parent).

Diethyl 2-methyl-4-phenylpyrrole 3-carboxamide (59)

Diethylamine (2 ml, 19.3 mmol) was stirred in 40 ml of dry acetone under nitrogen. Diketene (19.3 mmol) was added dropwise and the solution was stirred for three hours at room temperature. 2-Phenylazirine (2.0 ml) and 0.1 g of nickel acetylacetonate was added and the solution was stirred overnight. Water (120 ml) was added and the beige crystals were collected by filtration to yield 3.0 g (61%) of 59: mp 162-163°; IR (Nujol): 3125 and 3180 cm^{-1} (N-H), 1580 (C=O); PMR ($CDCl_3$): δ0.72 and 1.12 (two t, 6H, $CH_2C\underline{H}_3$), 1.98 (s, 3H, $C\underline{H}_3$), 3.00 and 3.47 (two q, 4H, $NC\underline{H}_2CH_3$), 6.50 (d, 1H, C_2-pyrrole-$\underline{H}$), 7.28 (m, 5H, $C_6\underline{H}_5$), 9.78 (broad s, 1H, N-$\underline{H}$O); ^{13}CMR ($CDCl_3$): δ9.35 (C_2-$\underline{C}H_3$), 10.78 and 11.74 ($\underline{C}H_2CH_3$'s), 41.00 ($N\underline{C}H_2CH_3$'s), 111.82, 112.84, 119.76, 123.29 (pyrrole carbons), 124.09 (ortho phenyl carbons), 124.83 (para phenyl carbon), 126.37 (meta phenyl carbons), 134.02 (quaternary phenyl carbon), 166.68 ($\underline{C}$=O); MS (70 eV): m/e = 56 (parent).

,4-Dipropylpyrrole (60), 3,4-dibutylpyrrole (61), 3,4-ipentylpyrrole (62), 3,4-dihexylpyrrole (63), 3,4-diheptylyrrole (64), and 3,4-dioctylpyrrole (65)

eneral Procedure:

Lithium aluminum hydride (50 ml of a 0.67 M ether soluion, 33.4 mmol), was added to a stirred solution of pyrrole

(**42**-**47**) (8.3 mmol) in 150 ml of tetrahydrofuran under nitrogen. The mixture was refluxed for three hours. To the cooled solution was added cautiously and in order water (1.3 ml), sodium hydroxide (1.3 ml of 15% w/w aqueous solution), and water (3.9 ml). The inorganic precipitate was filtered by suction and washed with tetrahydrofuran. The tetrahydrofuran was removed under reduced pressure. Yields are given in Table 4 on page 77. Spectral characteristics of **60**, **61**, **62**, **63**, **64**, and **65** are summarized below.

3,4-Dipropylpyrrole (**60**)

IR (Neat): 3380 cm^{-1} (N-H); PMR ($CDCl_3$): δ0.93 (t, 6H, $C\underline{H}_3$), 1.58 (hextet, 4H, $C\underline{H}_2CH_3$), 2.37 (t, 4H, $C\underline{H}_2$-pyrrole), 6.23 (d, 2H, pyrrole-$\underline{H}$), 7.42 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ13.98 ($\underline{C}H_3$), 23.47 ($\underline{C}H_2CH_3$), 27.30 ($\underline{C}H_2CH_2CH_3$), 114.73 (C_2- and C_5-pyrrole carbons), 122.53 (C_3- and C_4-pyrrole carbons).

3,4-Dibutylpyrrole (**61**)

IR (Neat): 3380 cm^{-1} (N-H); PMR ($CDCl_3$): δ0.95 (t, 6H, $\underline{H}_3$), 1.52 (m, 8H, $C\underline{H}_2C\underline{H}_2CH_3$), 2.43 (5, 4H, $C\underline{H}_2$-pyrrole), .41 (d, 2H, pyrrole-H), 7.67 (broad s, 1H, N-$\underline{H}$); ^{13}CMR $CDCl_3$): δ13.90 ($\underline{C}H_3$), 22.65 ($\underline{C}H_2CH_3$), 24.86 ($\underline{C}H_2(CH_2)_2CH_3$), 2.59 ($\underline{C}H_2CH_2CH_3$), 114.70 ($C_2$- and C_5-pyrrole carbons), 22.95 (C_3- and C_4-pyrrole carbons).

3,4-Dipentylpyrrole (62)

IR (Neat): 3375 cm^{-1} (N-H); PMR ($CDCl_3$): δ0.88 (t, 6H, $C\underline{H}_3$), 1.40 (m, 12H, $(C\underline{H}_2)_3CH_3$), 2.38 (t, 4H, $C\underline{H}_2$-pyrrole), 6.35 (d, 2H, pyrrole-$\underline{H}$), 7.56 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ13.90 ($\underline{C}H_3$), 22.47 ($\underline{C}H_2CH_3$), 25.16 ($\underline{C}H_2(CH_2)_3CH_3$), 30.10 ($\underline{C}H_2(CH_2)_2CH_3$), 31.84 ($\underline{C}H_2CH_2CH_3$), 114.70 ($C_2$- and C_5-pyrrole carbons), 122.94 (C_3- and C_4-pyrrole carbons).

3,4-Dihexylpyrrole (63)

IR (Neat): 3380 cm^{-1} (N-H); PMR ($CDCl_3$): δ0.87 (t, 6H, $C\underline{H}_3$), 1.35 (m, 16H, $(C\underline{H}_2)_4CH_3$), 2.36 (t, 4H, $C\underline{H}_2$-pyrrole), 6.27 (d, 2H, pyrrole-$\underline{H}$), 7.50 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ13.87 ($\underline{C}H_3$), 22.50 ($\underline{C}H_2CH_3$), 25.15 ($\underline{C}H_2(CH_2)_4CH_3$), 29.26 ($\underline{C}H_2(CH_2)_2CH_3$), 30.34 ($\underline{C}H_2(CH_2)_3CH_3$), 31.65 ($\underline{C}H_2CH_2CH_3$), 114.62 ($C_2$- and C_5-pyrrole carbons), 122.72 (C_3- and C_4-pyrrole carbons).

3,4-Diheptylpyrrole (64)

IR (Neat): 3380 cm^{-1} (N-H); PMR ($CDCl_3$): δ0.95 (t, 6H, $C\underline{H}_3$), 1.58 (m, 20H, $(C\underline{H}_2)_5CH_3$), 2.46 (t, 4H, $C\underline{H}_2$-pyrrole), 6.45 (d, 2H, pyrrole-$\underline{H}$), 7.73 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ13.90 ($\underline{C}H_3$), 22.54 ($\underline{C}H_2CH_3$), 25.18 ($\underline{C}H_2(CH_2)_5CH_3$), 29.13 ($\underline{C}H_2(CH_2)_2CH_3$), 29.58 ($\underline{C}H_2(CH_2)_3CH_3$), 30.41 ($\underline{C}H_2(CH_2)_4CH_3$), 31.77 ($\underline{C}H_2CH_2CH_3$), 114.65 ($C_2$- and C_5-pyrrole carbons), 122.81 (C_3- and C_4-pyrrole carbons).

3,4-Dioctylpyrrole (65)

IR (Neat): 3380 cm^{-1} (N-H); PMR ($CDCl_3$): δ0.85 (t, 6H, $\underline{H}_3$), 1.28 (m, 24H, $(C\underline{H}_2)_6CH_3$), 2.38 (t, 4H, $C\underline{H}_2$-pyrrole),

6.33 (d, 2H, pyrrole-$\underline{H}$), 7.57 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ13.84 ($\underline{C}H_3$), 22.51 ($\underline{C}H_2CH_3$), 25.14 ($\underline{C}H_2(CH_2)_6CH_3$), 29.19 ($\underline{C}H_2(CH_2)_2CH_3$), 29.40 ($\underline{C}H_2(CH_2)_3CH_3$), 29.59 ($\underline{C}H_2$-$(CH_2)_4CH_3$), 30.39 ($\underline{C}H_2(CH_2)_5CH_3$), 31.77 ($\underline{C}H_2CH_2CH_3$), 114.61 ($C_2$- and C_5-pyrrole carbons), 122.66 (C_3- and C_4-pyrrole carbons).

2-Formyl-3,4,5-trimethylpyrrole (67)

2-Cyano-3,4,5-trimethylpyrrole (6.7 g, 50 mmol) was stirred in 50 ml of benzene. Diisobutyl aluminum hydride (50 ml of a 1N hexane solution) was added slowly at room temperature under nitrogen. The initially colorless solution turned orange and warmed slightly as the reducing agent was added. After one hour 3 ml of methanol was added and the solution was stirred for 15 min. Water (5 ml) was added and the solution turned warm and gelatinous. The inorganics were removed by suction filtration and washed with methylene chloride. The solvent was removed from the filtrate under reduced pressure and the crude product recrystalized from methanol/water to yield 4.5 g (66%) of 67. IR (Nujol): 3245 cm^{-1} (N-H), 1635 (C=O); PMR ($CDCl_3$): δ1.85 (s, 3H, C_5-$C\underline{H}_3$), 2.19 (s, 6H, C_3- and C_4-$C\underline{H}_3$), 9.20 (s, 1H, C$\underline{H}$O), 10.04 (s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ8.05 (C_4-$\underline{C}H_3$), 8.60(C_3-$\underline{C}H_3$), 11.13 (C_5-$\underline{C}H_3$), 117.54 (C_4-pyrrole carbon), 27.53 (C_2-pyrrole carbon), 132.86 (C_5-pyrrole carbon), 36.71 (C_3-pyrrole carbon), 175.06 ($\underline{C}$=O); MS (70 eV): m/e = 37 (parent).

5-Acetoxymethyl-2-carbethoxy-3,4-decamethylenepyrrole (68)

2-Carbethoxy-3,4-decamethylene-5-methylpyrrole (5.82 g, 20 mmol) was dissolved in 200 ml of acetic acid. Lead tetraacetate (9.8 g) was added in small portions over one-half hour. The slurry was stirred for 15 min after completion of addition. Water (100 ml) was added and the crude product which precipitated was collected by filtration, washed with water and recrystalized from hexane to yield 5.7 g (82%) of 68: mp. 152-153°; IR (Nujol): 3285 cm^{-1} (N-H), 1710 (C=O); PMR ($CDCl_3$): δ1.32 (t, 3H, $CH_2C\underline{H}_3$), 1.43 (m, 16H, $-CH_2(C\underline{H}_2)CH_2-$), 2.05 (s, 3H, $C\underline{H}_3$), 2.65 (m, 4H, $-C\underline{H}_2(CH_2)_8C\underline{H}_2-$), 4.20 (q, 2H, $C\underline{H}_2CH_3$), 6.57 (s, 2H, $CH_3-COC\underline{H}_2-$), 9.05 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ14.31 ($OCH_2\underline{C}H_3$), 20.84, 22.39, 22.76, 25.51, 25.79, 26.34, 26.41, 28.42 ($-(\underline{C}H_2)_{10}-$), 29.72 ($CO\underline{C}H_3$), 57.28 ($\underline{C}H_2OCOCH_3$), 118.80 ($C_2$-pyrrole carbon), 125.34, 127.01 (C_4- and C_5-pyrrole carbons), 131.74 (C_3-pyrrole carbon), 161.00 (EtO$\underline{C}$=O), 171.45 ($CH_3\underline{C}$=O); MS (70 eV): m/e = 349 (parent).

2-Carbethoxy-5-formyl-3,4-decamethylenepyrrole (69)

2-Carbethoxy-3,4-decamethylene-5-methylpyrrole (5.82 , 20 mmol) was dissolved in 200 ml of acetic acid. Lead etraacetate (19.6 g) was added over 15 min at room temerature. The solution was heated on a steam bath for one our after completion of addition and then diluted with 00 ml of water. The product was extracted into methylene hloride. The methylene chloride was stripped off and the

product recrystalized from hexane to yield 3.35 g (55%) of 69: IR (Nujol): 3270 cm^{-1} (N-H), 1675 (C=O); PMR ($CDCl_3$): δ1.33 (t, 3H, $CH_2C\underline{H}_3$), 1.47 (m, 16H, $-CH_2(C\underline{H}_2)_8CH_2-$), 2.67 (t, 4H, $-C\underline{H}_2(CH_2)_8C\underline{H}_2-$), 4.28 (q, 2H, $C\underline{H}_2CH_3$), 8.67 (broad s, 1H, N-$\underline{H}$), 9.62 (s, 1H, C$\underline{H}$O); ^{13}CMR ($CDCl_3$): δ14.05 ($OCH_2\underline{C}H_3$), 20.69, 21.63, 22.18, 22.72, 25.09, 26.05, 26.31, 28.31, 31.05 ($-(\underline{C}H_2)_{10}-$), 60.69 ($O\underline{C}H_2CH_3$), 124.38 ($C_2$-pyrrole carbon), 129.88, 131.79 (C_4- and C_5-pyrrole carbons), 135.50 (C_3-pyrrole carbon), 160.51 (EtO$\underline{C}$=O), 179.46 (H$\underline{C}$=O); MS (70 eV): m/e = 305 (parent).

4-Acetyl-3-ethyl-2-iodopyrrole (70), 4-carbethoxy-3-methyl-2-iodopyrrole (71), 3-acetyl-5-methyl-4-phenyl-2-iodopyrrole (72), 3,4-dimethyl-5-formyl-2-iodopyrrole (73), 2,5-dimethyl-3,4-diiodopyrrole (77), and 5,5'-diiodo-2,2'-dipyrroketone (78)

General Procedure:

To a refluxing solution containing 12.5 mmol each of the appropriate pyrrole, acetic acid and 30% hydrogen peroxide in 15 ml of ethanol, there was added 12.5 mmol of potassium iodide in 10 ml of water. The rate of addition was adjusted so that the dark red color which immediately formed with each drop, rapidly disappeared. The solution was refluxed for one hour after completion of addition and allowed to sit at room temperature overnight. The white crystals were collected by suction filtration, washed with

95% ethanol, and allowed to dry. Spectral characteristics of 70, 71, 72, 73, 77, and 78 are summarized below.

4-Acetyl-3-ethyl-2-iodopyrrole (70)

mp. 146-147.5°; IR (Nujol): 3125 cm^{-1} (N-H), 1620 (C=O); PMR ($CDCl_3$): δ1.07 (t, 3H, $CH_2C\underline{H}_3$), 2.37 (s, 3H, $COC\underline{H}_3$), 2.67 (q, 2H, $C\underline{H}_2CH_3$), 7.30 (d, 1H, C_5-pyrrole-$\underline{H}$), 8.83 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ13.89 ($CH_2\underline{C}H_3$), 19.91 ($\underline{C}H_2CH_3$), 26.09 ($CO\underline{C}H_3$), 68.82 (C_2-pyrrole carbon), 122.72 (C_3-pyrrole carbon), 128.15 (C_5-pyrrole carbon), 130.15 (C_4-pyrrole carbon), 191.34 (C_4-pyrrole carbon); MS (70 eV): m/e = 263 (parent).

4-Carbethoxy-3-methyl-2-iodopyrrole (71)

IR (Nujol): 3235 cm^{-1} (N-H), 1660 (C=O); PMR ($CDCl_3$): δ1.30 (t, 3H, $CH_2C\underline{H}_3$), 2.20 (s, 3H, $C\underline{H}_3$), 4.17 (q, 2H, $C\underline{H}_2CH_3$), 7.28 (d, 1H, C_5-pyrrole-$\underline{H}$), 8.37 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ12.20 (C_3-$\underline{C}H_3$), 13.37 ($CH_2\underline{C}H_3$), 58.08 ($O\underline{C}H_2$), 67.35 (C_2-pyrrole carbon), 114.02 (C_5-pyrrole carbon), 126.76 (C_3- and C_4-pyrrole carbons), 161.29 (C=O); MS (70 eV): m/e = 279 (parent).

3-Acetyl-5-methyl-4-phenyl-2-iodopyrrole (72)

mp. 158-159°; IR (Nujol): 3145 cm^{-1} (N-H), 1615 (C=O); PMR ($CDCl_3$): δ1.81 (s, 3H, C_5-$C\underline{H}_3$), 2.45 (s, 3H, $COC\underline{H}_3$), .17 (s, 5H, $C_6\underline{H}_5$), 10.95 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): 12.48 (C_5-$\underline{C}H_3$), 28.75 ($CO\underline{C}H_3$), 64.84 (C_2-pyrrole carbon), 20.95, 125.51, 129.26, 135.46, 137.34 (C_3-, C_4-, C_5-pyrrole

carbons and quaternary and para phenyl carbons), 126.53 (ortho phenyl carbons), 128.90 (meta phenyl carbons), 192.66 ($\underline{C}$=O); MS (70 eV): m/e = 325 (parent).

3,4-Dimethyl-5-formyl-2-iodopyrrole (73)

IR (Nujol): 3195 cm^{-1} (N-H), 1620 (C=O); PMR ($CDCl_3$/DMSO-d_6): δ1.92 and 2.23 (two s, 6H, $C\underline{H}_3$), 9.18 (s, 1H, $C\underline{H}O$), 10.98 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$/DMSO-d_6): δ8.11, 10.00 ($\underline{C}H_3$), 80.36 (C_2-pyrrole carbon), 124.28, 128.09, 132.38 (C_3-, C_4-, and C_5-pyrrole carbons), 174.86 ($\underline{C}$=O); MS (70 eV): m/e = 249 (parent).

2,5-Dimethyl-3,4-diiodopyrrole (77)

mp. 113-114.5°; IR (Nujol): 3345 (N-H); PMR ($CDCl_3$/DMSO-d_6): δ2.23 (s, 6H, $C\underline{H}_3$), 10.10 (broad s, 1H, N-$\underline{H}$); ^{12}CMR ($CDCl_3$/DMSO-d_6): δ13.65 ($\underline{C}H_3$), 70.78 (C_3- and C_4-pyrrole carbons), 128.68 (C_2- and C_5-pyrrole carbons); MS (70 eV): m/e = 347 (parent).

5,5'-Diiodo-2,2'-dipyrroketone (78)

IR (Nujol): 3165 cm^{-1} (N-H); PMR (DMSO-d_6): δ7.22 (m, 4H, -pyrrole-$\underline{H}$); MS (70 eV): m/e = 412 (parent).

Ethyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate (74), diethyl 3-methyl-5-iodopyrrole-2,4-dicarboxylate (75), and 2-Benzyl 4-ethyl 5-iodo-3-methylpyrrole 2,4-dicarboxylate (76)

General Procedure:

The appropriate pyrrole-2-carboxylic acid[43] (200 mmol) was dissolved in 250 ml of ethanol and 365 ml of water

containing 43.6 g of sodium bicarbonate. The solution was warmed to 65° and a mixture of iodine (47.1 g) and potassium iodide (69 g) in 550 ml of water was added dropwise as fast as it was decolorized. After being stirred for an additional 10 min, the hot solution was filtered and allowed to cool. The product was collected by suction filtration. Spectral characteristics of 74, 75, and 76 are summarized below.

Ethyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate (74)

IR (Nujol): 3250 cm^{-1} (N-H), 1670 (C=O); PMR ($CDCl_3$): δ1.33 (t, 3H, $CH_2\underline{CH_3}$), 1.93, 2.27 (two s, 6H, $\underline{CH_3}$), 4.25 (q, 2H, $\underline{CH_2}CH_3$), 9.00 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ10.92, 11.66 (C_3- and C_4-$\underline{C}H_3$), 14.34 ($CH_2\underline{CH_3}$), 60.08 ($O\underline{C}H_2$), 73.36 (C_5-pyrrole carbon), 123.56, 126.68, 128.68 (C_3-, C_4-, and C_2-pyrrole carbons), 160.82 ($\underline{C}$=O); MS (70 eV): m/e = 293 (parent).

Diethyl 3-methyl-5-iodopyrrole-2,4-dicarboxylate (75)

IR (Nujol); 3240 cm^{-1} (N-H), 1665 and 1690 (C=O); PMR ($CDCl_3$): δ1.33 (t, 6H, $CH_2\underline{CH_3}$), 2.50 (s, 3H, C_3-$\underline{CH_3}$), 4.20 (q, 4H, $\underline{CH_2}CH_3$), 11.83 (broad s, 1H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ10.30 (C_3-$\underline{C}H_3$), 12.62, 12.70 ($CH_2\underline{C}H_3$), 57.88, 58.26 ($\underline{C}H_2CH_3$), 77.67 (C_5-pyrrole carbon), 118.08, 123.20, 128.48 (C_3-, C_4-, and C_2-pyrrole carbons), 158.46, 161.73 ($\underline{C}$=O); MS (70 eV): m/e = 351 (parent).

4-Benzyl 2-ethyl 5-iodo-3-methylpyrrole-2,4-dicarboxylate (76)

IR (Nujol): 3230 cm^{-1} (N-H), 1670 and 1685 (C=O); PMR ($CDCl_3$): δ1.50 (t, 3H, $CH_2C\underline{H}_3$), 2.68 (C_3-$C\underline{H}_3$), 4.38 (q, 2H, $C\underline{H}_2CH_3$), 5.37 (s, 2H, $C\underline{H}_2C_6H_5$), 7.35 (s, 5H, $C_6\underline{H}_5$), 9.48 (broad s, 1H, N-$\underline{H}$); MS (70 eV): m/e = 412 (parent).

Diethyl 3,3',4,4'-tetramethyl-2,2'-bipyrrole-5,5'-dicarboxylate (79), tetraethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3',5,5'-tetracarboxylate (81), and 5,5'-dibenzyl 3,3'-diethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3',5,5'-tetracarboxylate (82)

General Procedure:

The iodopyrrole (10 g) was dissolved in N,N-dimethylformamide (5 ml) and 1 g of copper bronze was added. The mixture was stirred at 100° for three hours. The copper was then filtered and washed with hot chloroform (4 X 50 ml). The filtrate and washings were extracted with 1N hydrochloric acid (2 X 100 ml) and with water (2 X 100 ml) and dried over magnesium sulfate. After removal of the solvent, the product was recrystalized from chloroform/hexane. The spectral characteristics of 79, 81, and 82 are summarized below.

Diethyl 3,3',4,4'-tetramethyl-2,2'-bipyrrole-5,5'-dicarboxylate (79)

IR (Nujol): 3240 cm^{-1} (N-H), 1655 (C=O); PMR ($CDCl_3$): δ1.28 (t, 6H, $CH_2C\underline{H}_3$), 1.95, 2.23 (two s, 12H, $C\underline{H}_3$), 4.17

(q, 4H, $C\underline{H}_2CH_3$), 11.00 (broad s, 2H, N-$\underline{H}$); MS (70 eV): m/e = 332 (parent).

Tetraethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3',5,5'-tetracarboxylate (81)

IR (Nujol): 1690 and 1615 (C=O); PMR ($CDCl_3$): δ1.55 (t, 12H, $CH_2C\underline{H}_3$), 2.55 (s, 6H, C_4-$C\underline{H}_3$), 4.28 (overlapping q, 4H, $C\underline{H}_2CH_3$), 13.98 (broad s, 2h, N-$\underline{H}$); MS (70 eV): m/e = 448 (parent).

5,5'-Dibenzyl 3,3'-diethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3',5,5'-tetracarboxylate (82)

IR (Nujol): 1720 and 1625 (C=O); PMR ($CDCl_3$): δ1.38 (t, 6H, $CH_2C\underline{H}_3$'s), 2.57 (s, 6H, C_4-$C\underline{H}_3$), 4.30 (q, 4H, $C\underline{H}_2CH_3$), 5.25 (s, 4H, $C\underline{H}_2C_6H_5$), 7.20 (m, 10H, $C_6\underline{H}_5$), 14.13 (broad s, 2H, N-$\underline{H}$); MS (70 eV): m/e = 572 (parent).

3,3',4,4'-Tetramethyl-2,2'-bipyrrole-5,5'-dicarboxylic acid (80)

In an oven-dried 100 ml flask, bis(triphenylphosphine)-nickel(II)dichloride (4.0 mmol), triphenylphosphine (8.0 mmol), and zinc dust (4.0 mmol) were stirred in 20 ml of oxygen-free N,N-dimethylformamide. The system was evacuated by a pump and flushed with nitrogen. This was repeated twice before the flask was immersed in an oil bath at 50^o and stirred for an hour. The deep blue solution turned green and then brown. Ethyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate (3.0 mmol) in 20 ml of oxygen-free N,N-dimethylformamide was added and the solution was stirred overnight.

The cooled solution was poured into 80 ml of 2% aqueous hydrochloric acid. The product was extracted into 120 ml of chloroform and diluted with 120 ml of ether. This solution was washed with water, then brine, and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residual solid and 1.0 g of potassium hydroxide was refluxed overnight in 50 ml of 1:1 ethanol/water. The cooled solution was extracted twice with ether. Acetic acid (1 ml) was added to the aqueous layer to precipitate a quantitative yield (contaminated by a small amount of triphenylphosphine) of 80: IR (Nujol): 3280 cm^{-1} (N-H), 1700 (C=O); PMR ($CDCl_3$/DMSO-d_6): δ1.93, 2.25 (two s, 12H, CH_3), 10.62 (broad s, 2H, N-H); MS (70 eV): m/e = 188 (parent).

3,3'-Diethyl-4,4'-dimethyl-2,2'-dipyrrole-3,3'-dicarboxylate-5,5'-dicarboxylic acid (83)

5,5'-Dibenzyl 3,3'-diethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3',5,5'-tetracarboxylate (1.4 mmol) and nickel(II)dichloride hexahydrate (27.2 mmol) were dissolved in 300 ml of absolute ethanol under nitrogen and cooled to 0°. Sodium borohydride (81.5 mmol) in 80 ml of water was added dropwise. The black mixture was refluxed for one hour after completion of addition. The black precipitate was removed by suction filtration and the solvent removed under reduced pressure. The residue was dissolved in ether and extracted with 10% aqueous sodium hydroxide. The basic

aqueous layer was neutralized to precipitate 1.1 mmol (78%) of 83: IR (Nujol): 3200-3400 cm^{-1} (N-H) and OH), 1635 (C=O); MS (70 eV): m/e = 348 (parent $-2CO_2$).

3-Acetyl-4-phenyl-2,2'-bipyrrole (87), 3-acetyl-3',4'-dimethyl-4-phenyl-2,2'-bipyrrole (88), 2-methyl-4-phenyl-3,2'-dipyrroketone (90), and 2,3',4'-trimethyl-4-phenyl-3,2'-dipyrroketone (91)

General Procedure:

2-Acetoacetylpyrrole (84 or 85) (12 mmol) and nickel acetylacetonate (0.1 g) were dissolved in 20 ml of acetone under nitrogen. 2-Phenylazirine (12 mmol) was added and the solution was stirred overnight. Water (75 ml) was added and the product collected by suction filtration. The crude product was chromatographed on silica gel using methylene chloride to elute bipyrrole (87 or 88) and 2% methanol in methylene chloride to elute dipyrroketone (90 or 91). Yields are given in Table 6 (page 81) and spectral characteristics are summarized below.

3-Acetyl-4-phenyl-2,2'-bipyrrole (87)

IR (Nujol): 3400 and 3200 cm^{-1} (N-H), 1600 (C=O); PMR ($CDCl_3$): δ2.02 ($COC\underline{H}_3$), 6.19-6.75 (four m, 4H, pyrrole-$\underline{H}$), 7.20 (s, 5H, $C_6\underline{H}_5$), 8.50 and 11.70 (two broad s, 2H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ31.02 ($CO\underline{C}H_3$), 105.78, 109.49 ($C_{3'}$- and $C_{4'}$-pyrrole carbons), 118.57, 116.95, 118.81, 124.03, 126.93, 127.66, 130.98 ($C_{2'}$-, $C_{5'}$-, C_2-, C_3-, C_4-, C_5-pyrrole and

para phenyl carbons), 128.24 (ortho phenyl carbons), 129.36 (meta phenyl carbons), 136.06 (quaternary phenyl carbon), 193.42 ($\underline{C}$=O); MS (70 eV): m/e = 250 (parent).

3-Acetyl-3',4'-dimethyl-4-phenyl-2,2'-bipyrrole (88)

IR (Nujol): 3330 and 3190 cm^{-1} (N-H), 1615 (C=O); PMR ($CDCl_3$): δ2.08 (s, 3H, $COC\underline{H}_3$), 2.13, 2.35 (C_3- and C_4-$C\underline{H}_3$), 6.63 (m, 2H, pyrrole-$\underline{H}$), 7.30 (s, 5H, $C_6\underline{H}_5$), 8.53, 11.22 (two broad s, 2H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ10.10, 10.85 ($\underline{C}H_3$), 31.10 ($CO\underline{C}H_3$), 116-136 (aromatic carbons), $\underline{C}$=O not observed; MS (70 eV): m/e = 278 (parent).

2-Methyl-4-phenyl-3,2'-dipyrroketone (90)

IR (Nujol): 3260 and 3185 cm^{-1} (N-H), 1570 (C=O); PMR ($CDCl_3$): δ2.40 (s, 3H, pyrrole-$C\underline{H}_3$), 6.00-6.80 (four m, 4H, pyrrole-$\underline{H}$), 7.17 (m, 5H, $C_6\underline{H}_5$), 8.43, 9.53 (two broad s, 2H, N-H): ^{13}CMR ($CDCl_3$): δ12.56 (C_2-$\underline{C}H_3$), 105-136 (aromatic carbons), $\underline{C}$=O not observed; MS (70 eV): m/3 = 250 (parent).

2,3',4'-Trimethyl-4-phenyl-3,2'dipyrroketone (91)

IR (Nujol): 3355 and 3150 cm^{-1} (N-H), PMR ($CDCl_3$): δ2.02, 2.05, 2.30 (three s, 9H, pyrrole-$C\underline{H}_3$), 6.60, 6.73 (two m, 2H, pyrrole-$\underline{H}$), 7.13 (m, 6H, $C_6\underline{H}_5$ and pyrrole-$\underline{H}$), 9.83, 10.42 (two broad s, 2H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$/DMSO-d_6): δ8.82, 9.02, 10.87 (pyrrole-$\underline{C}H_3$), 113-136 (aromatic carbons), $\underline{C}$=O not observed; MS (70 eV): m/e = 278 (parent).

5,5'-Dicarbethoxy-3,3',4,4'-tetramethyl-2,2'-dipyrromethane (93), 3,3',5,5'-tetracarbethoxy-4,4'-dimethyl-2,2'-dipyrromethane (94), and 5,5'-carbobenzyloxy-3,3',4,4'-tetramethyl-2,2'-dipyrromethane (95)

General Procedure:

The appropriate 2-methylpyrrole (300 mmol) was dissolved in 550 ml of acetic acid and warmed to 50^{o}. Sulfuryl chloride (300 mmol) in 30 ml of acetic acid was added dropwise over an hour. The crude chloromethylpyrrole was collected by suction filtration and used without further purification. The chloromethylpyrrole was refluxed in acetic acid (90 ml) and water (60 ml) for two hours. Water (30 ml) was added and the dipyrromethane was collected by filtration. Yields are given in Table 7 (page 83) and spectral characteristics are summarized below.

5,5'-Dicarbethoxy-3,3',4,4'-tetramethyl-2,2'-dipyrromethane (93)

IR (Nujol): 3320 cm^{-1} (N-H), 1670 and 1625 (C=O); PMR ($CDCl_3$): δ1.25 (t, 6H, $CH_2C\underline{H}_3$), 1.92, 2.20 (two s, 12H, pyrrole-$C\underline{H}_3$), 3.77 (s, 2H, pyrrole-$C\underline{H}_2$-pyrrole), 4.13 (q, 4H, $OC\underline{H}_2CH_3$), 9.15 (broad s, 2H, N-H); MS (70 eV): m/e = 346 (parent).

3,3',5,5'-Tetracarbethoxy-4,4'-dimethyl-2,2'-dipyrromethane (94)

IR (Nujol): 3410 cm^{-1} (N-H), 1725 and 1695 (C=O); PMR ($CDCl_3$): δ1.58 (overlapping q, 12H, $CH_2C\underline{H}_3$), 2.50 (s, 6H,

pyrrole-C$\underline{H}_3$), 4.20 (s, 2H, pyrrole-C$\underline{H}_2$-pyrrole), 4.37 (overlapping q, 8H, C$\underline{H}_2$CH$_3$), 10.00 (broad s, 2H, N-$\underline{H}$); ^{13}CMR (CDCl$_3$): δ11.76 (C$_4$-$\underline{C}$H$_3$), 14.20 (OCH$_2\underline{C}$H$_3$), 24.39 (pyrrole-$\underline{C}$H$_2$-pyrrole), 60.02 (O$\underline{C}$H$_2$), 112.98, 118.59, 129.58, 138.77 (pyrrole carbons), 160.93, 166.33 ($\underline{C}$=O); MS (70 eV): m/e = 462 (parent).

5,5'-Carbobenzyloxy-3,3',4,4'-tetramethyl-2,2'-dipyrromethane (95)

IR (Nujol): 3315 cm^{-1} (N-H), 1670 and 1640 (C=O); PMR (CDCl$_3$): δ1.93, 2.20 (two s, 12H, C$\underline{H}_3$), 3.70 (s, 2H, pyrrole-C$\underline{H}_2$-pyrrole), 5.13 (s, 4H, OC$\underline{H}_2$C$_6$H$_5$), 7.15 (s, 10H, C$_6\underline{H}_5$), 9.17 (broad s, 2H, N-H); ^{13}CMR (CDCl$_3$): δ8.70 (C$_4$-$\underline{C}$H$_3$), 10.71 (C$_3$-$\underline{C}$H$_3$), 22.70 (pyrrole-$\underline{C}$H$_2$-pyrrole), 65.49 (O$\underline{C}$H$_2$), 116.99 (C$_5$-pyrrole carbons), 117.09 (C$_3$-pyrrole carbons), 127.52 (ortho phenyl carbons), 127.67, 127.88 (C$_4$-pyrrole and para phenyl carbons), 128.23 (meta phenyl carbons), 130.63 (C$_2$-pyrrole carbons), 136.19 (quaternary phenyl carbon), 161.89 ($\underline{C}$ = O); MS (70 eV): m/e = 470 (parent).

3,3',4,4'-Tetramethyl-2,2'-dipyrromethane-5,5'-dicarboxylic acid (96) and diethyl 4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylic acid-3,3'-dicarboxylate (97)

General Procedure:

Dipyrromethane (93 or 94) (78.8 mmol) was heated to boiling in 350 ml of ethanol. Sodium hydroxide (20 ml of

a 4.1M aqueous solution, 82 mmol) was added and the solution was refluxed for three hours. Hydrochloric acid (20 ml) was diluted with 100 ml of ethanol and added to the cooled basic solution. The product was collected by suction filtration and washed with ethanol. Yields are given in Table 7 (page 83) and spectral characteristics of 96 and 97 are summarized below.

3,3',4,4'-Tetramethyl-2,2'-dipyrromethane-5,5'-dicarboxylic acid (96)

IR (Nujol): 3325 (N-H and O-H), 1670 (C=O); PMR ($CDCl_3/DMSO-d_6$): δ2.00, 2.23 (two s, 12H, $C\underline{H}_3$), 3.73 (s, 2H, pyrrole-$C\underline{H}_2$-pyrrole), 9.07 (broad s, 2H, N-$\underline{H}$); MS (70 eV): m/e = 290 (parent).

Diethyl 4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylic acid-3,3'-carboxylate (97)

IR (Nujol); 3420, 3365, and 3215 cm^{-1} (N-H and O-H), 1710 and 1650 (C=O); PMR ($CDCl_3/DMSO-d_6$): δ1.32 (t, 6H, $CH_2C\underline{H}_3$), 2.43 (s, 6H, $C\underline{H}_3$), 4.20 (q, 2H, pyrrole-$C\underline{H}_2$-pyrrole), 8.70 (broad s, 2H, N-$\underline{H}$); MS (70 eV): m/e = 406 (parent).

5,5'-Diethoxycarbonyl-3,3',4,4'-tetramethyl-2,2'-dipyrroketone (98)

Ethyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate (7 g, 23.9 mmol) and copper bronze (7 g) were stirred in 35 ml of N,N-dimethylformamide at 100° for three hours. The hot solution was filtered by gravity. The copper was washed

with chloroform (4 X 50 ml). The filtrate and combined washings were extracted with 1N hydrochloric acid (2 X 100 ml) and water (2 X 100 ml). The solvent was removed under reduced pressure and the crude product was recrystalized from chloroform/hexane to give 1.2 g (27%) of 98: mp. 210-211^{o} (lit.^{50} 212-214^{o}); IR (Nujol); 3255 cm^{-1} (N-H), 1665 and 1625 (C=O); PMR ($CDCl_3$): δ1.38 (t, 6H, $CH_2C\underline{H}_3$), 2.23, 2.28 (two s, 12H, $C\underline{H}_3$), 3.98 (q, 8H, $C\underline{H}_2CH_3$), 8.97 (broad s, 2H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ9.71, 10.04 (C_3- and C_4-$\underline{C}H_3$), 14.04 ($CH_2\underline{C}H_3$), 60.65 ($O\underline{C}H_2$), 121.78 (C_5-pyrrole carbon), 126.64, 126.80 (C_3- and C_4-pyrrole carbons), 131.59 (C_2-pyrrole carbon), pyrrole-$\underline{C}$=O-pyrrole not observed; MS (70 eV): m/e = 360 (parent).

3,3',4,4',5,5'-Hexamethyldipyrro-2,2'-trimethine hydrobromide (100) and 3,3',4,4',5,5'-hexamethyldipyrro-2,2'-hexacyclotrimethine hydrobromide (101)

General Procedure:

2-Carbo-t-butoxy-3,4,5-trimethylpyrrole (10 mmol) and 5 mmol of malonaldehyde bis-(dimethyl acetal) or 1,3-cyclohexadione were brought to a reflux in 40 ml of ethanol. Hydrobromic acid (1 ml) was added to the refluxing solution which immediately turned ink-blue. After refluxing for one-half hour, the solution was allowed to cool overnight. The product was collected by suction filtration and washed with ether. Yields and spectral characteristics of 100 and 101 are summarized below.

3,3',4,4',5,5'-Hexamethyldipyrro-2,2'-trimethine hydrobromide (100)

65%; IR (Nujol): 3125 cm^{-1} (N-H), 1560 (C=C); PMR ($CDCl_3$): δ1.98 (s, 6H, C_3- and $C_{3'}$-CH_3), 2.17 (s, 6H, C_4- and $C_{4'}$-$C\underline{H}_3$), 2.50 (s, 6H, C_5- and $C_{5'}$-$C\underline{H}_3$), 7.17 (m, 3H, vinyl-H); MS (70 eV): m/e = 254 (parent-HBr).

3,3',4,4',5,5'-Hexamethyldipyrro-2,2'-hexacyclo-trimethine hydrobromide (101)

33% yield; IR (Nujol): 3125 cm^{-1} (N-H), 1555 and 1510 (C=C); PMR ($CDCl_3$): δ1.97 (s, and m, 8H, C_3- and $C_{3'}$-$C\underline{H}_3$ and $C{=}CH\text{-}CH_2C\underline{H}_2$), 2.28 (s, 6H, C_4- and $C_{4'}$-$C\underline{H}_3$), 2.55 (s, 6H, C_5- and $C_{5'}$-$C\underline{H}_3$), 2.88 (t, 4H, $C{=}CH\text{-}C\underline{H}_2$), 7.95 (s, 1H, $C{=}C\underline{H}$), 11.88 (broad s, 2H, N-$\underline{H}$); ^{13}CMR ($CDCl_3$): δ8.74 (C_4-$\underline{C}H_3$), 12.31 (C_3-$\underline{C}H_3$), 13.77 (C_5-$C\underline{H}_3$), 27.15 ($C{=}CH\text{-}\underline{C}H_2$), 35.89 ($C{=}CH\text{-}CH_2\text{-}\underline{C}H_2$), 115.88, 123.98, 130.17, 134.47 (pyrrole carbons), 146.34 ($\underline{C}{=}CH$), 153.71 ($C{=}\underline{C}H$); MS (70 eV): m/e = 292 (parent-HBr).

1,5-Di-(5-carbo-t-butoxy-3,4-dimethyl-2-pyrro)-1,4-pentadiene-3-one (103) and 2,5-di-(5-carbo-t-butoxy-3,4-dimethyl-pyrr-2-ylmethylene)-cyclopentanone (104)

General Procedure:

To a stirred mixture of 5-carbo-t-butoxy-3,4-dimethylpyrrole-2-carboxaldehyde[43] (10 mmol), 4 ml of 15% NaOH, 10 ml of water and 14 ml of ethanol was added 5 mmol of acetone or cyclopentanone at room temperature. The mixture was stirred for two hours and then allowed to stand

overnight. The orange precipitate was collected by suction filtration to yield 1.5 g (65%) of 103 or 0.8 g (33%) of 104. Spectral characteristics are summarized below.

1,5-Di-(5-carbo-t-butoxy-3,4-dimethyl-2-pyrro)-1,4-pentadiene-3-one (103)

IR (Nujol): 3350 and 3225 cm^{-1} (N-H), 1655 (C=O), 1595 (C=C); PMR ($CDCl_3/DMSO-d_6$): δ1.57 (s, 18H, $C(C\underline{H}_3)_3$), 2.10, 2.17 (two s, 12H, $C\underline{H}_3$), 6.88-7.67 (AB q, 4H, J = 18 Hz, vinylic protons), 10.72 (broad s, 2H, N-$\underline{H}$); MS (70 eV): m/e = 468 (parent).

2,5-Di-(5-carbo-t-butoxy-3,4-dimethyl-pyrr-2-ylmethylene)-cyclopentanone (104)

IR (Nujol): 3460 cm^{-1} (N-H), 1655 (C=O), 1580 (C=C); PMR ($CDCl_3/DMSO-d_6$): δ1.58, 1.63 (two s, 18H, $C(C\underline{H}_3)_3$), 2.07, 2.12, 2.22 (three s, 12H, $C\underline{H}_3$), 2.95 (s, 4H, $-C\underline{H}_2C\underline{H}_2-$), 6.63, 7.35 (two s, 2H, vinylic protons), 8.67 (broad s, 2H, N-$\underline{H}$); MS (70 eV): m/e = 494 (parent).

APPENDIX

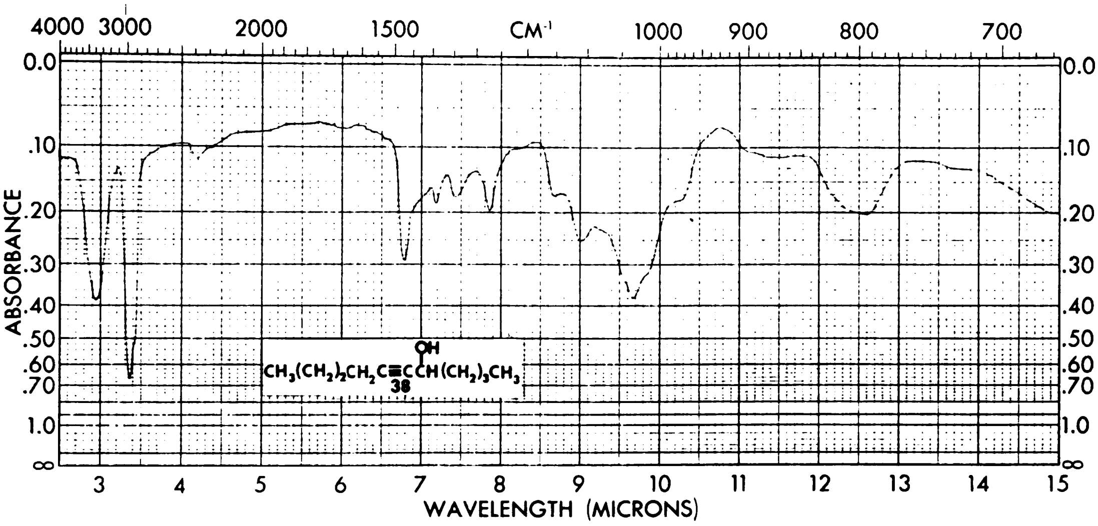


Figure 2. Infrared spectrum of 6-hydroxy-4-decyne (38).

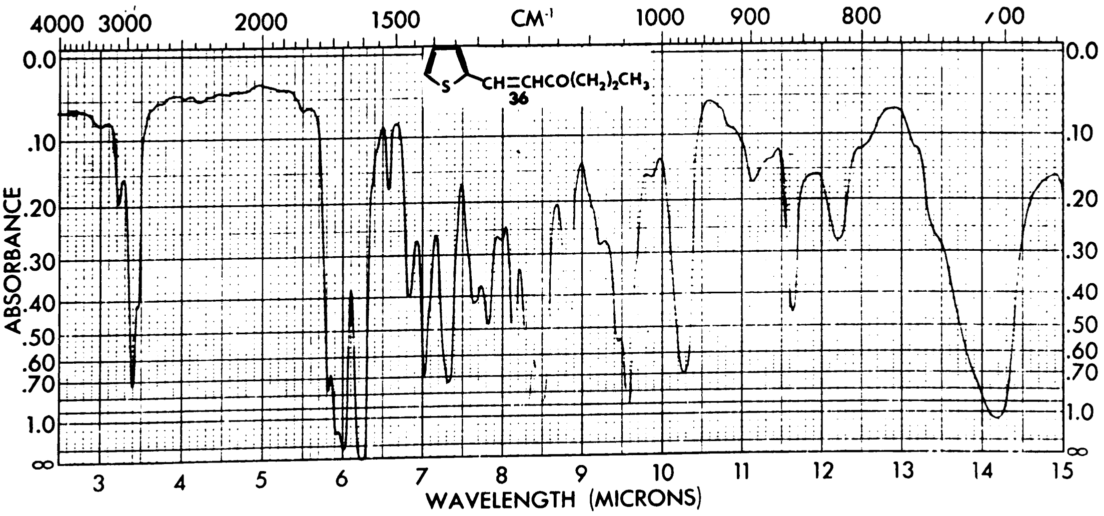
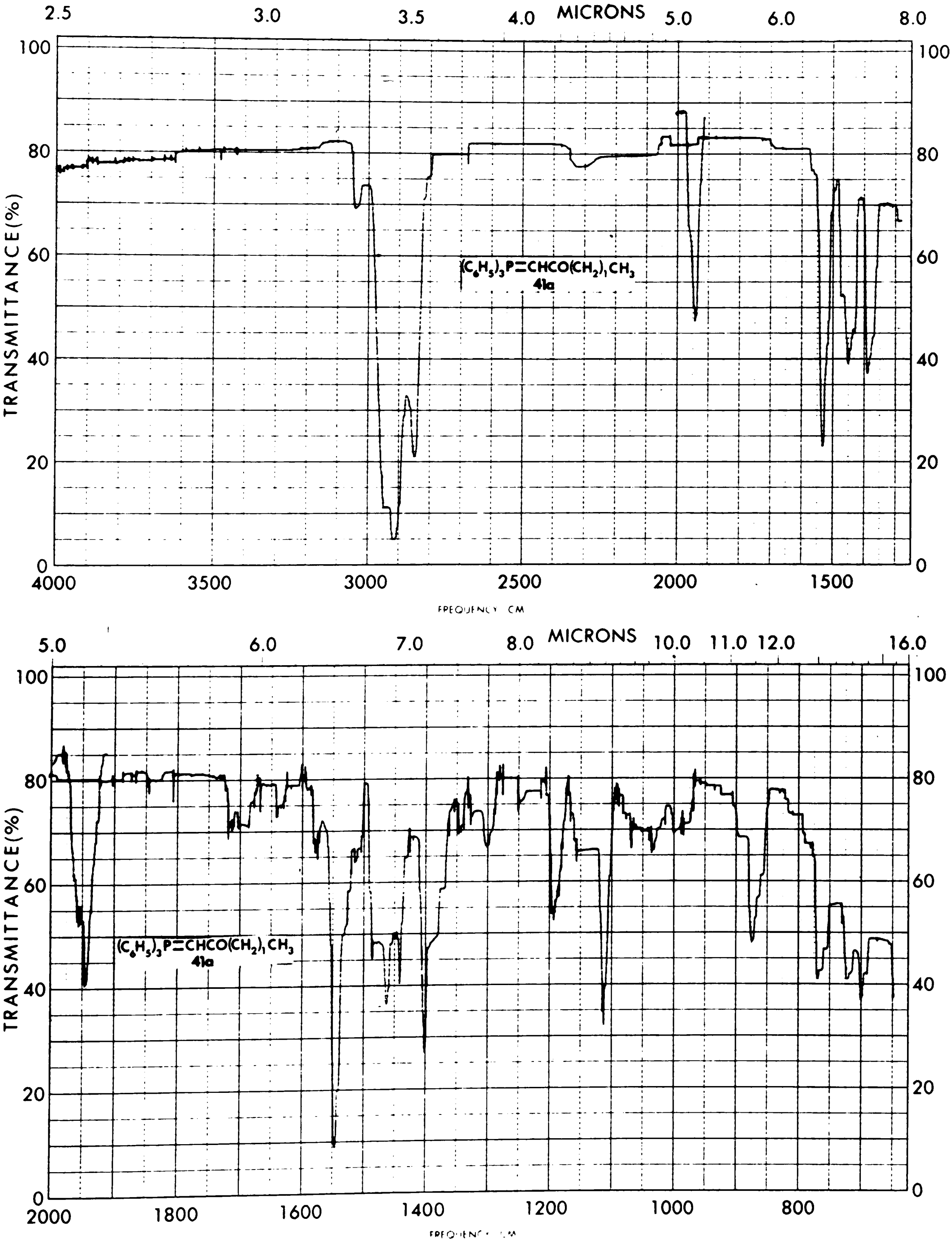


Figure 1. Infrared spectrum of 1-(2-thienyl)-hex-1-ene (36).



igure 3. Infrared spectrum of propyrylmethylenetriphenylphosphorane (41a).

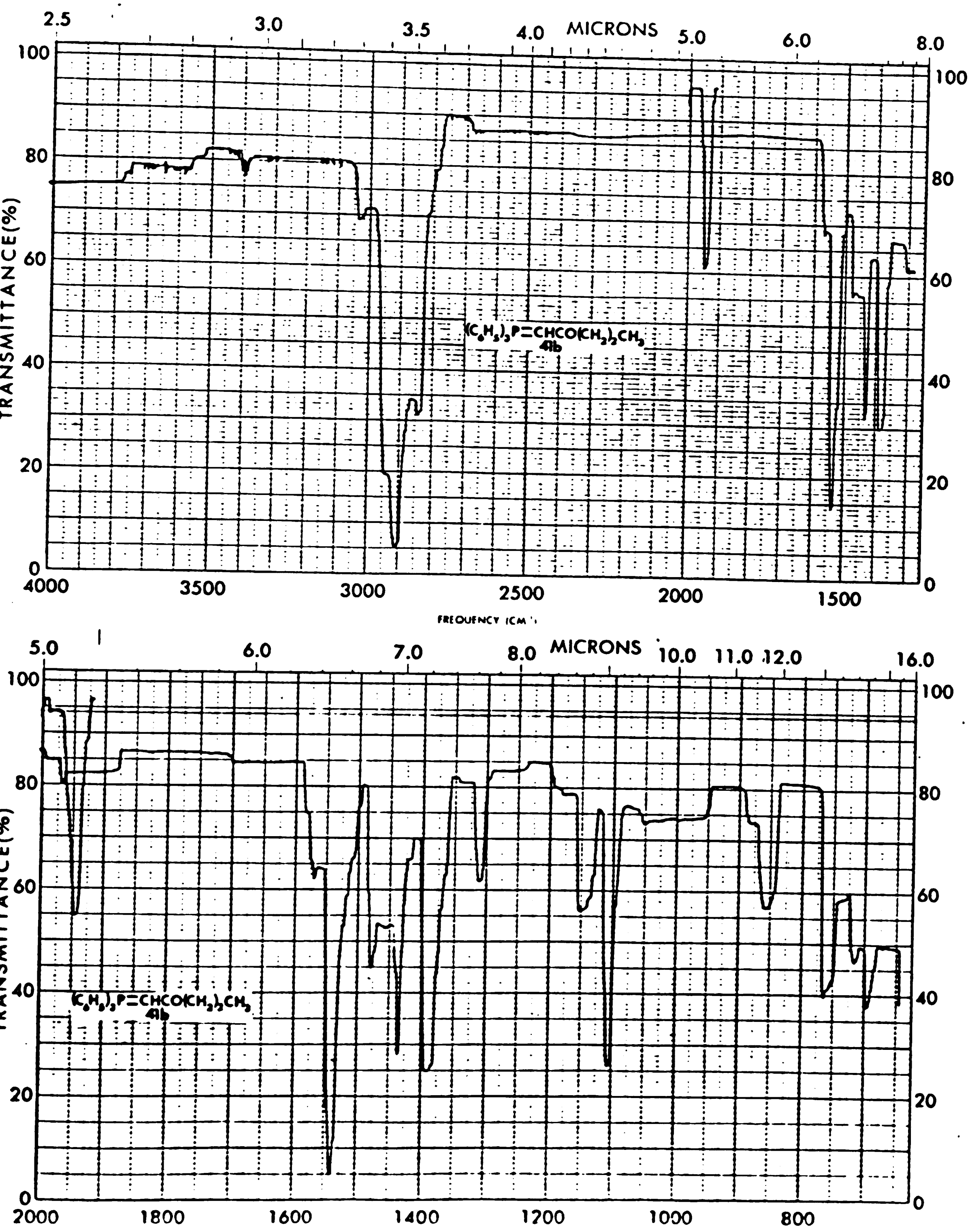
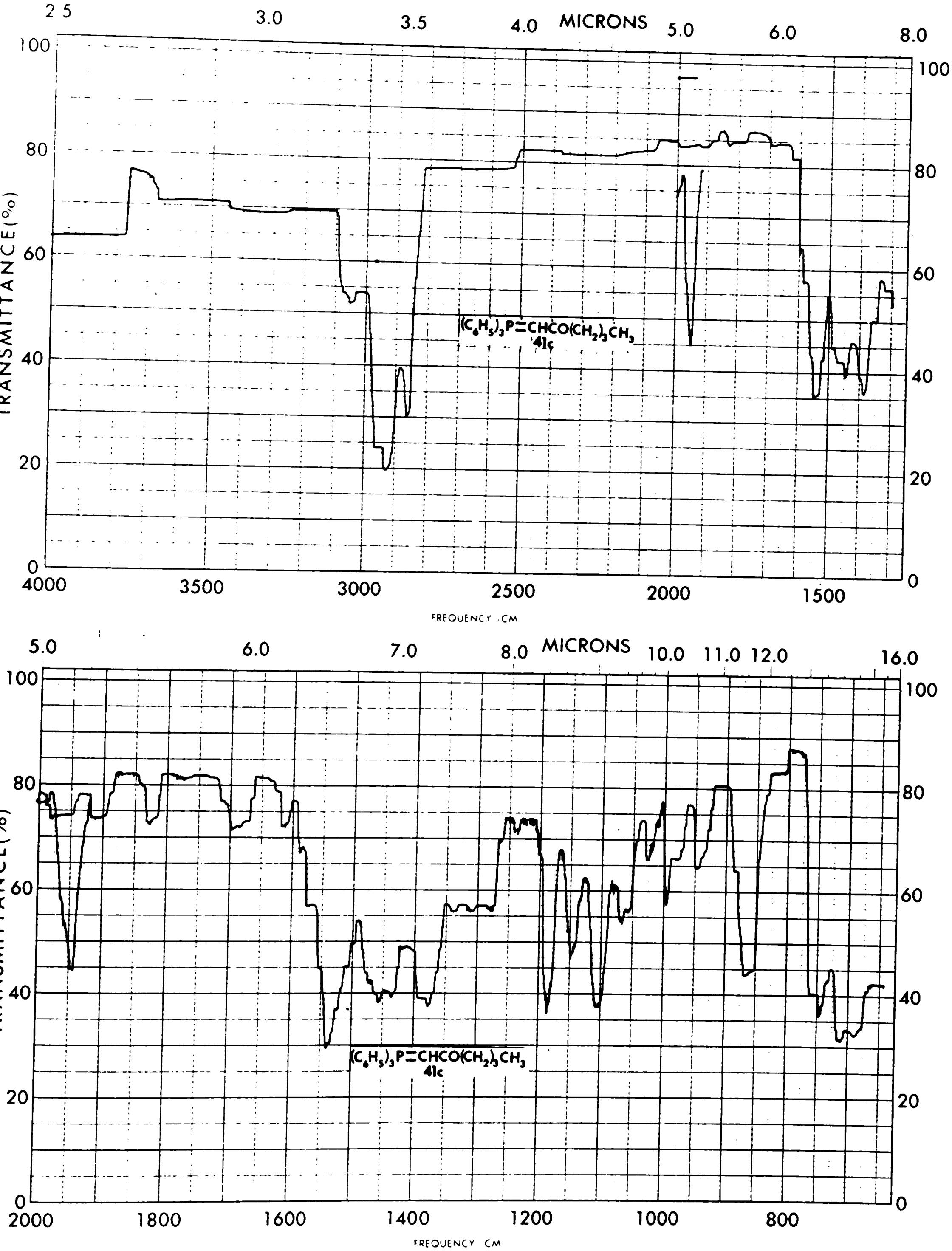


Figure 4. Infrared spectrum of butyrylmethylenetriphenylphosphorane (41b).



igure 5. Infrared spectrum of pentyrylmethylenetriphenylphosphorane (41c).

