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SYNTHESES OF PYRROLES AND PORPHYRINS

presented by

Ralph W. Kaesler

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Chemistry

Major professor

Eugene LeGoff

Date August 24, 1983

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SYNTHESES OF PYRROLES AND PORPHYRINS

By

Ralph W. Kaesler

A DISSERTATION

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

DOCTOR OF PHILOSOPHY

Department of Chemistry

1983

ABSTRACT

SYNTHESES OF PYRROLES AND PORPHYRINS

by

Ralph W. Kaesler

The syntheses of 2,5-unsubstituted and 2,5-dimethylpyrroles and their conversion to porphyrins have been investigated. Electrophilic substitution in the 3 and 4 positions of 2,5-dimethyl- and N-benzoyl-2,5-dimethylpyrroles gave 3,4-CH_2R-(R=CF_3, $CF_2CF_2CF_3$, $N(CH_3)_2$) as well as 3,4-dibromo- and 3,4-dichloropyrroles. Substitution of the dimethylamino group or its quaternary ammonium salt, allowed preparation of more functionalized derivatives (R=$C(CH_3)_2NO_2$, CN, $SO_2\phi CH_3$, $S\phi$). Hexafluorobut-2-yne and N-benzoyl-, N-benzoyl-2,5-dimethyl- and N-benzoyl-2-(1,3-dioxolan-2-yl)pyrroles reacted to form Diels-Alder adducts, which on selective hydrogenation of the less substituted double bond and pyrolytic cleavage of ethylene led to the corresponding 3,4-*bis*(trifluoromethyl)pyrroles. A two step synthesis of 3,4-*bis*-(carbethoxy)pyrrole from diethyl succinate allowed the efficient preparation of 2,5-unsubstituted 3,4-*bis*(N-methyl-, N,N-dimethyl-, N,N-diethyl- and morpholinecarboxamide)pyrroles.

The 2,5-dimethyl derivative of 3,4-*bis*(N,N-dimethylcarboxamide)pyrrole was obtained from the dimer of N,N-dimethylacetylacetamide.

The 2,5-dimethylpyrroles were converted to potential porphyrin precursors by oxidation of both methyl substituents. 2,5-*bis*(Acetoxy- and chloromethyl) derivatives were prepared by oxidation with $Pb(OAc)_4$ and SO_2Cl_2 respectively. Exhaustive chlorination with excess SO_2Cl_2 followed by hydrolysis and iodinative decarboxylation enabled the preparation of 2,5-diiodopyrroles.

Octakis(1H,1H-trifluoroeth-1-yl)- and octakis(1H,1H-heptafluorobut-1-yl)porphyrin were obtained from the acid catalyzed self-condensations of the corresponding 2,5-*bis*-(acetoxymethyl)pyrroles. Condensations of the 2,5-diiodo-derivatives with formaldehyde in acidified 1-propanol gave higher yields of the same porphyrins and also obviated the normally required prolonged air oxidation. Octakis(2-methyl-2-nitroprop-1-yl)- and octakis(N,N-dimethylcarboxamide)porphyrins were prepared in a similar fashion from the corresponding 2,5-diiodo- and 2,5-*bis*(acetoxymethyl)pyrroles. The latter porphyrin and its N,N-diethyl derivative were also synthesized *via* the condensations of the 2,5-unsubstituted pyrroles with formaldehyde. 2,5-*bis*(Acetoxymethyl)-3,4-dibromo-, chloro-, and (*p*-tolylsulfonylmethyl)pyrroles self-condensed to provide only trace amounts of porphyrin.

To
My Parents
and
My Wife Beth

ACKNOWLEDGEMENT

I am extremely indebted to Dr. Eugene LeGoff for his guidance, enthusiasm and friendship. His insights into chemistry and his willingness to help have made my graduate career both a pleasant and a fruitful one.

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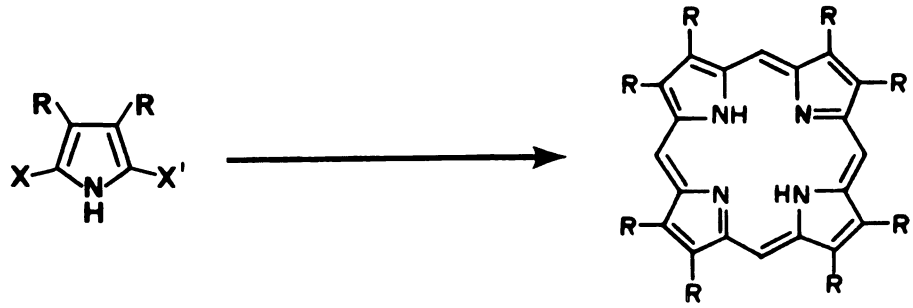
INTRODUCTION

The chemistry of porphyrins and their pyrrole precursors has been examined extensively over the past sixty years.[1-7] A considerable amount of this effort is devoted to the syntheses of porphyrins and numerous methods for their preparation are now available. These include the cyclization of pyrroles, dipyrromethanes, dipyrromethenes, dipyrroketones, (oxy-)bilanes, bilenes and biladienes.[8]

The condensation of monopyrroles bearing identical substituents in the 3 and 4 positions constitutes a useful route to symmetrically octasubstituted porphyrins. Porphine, octamethylporphyrin (OMP) and octaethylporphyrin (OEP) are the traditional targets of this method. Some of the most facile condensations leading to these porphyrins are summarized in Table 1. In general two types of α-pyrrole substitutions are involved: a) 2,5-unsubstituted pyrroles, which are condensed with formaldehyde or formic acid and b) α-hydroxymethyl or aminomethylpyrroles, which undergo self-condensation on treatment with acid (the 2-carboxy-5-CH_2R substituted pyrroles decarboxylate prior to

Table 1 Porphine, Octamethyl- and Octaethylporphyrin.



R	X, X'	Method	% Yield[a]	Reference
H	H, CHO	HCOOH, O_2	0.026	9
H	H	HCOH, MeOH Pyridine	0.021	10
H	H, CH_2OH	HOAc, ϕCOO_2H	5	11
H	H, CH_2OH	HOAc, O_2	5	12
H	H, CH_2OH	ϕEt, O_2	8-10	13
CH_3	H	HCOOH	12	14
CH_3	H	HCOH, AcOH Pyridine	77	15
CH_3	H	HCOH, HBr, EtOH	76	16
CH_3	CH_2OH, COOH	HCOOH	47	17
CH_3	CH_2NH_2, COOH	MeOH, $Cu(OAc)_2$	20[b]	18
CH_3	H, $CH_2N(CH_3)_2$	EtMgBr, Xylene	20-36[c]	19
CH_2CH_3	CH_2OH, COOH	HOAc, $K_3Fe(CN)_6$	44	20
CH_2CH_3	H, $CH_2N(CH_3)_2$	HOAc, O_2	52	21
CH_2CH_3	$CH_2N(CH_2CH_3)_2$, COOK	HOAc, O_2	52[d]	22
CH_2CH_3	H	HCOH, EtOH, HBr	65	16

[a]Yields of final condensation; [b]Yield of copper porphyrin; [c]Yield of magnesium porphyrin; [d]Yield based on ethylester precursor (Scheme 2).

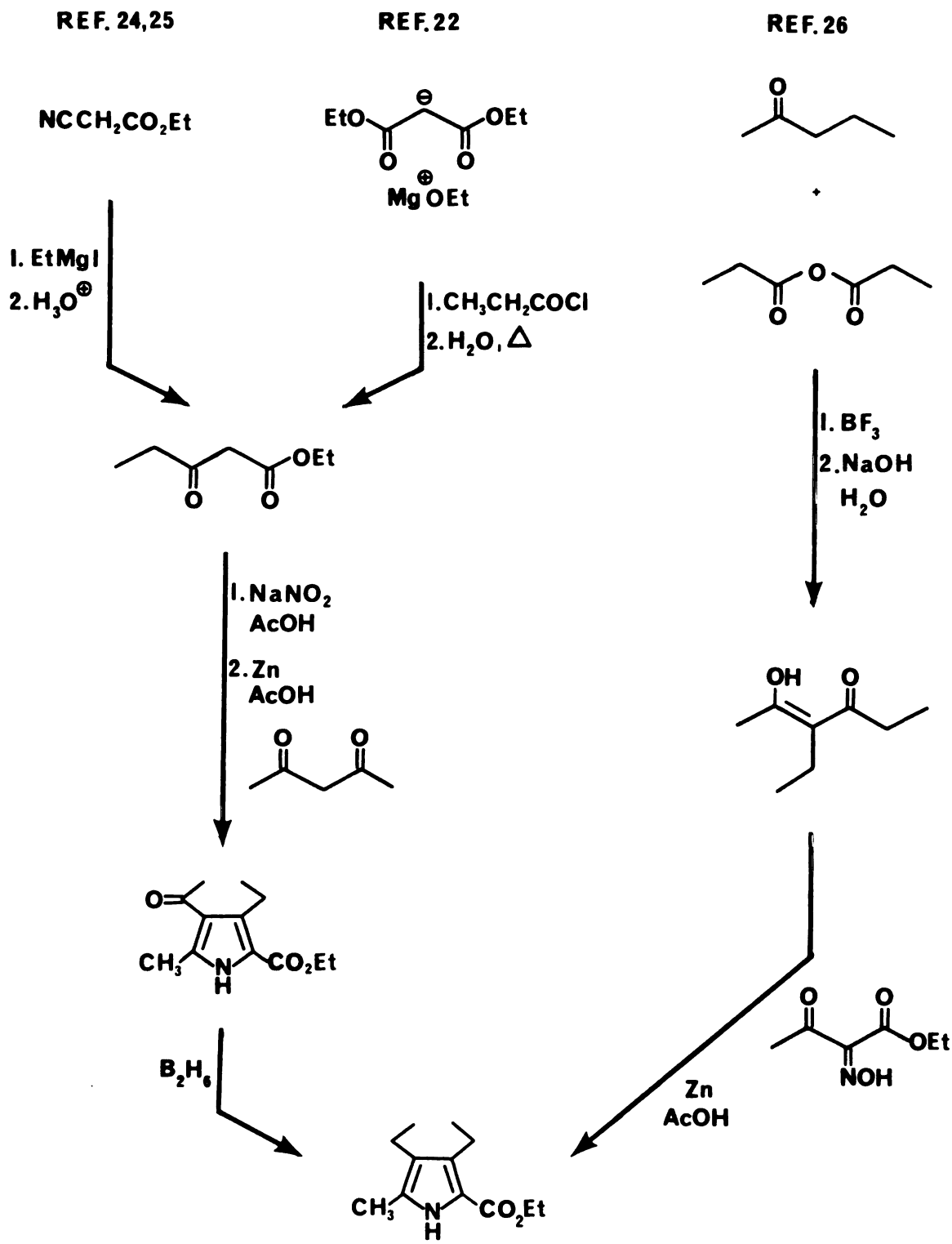
condensation). The mechanistic considerations of these reactions have been discussed elsewhere.[23]

The higher yields of OMP and OEP are attributed to a decrease in side reactions involving the β-positions of the pyrrole and an increase in reactivity of the α-positions toward electrophiles. One of the most efficient condensations ever reported involves Treibs and Häberle's synthesis of OMP from 3,4-dimethylpyrrole.[15] A yield of 77% was obtained for the final condensation, however, isolation of the porphyrin proved to be tedious. A more facile procedure entails heating 3,4-dimethylpyrrole and formaldehyde in acidified ethanol.[16] The porphyrin is collected by filtering the reaction mixture after air oxidation.

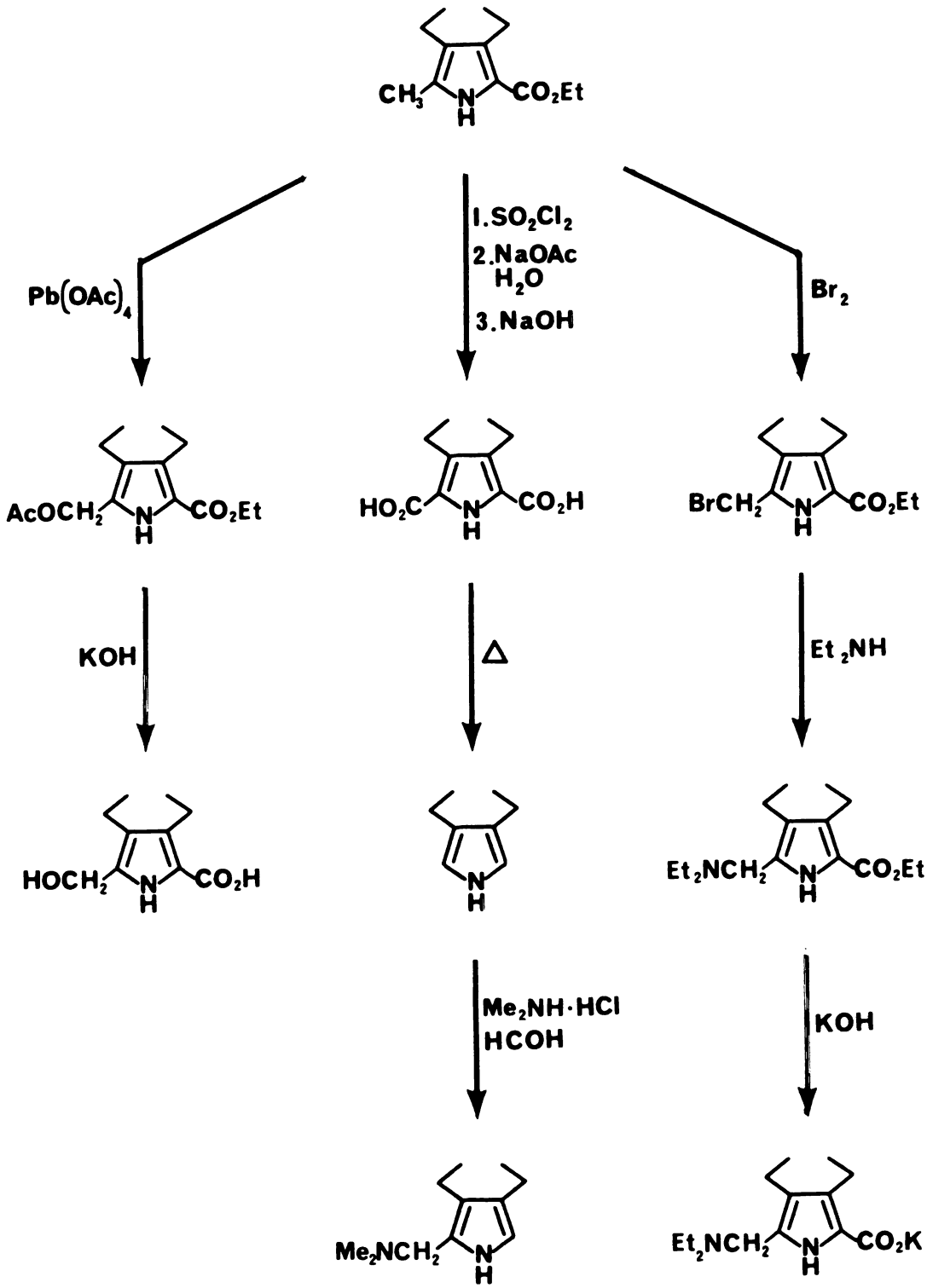
Octaethylporphyrin is one of the most widely used models in porphyrin chemistry and its synthesis has received considerable attention. The greatest challenges encountered en route to OEP (or any other porphyrin) are in the preparation of the pyrrole precursors. 2-Carbethoxy-3,4-diethyl-5-methylpyrrole is a commonly employed intermediate to OEP and three of its most important syntheses are outlined in Scheme 1. Conversion to precursors suitable for condensation (Table 1) requires further manipulations of the α-pyrrole substituents. These are illustrated in Scheme 2 for syntheses by Inhoffen,[20] Whitlock[21] and Dolphin.[22]

Except for the recent syntheses of octakis(2-methyoxycarbonylethyl)- and octakis(3-methoxycarbonylpropyl)porphyrin from the corresponding 2-acetoxymethyl-5-carboxypyr-

Scheme 1


REF. 24,25
REF. 22
REF. 26
NCCH2CO2Et
EtO
OEt
Mg OEt
1. EtMgI
2. H3O⊕
1. CH3CH2COCl
2. H2O, Δ
OEt
1. BF3
2. NaOH
H2O
1. NaNO2
AcOH
2. Zn
AcOH
OH
CH3
CO2Et
B2H6
Zn
AcOH
NOH
OEt

Scheme 2

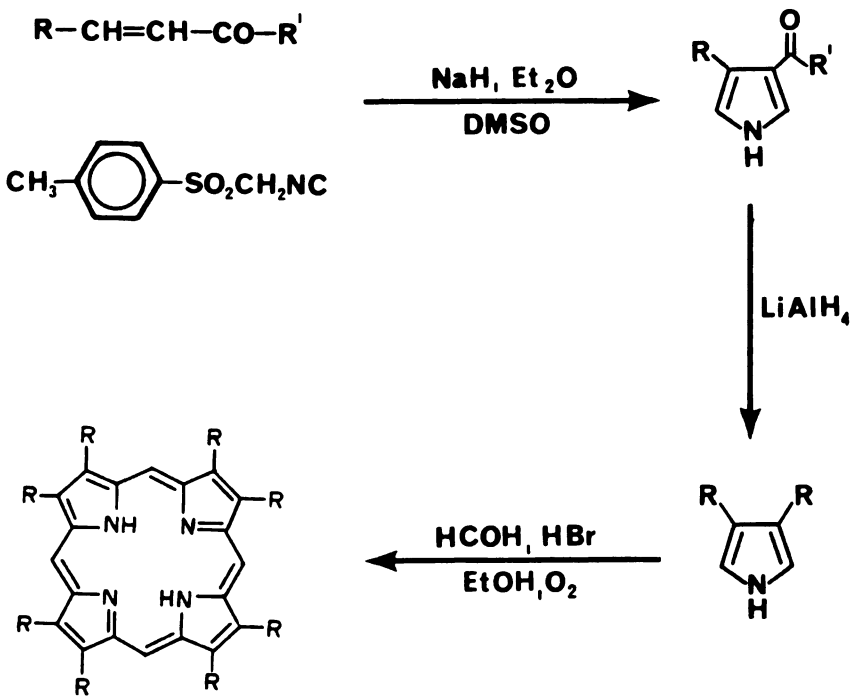

CH3
N
H
CO2Et
Pb(OAc)4
1.SO2Cl2
2.NaOAc
H2O
3.NaOH
Br2
AcOCH2
CO2Et
HO2C
CO2H
BrCH2
KOH
Δ
Et2NH
HOCH2
Et2NCH2
Me2NH·HCl
HCOH
KOH
Me2NCH2
CO2K

roles,[27a] other practical syntheses of symmetrically substituted porphyrins from monopyrroles have been limited to different alkyl and some aryl substituted cases. Octapropylporphyrin has been prepared from 2-hydroxymethyl-3,4-dipropylpyrrole, but the overall procedure was plagued by poor yields and sensitive intermediates.[17,27b] A more efficient synthesis of octapropylporphyrin as well as longer chain alkyl derivatives is outlined in Scheme 3.[28] The condensation of 3,4-diphenylpyrrole and formaldehyde[15] in acetic acid and pyridine as well as the self-condensations of 2-dimethylaminomethyl-3,4-diphenyl- and 3,4-*bis*(*p*-methoxyphenyl)pyrroles[29] have served as routes to octaarylporphyrins.

Table 2 summarizes the condensations of monopyrroles bearing both an alkyl (or aryl) and a strong electron withdrawing substituent in the β-positions.[16,30] Remarkably high yields are reported for some cases, however, due to the unsymmetrical nature of the pyrroles, mixtures of porphyrins could not be avoided. For example the condensation of 3-acetyl-4-ethylpyrrole with formaldehyde resulted in formation of three of the possible four isomers: 2,7,13,18-tetraacetyl-3,8,12,17-tetraethylporphyrin, 2,8,13,18-tetraacetyl-3,7,12,17-tetraethylporphyrin and 2,8,12,18-tetraacetyl-3,7,13,17-tetraethylporphyrin in ratios of 1:4:2 respectively.

Explored in this thesis are the applications of 2,5-dimethylpyrroles and highly deactivated 2,5-unsubstituted pyrroles in the syntheses of symmetrical, non-alkyl, octa-

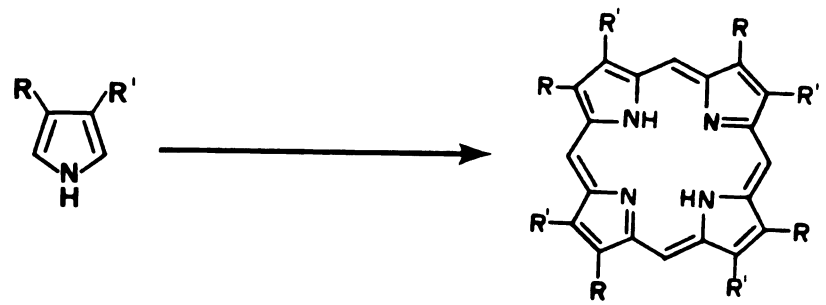
Scheme 3



R	% Yield[a]	Reference
$CH_3(CH_2)_2$	32	28
$CH_3(CH_2)_3$	33	28
$CH_3(CH_2)_4$	40	28
$CH_3(CH_2)_5$	11	28
$CH_3(CH_2)_6$	11	28
$CH_3(CH_2)_7$	22	28

[a]Yields of final condensation.

Table 2. Mixed Porphyrins



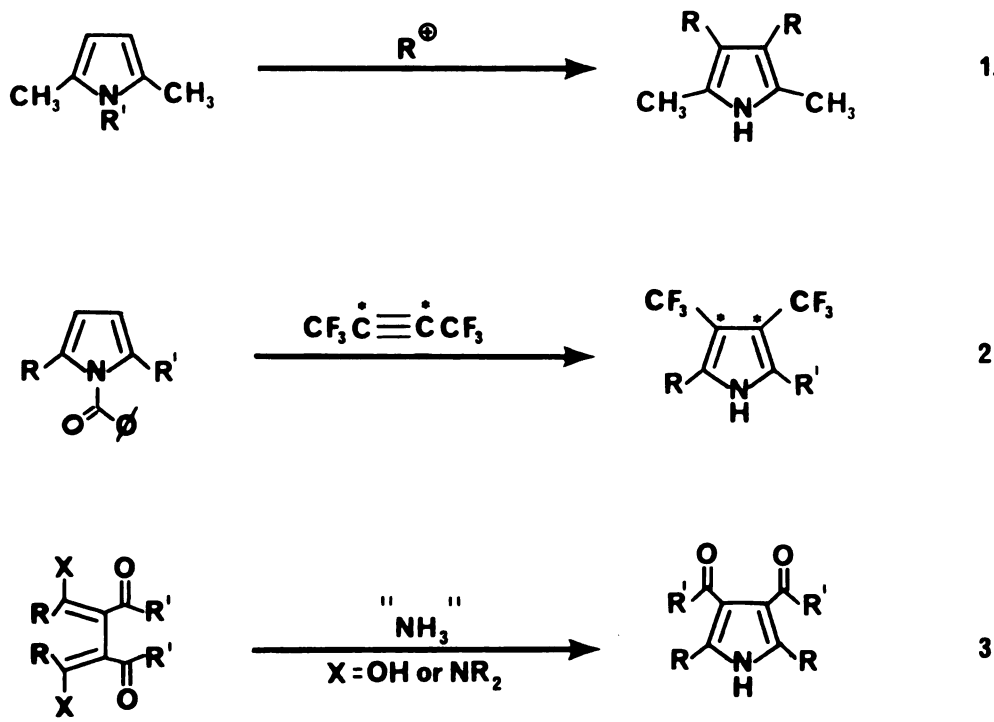
R, R'	% Yield	Reference
CH_3, CO_2Et	92	16
CH_3, $CO_2C_8H_{17}$	52	16
Ph, CO_2Et	86	16
CH_3, $COCH_3$	64	16
CH_2CH_3, $COCH_3$	96	16
$CH_3(CH_2)_n$, $CO(CH_2)_{n-1}CH_3$		
n=2	17	30
n=3	57	30
n=4	34	30
n=5	42	30

substituted porphyrins. This work is presented in three sections, describing, a) the syntheses of various 2,5-dimethyl and 2,5-unsubstituted pyrroles, b) the preparation of potential porphyrin precursors from 2,5-dimethyl pyrroles and c) the utility of the precursors in condensations leading to porphyrins.

A. SYNTHESES OF PYRROLES

Three fundamentally different approaches to 2,5-unsubstituted and 2,5-dimethylpyrroles have been investigated and their net transformations are summarized in Scheme 4. The first approach (eq. 1) involves electrophilic substitutions in the 3 and 4 positions of a 2,5-dimethylpyrrole,

Scheme 4

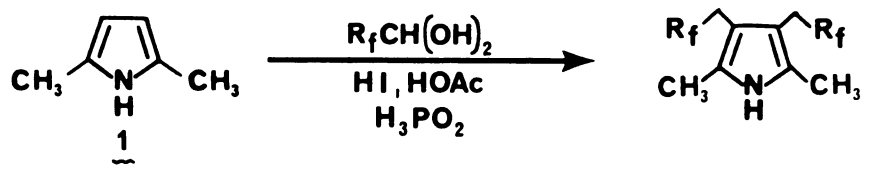


which proved useful in the preparation of 3,4-CH_2R pyrroles as well as halopyrroles. The second approach (eq. 2), leading to *bis*(trifluoromethyl)pyrroles, involves the exchange of the two acetylenic carbons in hexafluorobut-2-yne for the

β-carbons in a series of N-benzoylpyrroles. This was accomplished using a Diels-Alder, retro Diels-Alder reaction sequence. The third approach (eq. 3) provided various ester and amidepyrroles from the cyclizations of bisenamine and bisenol (diketone) precursors.

The 2,5-dimethyl-3,4-*bis*(polyfluoroalkyl)pyrroles 2a,b were prepared from readily available 2,5-dimethylpyrrole, 1, by reductive alkylation with heptafluorobutyraldehyde hydrate and trifluoroacetaldehyde hydrate (Scheme 5).

Scheme 5



1

2 a $R_f = CF_2CF_2CF_3$
b $R_f = CF_3$

This procedure is an extension of the pyrrole alkylations described by MacDonald, which have been useful in the preparation of several tetrasubstituted pyrroles.[31,32] The ^1H NMR of 2a includes a distinctive broad triplet for the polyfluorobutylmethylenes, a result of long-range coupling with adjacent fluorines. Similarly, a broad quartet is observed for the trifluoroethyl substituents in 2b. The ^{13}C proton decoupled NMR for both pyrroles show a single

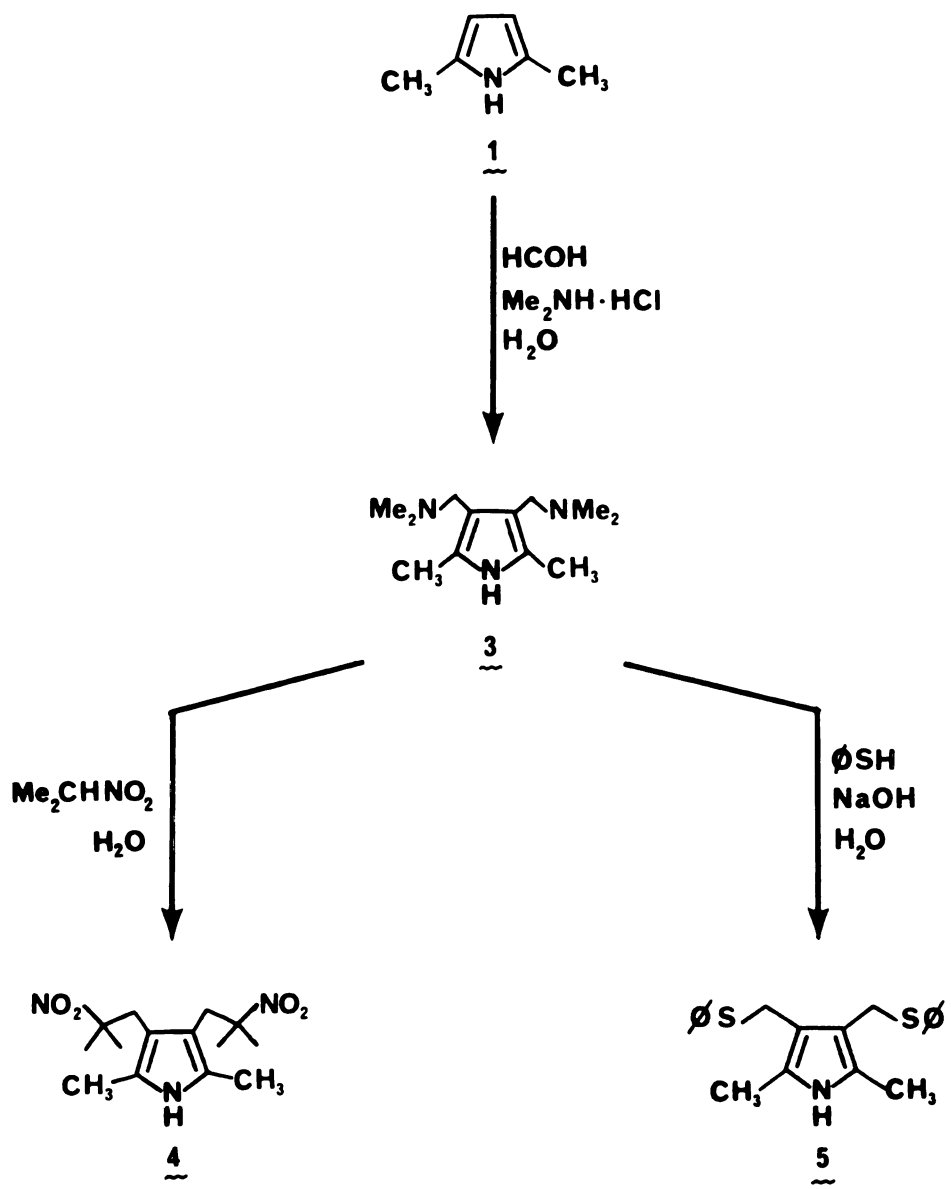
resonance for each of the α and β carbons, characteristic of symmetrically substituted pyrroles. The 1H,1H-heptafluorobutyl substituents give a distinctive ^{13}C-^{19}F coupling pattern, which is best seen in the 2,5-diiodo derivative of 2a and is discussed in detail on pg 36.

Further extension of MacDonald's method was not realized. Attempts to reductively dialkylate 1 with methyl-2,2-dimethoxyacetate under a variety of conditions failed to provide the desired 3,4-disubstituted pyrrole, despite a similar, reported monoalkylation of 2-carbethoxy-3-(2-methoxycarbonylethyl)-5-methylpyrrole.[32]

The substitutions of nucleophiles for the dimethylamino group of dimethylaminomethylpyrroles have been useful in the preparation of a variety of CH_2R substituted pyrroles.[33,34] Investigations into applying this method toward 2,5-dimethyl-3,4-CH_2R pyrroles revealed that heating 2,5-dimethyl-3,4-*bis*(dimethylaminomethyl)pyrrole, 3, (readily available from 1 by a double Mannich reaction[35]) with an excess of 2-nitropropane in water[36] affords a 70% yield of *bis*(nitroalkyl)pyrrole 4 (Scheme 6). Similarly, the *bis*(phenylthiomethyl)pyrrole 5 was prepared by heating 3 with thiophenol in the presence of NaOH.[37] The key mechanistic steps in these transformations are thought to entail formation of an azafulvene intermediate followed by addition of the nucleophile.

Analogous reactions of 3 with KCN or sodium *p*-toluenesulfinate in water failed to provide any *bis*-substitution

Scheme 6

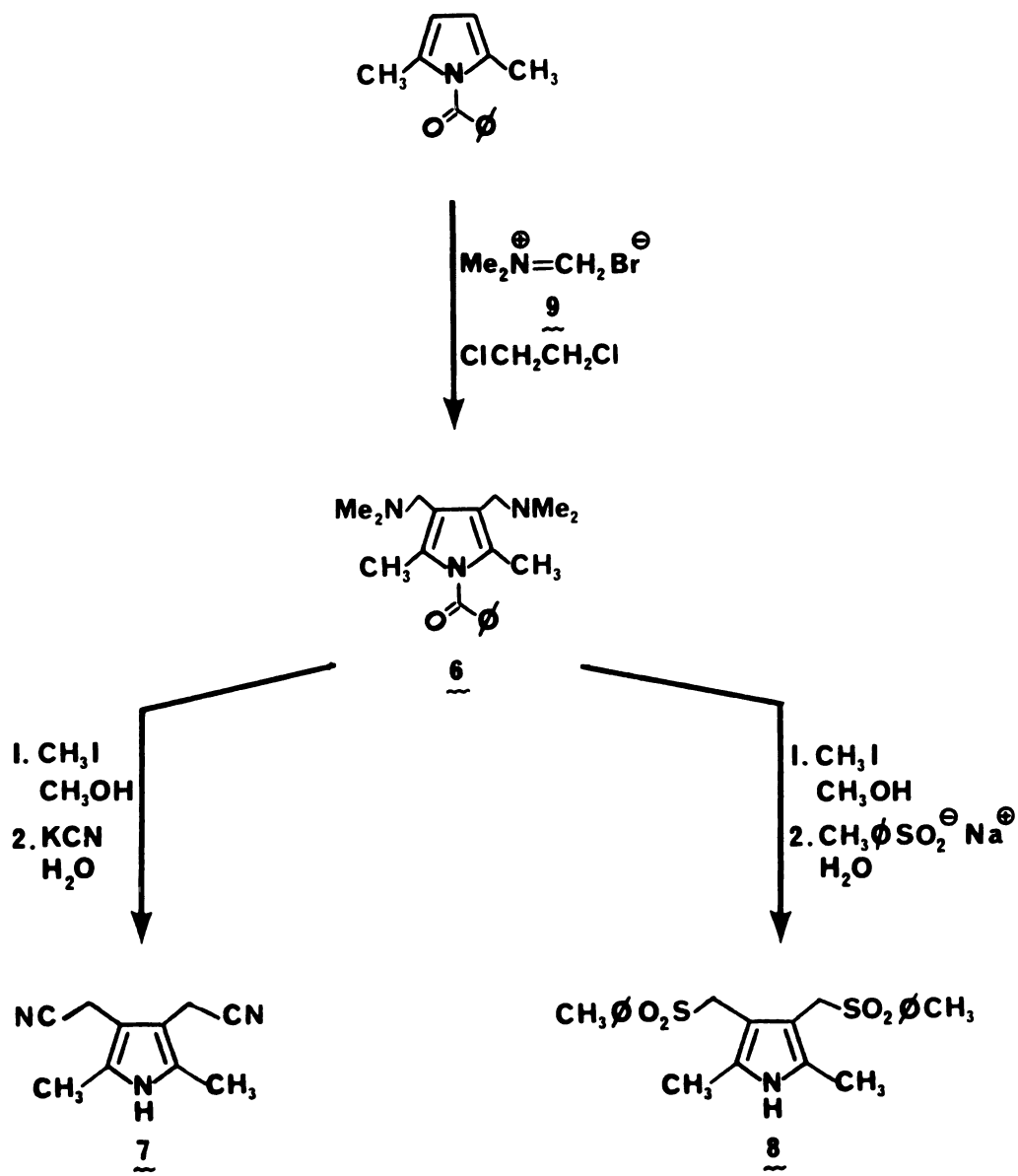


products. Heating of the corresponding *bis*(quaternary ammonium salt) with NaCN in DMSO reportedly affords a 40% yield of the desired nitrile.[38] The use of DMSO, however, makes isolation of the product tedious and attempts to

carry out the same reaction with KCN in water proved unsuccessful.

An alternate solution to this problem is summarized in Scheme 7. Quaternarization of the N-benzoylpyrrole 6 with

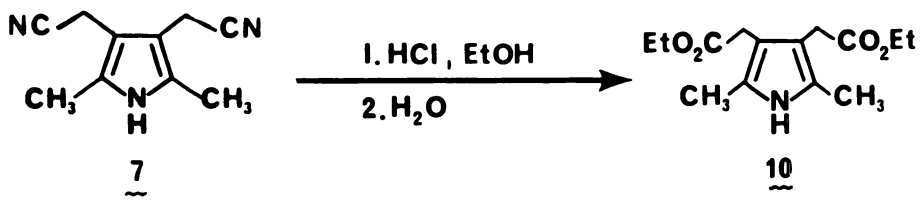
Scheme 7



methyl iodide followed by heating at 65°C with excess KCN or sodium *p*-toluenesulfinate led directly to dinitrile 7 (54%) and disulfone 8 (47%). None of the N-substituted benzoylnitrile or sulfone were observed and are presumably hydrolyzed in *situ*. Pyrrole 6 was conveniently prepared from N-benzoyl-2,5-dimethylpyrrole and the preformed Mannich reagent 9.[39] The difference in reactivity between the N-substituted and N-unsubstituted *bis*(quaternary ammonium salt) with KCN has not been explained.