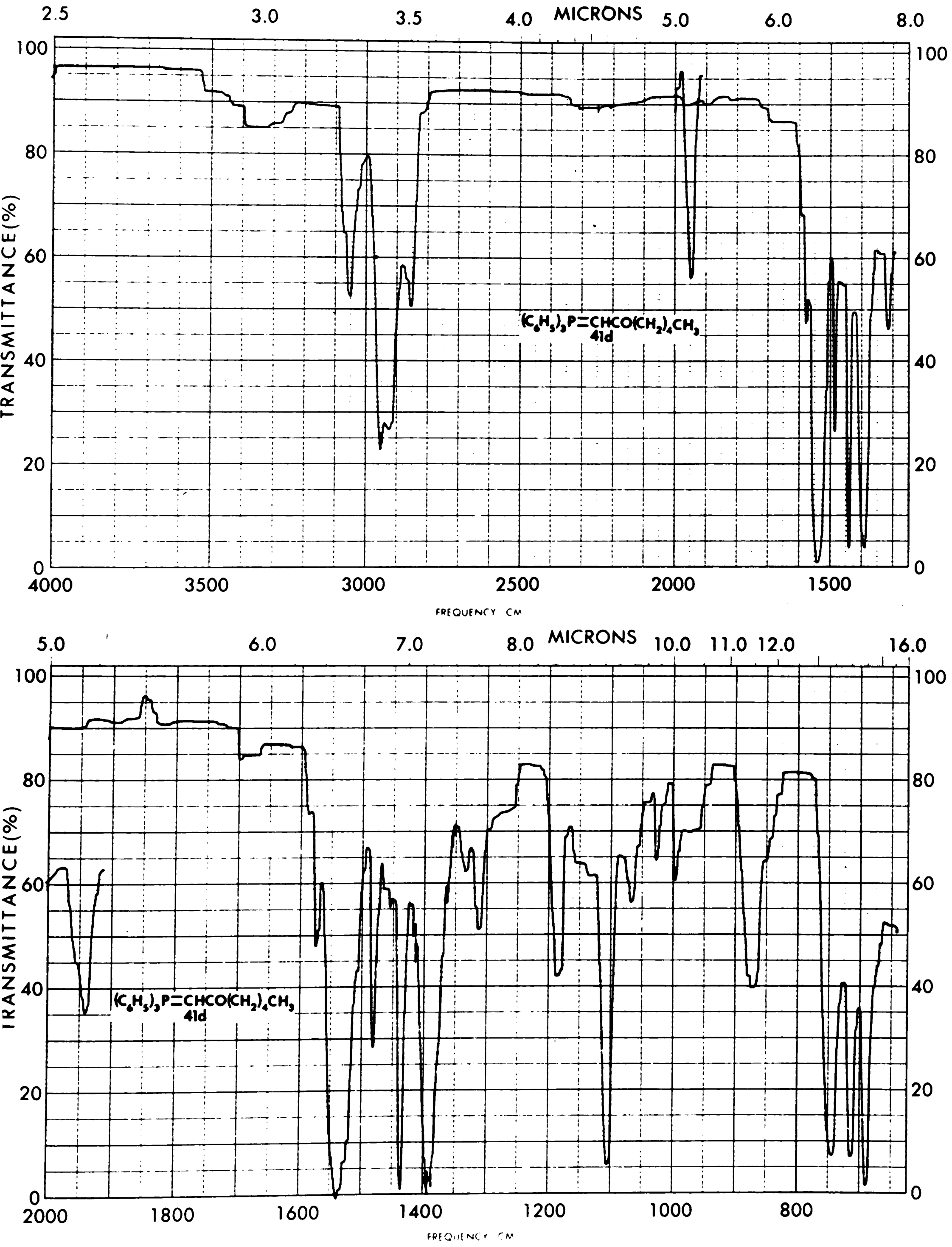


Figure 6. Infrared spectrum of hexyrylmethylenetriphenylphosphorane (41d).

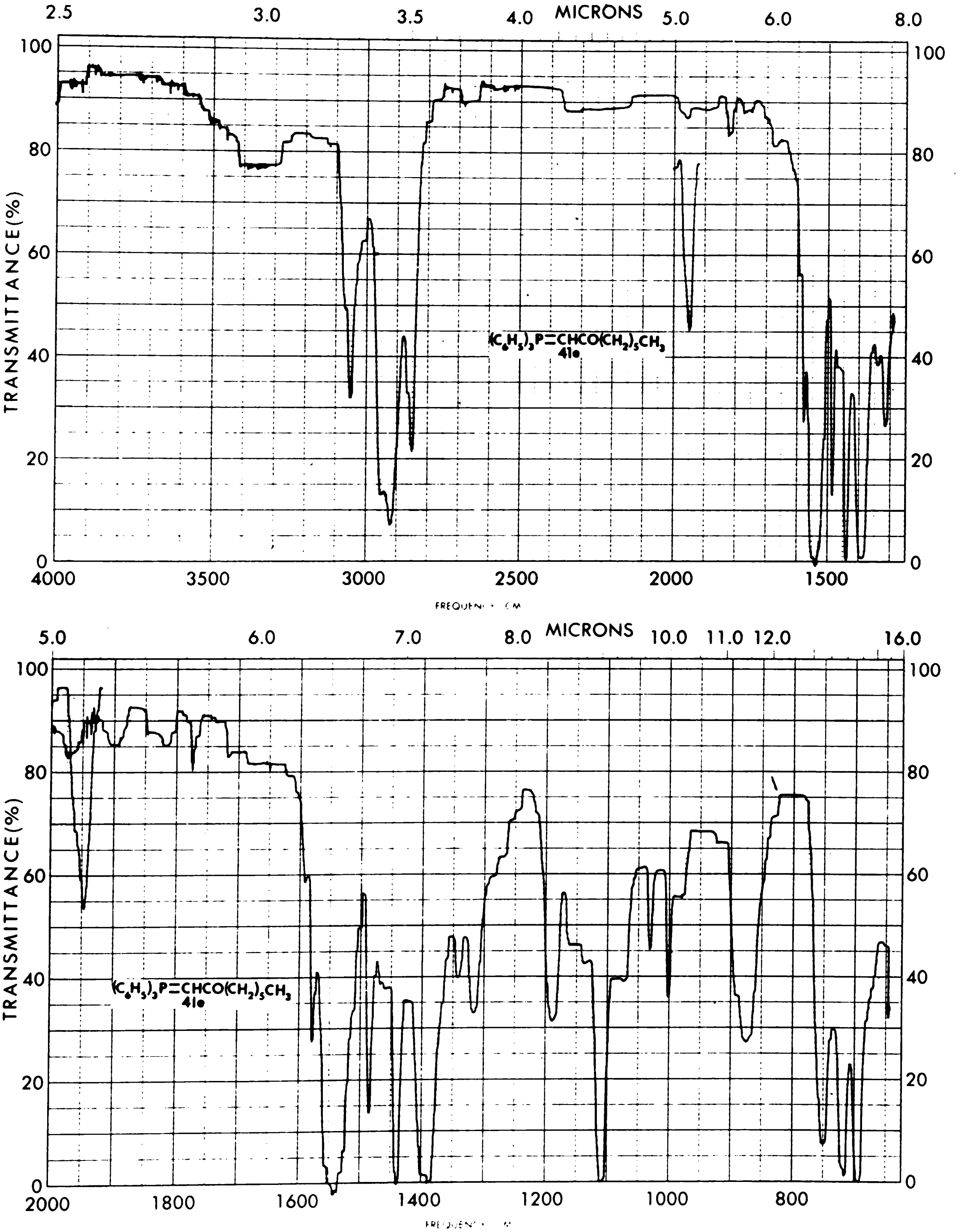


Figure 7. Infrared spectrum of heptyrylmethylenetriphenylphosphorane (41e).

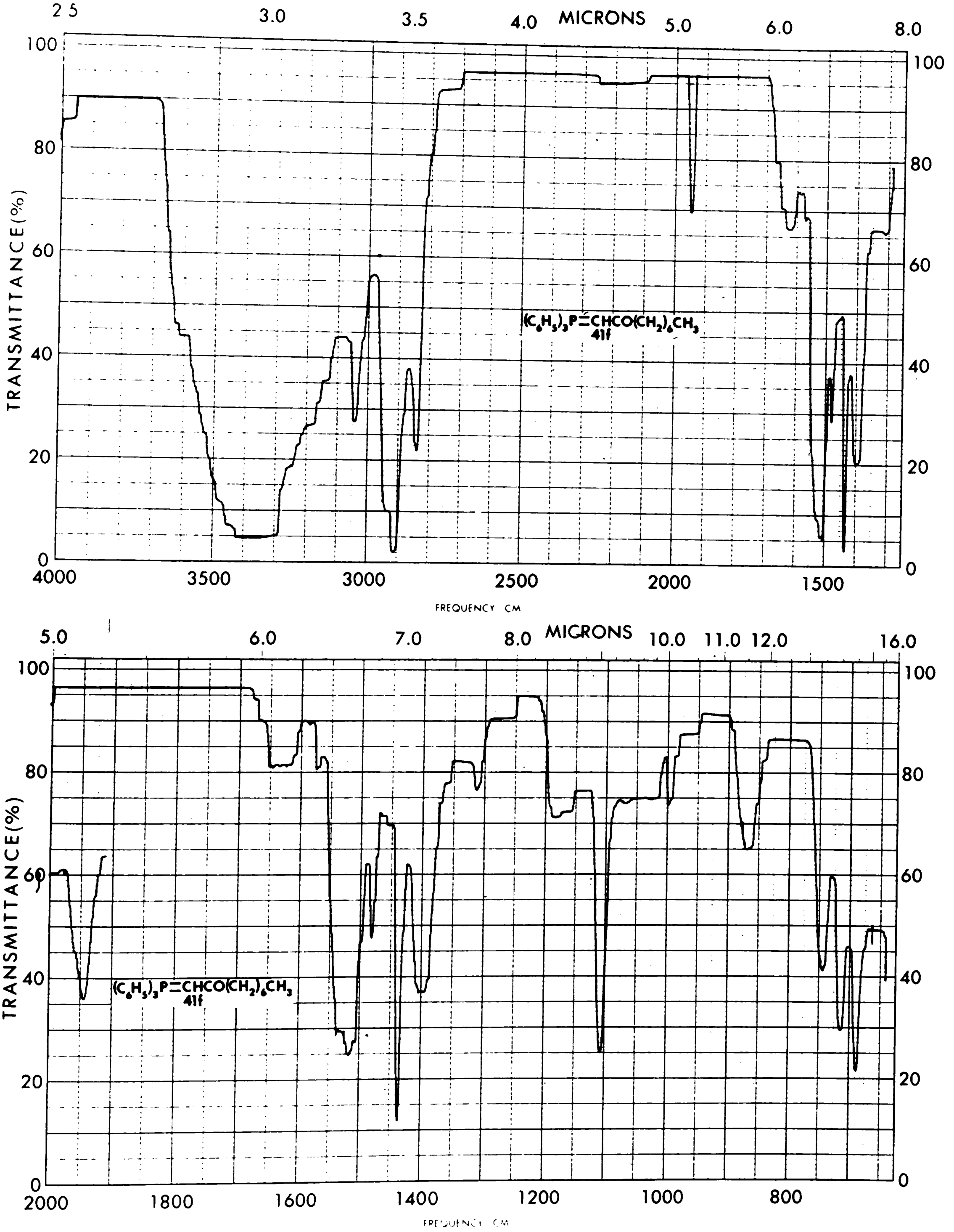
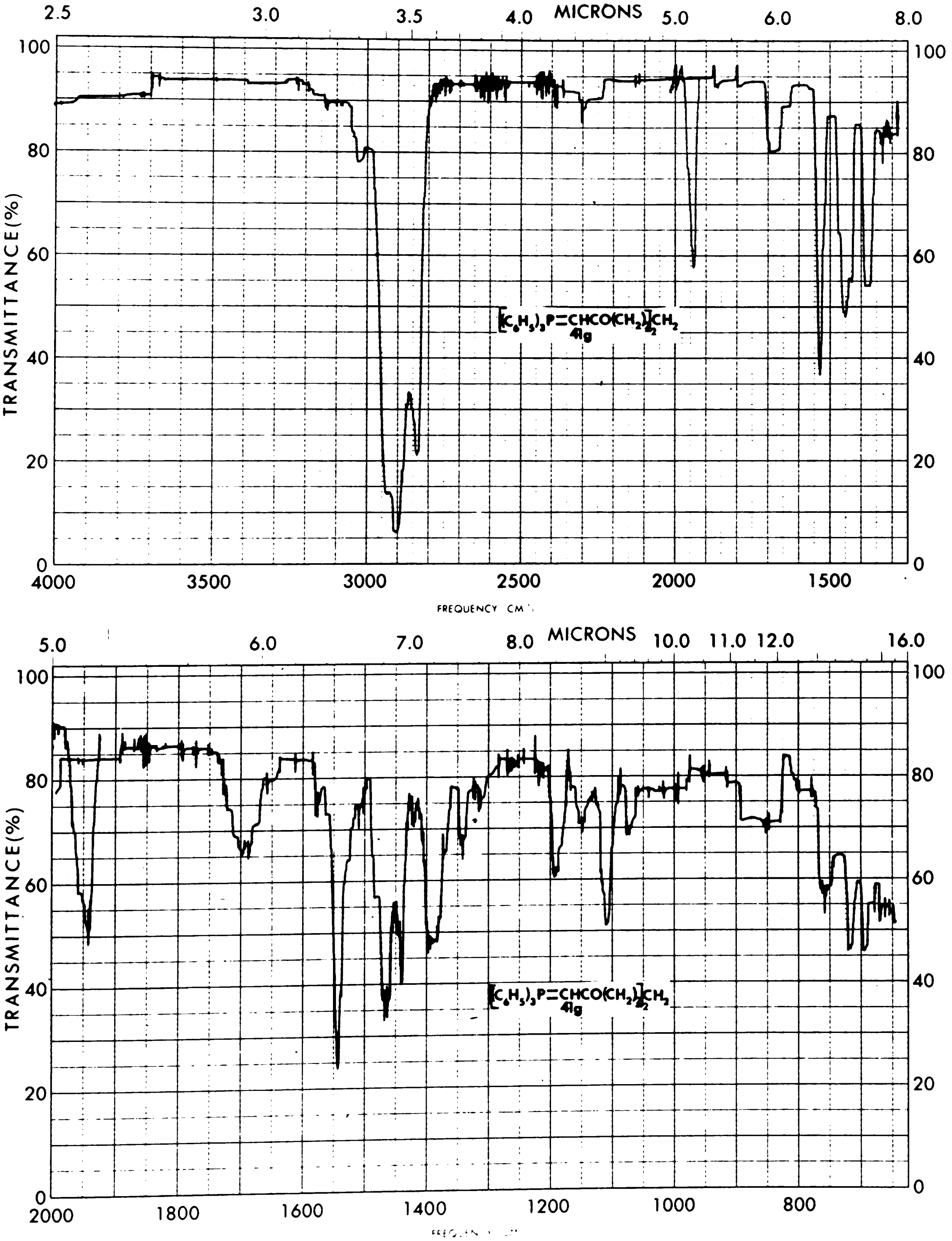


Figure 8. Infrared spectrum of octyrylmethylenetriphenylphosphorane (41f).



igure 9. Infrared spectrum of 1,3-diacetylmethylenetriphenylphosphorane (41g).

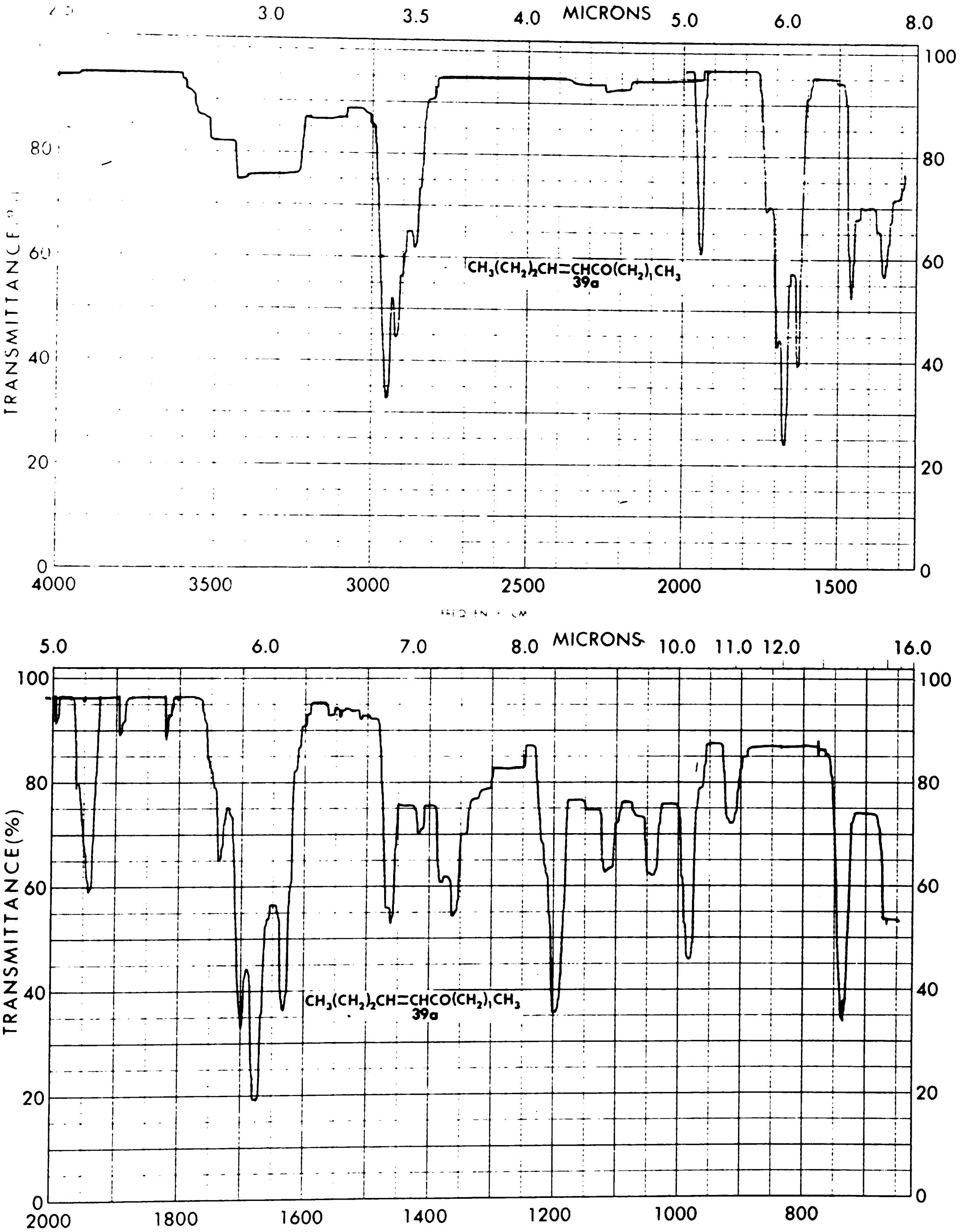
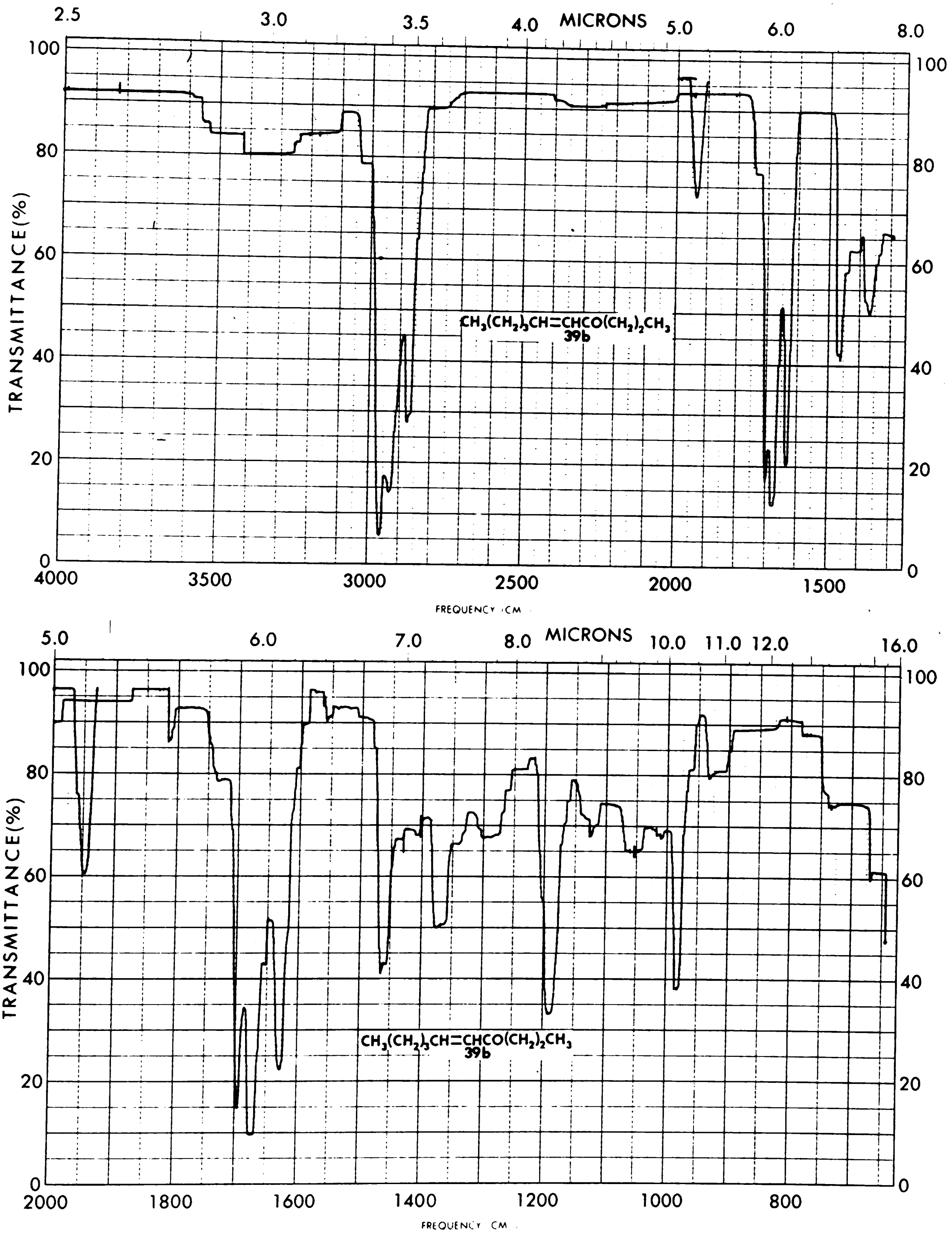
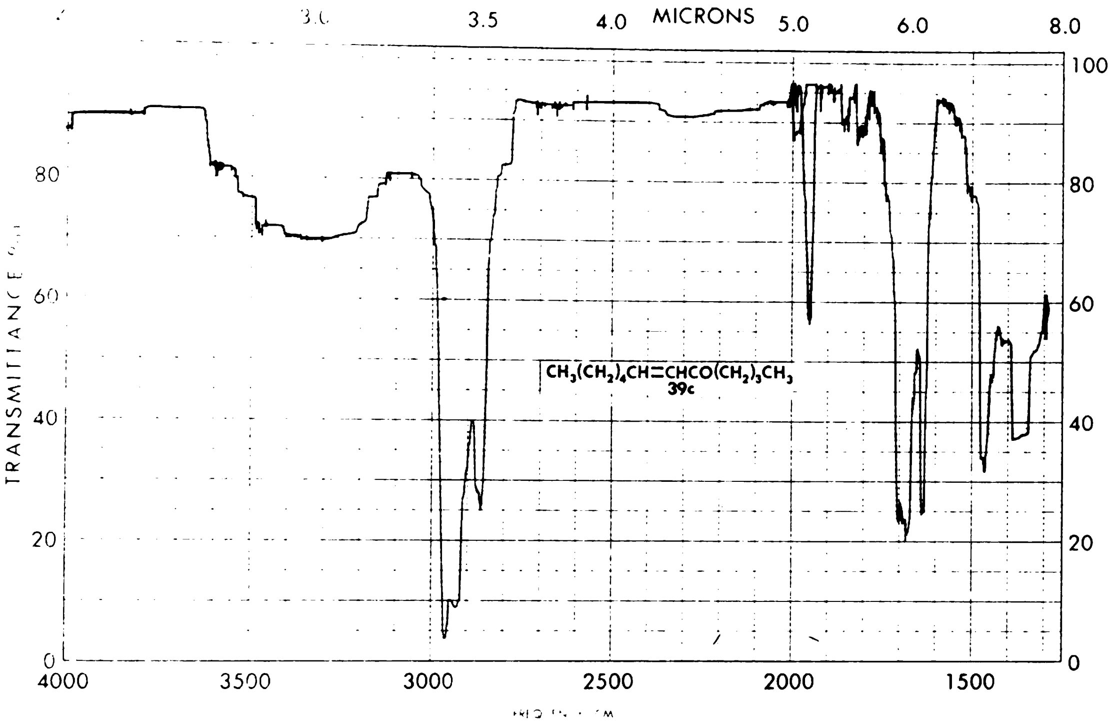


Figure 10. Infrared spectrum of 4-octene-3-one (39g).



igure 11. Infrared spectrum of 5-decene-4-one (39b).



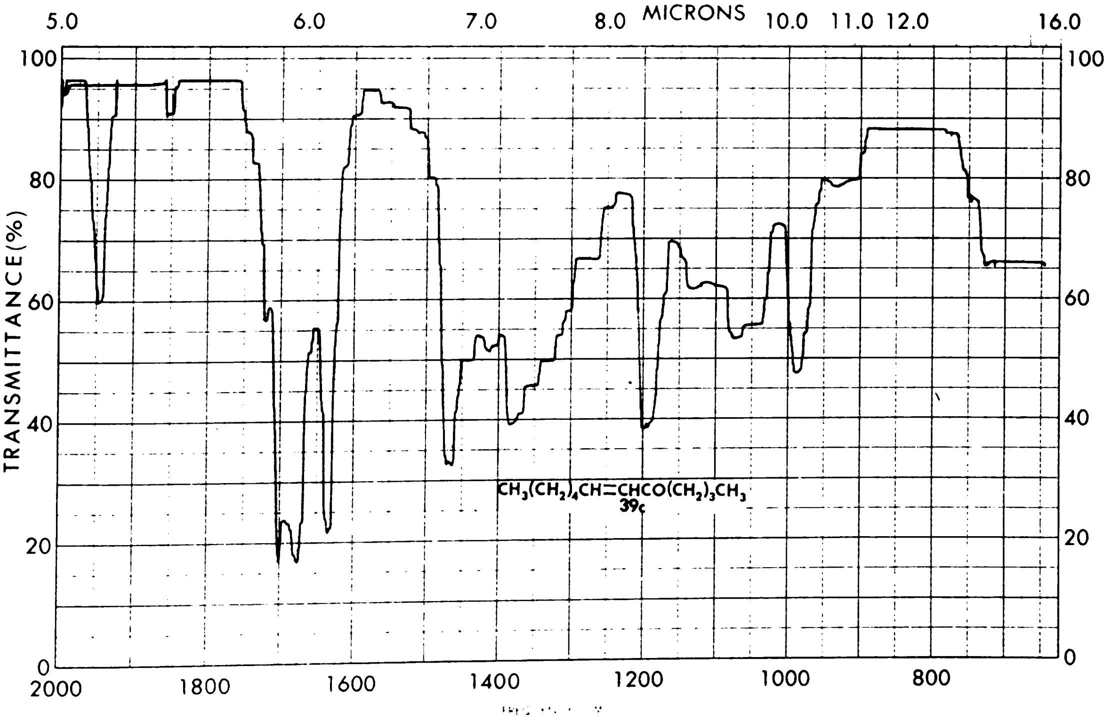
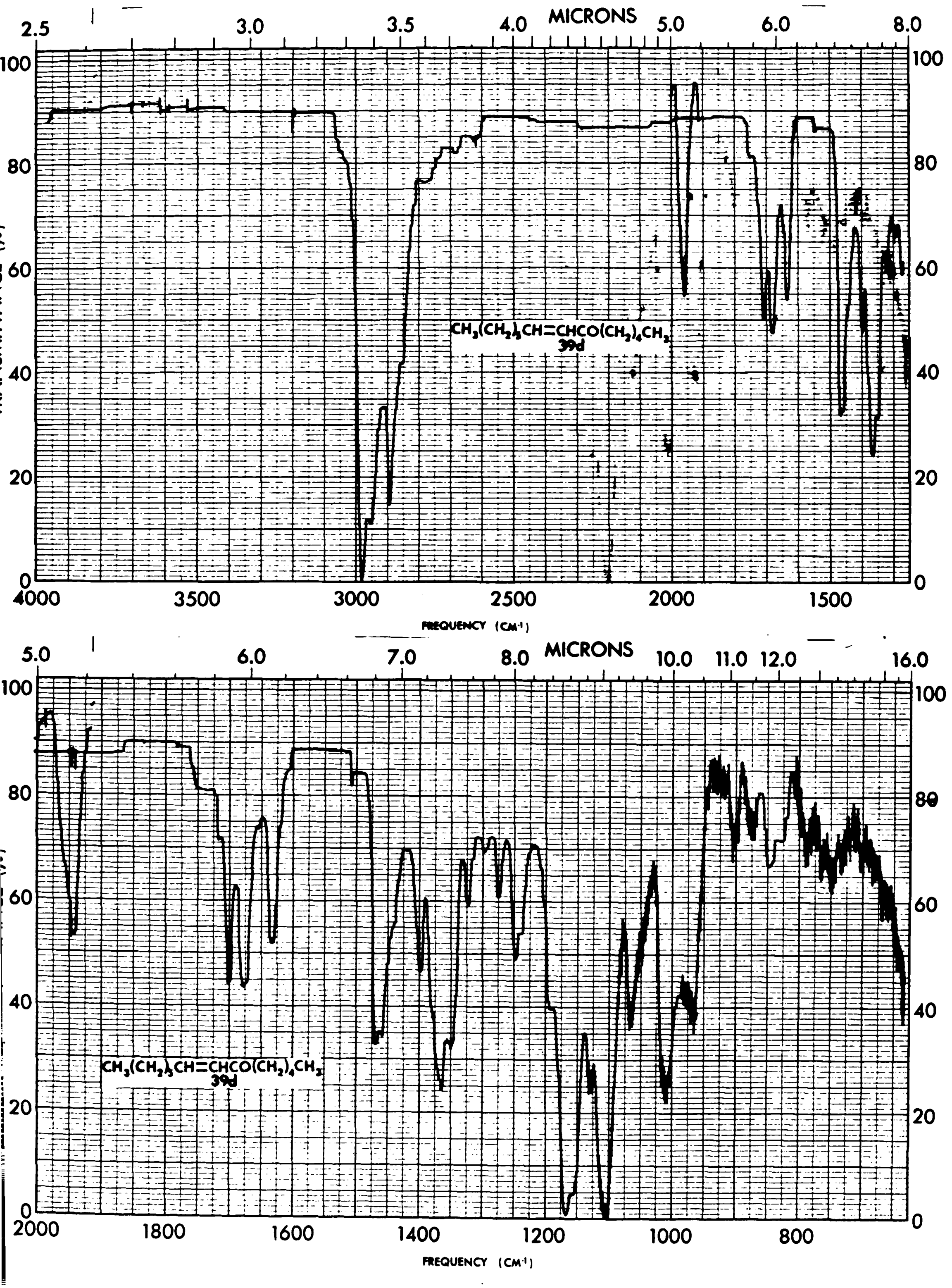


Figure 12. Infrared spectrum of 6-dodecene-5-one (39c).



igure 13. Infrared spectrum of 7-tetradecene-6-one (39d).

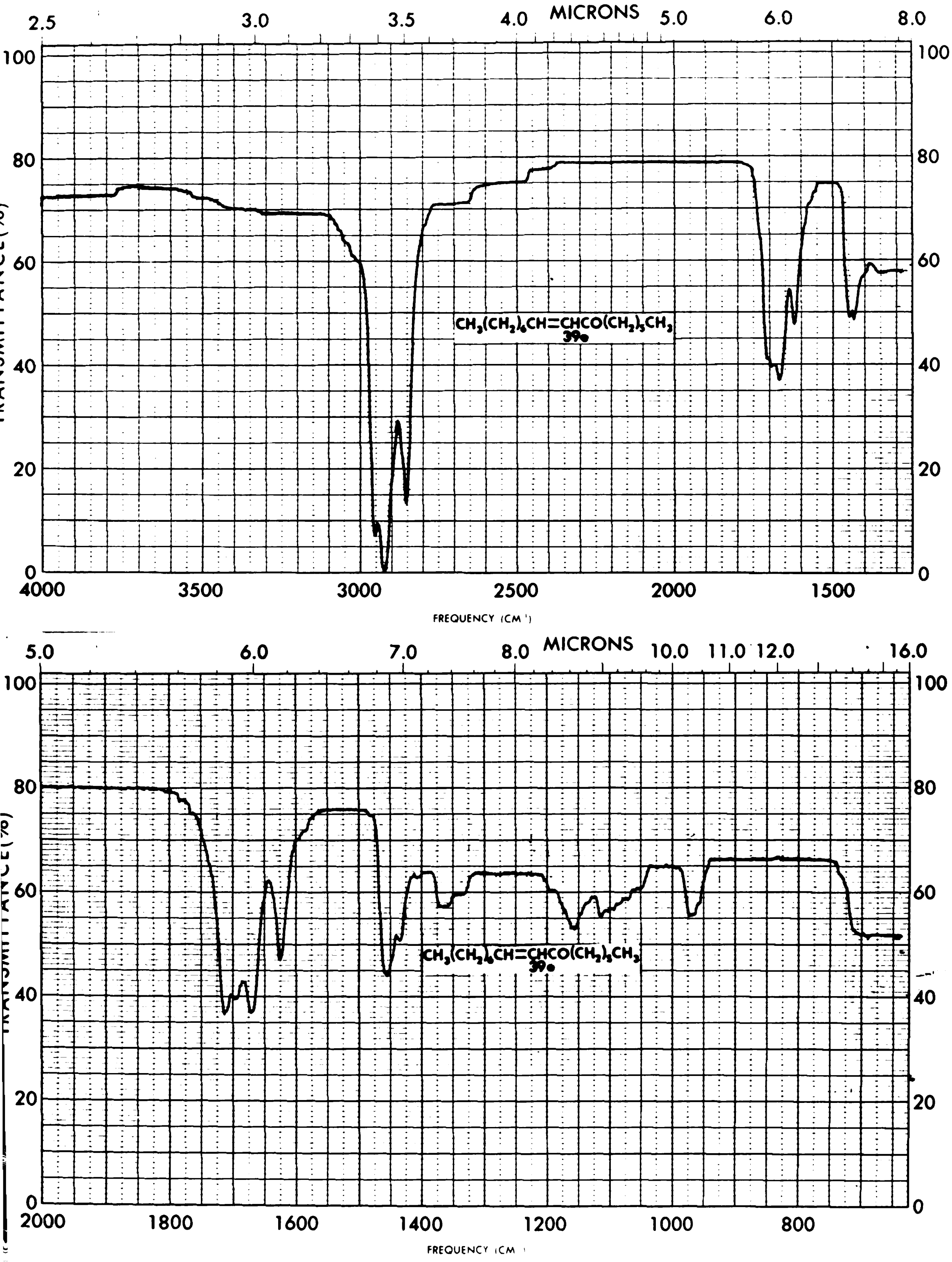


Figure 14. Infrared spectrum of 8-hexadecene-7-one (39e).

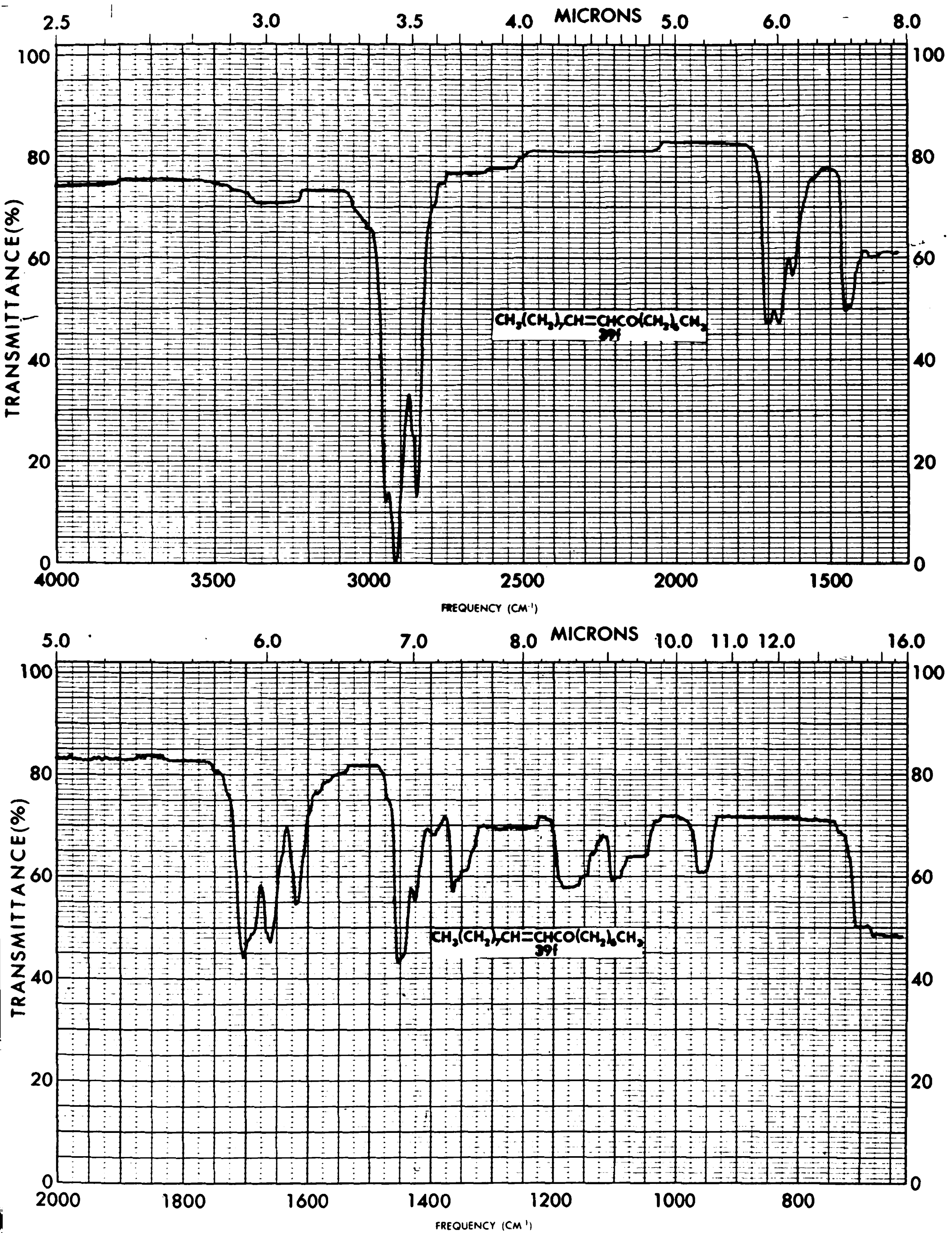
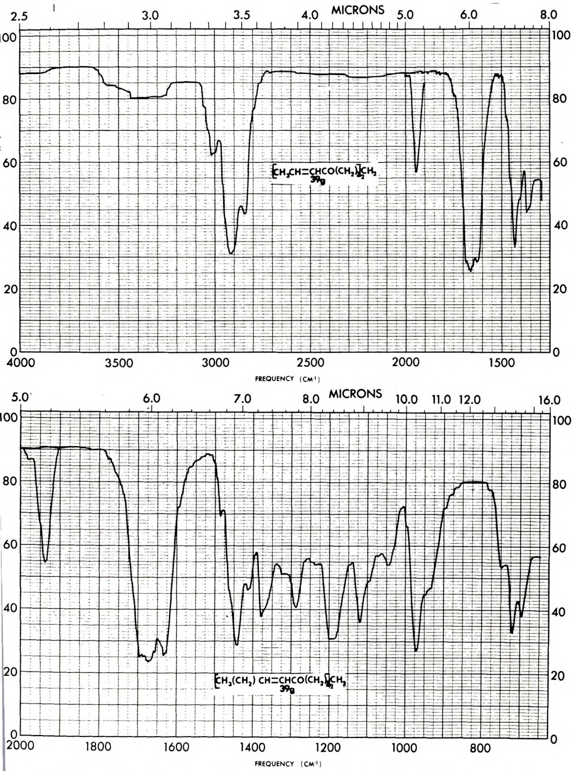


Figure 15. Infrared spectrum of 9-octadecene-8-one (39f).



igure 16. Infrared spectrum of 3,11-tridecadiene-4,10, dione (39g).

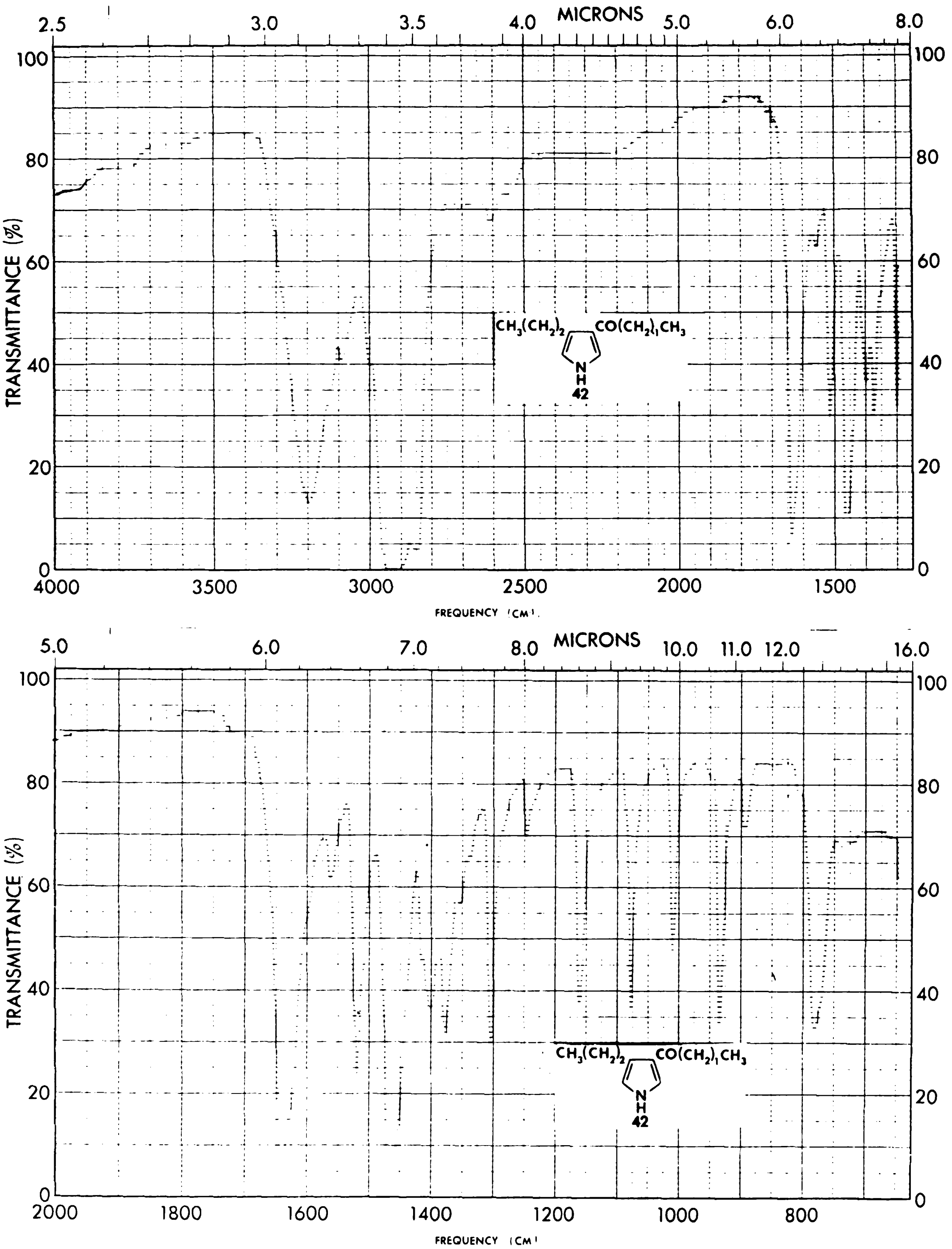


Figure 17. Infrared spectrum of 3-propyl-4-propyryl-pyrrole (42).

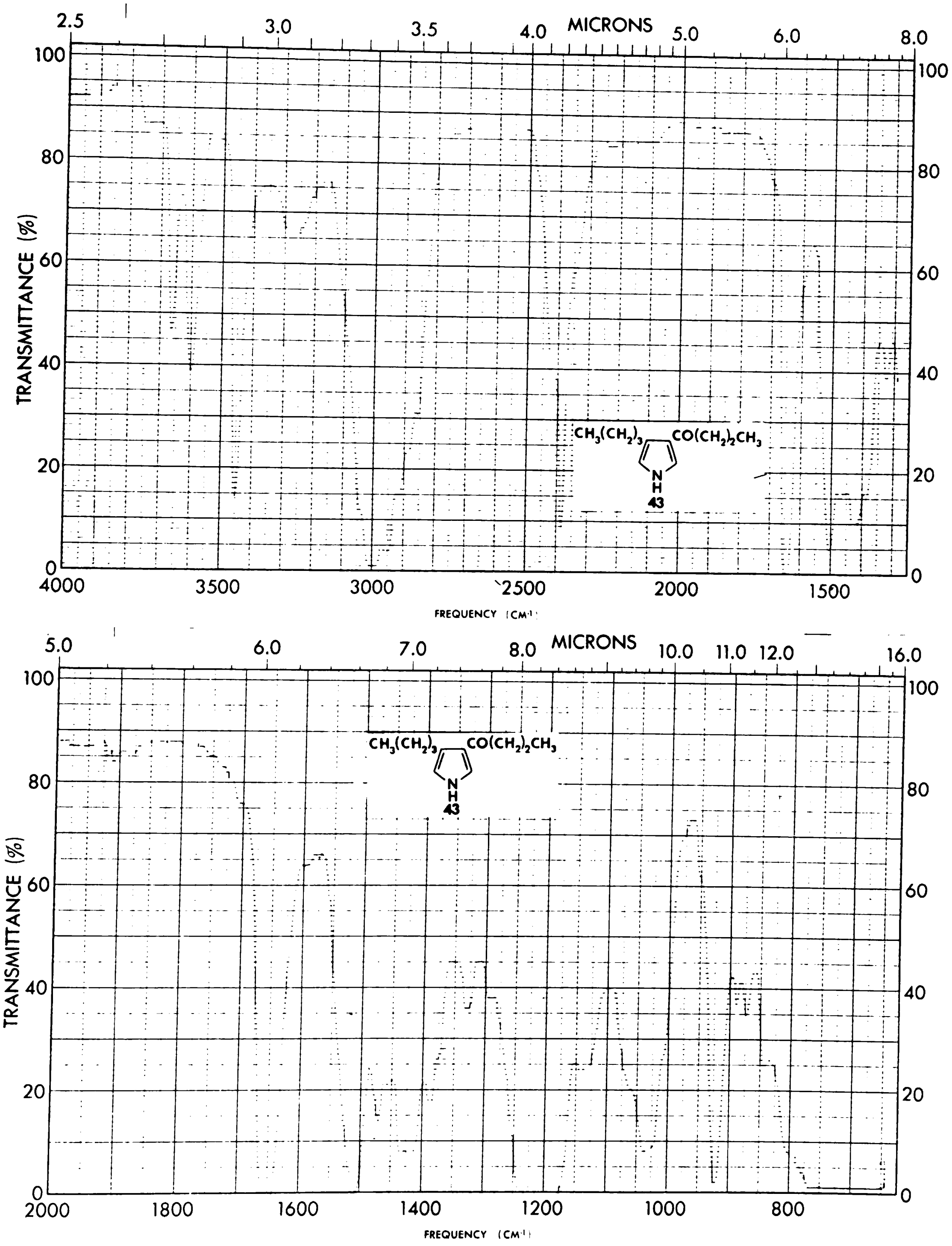


Figure 18. Infrared spectrum of 3-butyl-4-butyrylpyrrole (43).

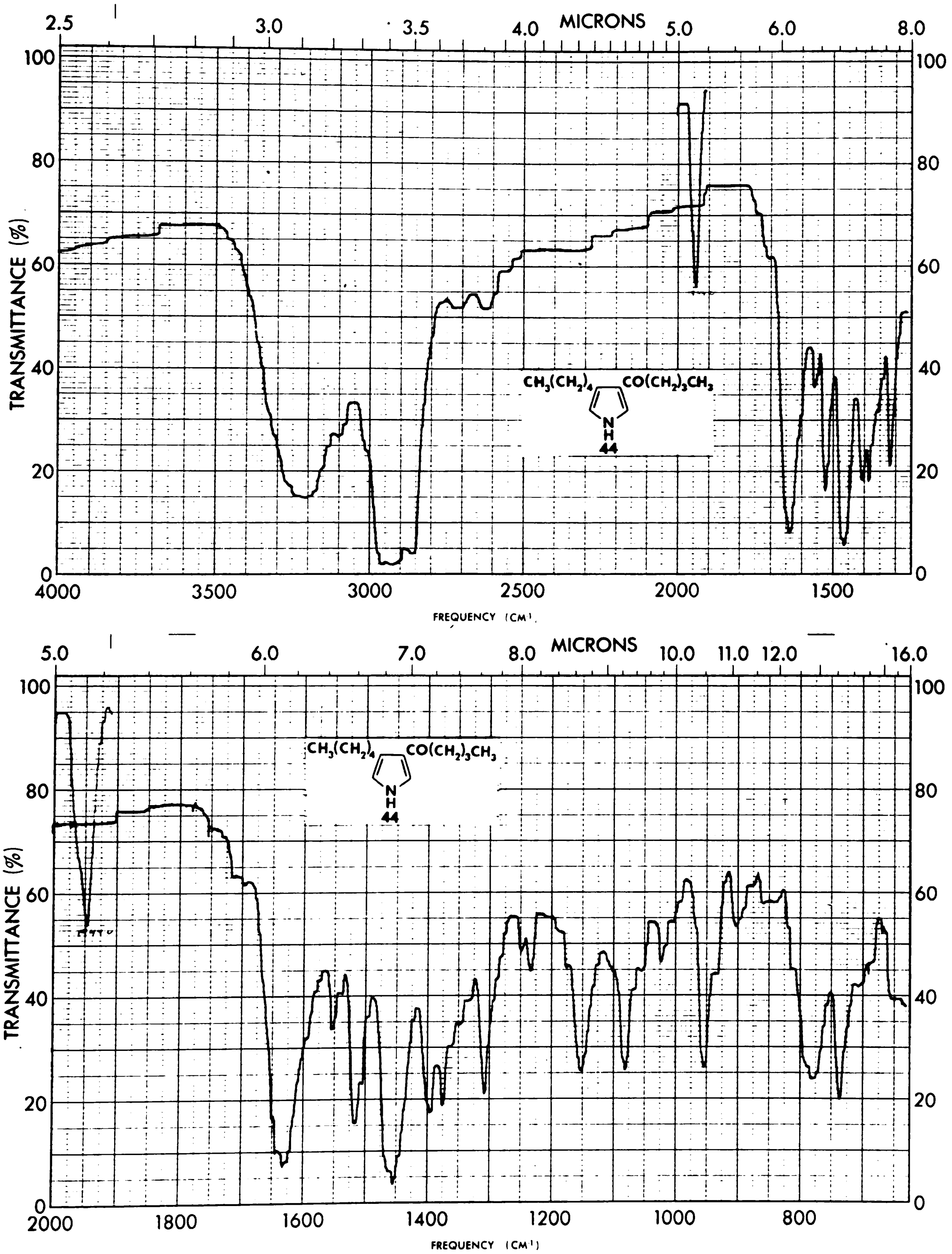


Figure 19. Infrared spectrum of 3-pentyl-4-pentyryl-pyrrole (44).

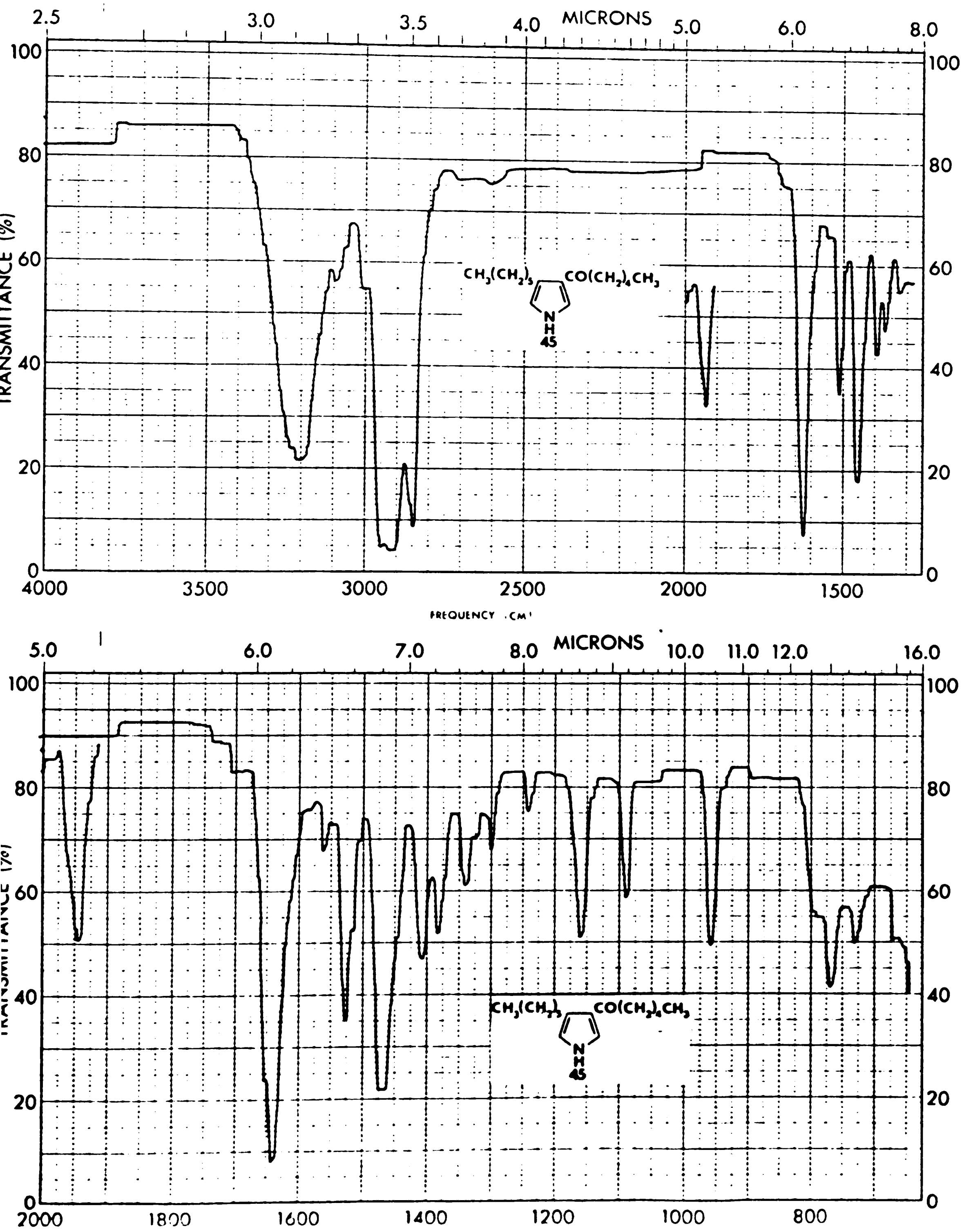


Figure 20. Infrared spectrum of 3-hexyl-4-hexyrylpyrrole (45).

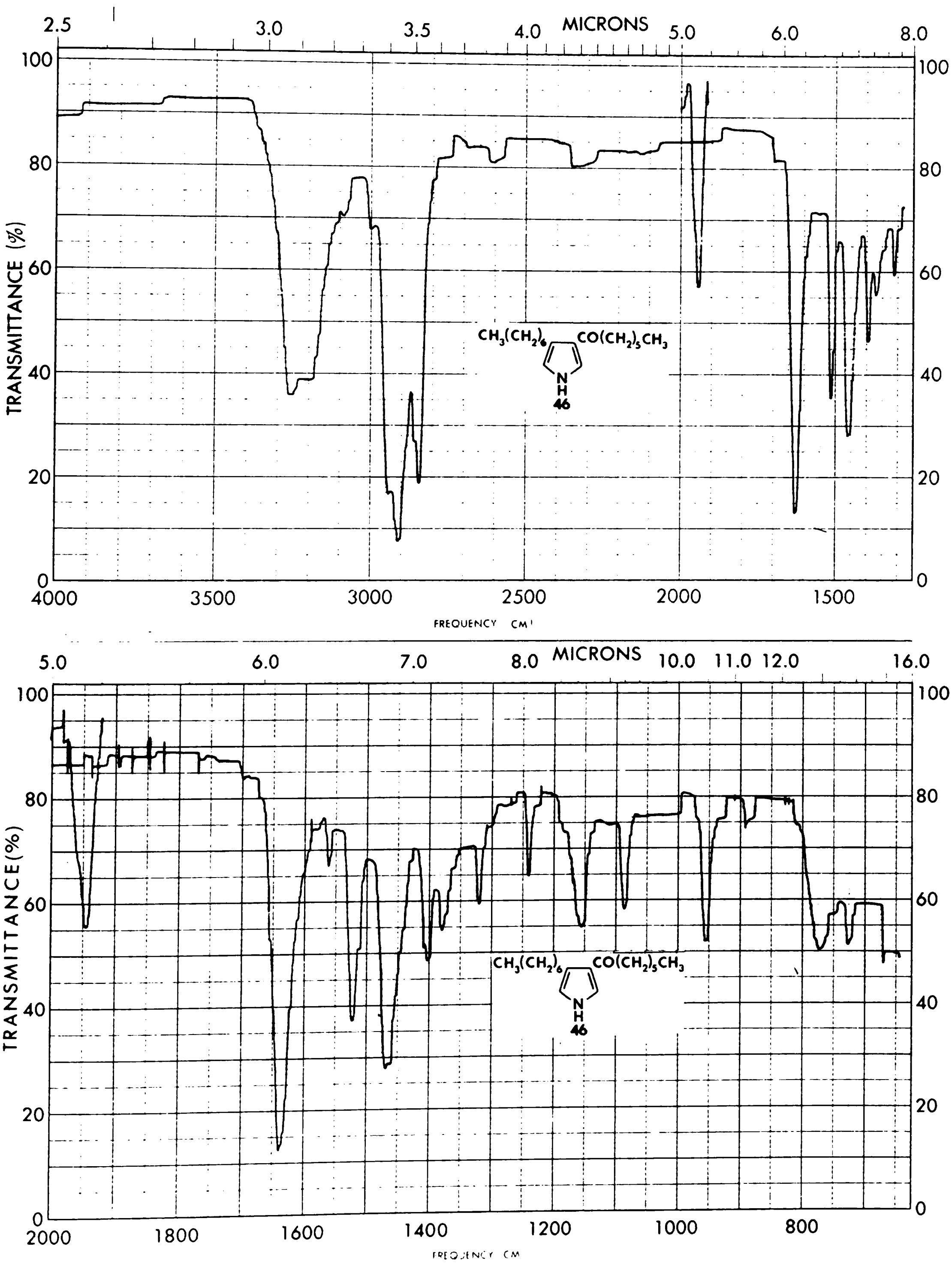


Figure 21. Infrared spectrum of 3-heptyl-4-heptyrylpyrrole. (46).

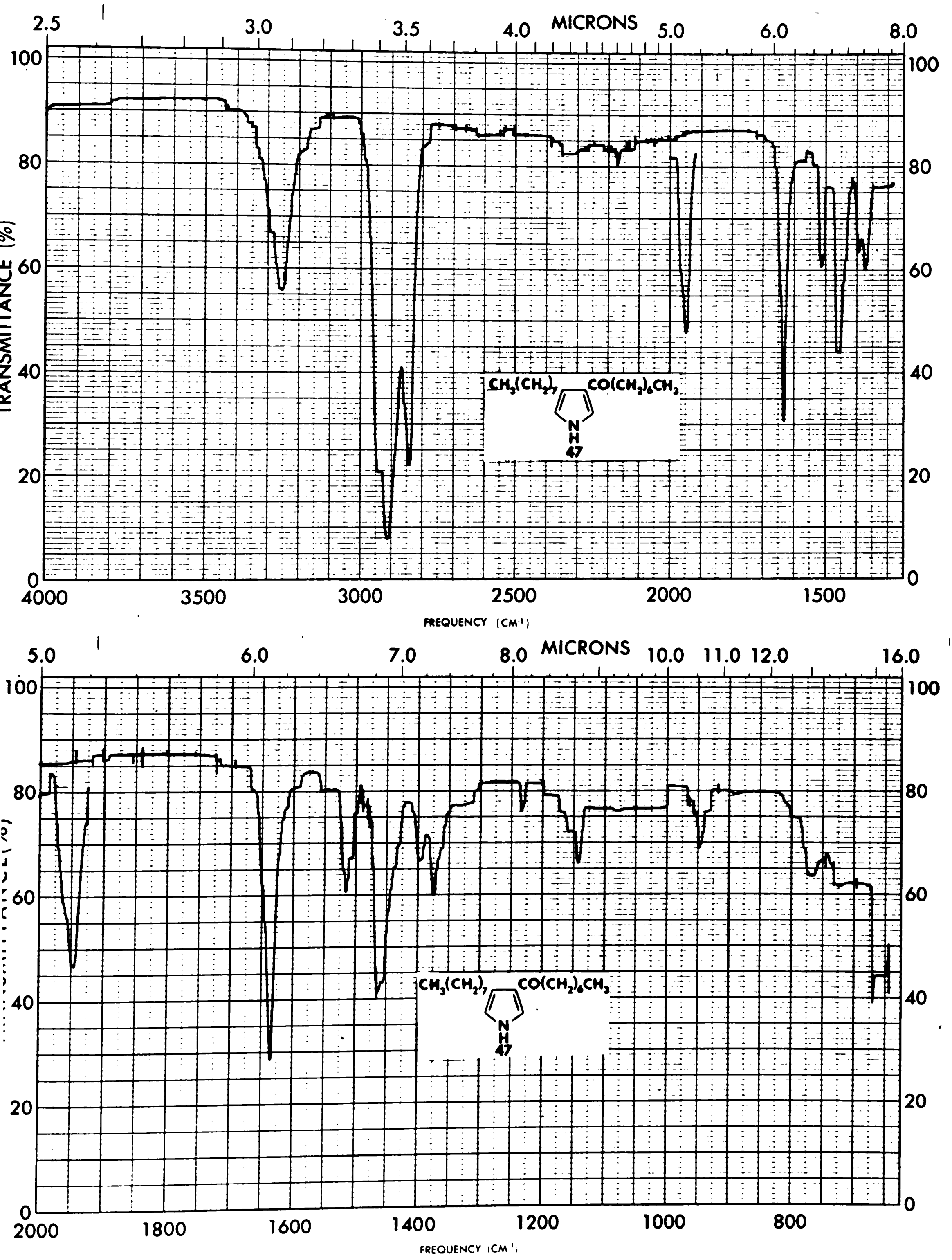


Figure 22. Infrared spectrum of 3-octyl-4-octyrylpyrrole (47).

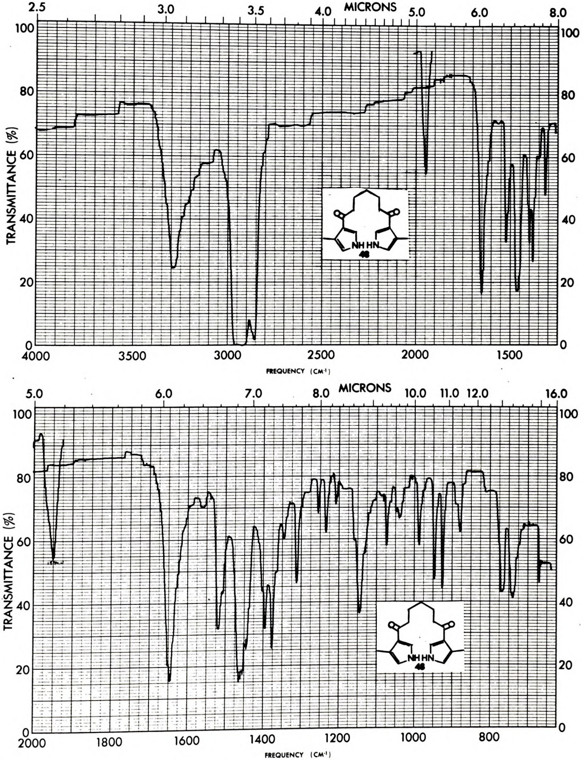
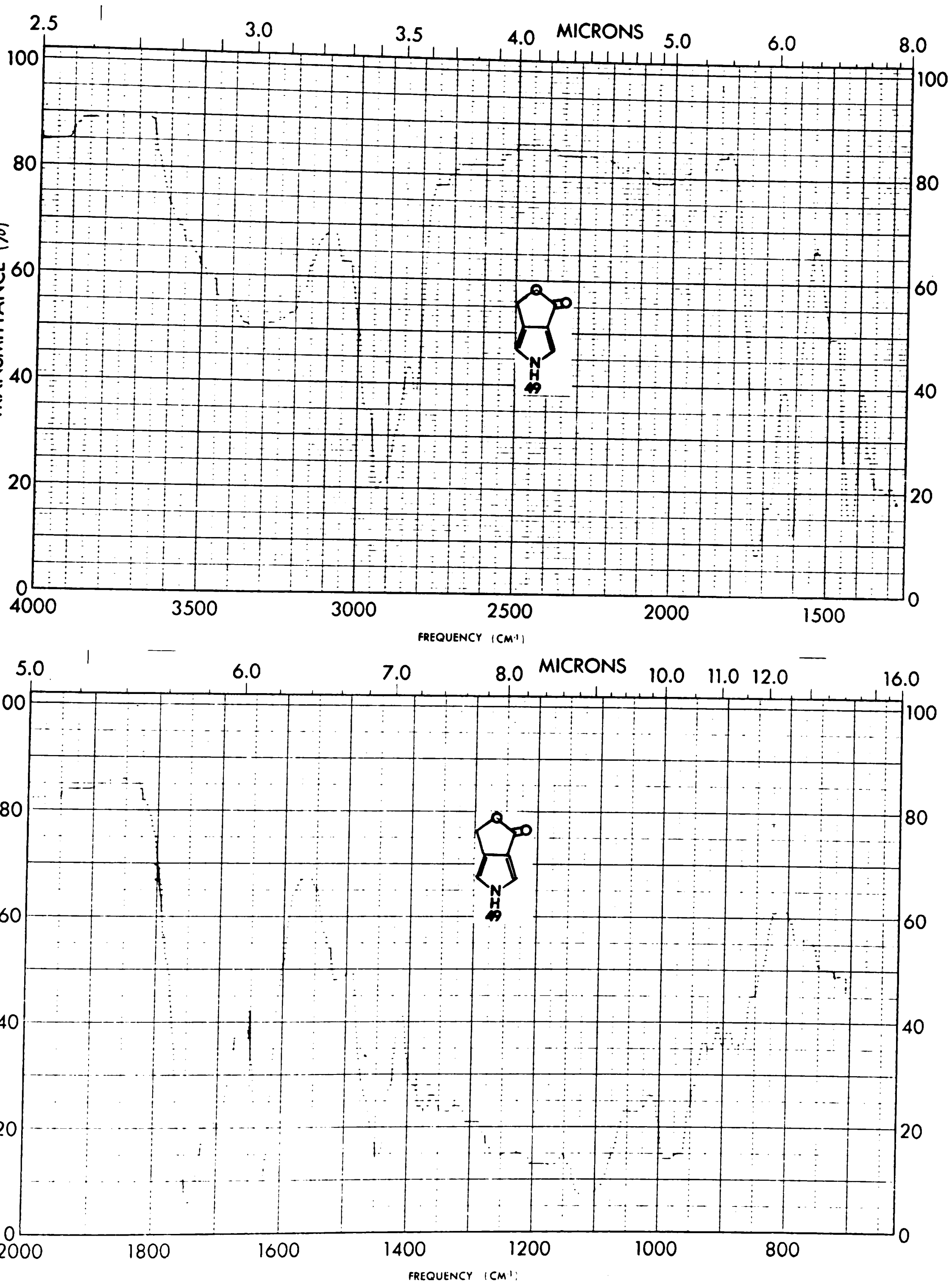


Figure 23. Infrared spectrum of 1,7-bis[-3-(4-methylpyrro)]-1,7-heptanedione (48).



igure 24. Infrared spectrum of 1H-pyrro-[3,4,a]-γ-butyrolactone (49).

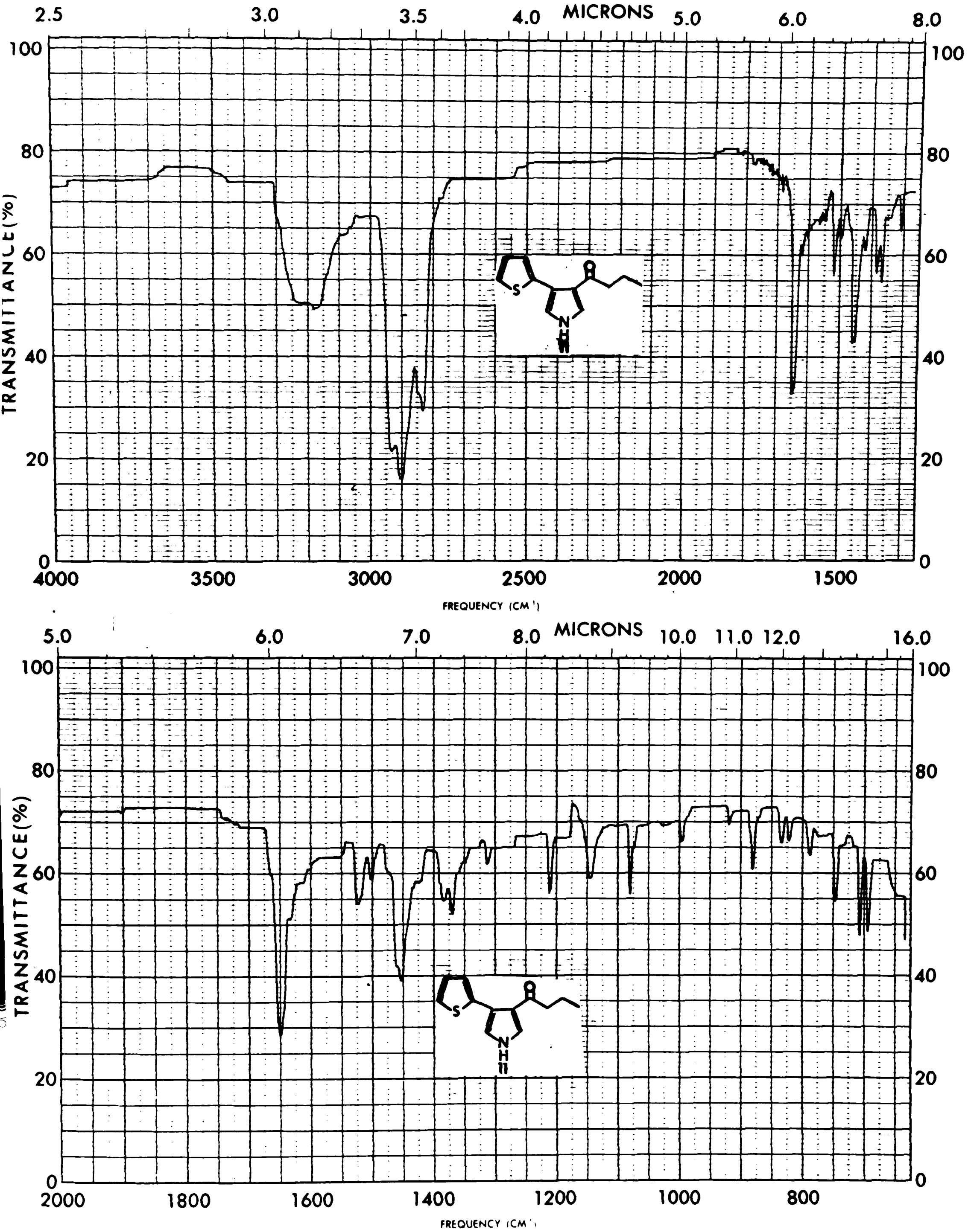
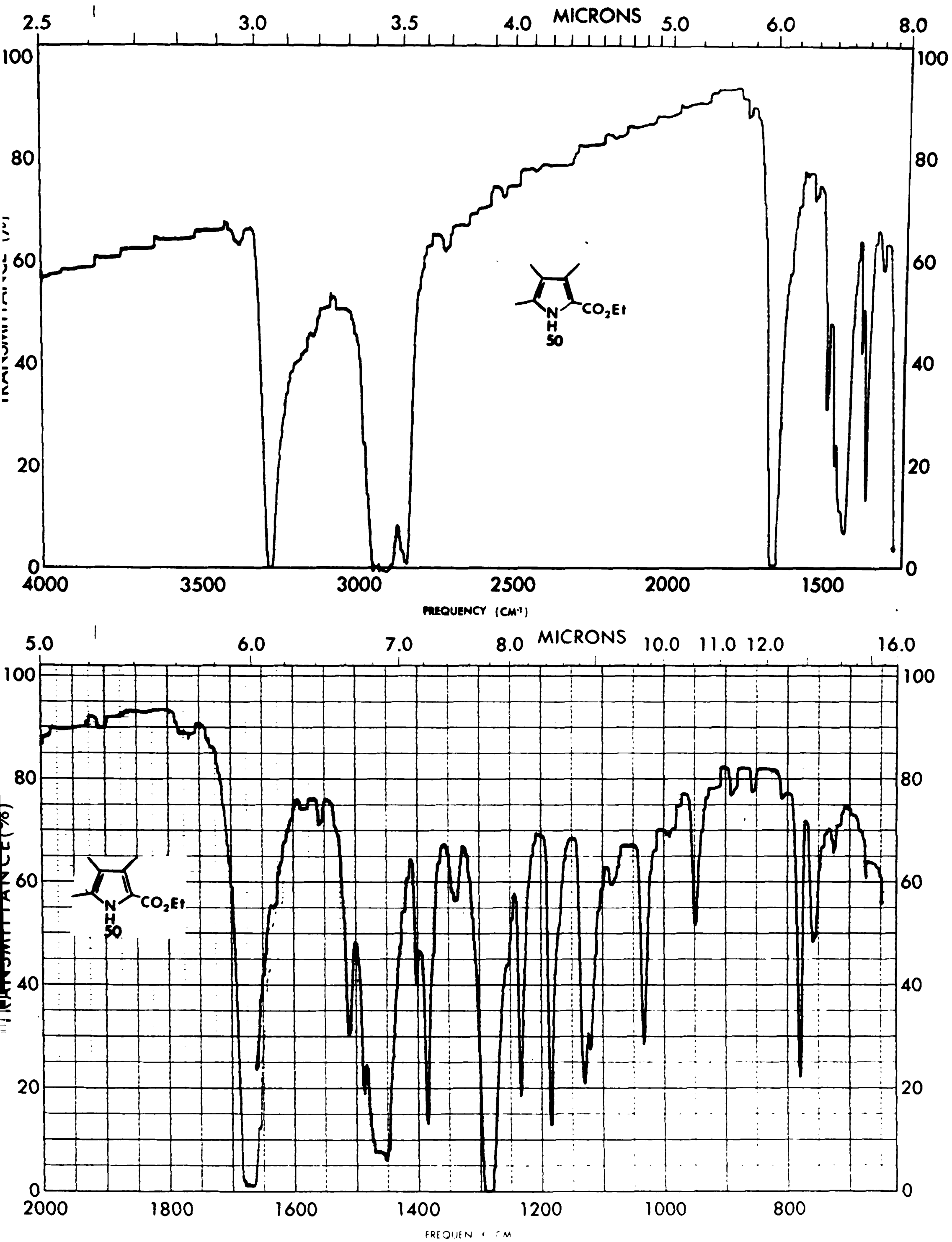


Figure 25. Infrared spectrum of 3-butyryl-4-(2-thienyl)-pyrrole (11).



'igure 26. Infrared spectrum of 2-carbethoxy-3,4,5-trimethylpyrrole (50).

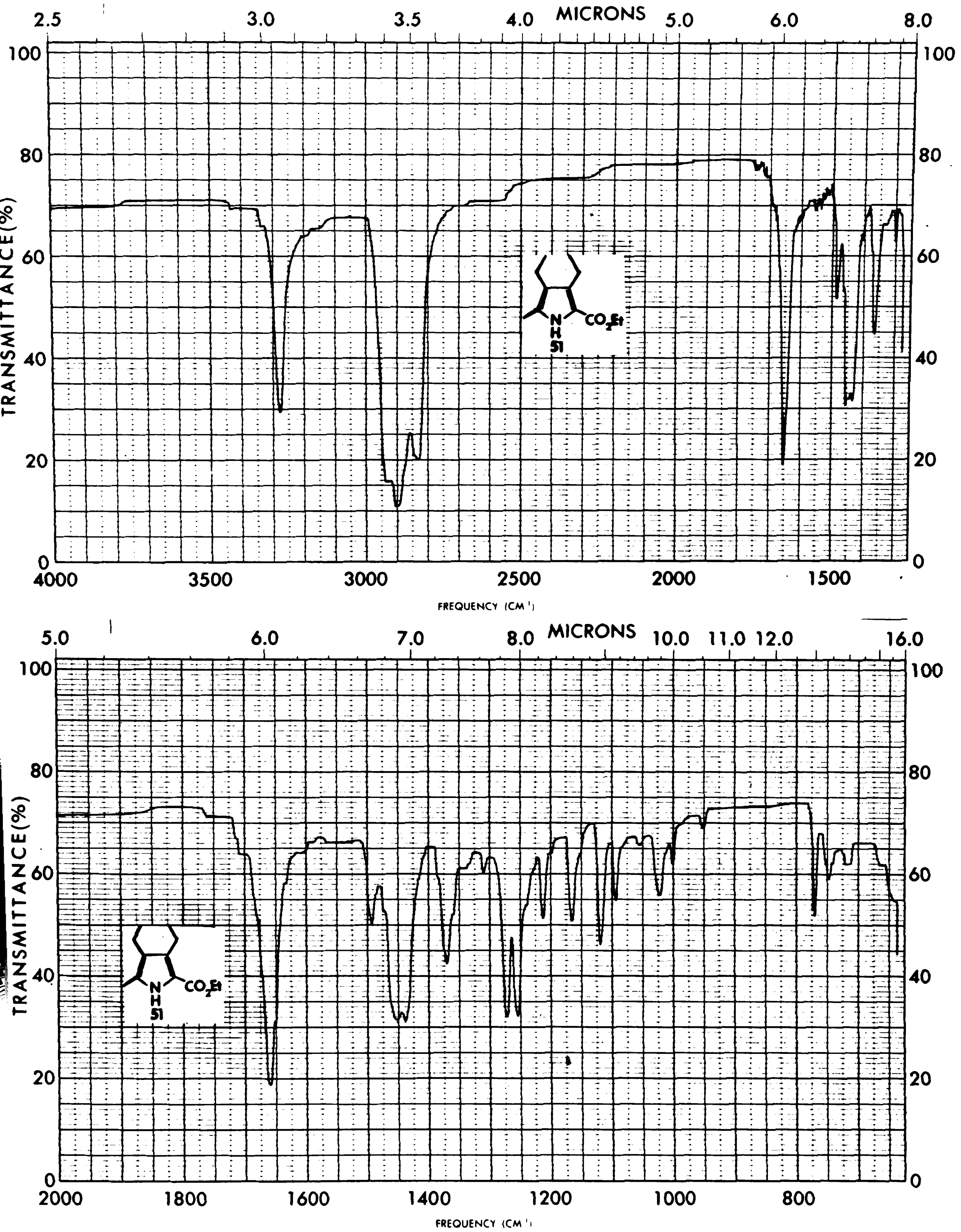


Figure 27. Infrared spectrum of 2-carbethoxy-3,4-diethyl-5-methylpyrrole (51).

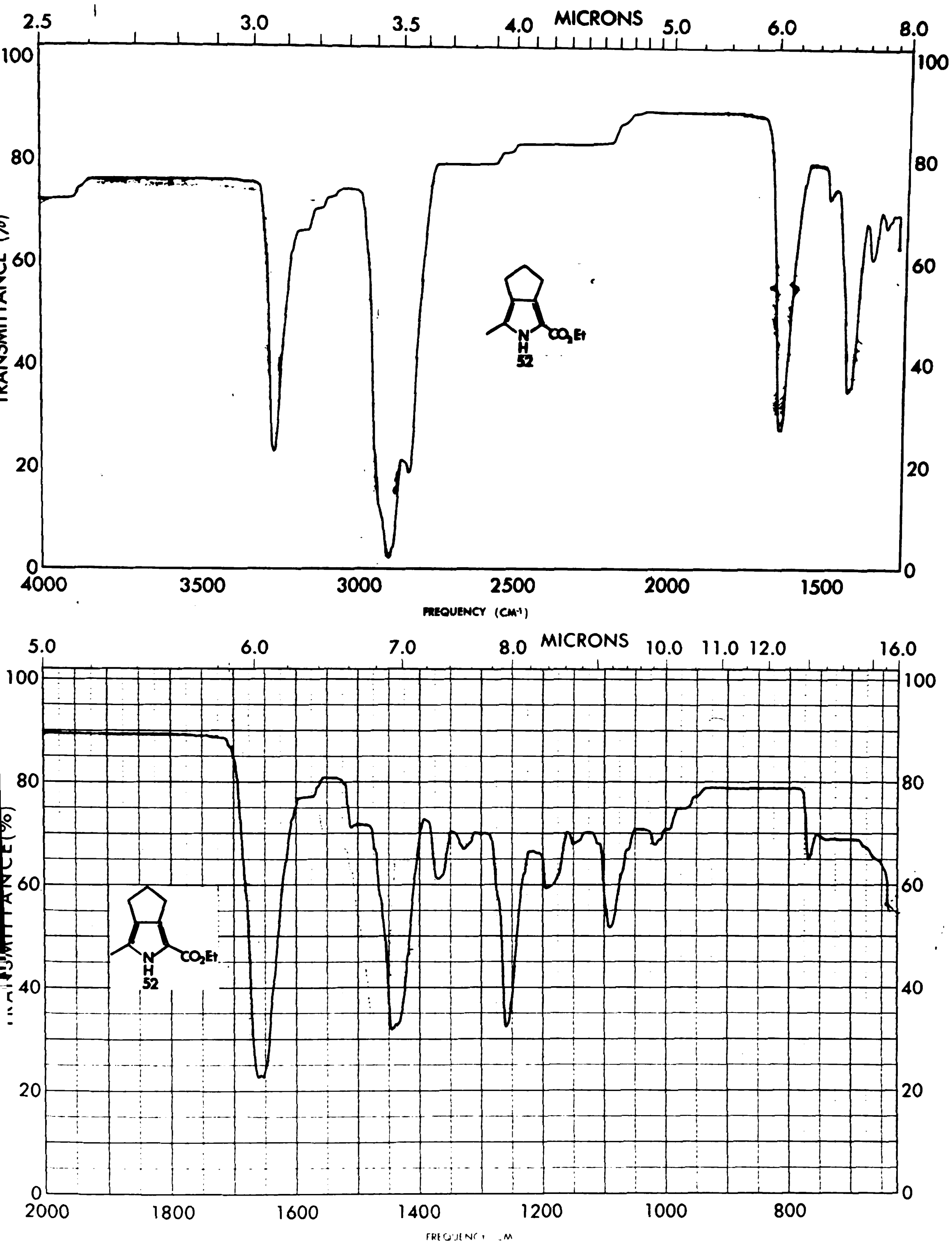


Figure 28. Infrared spectrum of 2-carbethoxy-3,4-trimethylene-5-methylpyrrole (52).

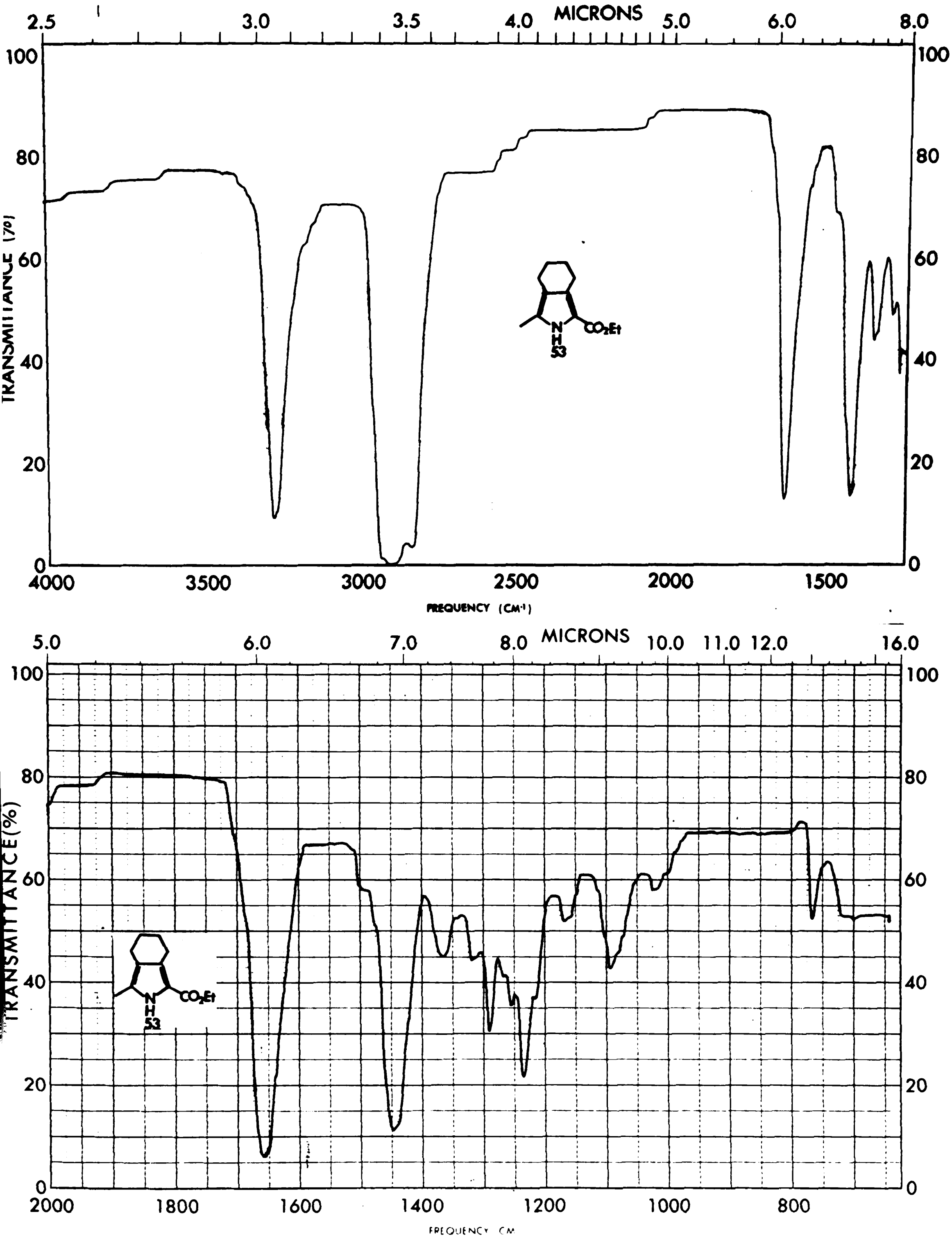


Figure 29. Infrared spectrum of 2-carbethoxy-3,4-tetramethylene-5-methylpyrrole (53).

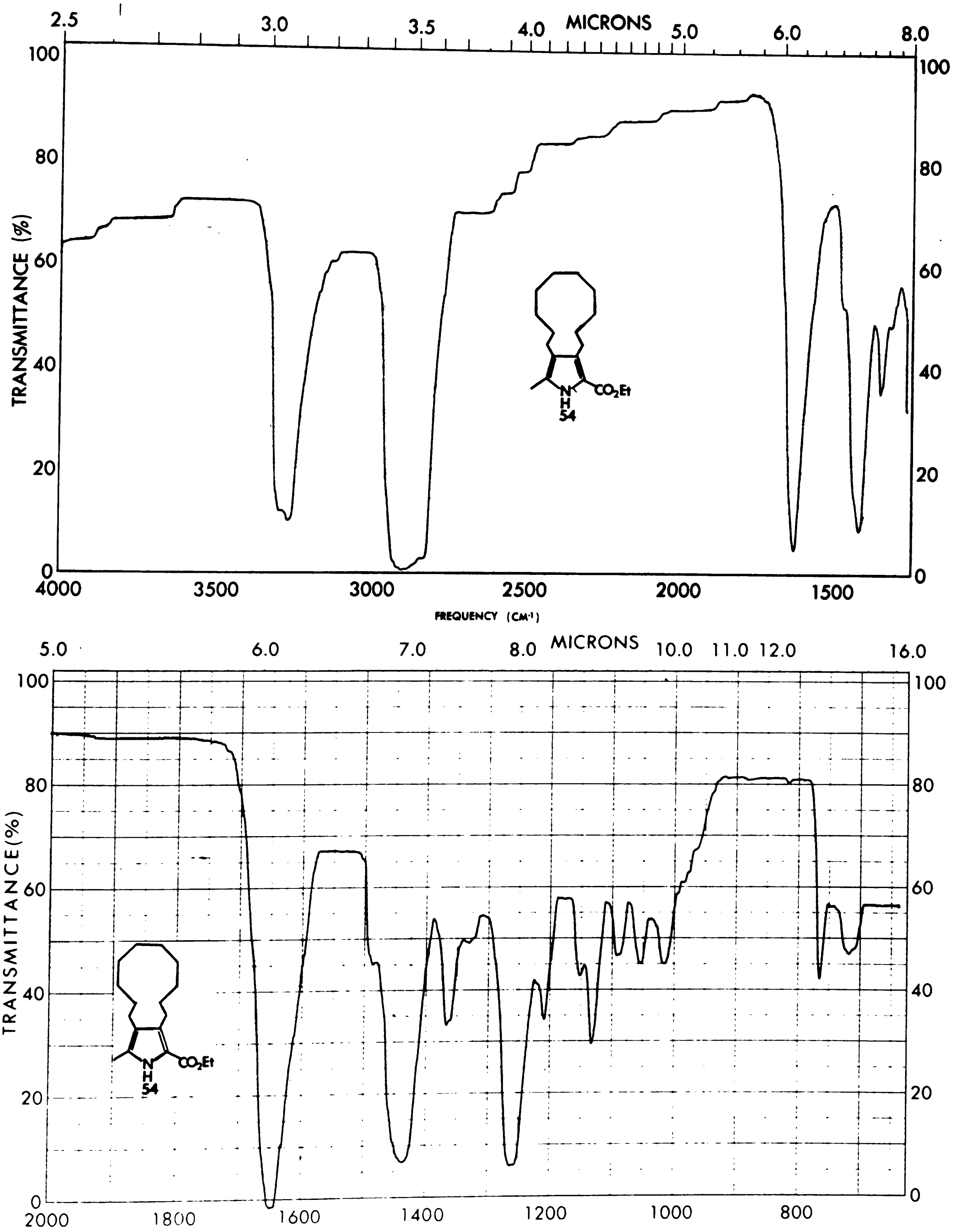


Figure 30. Infrared spectrum of 2-carbethoxy-3,4-decamethylene-5-methylpyrrole (54).

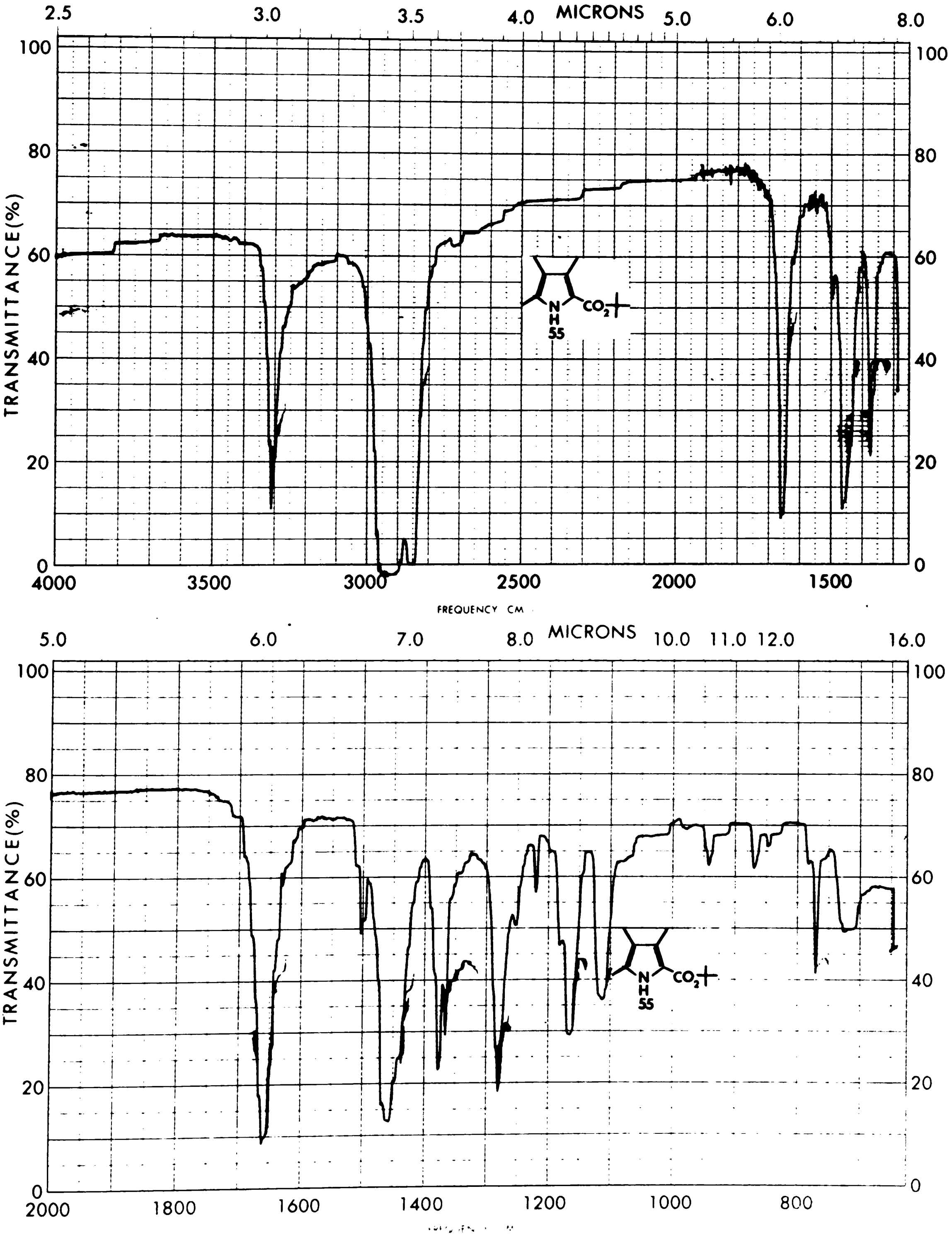
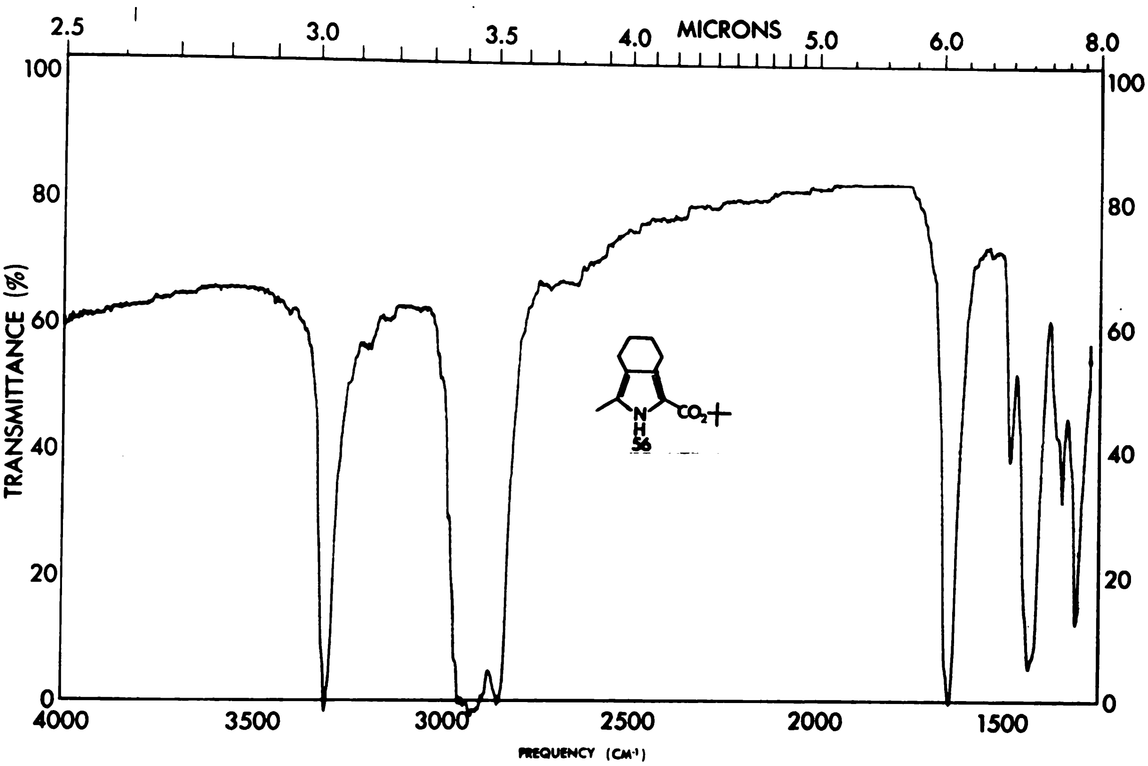


Figure 31. Infrared spectrum of 2-carbo-t-butoxy-3,4,5-trimethylpyrrole (55).



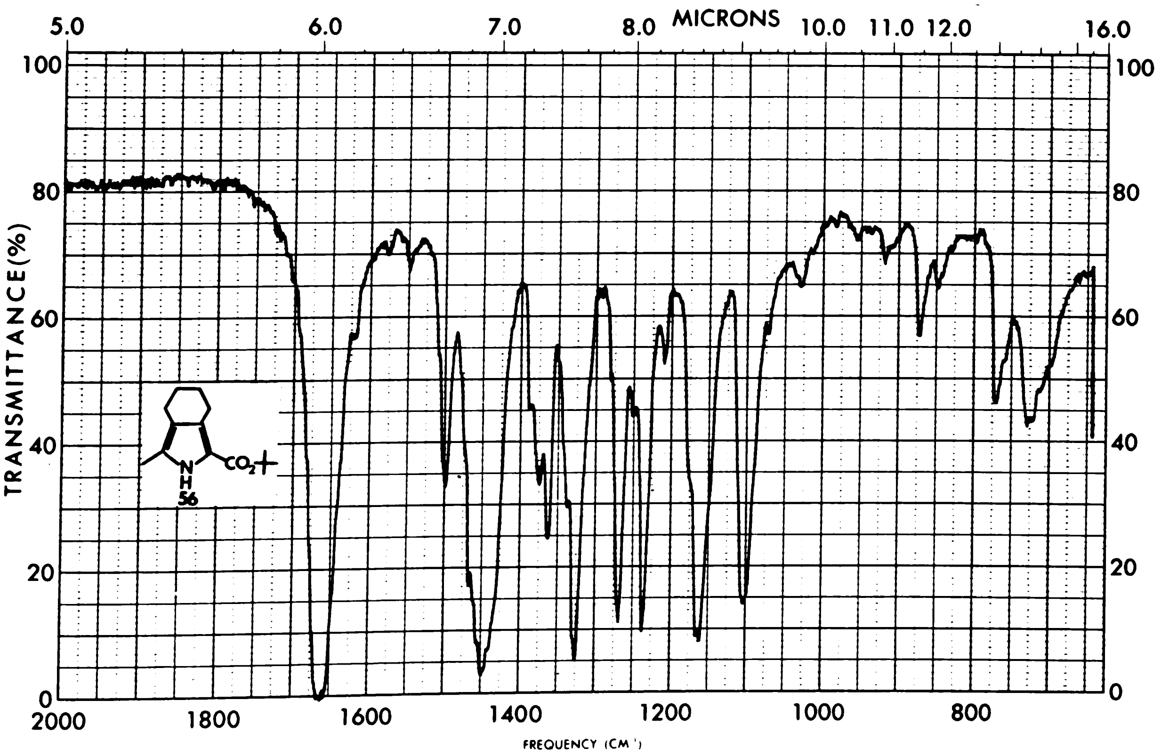


Figure 32. Infrared spectrum of 2-carbo-t-butoxy-3,4-tetramethylene-5-methylpyrrole (56).

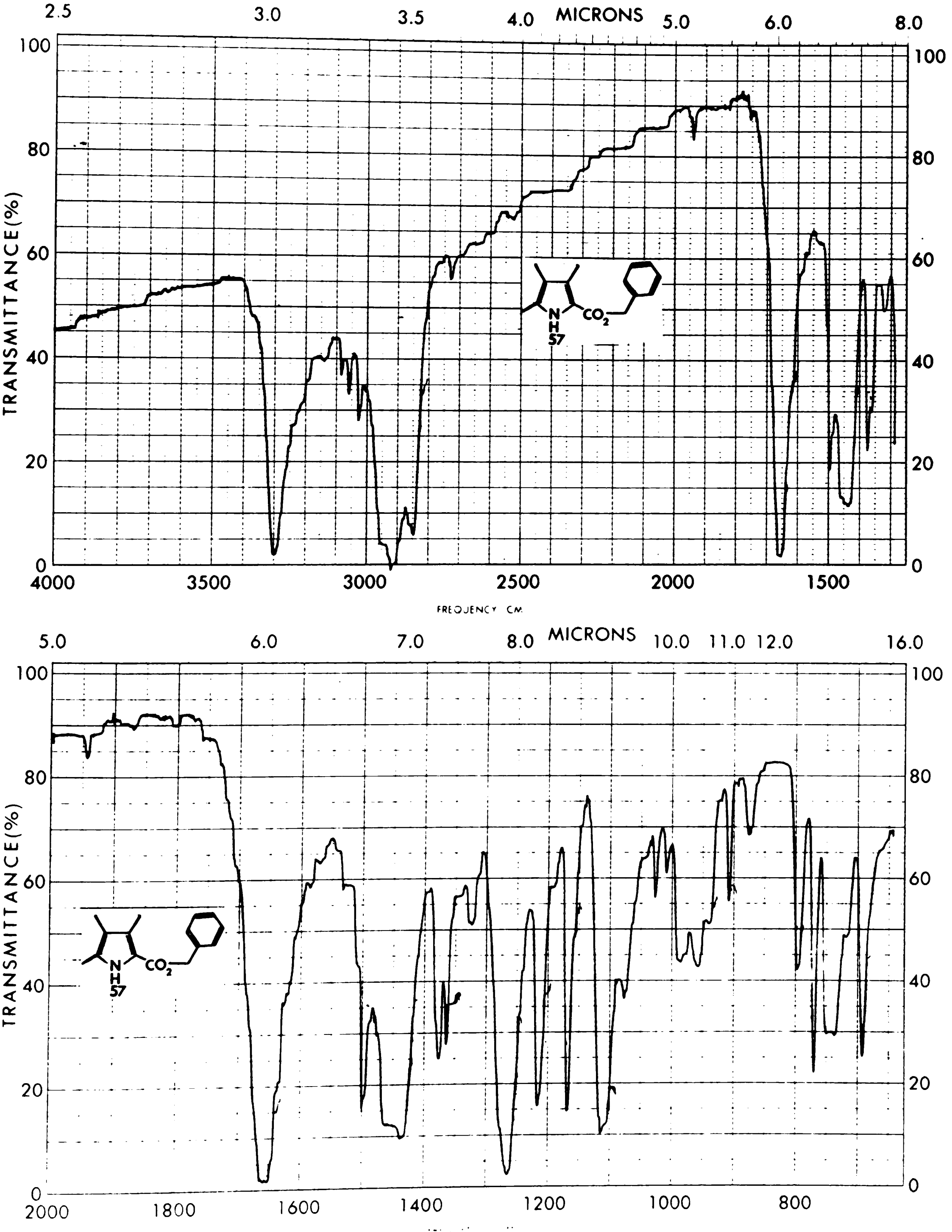


Figure 33. Infrared spectrum of 2-carbobenzyloxyl-3,4,5-trimethylpyrrole (57).

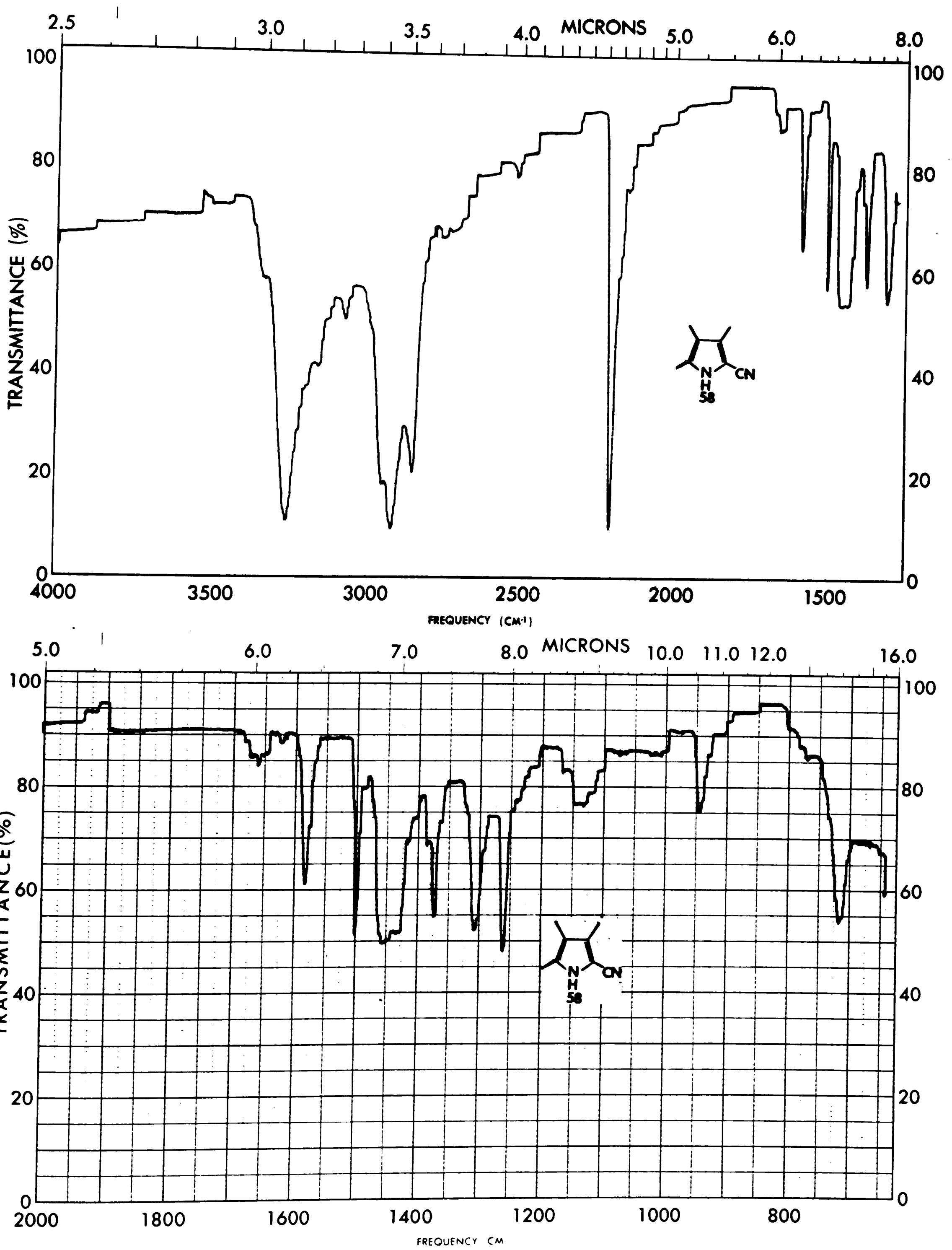


Figure 34. Infrared spectrum of 3,4,5-trimethyl-2-pyrrole carbonitrile (58).