Dinitrile 7 was examined as a possible precursor to the corresponding amide and esterpyrroles, however only the latter proved synthetically useful. As shown in Scheme 8

Scheme 8

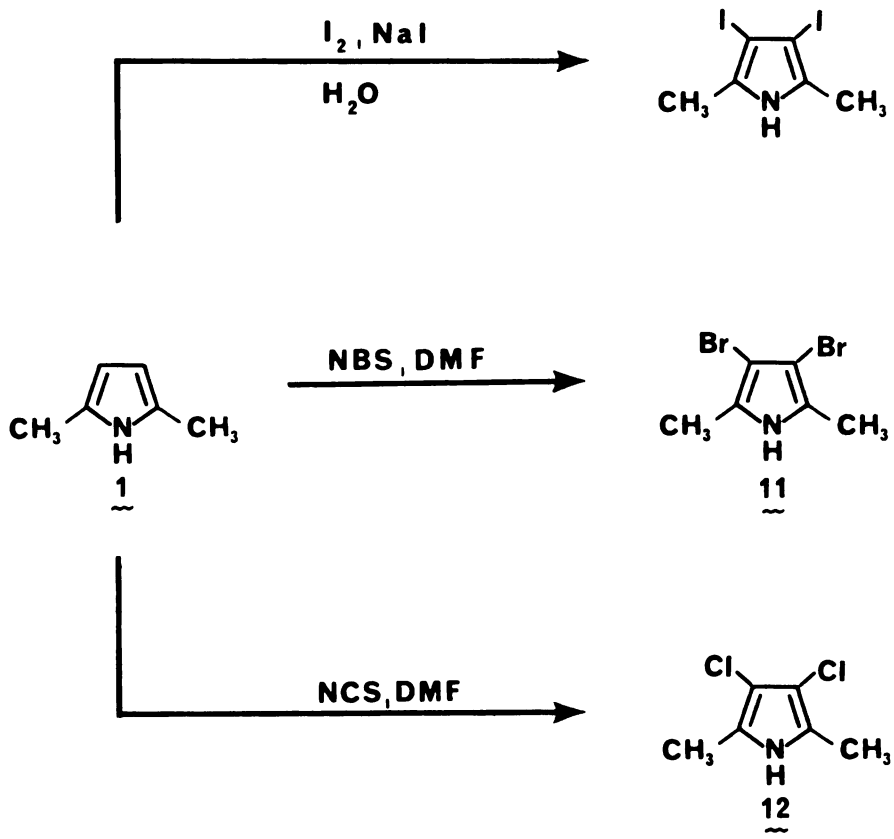


7 10

treatment of an ethanol solution of 7 with HCl gas over several days, followed by hydrolysis,[40] gave a 98% yield of diester 10.[41]

Scheme 9 summarizes the results of a third approach to 2,5-dimethyl-3,4-disubstituted pyrroles and involves the preparation of 3,4-dihalopyrroles 11 and 12 from 2,5-dimethylpyrrole. As reported by Treibs[42] 1 is readily diiodinated in the 3 and 4 positions with an aqueous solution

Scheme 9

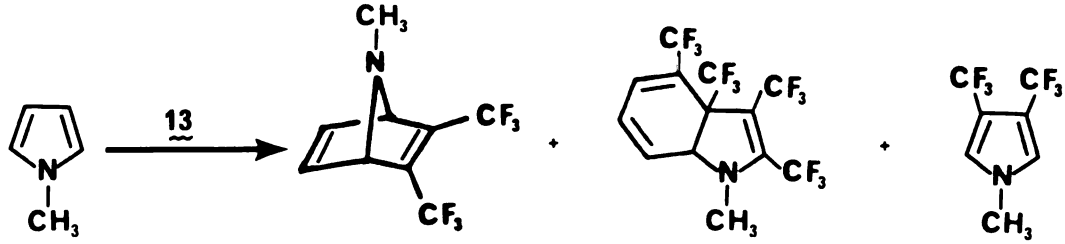


of KI_3. Similar chlorinations and brominations using chlorine, sulfuryl chloride or bromine are considerably less selective.[43] Recently N-bromosuccinimide (NBS) and N-chlorosuccinimide (NCS) have been reported as mild and selective pyrrole halogenating reagents in polar solvents such as THF or DMF.[44] Applying these methods it was found that the reactions of two equivalents of NBS or NCS in DMF with 1 give high yields of unstable dibromopyrrole 11 and dichloropyrrole 12. The ^{13}C NMR spectra of 11 and 12 display three resonances at δ 12.35, 96.72, 124.21, and 10.94,

107.30. 121.45 respectively, testifying to their symmetrical nature.

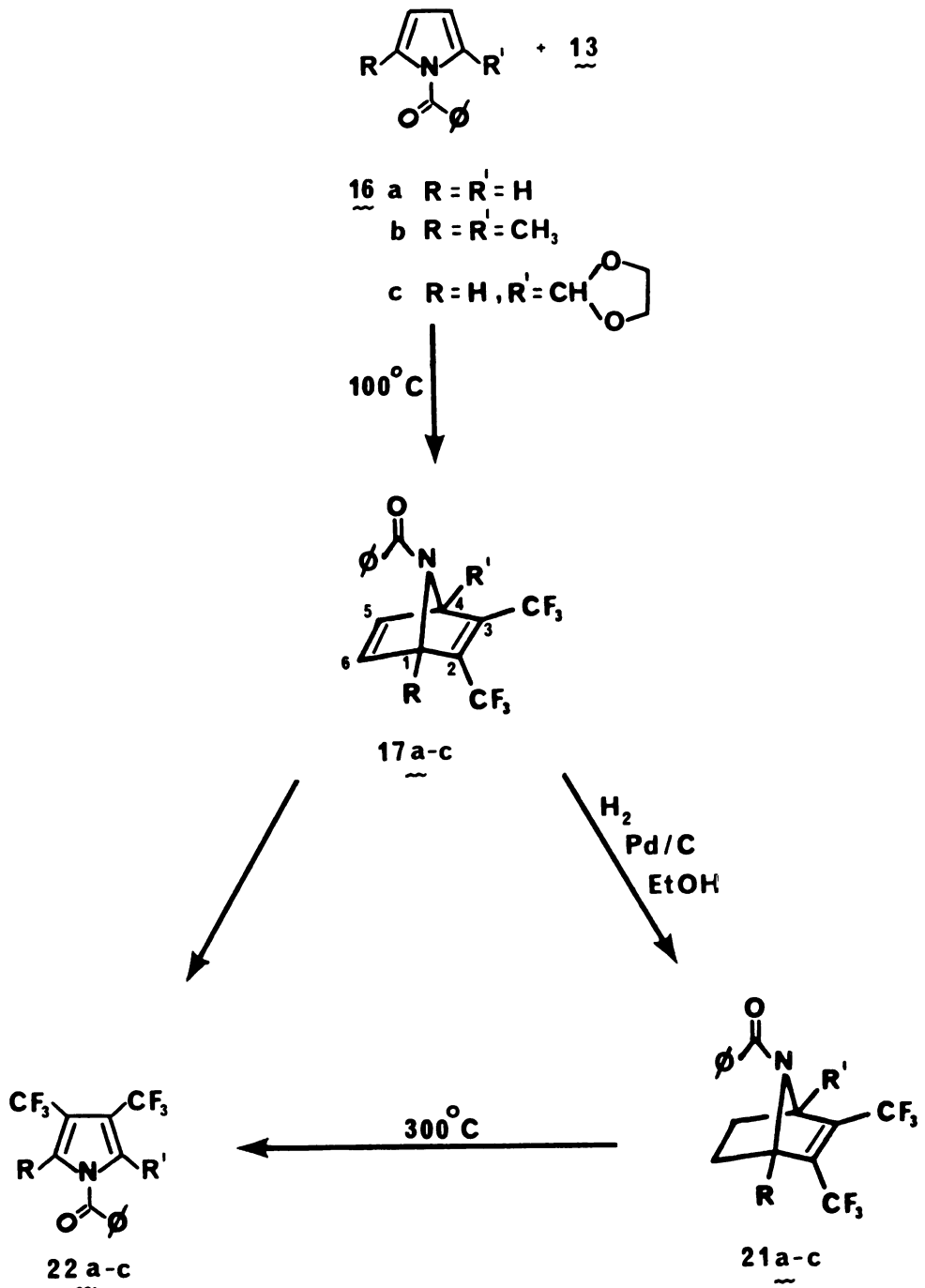
The introduction of ester substituents into the β-positions of the pyrrole ring can be achieved by Diels-Alder reactions of dialkyl acetylenedicarboxylates with various N- and C-substituted pyrroles followed by thermal cleavages of acetylene.[45-47] The efficient introduction of trifluoromethyl substituents with hexafluorobut-2-yne, 13, however, had not been realized at the onset of this study.[48] Wakselman reported the reaction of N-methylpyrrole with 13 to yield predominantly the N-methyl-7-azabicyclo[2.2.1]-hepta-2,5-diene 14 (30%) and the dihydroindole 15 (42%) along with only 2% of N-methyl-3,4-bis(trifluoromethyl)-pyrrole (Scheme 10).[49] Pyrrole itself gave lower yields

Scheme 10



of the N-unsubstituted dihydroindole (6%) in addition to 12% of the 1:1 Michael adduct of the diene and 13. No pyrrolic product was observed in the latter reaction.

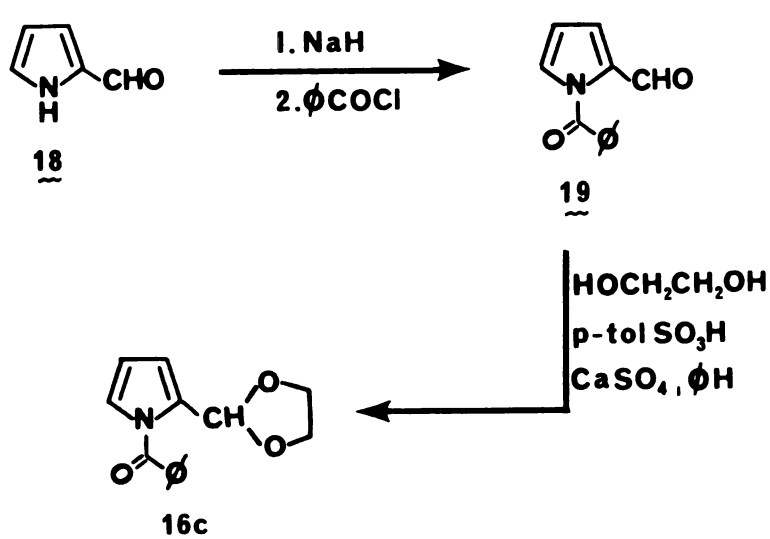
Scheme 11



The presence of an electron-withdrawing substituent on the pyrrole nitrogen facilitates the Diels-Alder reaction with dialkyl acetylenedicarboxylates as well as preventing the addition of a second molecule of dienophile.[47] A similar outcome was observed with the reactions of N-benzoylpyrroles 16a-c and hexafluorobut-2-yne. Quantitative yields of the mono adducts 17a-c were obtained on heating 16a-c with excess 13 inside a closed glass tube at 100°C (Scheme 11). Unlike N-methylpyrrole, none of the corresponding dihydroindole was observed.

The reported preparation[50] of the N-benzoyl-2-formylpyrrole precursor for 16c was found unsatisfactory. An alternate, more efficient procedure entails formation of the sodium salt of 18 with NaH followed by addition of one equivalent of benzoyl chloride. (Scheme 12). As expected

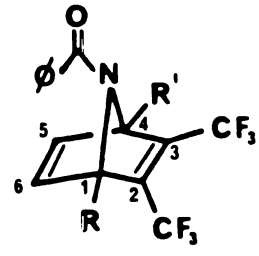
Scheme 12

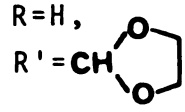


no Diels-Alder adduct was observed for the reaction of 19 with 13 and conversion to the less deactivated acetal 16c was required. This was accomplished by heating of 19 at 55-60°C with ethylene glycol in the presence of *p*-toluenesulfonic acid and anhydrous $CaSO_4$ in benzene. The conventional method of removing water from the reaction by azeotroping with benzene required prolonged heating at reflux and was accompanied by considerable destruction of the aldehyde. The use of $CaSO_4$ was very effective at the lower temperatures and greater than 95:5 ratios of product to starting material (as determined by ^1H NMR) were consistently obtained.

Table 3 summarizes the ^{13}C spectral data for the

Table 3. Selected ^{13}C NMR chemical shifts for N-benzoyl-2,3-*bis*(trifluoromethyl)-7-azabicyclo[2.2.1]-2,5-heptadienes 17a-c.

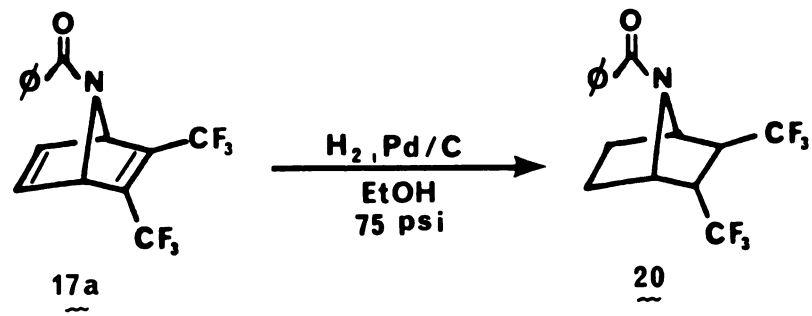


		1	4	2	3	5	6
17a	R=R'=H	66.59	69.76	140.90 (very broad)		142.65	144.48
17b	R=R'CH_3	78.44		150.90		148.00	
17c	R=H, R'= 	70.84	83.03	149.47	151.44	140.29	143.28

azanorbornene ring systems 17a-c. It is evident from the single absorptions recorded for each pair of carbons in adduct 17b that it possesses greater symmetry than either 17a or 17c. In 17a this can be accounted for by the benzamide existing in a preferred dipolar resonance form. In 17b steric interactions with the methyls prevent double bond character between the carbonyl carbon and the nitrogen, increasing the overall symmetry of the molecule. Adduct 17c is inherently less symmetrical than 17a or b and is expected to show six absorptions. ^{1}H NMR spectral data for the adducts support these observations.

Attempts to cleave acetylene from 17a,b by passing a benzene (or hexane) solution of the adduct through a column of glass beads at 300°C resulted in mixtures of starting material, retro Diels-Alder products 16a,b and only trace amounts of the desired pyrroles 22a,b. Weis reported the conversion of the 5,6-monoreduced Diels-Alder adduct of furan and 13 to 3,4-*bis*(trifluoromethyl)furan by thermal cleavage of ethylene.[51] A similar strategy was investigated here. Catalytic hydrogenation of adducts 17a-c with palladium on carbon at 70-80 psi resulted in the reduction of both C=C in 17a (Scheme 13) and only the 5,6 C=C in 17b,c (Scheme 11). The selective reduction of the less substituted C=C in 17a was possible using one equivalent of H_2 at atmospheric pressure. NMR spectral data for mono-reduced adducts 21a-c show a similar pattern with respect to symmetry as discussed for 17a-c. The subsequent cleavage of

Scheme 13

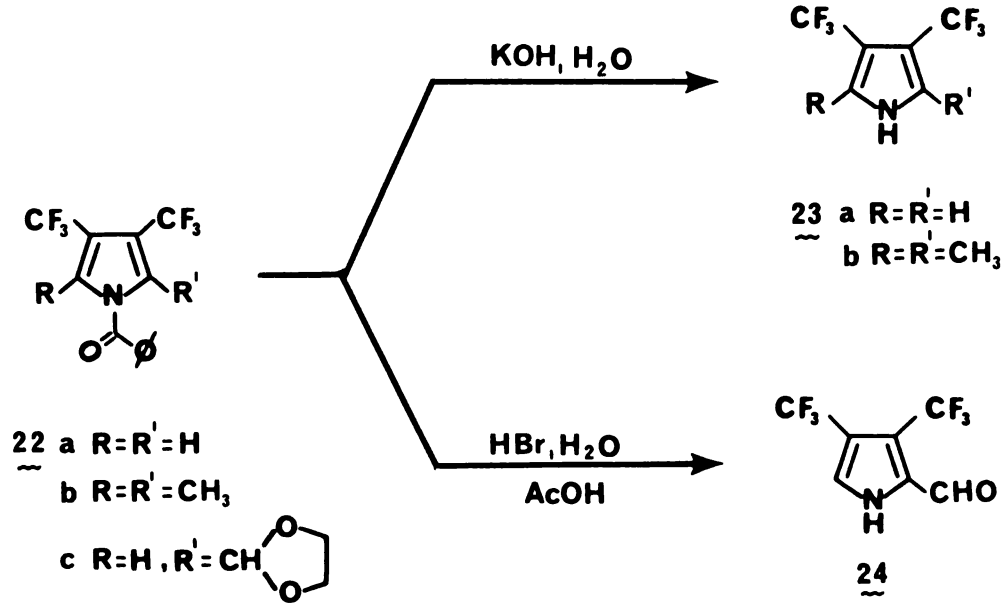


17a 20

ethylene from 21a-c occurred at 300°C affording N-benzoyl-pyrroles 22a-c in excellent yields.

Hydrolysis of the N-benzoyl protecting groups in 22a,b with aqueous KOH provided the desired 3,4-*bis*(trifluoromethyl)pyrrole, 23a, and 2,5-dimethyl-3,4-*bis*(trifluoromethyl)pyrrole, 23b, as volatile, crystalline solids (Scheme 14). Simultaneous hydrolysis of the acetal and the N-benzoyl group in 22c was accomplished by heating at 60°C in

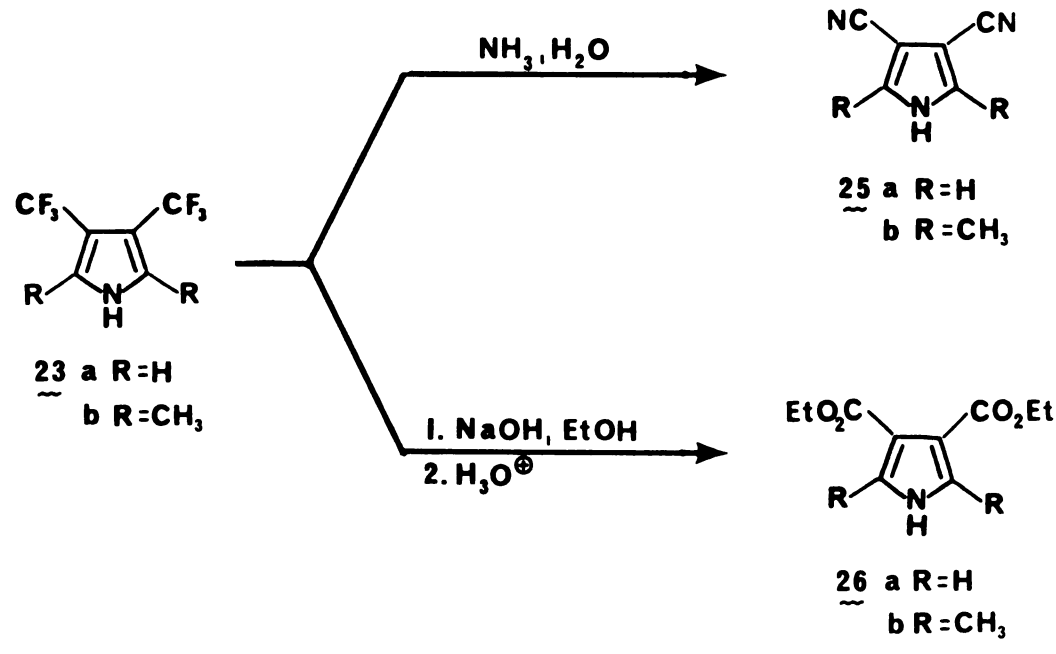
Scheme 14



aqueous acetic acid with HBr to give 2-formyl-3,4-*bis*-(trifluoromethyl)pyrrole 24.

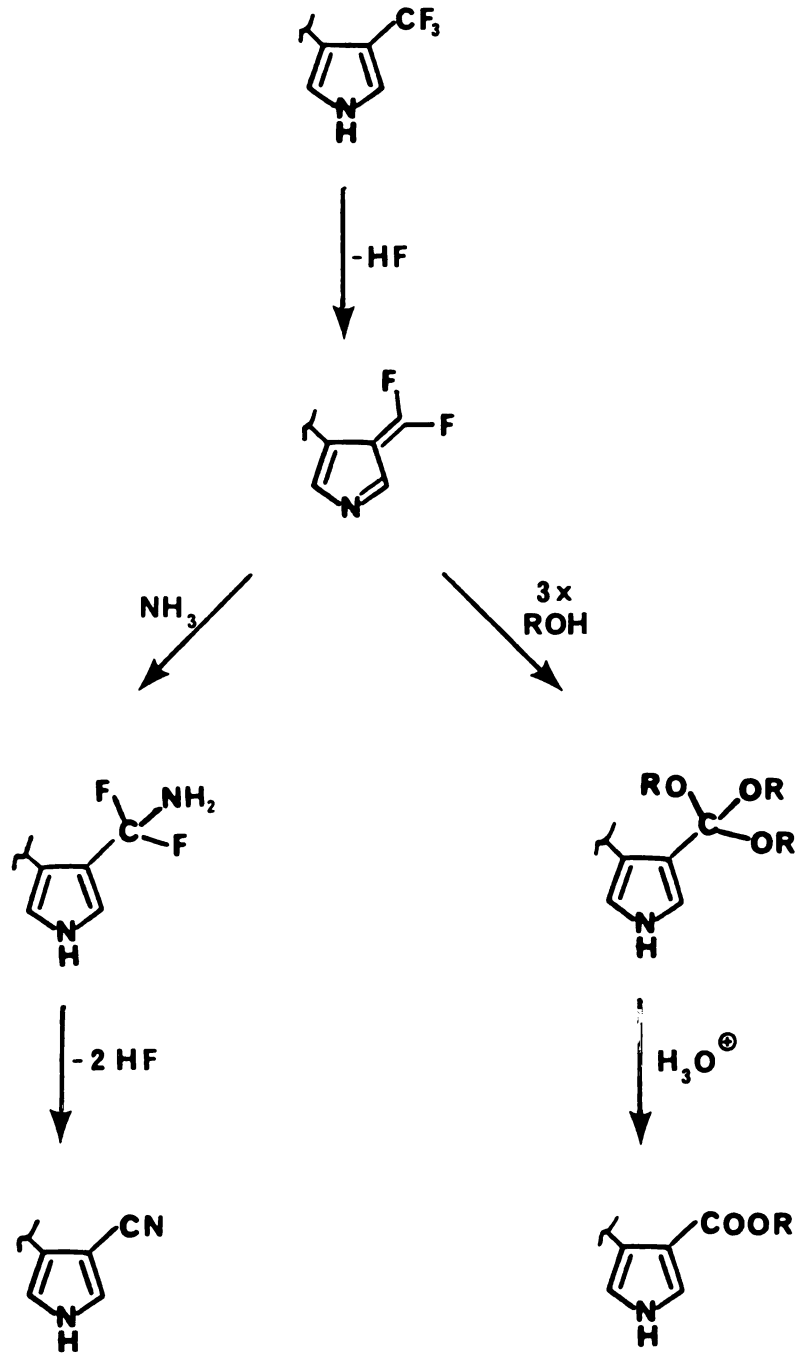
A recent report of the facile conversions of 2-(trifluoromethyl)imidazole to the corresponding ester and cyanoimidazole derivatives [52] prompted a similar study with pyrroles 23a,b. It was found that high yields of dicyanopyrroles 25a,b[53] are obtained on reaction of the trifluoromethylpyrroles with aqueous ammonia (Scheme 15). The structures of these pyrroles were readily confirmed by infrared and ^{13}C NMR. Similarly, heating of 23a,b with NaOH in ethanol provided the corresponding *bis*(orthoesters),

Scheme 15



which were hydrolyzed directly to give the known diesterpyrroles 26a,b[47,54] in 90% and 89% overall yields. A reasonable mechanism for these reactions is outlined in Scheme 16.

Scheme 16.

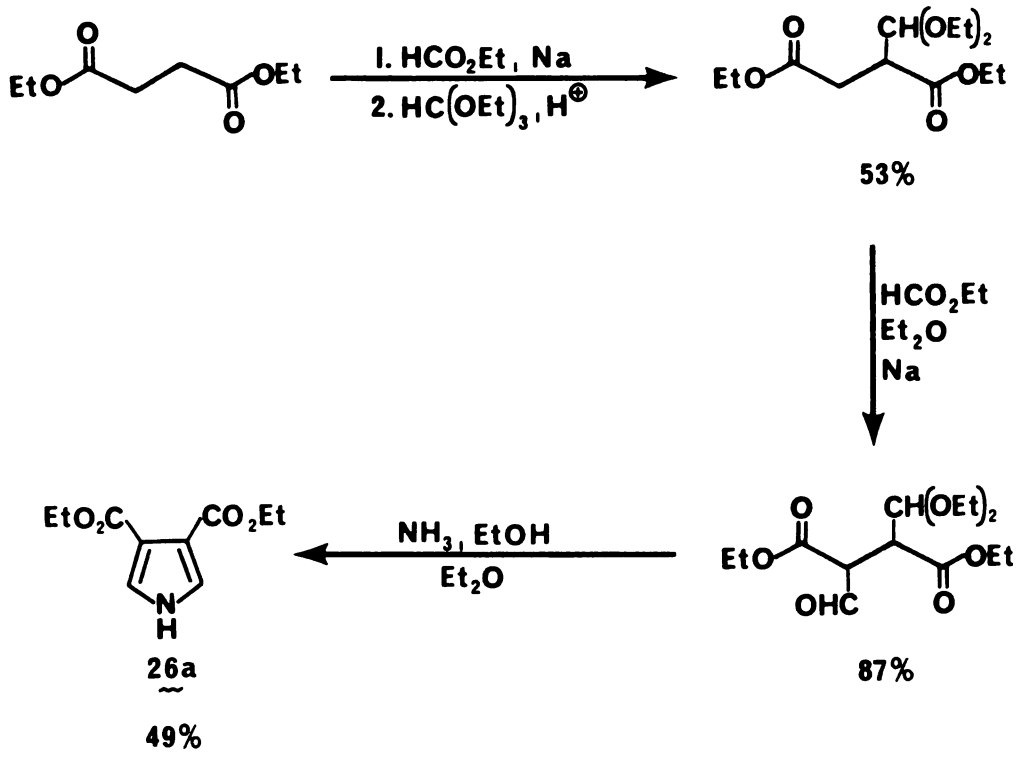


Under the basic conditions loss of HF generates an azafluvene intermediate which can add either one equivalent of ammonia, followed by further elimination of HF to provide a nitrile, or it can add three equivalents of alcohol (with concurrent elimination of two more equivalents of HF) to provide an orthoester, which may be hydrolyzed to the ester-pyrrole.

Two methods for the preparation of 3,4-*bis*(carboxamide)-pyrroles have been investigated. The first is summarized in Scheme 18 and involves the conversion of 3,4-*bis*(carbethoxy)pyrrole 26a to a series of α-unsubstituted carboxamide pyrroles 31a-d. The second method (Scheme 20) entails the preparation of 2,5-dimethyl-3,4-*bis*(N,N-dimethylcarboxamide)-pyrrole 37 from N,N-dimethylacetylacetamide, 35, a starting material which already incorporates the desired amide functionality.

Several syntheses of diester pyrrole 26a have been reported. Among the most practical are van Leusen's reaction of tosylmethylisocyanide with dimethyl fumarate[55] and the pyrolyses of the Diels-Alder adducts of dialkyl acetylenedicarboxylates and various N-substituted pyrroles (see page 16). Kornfeld described the cyclization of 1-diethyl-1-formyl-2-diethyoxymethylsuccinate to 3,4-furan, thiophene and pyrrole carboxylic esters (Scheme 17).[56] Modest yields are obtained for the cyclization as well as the three step preparation of the precursor. A single step

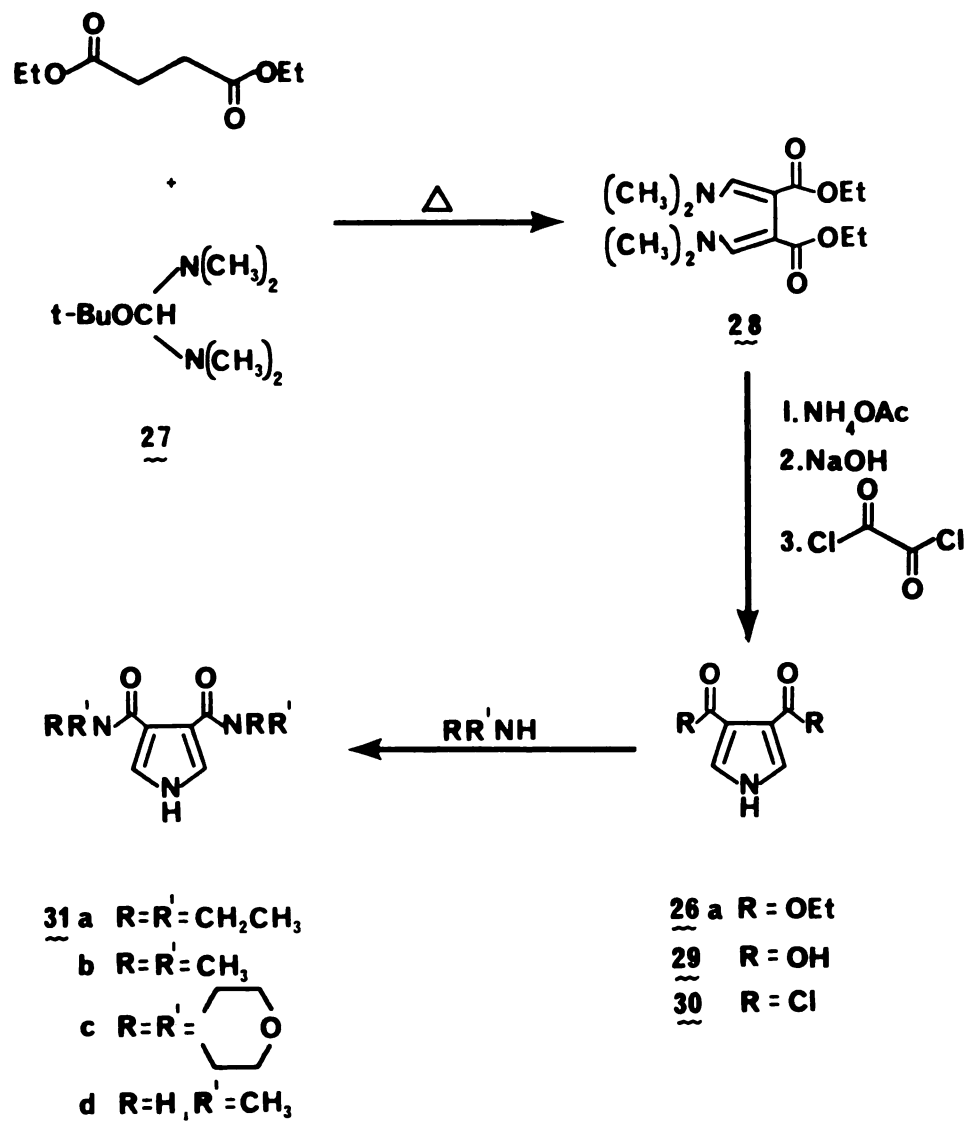
Scheme 17



synthesis of bisenamine 28 from diethylsuccinate by Bredereck[57] allowed a much more direct route to a similar dialdehyde equivalent. (Scheme 18). The bisenamine was prepared in 63% yield by heating a mixture of diethyl succinate and excess aminal ester 27[58] at 160°C. Subsequent reaction with ammonium acetate in 95% ethanol resulted in near quantitative cyclization, and completed an efficient two-step synthesis of 26a.

Basic hydrolysis of 26a to 3,4-dicarboxypyrrole 29 followed by heating with oxalyl chloride provided diacid chloride 30.[47] The usual conversion to amides by addition of the acid chloride to aqueous amines[59] was unsatisfactory.

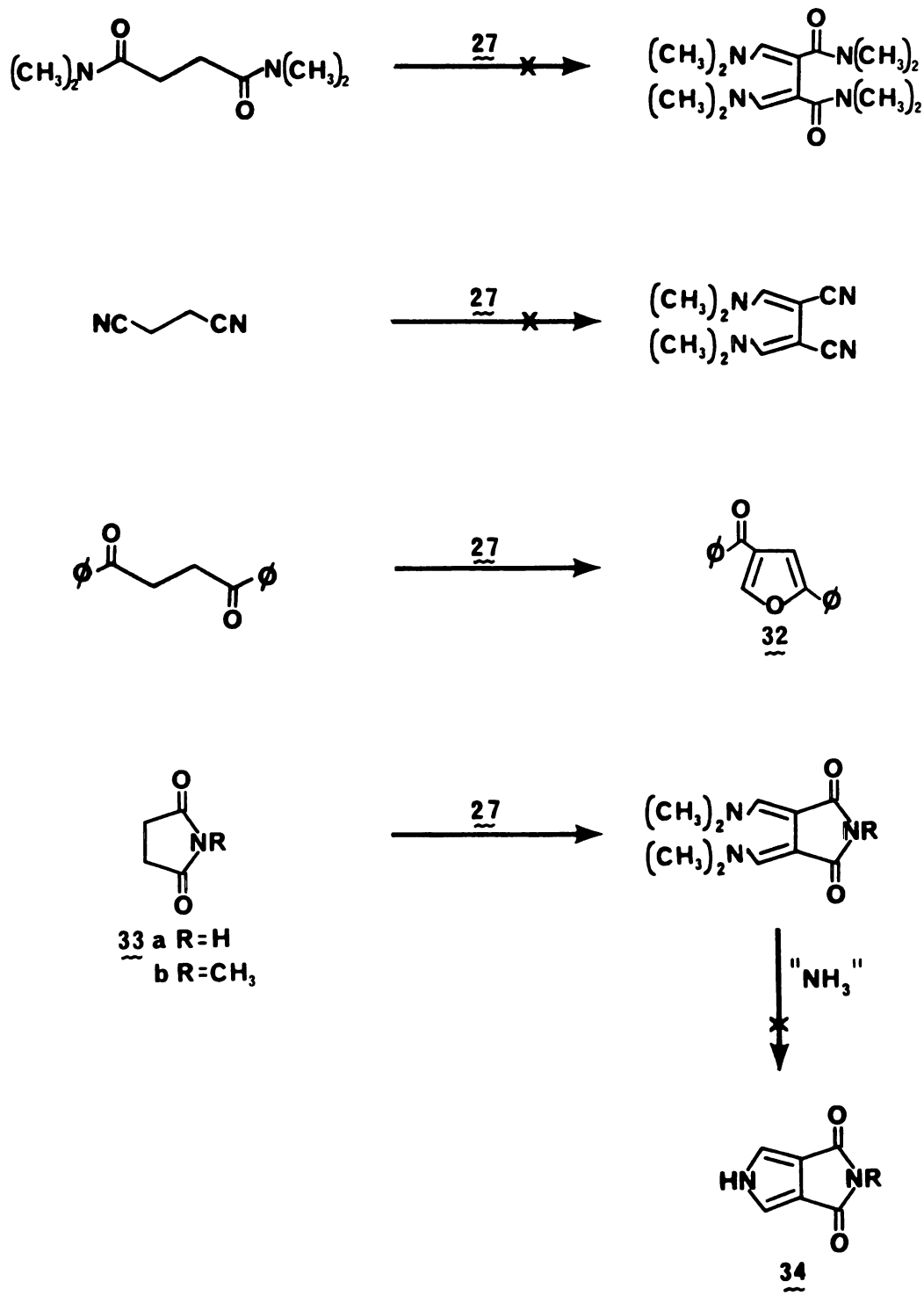
Scheme 18



Instead excellent yields of diamides 31a-d were obtained with the use of the corresponding anhydrous amines. For ease of workup it was essential that excess oxalyl chloride was removed prior to aminolysis. This was accomplished most efficiently by preparation of 30 in toluene, followed by evaporation of the oxalyl chloride under reduced pressure.