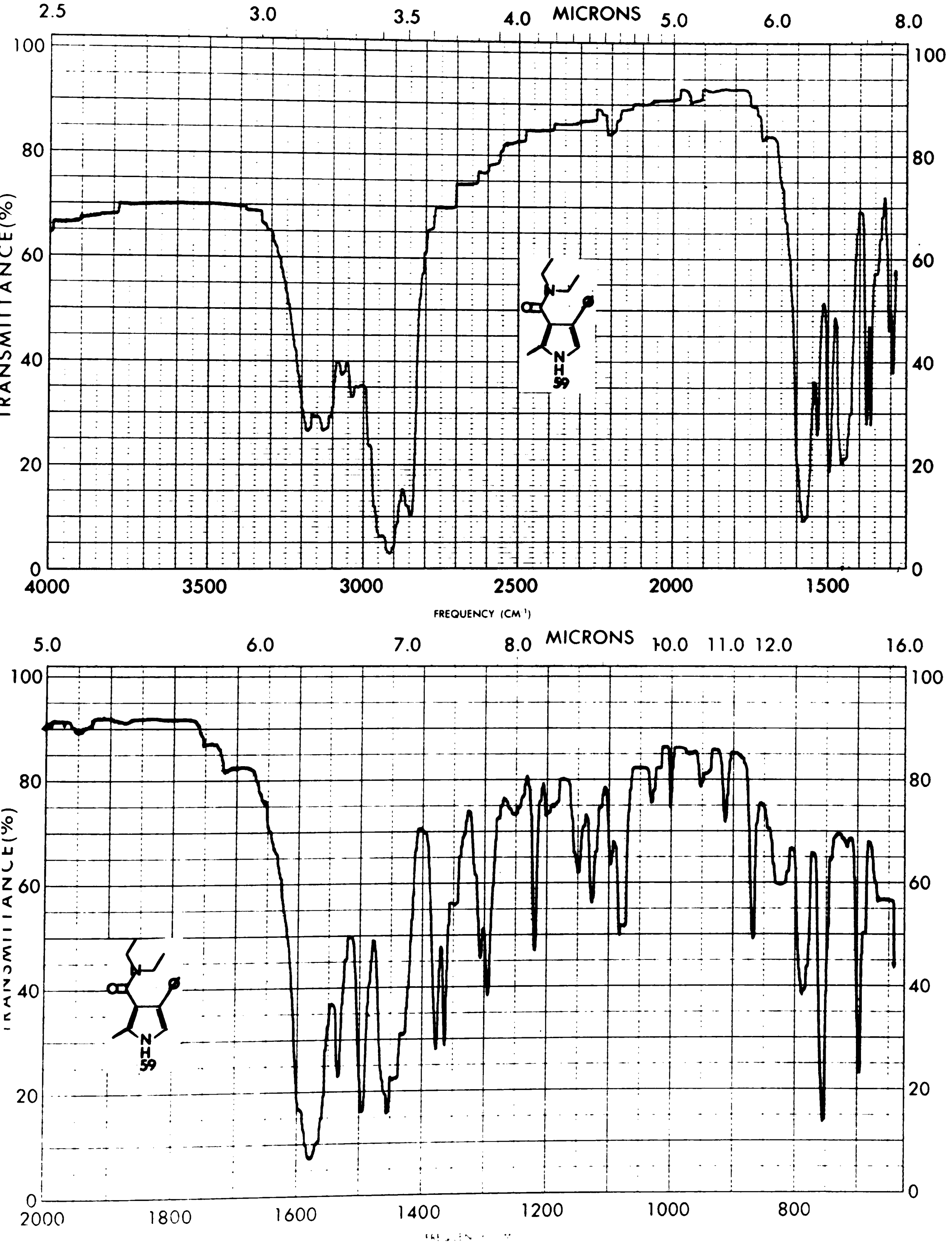


Figure 35. Infrared spectrum of diethyl 2-methyl-4-phenylpyrrole 3-carboxamide (59).

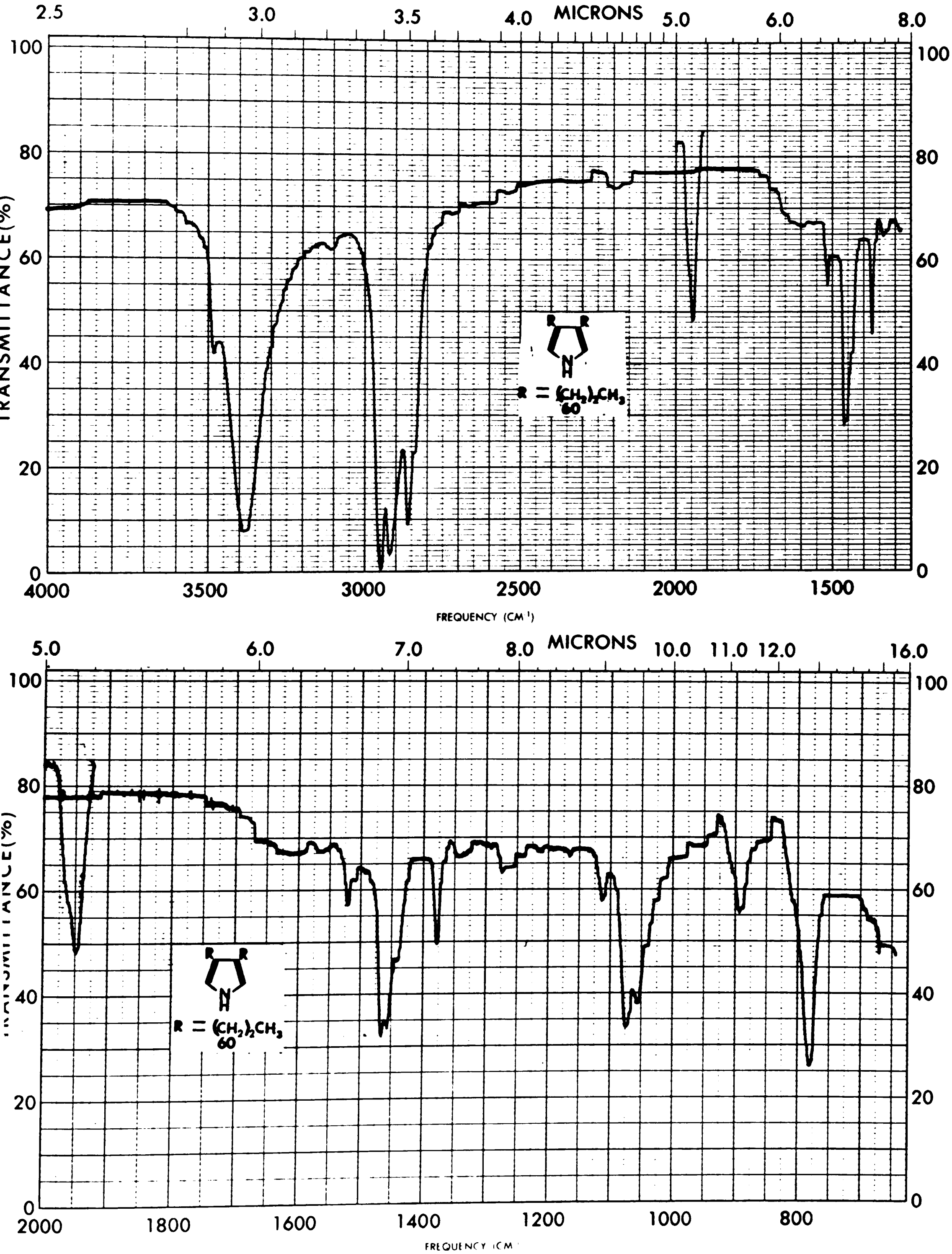


Figure 36. Infrared spectrum of 3,4-dipropylpyrrole (60).

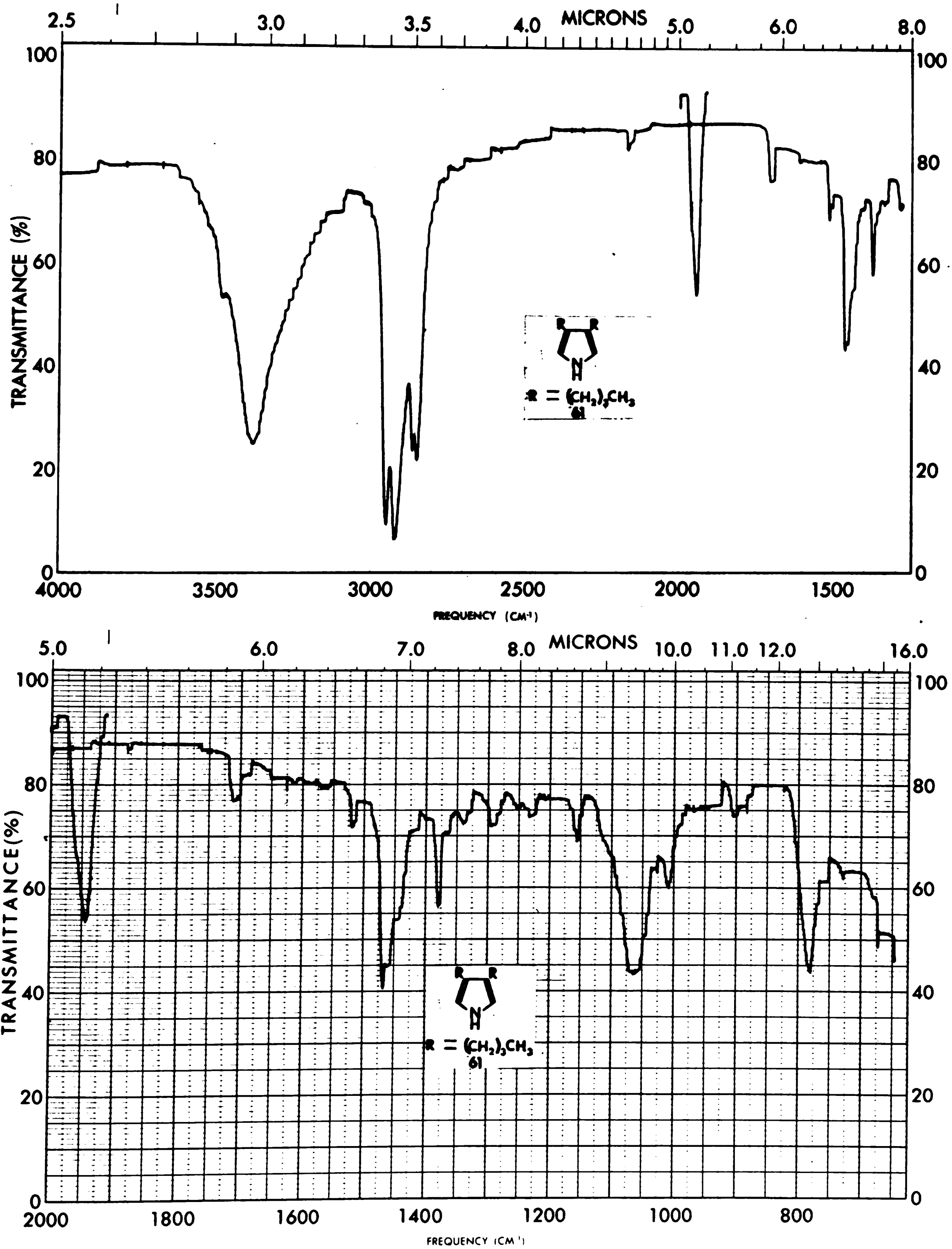


Figure 37. Infrared spectrum of 3,4-dibutylpyrrole (61).

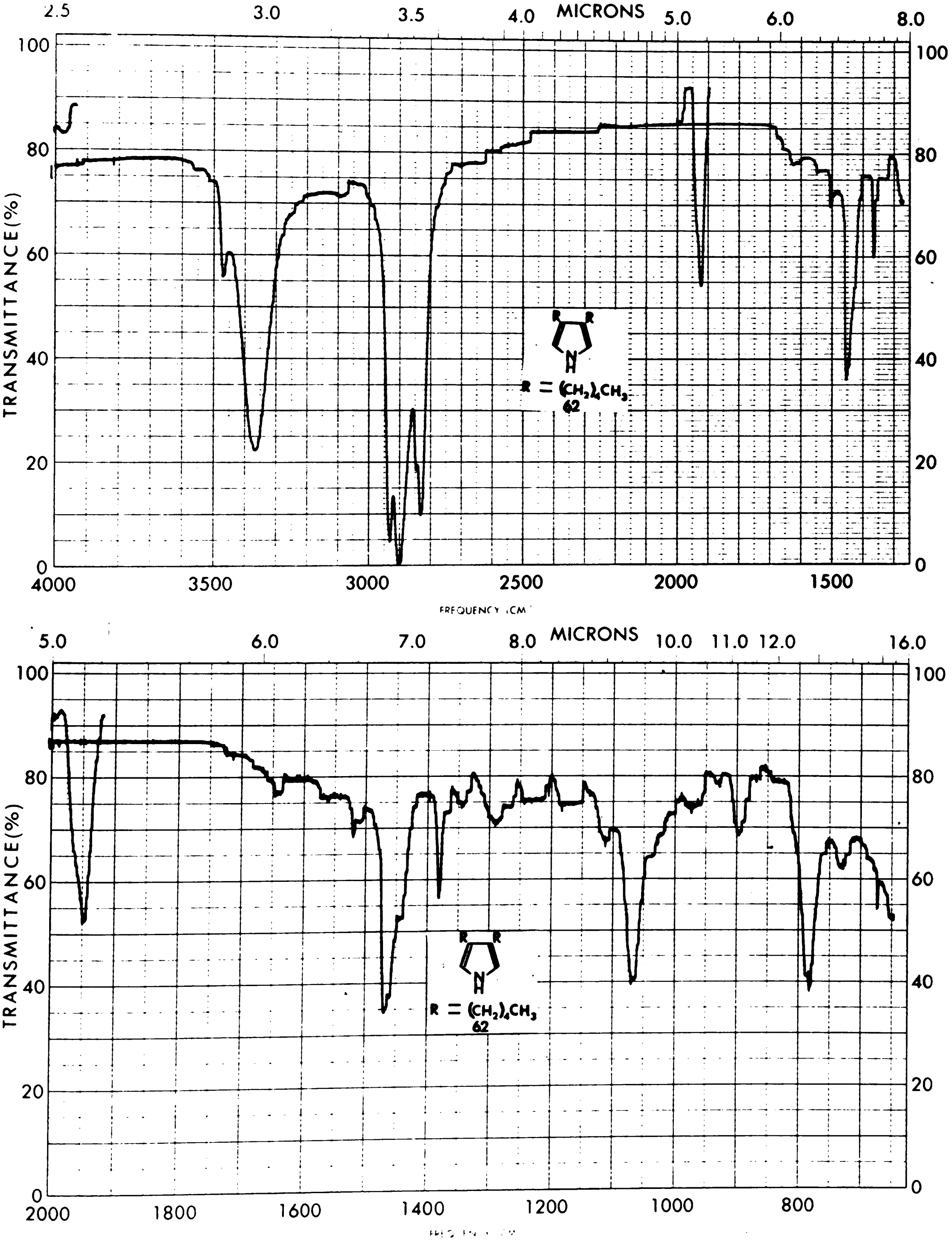


Figure 38. Infrared spectrum of 3,4-dipentylpyrrole (62).

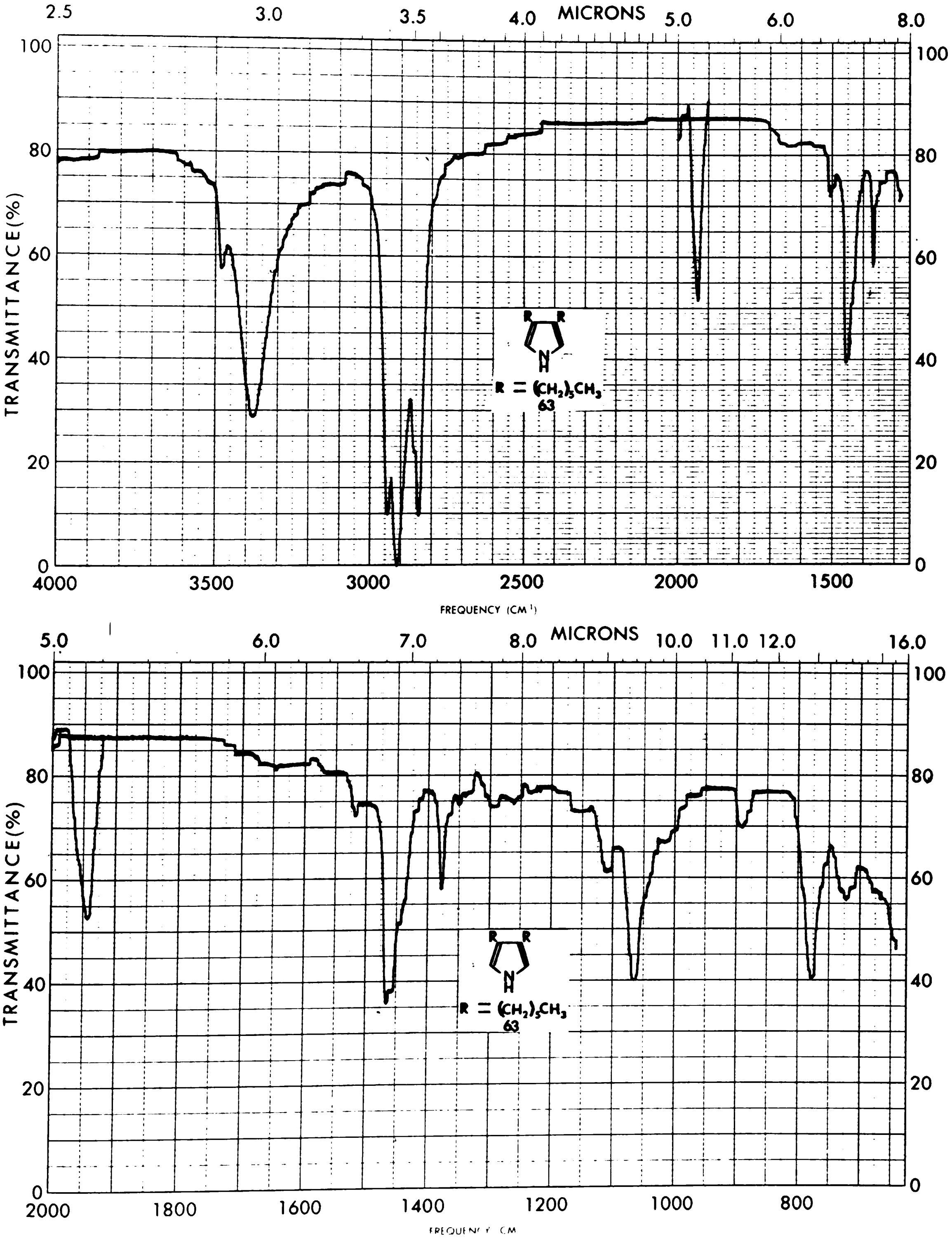


Figure 39. Infrared spectrum of 3,4-dihexylpyrrole (63).

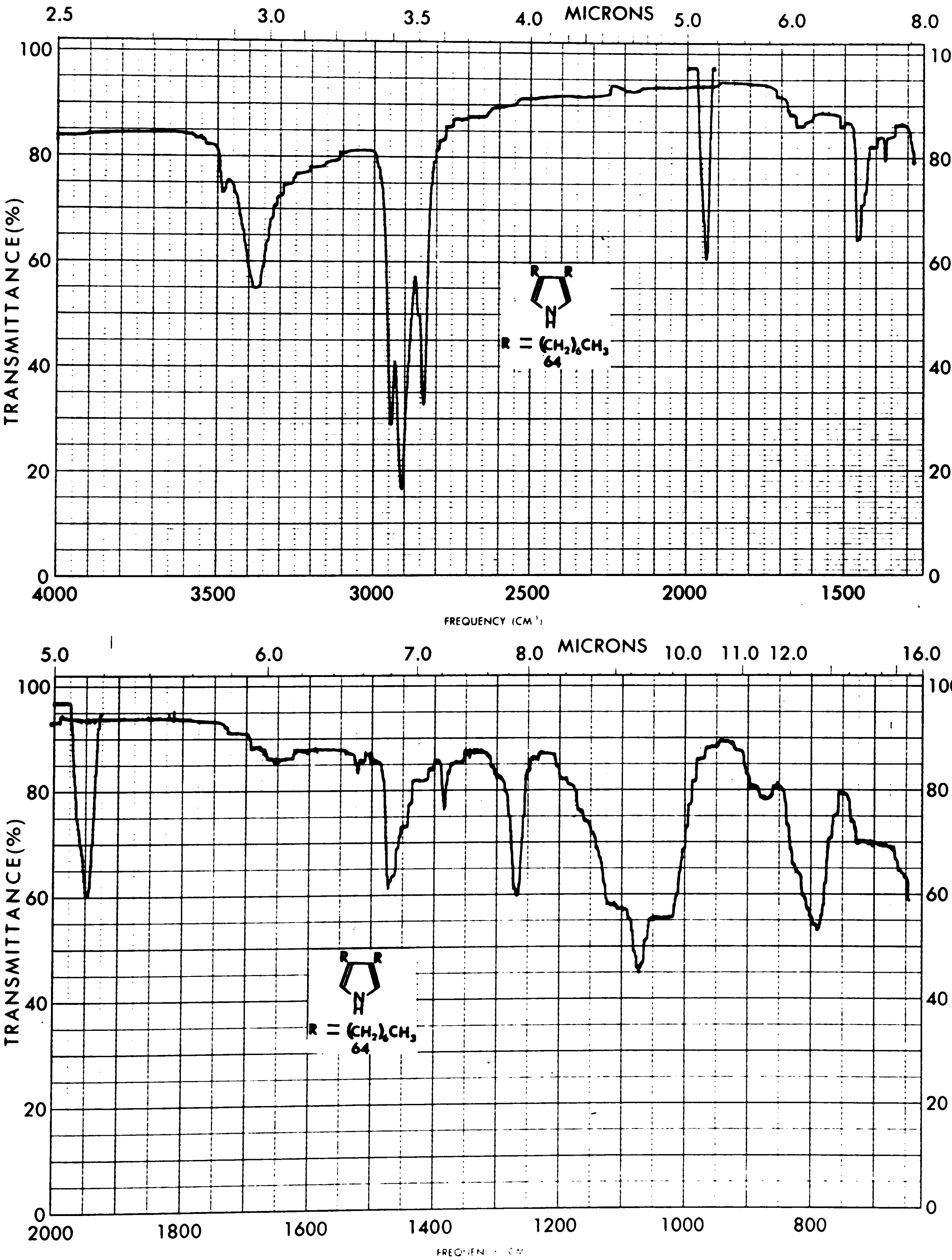


Figure 40. Infrared spectrum of 3,4-diheptylpyrrole (64).

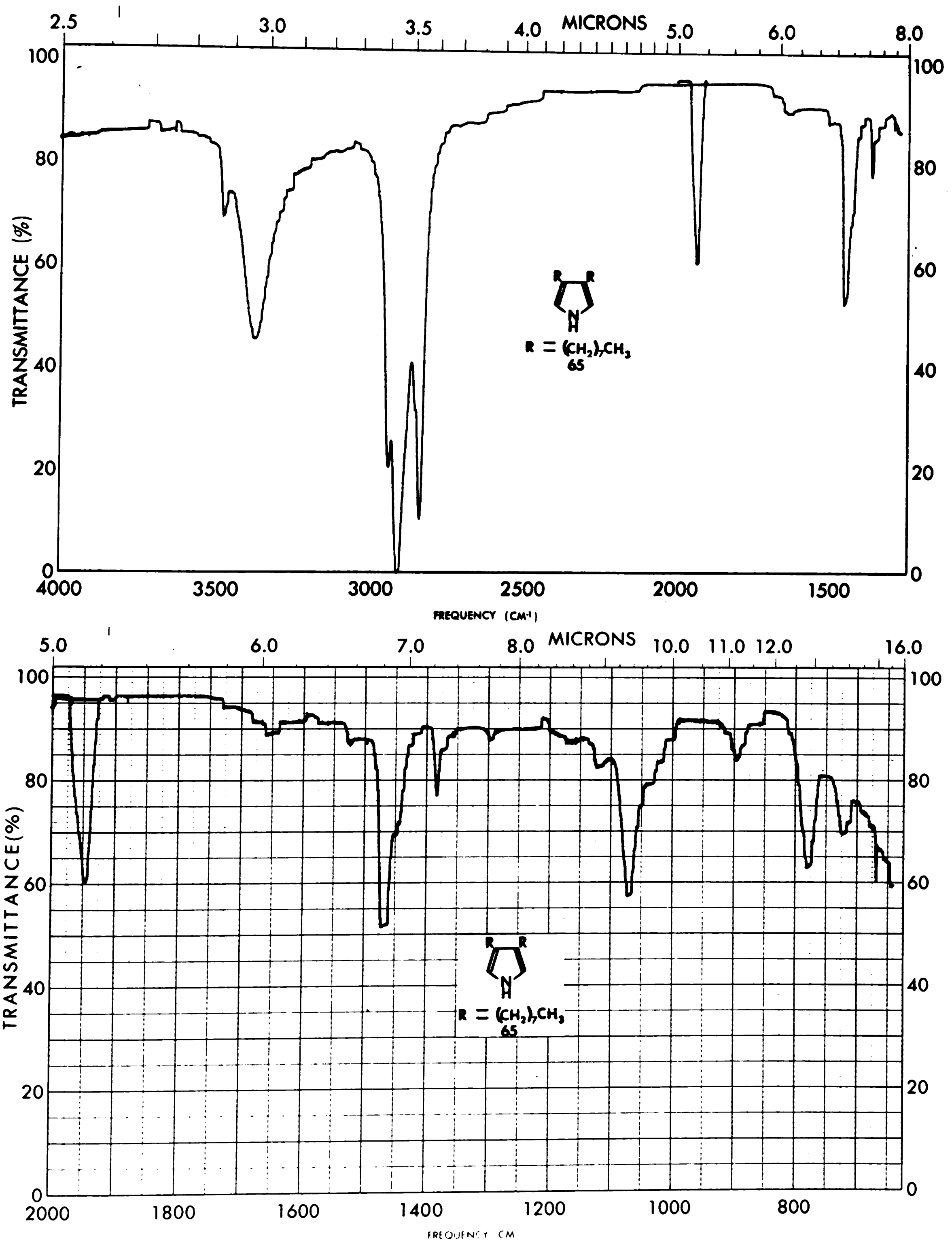


Figure 41. Infrared spectrum of 3,4-dioctylpyrrole (65).

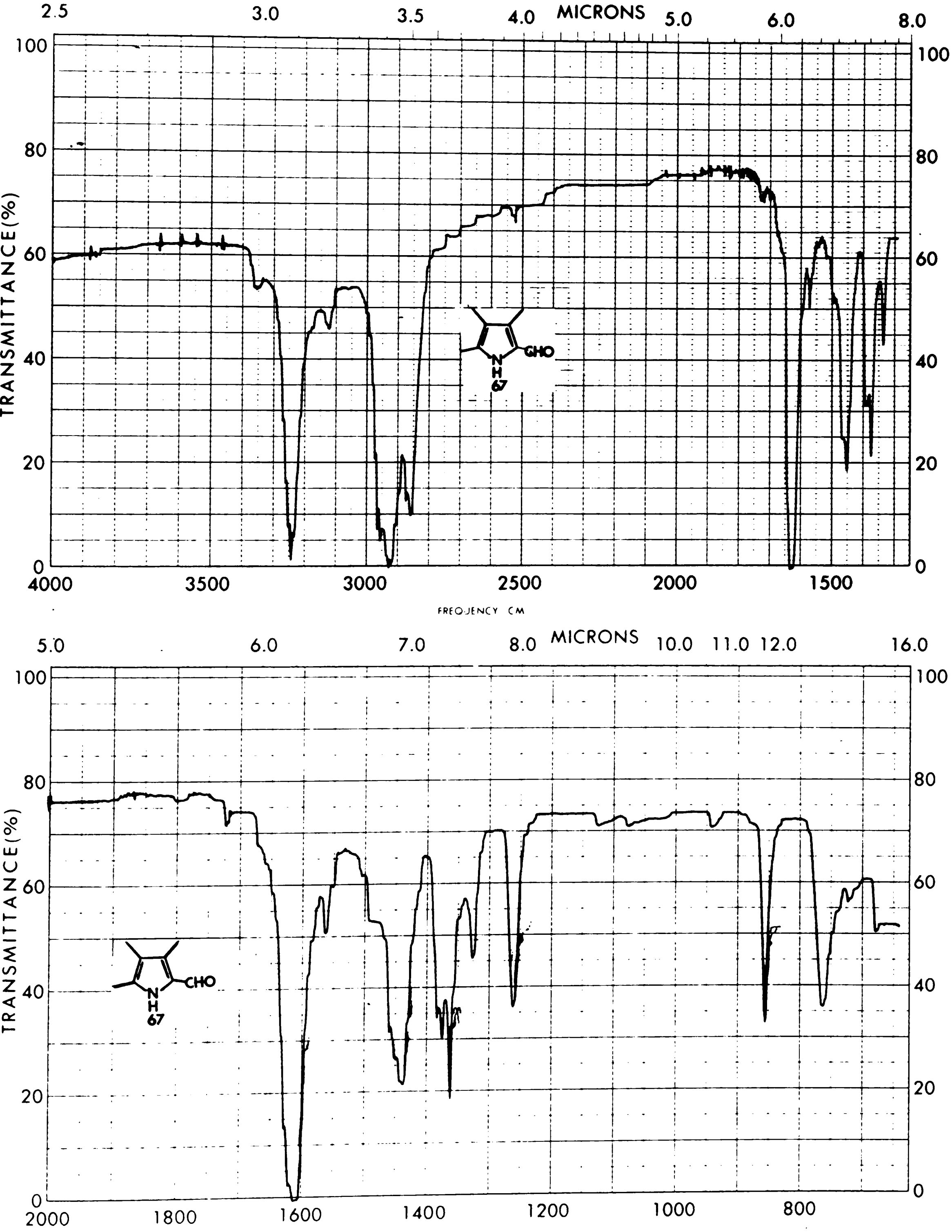


Figure 42. Infrared spectrum of 2-formyl-3,4,5-trimethylpyrrole (67).

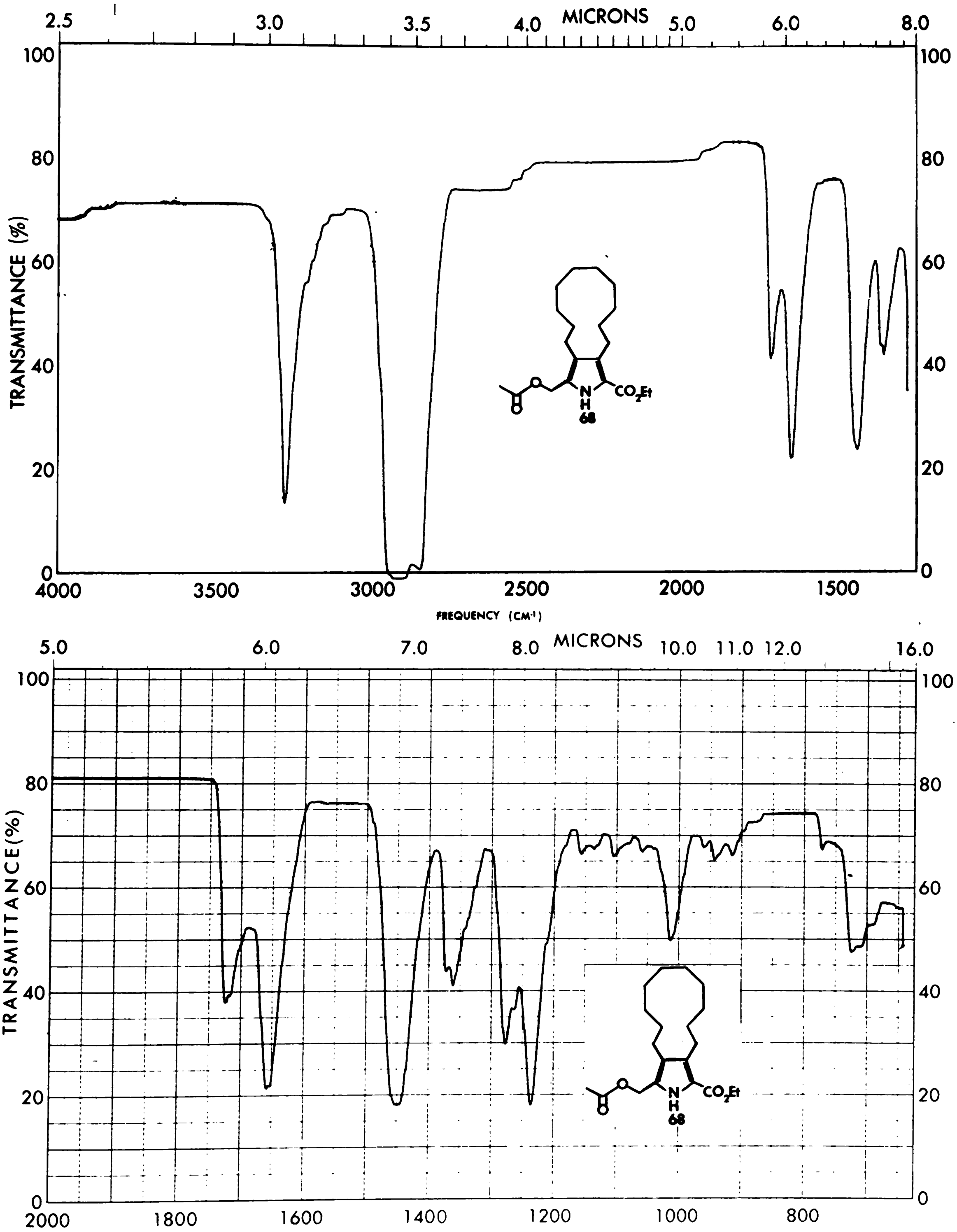


Figure 43. Infrared spectrum of 5-acetoxymethyl-2-carbethoxy-3,4-decamethylenepyrrole (68).

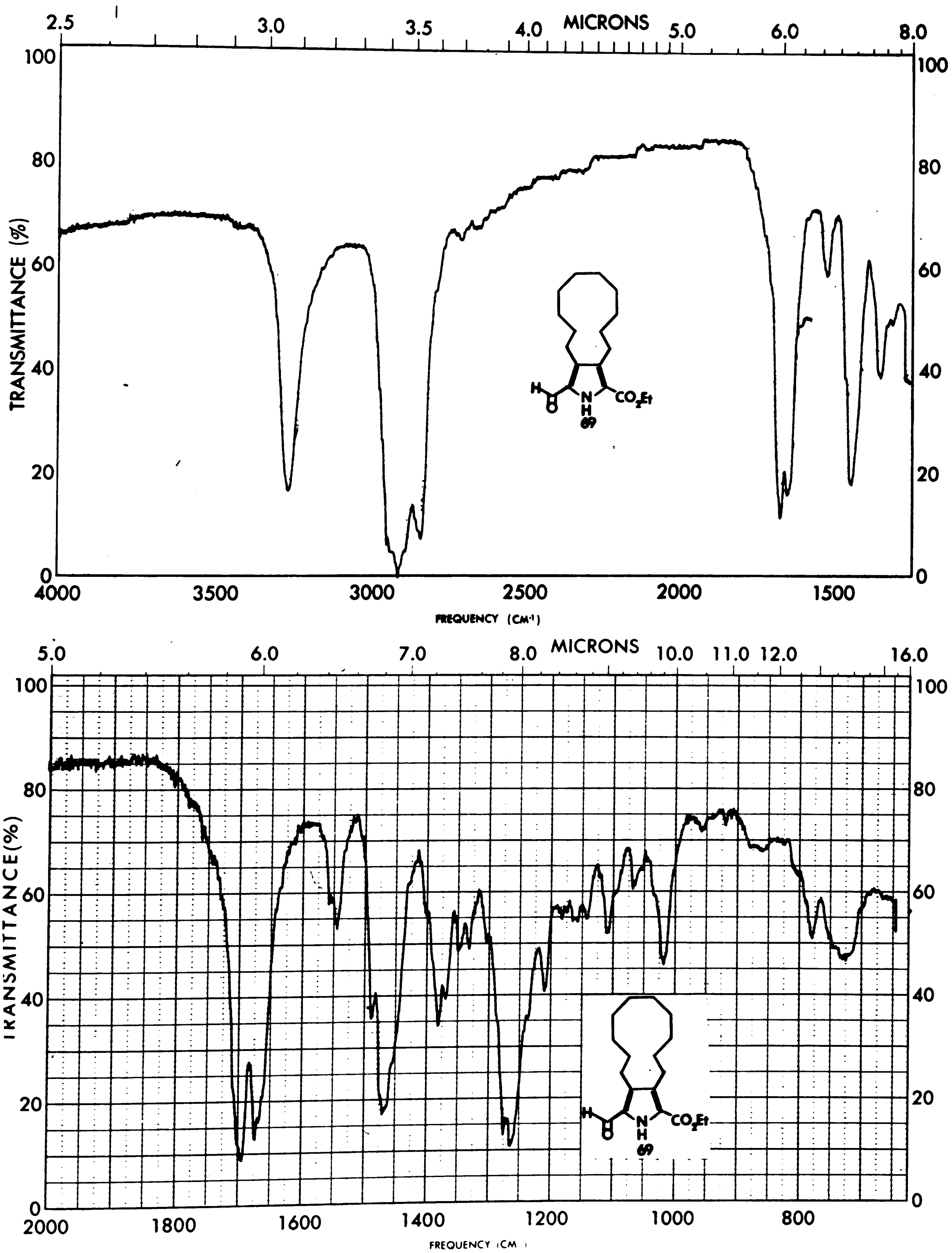


Figure 44. Infrared spectrum of 2-carbethoxy-5-formyl-3,4-decamethylenepyrrole (69).

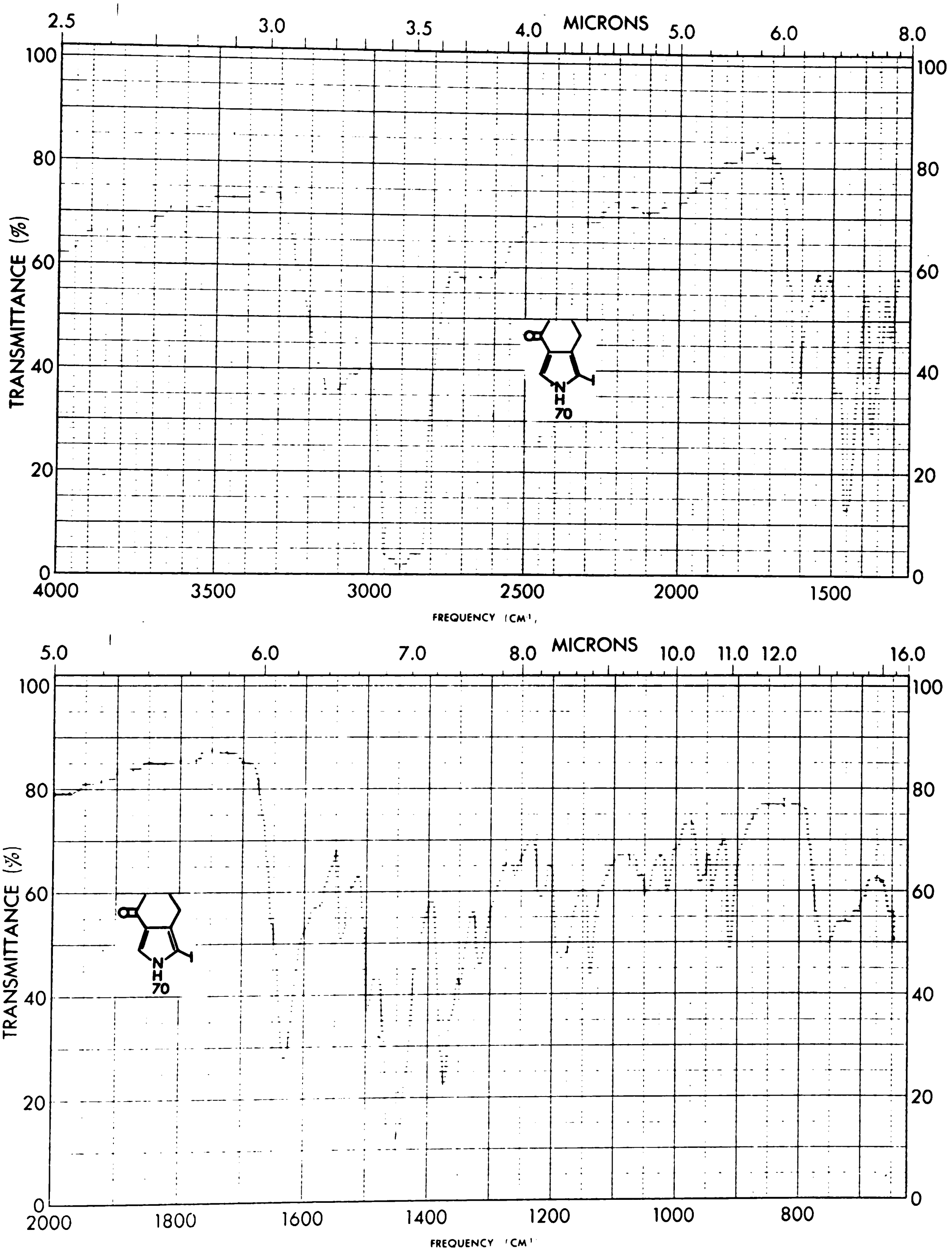


Figure 45. Infrared spectrum of 4-acetyl-3-ethyl-2-iodopyrrole (70).

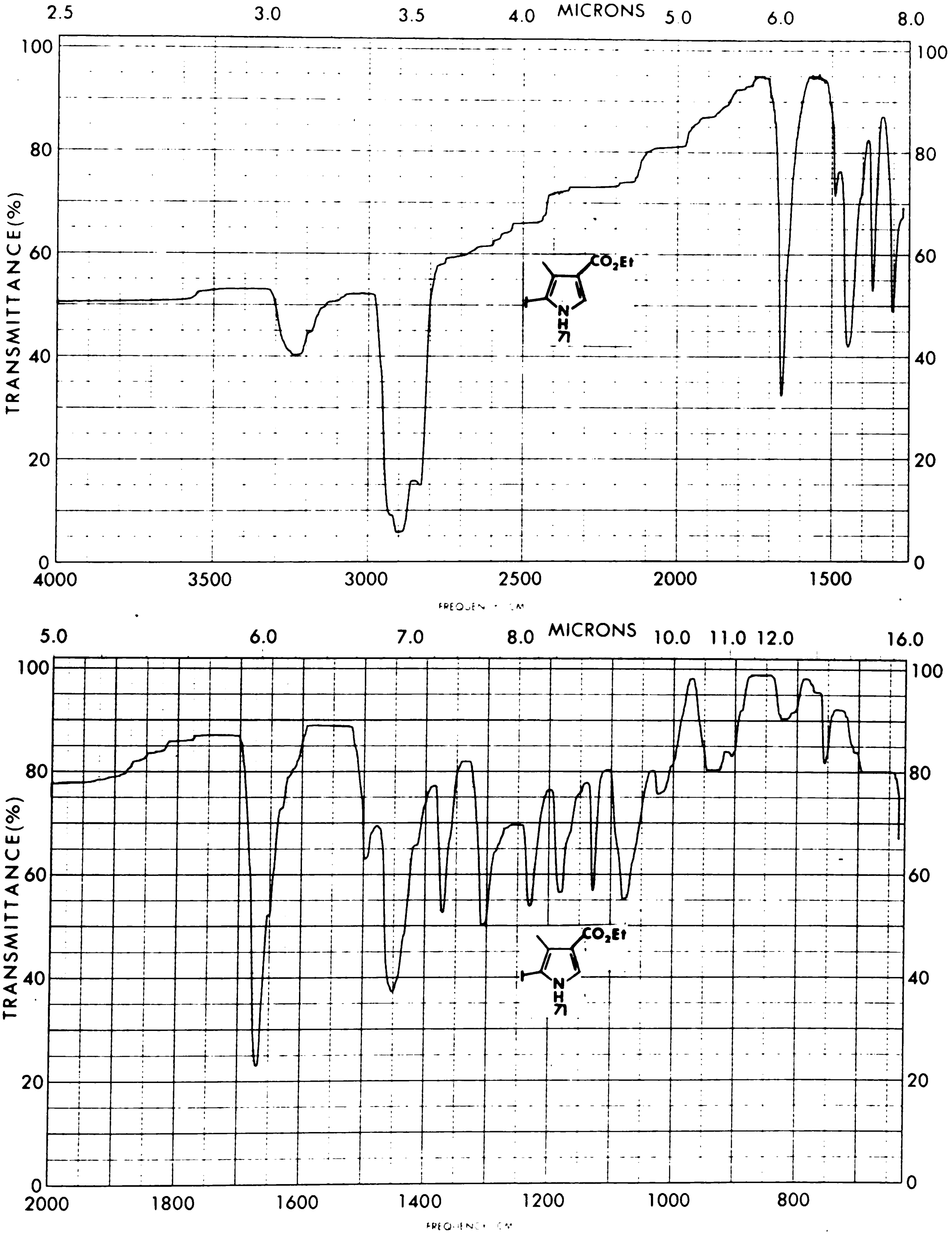


Figure 46. Infrared spectrum of 4-carbethoxy-3-methyl-2-iodopyrrole (71).

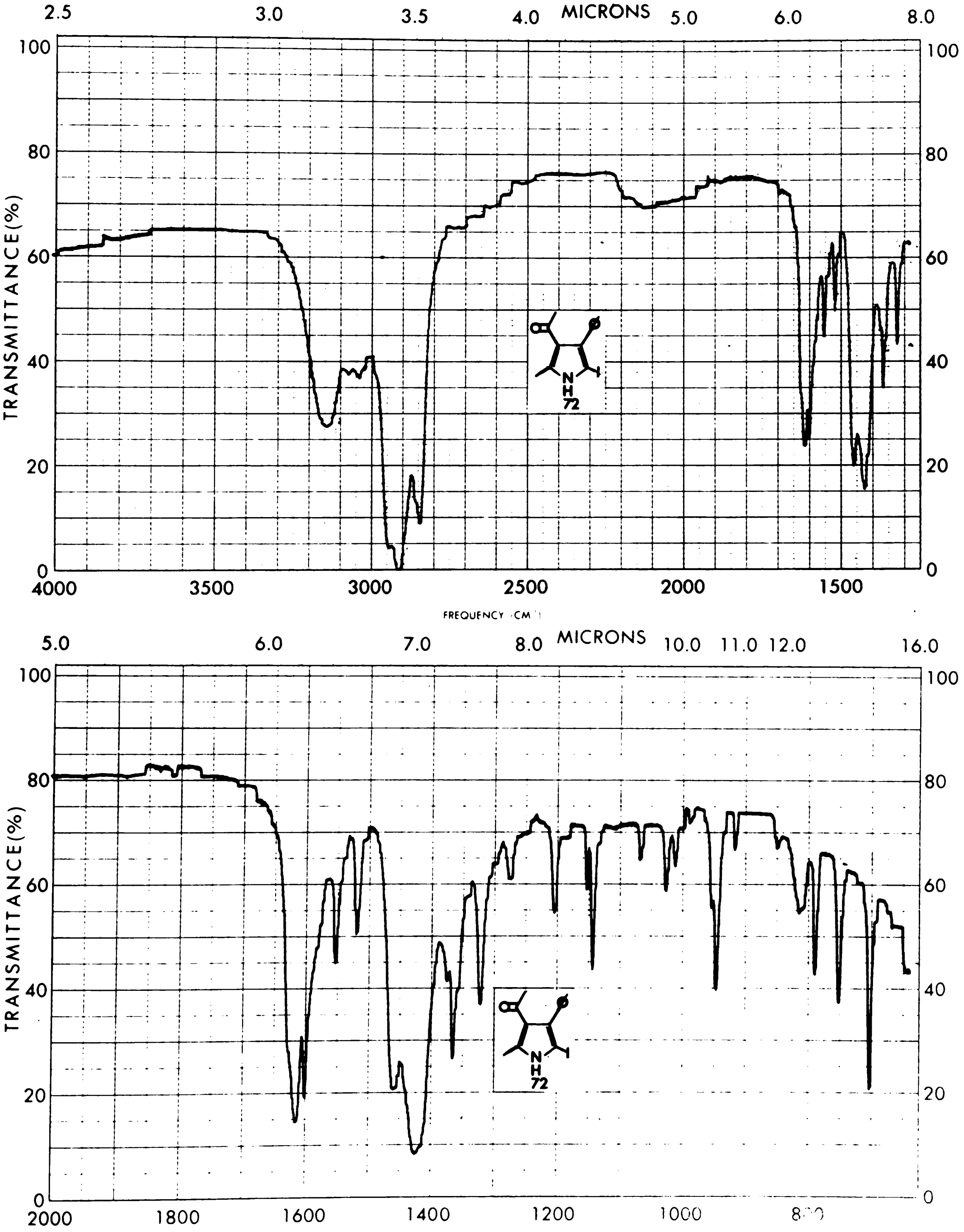


Figure 47. Infrared spectrum of 3-acetyl-5-methyl-4-phenyl-2-iodopyrrole (72).

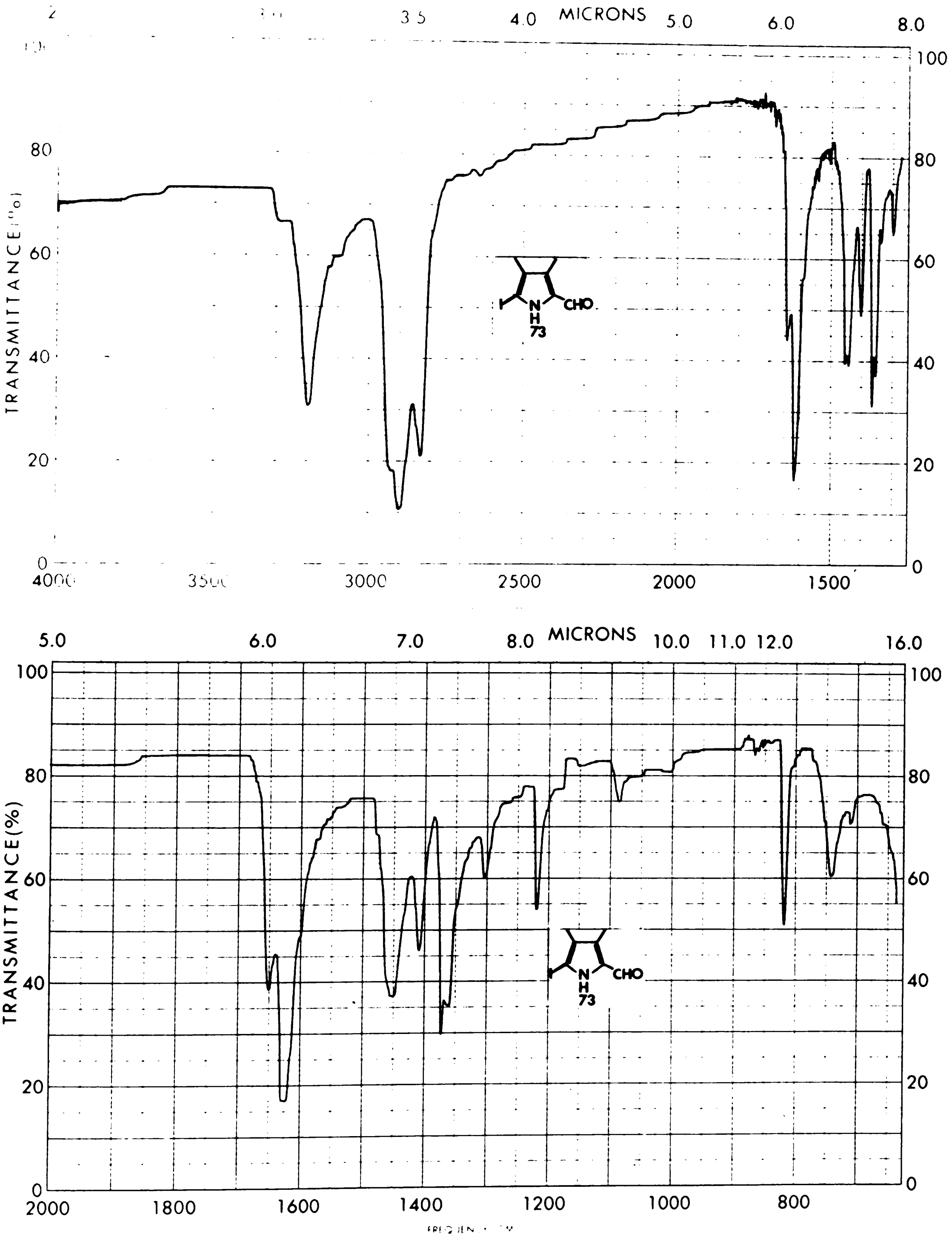


Figure 48. Infrared spectrum of 3,4-dimethyl-5-formyl-2-iodopyrrole (73).

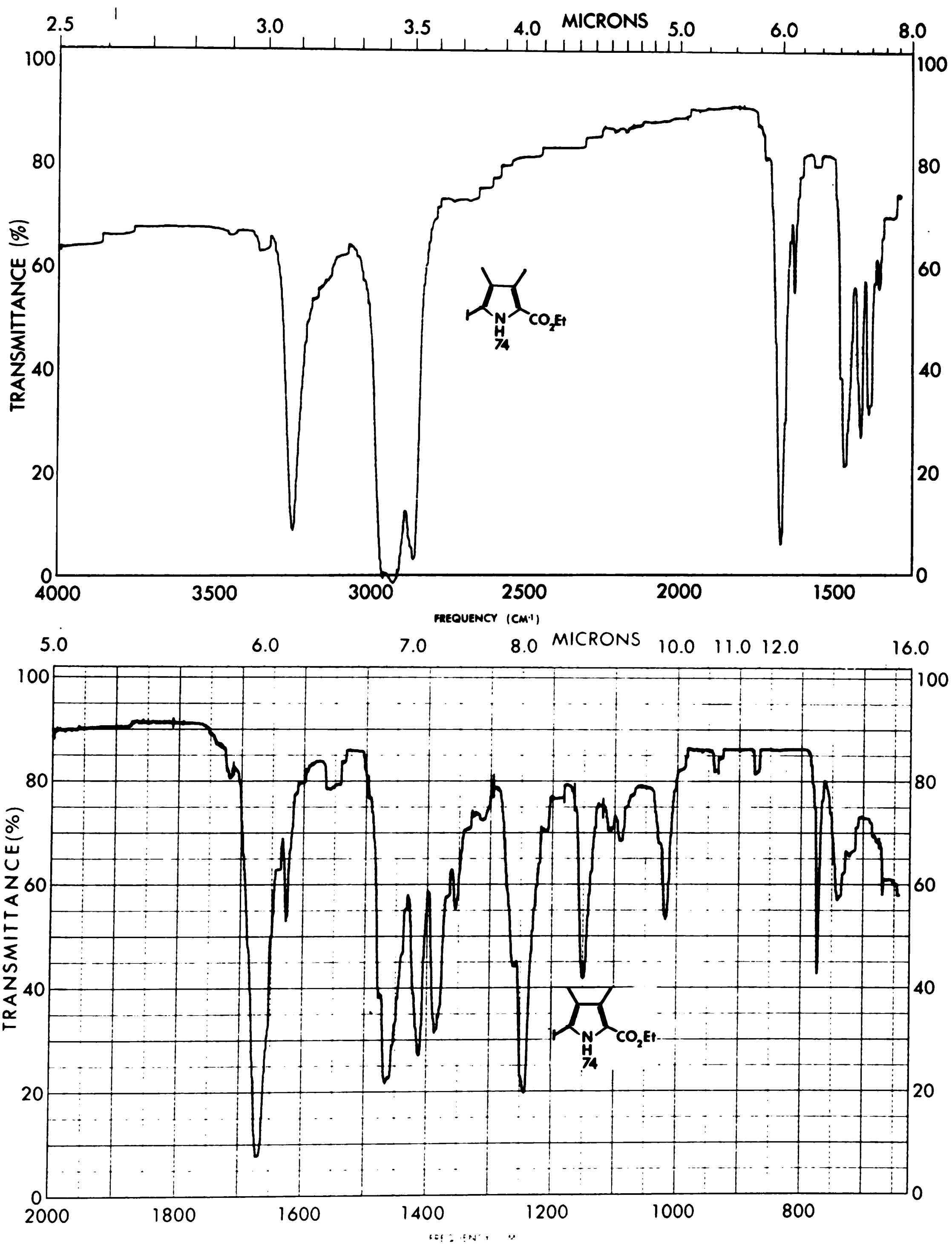
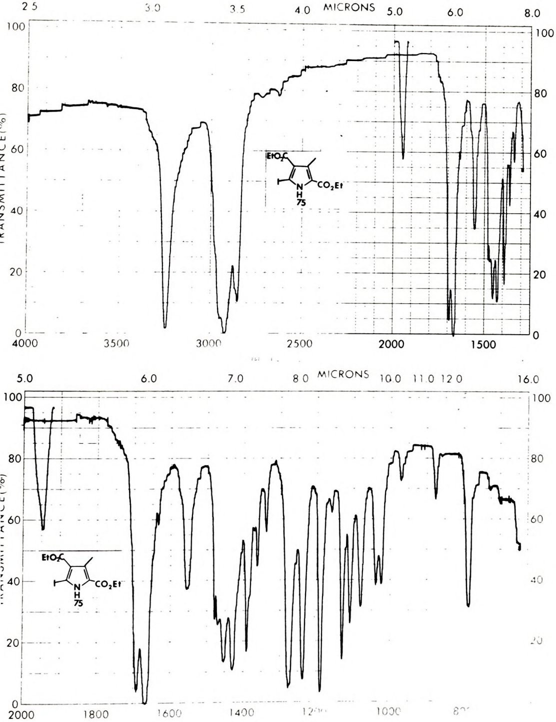


Figure 49. Infrared spectrum of ethyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate (74).



gure 50. Infrared spectrum of diethyl 3-methyl-5-iodo-pyrrole-2,4-dicarboxylate (75).

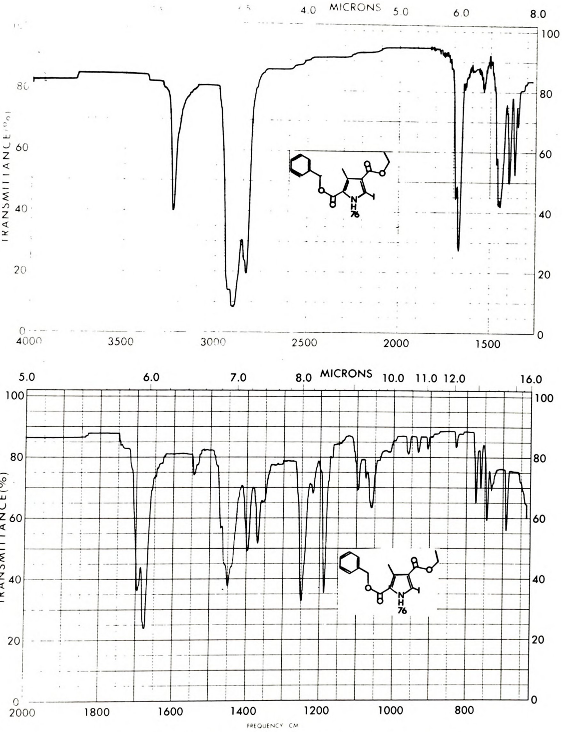
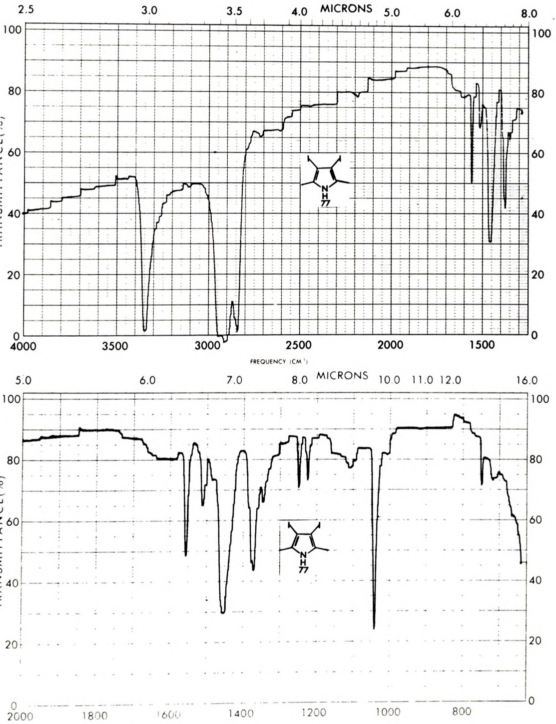
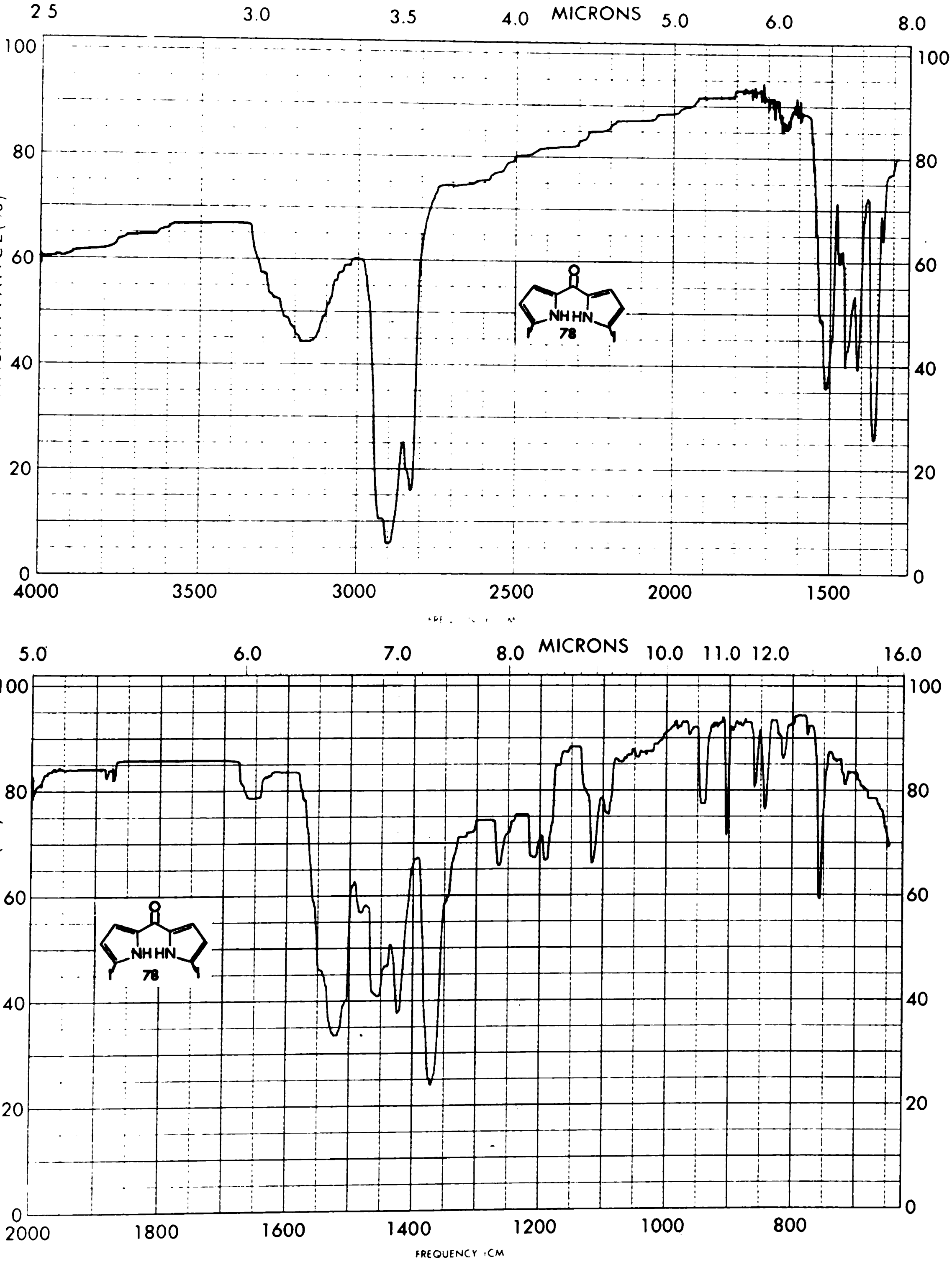


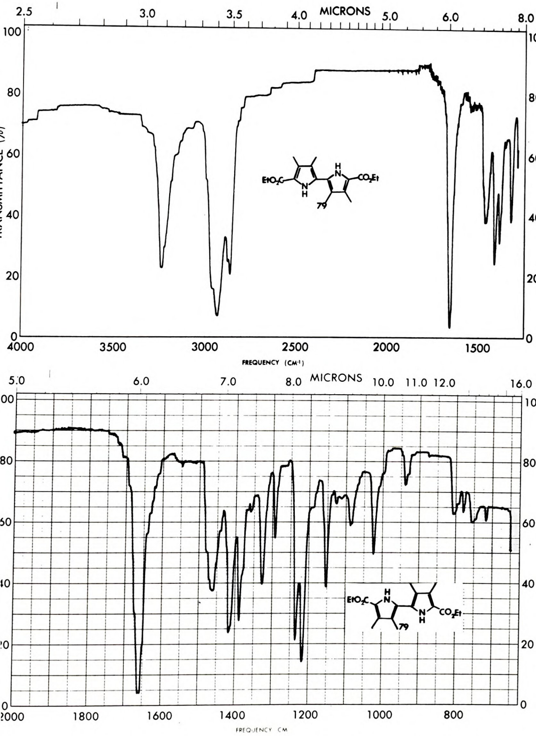
Figure 51. Infrared spectrum of 2-benzyl 4-ethyl 5-iodo-3-methylpyrrole-2,4-dicarboxylate (76).



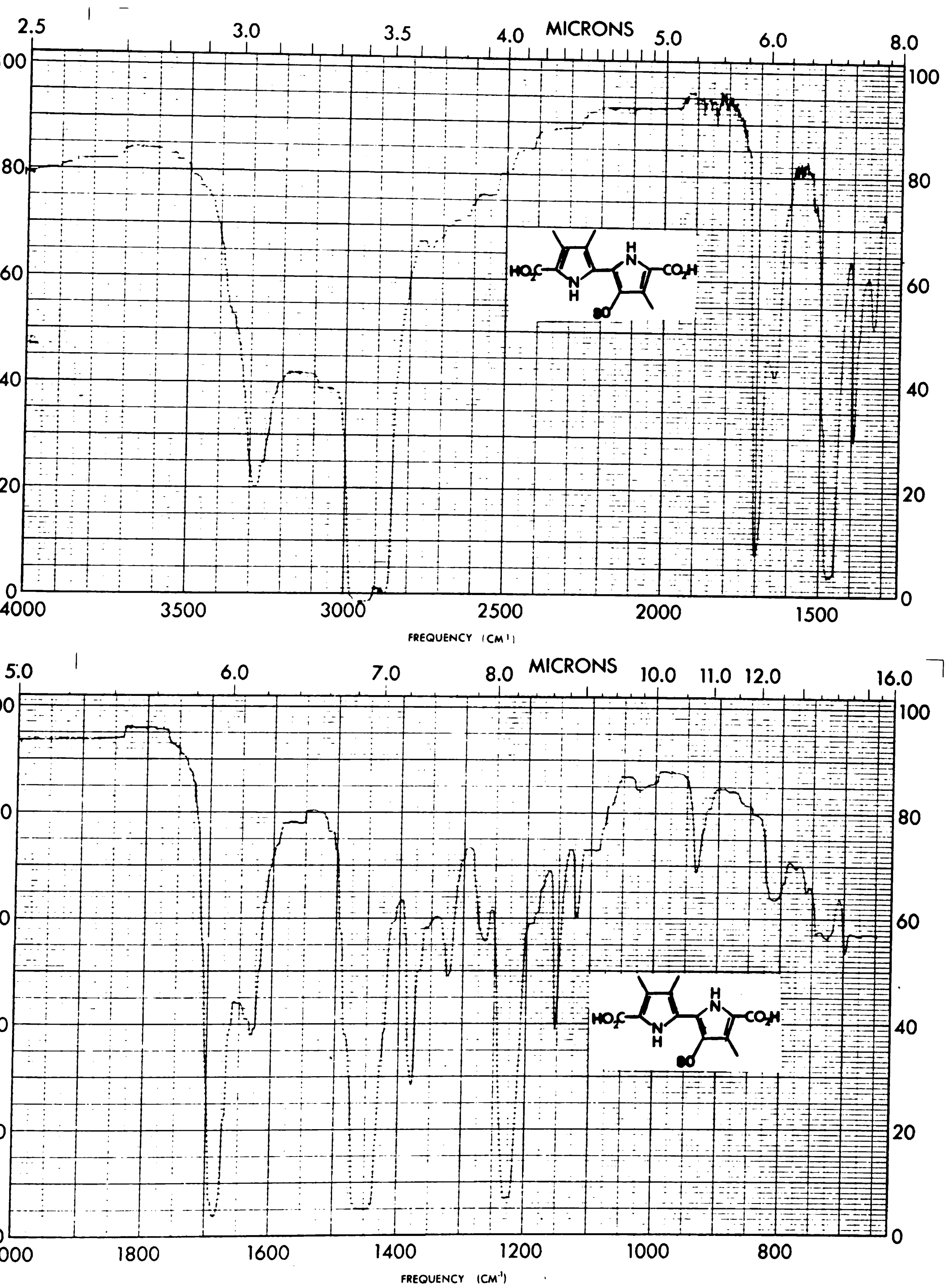
igure 52. Infrared spectrum of 2,5-dimethyl-3,4-diiodopyrrole (77).



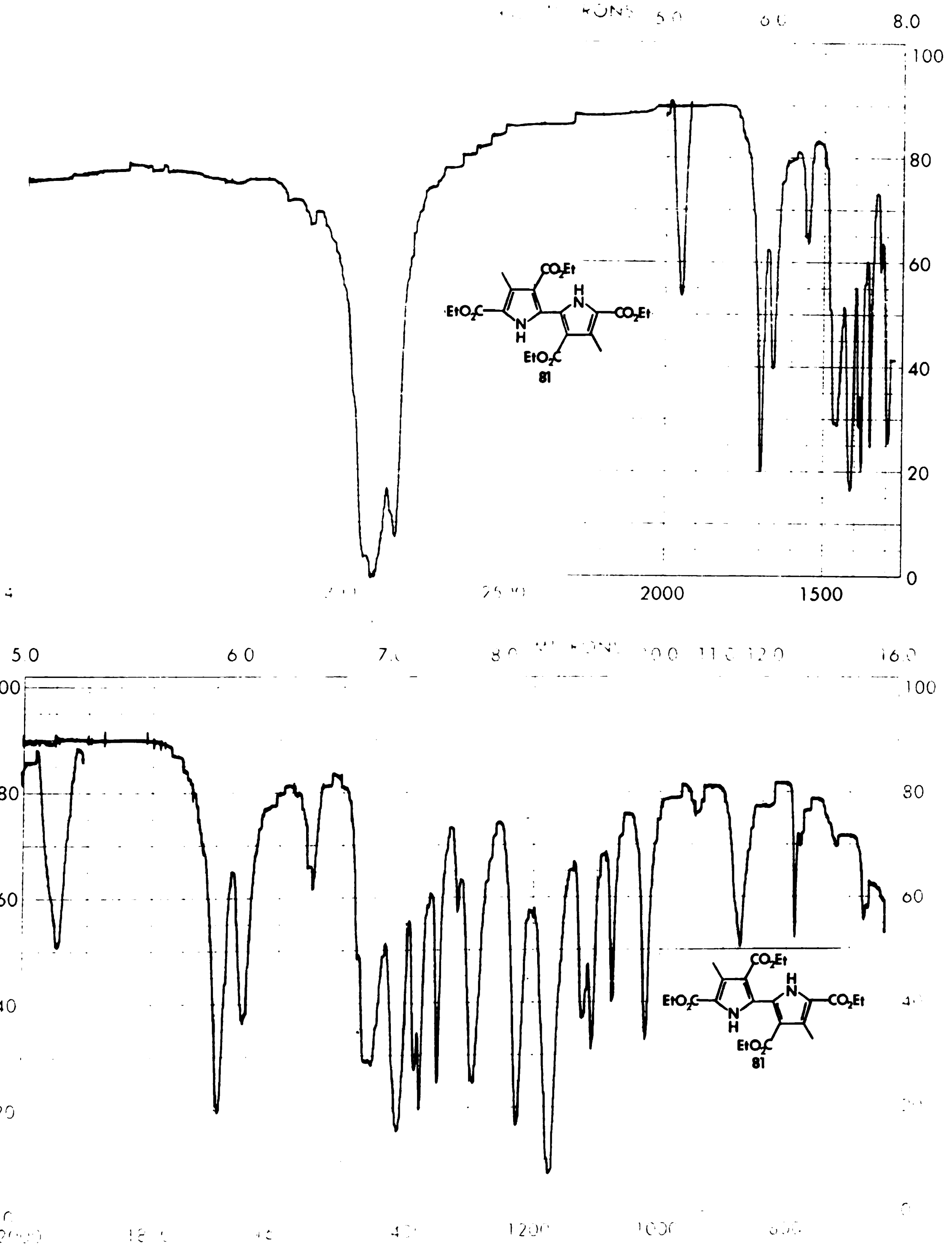
igure 53. Infrared spectrum of 5,5'-diiodo-2,2'-dipyrroketone (78).



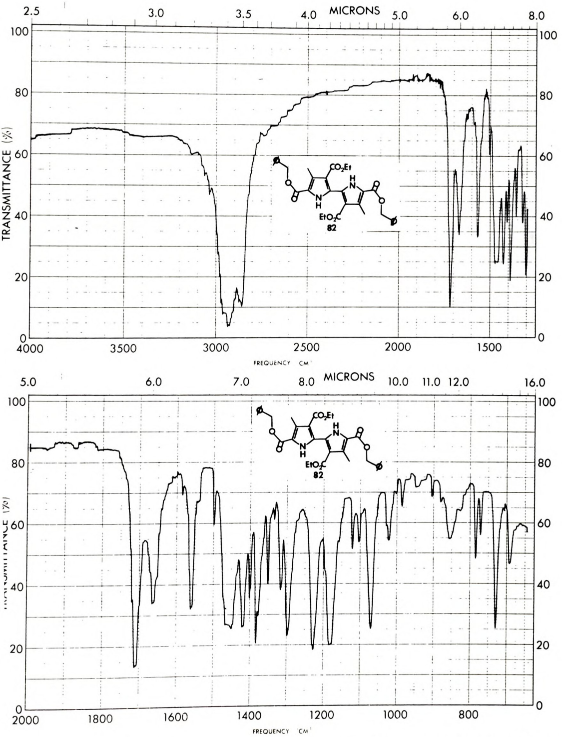
igure 54. Infrared spectrum of diethyl 3,3',4,4'-tetramethyl-2,2'-bipyrrole-5,5'-dicarboxylate (79).



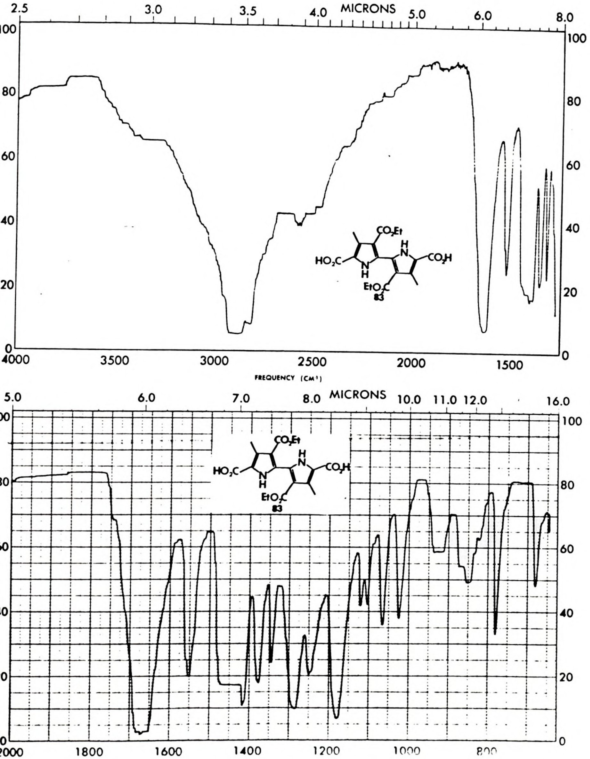
ure 55. Infrared spectrum of 3,3',4,4'-tetramethyl-2,2'-bipyrrole-5,5'-dicarboxylic acid (80).



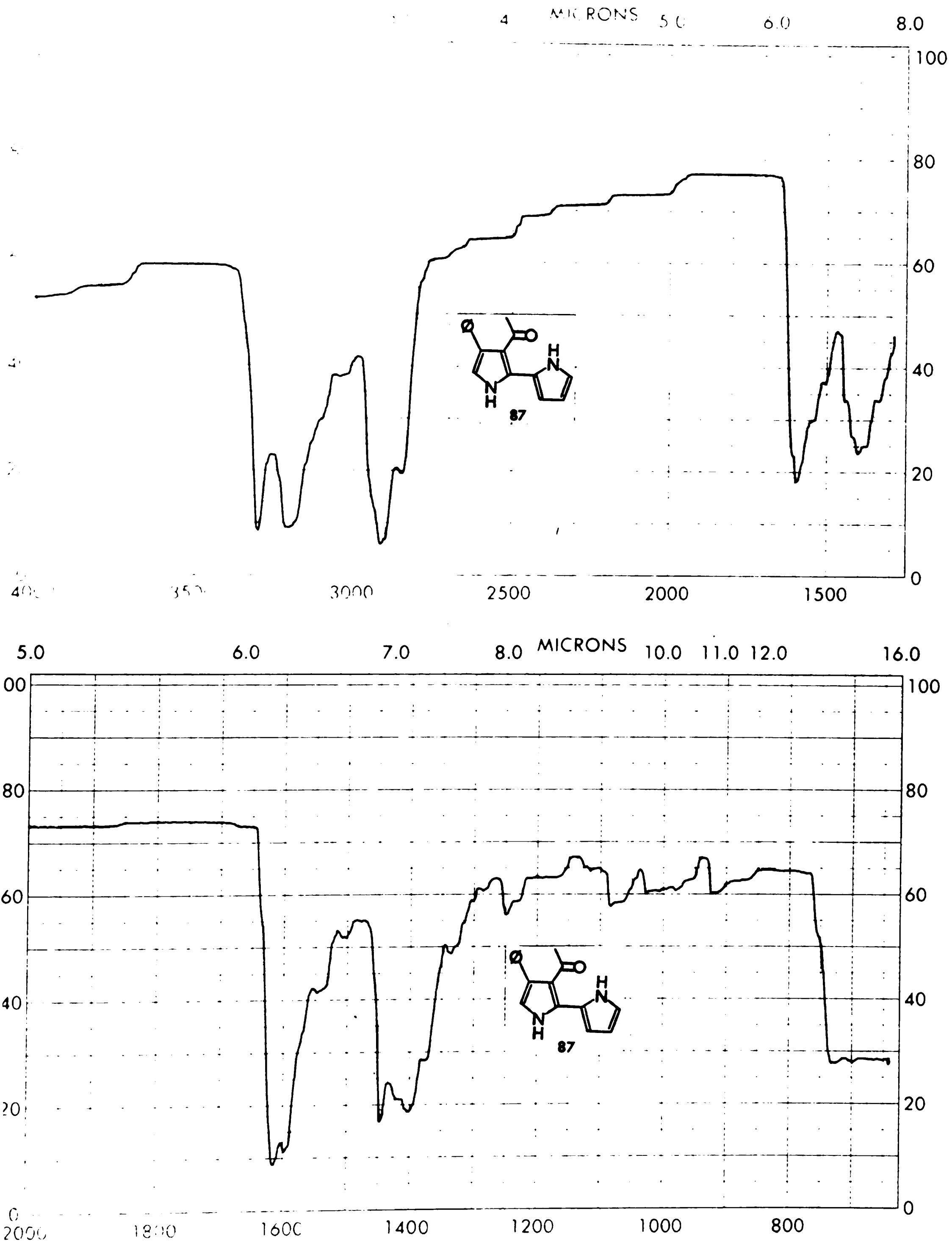
gure 56. Infrared spectrum of tetraethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3',5,5'-tetracarboxylate (81).



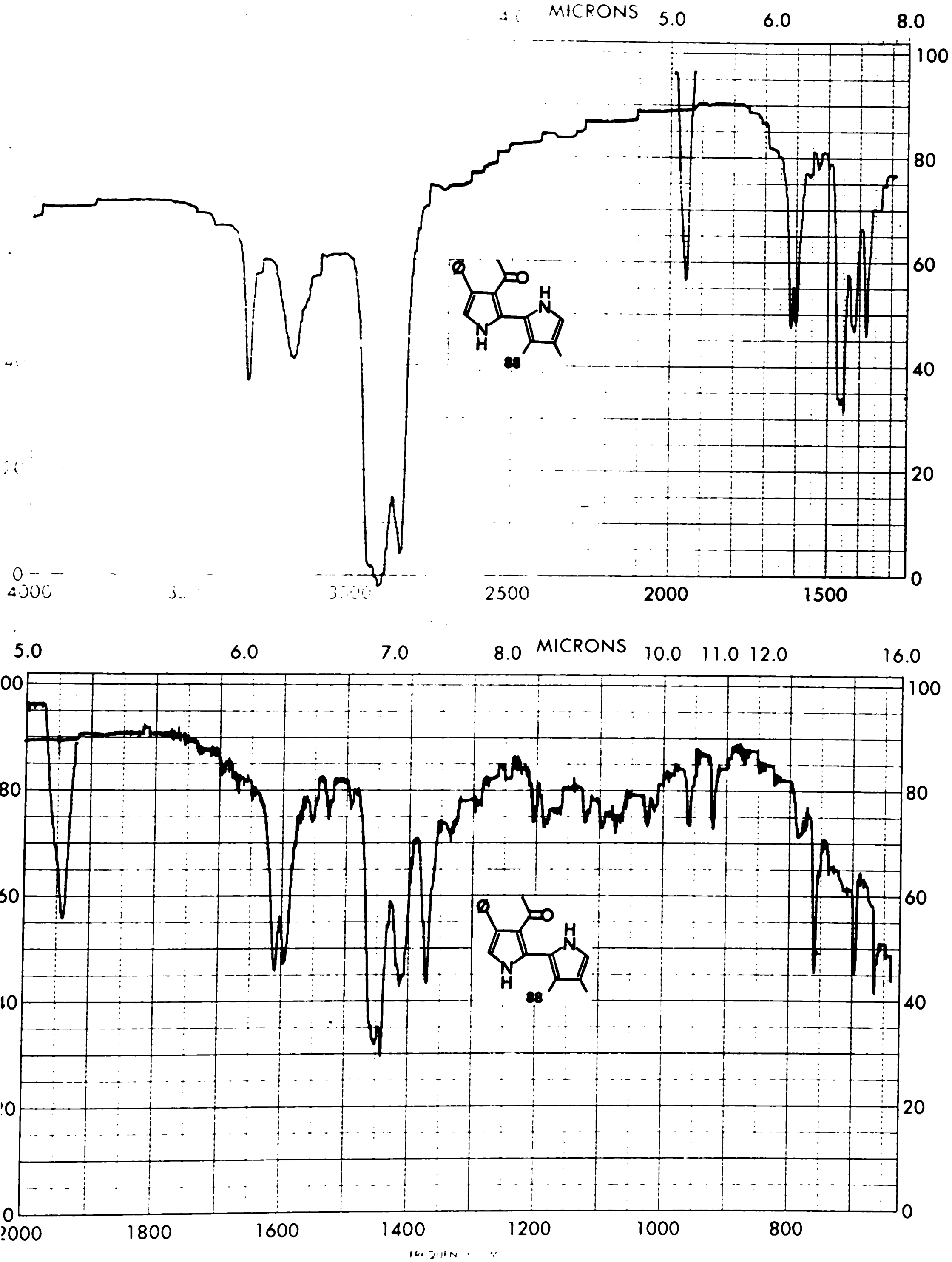
igure 57. Infrared spectrum of 5,5'-dibenzyl 3,3'-diethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3',5,5'-tetracarboxylate (82).



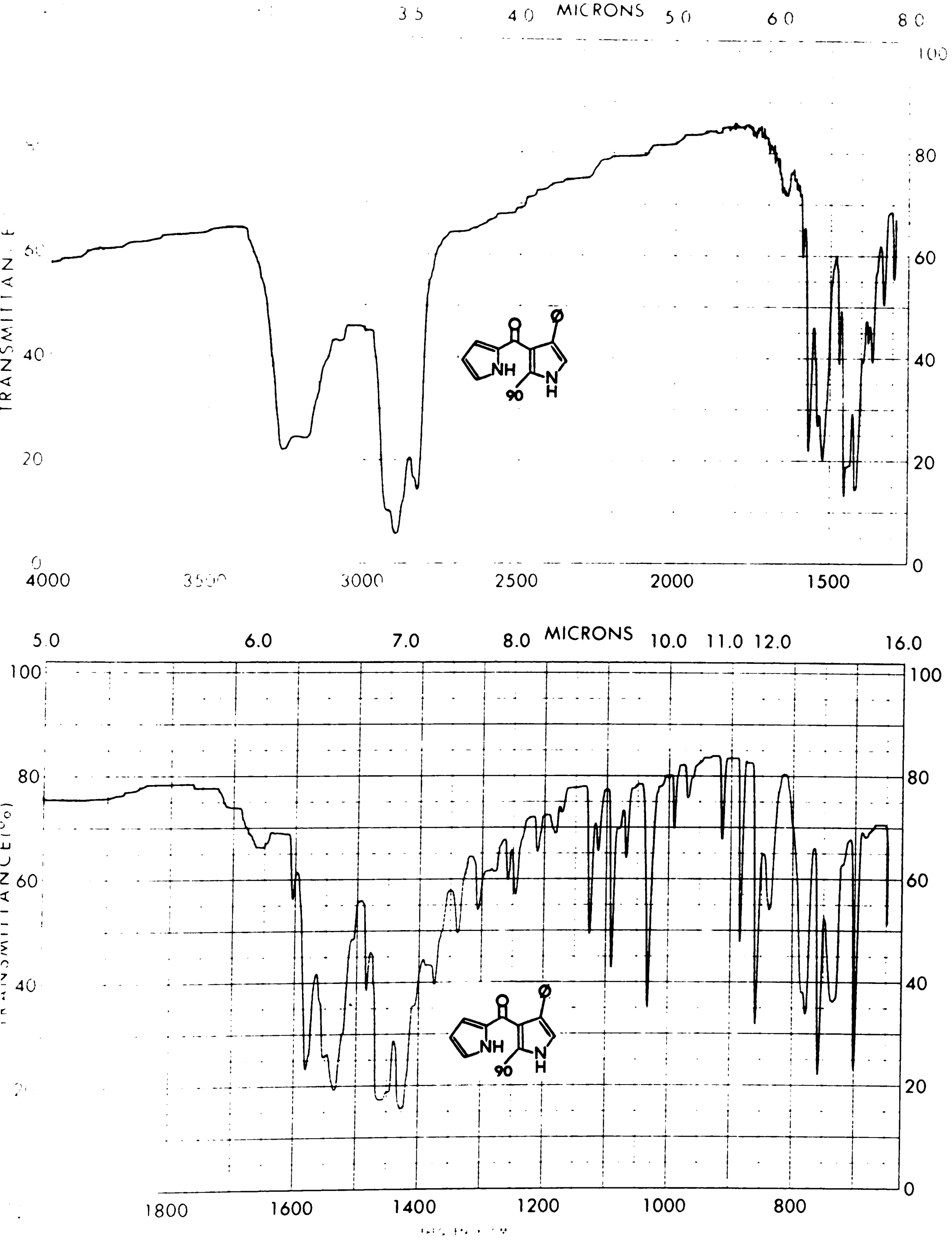
gure 58. Infrared spectrum of 3,3'-diethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3'-dicarboxylate-5,5'-dicarboxylic acid (83).



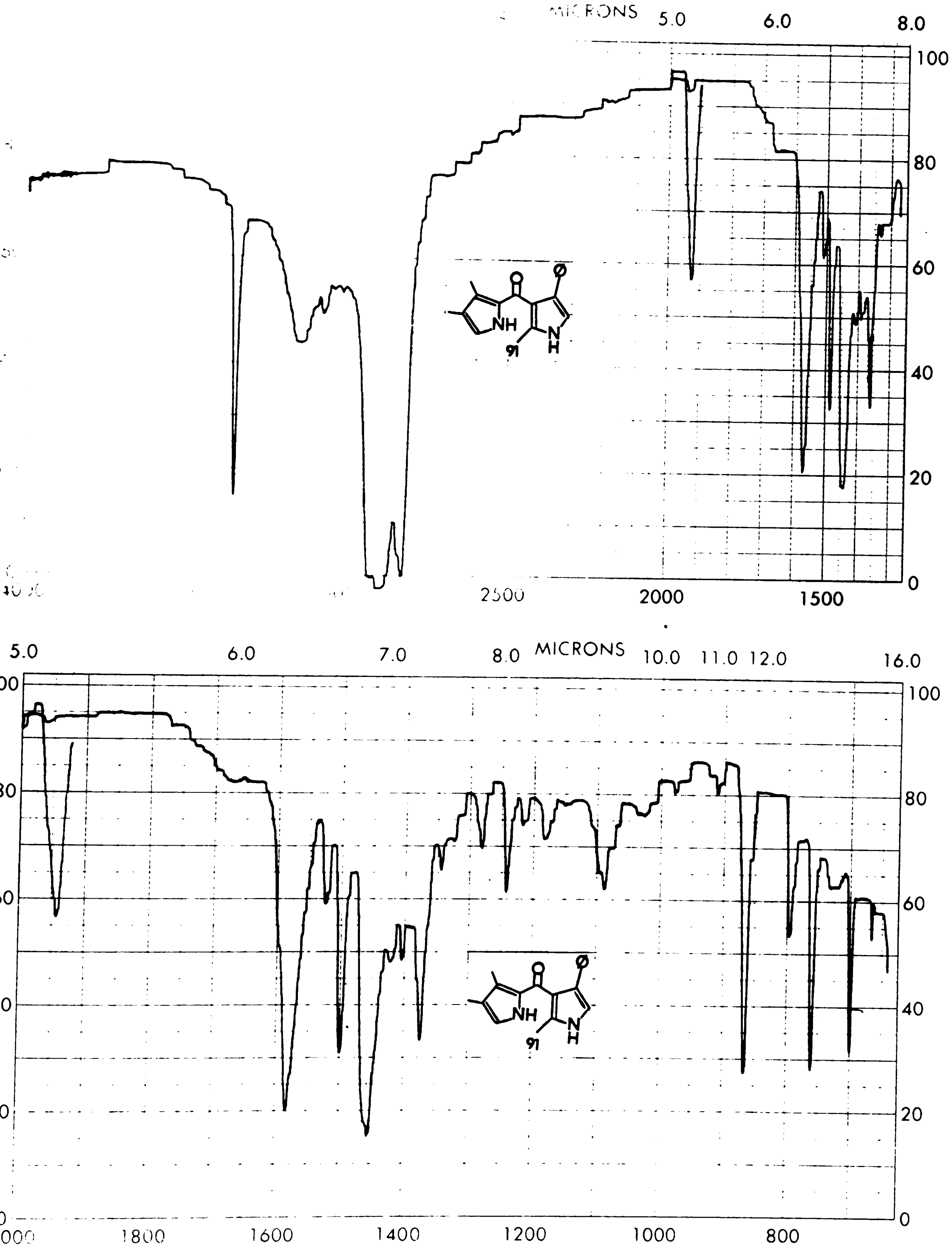
igure 59. Infrared spectrum of 3-acetyl-4-phenyl-2,2'-bipyrrole (87).



gure 60. Infrared spectrum of 3-acetyl-3',4'-dimethyl-4-phenyl-2,2'-bipyrrole (88).



igure 61. Infrared spectrum of 2-methyl-4-phenyl-3,2'-dipyrroketone (90).



gure 62. Infrared spectrum of 2,3',4'-trimethyl-4-phenyl-3,2'-dipyrroketone (91).

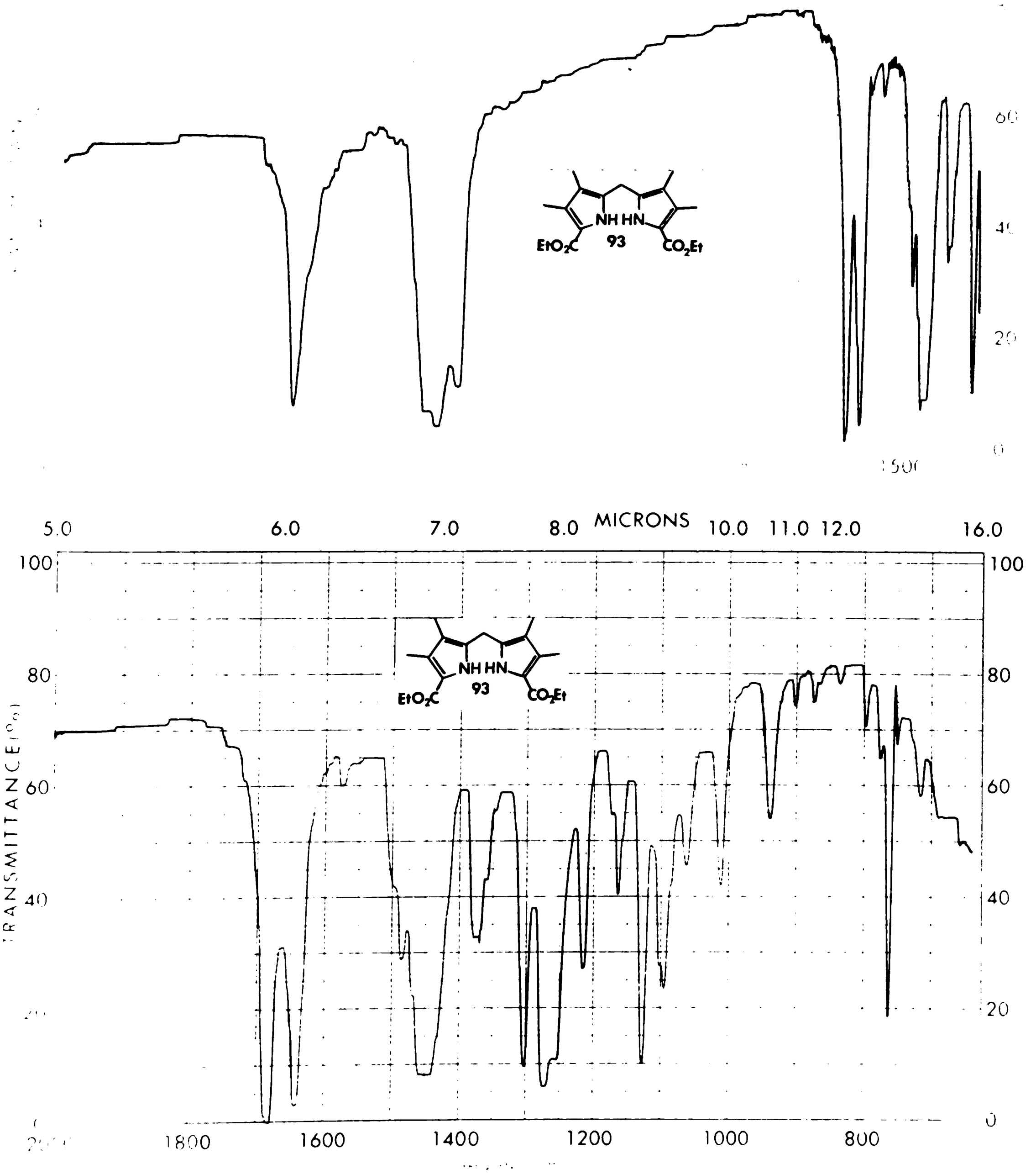
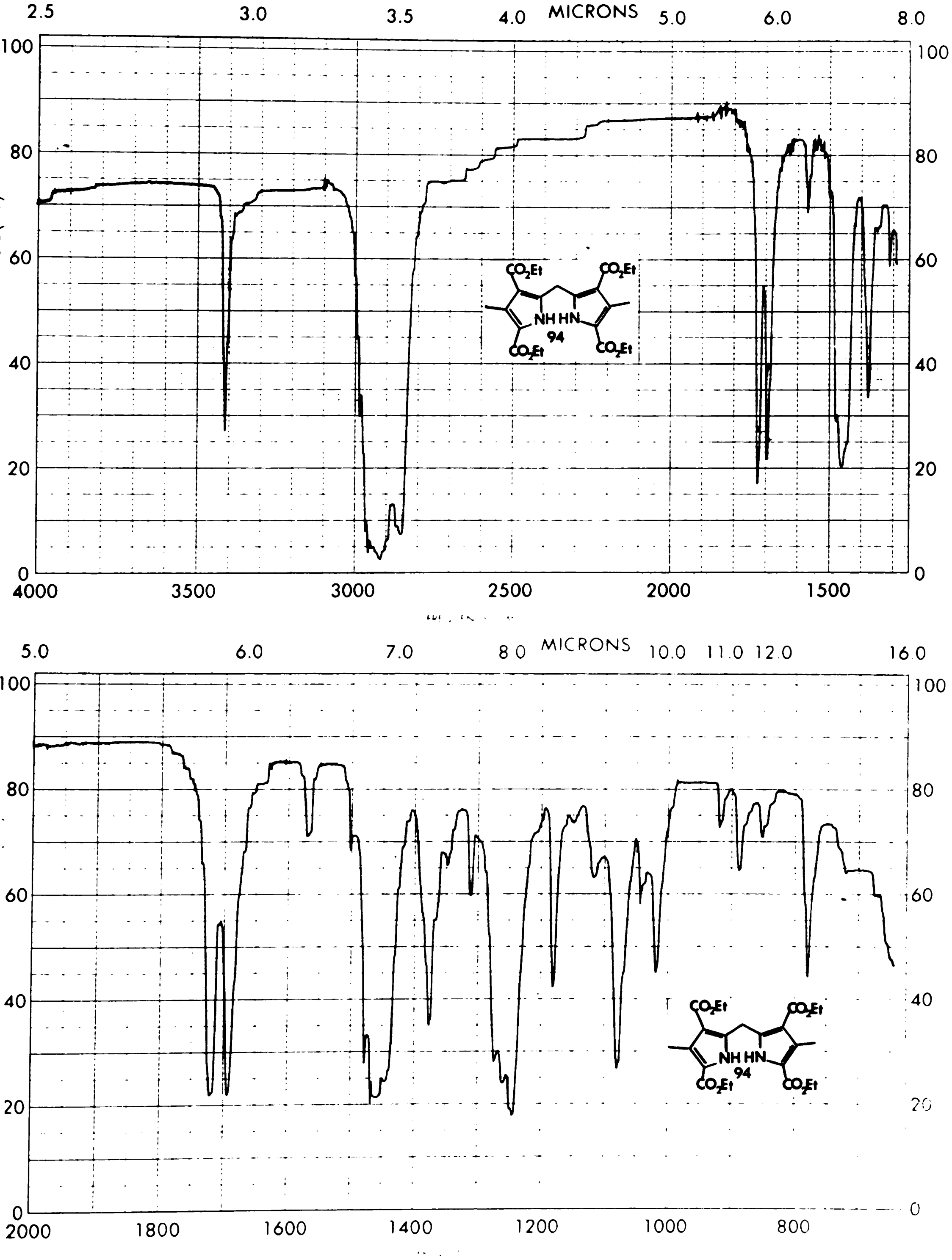
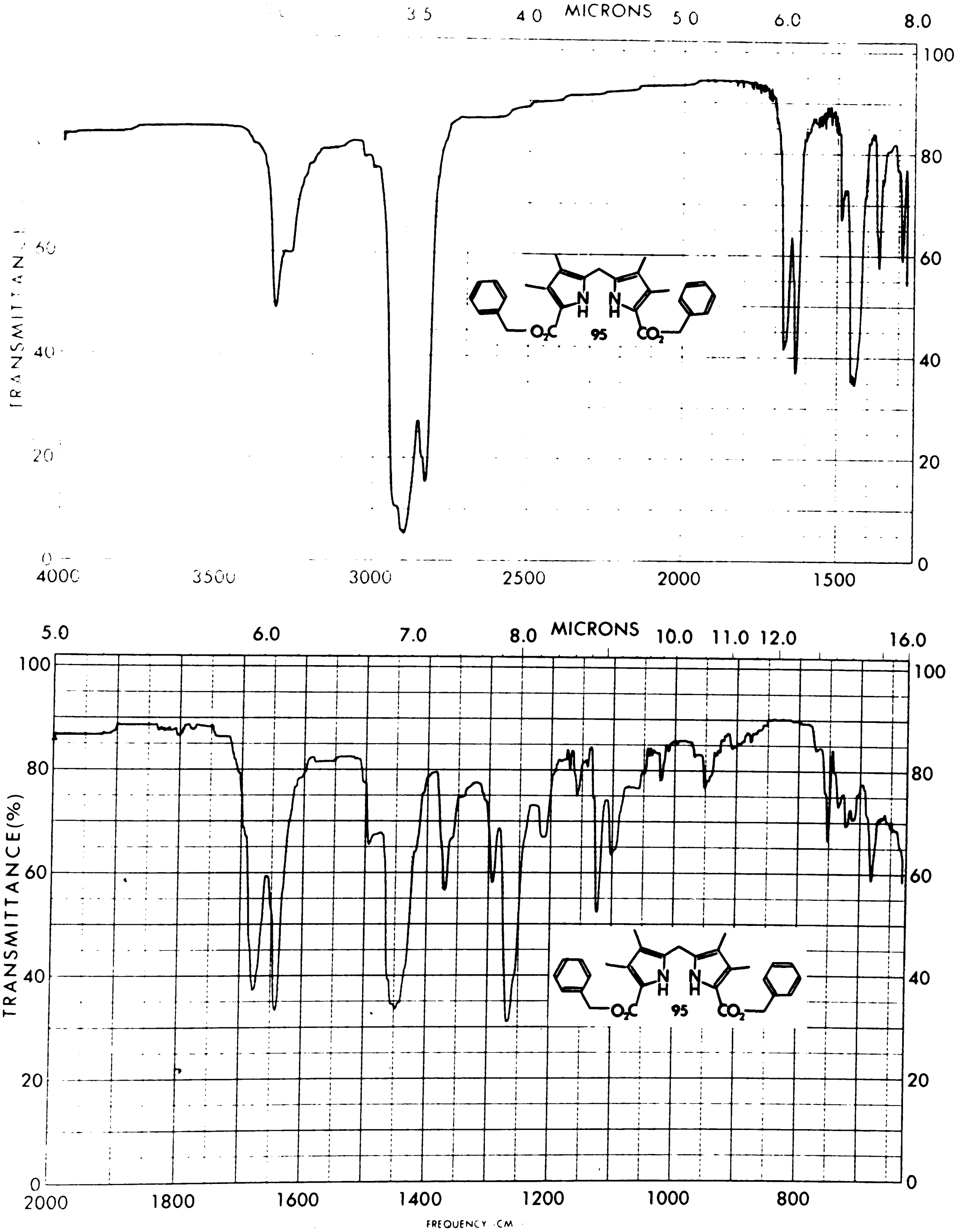


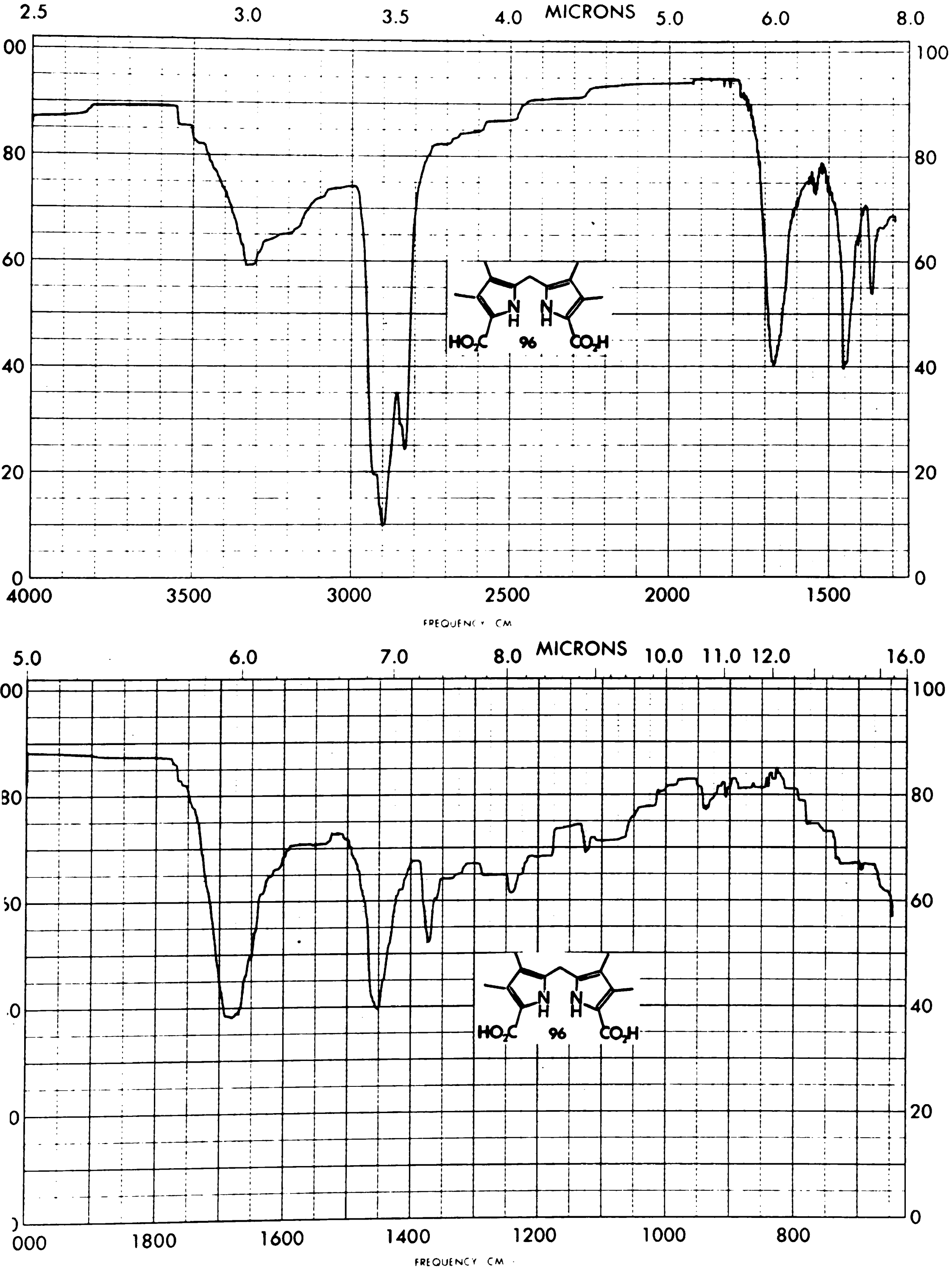
Figure 63. Infrared spectrum of 5,5'-dicarbethoxy-3,3',-4,4'-tetramethyl-2,2'-dipyrromethane (93).



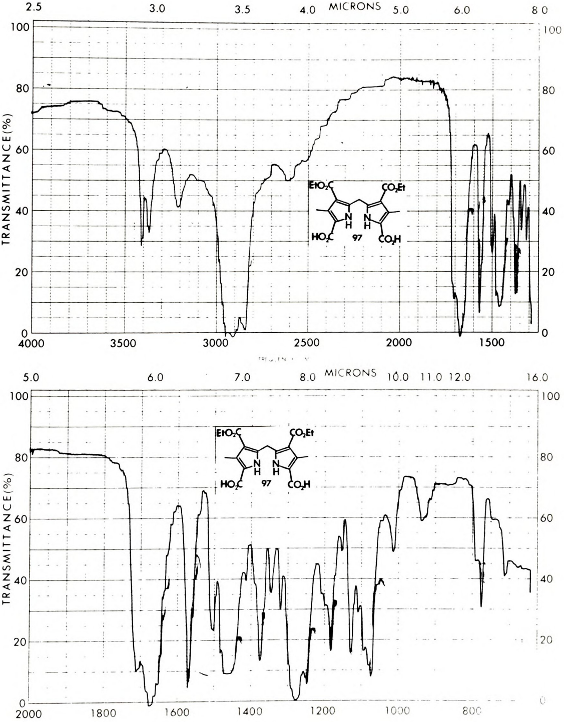
gure 64. Infrared spectrum of 3,3',5,5'-tetracarbethoxy-4,4'-dimethyl-2,2'-dipyrromethane (94).



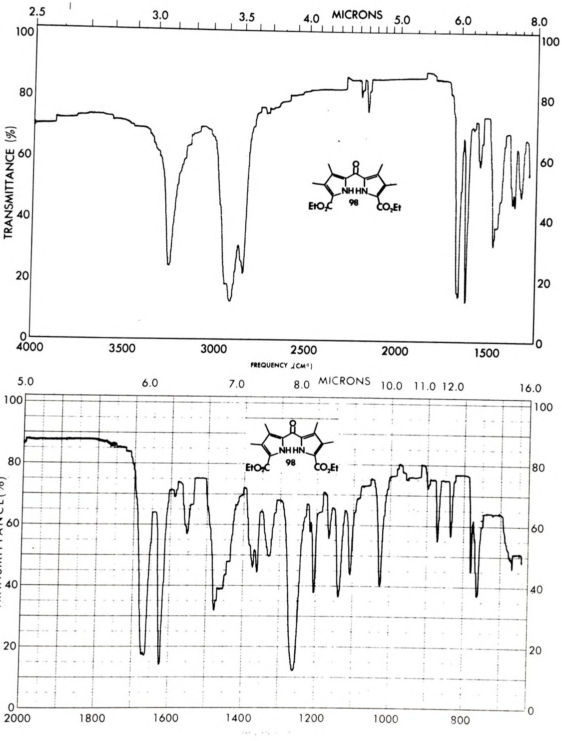
igure 65. Infrared spectrum of 5,5'-carbobenzyloxy-3,3',4,4'-tetramethyl-2,2'-dipyrromethane (95).



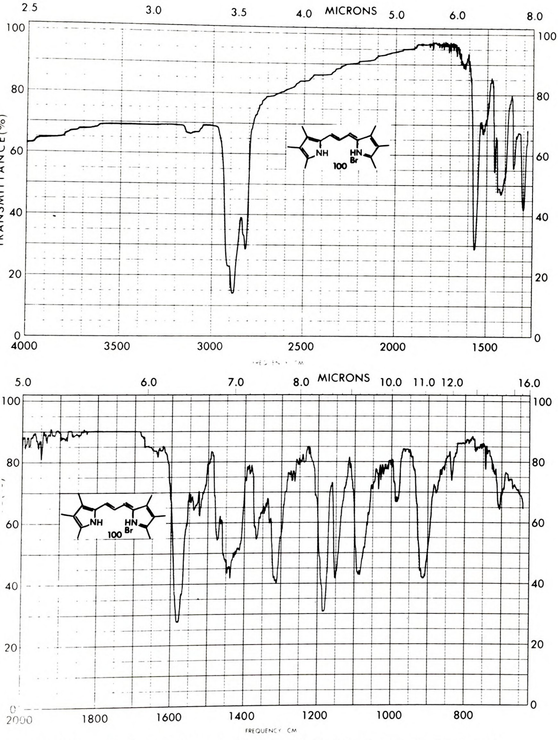
gure 66. Infrared spectrum of 3,3',4,4'-tetramethyl-2,2'-dipyrromethane-5,5'-dicarboxylic acid (96).