Scheme 19 summarizes the results of the attempted formation and cyclization of other bisenamines. The reaction

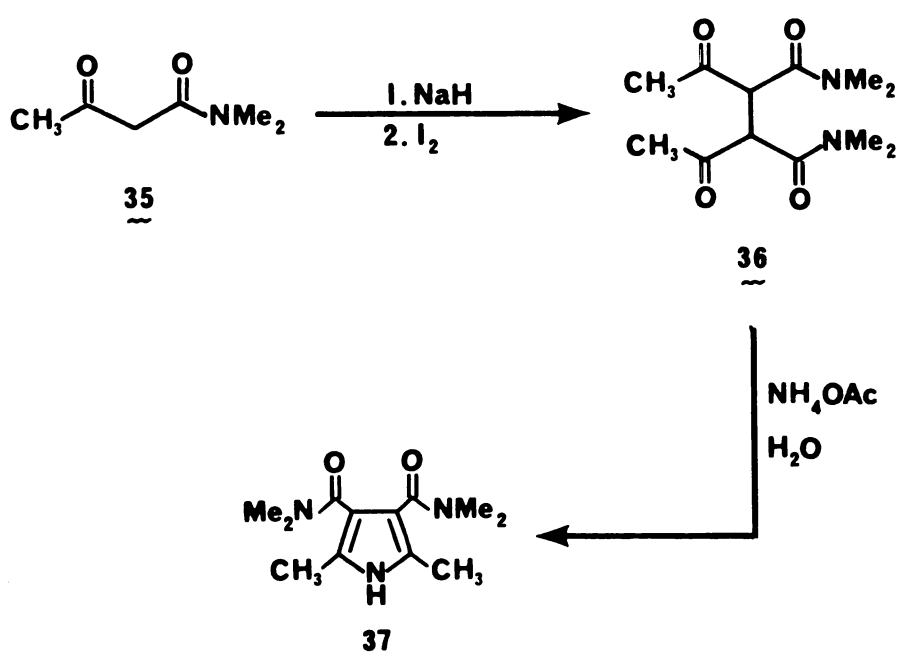
Scheme 19



of 27 with N,N-tetramethylsuccinamide, a potential precursor to pyrrole 31b, and succinonitrile resulted in the recovery of starting material and unidentified products. Only furan 32 could be isolated from the reaction of dibenzoylethane and excess 27 and is presumably formed from the cyclization of a monoenamine precursor. The bisenamines of succinimides 33a,b were prepared as described by Bredereck,[57] but conversion to pyrroles 34 could not be effected.

The second amide synthesis, modeled after a preparation of 2,5-dimethyl-3,4-*bis*(carbethoxy)pyrrole by Knorr,[54] is summarized in Scheme 20. Deprotonation of N,N-dimethylacetyl-

Scheme 20



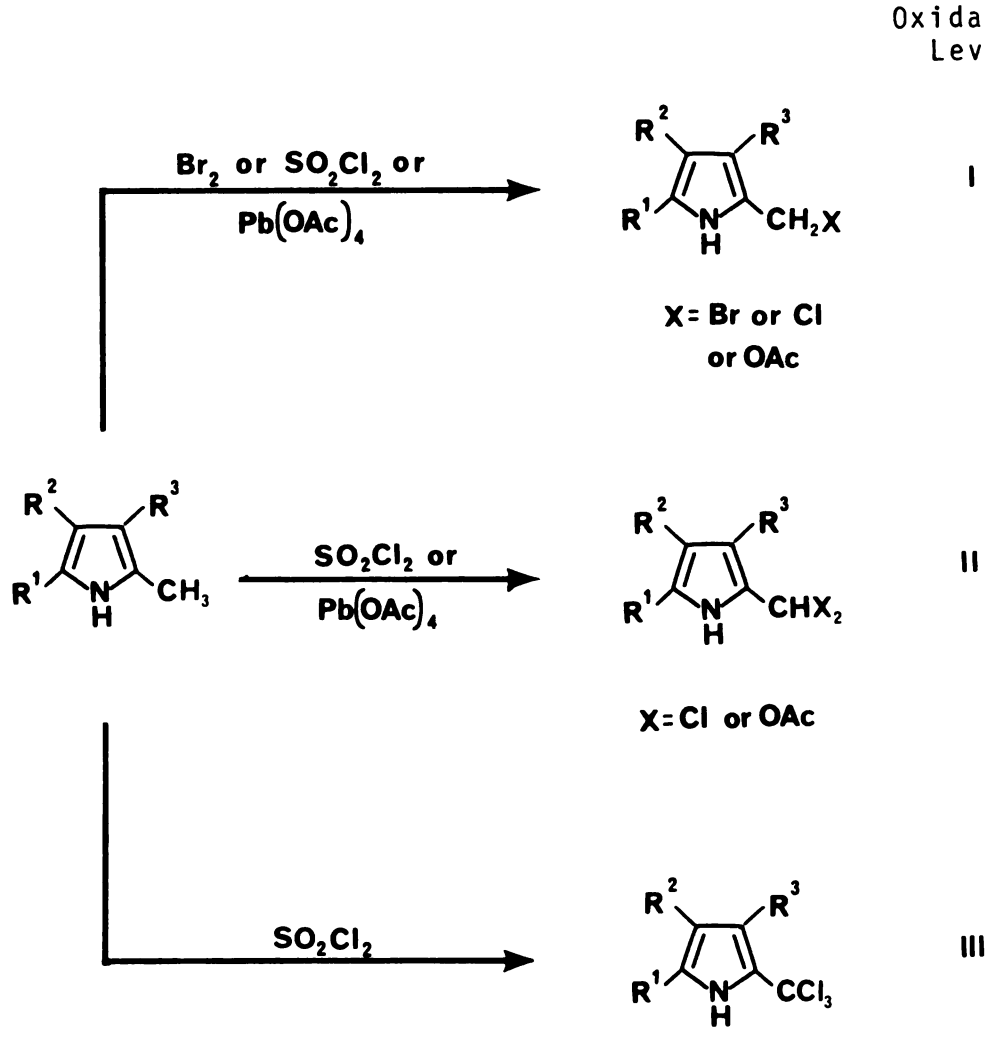
acetamide, 35, with NaH in ether, followed by addition of iodine gave dimer 36 as a mixture of diasteromers. The

mixture was identified on the basis of two sets of four singlets in the ^{1}H NMR (δ 2.13, 2.16; 2.91, 2.95; 3.23, 3.33; 4.66, 4.70). Due to the heterogeneous nature of the reaction mixture best results were obtained with finely divided NaH and excess iodine as well as vigorous mechanical stirring. Heating of purified dimer 36 with ammonium acetate in water allowed near quantitative conversion to pyrrole 37. Isolation of 36, however, was not necessary and a similar treatment of the crude dimer provided a 40% overall yield of 37 along with a considerable amount of starting material 35 (65% overall yield of 37 based on consumption of 35).

B. OXIDATION OF 2,5-DIMETHYLPYRROLES

Methyl substituents in the α-position of pyrroles can be oxidized with a variety of reagents.[60-62] Scheme 21 summarizes the most commonly used reagents for each oxidation level. Lead tetraacetate ($Pb(OAc)_4$) in acetic acid is the method of choice for mono-oxidation.[17,63] It avoids most of the disadvantages associated with bromine and sulfuryl chloride (SO_2Cl_2), which include ring oxidation of unsubstituted positions, formation of HBr or HCl, and the general instability of the halomethylpyrroles. The second oxidation level is best attained with two equivalents of SO_2Cl_2[64] or excess $Pb(OAc)_4$.[65] Temperatures near 90°C are normally required for a second equivalent of $Pb(OAc)_4$ to react and

Scheme 21



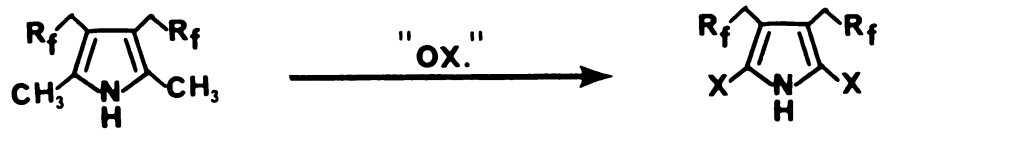
further oxidation is not observed. Complete oxidation (Level III) is most commonly effected with excess SO_2Cl_2.[21,64,66]

It has been observed that β-alkyl substituents are inert to oxidation.[60] Recently however, a high yield bromination of the β-methyls in 2,5-dicarbethoxy-3,4-dimethylpyrrole (Br_2, CCl_4, 70°C) was reported[67] and side reactions with β-alkyl substituents can thus not be completely precluded.

Described below are the α-methyl oxidations and subsequent reactions of the various 2,5-dimethylpyrroles prepared in Section A. Attention is focused on the preparation of first and third oxidation level products as well as the hydrolysis and *bis*decarboxylation of the latter in search of synthetically useful porphyrin precursors. Initial studies were conducted on 2,5-dimethyl-3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole, 2a. It was found that oxidation of the α-methyls could be successfully controlled to give every possible oxidation level, depending on reagents and reaction conditions employed. In no case was oxidation of the β-methylenes observed.

Stirring a solution of 2a with an excess of $Pb(OAc)_4$ in acetic acid at room temperature provided the stable *bis*(acetoxymethyl) derivative 38a in nearly quantitative yield (Scheme 22). The ^{1}H NMR of 38a included a singlet at

Scheme 22



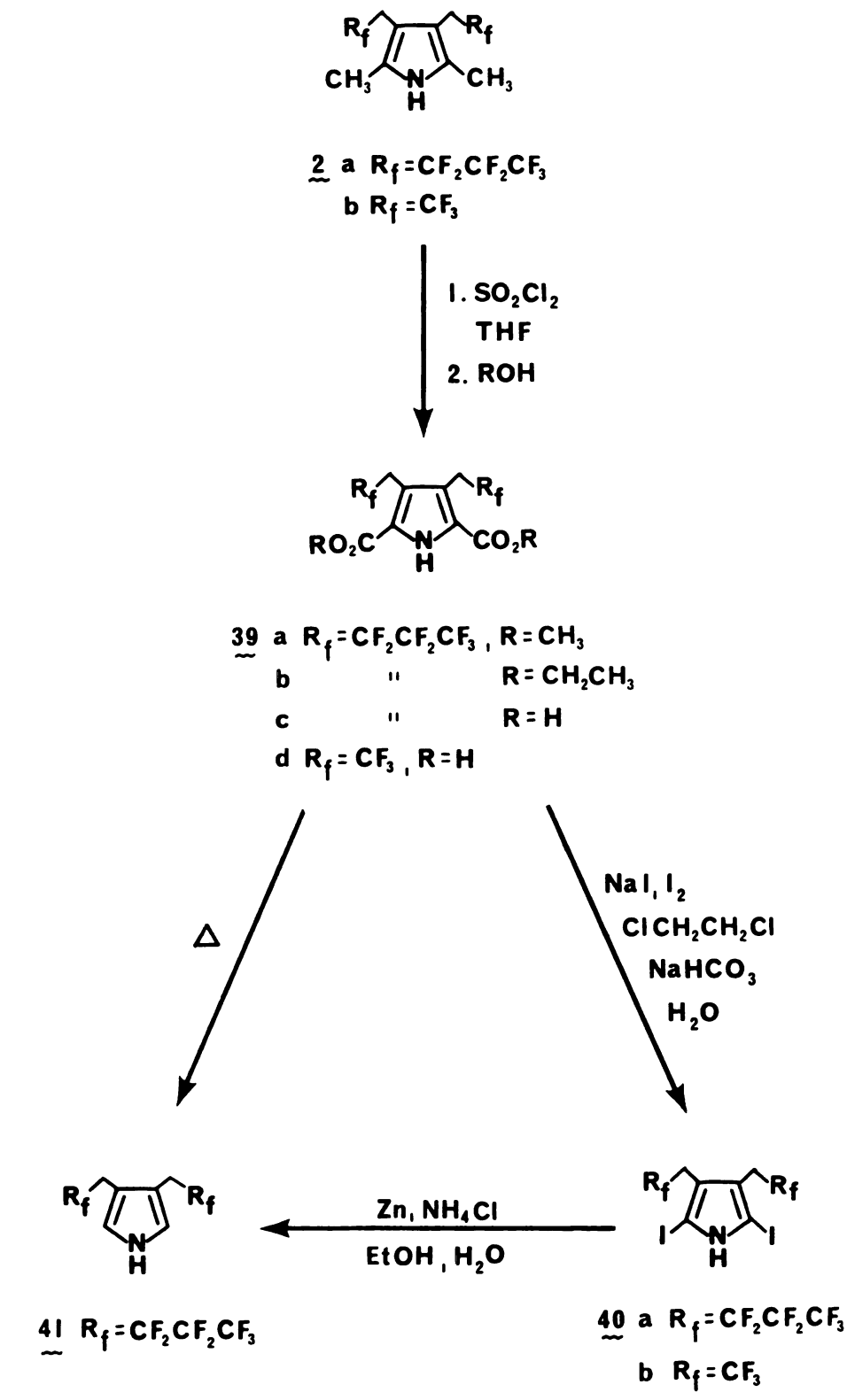
2 a R_f=$CF_2CF_2CF_3$
b R_f=CF_3

38 a R_f=$CF_2CF_2CF_3$, X=CH_2OAc
b " X=CH_2Br
c " X=CH_2Cl
d " X=$CHCl_2$
e " X=CHO
f R_f=CF_3, X=CH_2OAc

δ 5.02, testifying to the presence of an acetoxymethylene. The formation of other mono-oxidation derivatives proved to be less practical. *Bis*(bromomethyl)pyrrole 38b, prepared by refluxing a solution of 2a and N-bromosuccinimide, rapidly decomposed during isolation attempts. Identification was possibly only by ^{1}H NMR (CCl_4) of the crude reaction mixture. The spectrum exhibited a broad triplet at δ 3.20 (J=20 Hz) for the fluoroalkylmethylenes and a singlet at δ 4.40 for the bromomethyl substituents. Treatment of 2a with two equivalents of SO_2Cl_2 in CH_2Cl_2 at 0°C allowed formation of 38c (^{1}H NMR: broad triplet at δ 3.22 and singlet at δ 4.53), however contamination with either α-methyl- (at δ 2.30) or dichloromethyl- (at δ 6.13) pyrroles could not be avoided. Dichloronation of each methyl in 2a was controlled selectively with excess SO_2Cl_2 at 0-3°C to provide high yields of the 2,5-*bis*(dichloromethyl)-pyrrole 38d as a stable solid. The structure of 38d was confirmed by hydrolysis in aqueous THF to 2,5-diformyl-pyrrole 38e.

At low temperatures (0-3°C) trichlorination of 2a was not observed, however in refluxing THF[68] excess SO_2Cl_2 readily oxidized both α-methyl substituents to the corresponding trichloromethyls. The best procedure for this oxidation entailed rapid addition of SO_2Cl_2 to the dimethylpyrrole, dissolved in a minimum amount of refluxing THF (Scheme 23). Hydrolysis of the *bis*(trichloromethyl)pyrrole was studied in several solvents and isolation of the

Scheme 23


Rf
Rf
CH3
N
H
CH3
2 a Rf=CF2CF2CF3
b Rf=CF3
1. SO2Cl2
THF
2. ROH
RO2C
CO2R
39 a Rf=CF2CF2CF3, R=CH3
b " R=CH2CH3
c " R=H
d Rf=CF3, R=H
Δ
NaI, I2
ClCH2CH2Cl
NaHCO3
H2O
Zn, NH4Cl
EtOH, H2O
I
41 Rf=CF2CF2CF3
40 a Rf=CF2CF2CF3
b Rf=CF3

the intermediate was found unnecessary in all cases. Direct addition of hot 95% MeOH or EtOH to the reaction mixture gave excellent yields of the corresponding esters 39a (97%) and 39b (87%). Similarly, the 2,5-dicarboxypyrrole 39c was obtained in 80% yield on hydrolysis with hot aqueous THF. In an attempt to increase the overall yield of diacid 39c, the conversion of 39a to 39c was examined. The most efficient procedure involved S_N2 dealkylation of the ester with LiI in DMF,[69] but yields never exceeded 50-60%.

The final transformation investigated involved conversion of 39c to the 2,5-unsubstituted pyrrole 41. Thermal decarboxylation[70] at elevated temperatures (240-250°C) was accompanied by considerable destruction of the pyrrole nucleus. A more practical procedure proved to be iodinative decarboxylation with sodium triiodide in $ClCH_2CH_2Cl$ and water,[71] providing near quantitative conversion to diiodopyrrole 40a. As indicated by Paine[72] the two-phase system helps prevent formation of pyrrole-iodine charge-transfer complexes[42] by extraction of the iodopyrrole into the organic phase. Like most iodopyrroles, 40a is sensitive to light and required protection from direct illumination.

^1H NMR was of little value in confirming the structure of 40a, but the pyrrole was ideally suited for ^{13}C NMR analysis. Figure 1 shows the proton decoupled ^{13}C NMR spectrum of 40a in $CDCl_3$. It displays a characteristic triplet at δ 29.1 for the two methylenes (long range

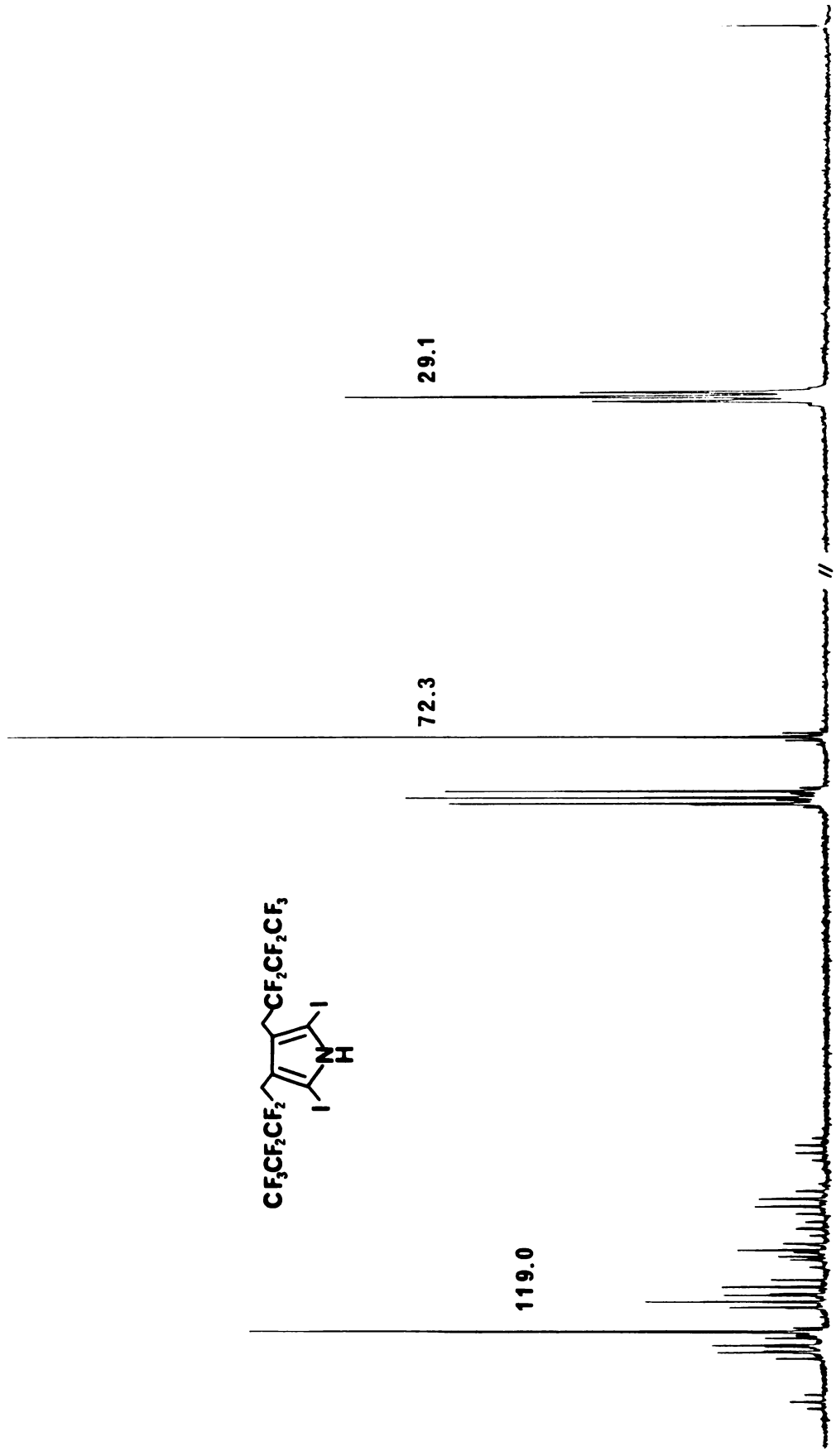


Figure 1. ^{13}C NMR spectrum of 2,5-diiodo-3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole.

coupling with adjacent fluorines), as well as singlets at δ 72.3 and 119.0 for the α- and β-pyrrole carbons. The unusual chemical shift of the α-carbons is not unexpected, since iodine is known to cause large up-field shifts in the ^{13}C NMR ("heavy atom effect"[73]). Figure 2 shows an expanded and particularly unobstructed view of the heptafluoropropyl carbons in 40a. Long-range ^{13}C-^{19}F coupling generates a complex coupling pattern, which is recognized as a triplet of triplets assigned to C-2, a triplet of quartets of triplets assigned to C-3, and a quartet of triplets assigned to C-4. Geminal and vicinal coupling constants are on the order of 260 and 40 Hz respectively. All pyrroles bearing heptafluorobutyl substituents display a similar coupling pattern.

The reduction of diiodopyrrole 40a to the 2,5-unsubstituted pyrrole 41 was readily accomplished by either catalytic hydrogenation with platinum oxide[74] or by reduction with zinc dust and ammonium chloride in aqueous ethanol.[42] Strong evidence for the structure of 41 was provided by the appearance of a doublet at δ 6.77 in the ^{1}H NMR.

The $Pb(OAc)_4$ oxidation of *bis*(trifluoroethyl)pyrrole 2b proved to be as efficient as the oxidation of 2a, affording a near quantitative yield of the *bis*(acetoxymethyl) derivative 38f (Scheme 22). Exhaustive oxidation with SO_2Cl_2 followed by hydrolysis to the diacid, however, resulted in low yields (45%), rendering the overall sequence from 2b to

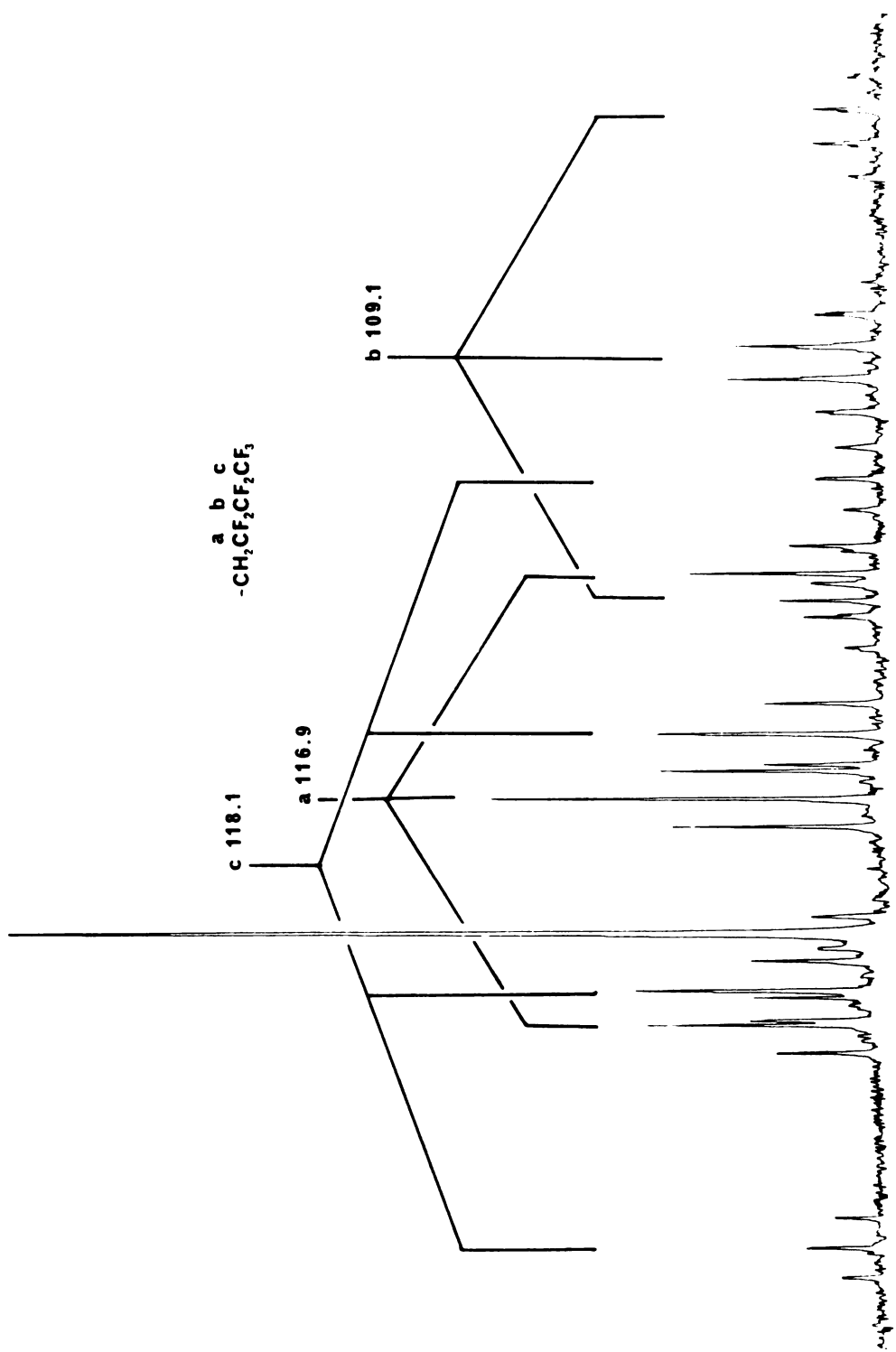


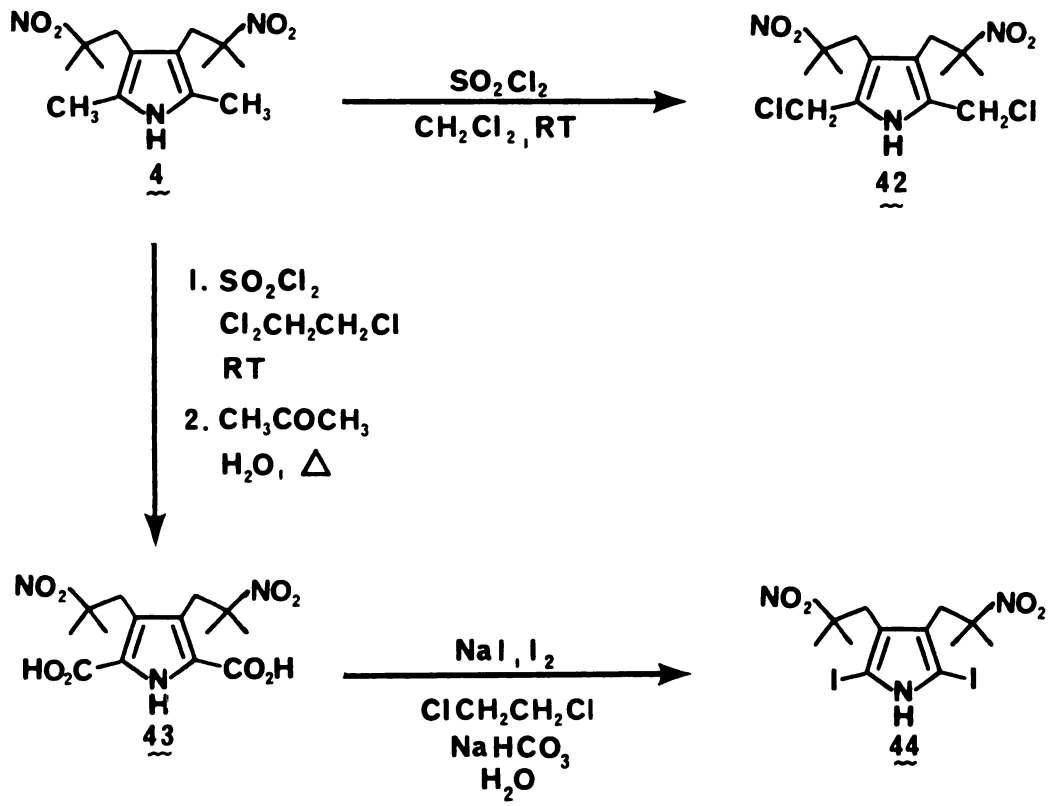
Figure 2. Expanded ^{13}C NMR of heptafluoropropyl carbons in 2,5-diiodo-3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole.

40b, despite facile conversion to diiodopyrrole (97%), impractical.

The β-substituents of the remaining 3,4-CH_2R-2,5-dimethylpyrroles are considerably more reactive toward oxidation than the polyfluoroalkyl groups in 2a,b. For cyanomethylpyrrole 7 neither selective mono-oxidation with $Pb(OAc)_4$ nor trichlorination with SO_2Cl_2 proved to be feasible. Although no identifiable products were isolated in these reactions, oxidation α to the cyano group is believed to be responsible. Selective oxidation of the α-methyls in carbethoxymethylpyrrole 10 was only possible with $Pb(OAc)_4$. However, serious contamination with aldehydes could not be avoided (^1H NMR of the crude reaction mixture contained peaks at δ 5.06 for CH_2OAc and at δ 9.60 for CHO). The $Pb(OAc)_4$ oxidation of nitroalkylpyrrole 4 (two equivalents or excess $Pb(OAc)_4$, HOAc, 25°C) gave similar results with ^1H NMR indicating products containing aldehyde, acetoxymethyl and methyl substituents. Aldehydes are normally not observed with $Pb(OAc)_4$ at ambient temperature[60] and further investigation is required to explore the scope of this reaction.

The use of SO_2Cl_2 allowed more reliable oxidation of 4. Slow addition of two equivalents of SO_2Cl_2 to 4 in CH_2Cl_2 at 25°C gave a blue solution which on evaporation to dryness and analysis by ^1H and ^{13}C NMR revealed surprisingly clean conversion to the *bis*(chloromethyl) derivative 42 (Scheme 24). Unfortunately 4 proved to be quite labile

Scheme 24



and decomposition (as indicated by the blue color) occured rapidly. Trichlorination of both methyls was possible with six equivalents of SO_2Cl_2 in $ClCH_2CH_2Cl$ at 25°C. It was found essential to add the oxidant as rapidly as possible to avoid decomposition of the intermediate chloromethylpyrrole (a blue color, which rapidly dissipated, was noticed at the first instant of SO_2Cl_2 addition). Hydrolysis in aqueous acetone, followed by iodinative decarboxylation under the conditions employed for polyfluoroalkylpyrroles 39c,d, gave diiodopyrrole 44. The structure of 44 was confirmed by ^{13}C NMR, which exhibited three peaks for the nitroalkyl

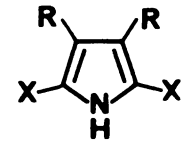
substituents (δ 26.20, 38.39, 89.74) and single peaks for the the α (δ 72.86) and β (δ 124.25) pyrrole carbons. Similar to diiodopyrrole 40a, the α carbons are shifted upfield due to the "heavy atom effect" of the iodines.

The oxidation of sulfone 8 with six equivalents of SO_2Cl_2 did not provide the desired product. This is most likely a result of the low solubility of 8 in solvents suitable for SO_2Cl_2 oxidation (i.e., Et_2O, THF, HOAc, $ClCH_2CH_2Cl$). Despite the low solubility, the oxidation of 8 with excess $Pb(OAc)_4$ in acetic acid (25°C, 70 h) allowed efficient conversion to the *bis*(acetoxymethyl) derivative 45. The ^1H NMR of 45 shows in addition to peaks for the *p*-tolysulfonylmethyl substituents singlets at δ 2.01 and 4.70 (in the ratio of 3:2), indicative of acetoxymethyl substituents.

Table 4 summarizes the oxidations of halo-, carbethoxy- N,N-dimethylcarboxamide- and trifluoromethyl-2,5-dimethylpyrroles. Mono-oxidation of both α-methyls with $Pb(OAc)_4$ was feasible for all cases except the *bis*(trifluoromethyl)pyrrole. Higher than normal reaction temperatures, however, were required for 26b and 37. Halopyrroles 11 and 12 are sensitive to excess oxidant and slightly less than two equivalents of $Pb(OAc)_4$ were used in each case.

Under no conditions could the *bis*(acetoxymethyl) derivative of 23b be prepared. Excess $Pb(OAc)_4$ at 100°C for 130 h provided only 8% of 2-acetoxymethyl-3,4-*bis*(trifluoromethyl)-5-methylpyrrole. It was isolated from the

Table 4. Oxidations of halo-, carbethoxy-, N,N-dimethylcarboxamide- and trifluoromethyl-2,5-dimethylpyrroles.



R	X	Pyrrole	Method	% Yield
I	CH_2OAc	46	A	95
Br	CH_2OAc	47	A[a]	96
Cl	CH_2OAc	48	A[a]	90
COOEt	CH_3	26b		
	CH_2OAc	49	B	74
	COOH	50	C	50
	I	51	D	90
$CONMe_2$	CH_3	37		
	CH_2OAc	52	E	b
	COOH	53	F	<15
	I	54	D	<15
CF_3	CH_3	23b		
	CH_2Cl	55	G	99
	CHO	56	H	80

[a] 1.75h

[b] not isolated

Method A: $Pb(OAc)_4$ (1.95 equiv), HOAc, 25°C, 4 h.
B: $Pb(AOc)_4$, HOAc, 90°C, 48 h. C: Br_2, SO_2Cl_2, HOAc, 60°C, 1 h; H_2O, 60°C, 1 h. D: NaI, I_2, $NaHCO_3$, H_2O, $ClCH_2CH_2Cl$, 85°C, 1 h. E: $Pb(OAc)_4$, HOAc, 50°C, 26 h. F: SO_2Cl_2, $ClCH_2CH_2Cl$, 25°C, 15 h; H_2O, 60°C, 1 h. G: SO_2Cl_2, $ClCH_2CH_2Cl$, 0-3°C, 10 h. H: Br_2, SO_2Cl_2, 3-25°C, 2 h; H_2O, 90°C, 28 h.

tarry reaction mixture by column chromatography (silica: hexane-CH_2Cl) and identified by mass spectrometry (M^+, 289) and ^1H NMR (broad singlets at δ 5.13 and 2.36 and a sharp singlet at δ 2.15). SO_2Cl_2 mono-chlorination of 23b proved to be considerably more effective, affording a high yield of the stable *bis*(chloromethyl)pyrrole 55.

The exhaustive chlorination, hydrolysis, and iodinative decarboxylation of pyrroles 26b, 37 and 23b were studied under a variety of conditions. The most effective procedure for the conversion of carbethoxypyrrole 26b to diacid 50 (M^+ at 299; ^1H NMR: triplet at δ 1.35 and quartet at δ 4.38) paralleled the reported oxidation of Knorr's pyrrole with SO_2Cl_2 and bromine in acetic acid.[75] The use of bromine in this reaction has not been explained, however poorer results were obtained without it. Iodinative decarboxylation of 50 at 90°C gave a good yield of 51, which displayed a triplet at δ 1.23 (J=7 Hz), quartet at δ 4.31 (J=7 Hz) and a broad singlet at δ 10.00 in the ^1H NMR (M^+ at 463).

Synthetically useful methods for the preparation of amide pyrroles 53 and 54 were not found. Various oxidation and decarboxylation attempts allowed isolation of only small amounts of each pyrrole. Spectral evidence for diiodopyrrole 54 included a singlet in the ^1H NMR (DMSO-d_6) at δ 2.88 and absorptions at δ 34.32, 38.34, 69.13, 125.97, 164.82 in the ^{13}C NMR (DMSO-d_6).