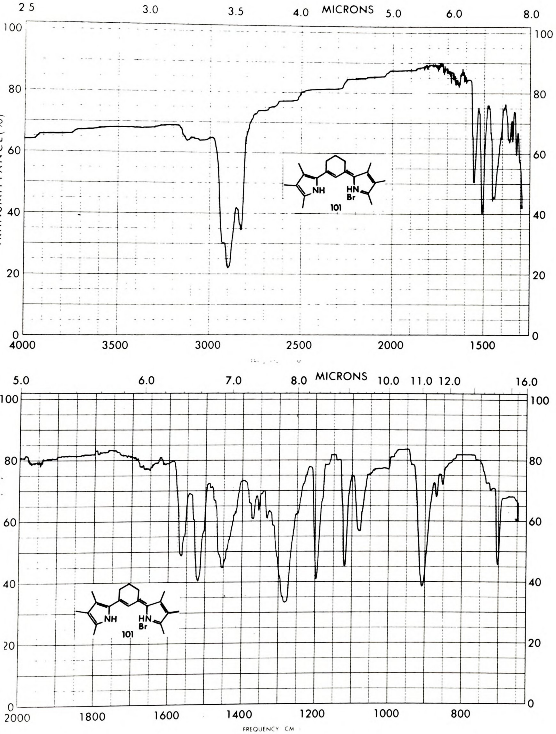
igure 67. Infrared spectrum of diethyl 4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylic acid-3,3'-dicarboxylate (97).



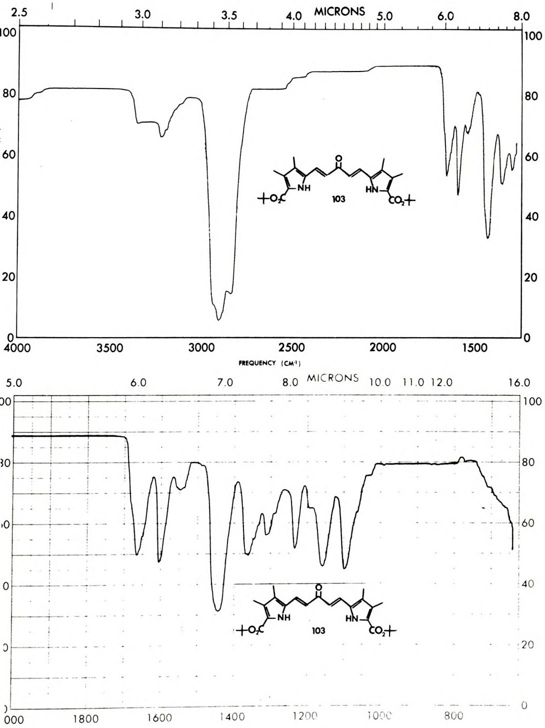
igure 68. Infrared spectrum of 5,5'-diethoxycarbonyl-3,3',4,4'-tetramethyl-2,2'-dipyrroketone (98).



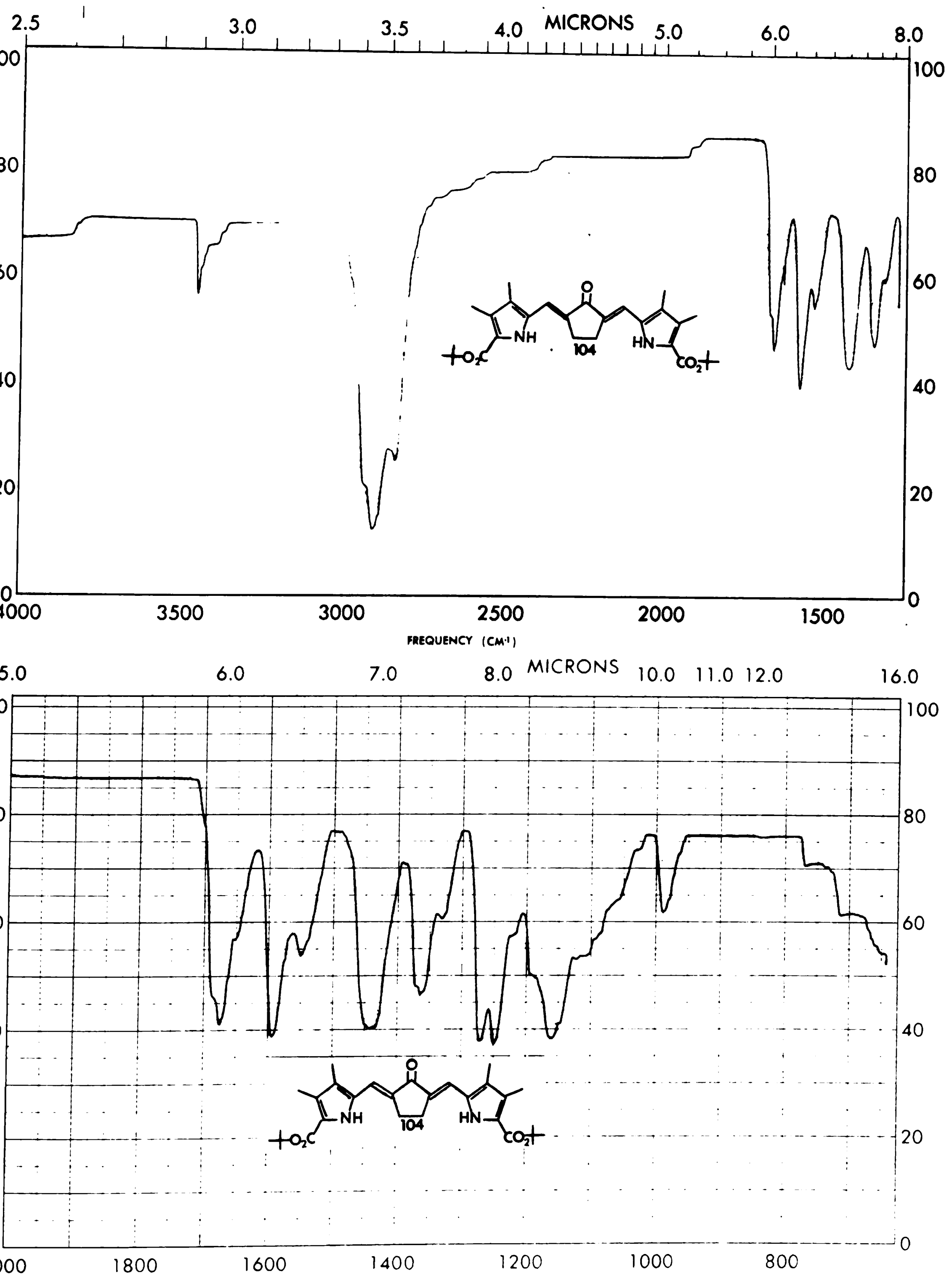
gure 69. Infrared spectrum of 3,3',4,4',5,5'-hexamethyldipyrro-2,2'-trimethine hydrobromide (100).



gure 70. Infrared spectrum of 3,3',4,4',5,5'-hexamethyldipyrro-2,2'-hexacyclotrimethine hydrobromide (101).



gure 71. Infrared spectrum of 1,5-di-(5-carbo-*t*-butoxy-3,4-dimethyl-2-pyrro)-1,4-pentadiene-$\overline{3}$-one (**103**).



gure 72. Infrared spectrum of 2,5-di-(5-carbo-*t*-butoxy-3,4-dimethylpyrr-2-ylmethylene)-cyclopentanone (104).

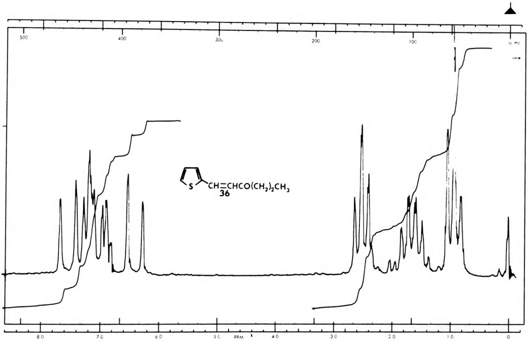


Figure 73. PMR spectrum of 1-(2-thienyl)-hex-1-ene (36).

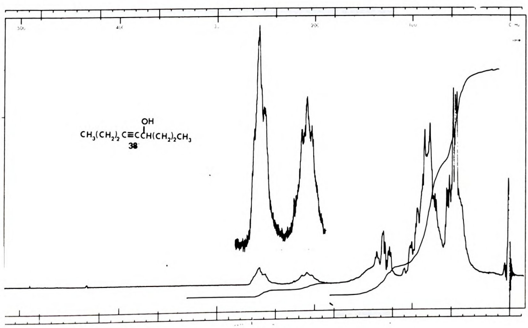


Figure 74. PMR spectrum of 6-hydroxy-4-decyne (38).

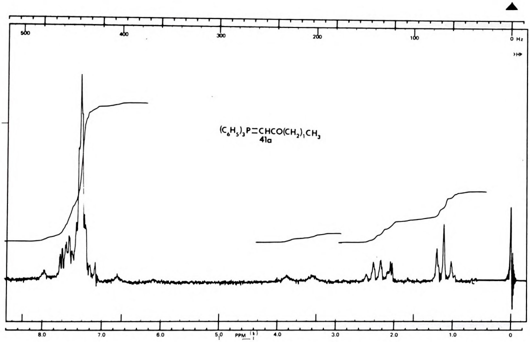


Figure 75. PMR spectrum of propyrylmethylenetriphenylphosphorane (41a).

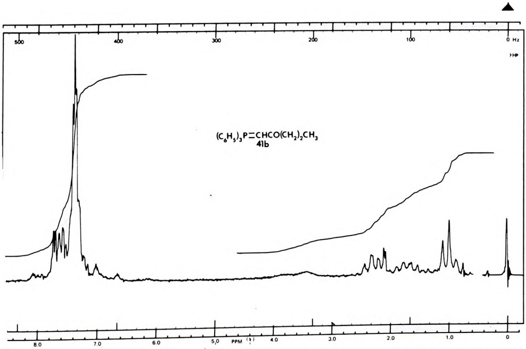


Figure 76. PMR spectrum of butyrylmethylenetriphenylphosphorane (41b).

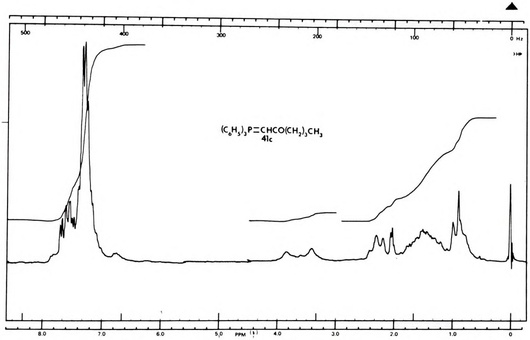


Figure 77. PMR spectrum of pentyrylmethylenetriphenylphosphorane (41c).

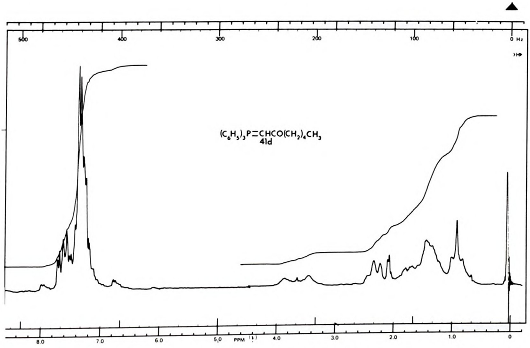


Figure 78. PMR spectrum of hexyrylmethylenetriphenylphosphorane (41d).

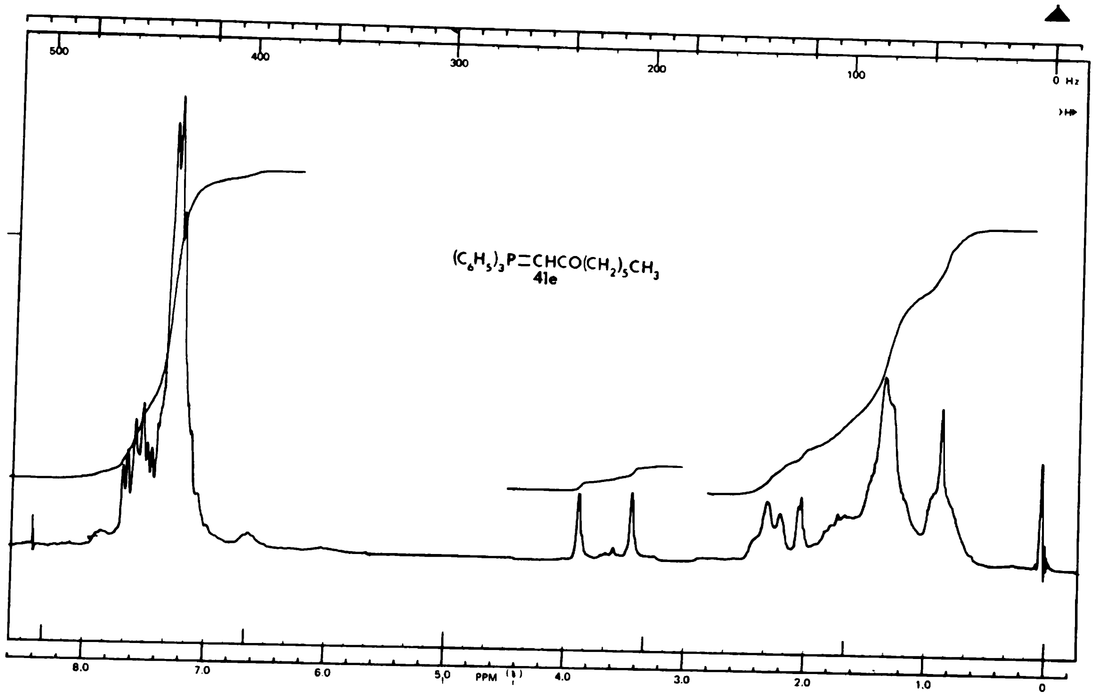


Figure 79. PMR spectrum of heptyrylmethylenetriphenylphosphorane (41e).

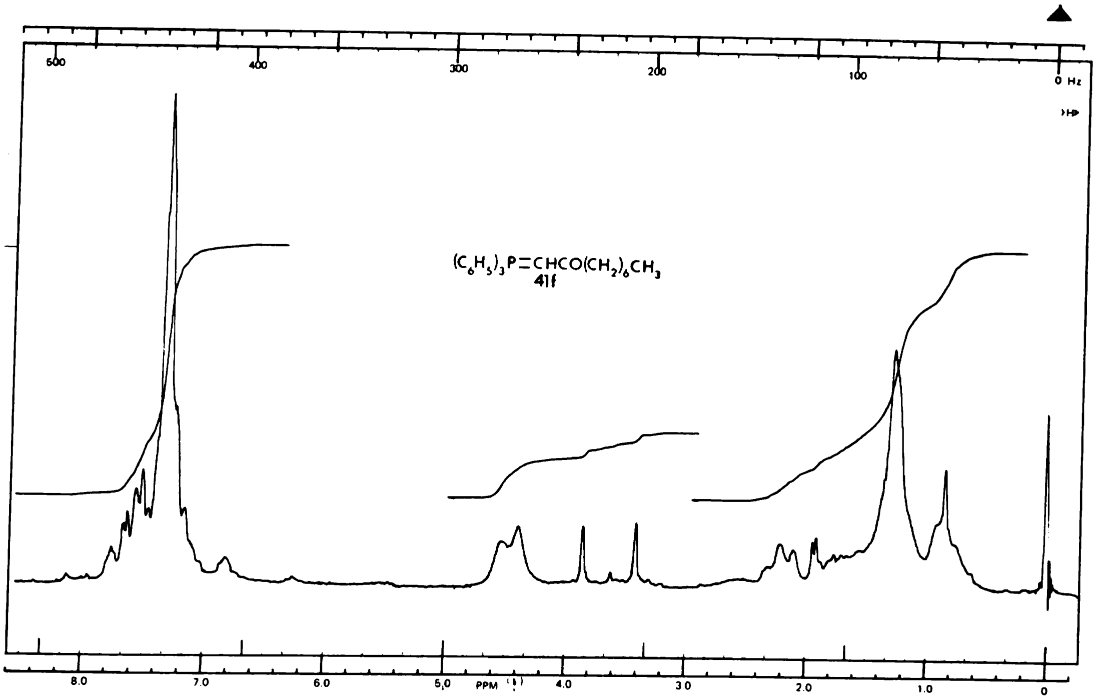


Figure 80. PMR spectrum of octyrylmethylenetriphenylphosphorane (41f).

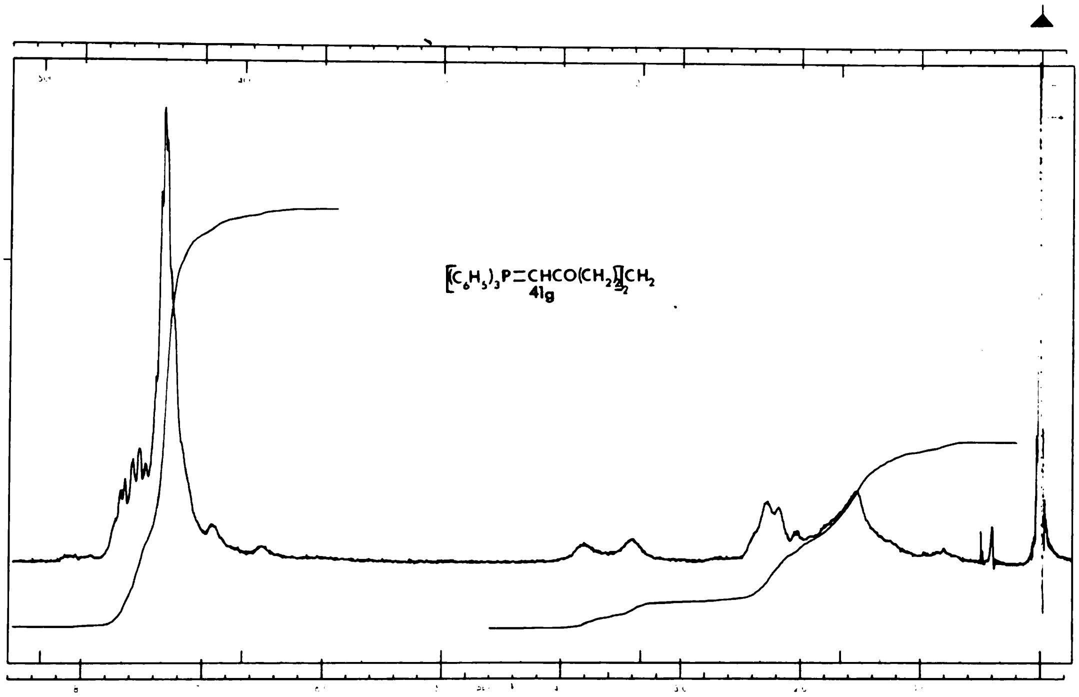


Figure 81. PMR spectrum of 1,3-diacetylmethylenetriphenylphosphorane (41g).

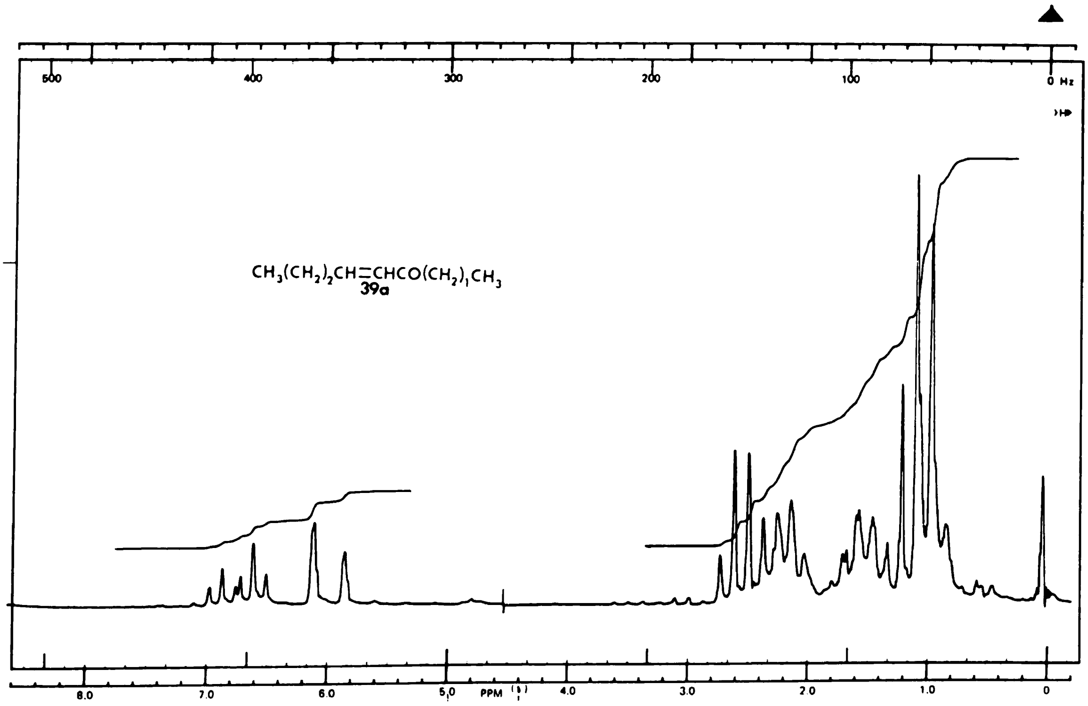


Figure 82. PMR spectrum of 4-octene-3-one (39a).

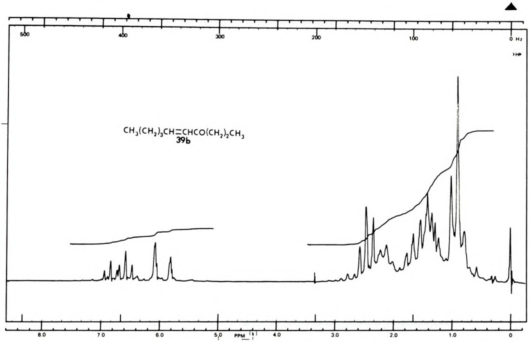


Figure 83. PMR spectrum of 5-decene-4-one (39b).

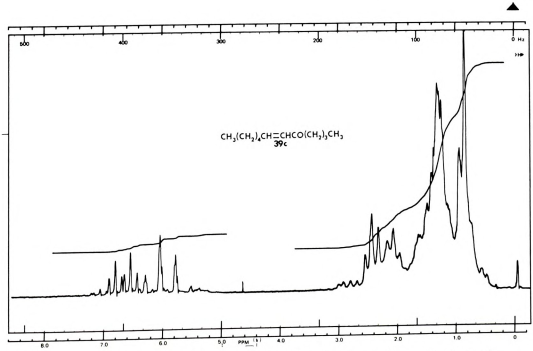


Figure 84. PMR spectrum of 6-dodecene-5-one (39c).

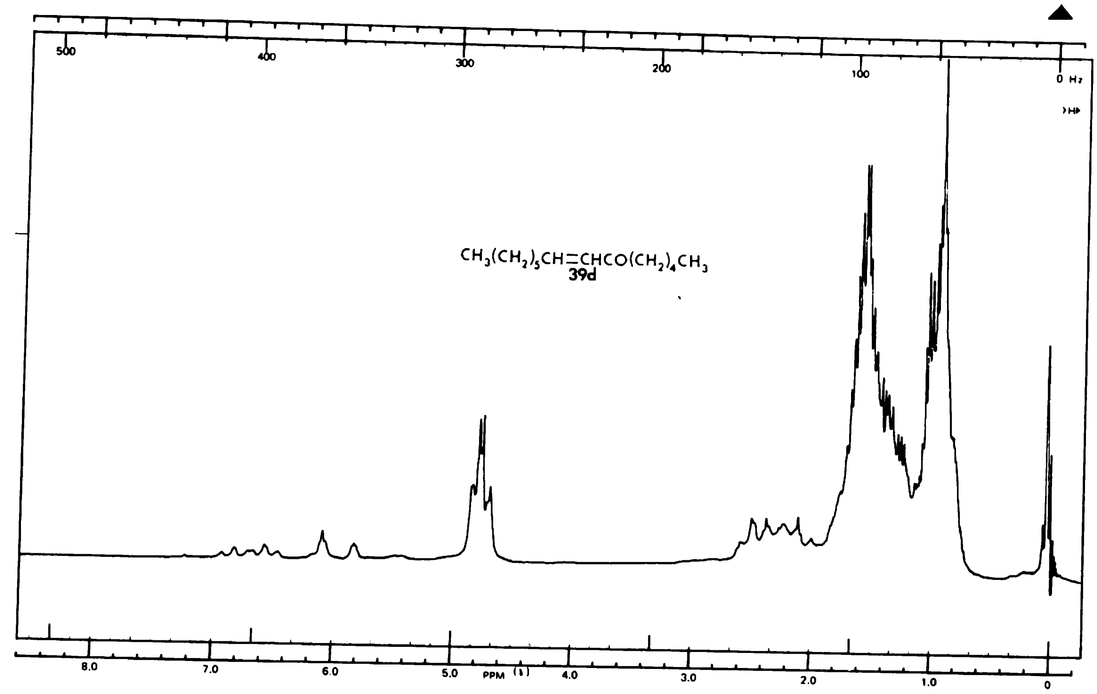


Figure 85. PMR spectrum of 7-tetradecene-6-one (39d).

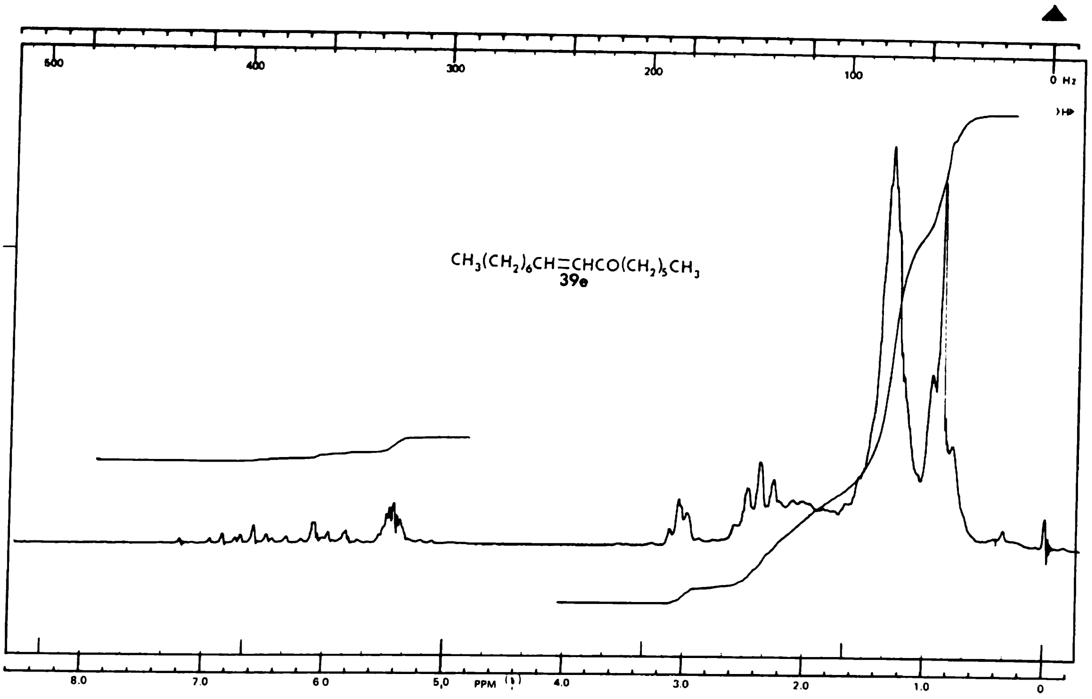


Figure 86. PMR spectrum of 8-hexadecene-7-one (39e).

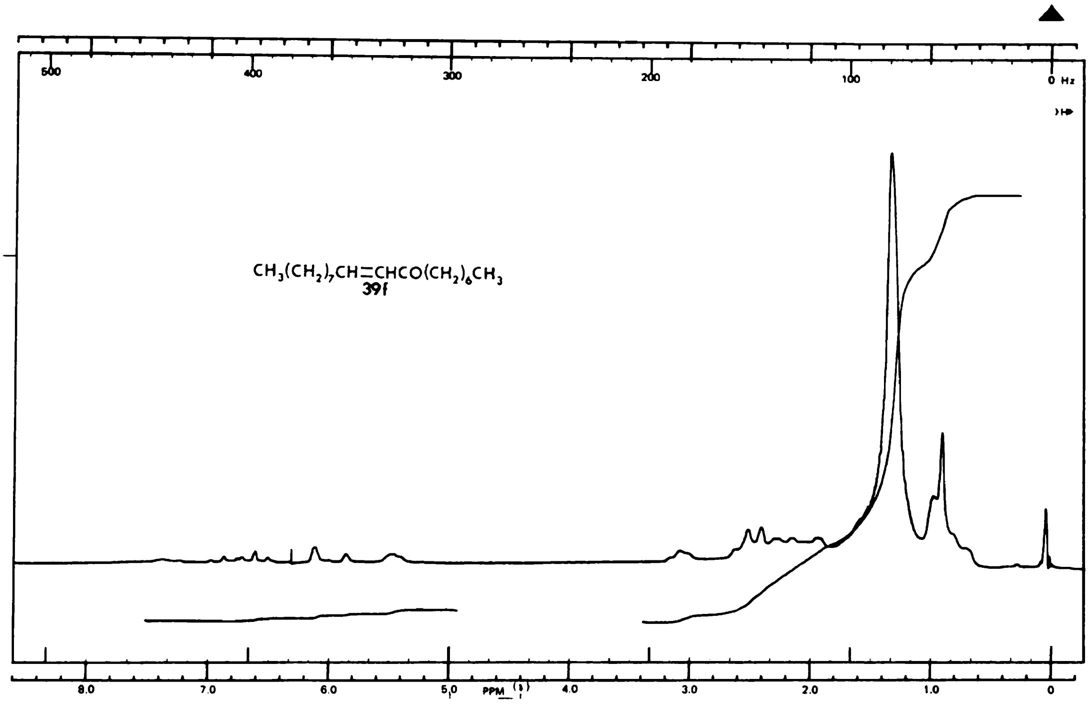


Figure 87. PMR spectrum of 9-octadecene-8-one (39f).

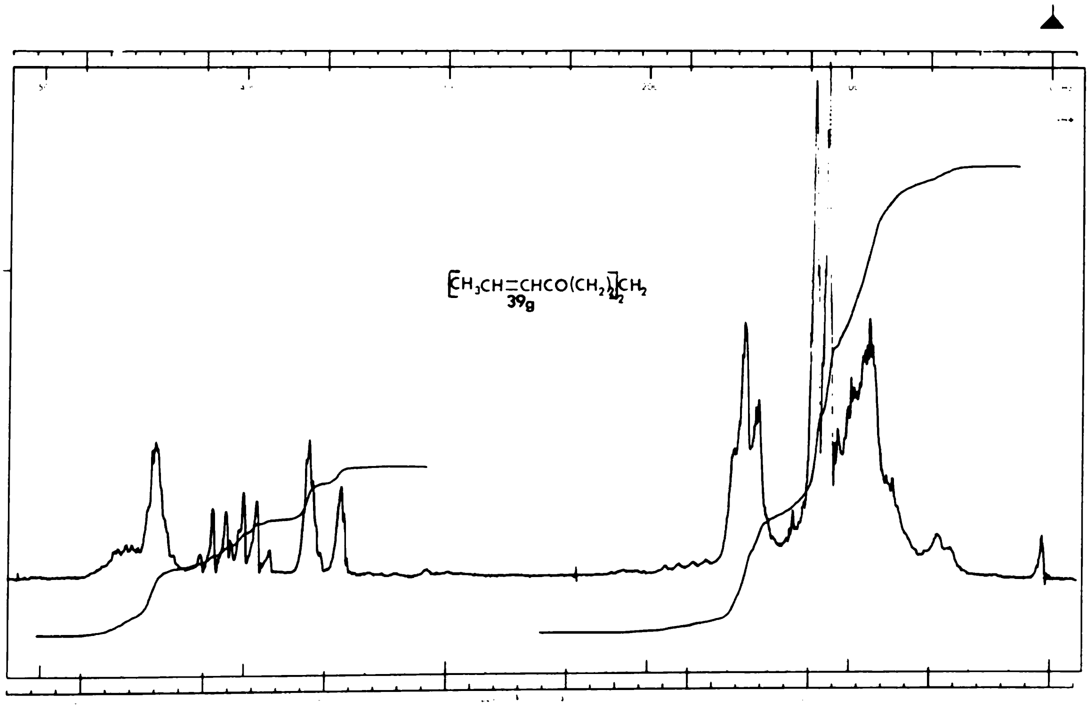


Figure 88. PMR spectrum of 3,11-tridecadiene-4,10, dione (39g).

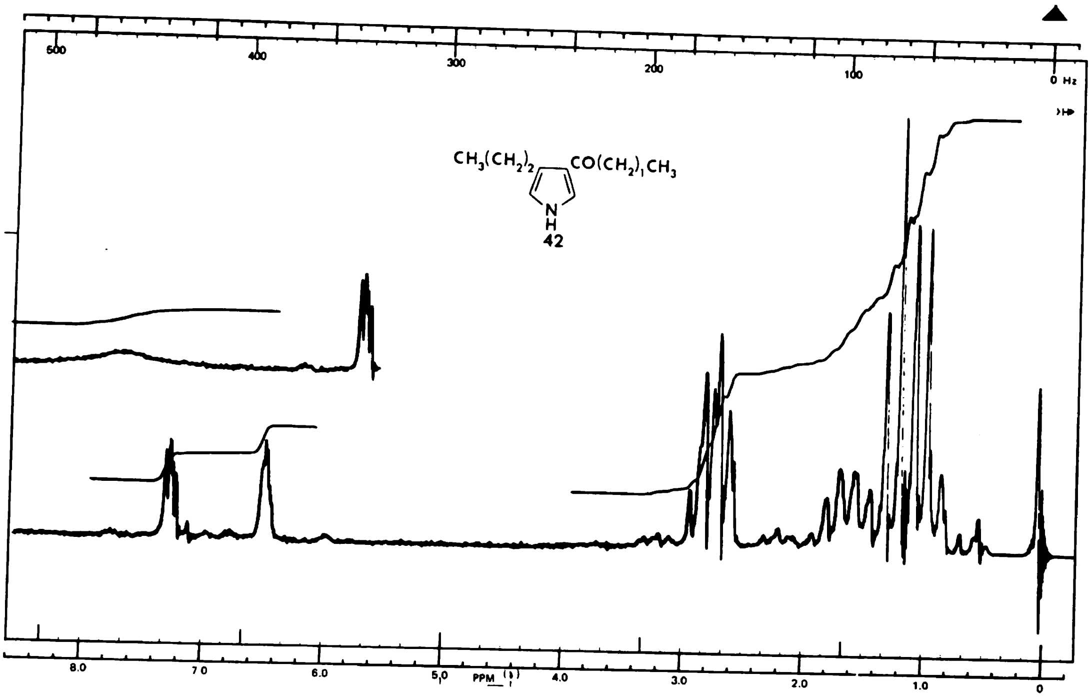


Figure 89. PMR spectrum of 3-propyl-4-propyrylpyrrole (42).

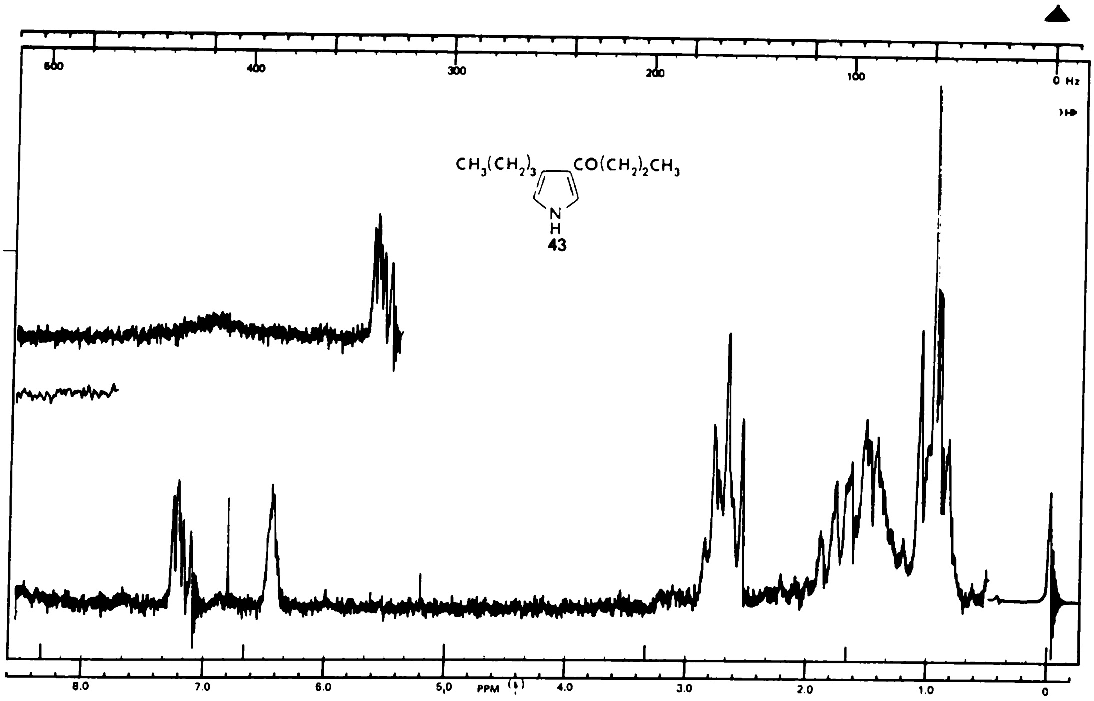


Figure 90. PMR spectrum of 3-butyl-4-butyrylpyrrole (43).

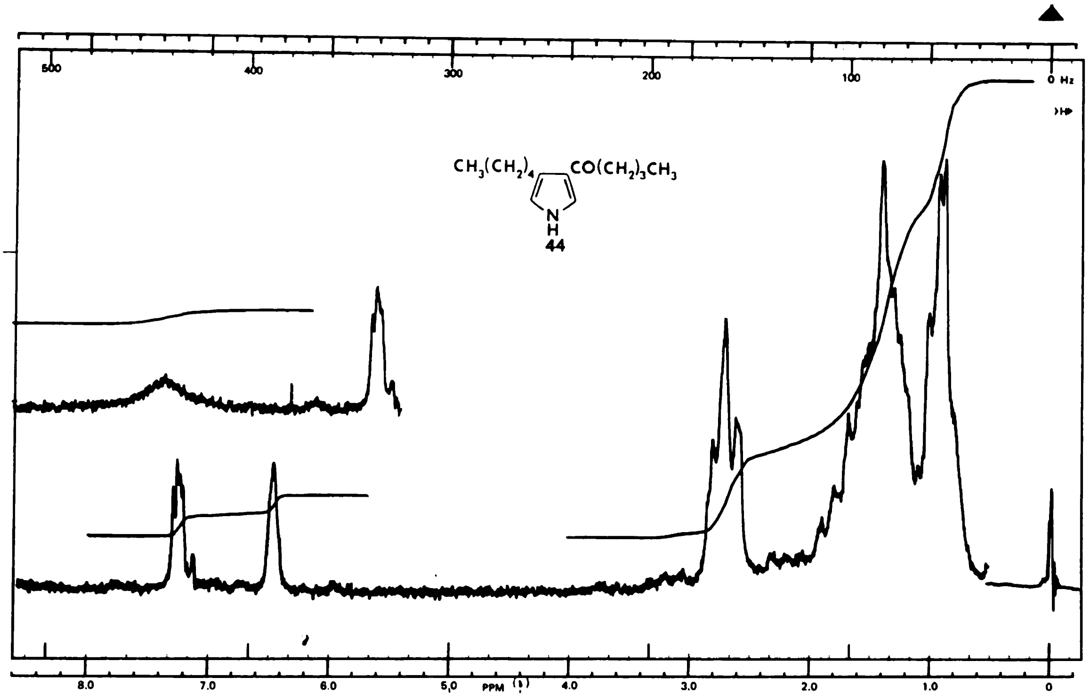


Figure 91. PMR spectrum of 3-pentyl-4-pentyrylpyrrole (44).

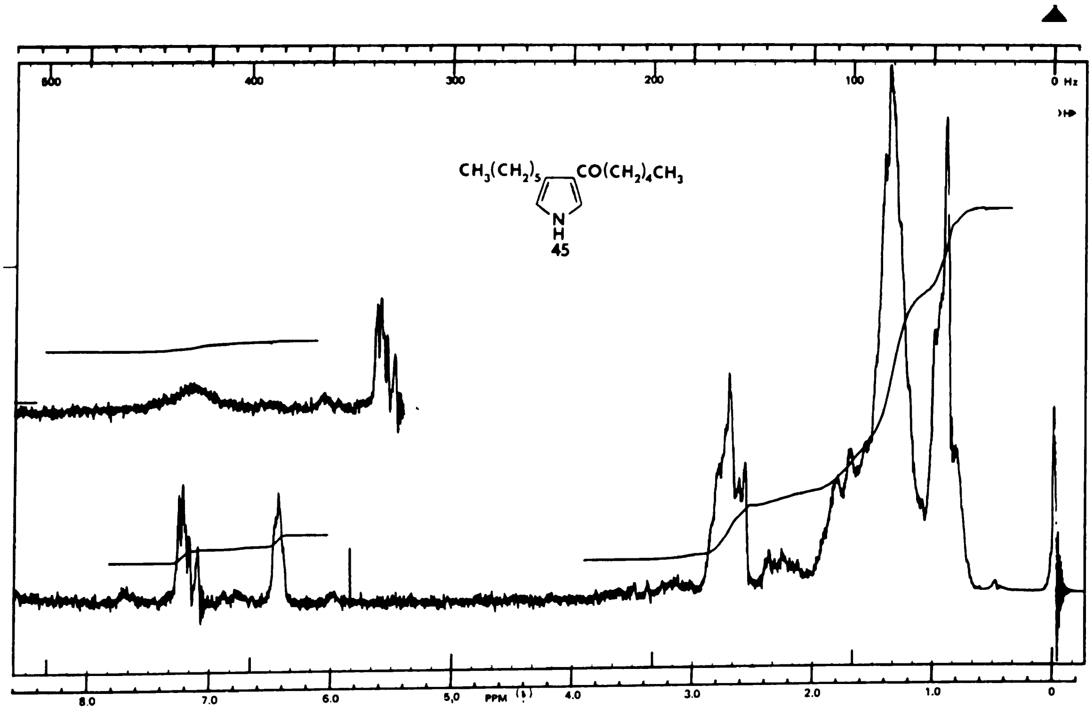
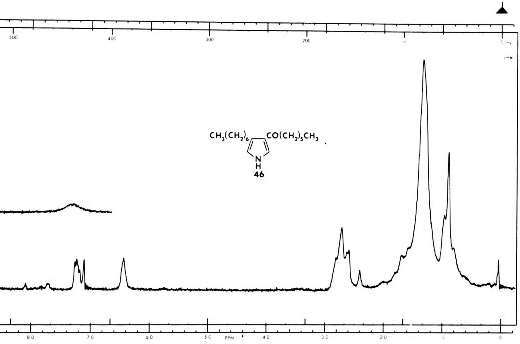
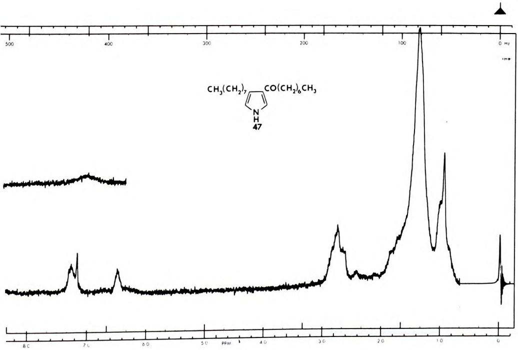


Figure 92. PMR spectrum of 3-hexyl-4-hexyrylpyrrole (45).



igure 93. PMR spectrum of 3-heptyl-4-heptyrylpyrrole (46).



gure 94. PMR spectrum of 3-octyl-4-octyrylpyrrole (47).

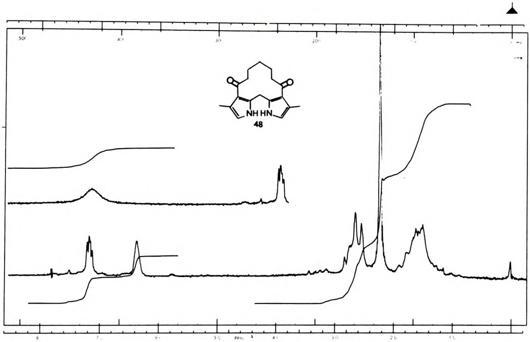


Figure 95. PMR spectrum of 1,7-bis[-3-(4-methylpyrro)]-1,7-heptanedione (48).

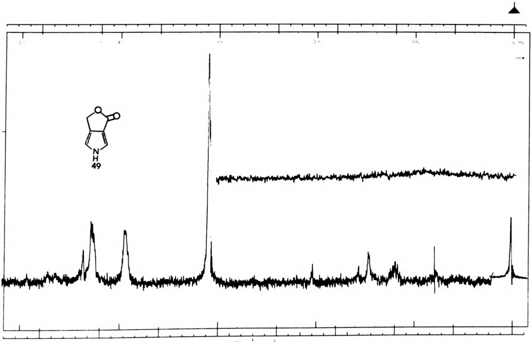


Figure 96. PMR spectrum of 1H-pyrro-[3,4,a]-γ-butyrolactone (49).

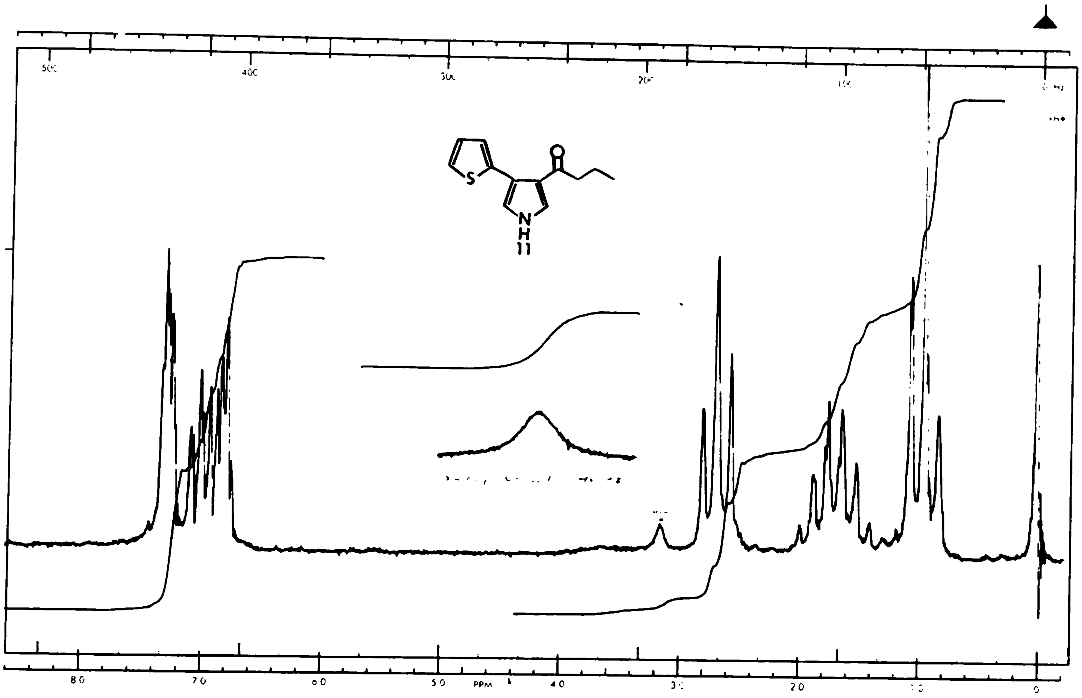


Figure 97. PMR spectrum of 3-butyryl-4-(2-thienyl-pyrrole (11).

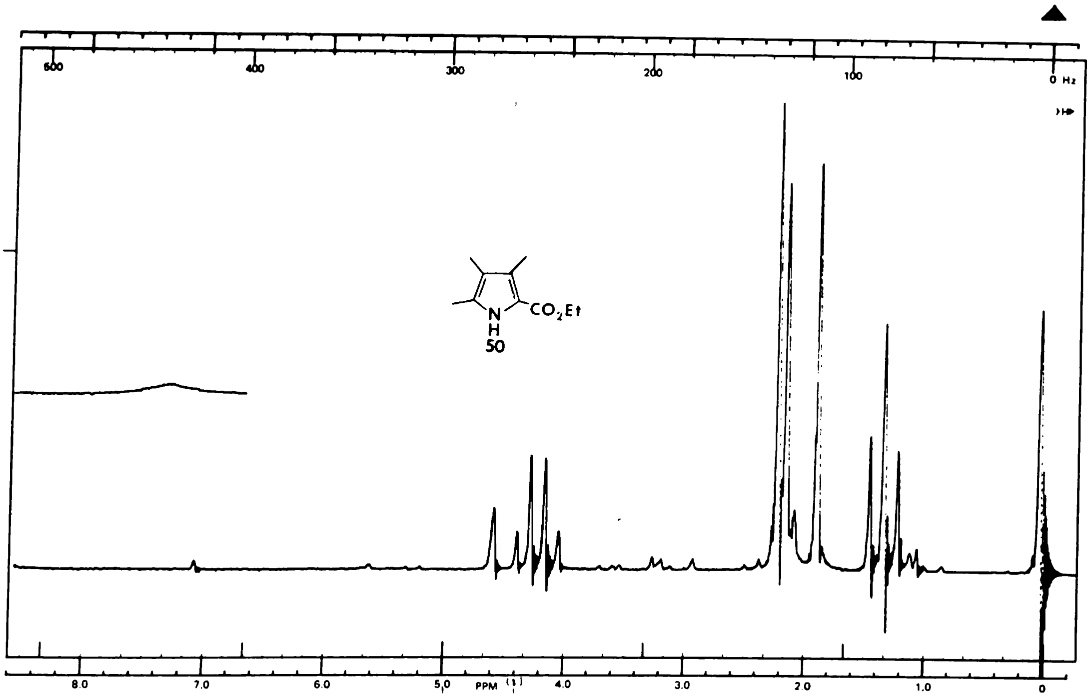


Figure 98. PMR spectrum of 2-carbethoxy-3,4,5-tri-methylpyrrole (50).

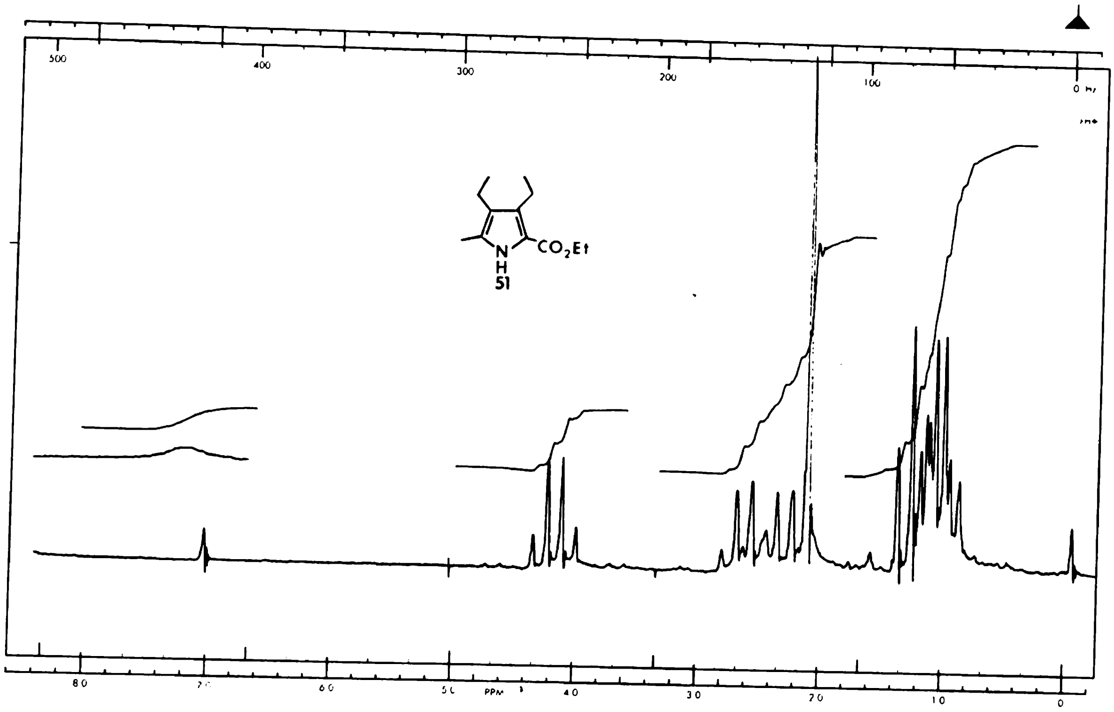
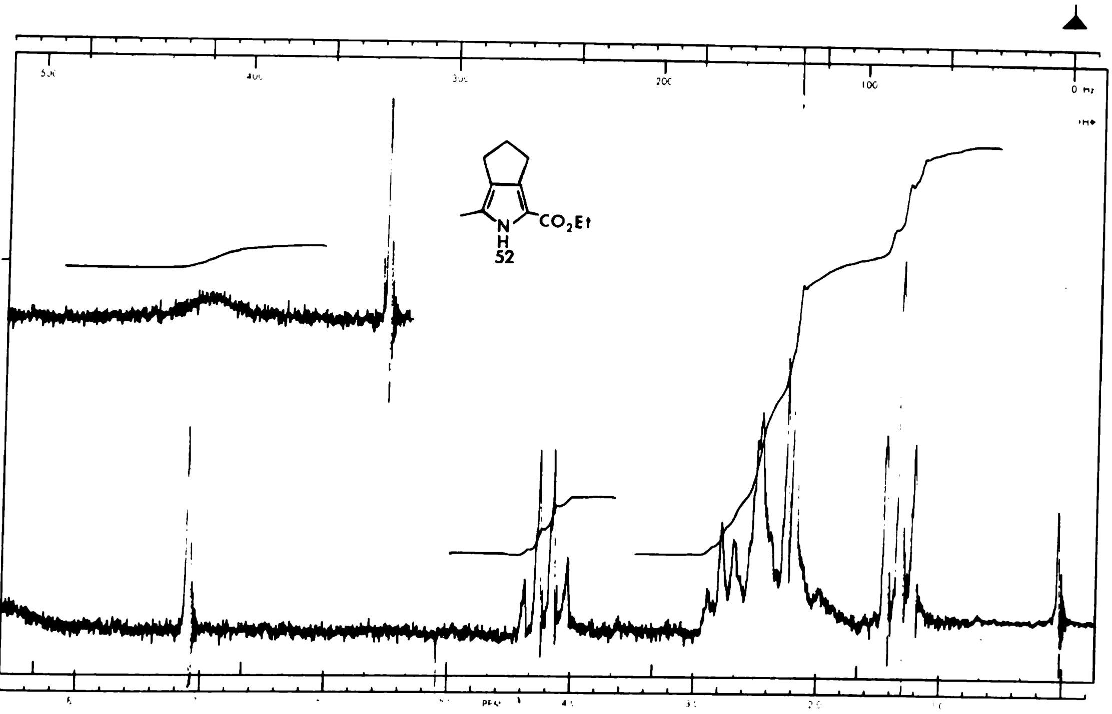


Figure 99. PMR spectrum of 2-carbethoxy-3,4-diethyl-5-methylpyrrole (51).