Dichlorination was the highest oxidation level feasible for *bis*(trifluoromethyl)pyrrole 23b. Conditions which

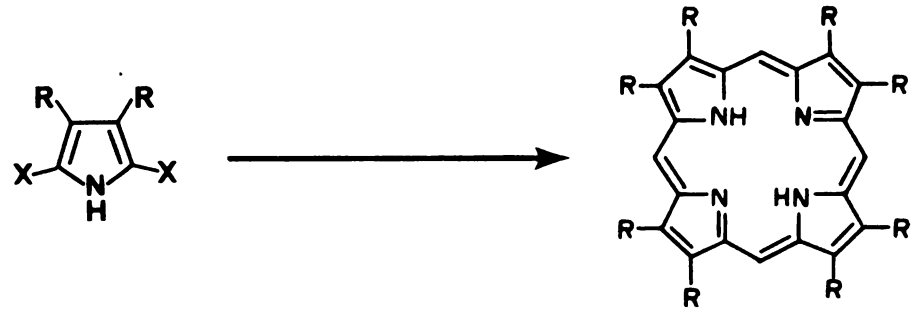
normally lead to trichlorination (Br_2, SO_2Cl_2, HOAc) only gave the *bis*(dichloromethyl) derivative (broad singlet at δ 6.93 in ^1H NMR). Direct hydrolysis provided diformylpyrrole 56 in 80% overall yield.

C. SYNTHESES OF PORPHYRINS

Dipyrromethanes and porphyrins have traditionally been prepared form pyrroles bearing a single α-chloro, bromo or acetoxymethyl substituent.[76,77] Initial investigations into the direct synthesis of porphyrins from pyrroles with two such α-substituents involved derivatives of heptafluorobutylpyrrole 2a (Table 5). It was found that heating *bis* (acetoxymethyl) derivative 38a under air in acidified alcohol allowed self-condensation and oxidation to symmetrically substituted octakis(1H,1H-heptafluorobut-1-yl)porphyrin 57.[78] Yields of 20% were obtained when the reaction was conducted at reflux in 1-propanol in the presence of a slow stream of oxygen and subsequently allowed to stand exposed to the atmosphere in a large open breaker for 14 days. The porphyrin precipitated slowly from the reaction mixture and was collected by filtration.

The mechanism of the condensation is envisioned to be similar to the one proposed for the formation of dipyrromethanes.[79] The key steps are summarized in Scheme 25 and involve the acid catalized solvolysis of the acetoxymethyls followed by self-condensation and elimination of formaldehyde.

Table 5. Preparations of octakis(1H,1H-heptafluorobut-1-yl)- and octakis(1H,1H-trifluoroeth-1-yl)porphyrins.

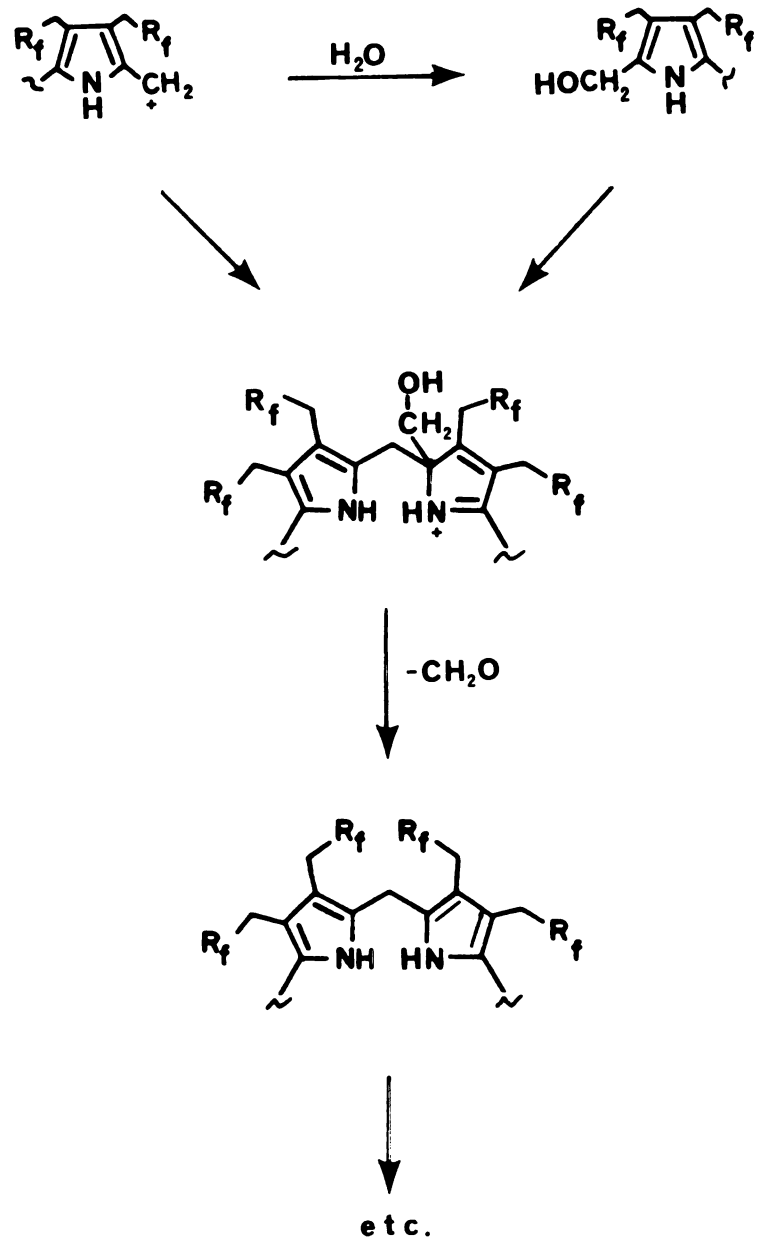


Pyrrole	R	X	Method	Porphyrin	% Yield
38a	$CH_2CF_2CF_2CF_3$	CH_2OAc	A	57	20
38b		CH_2Br	A		7
38c		CH_2Cl	A		15
58		CH_2NMe_2	A		0
41		H	B		30
40a		I	B		35
38f	CH_2CF_3	CH_2OAc	A	59	31
40b		I	B		40

Method A: HBr, 1-C_3H_7OH, O_2, 98°C. B: HBr, 1-C_3H_7OH, HCOH, 98°C.

An investigation of alternate sources of pyrrylcarbinyl cations revealed 38a to be the most practical porphyrin precursor. Both bromo- and chloromethyl derivatives 38b and 38c are considerably less stable and gave lower yields

Scheme 25



of porphyrin. Dimethylaminomethyl derivative, 58, prepared from 2,5-unsubstituted pyrrole 41 and excess N,N-dimethylmethyleneammonium bromide gave no evidence of porphyrin formation. Equimolar mixtures of 58 and 41 reacted to form 57, which suggests that self-condensation of 58 is

inhibited by deactivation of the pyrrole ring, possibly due to protonation of the second dimethylaminomethyl substituent.

Treibs reported the formation of dipyrromethenes from monoiodopyrroles and various aldehydes.[42] An extension of this method to the direct synthesis of porphyrins from α-diiodopyrroles was also investigated. It was found that reaction of 40a with formaldehyde and HBr in refluxing 1-propanol provides 57 in 31% yield. The porphyrin precipitated during the course of the reaction and was collected by filtration in an essentially pure form. Allowing the filtrate to stand exposed to air for 14 days provided only another 4% of 57. The condensation may entail elimination of I^+, an efficient internal oxidizing agent,[42] which obviates the use of oxygen and the normally required prolonged air oxidation. Although the yield of porphyrin is considerably greater than for 38a, a more direct comparison with the condensation of 41 and formaldehyde (30%) shows no major increase in yield in using the diiodo derivative.

Under conditions identical to the ones described above, *bis*(acetoxymethyl)- and diiodo(trifluoromethyl)pyrroles 38f and 40b condensed to form octakis(trifluoroethyl)porphyrin 59 (Table 5). Yields in both cases were slightly higher than for the corresponding heptafluorobutylpyrroles.

The ^1H NMR spectra for porphyrins 57 and 59 display the characteristic triplet (δ 5.34, J=18.4 Hz) and quartet

(δ 5.44, J=10.5 Hz) associated with the heptafluorobutyl and trifluoroethyl substituents. Singlet absorptions for the the *meso* (δ 10.62 for 57, δ 10.85 for 59) and NH protons (δ -3.21 for 57, δ -3.33 for 59) provide strong evidence for the symmetrical nature of the β-substitution pattern. The visible spectra (illustrated for 57 in Figure 3) display a phyllo-type absorption, which is in sharp contrast to the elio-type absorption normally observed for porphyrins of high substitution and symmetry (e.g., octabutyl[28] and octaethylporphyrin[80]).

Another surprising feature is the low solubility of 57 and 59 in normal organic solvents. This is illustrated in a comparison of solubilities between 57 and octabutylporphyrin, 60, summarized in Table 6. Unlike 60, heptafluorobutylporphyrin 57 is completely insoluble in hexane, benzene, and methylene chloride and demonstrates only moderate solubility in acetone and fluorinated solvents. A similar pattern in, although slightly higher overall, solubility is observed for octakis(trifluoroethyl)porphyrin.

The acid catalyzed self-condensation of 2,5-*bis*(acetoxymethyl)-3,4-*bis*(*p*-tolylsulfonylmethyl)pyrrole, 45, was considerably less efficient than the condensations for the corresponding polyfluoroalkylpyrroles. Optimum conditions, involving the heating of 45 (80°C, 60 h) under air in 1-propanol in the presence of HBr, allowed formation of only spectroscopic amounts of what is presumed to be the corresponding octasubstituted porphyrin. Evidence for the structure is provided by the UV-vis spectrum which displays

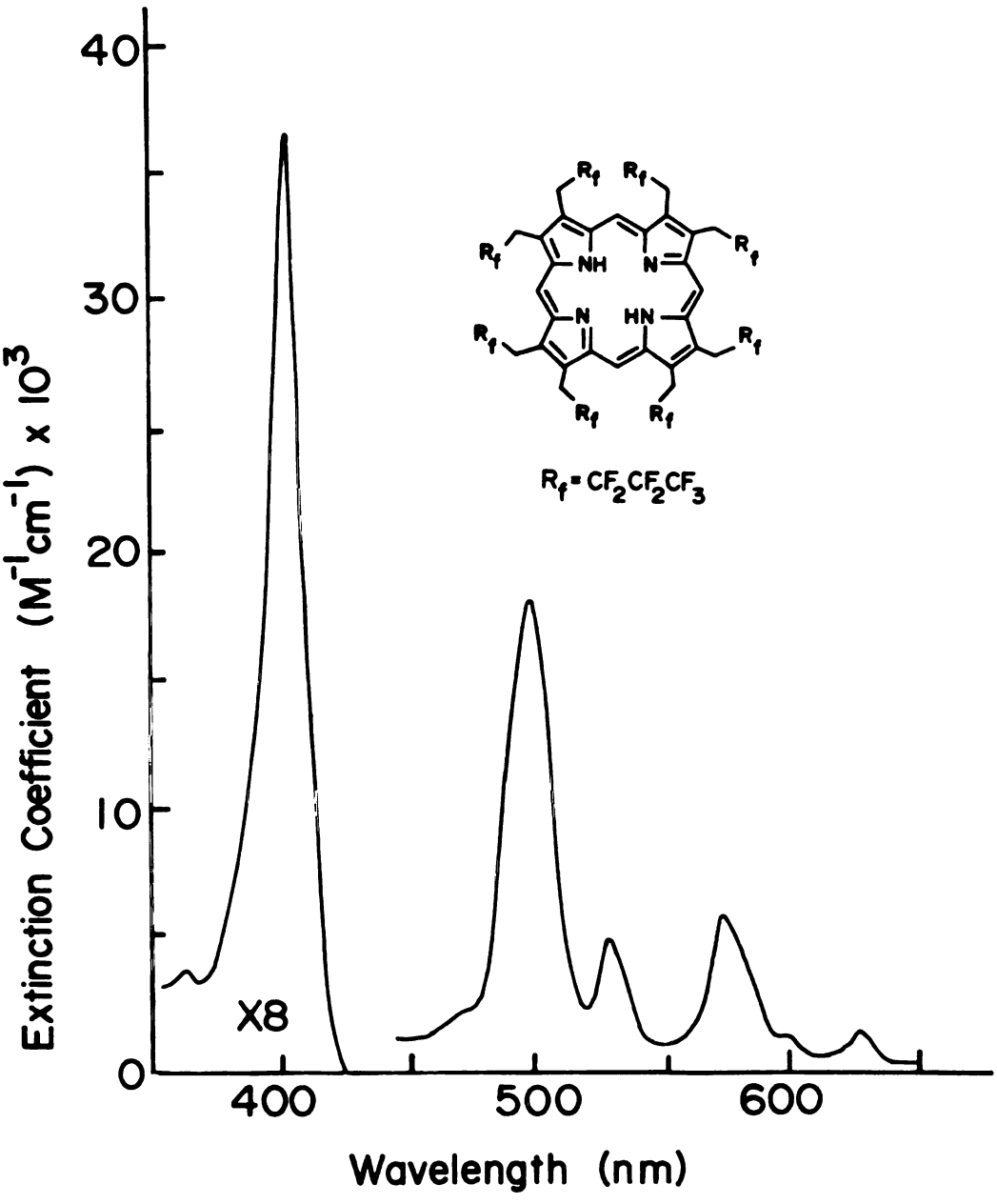


Figure 3. UV-vis spectrum of octakis(1H,1H-heptafluorobut-1-yl)porphyrin.

Table 6. Maximum solubilities of octakis(1H,1H-heptafluorobut-1-yl)- and octakis(1H,1H-trifluoroeth-1-yl)-porphyrins in grams/liter (moles/liter) at 25°C in selected solvents.

Solvents	57		60	
Hexane	insoluble		1.4	(1.9×10^{-4})
Benzene	insoluble		2.2	(2.9×10^{-3})
CH_2Cl_2	insoluble		6.5	(8.6×10^{-3})
Acetone	0.18	(1.0×10^{-4})	0.054	(7.2×10^{-5})
$Cl_2FCCClF_2$	0.064	(3.6×10^{-5})	0.097	(1.3×10^{-4})
Hexafluorobenzene	1.9	(1.1×10^{-3})	0.41	(5.4×10^{-4})

a Soret band (large ε) and a visible absorption pattern resembling the phyllo-type observed for polyfluoroalkylporphyrins 57 and 59 (λ_{max} in acetone 423.9, 514.0, 547.8, 587.3, 643.3).

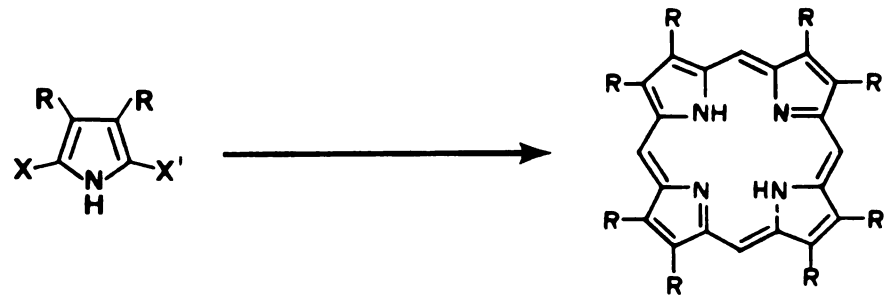
The unstable *bis*(chloromethyl) derivative of nitroalkylpyrrole 4 suffered a similar fate, providing only small amounts of porphyrin when heated with HBr in alcoholic solvents. Diiodonitroalkylpyrrole 44 on the other hand served as an efficient precursor to octakis(2-methyl-2-nitroprop-1-yl)porphyrin 61. Refluxing of 44 with formaldehyde and HBr in 1-propanol gave 25% yield of 61, which precipitated directly from the reaction mixture without the need for prolonged air oxidation. The structure and symmetrical

nature of 61 was determined by ^{1}H NMR, which in acetone-d_6 gave singlets at δ -3.50 (NH), 1.93 (nitroalkylmethyls), 4.96 (nitroalkylmethylene) and 10.05 (*meso* protons). The UV-vis spectrum shows a Soret band at 407.4 nm and a phyllo-type visible absorption pattern at 501.9, 534.2, 527.9 and 627.0 nm. The aliphatic nature of 61 gives it moderate solubility in chlorinated solvents as well as in acetone.

A study of the condensations of the various carboxamide pyrroles prepared in Sections A and B is summarized in Table 7. The reaction of N,N-diethylcarboxamidepyrrole 31a with formaldehyde gave a 25% yield of octakis(N,N-diethyl-carboxamide)porphyrin, 62a. It was successfully carried out in alcoholic solvents (ethanol and 1-propanol), water, or preferably a mixture of both, which allowed direct crystallization of 62a from the reaction mixture after air oxidation. Previous attempts to prepare a similar type of porphyrin, bearing eight strong electron-withdrawing groups, from 3,4-dibenzoyl- and dicarbethoxypyrroles had failed.[81] Success in this case is attributed to the slightly less deactivating nature of the dialkylcarboxamide substituents.

The condensation of N,N-dimethylcarboxyamidepyrrole 31b with formaldehyde proved to be solvent dependent, providing a 14% yield of octakis(N,N-dimethylcarboxamide)porphyrin, 62b, when carried out in water, but afforing no porphyrin in alcoholic solvents (methanol, ethanol, 1-propanol). This appears to be a result of the high solubility of pyrrole 31b in aqueous media. Unlike 62a, porphyrin 62b did not

Table 7. Preparations of octakis(N,N-dialkylcarboxamide)-porphyrins.



Pyrrole	X	X'	Method	Porphyrin	% Yield
31a	$CONEt_2$	H	A	62a	25
32b	$CONMe_2$	H	B	62b	14
52		CH_2OAc	C		10[a]
63	H	CH_2NMe_2	D		trace
54		I	—		0
31c	CON O	H	E	62c	trace
31d	CONHMe	H	—		0

[a] Pyrrole 52 was not isolated and yield is based on 37.

Method A: HBr, H_2O-EtOH, HCOH, 80°C. B: HBr, H_2O, HCOH, 100°C. C: HBr, H_2O, 75°C, N_2. D: HBr, H_2O, 100°C. E: HBr, EtOH or H_2O, HCOH reflux.

crystallize from the reaction mixture and isolation required extraction with CH_2Cl_2 followed by column chromatography (alumina, $CHCl_3$/3% sec-butanol).

Of the remaining N,N-dimethylcarboxamide derivatives only *bis*(acetoxymethyl)pyrrole 52 provided an alternate route to porphyrin 62b and best results were again obtained when water was used as the solvent. Monosubstituted dimethylaminomethylpyrrole 63, prepared from 31b and dimethylaminomethyleneammonium bromide, gave only trace amounts of 62b, whereas diiodopyrrole 54 surprisingly provided no evidence of porphyrin at all. The overall yields of porphyrin in both successful methods are comparable (7.6% from diethyl succinate and 4.0% from N,N-dimethylacetylacetamide), however in light of the shorter and more convenient preparation of precursor 52 (see page 28) synthesis of 62b *via* the *bis*(acetoxymethyl) derivative is more practical.

As was observed for the polyfluoroalkylporphyrins the visible spectra of 62a,b in $CHCl_3$ resemble a phyllo-type absorption more so than the expected etio-type[82] (Table 8). In water under neutral conditions 62b exhibits a true phyllo-type absorption: $\lambda_{max}(\varepsilon_M)$ 416 (264,000), 513 (17,500), 547 (6,800), 585 (7,400), 636 (2,900). Under basic conditions (KOH, H_2O, 25°C) the Soret band is shifted to longer wavelength with concurrent change in the visible bands: $\lambda_{max}(\varepsilon_m)$ 434 (215,000), 525 (sh, 6,700), 567 (14,200), 603 (sh, 6,100). Since the visible absorption pattern is very similar to the pattern normally observed for metalloporphyrins, this spectrum is attributed to the dianion of 62b. Also, acidification with HCl regenerates the original spectrum.

Table 8. ^{1}H and ^{13}C NMR chemical shifts and UV-vis absorptions of octakis(N,N-diethylcarboxamide)- and octakis(N,N-dimethylcarboxamide)porphyrins.

	62a	62b
λ_{max}, nm (ε_M)[a]	416 (249,000) 508 (20,000) 540 (7,800) 581 (3,600) 634 (2,900)	418 (241,000) 510 (17,000) 543 (6,000) 584 (6,000) 636 (2,000)
^{1}H NMR (δ)[b]		
NH	-3.36 s 10.10 s	-3.26 s 10.20 s
meso	1.16 t	3.27 s
NR_2	1.65 t 3.61 q 3.96 q	3.59 s
^{13}C NMR (δ)[b]		
meso	102.85 d	103.68 d
α-pyrrolic	142.80 s	142.65 d
β-pyrrolic	136.67 s	137.10 s
CO	165.74 s	166.60 s
NR_2	13.38 q 14.32 q 39.79 t 44.45 t	35.73 q 39.92 q

[a] recorded in $CHCl_3$

[b] recorded in $CDCl_3$

The ^{1}H NMR chemical shifts for the *meso* and NH protons as well as the ^{13}C NMR shifts for the *meso* and "pyrrolic" carbons in 62a,b compare closely with the values observed for other octasubstituted porphyrins.[83] Unlike their pyrrole precursors two distinct amide alkyl resonances are observed for 62a,b in the ^{1}H and ^{13}C NMR. For

the pyrroles the single resonance may be the result of delocalization of the amide carbonyl into the aromatic ring allowing rotation about the carbonyl-nitrogen bond. Since similar delocalization is also expected for the porphyrin, steric interactions of the amide alkyls with the *meso* protons appear to be the cause of the restricted rotation.

The solubilities of porphyrins 62a,b in selected solvents are summarized in Table 9. The values indicate a

Table 9. Maximum solubilities of octakis(N,N-diethylcarboxamide)- and octakis(N,N-dimethylcarboxamide)-porphyrins in grams/liter (moles/liter) at 25°C in selected solvents.

Solvent	62a		62b	
H_2O[a]	0.013	(1.2×10^{-5})	2.4	(2.7×10^{-3})
EtOH	3.5	(3.2×10^{-2})	1.6	(1.8×10^{-3})
EtOAc	2.2	(2.0×10^{-3})	0.097	(1.1×10^{-4})
CH_2Cl_2	96	(8.7×10^{-2})	65	(7.4×10^{-2})
Et_2O	0.051	(4.6×10^{-5})	0.004	(4.3×10^{-6})
Toluene	7.9	(7.2×10^{-3})	0.05	(5.7×10^{-5})

[a] Plots of the absorbance of the Soret band *vs* the concentration of 62a (1.2×10^{-5} to 1.0×10^{-7} M) and 62b (7.4×10^{-5} to 2.6×10^{-6} M) obey Beer's law, implying a lack of self-aggregation at these low concentrations.

a high degree of solubility in a wide range of organic solvents as well as in water. This latter property is

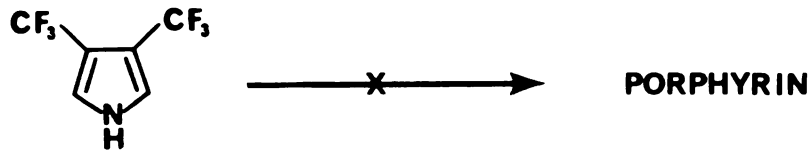
usually associated only with porphyrins bearing readily ionized substitutents such as carboxylate,[84] sulfonate[85] or quaternary ammonium salts.[86] Porphyrin 62b demonstrates considerably higher solubility in water, which is attributed to the less aliphatic nature of the carboxamide substituents.

Further reduction in the aliphatic character of the porphyrin could not be effected. Condensation of 3,4-*bis*-(N-methylcarboxamide)pyrrole 31d with formaldehyde under a variety of conditions failed to give any evidence of porphyrin formation. The condensation of *bis*(morpholinecarboxamide)pyrrole, 31c, possessing an additional heteroatom capable of hydrogen bonding with water, never proved practical, providing only spectroscopic amounts of the desired porphyrin 62c, (λ_{max}: 416.6, 509.7, 543.3, 584.4, 642.3).

Of the remaining oxidized pyrroles prepared in Section B only the self-condensations of the *bis*(acetoxymethyl)-3,4-dibromo- and dichloropyrroles were met with at least partial success. Optimum conditions for both condensations involved stirring of the pyrrole in acidified EtOH at 25°C for one week in the presence of air. The resulting residue was filtered and washed with EtOH, providing an insoluble black solid, which resisted all attempts of purification. Analysis of the solid was possible only by UV-vis spectroscopy in trifluoroacetic acid. The spectra display a Soret band (large ε) and absorptions in the visible region and are attributed to the diprotonated octabromo- and chloroporphyrins 64 and

65. (λ_{max} at 413.8, 560.5, 604.3 for 64 and 408.2, 554.6, 600.8 for 65). Additional evidence for the existance of 64 and 65 was provided by their conversion to zinc derivatives. This was accomplished by heating of the black solids with zinc acetate in dioxane at 90°C for 7-10 hours. The resulting crude reaction mixture gave UV-vis spectral data characteristic of zinc porphyrins:[87] λ_{max} at 420.9, 547.4,

Table 10. Reaction conditions for attempted conversions of 3,4-*bis*(trifluoromethyl)pyrrole to porphyrin.



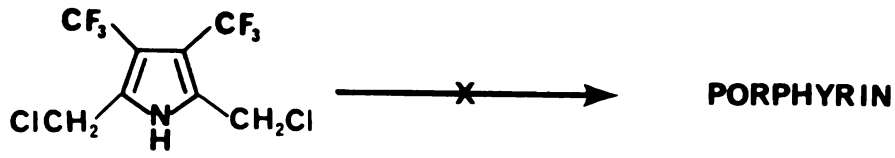
Aldehyde	Solvent	Catalyst	Temperature
HCOH	EtOH	HBr	79°C
HCOH	1-C_3H_7OH	HBr	98°C
HCOH	1-C_3H_7OH	HBr	170°C[a]
HCOH	H_2O	HBr	100°C
Paraform-aldehyde	o-dichloro-benzene	$ZnCl_2$	150°C[a]
ϕCOH	o-dichloro-benzene	$ZnCl_2$	150°C[a]
ϕCOH	1-C_3H_7OH	HBr	150°C[a]
ϕCOH	—	HBr	170°C[a]

[a]Reaction conducted inside a sealed heavy-walled glass tube.

583.8 for the bromo derivative and 417.0, 545.2, 580.3 for the chloro derivative.

Considerable effort was directed toward the preparation of octakis(trifluoromethyl)- and (carbethoxy)porphyrins. Tables 10 and 11 summarize the various reaction conditions

Table 11. Reaction conditions for attempted conversions of 2,5-*bis*(chloromethyl)-3,4-*bis*(trifluoromethyl)-pyrrole to porphyrin.



Solvent	Catalyst	Temperature
1-C_3H_7OH	HBr	98°C
1-C_3H_7OH	HBr	170°C[a]
1-C_3H_7OH	$ZnCl_2$	150°C[a]
o-dichloro-benzene	$ZnCl_2$	150°C[a]

[a] Reaction conducted inside a sealed heavy-walled glass tube.

examined for the condensations of 3,4-*bis*(trifluoromethyl)-pyrrole, 23a, and chloromethyl derivative 55. Neither for these, nor the condensations of 2,5-unsubsituted, 2,5-diiodo, and 2,5-*bis*(acetoxymethyl)-3,4-*bis*(carbethoxy)pyrroles (26a, 51 and 49), studied under similar sets of conditions, was any evidence of porphyrin observed.

To probe the reactivity of the *bis*(trifluoromethyl)-pyrrole nucleus two additional reactions of 23a were investigated. The Vilsmeier formylation of pyrroles bearing two electron-withdrawing substituents is reportedly a facile reaction,[88] however even at higher temperatures (90°C, 6 h and 130°C, 1 h) attempted formylation of 23a resulted in recovery of starting material. Treatment of 23a at 90°C for 3 h with excess dimethylmethyleneammonium bromide, conditions which successfully α-alkylated diamide pyrrole 31b (page 52), provided only N-dimethylaminomethyl-3,4-*bis*(trifluoromethyl)pyrrole (^{1}H NMR: singlets at δ 3.00, 5.80, 8.20 in ratios of 3:1:1). These results confirm that the α-positions of 3,4-*bis*(trifluoromethyl)-pyrroles are highly deactivated toward attack by electrophiles.

D. CONCLUSIONS

It has been demonstrated that octasubstituted porphyrins can be efficiently prepared from 2,5-dimethylpyrroles. The success of this method depends on the availability of the 2,5-dimethylpyrroles, the selective oxidation of the methyl substituents and the feasibility of the final condensation.

2,5-Dimethylpyrroles and its N-benzoyl derivative served as the preferred starting materials, allowing the facile introduction of a variety of substituents into the 3 and 4 positions. Selective oxidation of the α-methyls was influenced by the

nature of the β-substituents. Unreactive and slightly deactivating groups allowed efficient mono- and trioxidation, whereas more reactive substituents (e.g. CH_2CN and CH_2COOEt) interfered with the oxidation. Highly deactivated pyrroles required more severe reaction conditions, or did not react beyond the second oxidation level (CF_3).

Condensations leading to porphyrins were also dependent on the nature of the substituents. It was shown that pyrroles bearing electron-withdrawing dialkylamide substituents condensed to give porphyrins. More deactivated pyrroles, however, bearing esters, trifluoromethyls and monoalkylamides failed to do so. Slightly deactivated pyrroles gave the best results, providing porphyrins *via* their *bis*(acetoxy-, chloro- and bromomethyl), 2,5-diiodo and 2,5-unsubstituted derivatives.

Where comparisons are possible, the reactivity of the 2,5-*bis*(CH_2X)- and 2,5-diiodopyrroles toward condensations parallels the reactivity of the 2,5-unsubstituted pyrroles. This is consistent with the proposed mechanisms for the three types of condensations in which the key steps are very similar. The condensations of diiodopyrroles are more practical than the condensations of the corresponding *bis*(acetoxy- and chloromethyl)-pyrroles. They provide considerably higher yields and also avoid the usually required prolonged air oxidation.

Further investigations into the scope of the above porphyrin syntheses will depend largely on expanding existing and developing new routes to 2,5-dimethylpyrroles. For

example the reactions of malonate anions[33,34] with quaternary ammonium salts of 3 or 6 could prove useful in the preparation of ester (and eventaully amide) 3,4-*bis*(CH_2CH_2R)pyrroles. This may avoid the problems seen with pyrroles 7 and 10 and allow the preparation of 2,5-*bis*(CH_2X) derivatives. Another route to a similar pyrrole (and potentially numerous other pyrroles) could involve the use of 2,5-dimethyl-3,4-diformylpyrrole, which is readily available in large quantitites by Vilsmeier formylation of 2,5-dimethylpyrrole. Wittig olefination with carbethoxymethylenetriphenylphosphorane, followed by hydrogenation for example could lead to 2,5-dimethyl-3,4-*bis*(ethoxycarbonylethyl)pyrrole.

An alternate strategy to octakis(fluoromethyl)porphyrins may require the syntheses of less deactivated pyrrole derivatives. This could entail the preparation of 2,5-dimethyl-3,4-*bis*(difluoromethyl)pyrrole, which may be available by fluorination of 2,5-dimethyl-3,5-diformylpyrrole.

Investigations into the application of more reactive pyrroles could also prove useful. 3,5-Dimethyl-3,4-diethylpyrrole, available from 2,5-dimethylpyrrole by reductive alkylation,[32] may serve as an intermediate in what potentially is a three step octaethylporphyrin synthesis.

EXPERIMENTAL

General Methods

Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. NMR spectra were recorded on a Varian T-60 (^{1}H NMR at 60 MHz) or a Bruker WM-250 (^{1}H NMR at 250 MHz and ^{13}C NMR at 62.9 MHz) instrument in $CDCl_3$, or as noted, with Me_4Si as an internal standard. Electronic absorption spectra were measured on a Cary 219 spectrophotometer. Mass spectra were obtained on a Finnigan 4000 instrument at 70 eV or using ionized methane (CI). Infrared spectra were measured on a Perkin-Elmer 237 grating spectrophotometer as a Nujol mull for solids or neat for oils. Elemental analyses were performed by Galbraith Laboratories, Incorporated. Solvents were reagent grade and were not usually distilled prior to use. Dry benzene, toluene, and tetrahydrofuran (THF) were obtained by distillation from potassium-benzophenone. Dry methylene chloride (CH_2Cl_2) and 1,2-dichloroethane ($ClCH_2CH_2Cl$)

were obtained by passage through a column of alumina (Woelm B, Akt. I). All reactions unless otherwise noted were carried out under an atmosphere of nitrogen.

2,5-Dimethyl-3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole (2a).

According to the general procedure of MacDonald,[32] a solution of 1[89] (8.20 g, 86.3 mmol) and heptafluorobutyraldehyde hydrate[90] (46.6 g, 2.5 equiv) in acetic acid (100 mL), 47% HI (100 mL), and 58% H_3PO_2 (20 mL) was magnetically stirred at 100°C for 3.5 h. The dark red solution was diluted with water (100 mL) and CH_2Cl_2 (100 mL) and cooled in an ice bath. NH_4OH (400 mL) was added slowly with stirring and the mixture was extracted with CH_2Cl_2. The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated. Distillation (0.08 mm, 68°C) of the resulting dark red oil gave 25.4 g (64%) of 2a as a colorless oil, which solidified upon standing. An analytical sample was obtained by recrystallization from hexane: mp 32.5-33.0°C; ^{1}H NMR δ 2.18 (6H, s), 3.15 (4H, t, J=19.9 Hz), 7.69 (1H, br s); ^{13}C NMR δ 11.28, 26.15 (t, J=23.3 Hz), 106.72, 109.41 (t of q of t, J=261.5, 39.0, 39.1 Hz), 117.22 (t of t, J=251.6, 31.5 Hz), 118.21 (q of t, J=286.2, 33.3 Hz), 125.98; mass spectrum, m/e (relative intensity) 459 (15, M^+), 290 (100), 120 (34), 69 (17); IR 3525 (NH), 1230 (CF) cm^{-1}.

Anal. Calcd for $C_{14}H_{11}NF_{14}$: C, 36.60; H, 2.40.

Found: C, 36.40; H, 2.50.

2,5-Dimethyl-3,4-*bis*(1H,1H-trifluoroeth-1-yl)pyrrole (2b).

The above procedure was followed using 1 (7.00 g, 7.37 mmol) and trifluoroacetaldehyde hydrate[90] (21.4 g, 2.5 equiv) in acetic acid (90 mL), 47% HI (90 mL), and 58% H_3PO_2 (18 mL). Distillation (0.10 mm, 57°C) gave 7.6 g (40%) of 2b as a colorless oil which solidified upon standing. An analytical sample was obtained by recrystallization from hexane: mp 53.0-53.5°C; ^{1}H NMR δ 2.13 (6H, s), 3.18 (4H, q, J=11.0 Hz), 7.58 (1H, br s); ^{13}C NMR δ 11.03, 29.57 (q, J=30.5 Hz), 107.85, 125.42, 126.91 (q, J=276.5 Hz); mass spectrum, m/e (relative intensity) 259 (35, M^+), 258 (12), 190 (100); IR 3460 (NH), 1270, 1135 (CF) cm^{-1}.

Anal. Calcd for $C_{10}H_{11}NF_6$: C, 46.33; H, 4.25.
Found: C, 46.46; H, 4.24.

3,4-*bis*(Dimethylaminomethy)-2,5-dimethylpyrrole (3).

According to the procedure of Hertz[35] a solution of dimethylamine hydrochloride (17.0 g, 0.210 mol) in 37% formaldehyde (15.8 g, 0.210 mol) was added dropwise to 1[89] (10.0g, 0.105 mol) at such a rate that the temperature did not exceed 55°C. This was stirred another 1 h, diluted with water (150 mL) and extracted twice with ether. The aqueous layer was poured into a 25% NaOH solution (40 mL). The white precipitate was filtered, washed with small portions of cold water and dried under vacuum, yielding 19.8 g

(90%) of 3, which appeared pure by NMR and was used directly in subsequent reactions: ^{1}H NMR δ 2.07 (6H, s), 2.17 (12H, s), 3.20 (4H, s), 7.92 (1H, br s); ^{13}C NMR δ 11.12, 45.20, 53.78, 115.51, 123.47; mass spectrum, m/e (relative intensity) 209 (2, M^+), 164 (76), 149 (100), 120 (90), 85 (25), 77 (27), 58 (42), 44 (67).

3,4-*bis*(2-Methyl-2-nitroprop-1-yl)-2,5-dimethylpyrrole (4).

A solution of 3 (18.0 g, 0.0861 mol) and 2-nitropropane (31.0 mL, 0.341 mol) in water (500 mL) was stirred at 90°C for 35 h. The yellow precipitate was filtered from the cooled reaction mixture and thoroughly washed with water. Recrystallization from $CHCl_3$-hexane gave 17.9 g (70%) of 4: mp 127-130°C; ^{1}H NMR δ 1.51 (12H, s), 2.06 (6H, s), 2.95 (4H, s), 7.64 (1H, br s); ^{13}C NMR δ 11.82, 25.52, 36.55, 89.57, 112.24, 124.27; mass spectrum, m/e (relative intensity) 297 (73, M^+), 251 (14), 204 (32), 179 (41), 162 (100), 146 (33), 136 (28), 121 (86); IR 3450 (NH), 1540 (NO_2) cm^{-1}.

3,4-*bis*(Phenylthiomethyl)-2,5-dimethylpyrrole (5).

A solution of 3 (0.588 g, 2.67 mmol) and thiophenol (0.800 mL, 7.80 mmol) in H_2O (27 mL) was purged of oxygen

by bubbling a rapid stream of nitrogen through the solution at 25°C for 30 min. To this was added NaOH (0.160 g) and then stirred at 95°C for 17 h. The oily precipitate was filtered from the cooled solution and washed with water. Recrystallization from MeOH gave 0.75 g (83%) of 5 as a tan solid: mp 111-112.5°C; ^{1}H NMR δ 2.00 (6H, s), 4.00 (4H, s), 7.16 (10H, m); ^{13}C NMR δ 10.85, 29.55, 112.77, 124.09, 125.94, 128.68, 129.97, 137.74; mass spectrum, m/e (relative intensity) 339 (5, M^+), 230 (100), 121 (50), 120 (45), 108 (11); IR 3400 (NH) cm^{-1}.

N-Benzoyl-3,4-*bis*(dimethylaminomethyl)-2,5-dimethylpyrrole (6).

A solution of N-benzoyl-2,5-dimethylpyrrole[91] (3.00 g, 15.1 mmol) and N,N-dimethylmethyleneammonium bromide[39] (6.00 g, 43.5 mmol) in $CHCl_3$ (50 mL) was stirred at 58°C for 31 h. During the course of the reaction a white precipitate formed. The mixture was poured into a saturated, aqueous Na_2CO_3 solution (100 mL) and extracted with CH_2Cl_2. The organic layer was extracted with aqueous Na_2CO_3 and dried over Na_2SO_4. Evaporation of the solvent gave 4.48 g (95%) of 6 as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 2.00 (6H, s), 2.20 (12H, s), 3.27 (4H, s), 7.50 (5H, m); ^{13}C NMR δ 12.15, 45.35, 53.29, 120.33, 127.25, 128.60, 129.99, 133.07, 135.94, 171.00; mass spectrum, m/e (relative intensity)

313 (5, M^+), 268 (27), 163 (44), 105 (80), 77 (43), 58 (100); IR 3450 (NH), 2800 (CH), 1710 (CO) cm^{-1}.

3,4-*bis*(Cyanomethyl)-2,5-dimethylpyrrole (7).

A solution of pyrrole 6 (3.60 g, 11.5 mmol) and CH_3I (33 mL) in MeOH (33 mL) was stirred at 40°C for 2.5 h and then evaporated to complete dryness. The residue was dissolved in a solution of water (125 mL) and KCN (14 g), heated at 65°C for 5 min and suction filtered, removing any undissolved materials. The filtrate was then stirred at 65°C for 25 h. Filtration of the cooled solution gave 1.08 g (54%) of 7 as a tan solid, which appeared pure by NMR and was used without further purification in subsequent reactions: mp 166-169°C (lit.[38] mp 171-172°C); ^1H NMR δ 2.17 (6H, s), 3.47 (4H, s), 7.70 (1H, br s); ^{13}C NMR δ 10.62, 12.91, 107.07, 119.15, 124.56; mass spectrum, m/e (relative intensity) 173 (59, M^+), 147 (21), 146 (100), 145 (50), 133 (23), 85 (13); IR 3300 (NH), 2250 (CN) cm^{-1}.

3,4-*bis*(*p*-Tolylsulfonylmethyl)-2,5-dimethylpyrrole (8).

A solution of pyrrole 6 (0.543 g, 1.74 mmol) and CH_3I (5.5 mL) in MeOH (5.5 mL) was stirred at 40°C for 2.5 h and then evaporated to complete dryness. The resinous material was dissolved in water (17 mL) and stirred at 65°C with sodium *p*-toluenesulfinate (3.00 g, 16.9 mmol) for 12 h.

The resulting white solid was filtered from the cooled mixture, washed with water and dried under vacuum, yielding 0.354 g (47.4%) of 8: mp 240-245°C (dec.); ^{1}H NMR δ 1.77 (6H, s), 2.40 (6H, s), 4.20 (4H, s), 7.20 (4H, d, J=8 Hz), 7.57 (4H, d, J=8 Hz); mass spectrum, m/e (relative intensity) 431 (1, M^+), 276 (40), 212 (31), 121 (98), 120 (100), 92 (20), 91 (50), 77 (27), 65 (30); IR 3500 (NH), 1320 and 1170 (SO_2) cm^{-1}.

3,4-*bis*(Carbethoxymethyl)-2,5-dimethylpyrrole (10).

According to the method of Treibs,[40] a solution of pyrrole 7 (0.369 g, 2.13 mmol) in absolute EtOH (10 mL) was saturated with gaseous HCl at 3°C for 4 h and then stored at 25°C for 10 days. The solution was evaporated to dryness and the residue heated on a steam bath for 10 min. Extraction with CH_2Cl_2 and drying of the combined organic fractions over anhydrous Na_2SO_4 gave 0.514 g (99%) of 10 as a yellow oil: ^{1}H NMR δ 1.20 (6H, t, J=7 Hz), 2.07 (6H, s), 3.35 (4H, s), 4.05 (4H, q, J=7 Hz), 7.91 (1H, br s); ^{13}C NMR δ 11.14, 14.22, 30.63, 60.46, 111.09, 123.15, 172.48; mass spectrum, m/e (relative intensity) 267 (29, M^+), 221 (25), 194 (75), 122 (100), 120 (56); IR 3350 (NH), 1725 (CO) cm^{-1}.

3,4-Dibromo-2,5-dimethylpyrrole (11).

N-Bromosuccinimide (3.69 g, 1.95 equiv) was added in small portions over 30 min to pyrrole 1 (1.01 g, 10.6 mmol) in DMF (50 mL) at 25°C. The solution was stirred for 2.5 h, diluted with $CHCl_3$ (100 mL) and thoroughly washed with water, removing all of the DMF. The organic layer was dried over anhydrous Na_2SO_4 and the solvent evaporated, yielding 1.90 g (71%) of 11 as an unstable, slightly red solid, which appeared pure by NMR and was used directly in the preparation of 64: mp 67-70°C (dec); ^1H NMR δ 2.17 (6H, s), 7.63 (1H, br s); ^{13}C NMR δ 12.35, 96.72, 124.21; mass spectrum, m/e (relative intensity) 255 (8, M^+), 254 (8), 253 (17, M^+), 252 (14), 251 (10, M^+), 250 (17), 174 (19), 172 (21), 93 (20), 73 (19), 65 (27), 51 (70), 42 (100); IR 3450 (NH) cm^{-1}.

3,4-Dichloro-2,5-dimethylpyrrole (12).

N-Chlorosuccinimide (2.47 g, 2.00 equiv) was added in small portions over 20 min to pyrrole 1 (0.855 g, 9.00 mmol) in DMF (40 mL) at 2°C. The solution was stirred for 2.5 h, diluted with $CHCl_3$ (100 mL) and thoroughly washed with water, removing all of the DMF. The organic layer was dried over anhydrous Na_2SO_4 and the solvent evaporated, yielding a dark oil. Filtration through a short column of silica gel (CH_2Cl_2) gave 0.400 g (27%) of 12 as an unstable oily

solid: ^{1}H NMR δ 2.13 (6H, s), 7.10 (1H, br s); ^{13}C NMR δ 10.94, 107.30, 121.45; mass spectrum, m/e (relative intensity) 167 (5, M^+), 166 (12), 165 (38, M^+), 164 (66), 163 (65, M^+), 162 (100), 128 (53), 85 (16), 65 (12), 51 (38), 50 (27), 42 (75); IR 3500 (NH).

N-Benzoyl-2-formylpyrrole (19).

A 50% mineral oil dispersion of NaH (8.82 g, 0.184 mol) was washed thoroughly with dry ether inside a 1000 mL flask, equipped with an efficient condenser and mechanical stirrer. To this was added dry ether (250 mL) followed by 2-formylpyrrole[92] (11.7 g, 0.123 mol) in ether (75 mL) and then heated at gentle reflux for 3 h. The suspension was cooled to 25°C and benzoyl chloride was added carefully (exothermic reaction) in portions (5.00, 5.00, 3.56 mL). This was then stirred at gentle reflux for 4 h and at 25°C for 15 h. The reaction was monitored by TLC (silica, CH_2Cl_2) and additional benzoyl chloride was added in small amounts as needed. The reaction mixture was rapidly suction filtered and the filtrate evaporated to dryness. Recrystallization of the residue from MeOH yielded 12.9 g (53%) of 19: mp 89-90°C (lit.[50] mp 90°C); ^{1}H NMR δ 6.30 (1H, m), 7.17 (2H, m), 7.60 (5H, m), 9.90 (1H, s); ^{13}C NMR δ 111.81, 122.31, 129.06, 128.52, 129.78, 132.37, 135.22, 135.37, 167.88, 180.54; mass spectrum, m/e (relative intensity) 199 (61, M^+), 105 (100), 77 (54), 51 (16).

N-Benzoyl-2-(1,3-dioxolan-2-yl)pyrrole (16c).

A solution of aldehyde 19 (2.95 g, 14.8 mmol) and ethylene glycol (4.1 mL) in benzene (100 mL) was mechanically stirred with $CaSO_4$ (~4 g) at 55°C for 1 h. To this was added p-toluenesulfonic acid (0.10 g) and stirred at 55°C for 6 h. The cooled mixture was filtered and the filtrate diluted with CH_2Cl_2 (300 mL) and thoroughly extracted with saturated aqueous $NaHCO_3$. Drying of the organic fraction over anhydrous Na_2SO_4 and evaporation of the solvent provided 3.55 g (99%) of a yellow oil, consisting as indicated by TLC (silica, CH_2Cl_2) and NMR of a small amount of 19 and 16d: ^{1}H NMR δ 4.00 (4H, s), 6.10 (1H, m), 6.53 (2H, m), 6.82 (1H, m), 7.55 (5H, m); ^{13}C NMR δ 64.51, 98.01, 110.16, 113.24, 124.51, 128.01, 128.39, 129.44, 132.14, 133.20, 168.01; mass spectrum, m/e (relative intensity) 243 (5, M^+), 215 (4), 149 (5), 138 (4), 105 (100), 77 (31), 51 (7); IR 1690 (CO) cm^{-1}.

N-Benzyol-2,3-*bis*(trifluoromethyl)-7-azabicyclo[2.2.1]-2,5-heptadiene (17a).

Hexafluorobut-2-yne, 13,[90] (7.60 g, 46.9 mmol) was condensed at -78°C into a heavy-walled glass tube containing N-benzoylpyrrole, 16a,[91] (4.0 g, 23.4 mmol) and THF (15 mL). The closed tube was heated inside a steam bath for 5 h. The solvent and excess 13 were evaporated on a rotary

evaporator, affording 7.79 g (100%) of 17a as a yellow oil. This product appeared pure by NMR and TLC and was used directly in the preparation of 20 and 21a: ^{1}H NMR δ 5.56 (2H, br s), 7.10 (2H, m), 7.35 (5H, br s); ^{13}C NMR δ 66.59, 69.76, 120.89 (q, J=269.8 Hz), 128.10, 128.86, 132.16, 132.80, 142.65, 144.48, 148.98 (broad), 169.12; mass spectrum, m/e (relative intensity) 333 (10, M^{+}), 105 (100), 77 (40), 51 (13); IR 3350, 3060, 1675, 1350, 1290, 1180, 1130 cm^{-1}.

N-Benzoyl-2,3-*bis*(trifluoromethyl)-1,4-dimethyl-7-azabicyclo[2.2.1]-2,5-heptadiene (17b).

Pyrrole 17b was prepared as above in 100% yield by heating 16b and 13 for 9 h: ^{1}H NMR δ 1.67 (6H, s), 6.80 (2H, s), 7.40 (5H, m); ^{13}C NMR δ 16.00, 78.44, 121.76 (q, J= 273.0), 128.49, 129.24, 132.39, 137.28, 148.00, 150.90, 174.70; mass spectrum (CI, CH_4), m/e 362 (M^{+} + 1); IR 3300, 3000, 1660, 1450, 1325, 1250, 1150, 700 cm^{-1}.

N-Benzoyl-2,3-*bis*(trifluoromethyl)-1-(1,3-dioxolan-2-yl)-7-azabicyclo[2.2.1]-2,5-heptadiene (17c).

Pyrrole 17c was prepared as above in 95% yield by heating 16c and 13 for 23 h in dry benzene: ^{1}H NMR δ 4.05 (4H, m), 5.37 (1H, m), 6.37 (1H, br s), 7.40 (7H, m); ^{13}C NMR δ 65.27, 65.90, 70.84, 83.03, 98.18, 120.31 (q, J =

268.6 Hz), 120.61 (q, J=273.6 Hz), 127.92, 128.39, 131.97, 132.57, 140.29, 143.28, 149.47 (br q, J=36 Hz). 151.44 (br q, J=45 Hz), 171.17; mass spectrum (CI, CH_4), m/e 406 (M^+ + 1); IR 1660 (CO) cm^{-1}.

N-Benzoyl-2,3-*bis*(trifluoromethyl)-7-azabicyclo[2.2.1]-heptane (20).

A solution of 17a (0.50 g, 1.5 mmol) in EtOH (20 mL) was hydrogenated in a Parr apparatus at 75 lbs/sq. in. for 2 h in the presence of 10% palladium on activated carbon (10 mg). The solution was filtered and concentrated *in vacuo*. The resulting solid was recrystallized from hexane, yielding 0.49 g (97%) of 20 as colorless crystals: mp 114-115°C; ^1H NMR δ 2.00 (4H, m), 3.06 (2H, m), 4.60 (2H, m), 7.40 (5H, m); ^{13}C NMR δ 24.05, 44.88, 58.86, 124.65 (q, J=280.5 Hz), 128.13, 128.84, 131.92, 134.08, 169.98; mass spectrum, m/e (relative intensity) 337 (21, M^+), 105 (100), 77 (33), 51 (8); IR 3300, 1630, 1410, 1305, 1275, 1230, 725 cm^{-1}.

Anal. Calcd for $C_{15}H_{13}NOF_6$: C, 53.41; H, 3.86.
Found: C, 53.42; H, 3.99.

N-Benzoyl-2,3-*bis*(trifluoromethyl)-7-azabicyclo[2.2.1]-2-heptene (21a).

A solution of 17a (2.65 g, 7.96 mmol) in EtOH (20 mL) was hydrogenated at 1 atm in the presence of 10% palladium on activated carbon (30 mg). The uptake of hydrogen dropped sharply after 1 equiv (180 mL) and the solution was filtered and concentrated *in vacuo* yielding 2.58 g (97%) of 21a as a yellow oil. The product appeared pure by NMR and TLC and was used directly in the preparation of 22a: ^{1}H NMR δ 1.47 (2H, m), 2.13 (2H, m), 5.13 (2H, m), 7.36 (5H, br s); ^{13}C NMR δ 24.15, 61.41, 120.20 (q, J=271.3 Hz), 128.86, 128.88, 131.95, 133.30, 139.44, 169.47; mass spectrum (CI, CH_4) m/e: 336 (M^+ + 1); IR 3250, 3050, 2960, 1670, 1370, 1300, 1180, 1150, 1040, 730, 710 cm^{-1}.

N-Benzoyl-2,3-*bis*(trifluoromethyl)-1,4-dimethyl-7-azabicyclo[2.2.1]-2-heptene (21b).

Hydrogenation of 17b as above gave 21b (95% yield) as a yellow oil: ^{1}H NNR δ 1.53 (6H, s), 1.58 (2H, m), 2.03 (2H, m), 7.40 (5H, m); ^{13}C NMR δ 18.41, 34.39, 72.79, 121.24 (q, J=273.7), 128.43, 129.52, 132.47, 138.00, 140.90 (br), 176.43; mass spectrum (CI, CH_4) m/e 364 (M^+ + 1); IR 3260, 2950, 1675, 1450, 1335, 1270, 1170, 945, 840, 760, 710 cm^{-1}.

N-Benzoyl-2,3-*bis*(trifluoromethyl)-1-(1,3-dioxolan-2-yl)-7-azabicyclo[2.2.1]-2-heptene (21c).

Hydrogenation of 17c as described for 20 gave 21c (95% yield) as an oily solid: ^{1}H NMR δ 1.50 (2H, m), 2.40 (2H, m), 4.02 (4H, s), 4.90 (1H, m), 6.33 (1H, s), 7.47 (5H, m); ^{13}C NMR δ 24.18, 24.68. 65.57, 65.90, 66.03, 76.66, 99.53, 120.10 (q, J=278.6 Hz), 120.29 (q, J=270.5 Hz), 128.22, 128.56, 132.06, 133.92, 139.91 (q, J=37.1 Hz), 141.89 (q, J=37.1 Hz), 172.10; mass spectrum (CI, CH_4), m/e 408 (M^+ + 1); IR 2950 (CH), 1660 (CO) cm^{-1}.

N-Benzoyl-3,4-*bis*(trifluoromethyl)pyrrole (22a).

A solution of 21a (2.20 g, 6.57 mmol) in benzene (100 mL) was passed dropwise in a slow stream of nitrogen through a tube packed with glass beads and heated to 300°C. The product was collected in a flask, cooled to -78°C. The column was washed with additional benzene (20 mL) and the solution was concentrated *in vacuo*. Distillation (0.15 mm, 84°C) gave 1.90 g (94%) of 22a as a colorless oil: ^{1}H NMR δ 7.56 (7H, m); ^{13}C NMR δ 115.70 (q, J=37.7 Hz), 121.75 (q, J=270.5 Hz), 123.5, 129.40, 130.00, 130.70, 134.20, 166.50; mass spectrum (CI, CH_4), m/e 308 (M^+ + 1); IR 3360, 3160, 1730, 1560, 1320, 1250, 1150, 980, 900, 725 cm^{-1}.

N-Benzoyl-3,4-*bis*(trifluoromethyl)-2,5-dimethylpyrrole (22b).

Pyrolysis of 21b as above gave 22b (95% yield) as colorless crystals from hexane: mp 69.5-70.5°C; ^{1}H NMR δ 2.17 (6H, s), 7.60 (5H, m); ^{13}C NMR δ 12.00, 110.09 (q, J=38.8 Hz), 116.92, 123.35 (q, J=269.1 Hz), 129.78, 130.81, 133.16, 135.85, 169.98; mass spectrum, m/e (relative intensity) 335 (1, M^+), 105 (100), 77 (57), 51 (11); IR 3350, 1725, 1370, 1260, 1200, 1150, 1110, 925, 725 cm^{-1}.

Anal. Calcd for $C_{15}H_{11}NOF_6$: C, 53.73; H, 3.28.
Found: C, 53.73; H, 3.31.

N-Benzoyl-3,4-*bis*(trifluoromethyl)-2-(1,3-dioxolan-2-yl)-pyrrole (22c).

Pyrolysis of 21c as above gave 22c (82% yield) as colorless crystals from $CHCl_3$-hexane: mp 87.5-89.0°C; ^{1}H NMR δ 3.75 (4H, m), 6.07 (1H, br s), 7.20 (1H, br s), 7.58 (5H, m); ^{13}C NMR δ 65.48, 96.62, 113.81 (q, J=40.3 Hz), 114.15 (q, J=39.6 Hz), 121.87 (q, J=268.0 Hz), 122.08 (q, J=268.0 Hz), 128.83, 129.15, 130.83, 131.68, 133.03, 135.05, 167.80; mass spectrum, m/e (relative intensity) 379 (9, M^+), 105 (100), 77 (42), 51 (11); IR 1725 (CO) cm^{-1}.

3,4-*bis*(Trifluoromethyl)pyrrole (23a).

A solution of 22a (1.30 g, 4.23 mmol) and KOH (0.24 g, 1 equiv) in diethyl ether (60 mL) and water (3 mL) was stirred at RT for 6 h. The reaction was monitored by TLC (silica, CH_2Cl_2) and additional KOH was added in small amounts as needed. Water (200 mL) was added and the solution was extracted with CH_2Cl_2. The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Recrystallization from hexane-$CHCl_3$ (3:1) gave 0.77 g (90%) of 23a as volatile, colorless crystals: mp 36.5-37.5°C; ^1H NMR δ 7.16 (2H, d, J=3 Hz), 8.53 (1H, br s); ^{13}C NMR δ 112.75 (q, J=39.0 Hz), 121.18, 122.96 (q, J=266.7 Hz); mass spectrum, m/e (relative intensity) 203 (38, M^+), 184 (100), 153 (8), 134 (3); IR 3475, 3300, 1560, 1450, 1370, 1330, 1230, 1130, 980.

Anal. Calcd for $C_6H_3NF_6$: C, 35.47; H, 1.48.
Found: C, 35.00; H, 1.51.

3,4-*bis*(Trifluoromethyl)-2,5-dimethylpyrrole (23b).

A solution of 22b (2.00 g, 5.97 mmol) and KOH (0.34 g, 1 equiv) in THF (130 mL) and water (7 mL) was stirred at RT for 6 h. The reaction was monitored by TLC (silica, hexane-CH_2Cl_2) and additional KOH was added in small amounts as needed. Water (300 mL) was added and the solution was extracted with CH_2Cl_2. The combined organic fractions were

dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Recrystallization from hexane gave 1.27 g (92%) of 23b as colorless crystals: mp 95.5-96.5°C; ^1H NMR δ 2.27 (6H, s), 7.87 (1H, br s); ^{13}C NMR δ 12.04, 108.23 (q, J= 39.7 Hz), 123.89 (q, J=267.3 Hz), 128.94; mass spectrum, m/e (relative intensity) 231 (62, M^+), 230 (80), 212 (46), 162 (100), 69 (19), 42 (30); IR 3450, 3250, 1330, 1220, 1150, 1110, 1055 cm^{-1}.

Anal. Calcd for $C_8H_7NF_6$: C, 41.56; H, 3.03.
Found: C, 41.37; H, 3.16.

3,4-*bis*(Trifluoromethyl)-2-formylpyrrole (24).

A solution of 22c (1.00 g, 2.64 mmol) and 48% HBr (0.20 mL) in acetic acid (30 mL) and H_2O (4 mL) was stirred at 60°C for 4.5 h. CH_2Cl_2 (150 mL) was added and the solution was washed with water followed by saturated aqueous $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. Recrystallization from $CHCl_3$ at -10°C gave 0.35 g (58%) of 24 as colorless crystals: mp 108.5-110°C; ^1H NMR (acetone-d_6) δ 7.67 (1H, br s), 9.80 (1H, br s); ^{13}C NMR (acetone-d_6) δ 114.72 (q, J=37.1 Hz), 116.9 (q, J=37.1 Hz), 123.20 (q, J=265.4 Hz), 123.43 (q, J=268.0 Hz), 127.74, 133.15, 180.20; mass spectrum, m/e (relative intensity) 231 (100, M^+), 212 (25), 210 (79), 192 (23), 184 (27), 183 (43), 182 (31), 164 (14), 156 (20), 114 (18), 69 (15); IR 3200 (NH), 1675 (CO) cm^{-1}.

3,4-Dicyanopyrrole (25a).

A suspension of pyrrole 23a (0.339 g, 1.67 mmol) was stirred at 25°C in 7.5% aqueous ammonia (45 mL). After 5 days the solution was filtered yielding 0.074 g of 25a as a white powder. The filtrate was thoroughly extracted with CH_2Cl_2 and the combined organic fractions dried over anhydrous Na_2SO_4. Evaporation of the solvent gave another 0.090 g of 25a (total yield: 84%) as a white solid: mp 226-228°C; ^1H NMR (acetone-d_6) δ 7.66 (2H, s), 10.23 (1H, br s); ^{13}C NMR (acetone-d_6) δ 96.41, 114.13, 129.40; mass spectrum, m/e (relative intensity) 117 (100, M^+), 90 (13), 66 (10), 63 (26), 51 (11), 41 (20); IR 3350 (NH), 2250 (CN) cm^{-1}.

3,4-Dicyano-2,5-dimethylpyrrole (25b).

A heavy-walled glass tube was charged with 23b (0.108 g, 0.468 mmol) and 7.5% aqueous ammonia (19 mL) and heated inside a steam bath for 20 h. The cooled reaction mixture was filtered and the product washed with water yielding 0.064 g (95%) of 25b as a crystalline solid: mp 238-240°C (lit.[53] mp 239°C); ^1H NMR (acetone-d_6) δ 2.33 (6H, s); ^{13}C NMR (acetone-d_6) δ 11.86, 93.20, 114.51, 139.19; mass spectrum, m/e (relative intensity) 145 (63, M^+), 144 (100), 130 (9), 76 (10), 42 (20), 41 (10); IR 3225 (NH), 2220 (CN) cm^{-1}.

3,4-*bis*(Carbethoxy)-2,5-dimethylpyrrole (26b) prepared from 23b.

A solution of pyrrole 23b (0.103 g, 0.446 mmol) and KOH (0.25 g) in EtOH (10 mL) was heated at 55°C for 4 h. The cooled solution was stirred in 5% HCl (50 mL) for 30 min and then extracted with CH_2Cl_2. The combined organic fractions were washed with saturated aqueous $NaHCO_3$ and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave 0.095g (89%) of 26b as a crystalline solid which was identical in all respects to an authentic sample.[54]

3,4-*bis*(Carbethoxy)pyrrole (26a) prepared from 23a.

Pyrrole 26a was prepared as described for 26b by heating 23a and KOH in EtOH for 20 h. Recrystallization from THF gave 26a (90% yield) as a colorless solid, which was identical in all respects to an authentic sample (see pg 80).

bis(Dimethylaminomethylene)diethylsuccinate (28).

According to the method of Bredereck,[57] a solution of diethyl succinate (2.00 g, 11.5 mmol) and *t*-butoxy*bis*-(dimethylamino)methane,[58] 27 (6.00 g, 34.5 mmol), was heated under a nitrogen atmosphere for 5 h at 160°C in a magnetically stirred flask, equipped with a distilling head and condenser. The flask was cooled to 50°C, evacuated to 0.3 mm pressure and heated at 110°C for another 45 min.

During the course of this procedure a clear liquid distilled from the reaction mixture. The remaining dark oil was cooled at -10°C overnight and the resulting crystals were triturated with ether (4 mL) and cooled at -10°C for 5 h. The ether was decanted and the process repeated. Recrystallization from hexane gave 2.05 g (63%) of 28 as yellow needles: mp 73.5-74.5°C (lit.[57] mp 70.5°C); ^{1}H NMR (60 MHz) δ 1.16 (6H, t, J=7 Hz), 2.90 (12H, s), 4.02 (4H, q, J=7 Hz), 7.25 (2H, s).

3,4-*bis*(Carbethoxy)pyrrole (26a).

A solution of bisenamine 28 (2.00 g, 7.11 mmol) and ammonium acetate (2.74 g, 35.5 mmol) in 95% ethanol (40 mL) was heated under reflux for 24 h. The solution was cooled, poured into water (250 mL) and extracted with CH_2Cl_2. The combined organic fractions were washed with saturated aqueous $NaHCO_3$ and dried over anhydrous Na_2SO_4. Evaporation of the solvent and recrystallization from THF gave 1.45 g (97%) of 26a as colorless crystals: mp 150-151°C (lit.[47] mp 151-152°C); ^{1}H NMR (250 MHz) δ 1.33 (6H, t, J=7 Hz), 4.29 (4H, q, J=7 Hz), 7.42 (2H, d, J=3 Hz), 10.50 (1H, br s); ^{13}C NMR δ 14.35, 60.24, 115.04, 126.43, 164.41; mass spectrum, m/e (relative intensity) 211 (12, M^+), 166 (34), 138 (100), 94 (16), 66 (20).

3,4-Dicarboxypyrrole (29).

According to the procedure of Groves[47] a solution of diester 26a (1.50 g, 7.10 mmol) and NaOH (1.40 g) in 50% EtOH (15 mL) was heated under reflux for 2 h. The solution was diluted with water (50 mL), warmed on a steam bath and slowly acidified with 10% HCl. Suction filtration and thorough washing with water gave 1.05 g (95%) of 29 as an insoluble white powder: mp 300°C, dec. (lit.[47] 300°C, dec.); IR 3160 (NH), 2000-3000 (OH), 1590 (CO) cm^{-1}; mass spectrum, m/e (relative intensity) 155 (100, M^+).

3,4-*bis*(N,N-Diethylcarboxamide)pyrrole (31a).

A suspension of diacid 29 (0.960 g, 6.19 mmol) and oxalyl chloride (8.0 mL) in dry toluene (100 mL) was magnetically stirred under an inert atmosphere in a flask equipped with an efficient condenser. Four drops of DMF were added and the suspension was heated to 85°C. After 50 min the yellow, homogeneous solution was cooled to 40°C and evacuated for 30 min (0.5 mm pressure) keeping the temperature at 40-50°C. (This efficiently removed excess oxalyl chloride without destruction of the diacid chloride 30.) The warm toluene solution (approximately 60mL) was added slowly *via* cannula to a flask, equipped with a drying tube and containing a cooled (ice bath) solution of diethylamine (40 mL) and toluene (40 mL). This was stirred

overnight allowing the temperature to rise to 25°C. The mixture was concentrated on a rotary evaporator, dissolved in water (250 mL) and extracted thoroughly first with ether and then with $CHCl_3$. The combined $CHCl_3$ fractions were dried over anhydrous Na_2SO_4 and concentrated. The resulting yellow oil was treated with ether (10 mL) and cooled at -10°C overnight. The solid was suction filtered and washed with ether. Recrystallization from toluene gave 1.46 g (89%) of 31a as colorless crystals: mp 123-124°C; ^1H NMR (60 MHz) δ 1.12 (12H, t, J=7 Hz), 3.42 (8H, q, J= 7Hz), 6.66 (2H, d, J=2.5 Hz), 10.96 (1H, br s); ^{13}C NMR δ 13.50, 41.06, 117.94, 118.24, 167.42; mass spectrum, m/e (relative intensity) 265 (12, M^+), 193 (67), 192 (62), 122 (41), 72 (100); IR 3170 (NH), 1620 (CO) cm^{-1}.

Anal. Calcd for $C_{14}N_{23}H_3O_2$: C, 63.40; H, 8.68.
Found: C, 63.44; H, 8.94.

3,4-*bis*(N,N-Dimethylcarboxamide)pyrrole (31b).

Diacid chloride 30 was prepared in toluene as described above and added slowly *via* cannula to a flask equipped with a drying tube, dry-ice condenser and magnetic stirrer and containing anhydrous dimethylamine (approximately 100 mL) at -78°C. This was stirred overnight allowing the reaction to warm slowly to 25°C and the dimethylamine to evaporate. The mixture was heated on a steam bath for 30 min, removing residual dimethylamine, and was then

cooled in an ice bath. The white, crystalline solid was suction filtered, washed with cold toluene and air dried. This was dissolved in a saturated, aqueous $NaHCO_3$ solution (30 mL) and stirred overnight with an equal volume of CH_2Cl_2. (For maximum yield of the water-soluble pyrrole, this extraction was repeated.) The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated. Recrystallization from THF-CH_2Cl_2 (15:1) gave 1.2 g (93%) of 31b as colorless needles: mp 206-207°C: ^1H NMR (250 MHz) δ 3.02 (12H, s), 6.72 (2H, d, J=2.75 Hz), 11.22 (1H, br s); ^{13}C NMR δ 37.37, 118.02, 119.81, 167.98; mass spectrum, m/e (relative intensity) 209 (29, M^+), 165 (40), 164 (59), 122 (100), 94 (21), 44 (20); IR 3110 (NH), 1630 and 1610 (CO) cm^{-1}.

Anal. Calcd for $C_{10}H_{15}N_3O_2$: C, 57.42; H, 7.18.
Found: C, 57.11; H, 7.35.

3,4-*bis*(N-Morpholinecarboxamide)pyrrole (31c).

Diacid chloride 30 was prepared in toluene as described above and added slowly *via* cannula to a flask equipped with a drying tube and containing morpholine (25 mL) in toluene (75 mL) at 2°C. This was stirred overnight, allowing the reaction to warm to 25°C. The mixture was evaporated to dryness and added to water (40 mL). The aqueous solution was acidified with conc. HCl, saturated with NaCl and then thoroughly extracted with CH_2Cl_2. The combined

organic fractions were dried over anhydrous Na_2SO_4 and evaporated. Purification by flash column chromatography[95] (THF) gave 31c (91%) as a colorless solid: mp 153-157°C; ^1H NMR δ 3.61 (16H, br s), 6.71 (2H, d, J=2.5 Hz), 10.72 (1H, br s); ^{13}C NMR δ 45.37, 66.85, 117.19, 120.06, 166.39; mass spectrum, m/e (relative intensity) 293 (8, M^+), 207 (50), 122 (100), 94 (30), 86 (71), 70 (24), 56 (23), 42 (20); IR 3375 (NH), 1620 (CO) cm^{-1}.

3,4-*bis*(N-Methylcarboxamide)pyrrole (31d).

Pyrrole 31d was prepared as described for 31b using anhydrous methylamine. After heating on a steam bath to remove residual methylamine, the mixture was filtered. The white solid was washed with cold acetone followed by cold water. Recrystallization from hot water provided 31d as a white solid: mp 228-229.5°C; ^1H NMR (in warm D_2O, acetone-H_6 as a reference) δ 2.33 (6H, s), 7.15 (2H, s); mass spectrum, m/e (relative intensity) 181 (55, M^+), 151 (49), 150 (47), 122 (100), 94 (30); IR 1620 (CO) cm^{-1}.

2,5-Dimethyl-3,4-*bis*(N,N-dimethylcarboxamide)pyrrole (37).

A 2000 mL flask, equipped with a mechanical stirrer and an efficient condenser, was charged under nitrogen with NaH[94] (10.0 g, 0.208 mol) and anhydrous Et_2O (1200 mL). This was stirred and warmed to a gentle reflux and

N,N-dimethylacetylacetamide, 35,[95] (20.0 g, 0.155 mol) was added dropwise over 30 min. After 24 h I_2, dissolved in a minimum amount of Et_2O, was added dropwise in portions (20, 10, 5, 5 g) at 1 h intervals to the vigorously stirred suspension. This was stirred at gentle reflux for another 24 h, cooled to RT and a solution of $NaHSO_3$ (10 g), NH_4OAc (30 g) in water (300 mL) was added slowly. The ether was removed on a rotary evaporator and the remaining aqueous solution was stirred at 70°C for 15 h, cooled to 25°C, neutralized with $NaHCO_3$, and thoroughly extracted with ether. The aqueous layer was saturated with NaCl and stirred overnight with an equal volume of CH_2Cl_2. (For a maximum yield of the water-soluble pyrrole, this extraction was repeated.) The CH_2Cl_2 layer was dried over anhydrous Na_2SO_4 and concentrated, providing 15.5 g of a dark oil. Recrystallization from a minimum amount of THF gave 8.15 g of crude starting material, 35, and 7.35 g (40%) of 37 as colorless crystals: mp 183-184.5°C; ^1H NMR (250 MHz) δ 2.10 (6H, s), 2.97 (12H, s), 9.37 (1H, br s); ^{13}C NMR δ 11.56, 35.33, 38.65, 114.17, 127.37, 168.82; mass spectrum, m/e (relative intensity) 237 (20, M^+), 192 (30), 150 (100), 122 (24), 121 (30), 42 (34); IR 3200 (NH), 1620 (CO) cm^{-1}.

Anal. Calcd for $C_{12}H_{19}N_3O_2$: C, 60.76; H, 8.02.

Found: C, 60.60; H, 8.12.

2,5-*bis*(Acetoxymethyl)-3,4-*bis*(1H,1H-heptafluorobut-1-yl)-pyrrole (38a).

A solution of 2a (2.00 g, 4.36 mmol) and $Pb(OAc)_4$[96] (4.26 g, 2.2 equiv) in acetic acid (50 mL) and acetic anhydride (2.0 mL) was stirred under a nitrogen atmosphere at 25°C for 20 h. CH_2Cl_2 (150 mL) was added and the solution was washed with water followed by saturated aqueous $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. Recrystallization from CH_2Cl_2-hexane gave 2.40 g (96%) of 38a as colorless crystals: mp 60-61°C; ^1H NMR δ 2.07 (6H, s), 3.31 (4H, t, J=19.5 Hz), 5.02 (4H, s), 9.37 (1H, br s); ^{13}C NMR δ 20.85, 25.85 (t, J=24.1 Hz), 56.99, 110.89, 109.40 (t of q of t, J=265.2, 37.9, 38.0 Hz), 116.61 (t of t, J=252.5, 31.5 Hz), 118.19 (q ot t, J=287.6, 34.2 Hz), 127.83, 172.11; mass spectrum, m/e (relative intensity) 575 (4, M^+), 516 (16), 473 (20), 43 (100); IR 3350 and 3250 (NH), 1750 and 1720 (CO), 1220 (CF) cm^{-1}.