'igure 100. PMR spectrum of 2-carbethoxy-3,4-trimethylene-5-methylpyrrole (52).

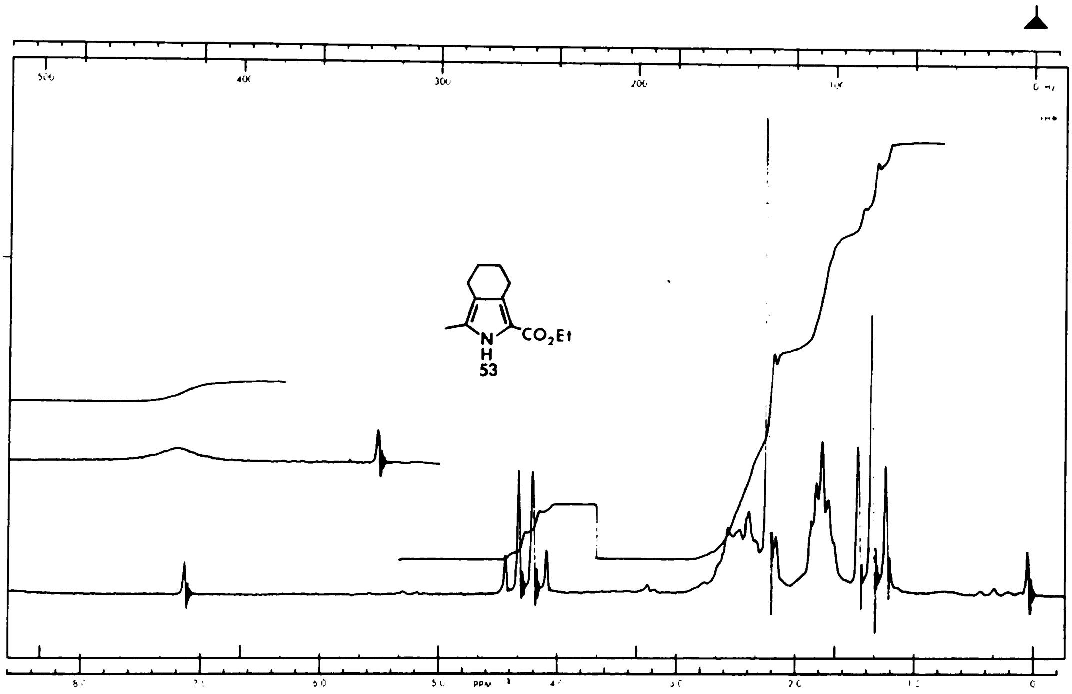


Figure 101. PMR spectrum of 2-carbethoxy-3,4-tetramethylene-5-methylpyrrole (53).

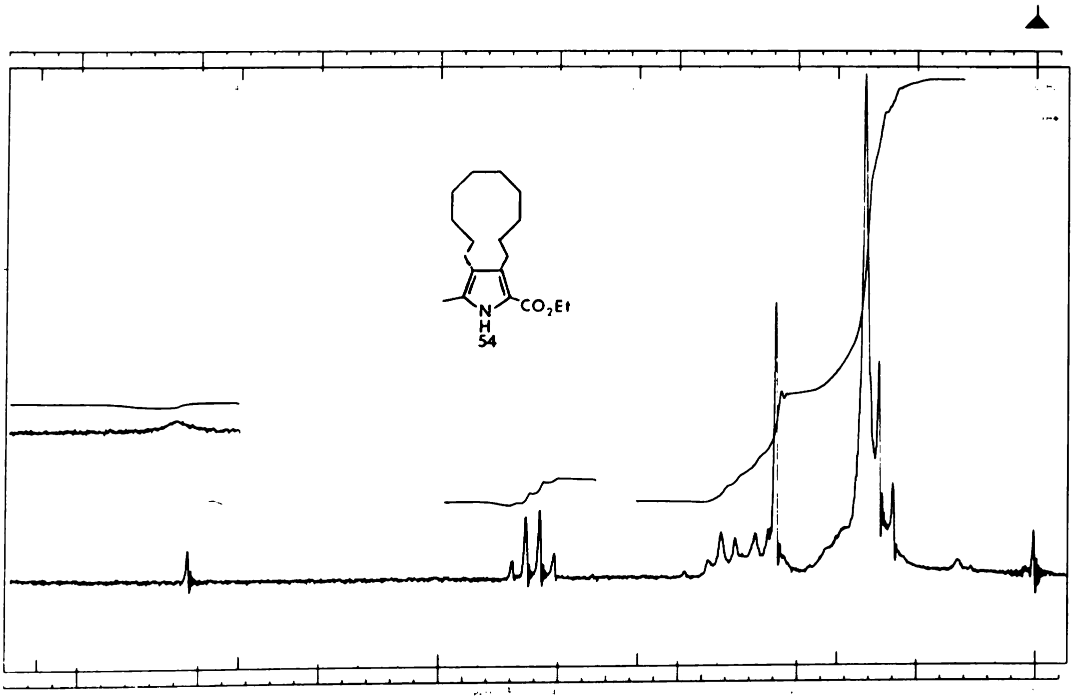


Figure 102. PMR spectrum of 2-carbethoxy-3,4-decamethylene-5-methylpyrrole (54).

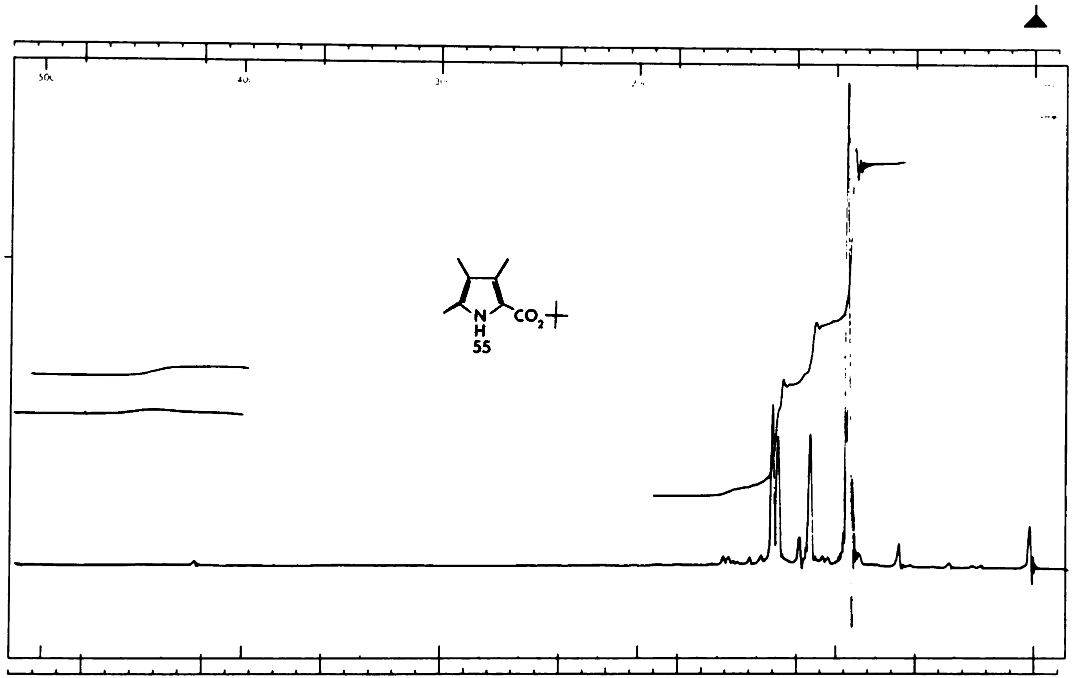


Figure 103. PMR spectrum of 2-carbo-t-butoxy-3,4,5-trimethylpyrrole (55).

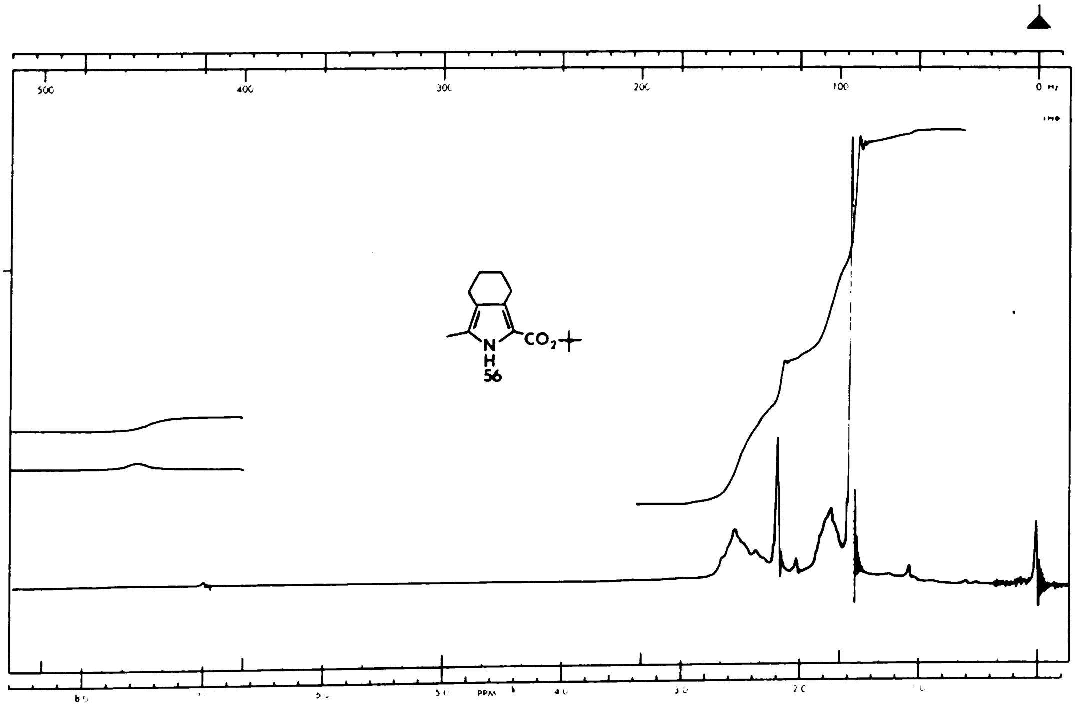


Figure 104. PMR spectrum of 2-carbo-t-butoxy-3,4-tetramethylene-5-methylpyrrole (56).

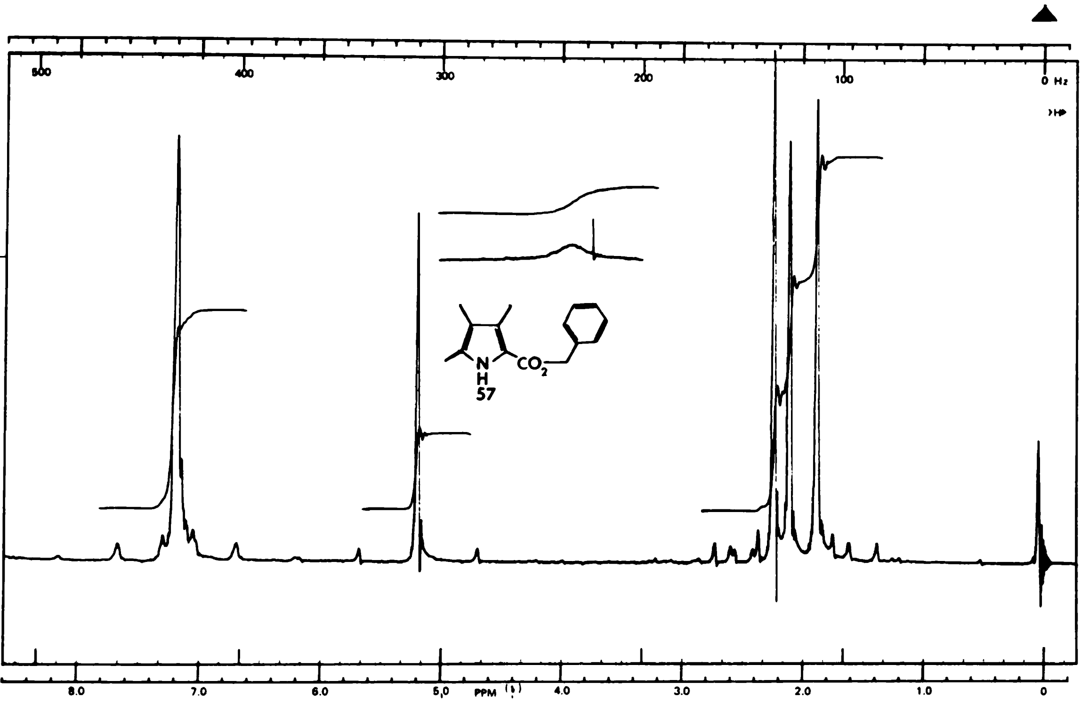


Figure 105. PMR spectrum of 2-carbobenzyloxyl-3,4,5-trimethylpyrrole (57).

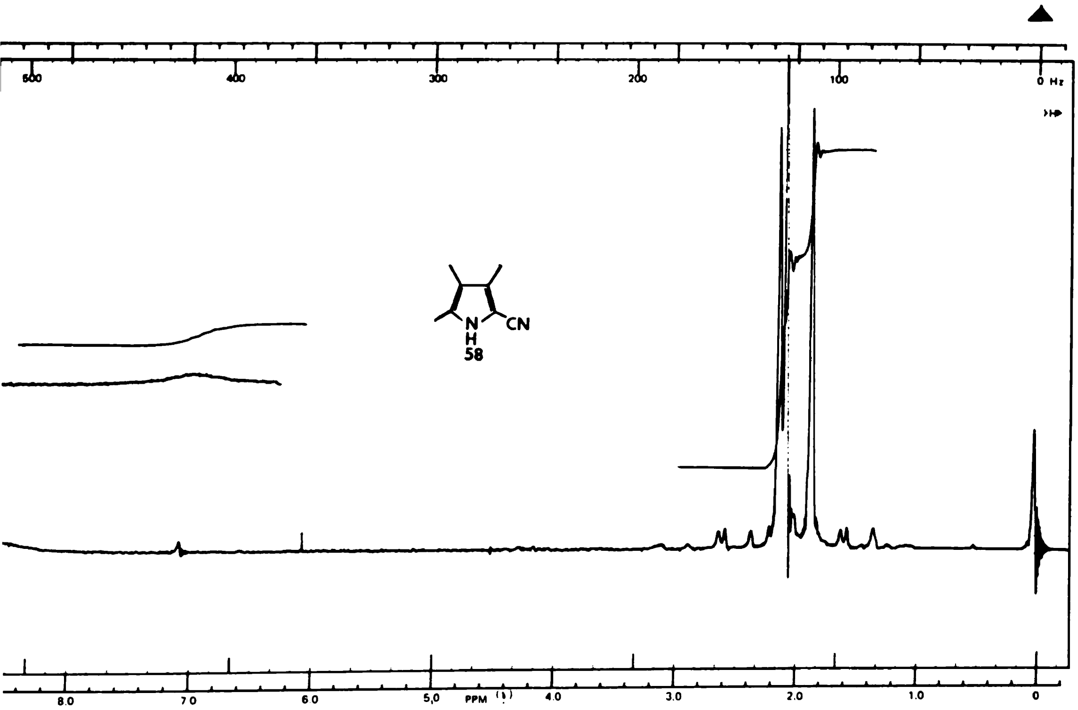


Figure 106. PMR spectrum of 3,4,5-trimethyl-2-pyrrole carbonitrile (58).

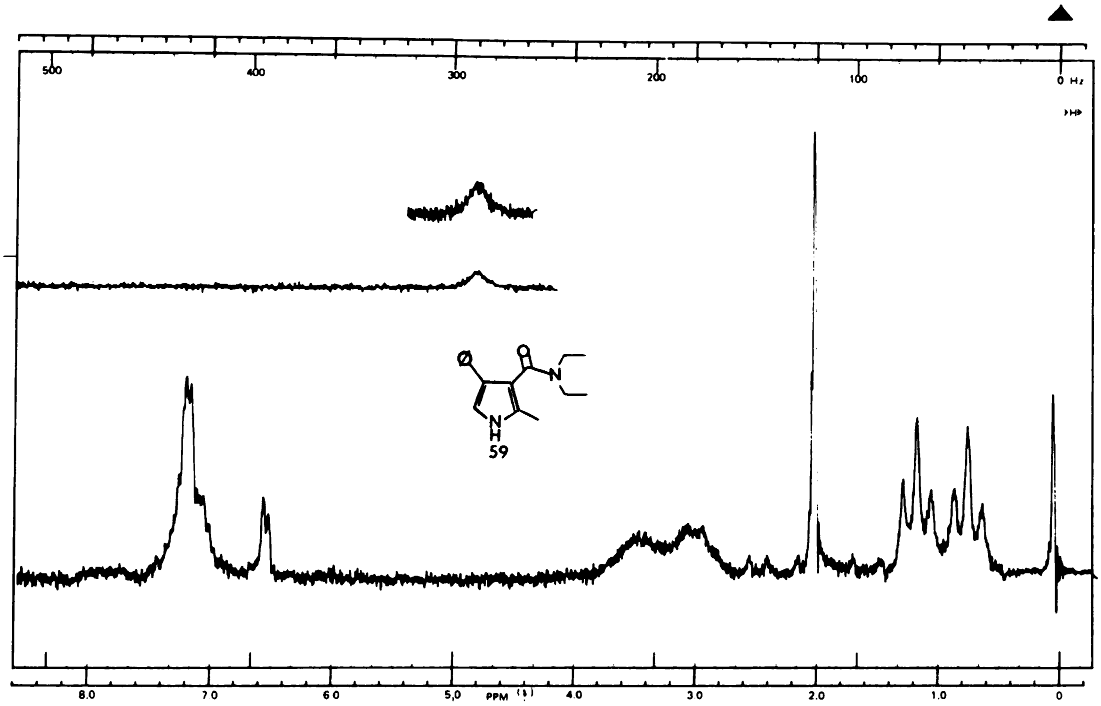


Figure 107. PMR spectrum of diethyl 2-methyl-4-phenylpyrrole 3-carboxamide (59).

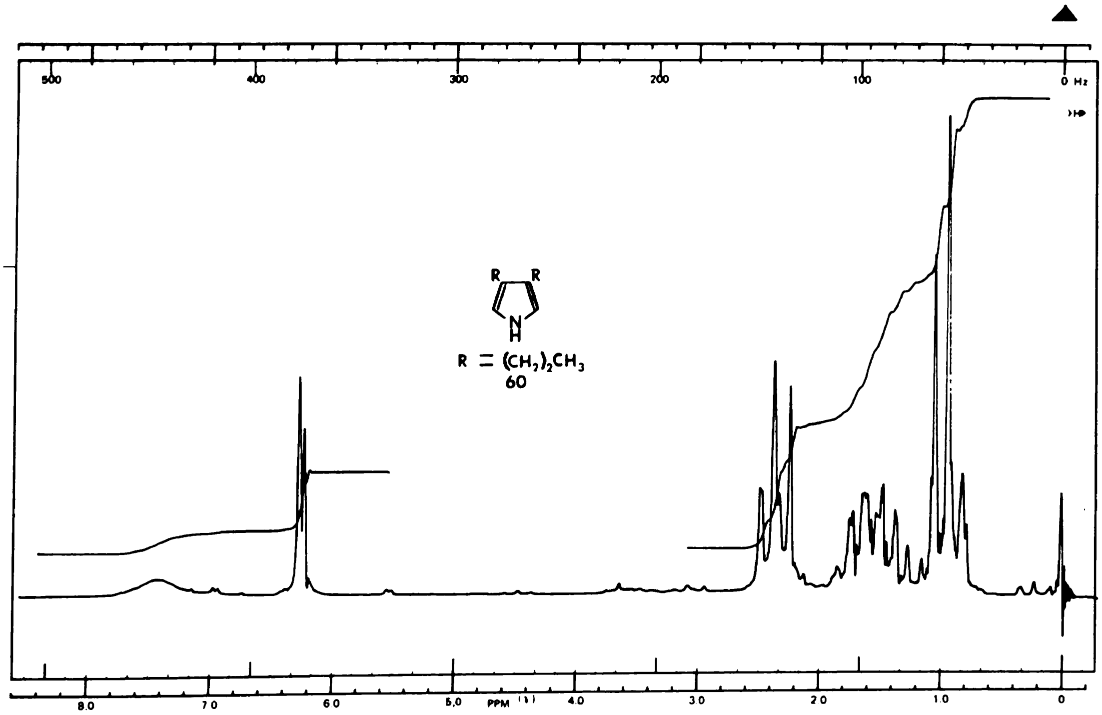


Figure 108. PMR spectrum of 3,4-dipropylpyrrole (60).

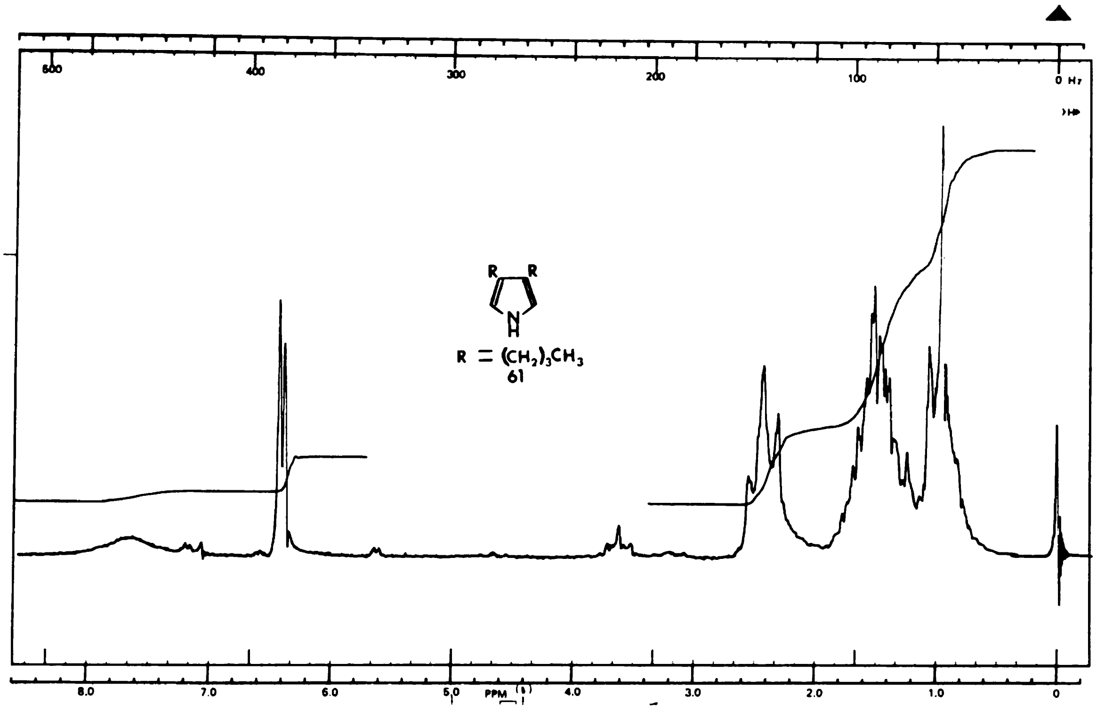


Figure 109. PMR spectrum of 3,4-dibutylpyrrole (61).

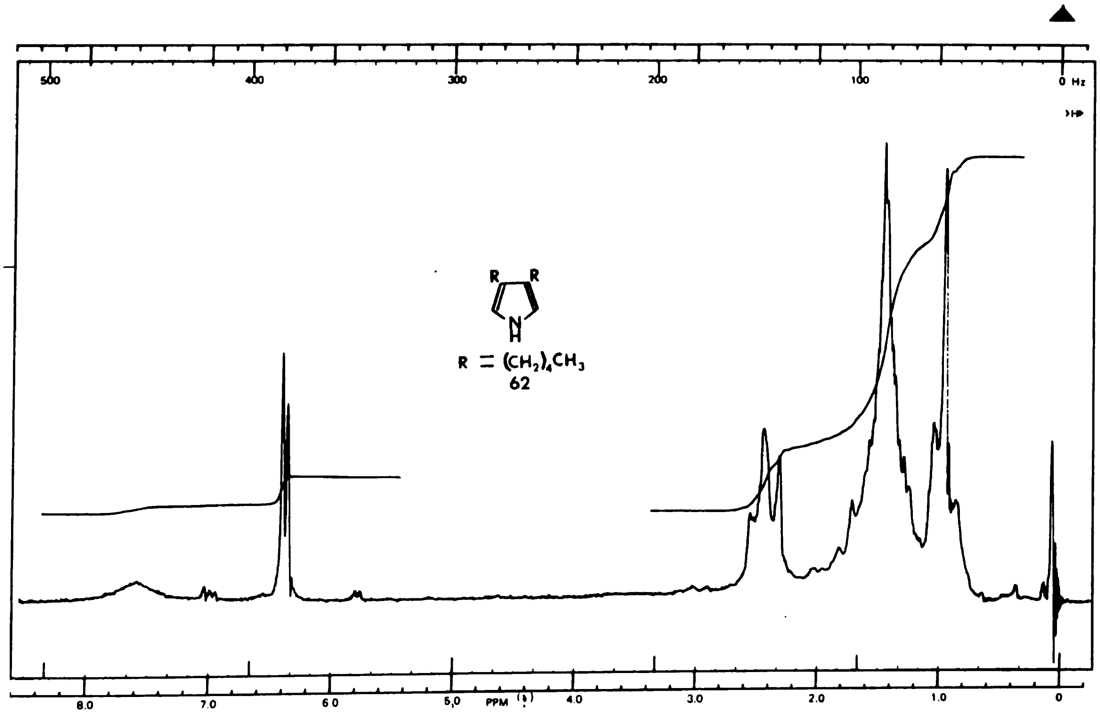


Figure 110. PMR spectrum of 3,4-dipentylpyrrole (62).

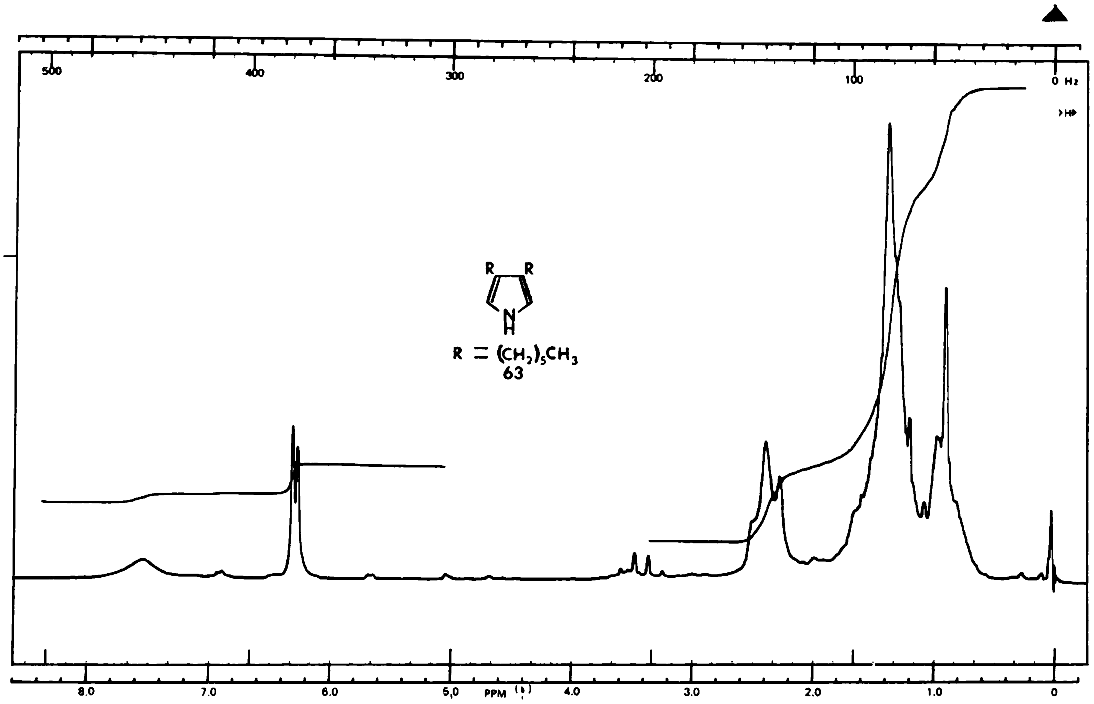


Figure 111. PMR spectrum of 3,4-dihexylpyrrole (63).

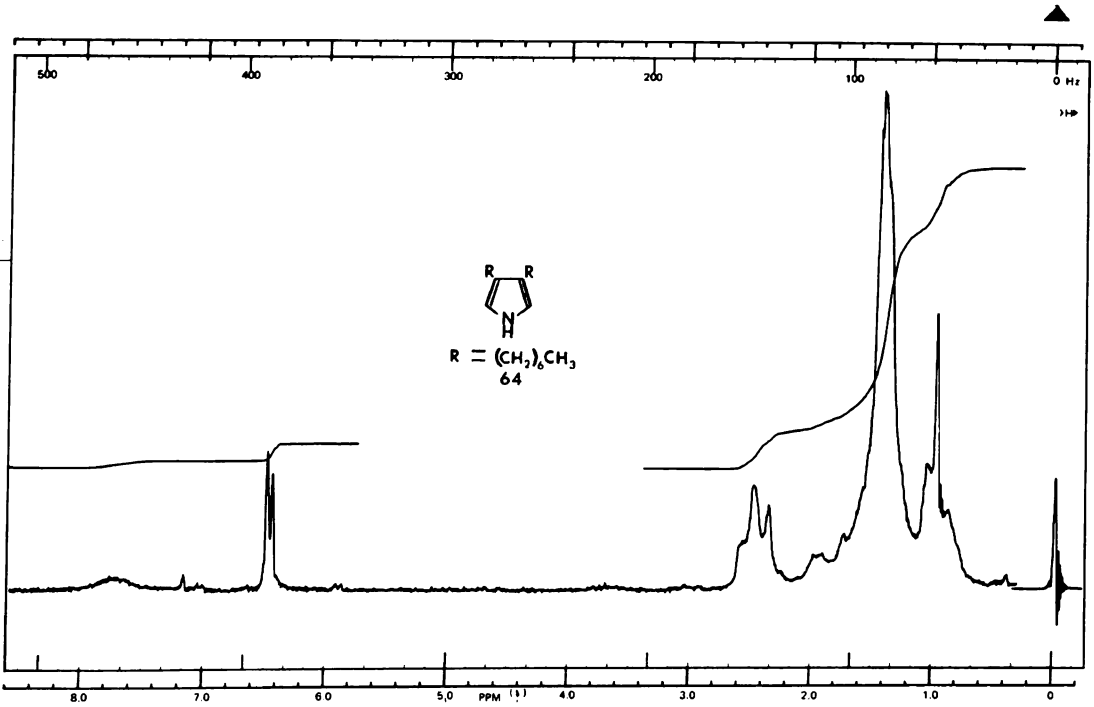


Figure 112. PMR spectrum of 3,4-diheptylpyrrole (64).

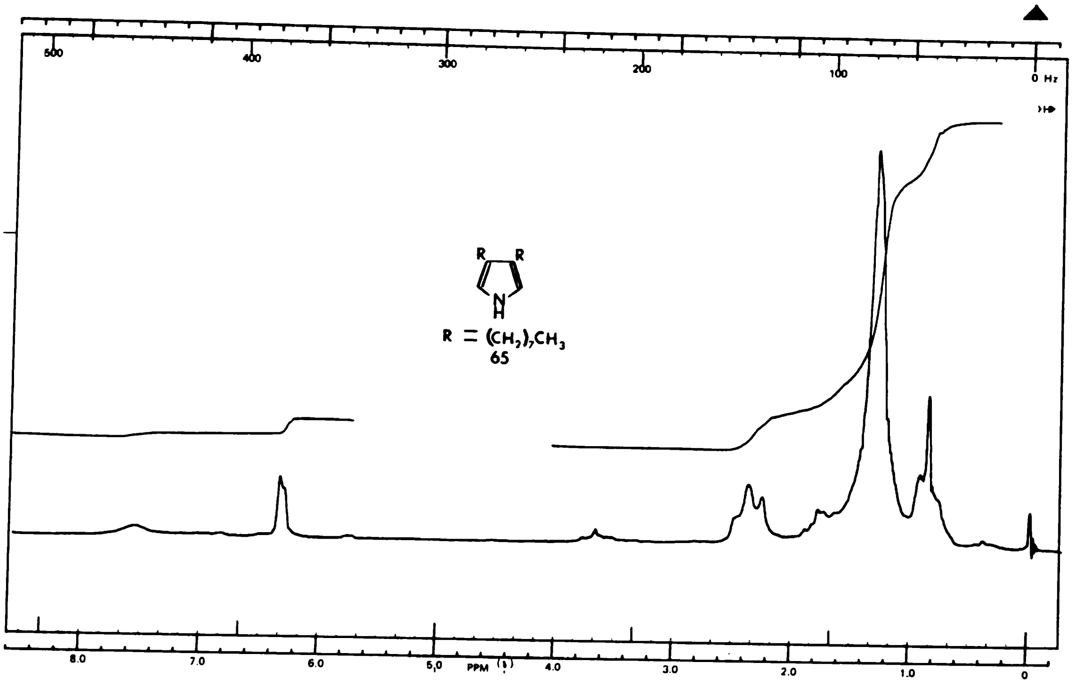


Figure 113. PMR spectrum of 3,4-dioctylpyrrole (65).

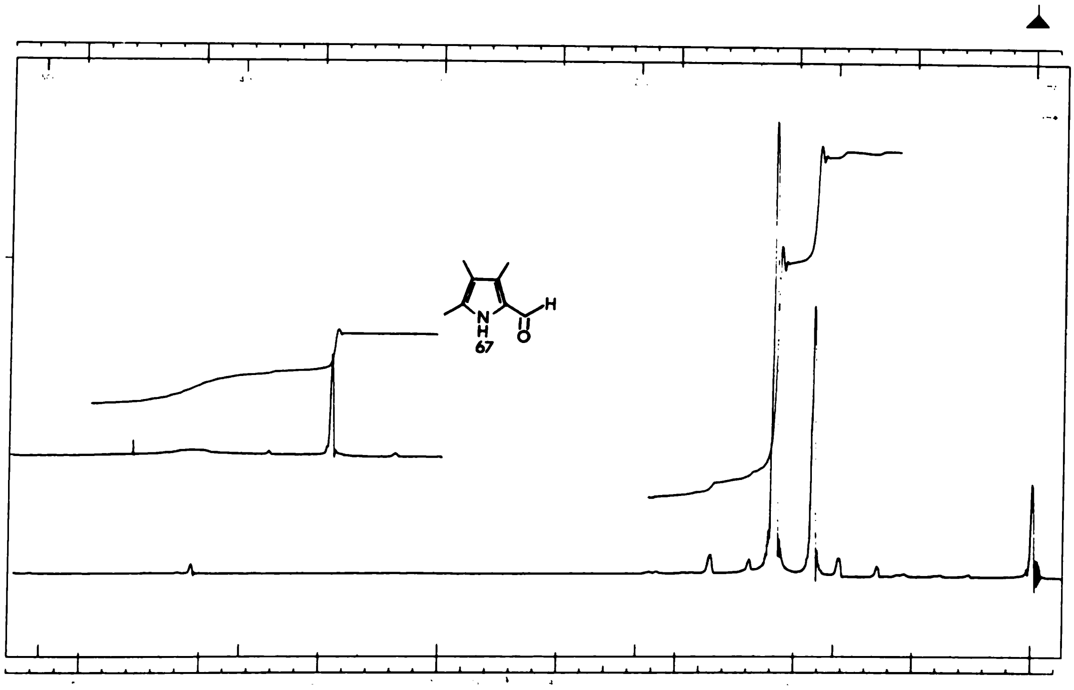


Figure 114. PMR spectrum of 2-formyl-3,4,5-trimethylpyrrole (67).

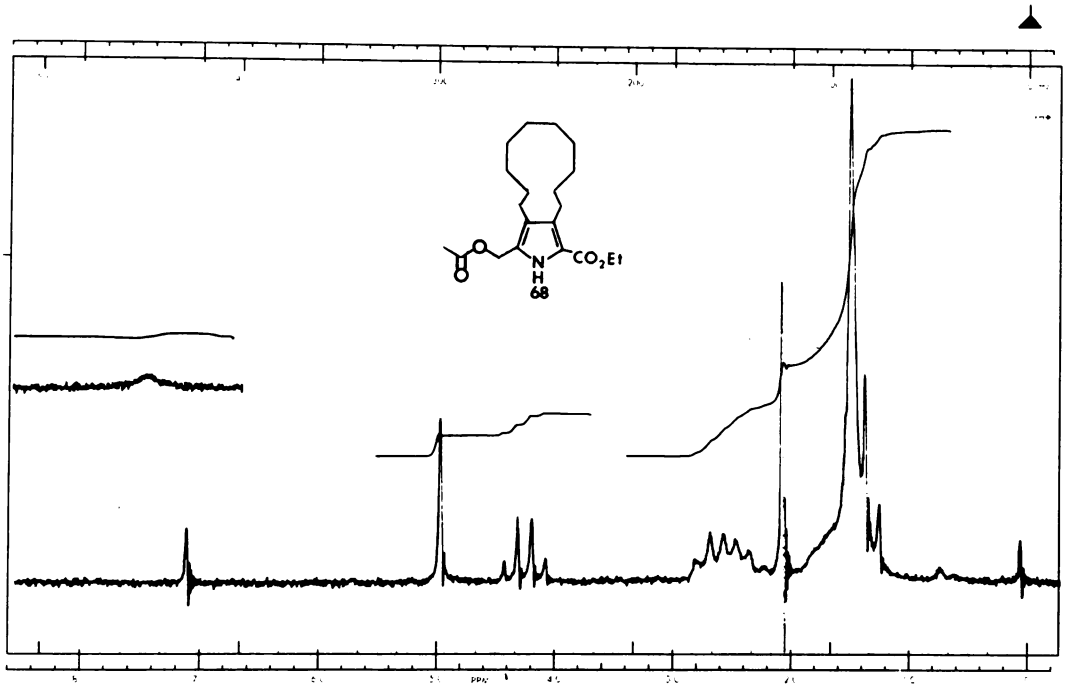


Figure 115. PMR spectrum of 5-acetoxymethyl-2-carbethoxy-3,4-decamethylenepyrrole (68).

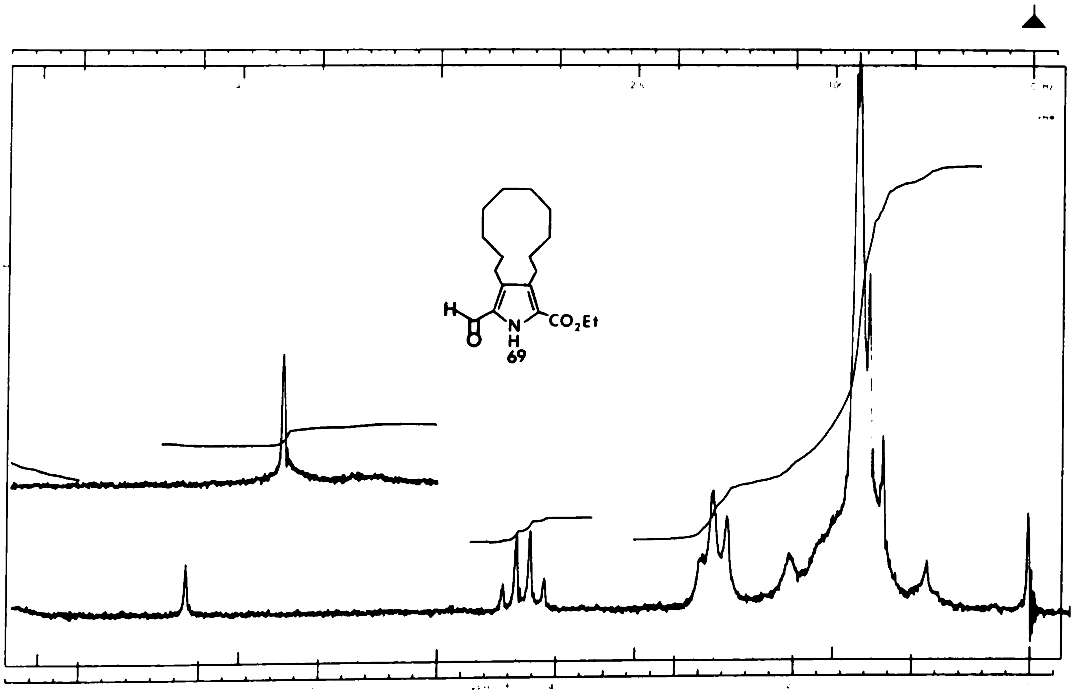


Figure 116. PMR spectrum of 2-carbethoxy-5-formyl-3,4-decamethylenepyrrole (69).

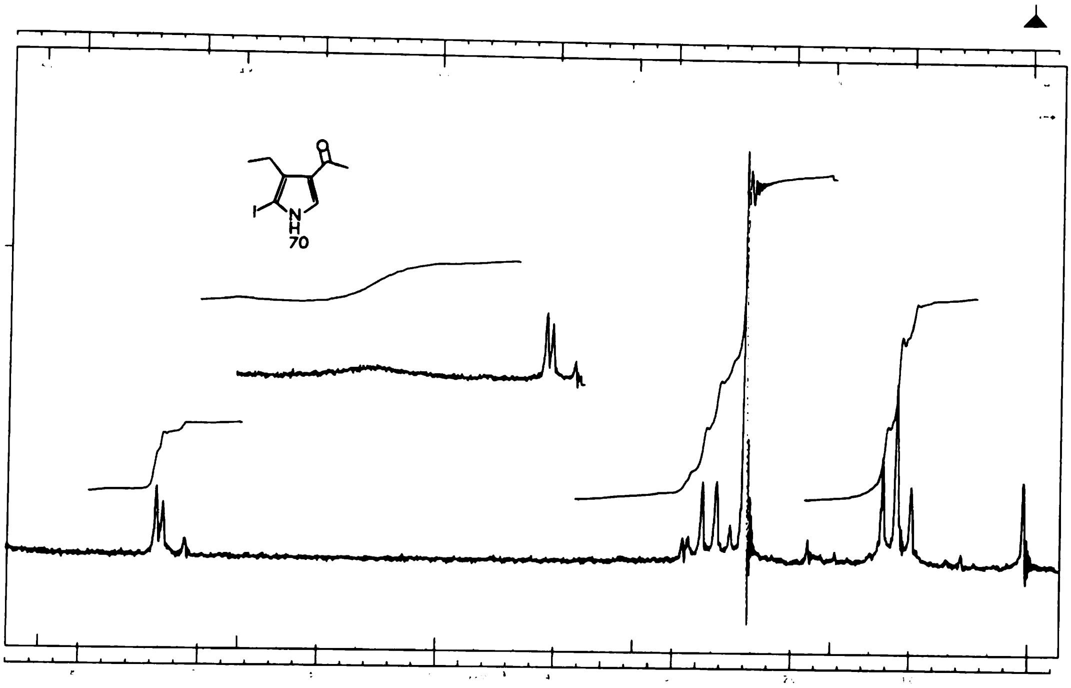


Figure 117. PMR spectrum of 4-acetyl-3-ethyl-2-iodopyrrole (70).

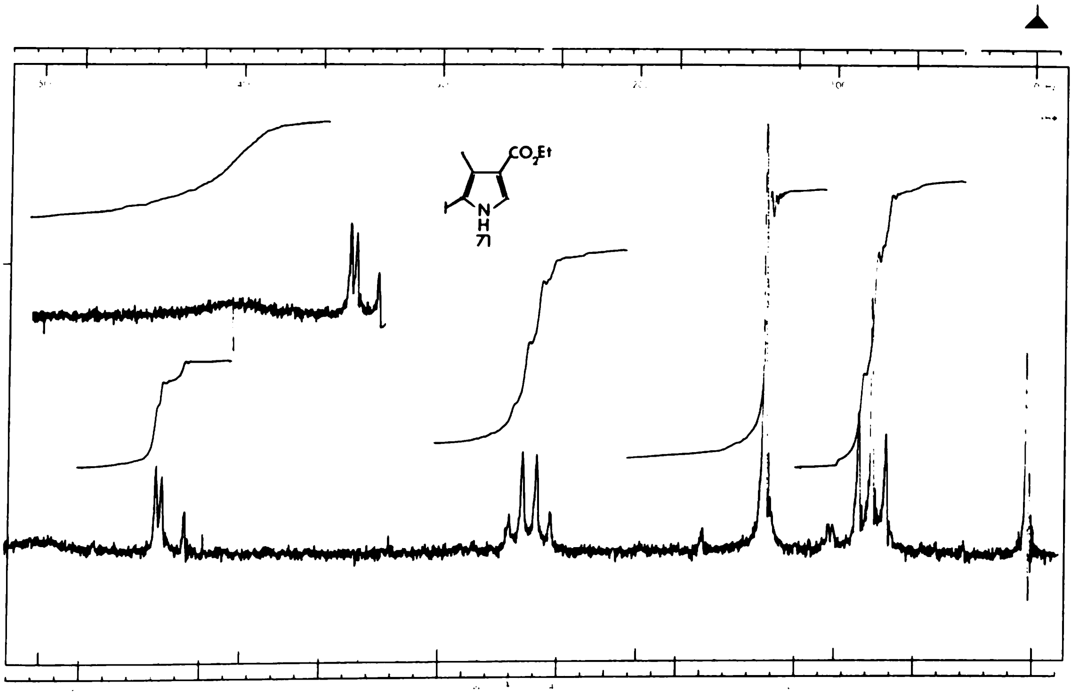


Figure 118. PMR spectrum of 4-carbethoxy-3-methyl-2-iodopyrrole (71).

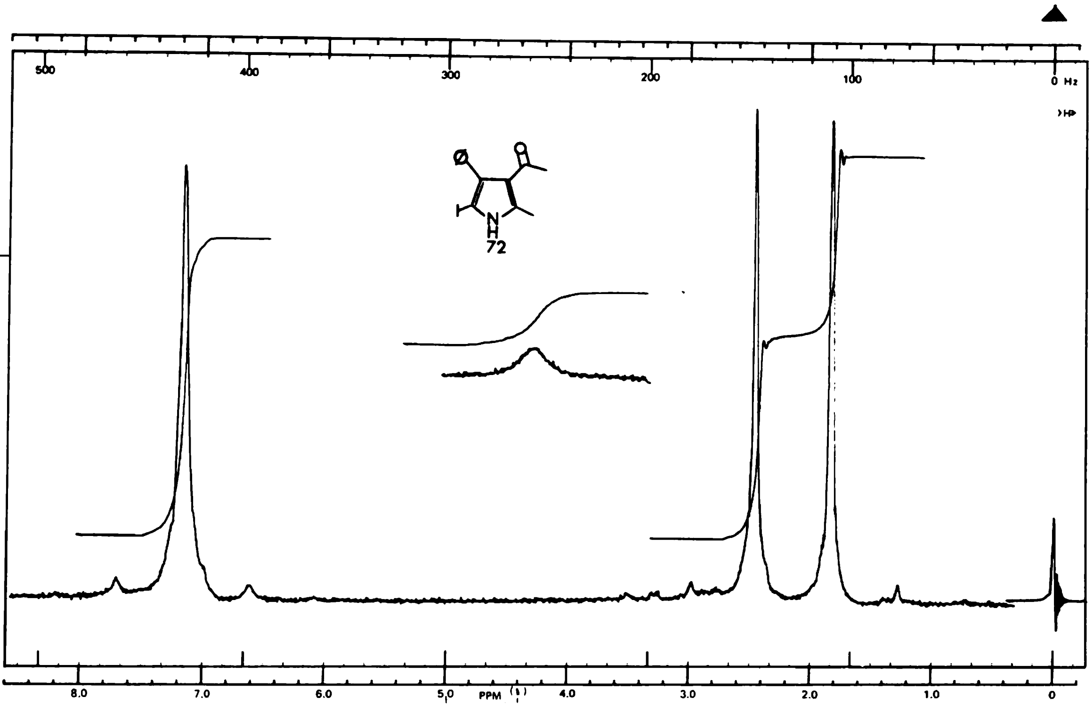
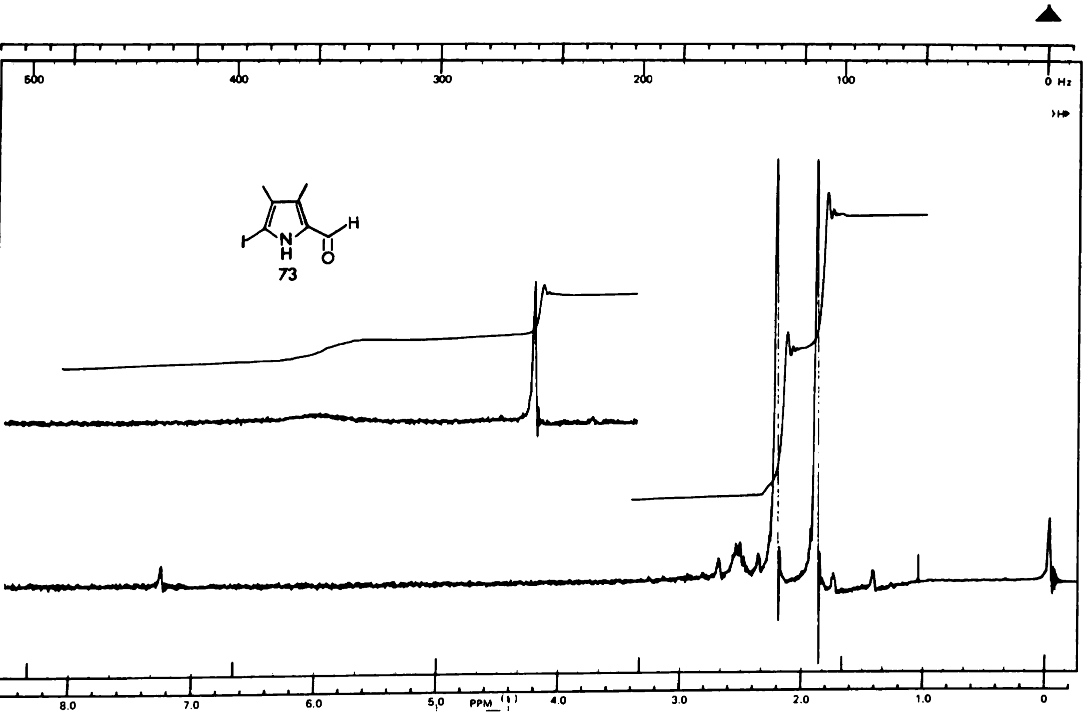


Figure 119. PMR spectrum of 3-acetyl-5-methyl-4-phenyl-2-iodopyrrole (72).



igure 120. PMR spectrum of 3,4-dimethyl-5-formyl-2-iodopyrrole (73).

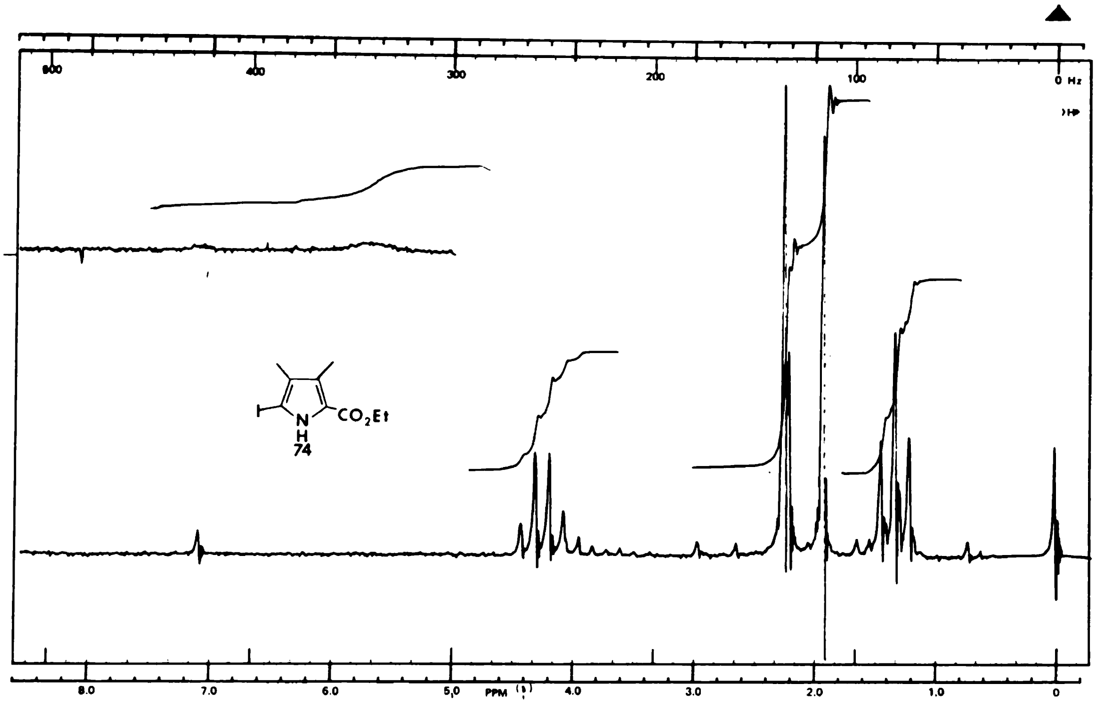


Figure 121. PMR spectrum of ethyl 3,4-dimethyl-5-iodopyrrole-2-carboxylate (74).

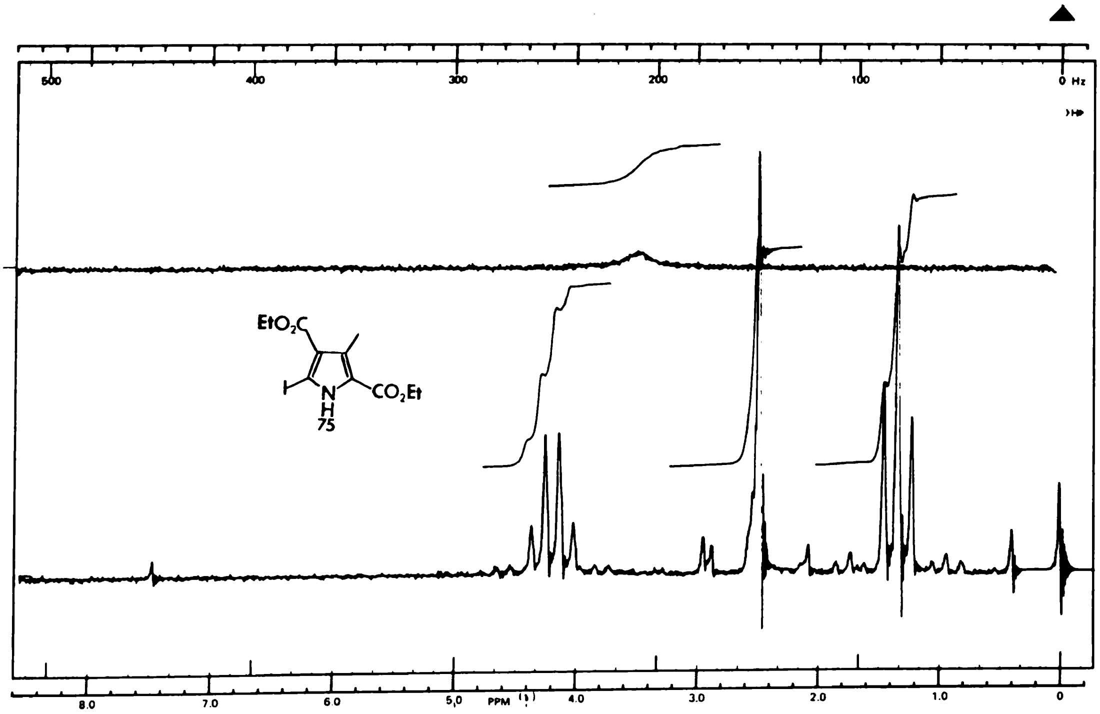


Figure 122. PMR spectrum of diethyl 3-methyl-5-iodopyrrole-2,4-dicarboxylate (75).