Anal. Calcd for $C_{18}H_{15}NO_4F_{14}$: C, 37.56; H, 2.61.
Found: C, 37.45; H, 2.63.

2,5-*bis*(Bromomethyl)-3,4-*bis*(1H,1H-heptafluorobut-1-yl)-pyrrole (38b).

Pyrrole 2a (0.500 g, 1.09 mmol) and N-bromosuccinimide (0.425 g, 2.1 equiv) in CCl_4 (30 mL) were heated at 70°C for 50 min. The dark reaction mixture was cooled to 3°C for 30 min and then suction filtered. The filtrate was

concentrated at 0.2 mm Hg pressure yielding a sensitive dark red oil which was used directly in the preparation of 38a: ^{1}H NMR δ 3.20 (4H, t, J=20 Hz), 4.40 (4H, s).

2,5-*bis*(Dichloromethyl)-3,4-*bis*(1H,1H-heptafluorobut-1-yl)-pyrrole (38d).

SO_2Cl_2 (0.700 mL, 8.61 mmol) was added to a solution of pyrrole 2a (0.600 g, 1.31 mmol) in CH_2Cl_2 (10 mL) at 3°C and stirred for 3 h. Water was added and the solution was extracted with CH_2Cl_2. The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated yielding 0.720 g (92%) of 38d as a stable yellow oil which appeared pure by NMR and was used directly in the preparation of 38e: ^{1}H NMR δ 3.23 (4H, t, J=20 Hz), 6.67 (2H, s), 9.13 (1H, br s).

3,4-*bis*(1H,1H-Heptafluorobut-1-yl)-2,5-diformylpyrrole (38e).

A solution of pyrrole 38d (0.620 g, 1.04 mmol) in THF (30 mL) and water (6 mL) was stirred at 40°C for 6 h. Water (150 mL) was added and the solution extracted with CH_2Cl_2. The combined organic fractions were washed with saturated aqueous $NaHCO_3$ and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave 0.40 g (80%) of 38e as a slightly yellow solid: mp 51-54°C; ^{1}H NMR δ 3.58 (4H, t, J=18 Hz), 9.73 (2H, s); mass spectrum, m/e (relative intensity) 487 (33, M^+), 468 (18), 348 (100), 318 (58), 69 (34); IR 3500 (NH), 1690 (CO), 1220 (CF) cm^{-1}.

2,5-*bis*(Acetoxymethyl)-3,4-*bis*(1H,1H-trifluoroeth-1-yl)-pyrrole (38f).

The procedure for 38a was followed by using 2b (1.00 g, 3.86 mmol) and $Pb(OAc)_4$ (3.8 g, 2.2 equiv) in acetic acid (70 mL) and acetic anhydride (2.0 mL). Recrystallization from CH_2Cl_2-hexane gave 1.40 g (97%) of 38f as colorless crystals: mp 117.5-118.5°C; ^1H NMR δ 2.05 (6H, s), 3.34 (4H, q, J=10.8 Hz), 5.03 (4H, s), 9.23 (1H, br s); ^{13}C NMR δ 20.79, 29.14 (q, J=31.5 Hz), 56.84, 111.96, 126.08 (q, J=276.51), 127.11, 171.96; mass spectrum, m/e (relative intensity) 375 (7, M^+), 316 (27), 274 (47), 273 (61), 43 (100); IR 3330 (NH), 1750 and 1725 (CO), 1245 (CF), 1145 cm^{-1}.

Anal. Calcd for $C_{14}H_{15}NO_4F_6$: C, 44.80; H, 4.00.
Found: C, 45.01; H, 4.06.

2,5-*bis*(Carbmethoxy)-3,4-(1H,1H-heptafluorobut-1-yl)pyrrole (39a).

To a magnetically stirred 500-mL flask equipped with an efficient condenser and containing 2a (2.00 g, 4.36 mmol) in dry THF (10 mL) at 60°C was added SO_2Cl_2 (5 mL) *via* pipet as rapidly as possible (vigorous reaction!). This was stirred for 2 min and additional SO_2Cl_2 (2 mL) was added. After 2 min, warm (40°C) 95% MeOH (40 mL) was added (vigorous reaction) and the solution refluxed for 90 min. This was

cooled and extracted with Et_2O. The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated. Recrystallization from hexane (25°C— -10°C) gave 2.30 g (97%) of 39a as a colorless solid: mp 85-87°C; ^1H NMR δ 3.67 (4H, t, J=19 Hz), 3.85 (6H, s); mass spectrum (CI, CH_4), m/e 548 (M^++1); IR 3300 (NH), 1750 and 1725 (CO) cm^{-1}.

2,5-*bis*(Carbethoxy)-3,4-(1H,1H-heptafluorobut-1-yl)pyrrole (39b).

Pyrrole 2a was oxidized with SO_2Cl_2 as described above and hydrolyzed in 95% EtOH under reflux for 1 h. Water was added and the solution extracted with CH_2Cl_2. The combined organic fractions were washed with saturated aqueous $NaHCO_3$, dried over anhydrous Na_2SO_4 and concentrated, affording 39b as a yellow oil (87%): ^1H NMR δ 1.33 (6H, t, J= 7 Hz), 3.67 (4H, t, J=19 Hz), 4.27 (4H, q, J=7 Hz); mass spectrum, m/e (relative intensity) 575 (49, M^+), 530 (13), 484 (28), 436 (48), 408 (41), 378 (30), 332 (66), 119 (100), 69 (74).

2,5-Dicarboxy-3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole (39c).

To a magnetically stirred 1000-mL flask equipped with an efficient condenser and containing 2a (7.00 g, 15.3 mmol) in dry THF (30 mL) at 60°C was added SO_2Cl_2 (12 mL) *via* pipett as rapidly as possible (vigorous reaction!).

This was stirred for 3 min and additional SO_2Cl_2 (6 mL) was added. After 3 min hot (60°C) 80% aqueous THF (200 mL) was added (vigorous reaction!) and the solution was refluxed for 3 h. The mixture was poured into water (500 mL) and thoroughly extracted with Et_2O. The Et_2O fractions were combined and extracted with saturated aqueous $NaHCO_3$. The combined $NaHCO_3$ fractions were washed with Et_2O, heated on a steam bath and slowly acidified with concentrated HCl. Suction filtration and thorough washing with water gave 6.33 g (80%) of 39c as a white powder. An analytical sample was obtained by recrystallization from hexane-Et_2O (20:1); mp 270-272°C(dec.); ^1H NMR (acetone-d_6) δ 3.92 (4H, t, J= 20.0 Hz); ^{13}C NMR δ 26.38 (t, J=22.6 Hz), 110.09 (t of q of t, J=262.6, 37.1, 37.2 Hz), 117.67 (t of t, J=253.5, 31.5 Hz), 118.98 (q of t, J=286.8, 33.3 Hz), 119.20, 126.05, 161.52; mass spectrum (CI, CH_4), m/e 520 (M+1 ion); IR 3420 (NH), 3150-2460 (OH), 1680 (CO), 1220 (CF) cm^{-1}.

Anal. Calcd for $C_{14}H_7NO_4F_{14}$: C, 32.37; H, 1.35.
Found: C, 32.46; H, 1.37.

2,5-Dicarboxy-3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole (39c) prepared from 39a.

A mixture of 39a (0.300 g, 0.548 mmol) and lithium iodide (1.32 g) in DMF (20 mL) was refluxed for 3 h. The dark solution was diluted with H_2O (100 mL), acidified with 5% HCl and then extracted with Et_2O. The organic fractions

were combined and extracted with saturated aqueous $NaHCO_3$. The combined $NaHCO_3$ fractions were acidified and then extracted with ether. The organic layer was dried over anhydrous Na_2SO_4 and concentrated affording 0.160 g (56%) of 39c as a white powder.

2,5-Dicarboxy-3,4-*bis*(1H,1H-trifluoroeth-1-yl)pyrrole (39d).

Pyrrole 39d was prepared from 2b in 45% yield as described for 39c: mp 294-296°C (dec.); ^1H NMR (acetone-d_6) δ 3.91 (4H, t, J=11 Hz); mass spectrum (CI, CH_4) 320 (M^++1); IR 2700 (OH), 1700 and sh at 1680 (CO) cm^{-1}.

2,5-Diiodo-3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole 40a.

Precautions against direct illumination were taken during all the following operations. A solution of I_2 (3.0 g) and NaI (3.2 g) in water (14 mL) was added to a flask wrapped in aluminum foil and charged with 39c (1.0 g, 1.93 mmol) and $NaHCO_3$ (1.5 g) in water (40 mL) and $ClCH_2CH_2Cl$ (40 mL). The two-phase mixture was stirred under a nitrogen atmosphere at 25°C for 48 h. $NaHSO_3$ was added slowly until the red color dissipated and the solution was extracted with CH_2Cl_2. The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated on a rotary evaporator yielding 1.27 g (97%) of 40a as a slightly red solid. This product appeared quite pure by NMR and TCL and was used

directly in subsequent reactions. An analytical sample was obtained by recrystallization from petroleum ether at -10°C: mp 78-82°C (dec.); ^{1}H NMR δ 3.28 (4H, t, J=19.0 Hz), 8.25 (1H, br s); ^{13}C NMR δ 29.13 (t, J=23.1 Hz), 72.29, 109.14 (t of q of t, J=264.2, 38.9, 39.0 Hz), 116.90; (t of t, J=253.4, 30.5 Hz), 118.07 (q of t, J=290.8, 34.2 Hz), 119.02; mass spectrum, m/e (relative intensity) 683 (58, M^+), 514 (78), 345 (23), 268 (51), 114 (34), 69 (100); IR 3470 (NH), 1230 (CF) cm^{-1}.

Anal Calcd. for $C_{12}H_{15}NF_{14}I_2$: C, 21.08; H, 0.73.
Found: C, 21.45; H, 0.80.

2,5-Diiodo-3,4-*bis*(1H,1H-trifluoroeth-1-yl)pyrrole (40b).

Pyrrole 40b was prepared from 39d in 97% yield as described for 40a: mp 87-88.5°C; ^{1}H NMR (acetone-d_6) δ 3.23 (4H, q, J=11 Hz), 8.80 (1H, br s); mass spectrum, m/e (relative intensity) 483 (100, M^+), 464 (2), 414 (72), 306 (13), 160 (12), 113 (11), 69 (31), 63 (16), 40 (11).

3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole (41).

A suspension of 40a (1.60 g, 2.34 mmol), zinc dust (1.00 g), NH_4Cl (1.60 g) and 95% EtOH (40 mL) was stirred under a nitrogen atmosphere at 75°C for 15 h. The excess zinc was filtered and washed with CH_2Cl_2 (20 mL). The filtrate was diluted with water (100 mL) and extracted with

CH_2Cl_2. The combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated yielding 0.98 g (98%) of 41 as a pale yellow oil. This product appeared quite pure by NMR and TLC and was used directly in the preparation of 57: ^1H NMR δ 3.24 (4H, t, J=19.5 Hz), 6.77 (2H, d, J=2.75 Hz), 8.22 (1H, br s); ^{13}C NMR δ 27.22 (t, J=23.8 Hz), 109.62 (t of q of t, J=263.6, 37.9, 38.0 Hz), 110.76, 116.78 (t of t, J=252.5, 30.5 Hz), 118.37 (q of t, J=287.6, 34.2 Hz), 119.53; mass spectrum, m/e (relative intensity) 431 (14, M^+), 412 (8), 262 (100), 142 (15), 93 (31), 69 (39); IR (neat) 3500 (NH), 1220 (CF) cm^{-1}.

3,4-*bis*(1H,1H-Heptafluorobut-1-yl)pyrrole(41)prepared from 40a by catalytic hydrogenation.

Precautions against direct illumination were taken during all the following operations. A solution of 40a (1.00 g, 1.46 mmol) in MeOH (15 mL) was hydrogenated in a Parr apparatus at 75 lbs/in.^{2} of H_2 for 40 h in the presence of PtO_2 (10 mg) and NaOAc (0.40 g). CH_2Cl_2 (100 mL) was added and the solution was washed with water followed by aqueous $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4 and concentrated, providing 0.53 g (84%) of 41.

2,5-*bis*(Chloromethyl)-3,4-*bis*(2-methyl-2-nitroprop-1-yl)-pyrrole (42).

SO_2Cl_2 (0.200 mL, 2.46 mmol) in $ClCH_2CH_2Cl$ (5 mL) was added dropwise over 30 min to pyrrole 4 (0.367 g, 1.24 mmol) in $ClCH_2CH_2Cl$ (8 mL) at 25°C and stirred for another 30 min. The dark-blue solution was evaporated to dryness at 0.2 mmHg to yield 0.45 g (99%) of 42: ^{1}H NMR δ 1.53 (12H, s), 3.00 (4H, s), 4.43 (4H, s); ^{13}C NMR δ 25.73, 35.70. 37.14, 88.80, 115.77, 127.35.

3,4-*bis*(2-Methyl-2-nitroprop-1-yl)-2,5-dicarboxypyrrole (43).

To a magnetically stirred 1000-mL flask equipped with an efficient condenser and containing 4 (2.43 g, 8.18 mmol) in $ClCH_2CH_2Cl$ (15 mL) at 25°C was added SO_2Cl_2 (4.00 mL, 6.00 equiv) *via* pipett (vigorous reaction!) and then stirred for 4.5 h. To this was added aqueous 80% acetone (200 mL) and then heated under gentle reflux for 5 h. The reaction mixture was evaporated to dryness and the residue dissolved in saturated aqueous $NaHCO_3$ (100 mL). The solution was thoroughly washed with CH_2Cl_2 and then acidified with concentrated HCl. Suction filtration and washing with water gave 1.46 g (50%) of 43 as a white powder which appeared pure by NMR and was used directly in the preparation of 44: ^{1}H NMR δ 1.55 (12 H, s), 3.45 (4H, s), 8.90 (1H, br s);

mass spectrum, m/e (relative intensity) 357 (2, M^+), 280 (48), 264 (94), 223 (100), 208 (60), 204 (45), 186 (70), 181 (41); IR 3380 (NH), 1690 (CO) cm^{-1}.

3,4-*bis*(2-Methyl-2-nitroprop-1-yl)-2,5-diiodopyrrole (44).

Pyrrole 44 was prepared from 43 in 96% yield as described for 40a. The product appeared pure by NMR and was used directly in the preparation of 61: ^1H NMR (acetone-d_6) δ 1.60 (12H, s), 3.03 (4H, s), 10.67 (1H, br s); ^{13}C NMR (acetone-d_6) δ 26.20, 38.39, 72.86, 89.74, 124.25; mass spectrum, m/e (relative intensity) 521 (29, M^+), 428 (32), 345 (47), 317 (33), 259 (46), 207 (38), 164 (79), 132 (100), 118, (64), 91 (35), 77 (40).

2,5-*bis*(Acetoxymethyl)-3,4-*bis*(*p*-tolysulfonylmethyl)pyrrole (45).

The procedure for 38a was followed by using 8 (0.243 g, 0.564 mmol) and $Pb(OAc)_4$ (0.625 g, 2.5 equiv) in acetic acid (15 mL) at 25°C for 70 h. This provided 0.277 g (90%) of 45 as a yellow-orange foam. Due to the sensitive nature of 45, it was used directly in subsequent reactions: ^1H NMR δ 2.01 (6H, s), 2.40 (6H, s), 4.30 (4H, s), 4.70 (4H, s), 7.22 (4H, d, J=8 Hz), 7.58 (4H, d, J=8 Hz); ^{13}C NMR δ 20.88, 21.62, 52.56, 56.17, 110.08, 128.29, 128.71, 129.84, 135.82, 144.90, 171.64; IR 3300 (NH), 1730 (CO) cm^{-1}.

2,5-*bis*(Acetoxymethyl)-2,5-diiodopyrrole (46).

The procedure for 38a was followed by using 2,5-dimethyl-3,4-diiodopyrrole[42] (0.410g, 1.18 mmol) and $Pb(OAc)_4$ (1.04 g, 1.98 equiv) in acetic acid (20 mL) and acetic anhydride (0.25 mL) for 4 h under complete exclusion of light. This gave 0.520 g (95%) of 46 as a brown oil: ^1H NMR δ 2.08 (6H, s), 5.08 (4H, s), 9.51 (1H, br s); ^{13}C NMR δ 20.84, 60.12, 78.43, 130.92, 172.01; mass spectrum, m/e (relative intensity) 463 (4, M^+), 361 (9), 276 (12), 60 (15), 43 (100); IR 3300 (NH), 1725 (CO) cm^{-1}.

2,5-*bis*(Acetoxymethyl)-2,5-dibromopyrrole (47).

The procedure for 38a was followed by using 11 (1.00 g, 3.95 mmol) and $Pb(OAc)_4$ (3.42 g, 1.95 equiv) in acetic acid (50 mL) and acetic anhydride (1 mL) for 1.75 h, providing 1.40 g (96%) of 47 as a sensitive red oil: ^1H NMR δ 2.06 (6H, s), 5.00 (4H, s); ^{13}C NMR δ 20.80, 57.59, 101.17, 125.77, 172.05; mass spectrum m/e (relative intensity) 371 (1, M^+), 370 (1), 369 (2, M^+), 368 (1), 367 (1, M^+), 310 (7), 268 (13), 267 (14), 43 (100).

2,5-*bis*(Acetoxymethyl)-2,5-dichloromethylpyrrole (48).

The above procedure was followed for 12 providing 48 as a sensitive yellow oil (90%): ^1H NMR δ 2.08 (6H, s), 5.00 (4H, s).

2,5-*bis*(Acetoxymethyl)-3,4-*bis*(carbethoxy)pyrrole (49).

The procedure for 38a was followed by using 26b (0.182 g, 0.761 mmol) and $Pb(OAc)_4$ (0.90 g, 2.66 equiv) in acetic acid (10 mL) and acetic anhydride (0.25 mL) at 90°C for 48 h. Recrystallization from petroleum ether (30—60°C)—Et_2O gave 0.20 g (74%) of 49 as a white solid: mp 74-75°C; ^1H NMR δ 1.33 (6H, t, J=7 Hz), 2.07 (6H, s), 4.27 (4H, q, J=7 Hz), 5.22 (4H, s); ^{13}C NMR δ 14.25, 20.78, 57.27, 60.72, 115.62, 130.87, 164.10, 171.93; mass spectrum, m/e (relative intensity) 355 (4, M^+), 310 (5), 296 (6), 253 (25), 224 (15), 207 (38), 178 (17), 162 (10), 43 (100); IR 3350 (NH), 1720 (CO) cm^{-1}.

2,5-*bis*(Acetoxymethyl)-3,4-*bis*(N,N-dimethylcarboxamide)-pyrrole (52).

A solution of 37 (4.00 g, 16.9 mmol) and $Pb(OAc)_4$ (18.7 g, 2.5 equiv) in acetic acid (70 mL) and acetic anhydride (1.2 mL) was stirred under nitrogen at 50°C for 26 h. This was cooled to 25°C, added to a saturated, aqueous NaCl solution (250 mL), and stirred overnight with an equal volume of $CHCl_3$. The $CHCl_3$ layer was dried over Na_2SO_4 and concentrated, affording 8.0 g of a yellow oil, consisting of 52 and acetic acid. Due to the high solubility of 52 in water and sensitivity to base, this mixture was used directly in the preparation of 62b. An analytical sample

was obtained by recrystallization from THF-Et_2O: mp 117-118°C; ^1H NMR (250 MHz) δ 2.07 (6H, s), 2.99 (12H, s), 5.08 (4H, s), 9.60 (1H, br s); ^{13}C NMR δ 20.88, 35.17, 39.08, 57.22, 118.18, 126.88, 166.61, 171.96; mass spectrum, m/e (relative intensity) 309 [1, $(M-(CH_3)_2N)^+$], 293 [4, $(M-CH_3CO_2H)^+$], 250 (8), 207 (23), 190(9), 147 (11), 60 (43), 45 (72), 43 (100); IR 3140 (NH), 1750 (CO), 1625 (CO) cm^{-1}.

Anal. Calcd for $C_{16}H_{23}N_3O_6$: C, 54.39; H, 6.52.
Found: C, 54.52; H, 6.55.

2,5-*bis*(Chloromethyl)-3,4-*bis*(trifluoromethyl)pyrrole (55).

SO_2Cl_2 (1.0 mL, 12.3 mmol) was added to a solution of pyrrole 23b (0.198 g, 0.857 mmol) in $ClCH_2CH_2Cl$ (6 mL) at 3°C and stirred for 10 h. The mixture was evaporated to dryness at 0.2 mmHg pressure affording 0.254 g (99%) of 55 as a slightly red oil: ^1H NMR δ 4.70 (4H, br s), 8.80 (1H, br s); ^{13}C NMR δ 35.71, 110 (q, J=41.0 Hz), 122.26 (q, J=269.8 Hz), 129.00; mass spectrum (CI, CH_4), m/e 300 (M^++1).

3,4-*bis*(Trifluoromethyl)-2,5-diformylpyrrole (56).

Bromine (1.8 mL) was added to a solution of 23b (1.87 g, 8.10 mmol) in HOAc (40 mL) at 25°C and stirred for 3 min. The mixture was rapidly cooled to 3°C and SO_2Cl_2

(7.4 mL) added in one portion. After 5 min the reaction mixture was allowed to warm to 25°C and stirred for another 2 h. Water (9 mL) was added carefully to the ice-cooled solution and then heated at 90°C for 28 h. The cooled solution was made basic with saturated aqueous $NaHCO_3$ and thoroughly extracted with CH_2Cl_2. The combined organic fractions were dried over anhydrous $NaHCO_3$ and concentrated. Recrystallization from CH_2Cl_2 gave 1.68 g (80%) of 56 as colorless crystals: mp 120-121.5°C; ^1H NMR (acetone-d_6) δ 9.93 (2H, s); ^{13}C NMR (acetone-d_6) δ 117.69 (q, J=45.3 Hz), 122.92 (q, J=268.0 Hz), 134.04, 181.08; mass spectrum, m/e (relative intensity) 259 (100, M^+), 240 (16), 238 (67), 211 (18), 210 (16), 182 (27), 114 (35), 69 (59), IR 3150 (NH), 1690 and 1720 (CO) cm^{-1}.

Octakis(1H,1H-heptafluorobut-1-yl)porphyrin (57) prepared from 38a.

A solution of 38a (0.48 g, 0.835 mmol) and 48% HBr (3.0 mL) in *n*-propanol (20 mL) was heated at 100°C for 60 h with a slow stream of O_2 bubbled through the reaction mixture. The solution was then allowed to stand in a large open beaker for 14 days. Filtration and recrystallization from acetone gave 0.073 g (20%) of 57: mp 282-283°C: ^1H NMR (acetone-d_6, 80°C) δ -3.21 (2H, br s), 5.34 (16H, t, J=18.4 Hz), 10.62 (4H, s); UV-vis (acetone)

$\lambda_{max}(\varepsilon_M)$ 402 (294,000), 499 (17,800), 529 (4900), 574 (5900), 599 (1200), 627 (1400); IR 3275 (NH), 2850 (CH), 1220 (CF) cm^{-1}.

Anal. Calcd for $C_{52}H_{22}F_{56}N_4$: C, 35.33; H, 1.25.
Found: C, 35.38; H, 1.16.

Octakis(1H,1H-heptafluorobut-1-yl)porphyrin (57) prepared from 38b.

A solution of crude pyrrole 38b (as prepared above) and 48% HBr (2.5 mL) in 1-propanol (20 mL) was heated at 100°C for 65 h with a slow stream of O_2 bubbled through the reaction mixture. The solution was then allowed to stand in a large open beaker for 28 days. Filtration and recrystallization from acetone gave 0.0337 g (7.0%) of 57.

Octakis(1H,1H-heptafluorobut-1-yl)porphyrin (57) prepared from 39c.

SO_2Cl_2 (0.152 mL, 1 equiv) was added to pyrrole 2a (0.43 g, 0.937 mmol) in CH_2Cl_2 (20 mL) at 3°C and stirred for 1 h. This was followed by evaporation of the solvent at 0.2mmHg pressure. 1-Propanol (20 mL) and 48% HBr (1.5 mL) were added and the solution was heated at 100°C for 70 h with a slow stream of O_2 bubbled through the reaction mixture. This was allowed to stand in a large open beaker for 28 days. Filtration and recrystallization from acetone gave 0.062 g (15%) of 57.

Octakis(1H,1H-heptafluorobut-1-yl)porphyrin (57) prepared from 40a.

A solution of 40a (1.19 g, 1.74 mmol), 37% formaldehyde (8.0 mL) and 48% HBr (2.5 mL) in 1-propanol (70 mL) was heated at 100°C for 35 h. The mixture is cooled and suction filtered. Recrystallization from acetone gave 0.238 g (31%) of 57. The filtrate was allowed to stand in a large open beaker for 14 days. Filtration and recrystallization from acetone gave another 0.030 g (4%) of 57.

Octakis(1H,1H-heptafluorobut-1-yl)porphyrin (57) prepared from 41.

A solution of 41 (0.78 g, 1.80 mmol), 37% formaldehyde (7.0 mL) and 48% HBr (1.6 mL) in 1-propanol (60 mL) was heated at 100°C for 48 h. The mixture was allowed to stand in a large open beaker for 21 days. Filtration of the reaction mixture and recrystallization from acetone gave 0.240 g (30%) of 57.

2,3-*bis*(Dimethylaminomethyl)3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole (58).

Pyrrole 41 (0.20 g, 0.464 mmol) and excess 9 (0.30 g) in $ClCH_2CH_2Cl$ (8 mL) were stirred at 80°C for 17 h. CH_2Cl_2 (50 mL) was added and the solution was thoroughly washed

with saturated aqueous $NaHCO_3$. The organic layer was dried over anhydrous Na_2SO_4 and concentrated, yielding 0.210 g (83%) of 58 as a yellow oil: ^1H NMR δ 2.21 (12H, s), 3.20 (4H, t, J=20 Hz), 3.30 (4H, s), 8.98 (1H, br, s); ^{13}C NMR δ 25.70 (t, J=23.3 Hz), 45.21, 54.78, 107.55, 109.42 (t of q of t, J=265.0, 37.2, 37.1 Hz), 116.90 (t of t, J=251.4, 30.5 Hz), 118.17 (q of t, J=286.7, 34.2 Hz), 128.69; mass spectrum, m/e (relative intensity) 545 (0.4, M^+), 501 (7), 457 (7), 338 (4), 169 (3), 119 (2), 106 (2), 73 (3), 58 (100), 45 (10), 44 (24), 42 (18); IR 3200 (NH), 1230 (CF) cm^{-1}.

Octakis(1H,1H-trifluoroeth-1-yl)porphyrin (59) prepared from 38f.

Porphyrin 59 was prepared from 39f (0.68 g, 1.81 mmol) and 48% HBr (9.0 mL) in 1-propanol (50 mL) as described for the preparation of 57 from 38a. Recrystallization from 1-propanol/acetone gave 0.135 g (31%) of 59: mp > 310°C; ^1H NMR (acetone-d_6) δ -3.33 (2H, br s), 5.44 (16H, q, J=10.5 Hz), 10.85 (4H, s); mass spectrum, m/e (relative intensity) 966 (31, M^+), 965 (10), 483 (27), 105 (25), 44 (100), 40 (13), UV-vis (acetone) $\lambda_{max}(\varepsilon_M)$ 401 (276,000), 498 (17,600), 527 (5100), 572 (6000), 599 (1300), 627 (1500), IR 3325 (NH), 2850, (CH), 1230 (CF), 1170 cm^{-1}.

Anal. Calcd for $C_{36}H_{22}F_{24}N_4$: C, 44.72; H, 2,28

Found: C, 44.77; H, 2.55.

Octakis(1H,1H-trifluoroeth-1-yl)porphyrin (59) prepared from 40b.

Porphyrin 59 was prepared from 40b (0.500 g, 1.03 mmol), 37% formaldehyde (4.8 mL) and 48% HBr (1.5 mL) in 1-propanol (40 mL) as described for the preparation of 57 from 40a. Recrystallization from 1-propanol/acetone gave 0.10 g (40%) of 59.

Octakis(2-methyl-2-nitroprop-1-yl)porphyrin (61).

Porphyrin 61 was prepared from 44 as described for the preparation of 57 from 40a. Recrystallization from 1-propanol/acetone gave a 25% yield of 61 as a purple solid: mp 267-268°C: ^{1}H NMR δ -3.50 (2H, s), 1.93 (48H, s), 4.96 (16H, s), 10.05 (4H, s); UV-vis (acetone) $\lambda_{max}(\varepsilon_M)$ 407 (270,000), 502 (19,000), 534 (8,400), 573 (7,300), 627 (3,300); IR 3450 (NH), 2850 (CH), 1530 (NO_2) cm^{-1}.

Octakis(N,N-diethylcarboxamide)porphyrin (62a).

A solution of 3,4-*bis*(N,N-diethylcarboxamide)pyrrole, 31a (0.70 g, 2.64 mmol), 37% formaldehyde (4.0 mL) and 48% HBr (1.4 mL) in water (85 mL) and EtOH (20 mL) was heated under a nitrogen atmosphere at 85°C for 36 h and then allowed to stand in a large open beaker for 14 days (slow air oxidation). Filtration of the reaction mixture and recry-

stallization of the solid from H_2O-MeOH (20:1) gave 0.182 g (25%) of 62a as purple crystals: mp > 350°C; ^1H NMR δ -3.36 (2H, s), 1.16 (24H, br t, J=7 Hz), 1.65 (24H, br t, J=7 Hz), 3.61 (16H, br q, J=7 Hz), 3.96 (16H, br q, J=7 Hz), 10.10 (4H, s); ^{13}C NMR δ 13.38 (q), 14.32 (q), 39.79 (t), 44.45 (t), 102.85 (d), 136.67 (s), 142.80 (s), 165.74 (s); UV-vis ($CHCl_3$) $\lambda_{max}(\varepsilon_M)$ 416 (249,000), 508 (20,000), 540 (7,800), 581 (3,600), 634 (2,900); IR 3350 (NH), 2820 (CH), 1630 (CO) cm^{-1}.

Anal. Calcd for $C_{60}H_{86}N_{12}O_8$: C, 65.34; H, 7.80.
Found: C, 65.86; H, 7.53.

Octakis(N,N-dimethylcarboxamide)porphyrin (62b).

A solution of 3,4-*bis*(N,N-dimethylcarboxamide)pyrrole, 31b (0.70 g, 3.35 mmol), 37% formaldehyde (4.0 mL) and 48% HBr (1.4 mL) in water (105 mL) was refluxed for 36 h and then allowed to stand in a large open beaker for 14 days. This was extracted with CH_2Cl_2 and the combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated. Chromatography of the residue (activity I, neutral alumina, elution with $CHCl_3$/3% sec-butanol) and recrystallization from CH_2Cl_2-Et_2O gave 0.10 g (14%) of 62b as purple needles: mp > 350°C; ^1H NMR δ -3.26 (2H, s), 3.27 (24H, s), 3.59 (24H, s), 10.21 (4H, s); ^{13}C NMR δ 35.73 (q), 39.92 (q), 103.68 (d), 137.10 (s), 142.65 (s), 166.60 (s); UV-vis ($CHCl_3$) $\lambda_{max}(\varepsilon_M)$ 418 (241,000), 510 (17,000), 543 (6,000), 584

(6,000), 636 (2,000); IR 3350 (NH), 2860 (CH), 1675 (CO) cm^{-1}.

Anal. Calcd for $C_{44}H_{54}N_{12}O_8 \cdot H_2O$: C, 58.93; H, 6.25
Found: C, 59.11; H, 6.29.

Octakis(N,N-dimethylcarboxamide)porphyrin (62b) prepared from 52.

A solution of crude 52 (8.0 g) in H_2O (750 mL) was purged of oxygen by bubbling a strong stream of nitrogen through the solution at 60°C for 3 h. To this was added 48% HBr (29 mL), heated under nitrogen at 75°C for 100 h, and then allowed to stand in a large open beaker for 14 days. This was extracted with CH_2Cl_2 and the combined organic fractions were dried over anhydrous Na_2SO_4 and concentrated. Chromatography of the residue (activity I, basic alumina, elution with $CHCl_3$/3% sec-butanol) and recrystallization from CH_2Cl_2-Et_2O gave 0.37 g of 62b (10%, based on 16.9 mmol of 37).

3,4-*bis*(N,N-dimethylcarboxamide)-2-dimethylaminomethylpyrrole (63).

Pyrrole 31b (0.19 g, 0.603 mmol) and 9 (0.126 g, 1 equiv) were stirred in $ClCH_2CH_2Cl$ (10 mL) at relux for 6 h. This was added to saturated aqueous $NaHCO_3$ (20 mL) and thoroughly extracted with CH_2Cl_2. The organic layer was

dried over anhydrous Na_2SO_4 and concentrated, yielding 0.110 g (45.3%) of 63 as a colorless oil: ^1H NMR δ 2.23 (6H, s), 2.93 (6H, s), 2.96 (6H, s), 3.53 (2H, s), 6.81 (1H, s); ^{13}C NMR δ 35.3-38.7 (four broad absorptions for amide methyls), 44.90, 54.27, 117.39, 118.00, 119.27, 128.96, 167.14, 167.72; mass spectrum (CI, CH_4), m/e 267 ($M^+ + 1$); IR 3400 (NH), 1620 (CO) cm^{-1}.

APPENDIX

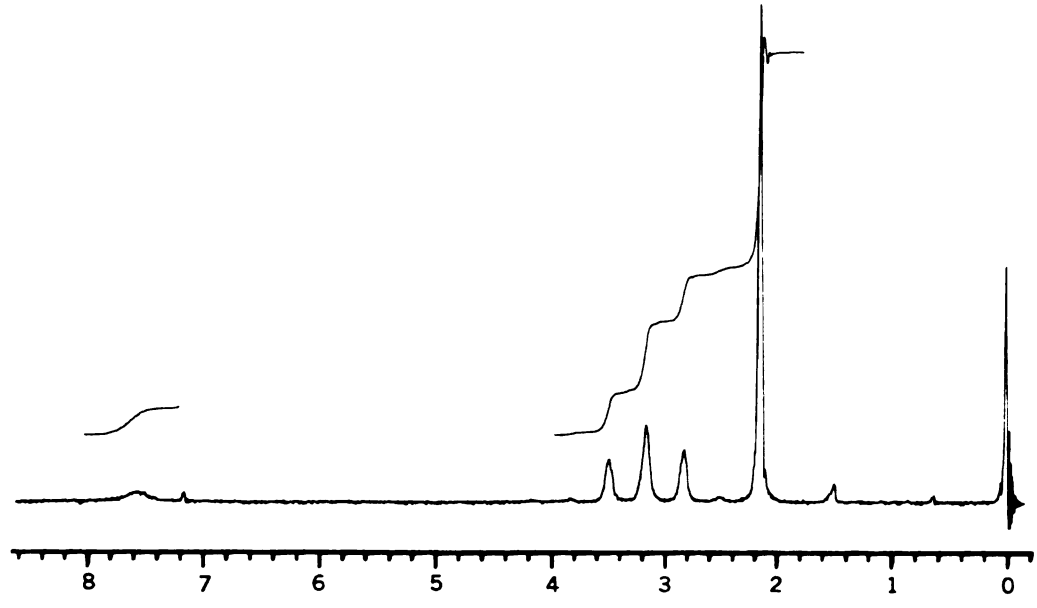


Figure A1. 60 MHz ^{1}H NMR spectrum of 2,5-dimethyl-3,4-*bis*-(1H,1H-heptafluorobut-1-yl)pyrrole (2a).