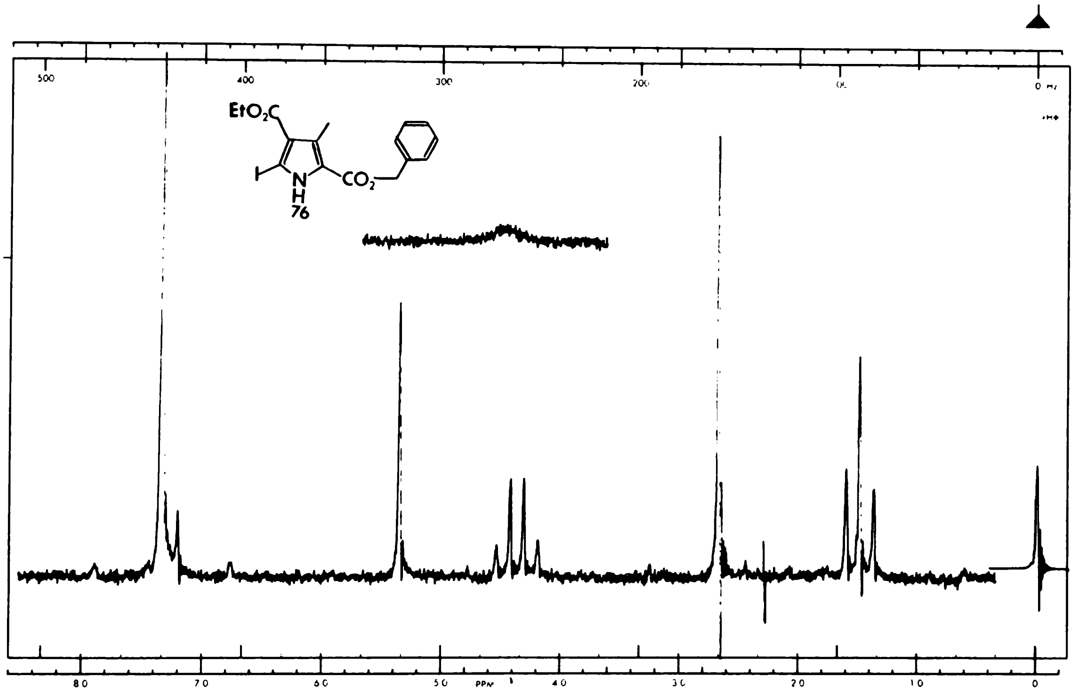


Figure 123. PMR spectrum of 2-benzyl 4-ethyl 5-iodo-3-methylpyrrole-2,4-dicarboxylate (76).

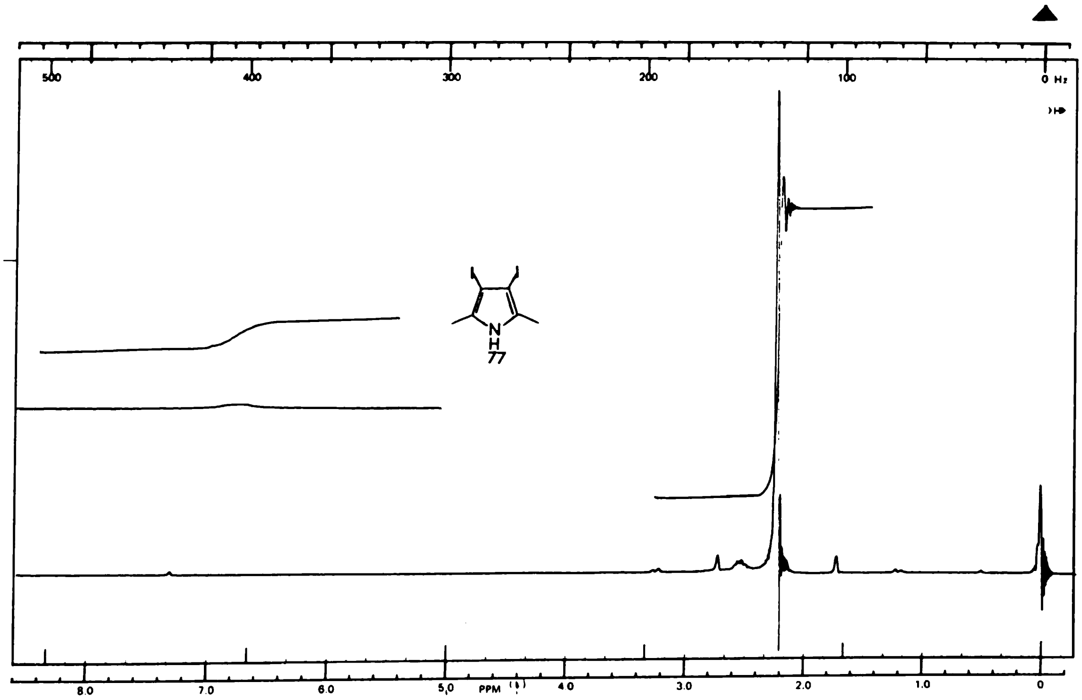


Figure 124. PMR spectrum of 2,5-dimethyl-3,4-diiodopyrrole (77).

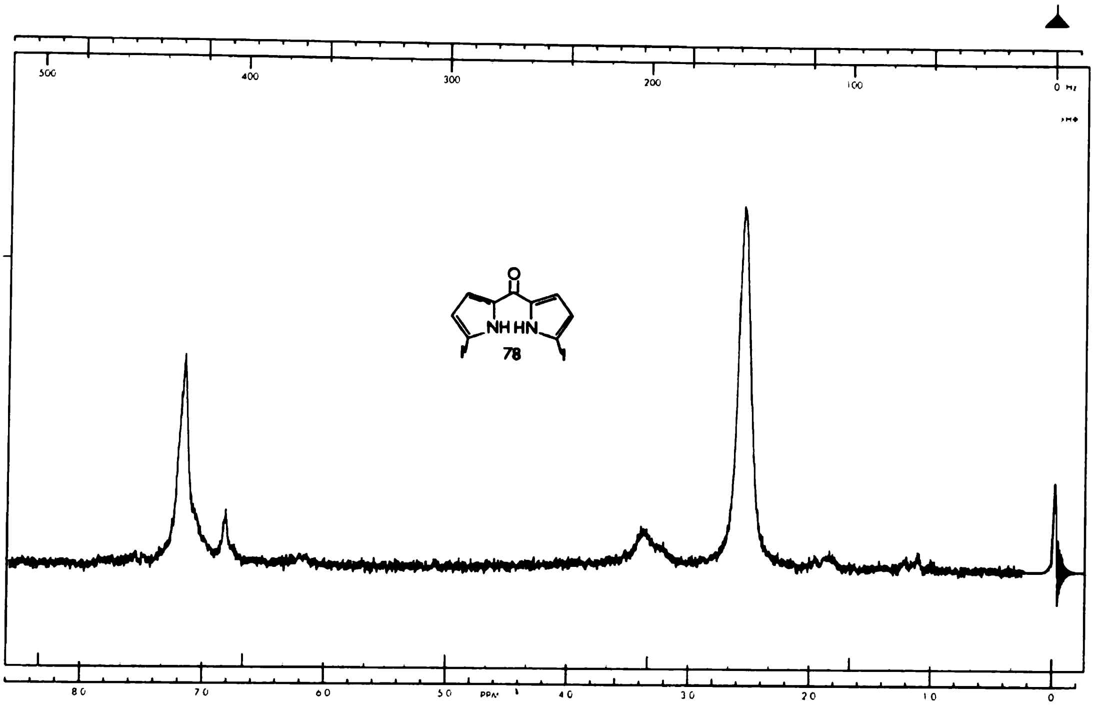


Figure 125. PMR spectrum of 5,5'-diiodo-2,2'-dipyrroketone (78).

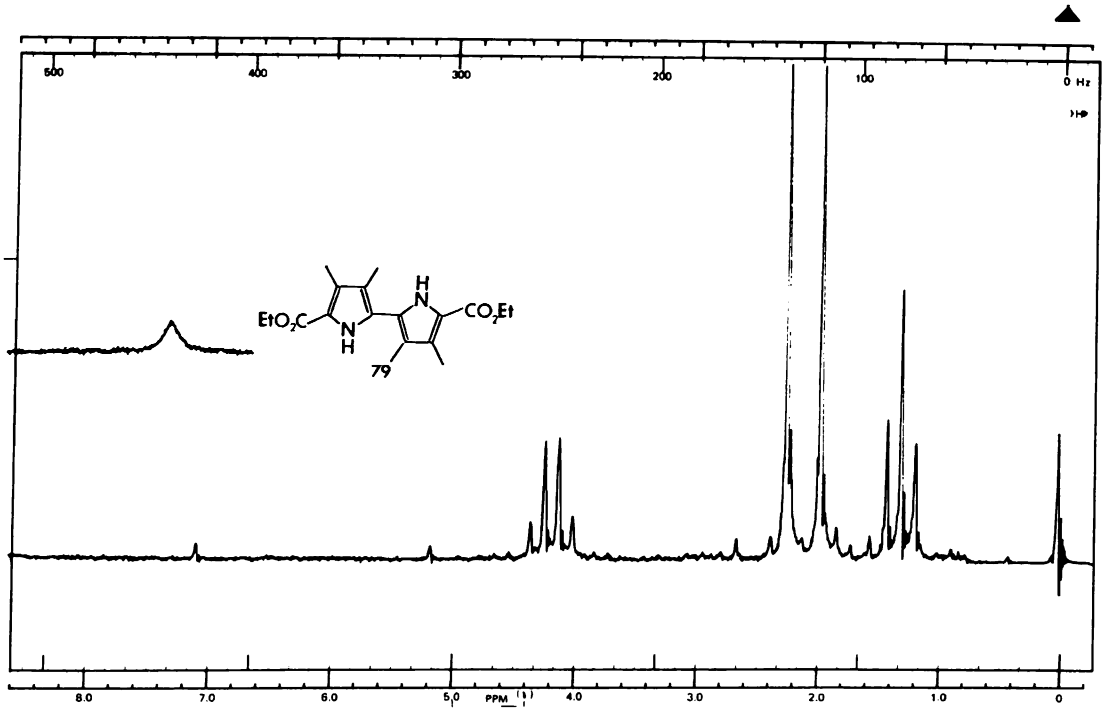


Figure 126. PMR spectrum of diethyl 3,3',4,4'-tetramethyl-2,2'-bipyrrole-5,5'-dicarboxylate (79).

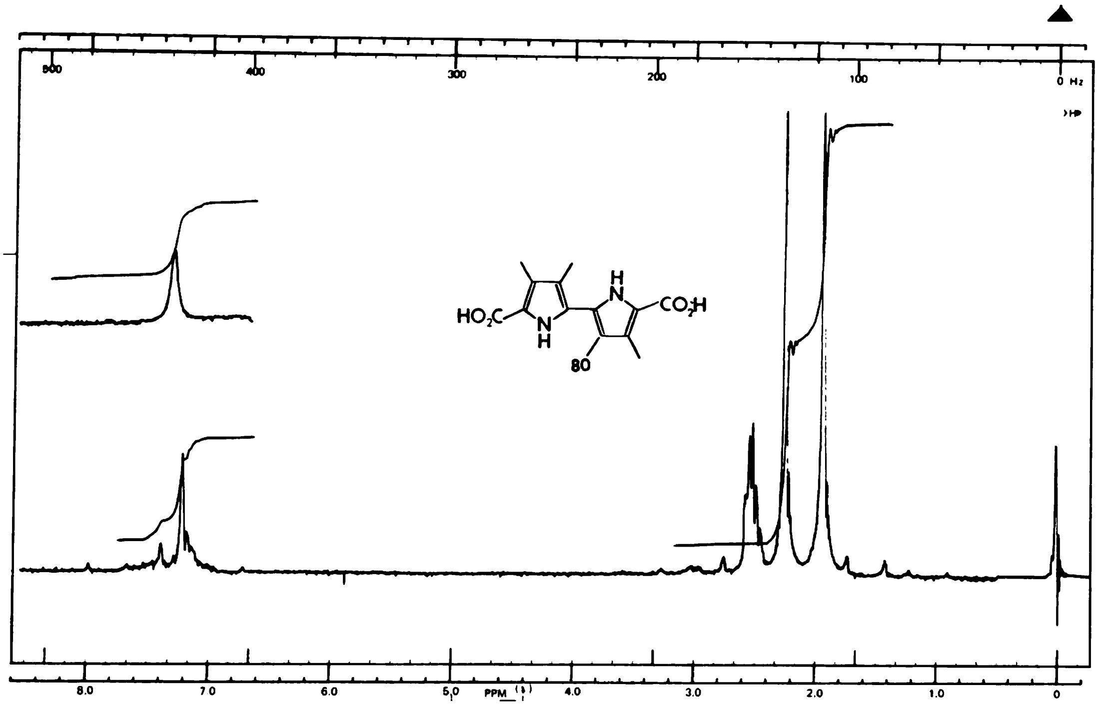


Figure 127. PMR spectrum of 3,3',4,4'-tetramethyl-2,2'-bipyrrole-5,5'-dicarboxylic acid (80).

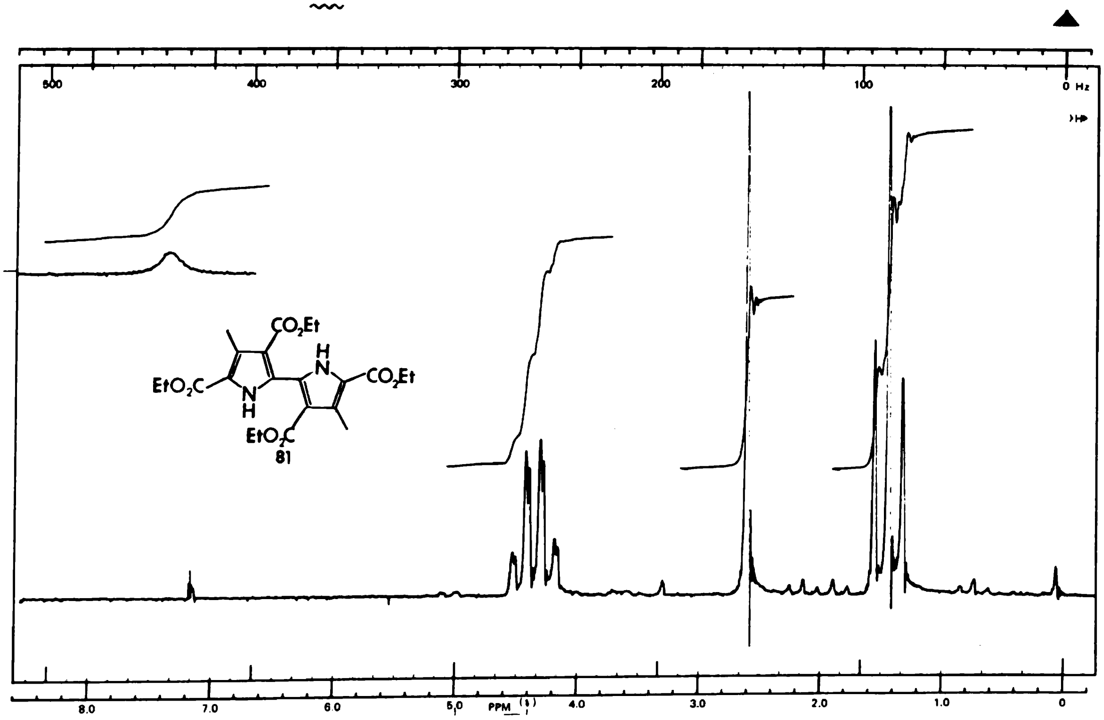


Figure 128. PMR spectrum of tetraethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3',5,5'-tetracarboxylate (81).

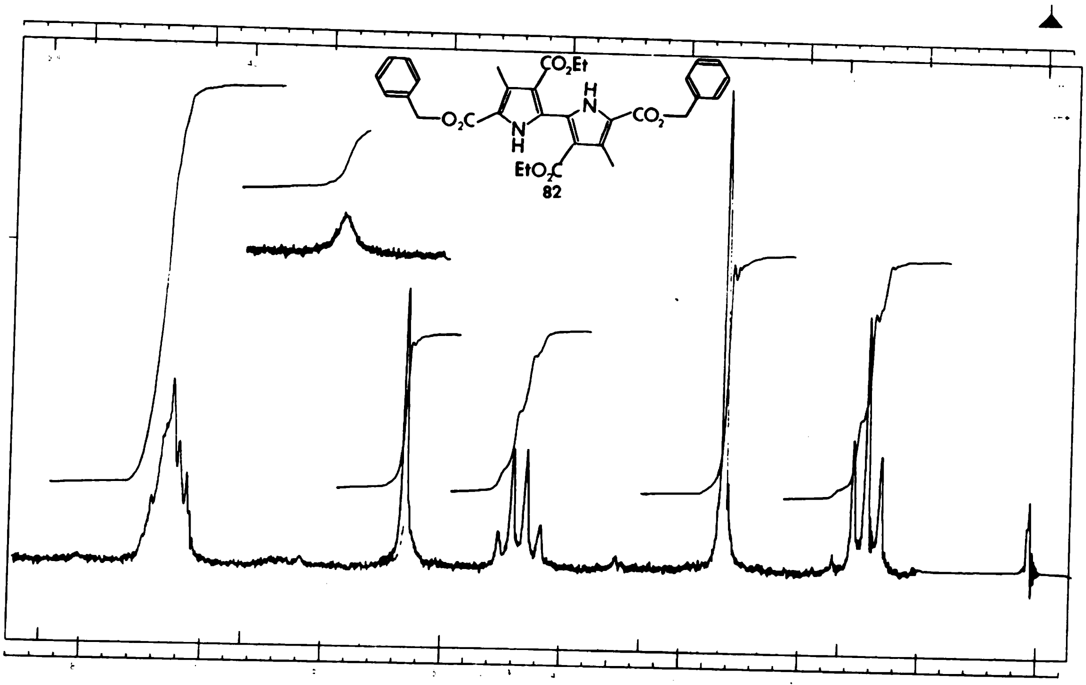


Figure 129. PMR spectrum of 5,5'-dibenzyl 3,3'-diethyl 4,4'-dimethyl-2,2'-bipyrrole-3,3',5,5'-tetracarboxylate (82).

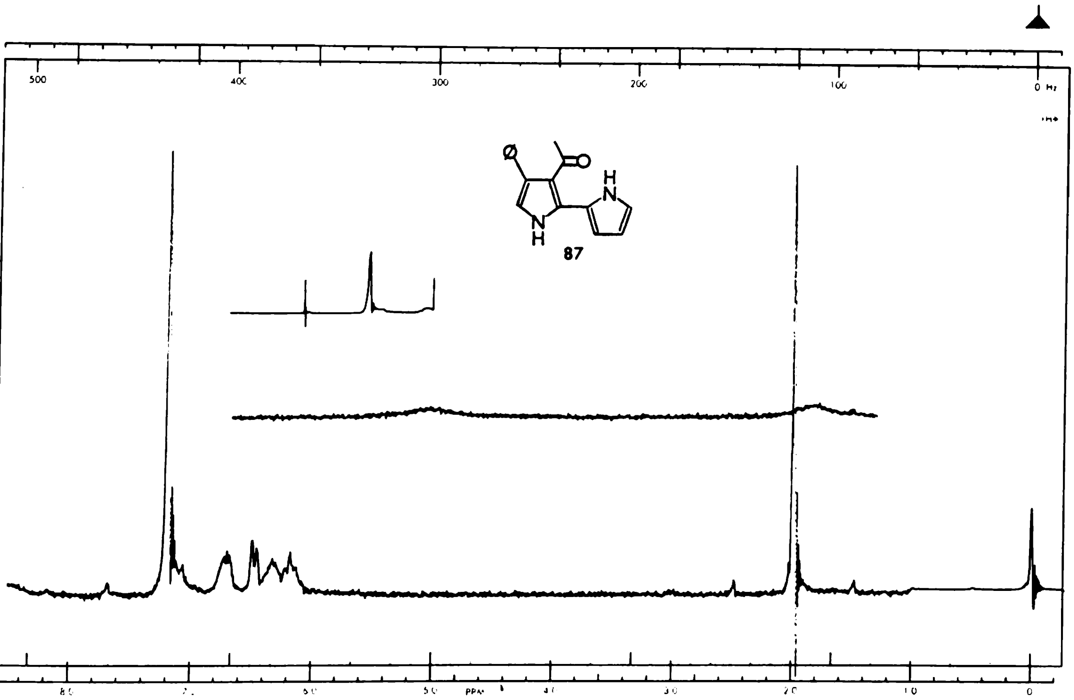


Figure 130. PMR spectrum of 3-acetyl-4-phenyl-2,2'-bipyrrole (87).

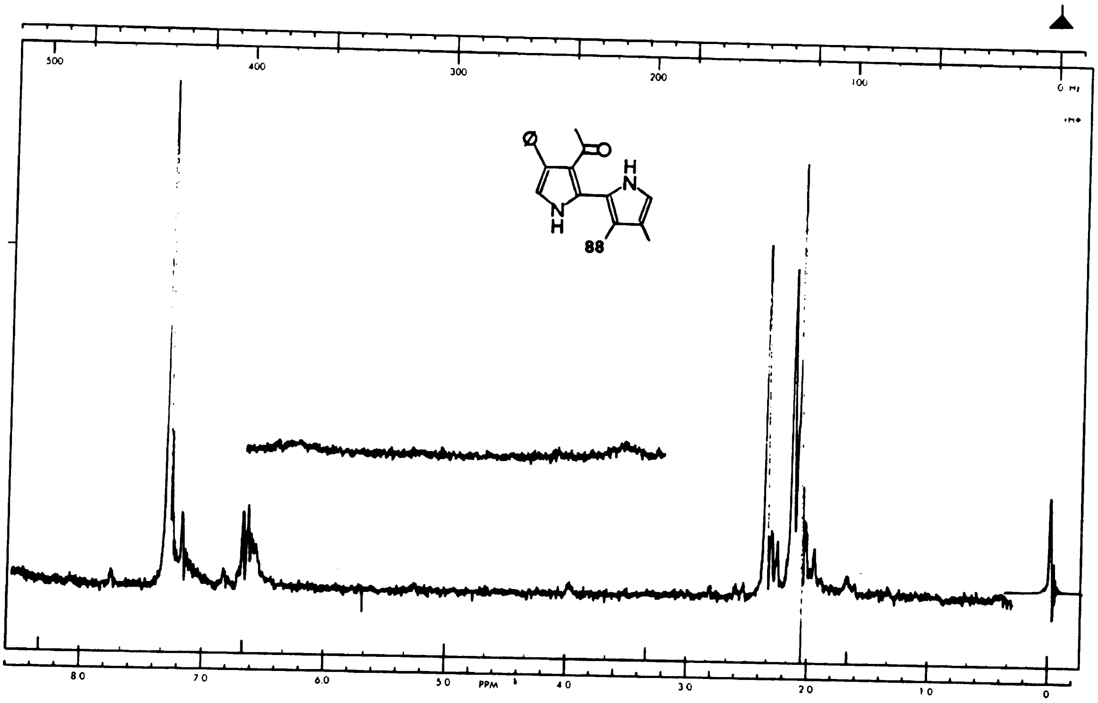


Figure 131. PMR spectrum of 3-acetyl-3',4'-dimethyl-4-phenyl-2,2'-bipyrrole (88).

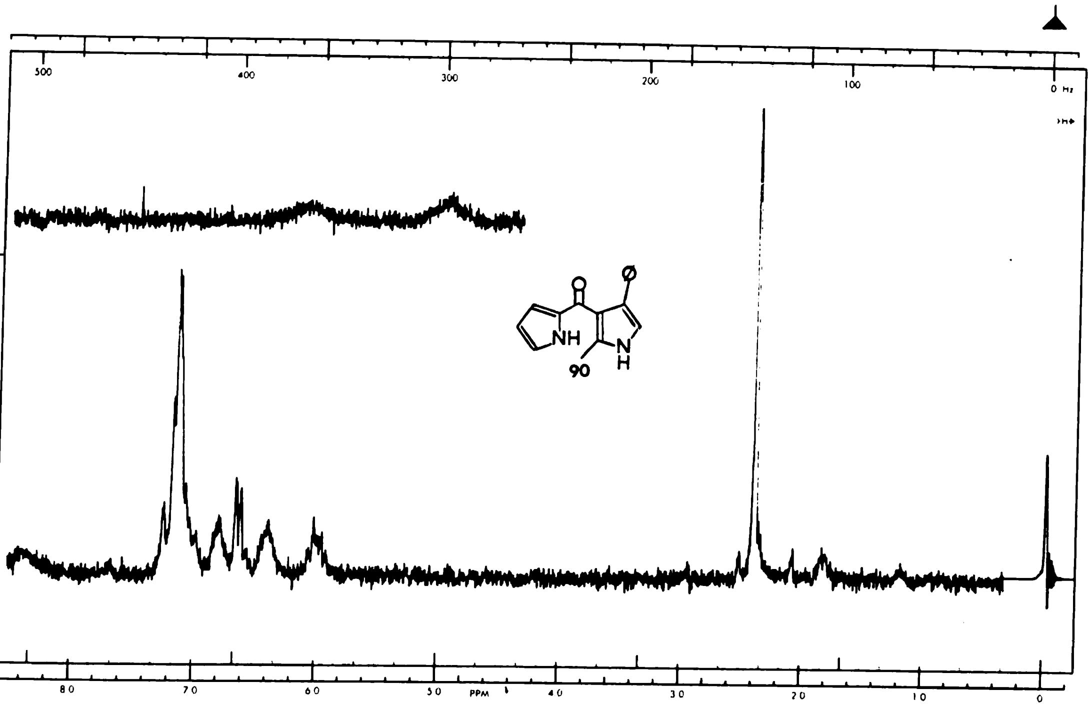


Figure 132. PMR spectrum of 2-methyl-4-phenyl-3,2'-dipyrroketone (90).

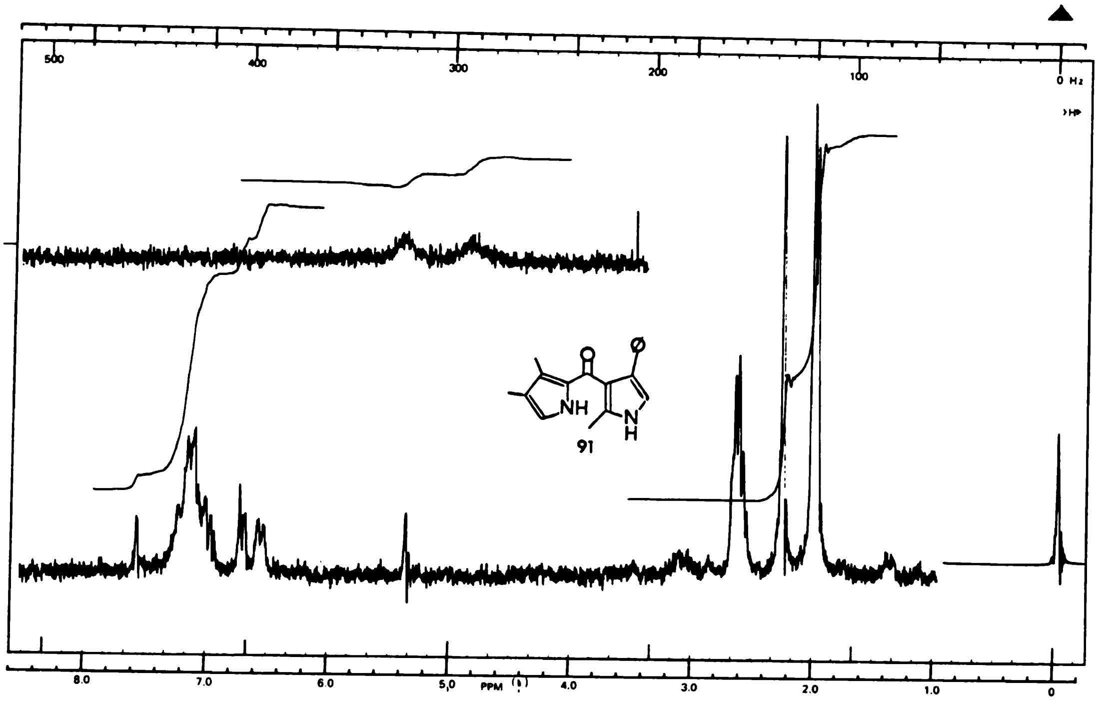


Figure 133. PMR spectrum of 2,3',4'-trimethyl-4-phenyl-3,2'-dipyrroketone (91).

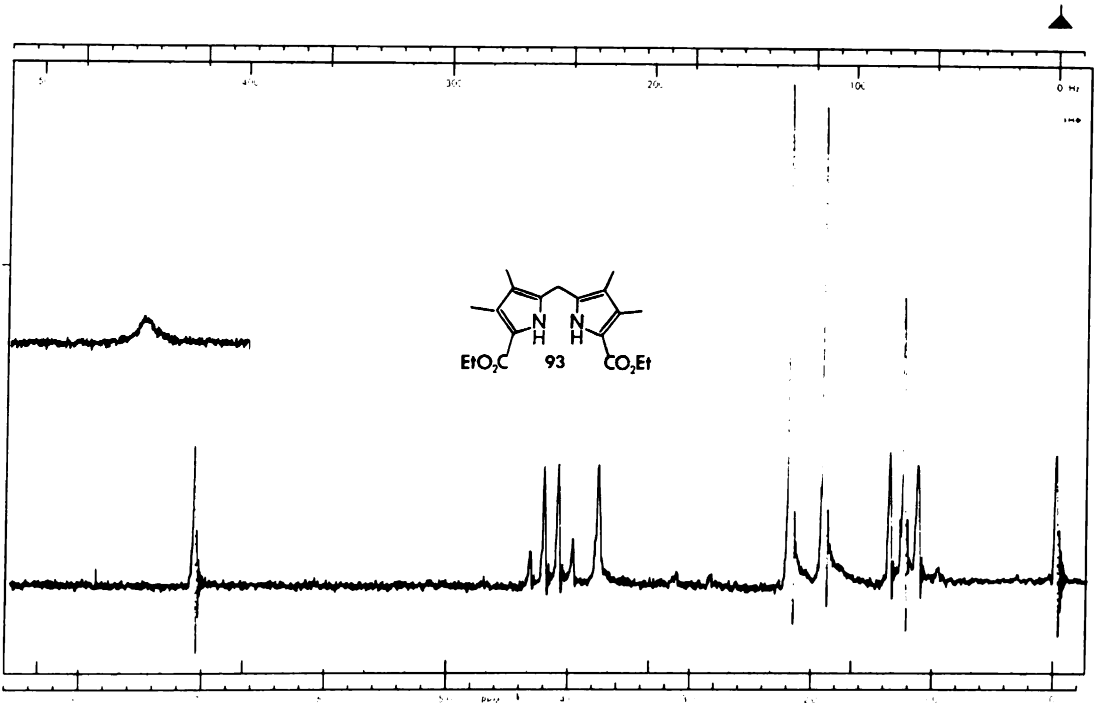


Figure 134. PMR spectrum of 5,5'-dicarbethoxy-3,3',4,4'-tetramethyl-2,2'-dipyrromethane (93).

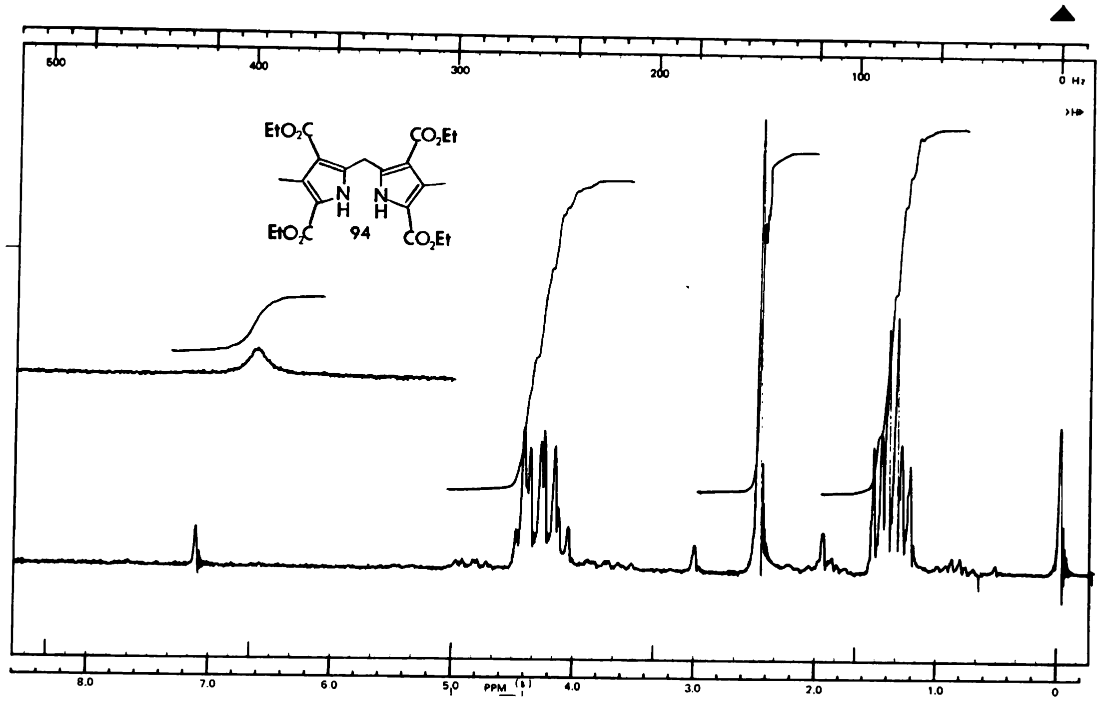


Figure 135. PMR spectrum of 3,3',5,5'-tetracarbethoxy-4,4'-dimethyl-2,2'-dipyrromethane (94).

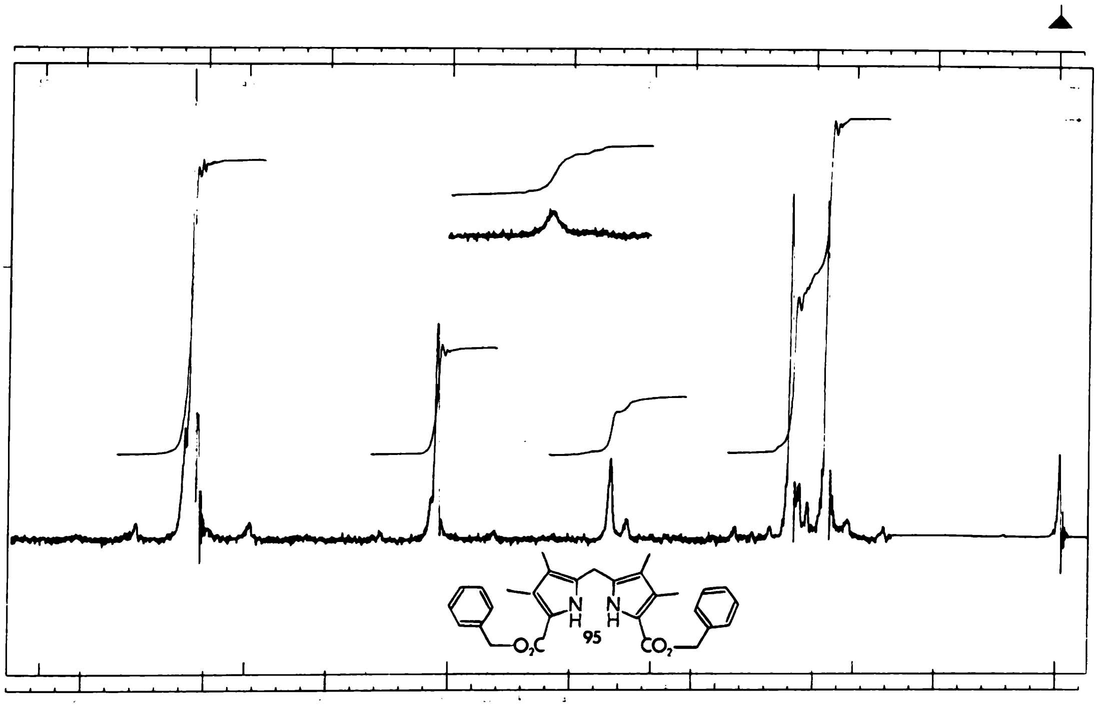


Figure 136. PMR spectrum of 5,5'-carbobenzyloxy-3,3',-4,4'-tetramethyl-2,2'-dipyrromethane (95).

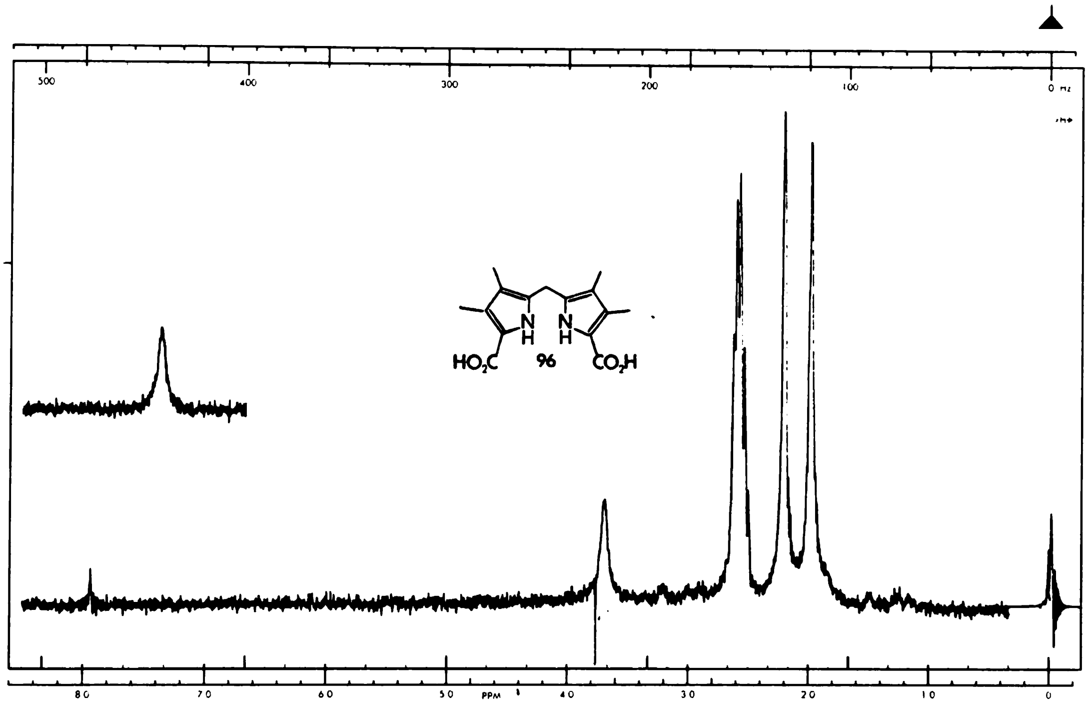


Figure 137. PMR spectrum of 3,3',4,4'-tetramethyl-2,2'-dipyrromethane-5,5'-dicarboxylic acid (96).

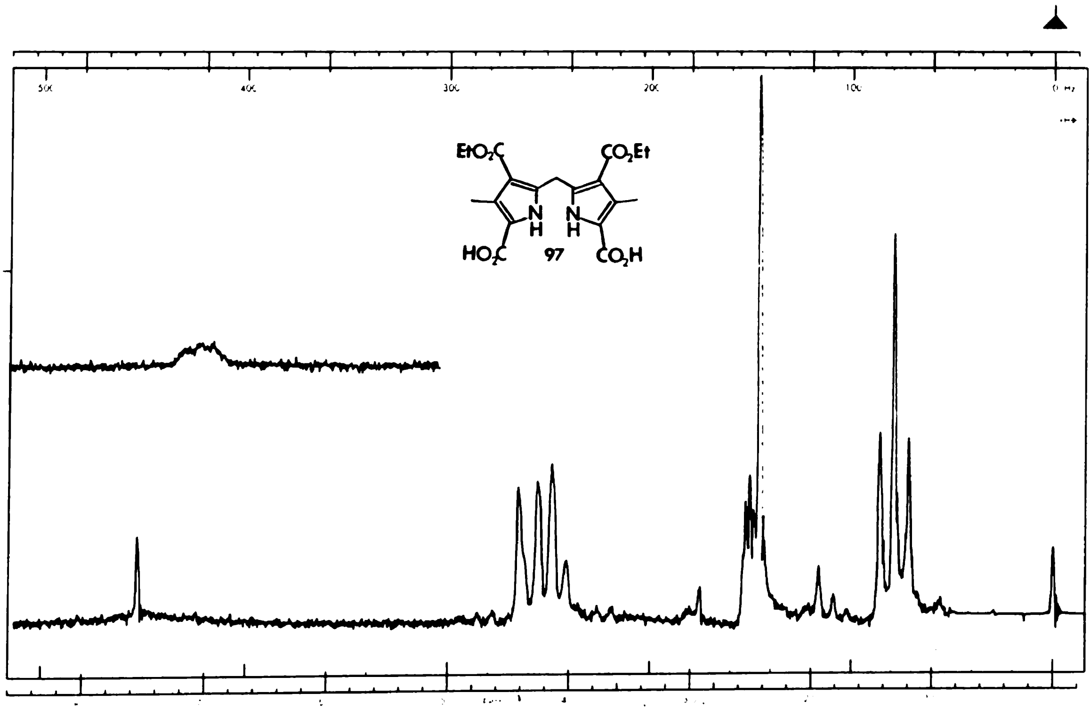


Figure 138. PMR spectrum of diethyl 4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylic acid-3,3'-dicarboxylate (97).

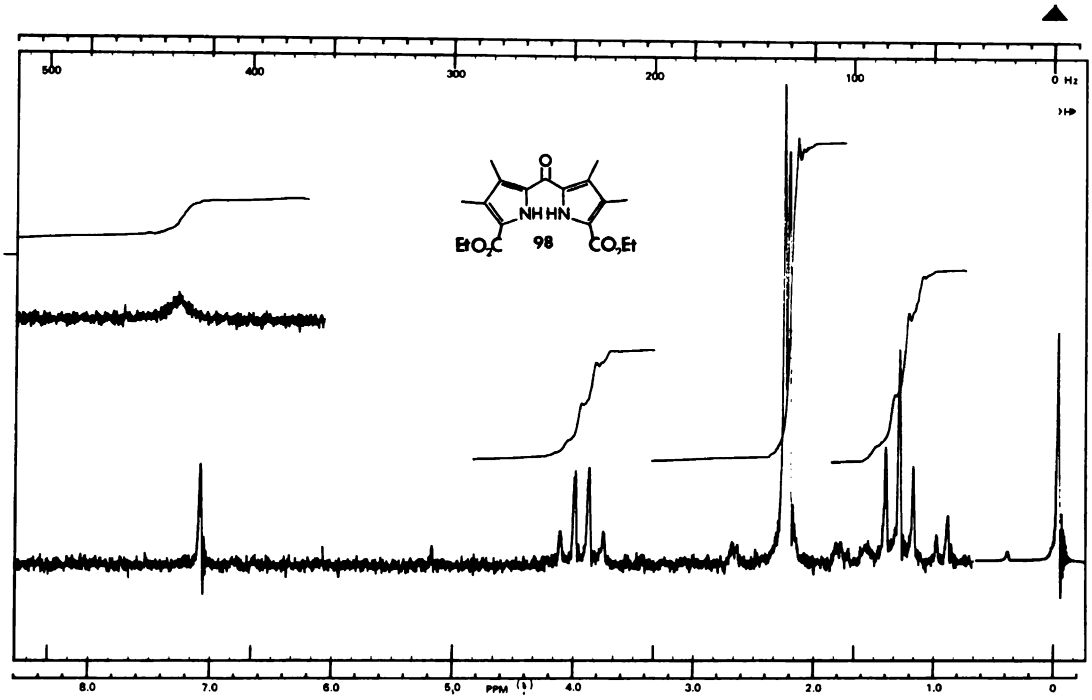


Figure 139. PMR spectrum of 5,5'-diethoxycarbonyl-3,3',-4,4'-tetramethyl-2,2'-dipyrroketone (98).

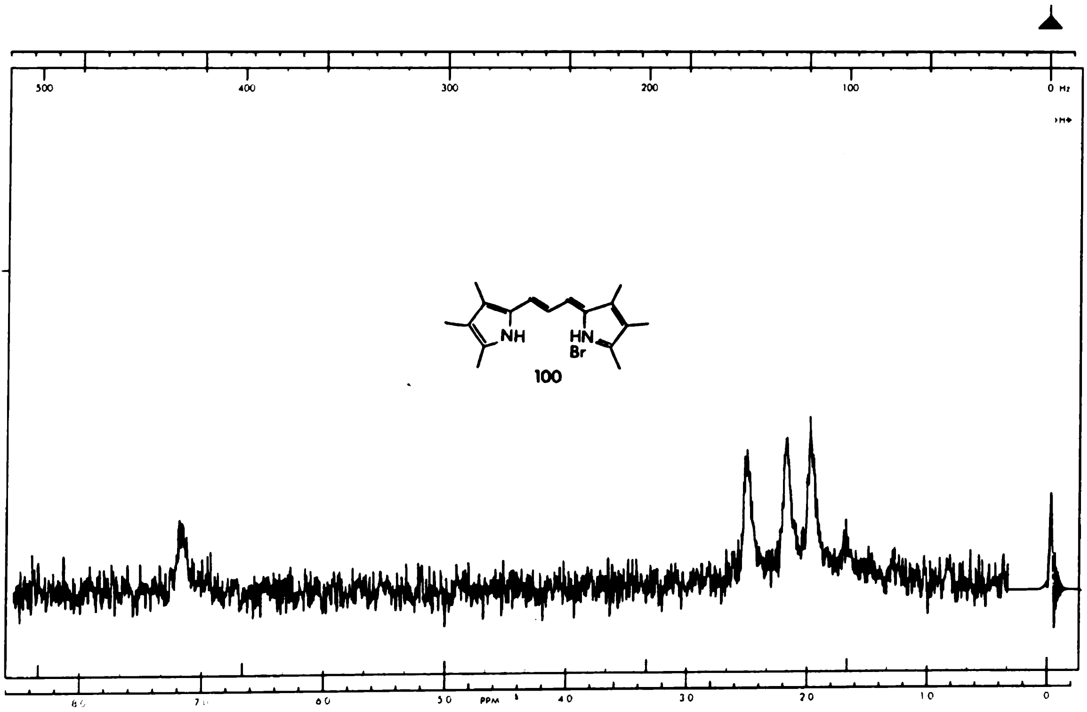


Figure 140. PMR spectrum of 3,3',4,4',5,5'-hexamethyldipyrro-2,2'-trimethine hydrobromide (100).

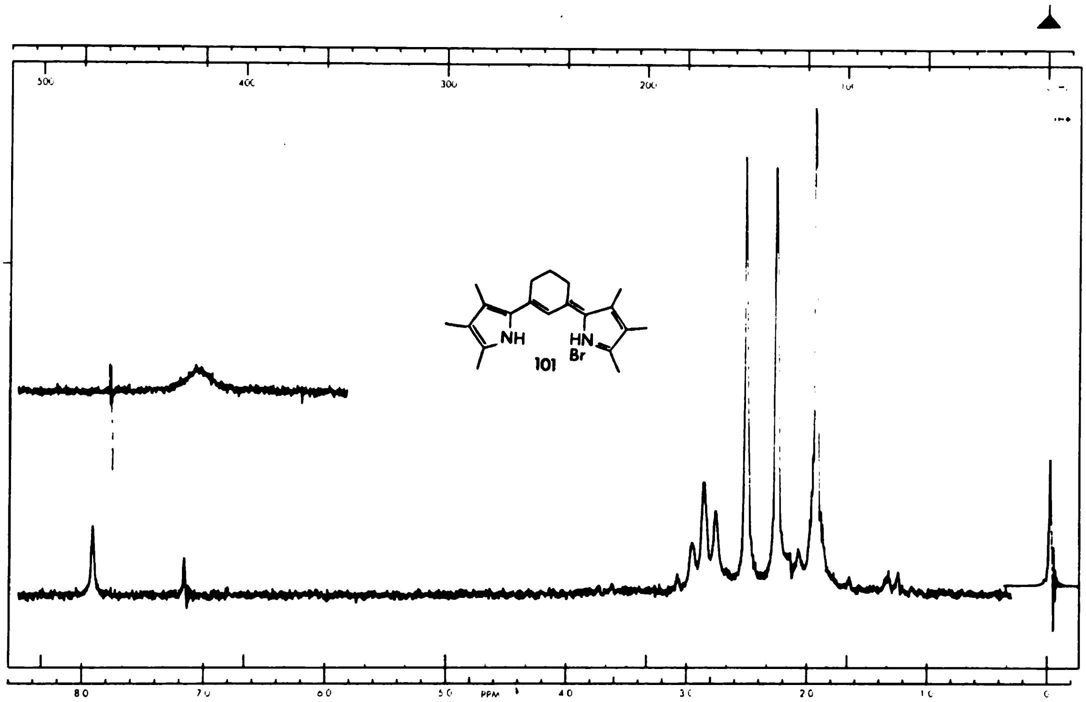


Figure 141. PMR spectrum of 3,3',4,4',5,5',-hexamethyldipyrro-2,2'-hexacyclotrimethine hydrobromide (101).

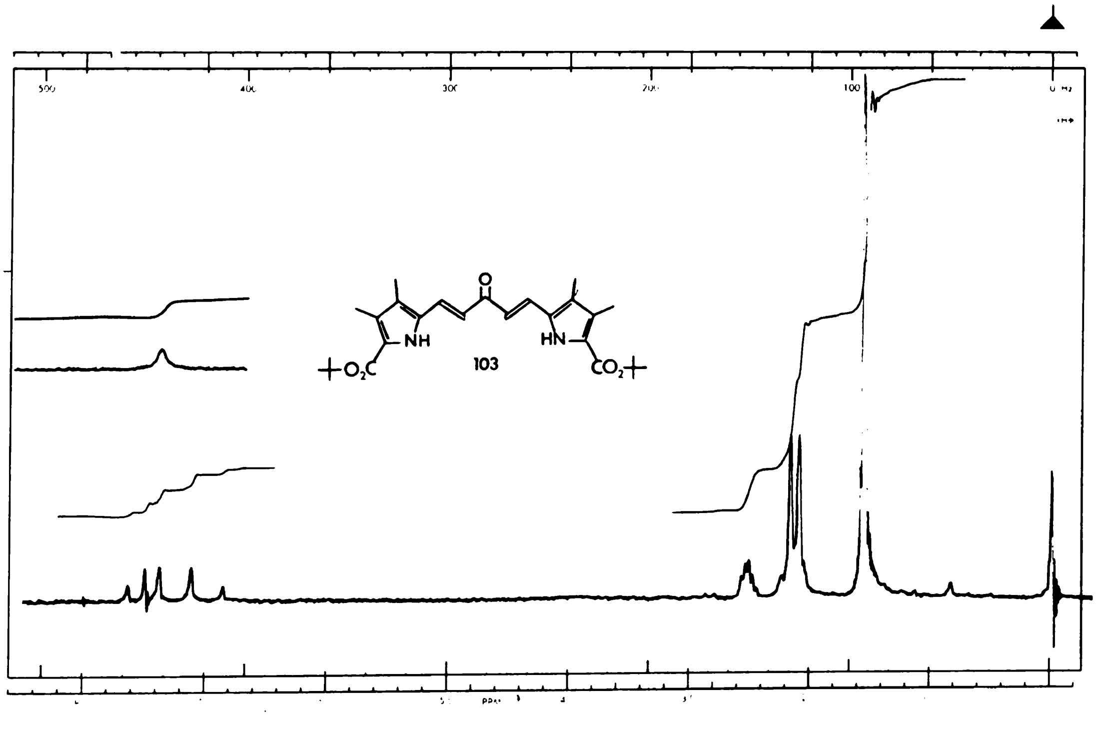


Figure 142. PMR spectrum of 1,5-di-(5-carbo-*t*-butoxy-3,4-dimethyl-2-pyrro)-1,4-pentadiene-3-one (103).

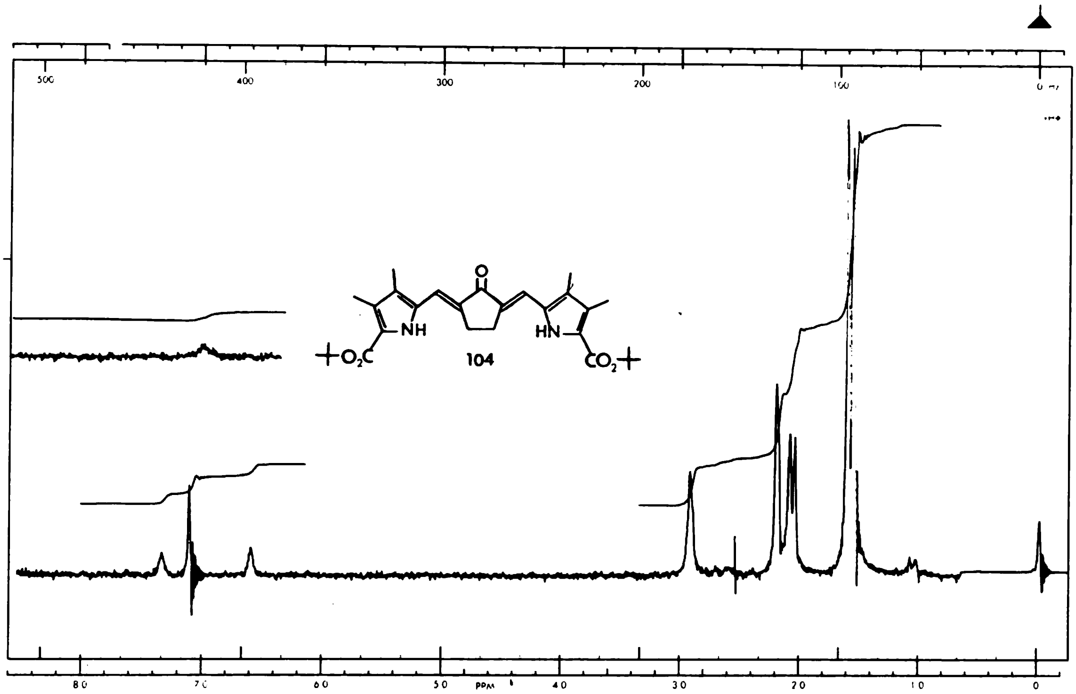


Figure 143. PMR spectrum of 2,5-di-(5-carbo-*t*-butoxy-3,4-dimethyl-pyrr-2-ylmethylene)-cyclopentanone (104).

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