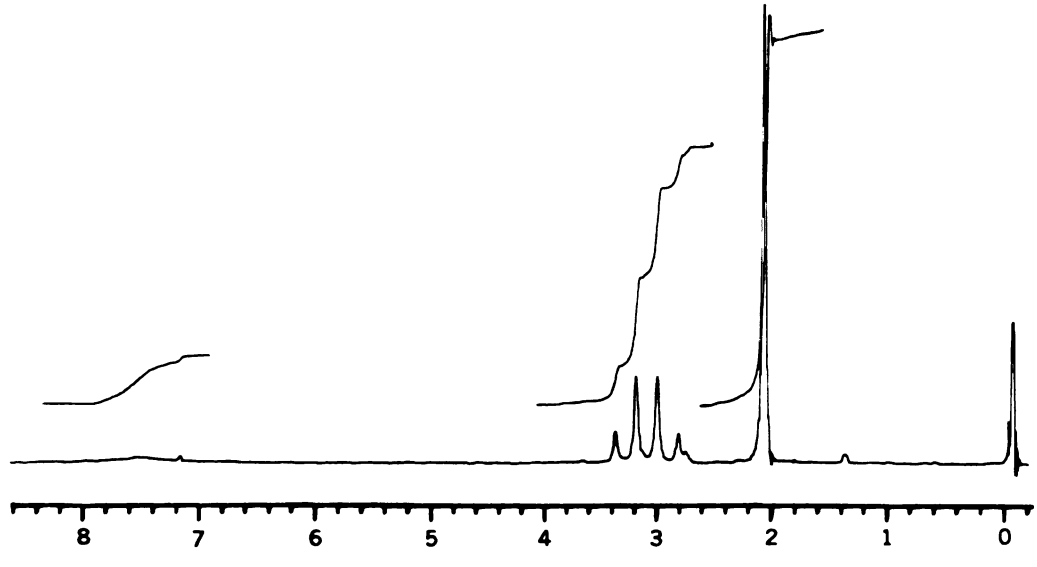


Figure A2. 60 MHz ^{1}H NMR spectrum of 2,5-dimethyl-3,4-*bis*-(1H,1H-trifluoroeth-1-yl)pyrrole (2b).

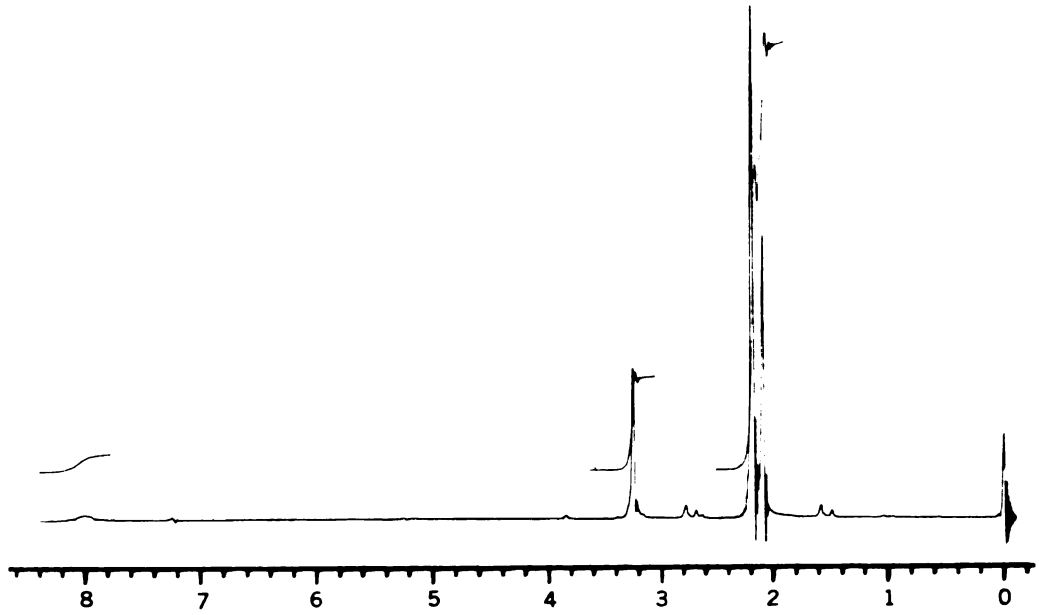


Figure A3. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(dimethylaminomethyl)-2,5-dimethylpyrrole (3).

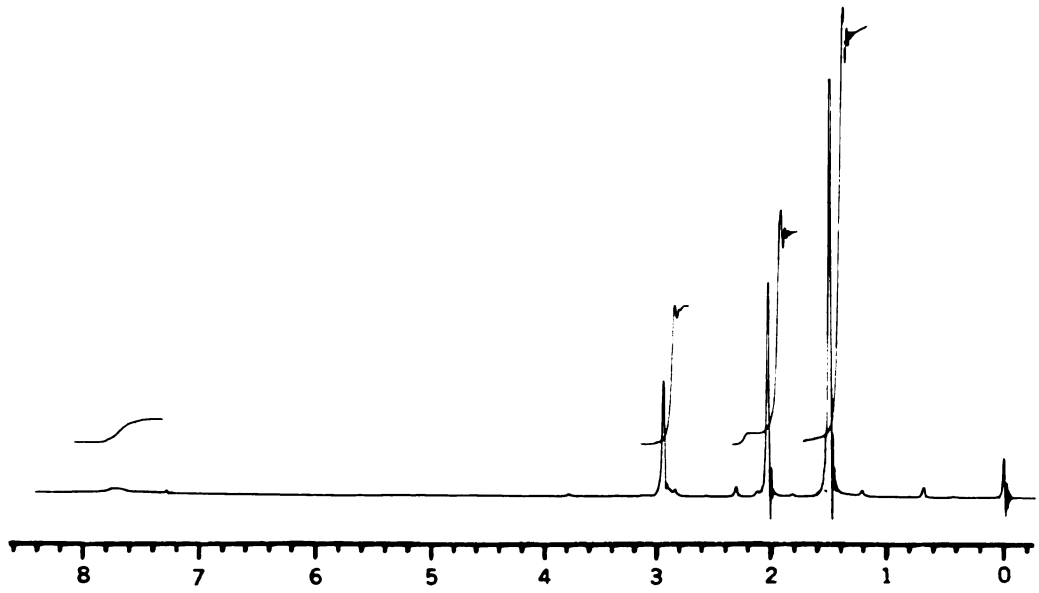


Figure A4. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(2-methyl-2-nitroprop-1-yl)-2,5-dimethylpyrrole (4).

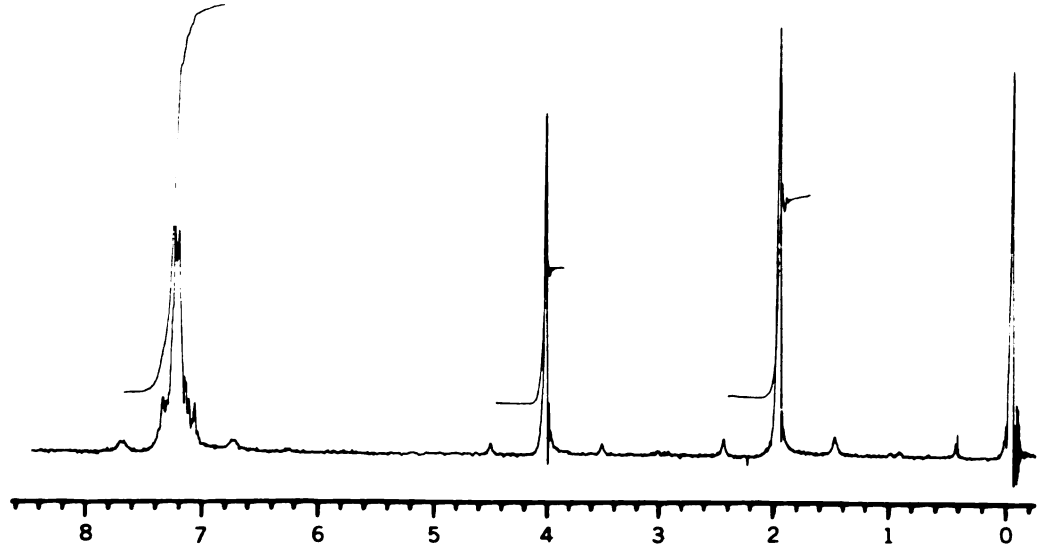


Figure A5. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(phenylthiomethyl)-2,5-dimethylpyrrole (5).

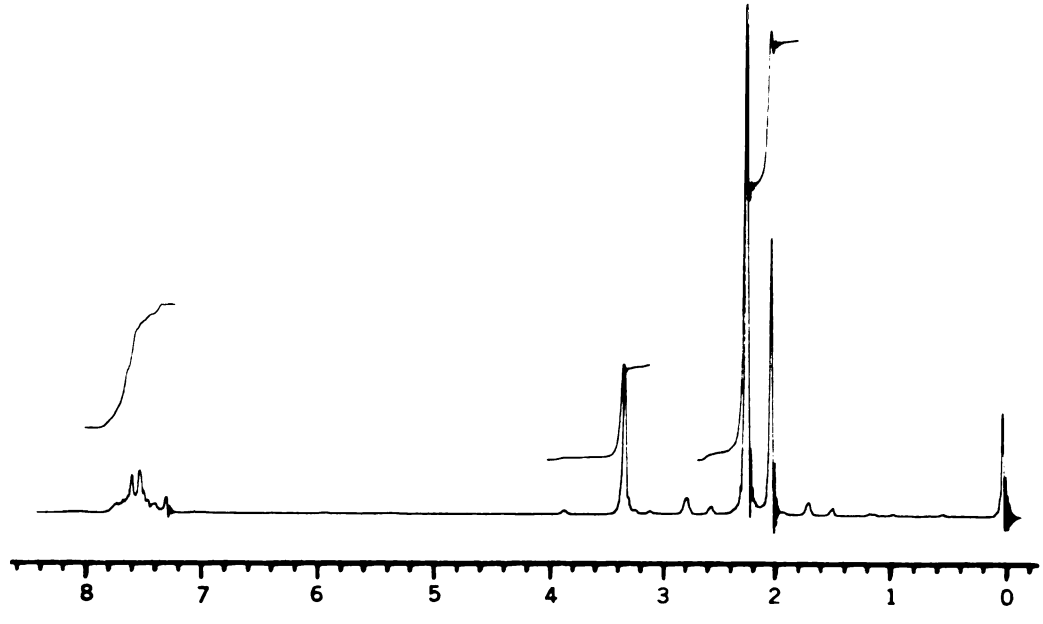


Figure A6. 60 MHz ^{1}H NMR spectrum of N-benzoyl-3,4-*bis*-(dimethylaminomethyl)-2,5-dimethylpyrrole (6).

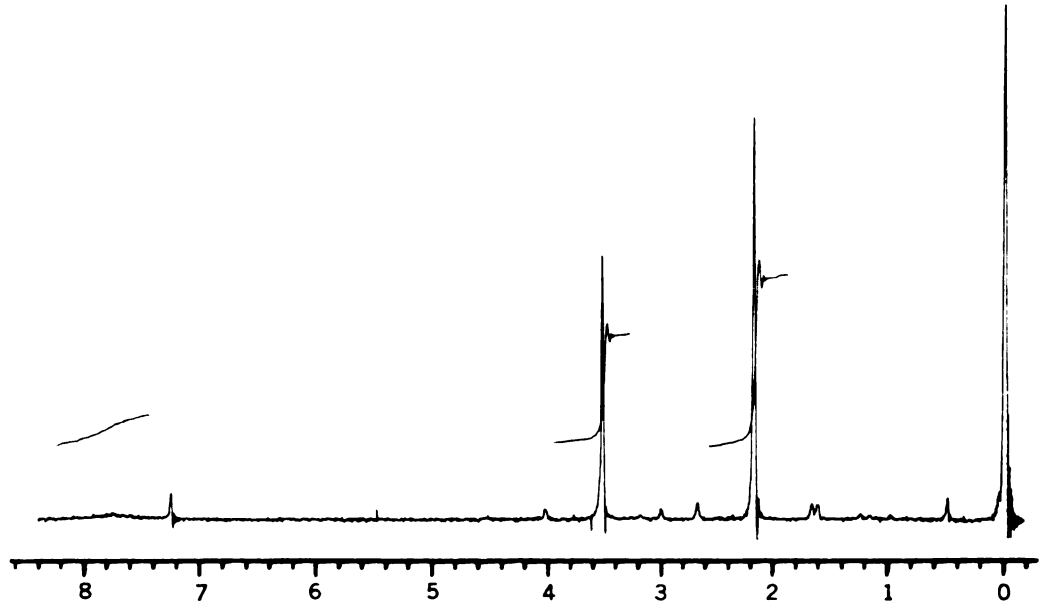


Figure A7. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(cyanomethyl)-2,5-dimethylpyrrole (7).

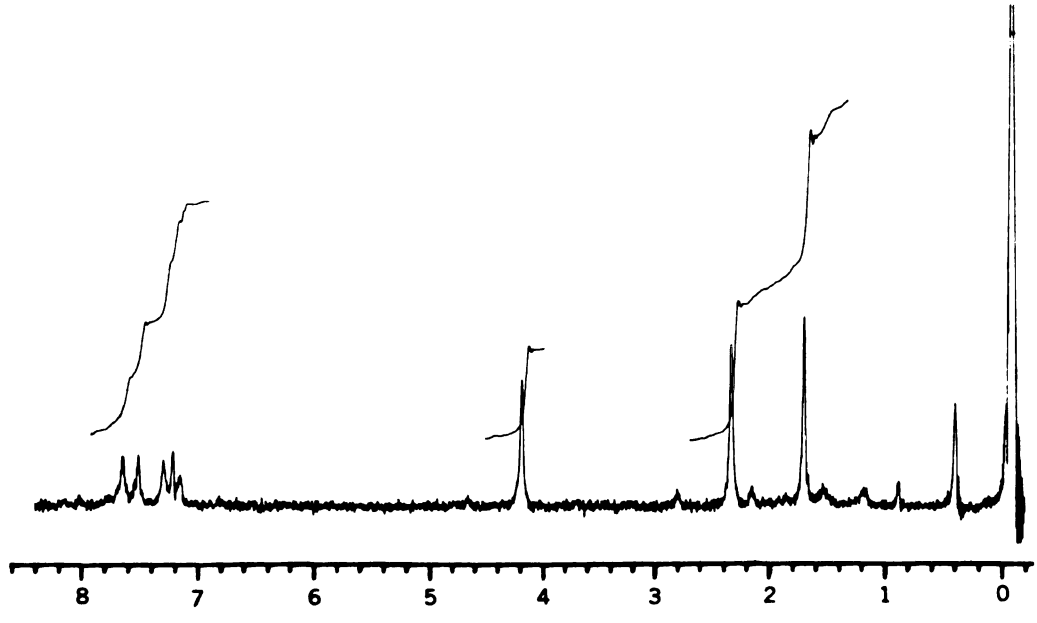


Figure A8. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(*p*-tolylsulfonylmethyl)-2,5-dimethylpyrrole (8).

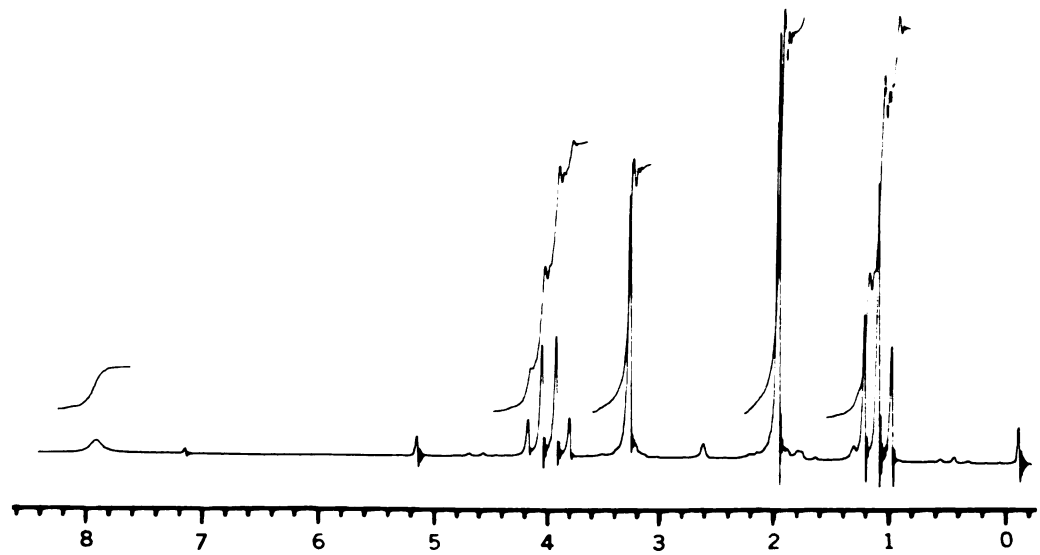


Figure A9. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(carbethoxymethyl)-2,5-dimethylpyrrole (10).

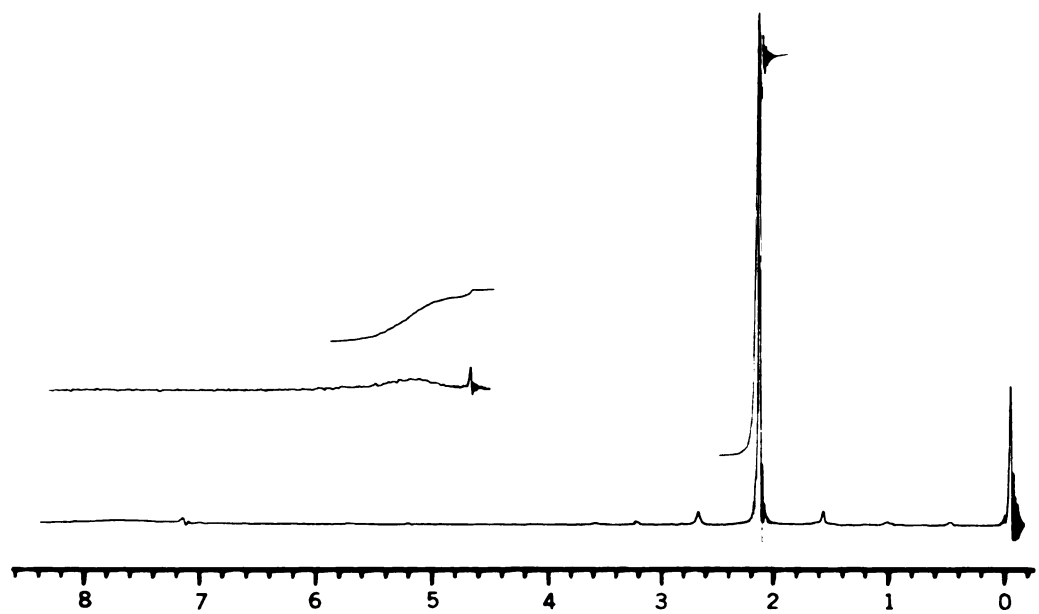


Figure A10. 60 MHz ^{1}H NMR spectrum of 2,5-dibromo-3,4-dimethylpyrrole (11).

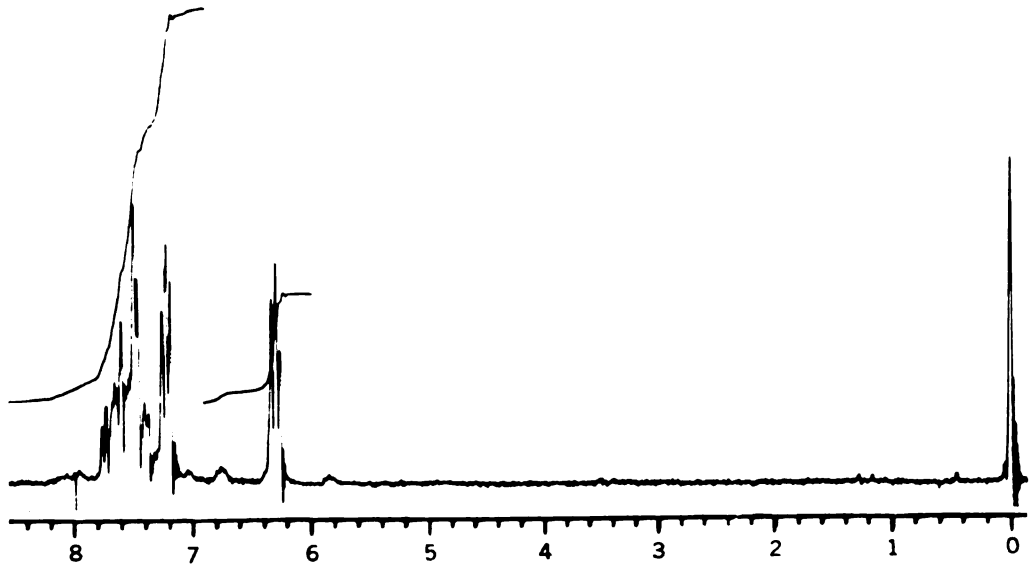


Figure A11. 60 MHz ^{1}H NMR spectrum of N-benzoylpyrrole (16a).

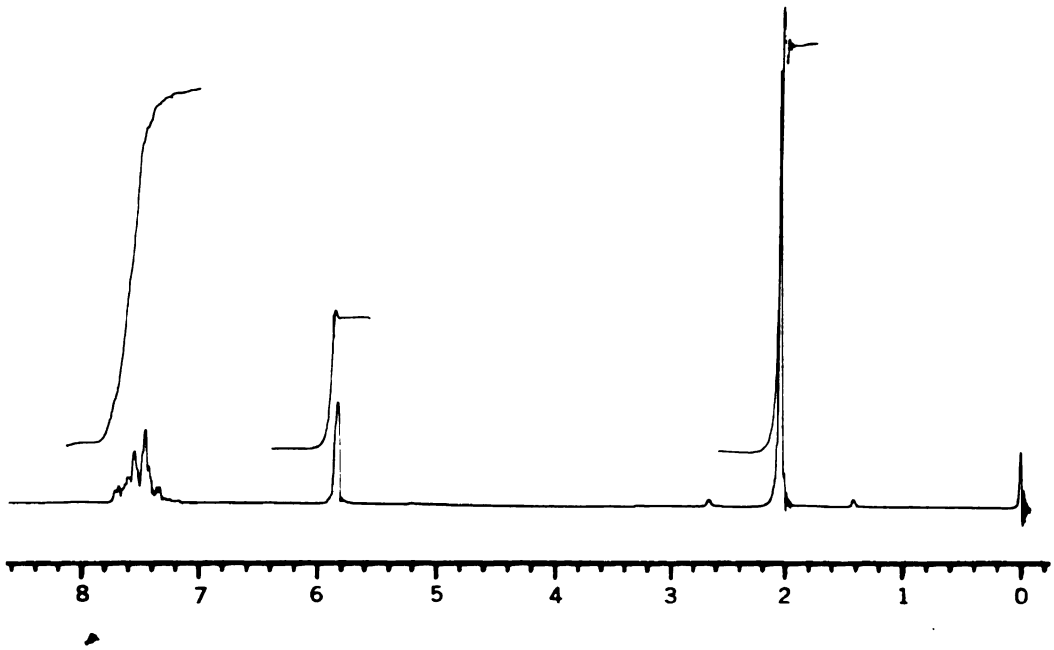


Figure A12. 60 MHz ^{1}H NMR spectrum of N-benzoyl-2,5-dimethylpyrrole (16b).

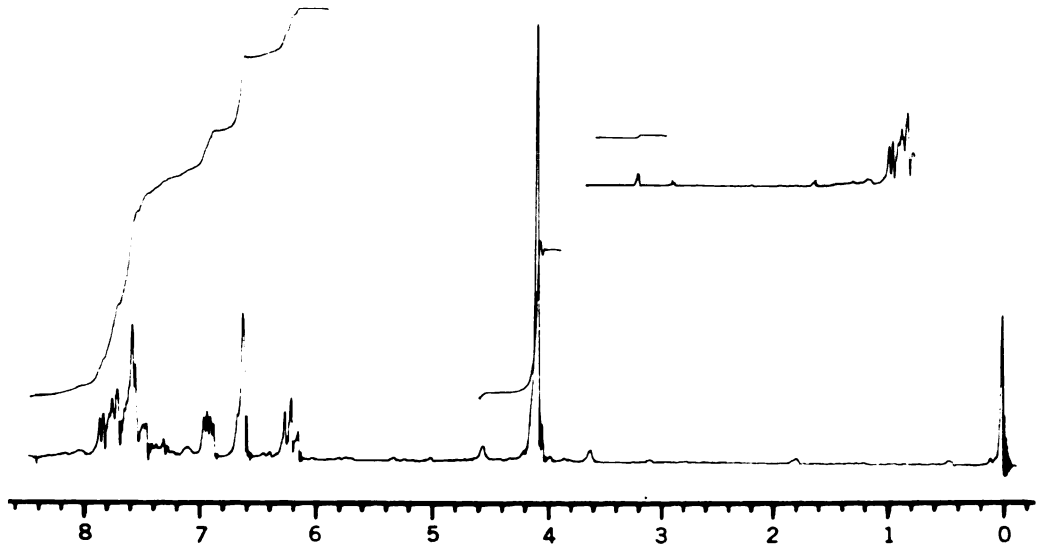


Figure A13. 60 MHz ^{1}H NMR spectrum of N-benzoyl-2-(1,3-dioxolan-2-yl)pyrrole (16c).

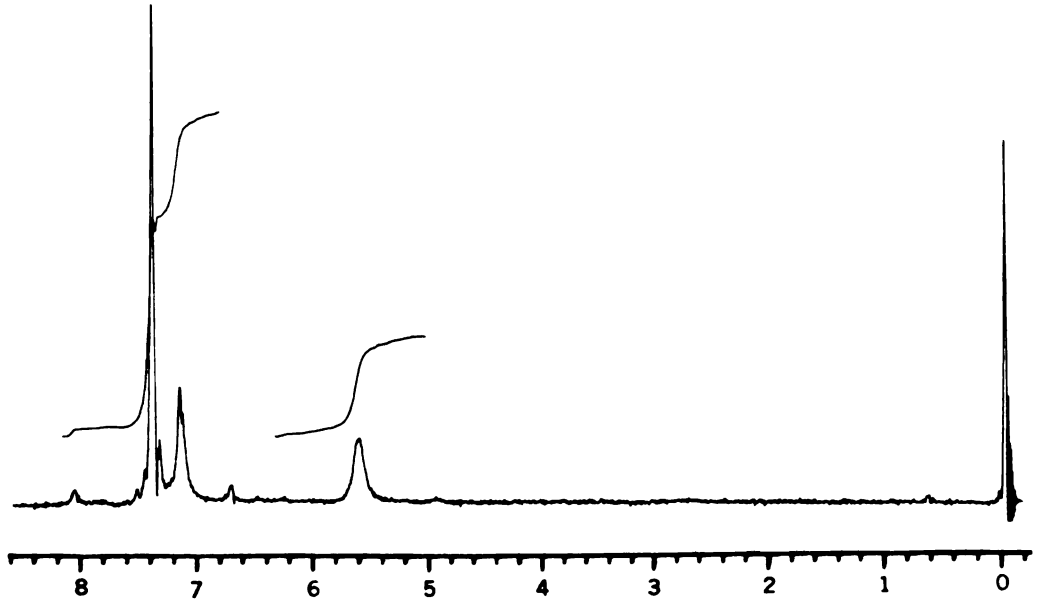


Figure A14. 60 MHz ^{1}H NMR spectrum of N-benzoyl-2,3-*bis*-(trifluoromethyl)-7-azabicyclo[2.2.1]-2,5-heptadiene (17a).

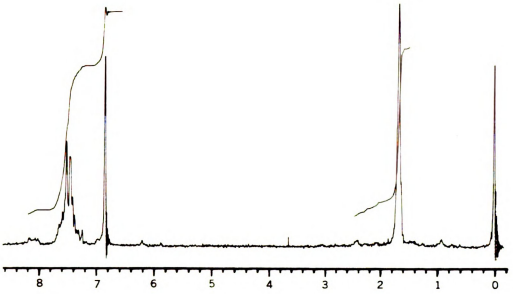


Figure A15. 60 MHz ^{1}H NMR spectrum of N-benzoyl-2,3-*bis*-(trifluoromethyl)-1,4-dimethyl-7-azabicyclo-[2.2.1]-2,5-heptadiene (17b).

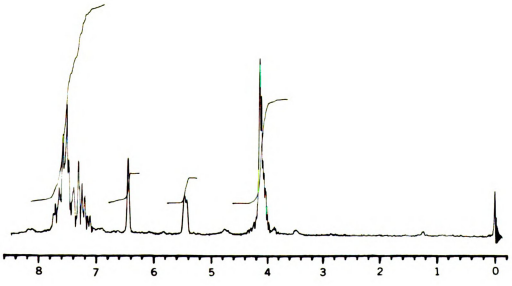


Figure A16. 60 MHz ^{1}H NMR spectrum of N-benzoyl-2,3-*bis*-(trifluoromethyl)-1-(1,3-dioxolan-2-yl)-7-azabicyclo[2.2.1]-2,5-heptadiene (17c).

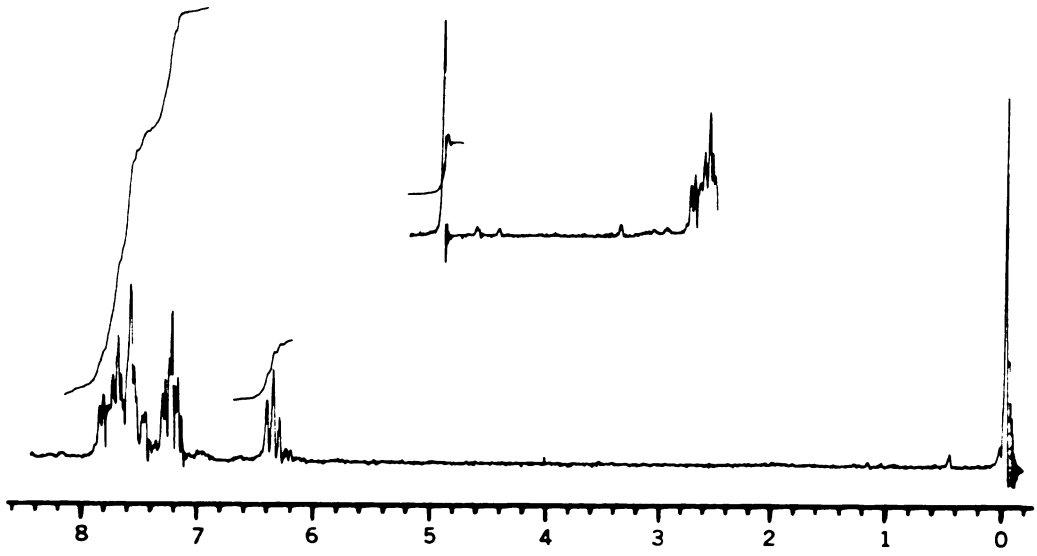


Figure A17. 60 MHz ^{1}H NMR spectrum of N-benzoyl-2-formyl-pyrrole (19).

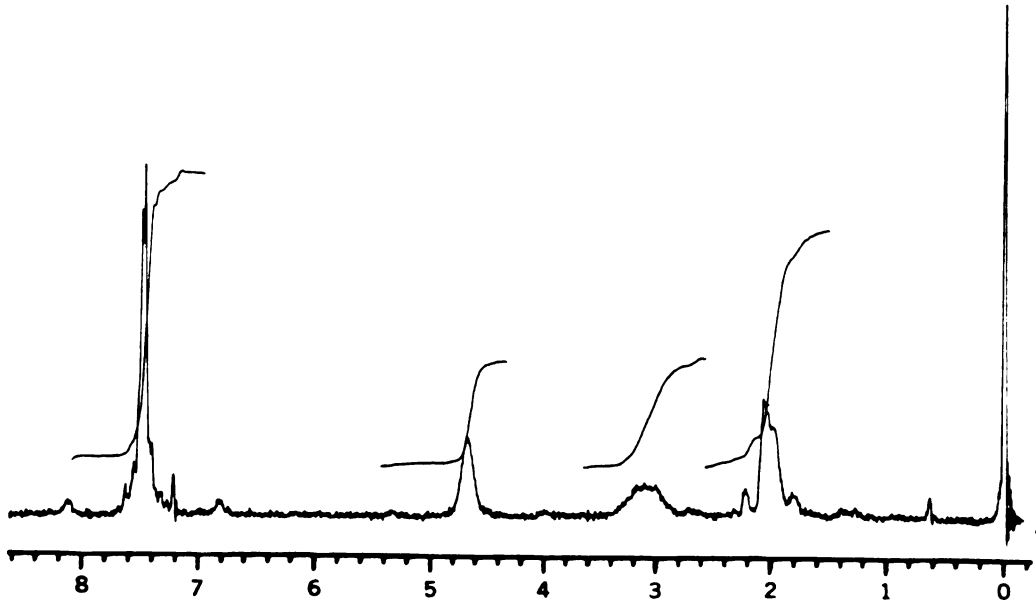


Figure A18. 60 MHz ^{1}H NMR spectrum of N-benzoyl-2,3-*bis*-(trifluoromethyl)-7-azabicyclo[2.2.1]-heptane (20).

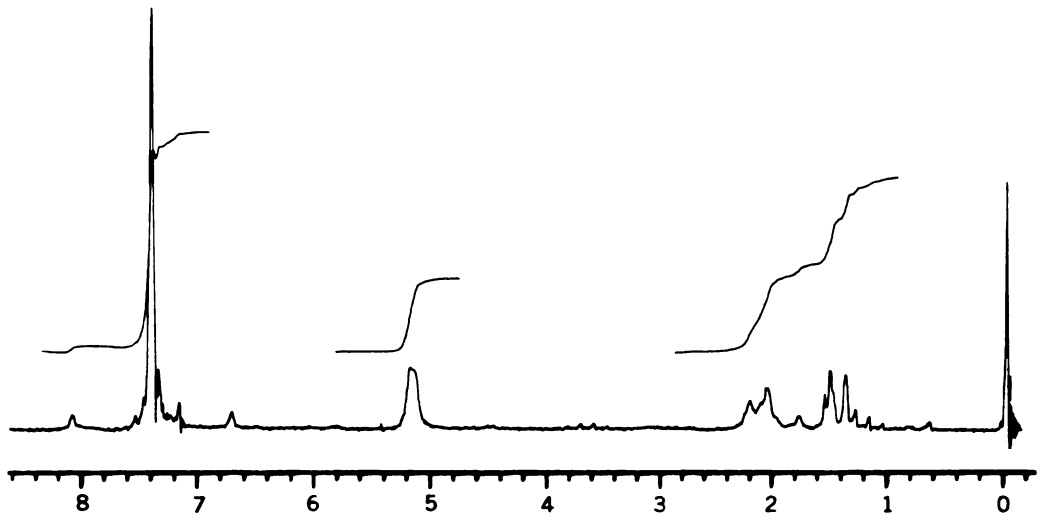


Figure A19. 60 MHz ^{1}H NMR spectrum of N-benzoyl-2,3-*bis*-(trifluoromethyl)-7-azabicyclo[2.2.1]-2-heptene (21a).

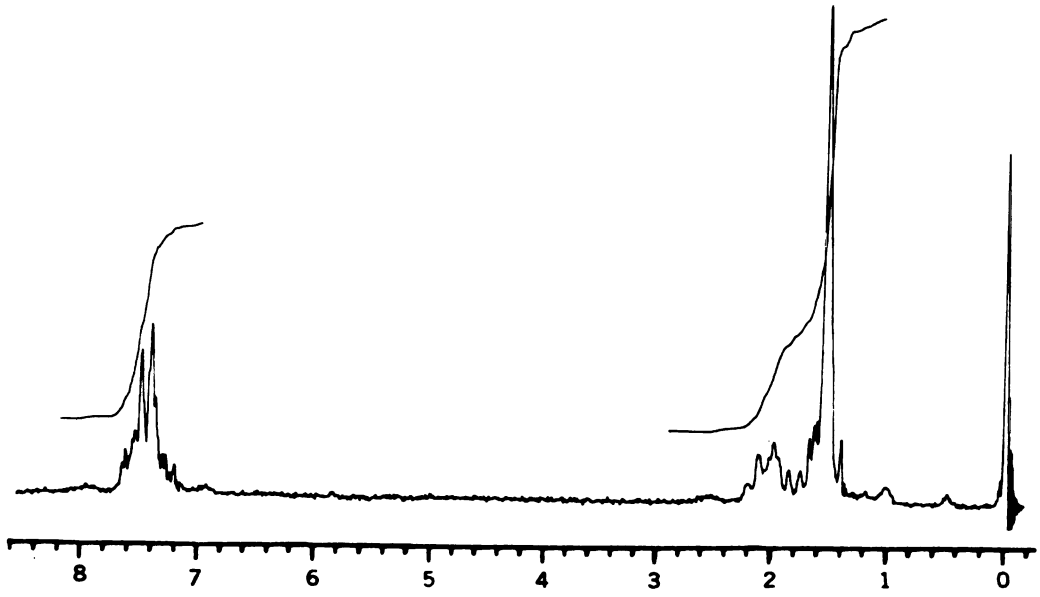


Figure A20. 60 MHz ^{1}H NMR spectrum of N-benzoyl-2,3-*bis*-(trifluoromethyl)-1,4-dimethyl-7-azabicyclo-[2.2.1]-2-heptene (21b).

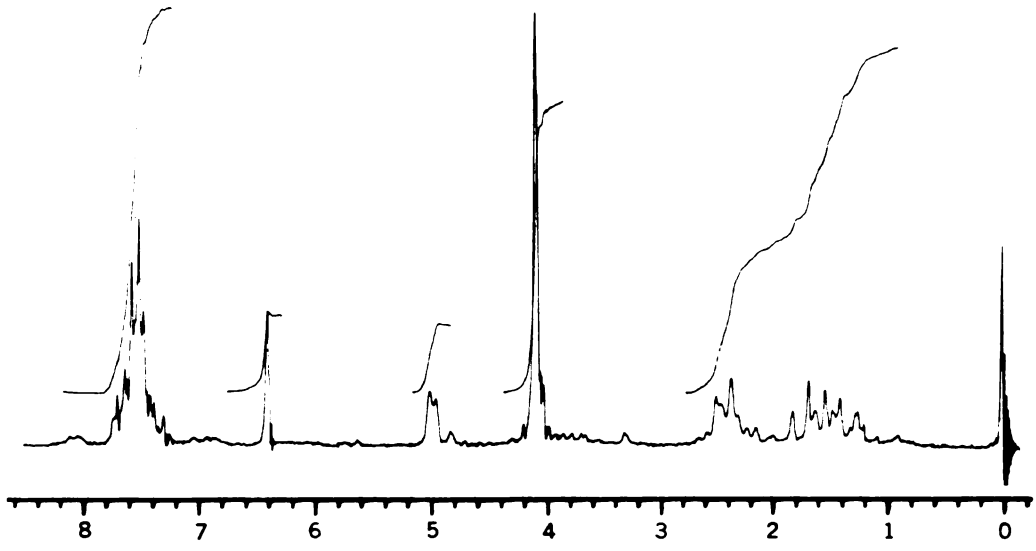


Figure A21. 60 MHz ^{1}H NMR spectrum of N-benzoyl-2,3-*bis*-(trifluoromethyl)-1-(1,3-dioxolan-2-yl)-7-azabicyclo[2.2.1]-2-heptene (21c).

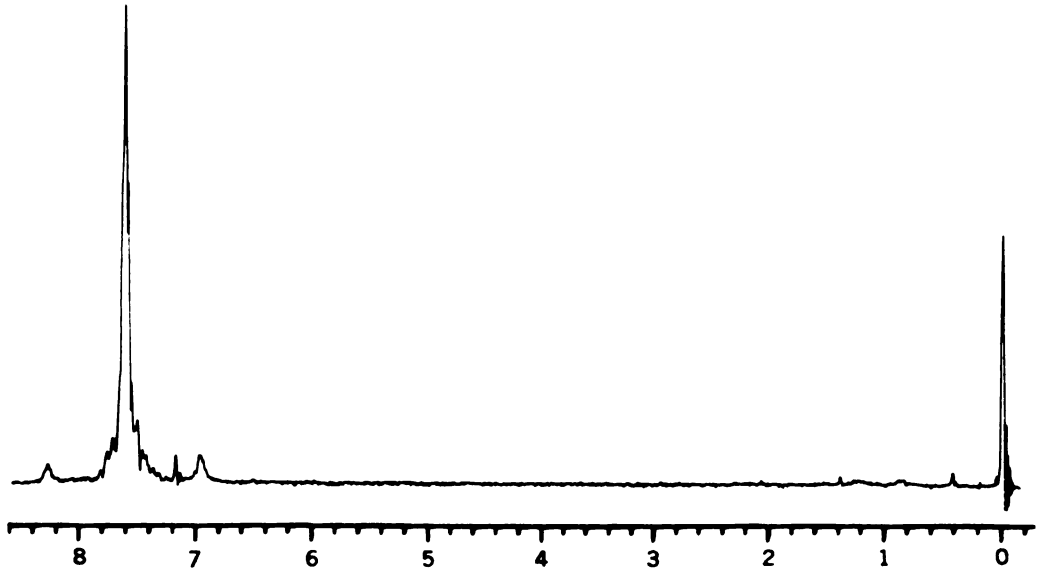


Figure A22. 60 MHz ^{1}H NMR spectrum of N-benzoyl-3,4-*bis*-(trifluoromethyl)pyrrole (22a).

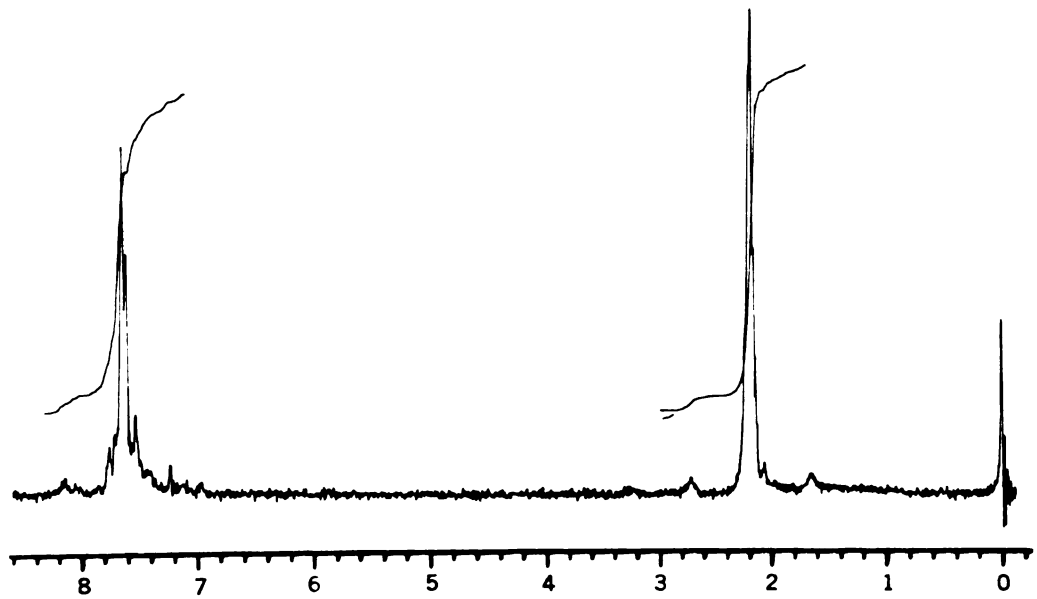


Figure A23. 60 MHz ^{1}H NMR spectrum of N-benzoyl-3,4-*bis*-(trifluoromethyl)-2,5-dimethylpyrrole (22b).

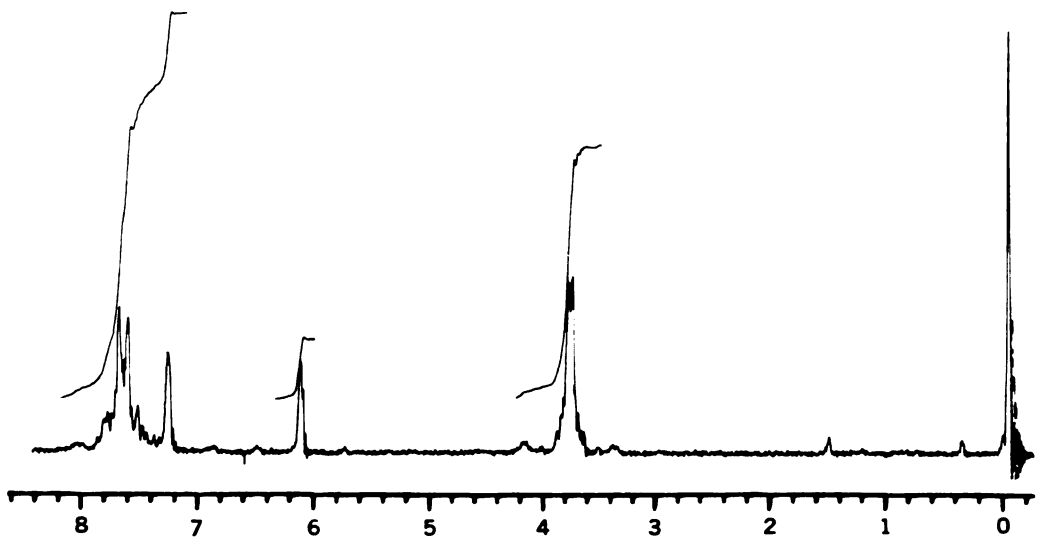


Figure A24. 60 MHz ^{1}H NMR spectrum of N-benzoyl-3,4-*bis*-(trifluoromethyl)-2-(1,3-dioxolan-2-yl)pyrrole (22c).

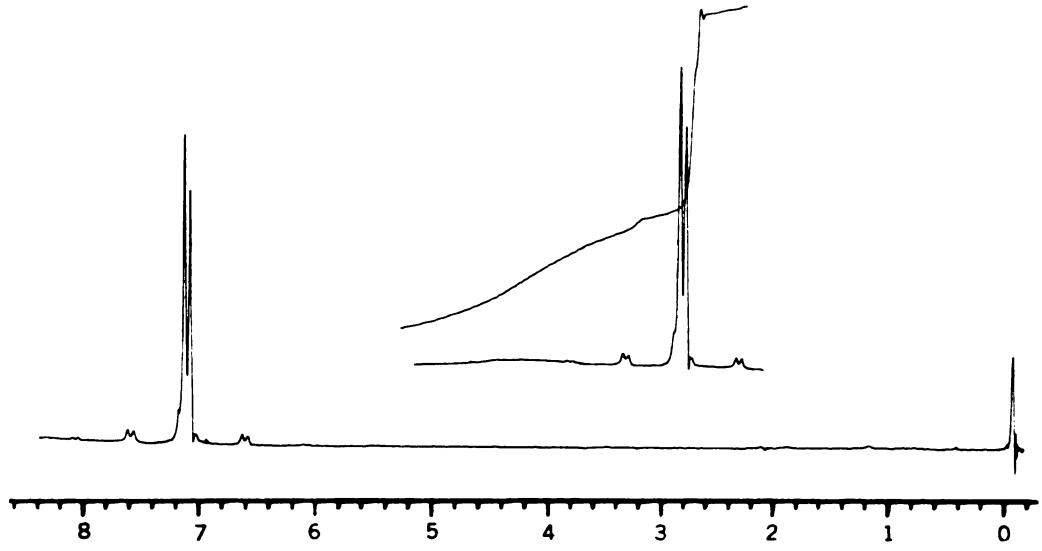


Figure A25. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(trifluoromethyl)pyrrole (23a)

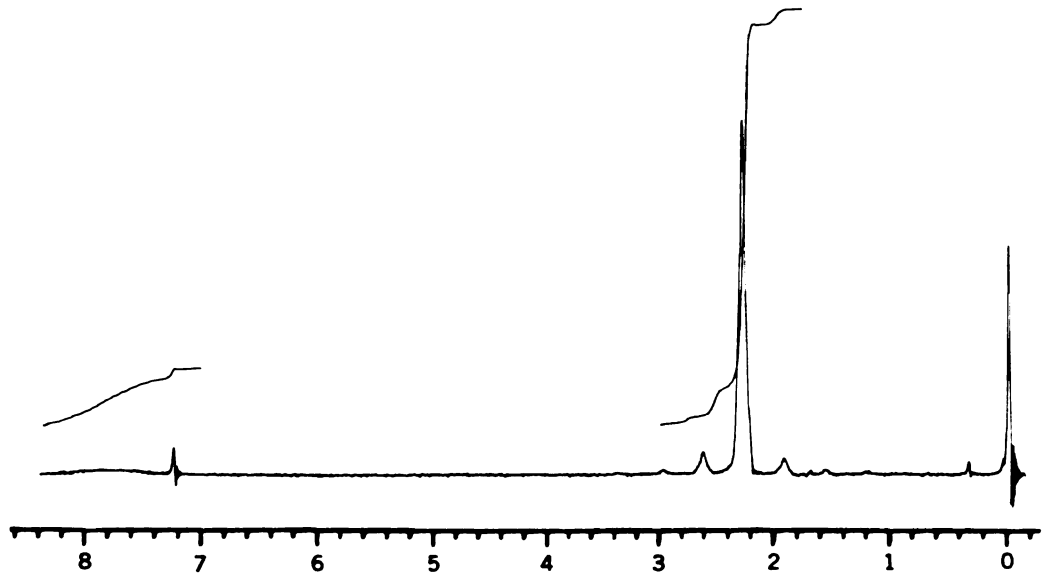


Figure A26. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(trifluoromethyl)-2,5-dimethylpyrrole (23b).

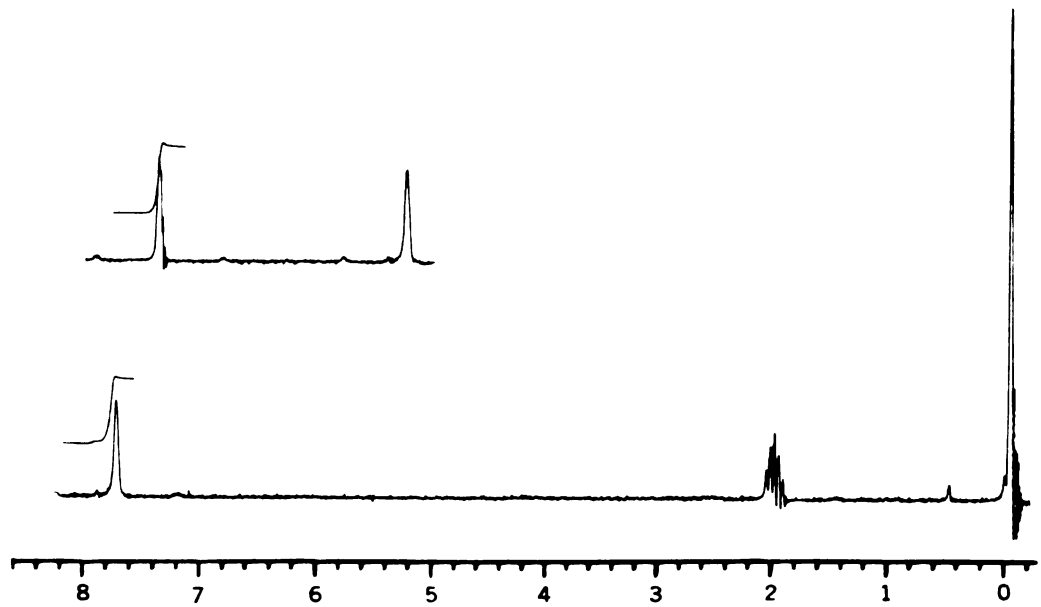


Figure A27. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(trifluoromethyl)-2-formylpyrrole (24).

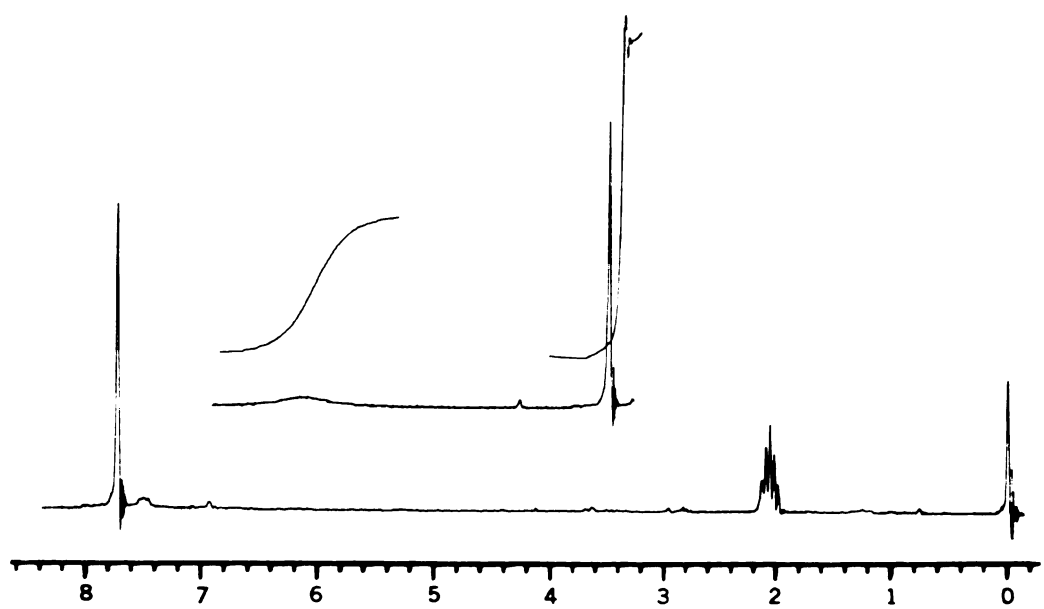


Figure A28. 60 MHz ^{1}H NMR spectrum of 3,4-dicyanopyrrole (25a).

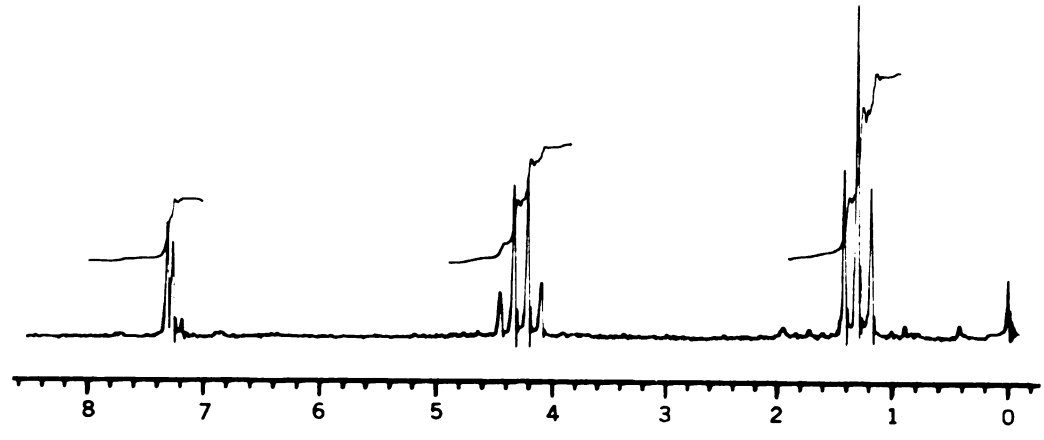


Figure A29. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(carbethoxy)-pyrrole (26a).

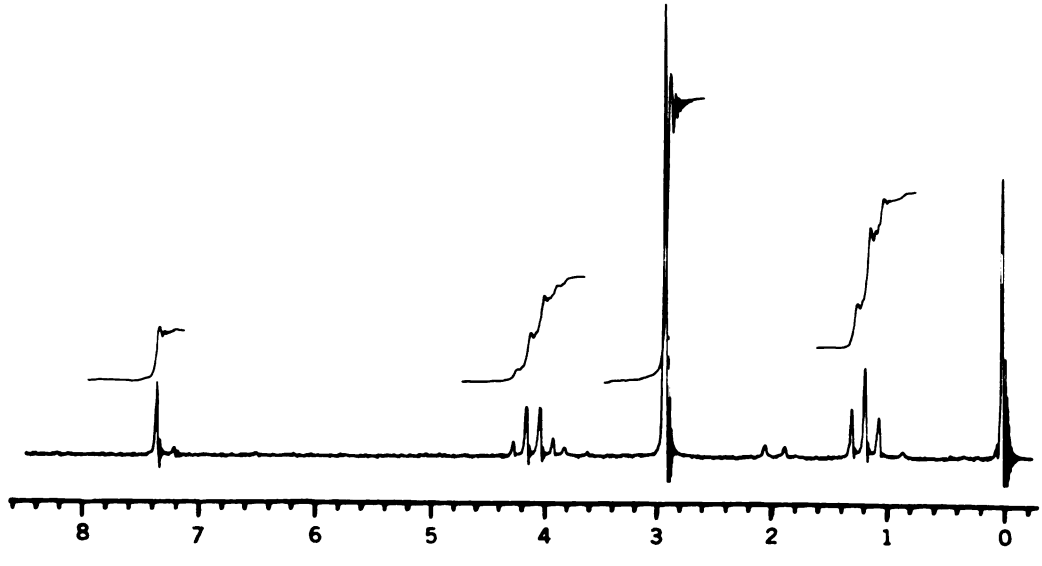


Figure A30. 60 MHz ^{1}H NMR spectrum of *bis*(dimethylamino-methylene)diethylsuccinate (28).

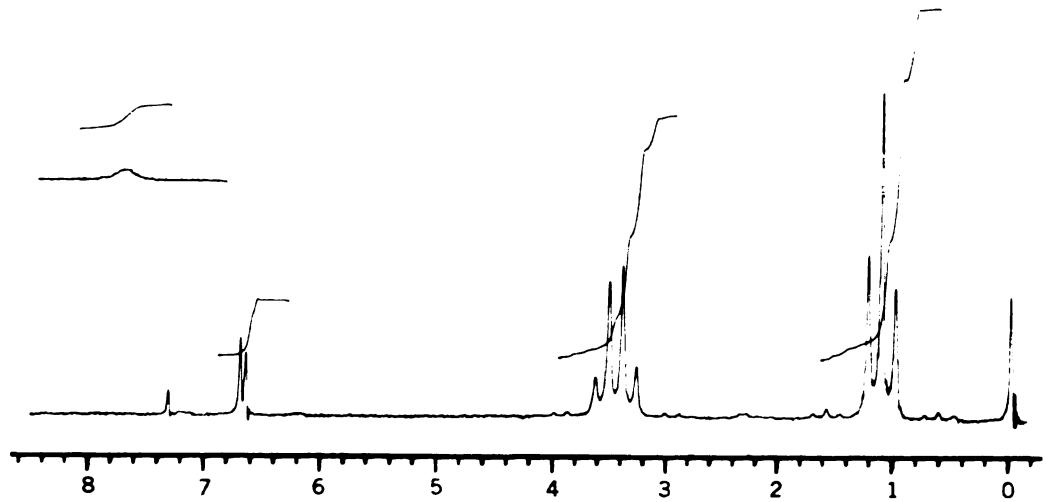


Figure A31. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(N,N-diethylcarboxamide)pyrrole (31a).

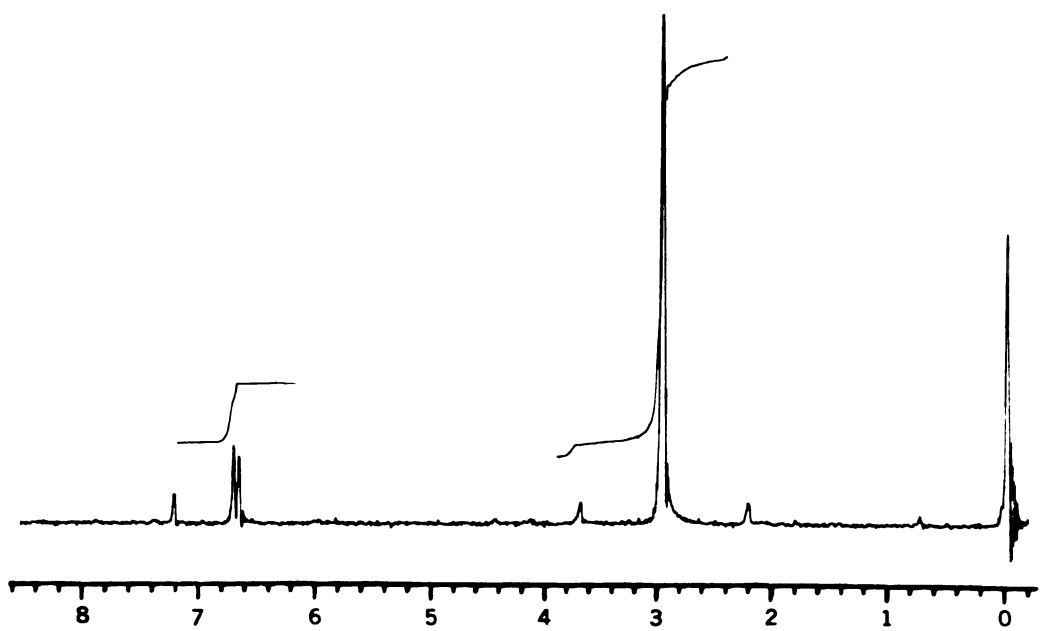


Figure A32. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(N,N-dimethylcarboxamide)pyrrole (31b).

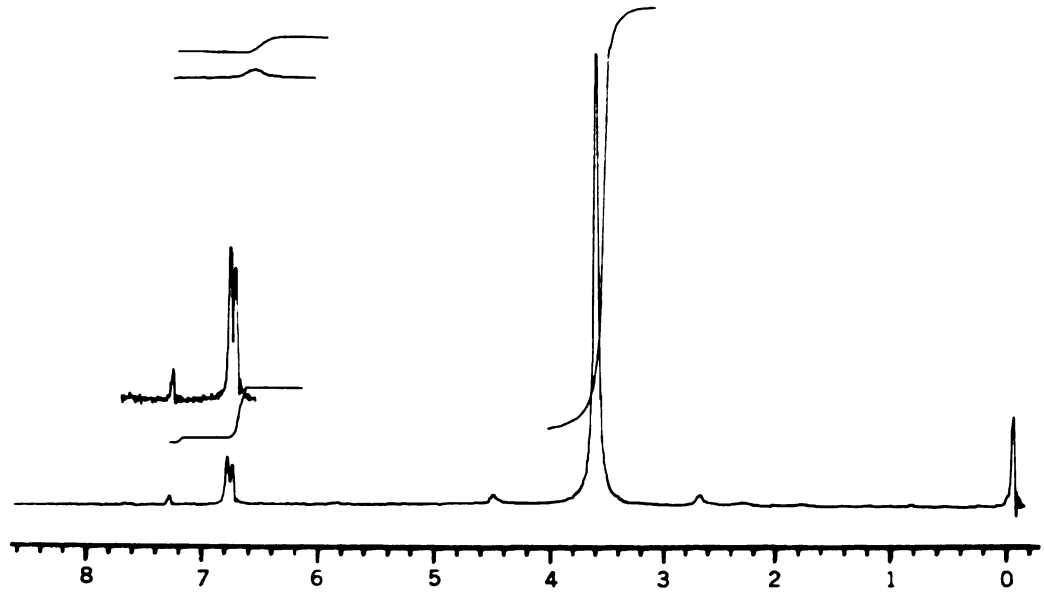


Figure A33. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(N-morpholine-carboxamide)pyrrole (31c).

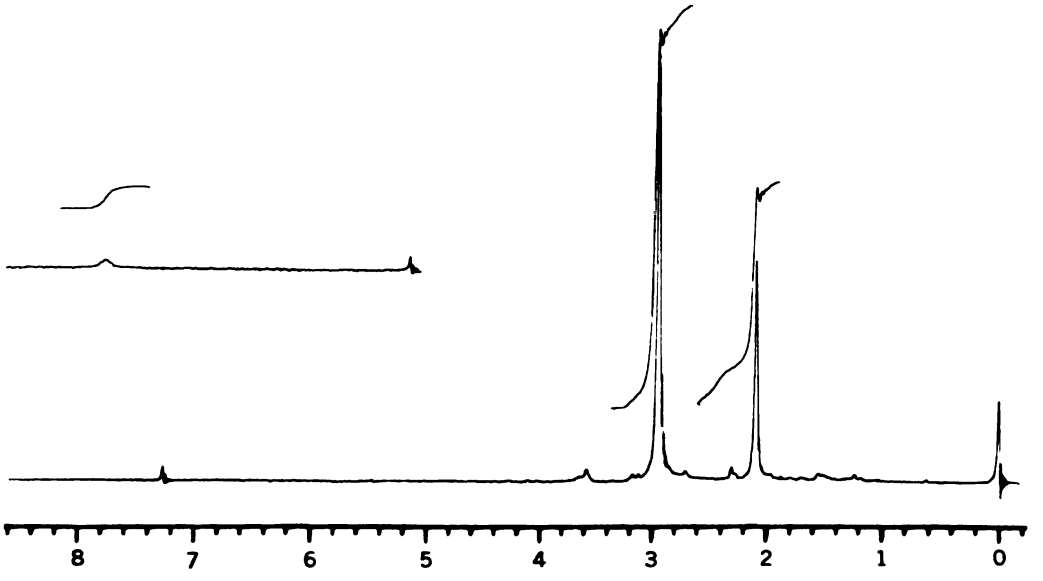


Figure A34. 60 MHz ^{1}H NMR spectrum of 2,5-dimethyl-3,4-*bis*-(N,N-dimethylcarboxamide)pyrrole (37).

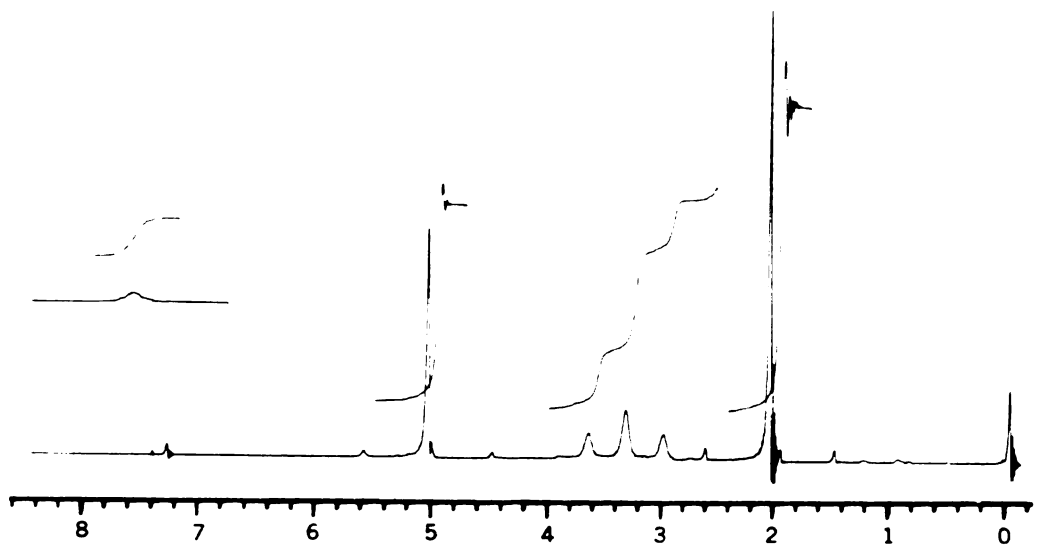


Figure A35. 60 MHz ^{1}H NMR spectrum of 2,5-*bis*(acetoxymethyl)-3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole (38a).

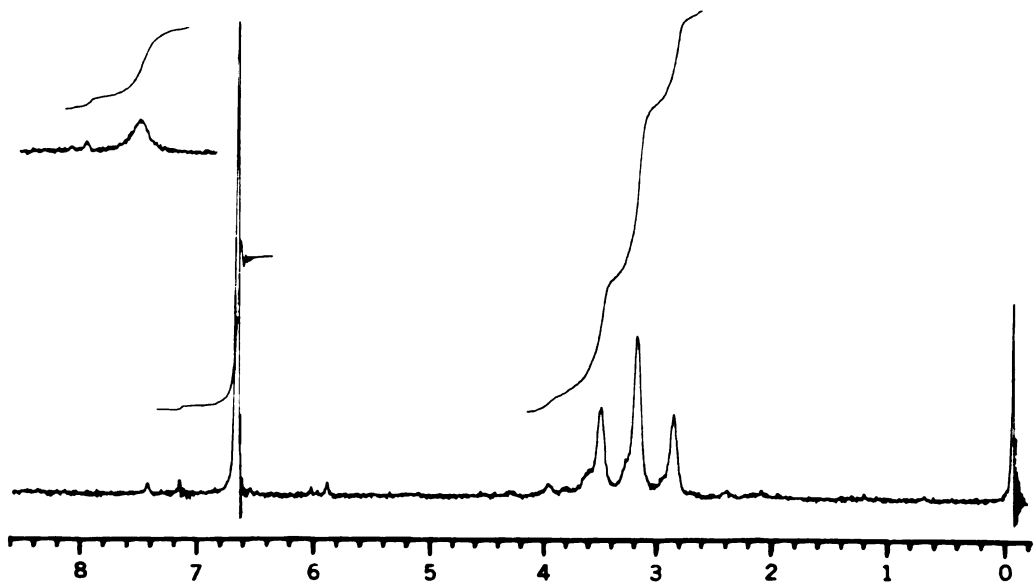


Figure A36. 60 MHz ^{1}H NMR spectrum of 2,5-*bis*(dichloromethyl)-3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole (38d).

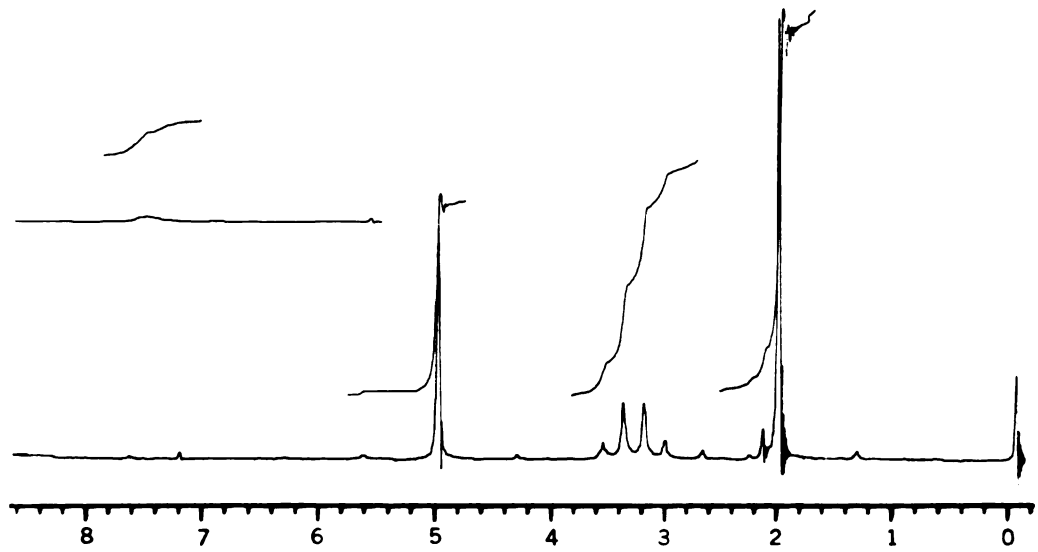


Figure A37. 60 MHz ^{1}H NMR spectrum of 2,5-*bis*(acetoxymethyl)-3,4-*bis*(1H,1H-trifluoroeth-1-yl)pyrrole (38f).

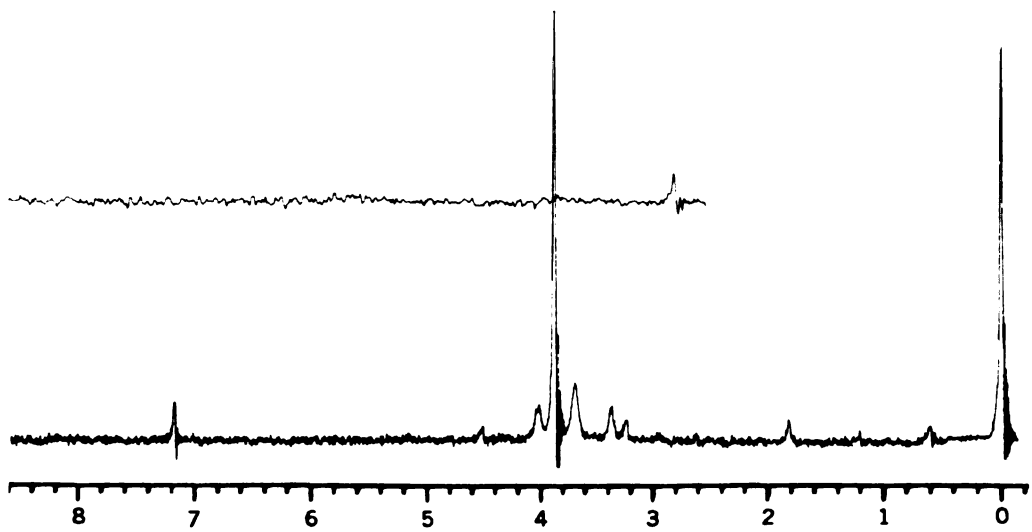


Figure A38. 60 MHz ^{1}H NMR spectrum of 2,5-*bis*(carbmethoxy)-3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole (39a).

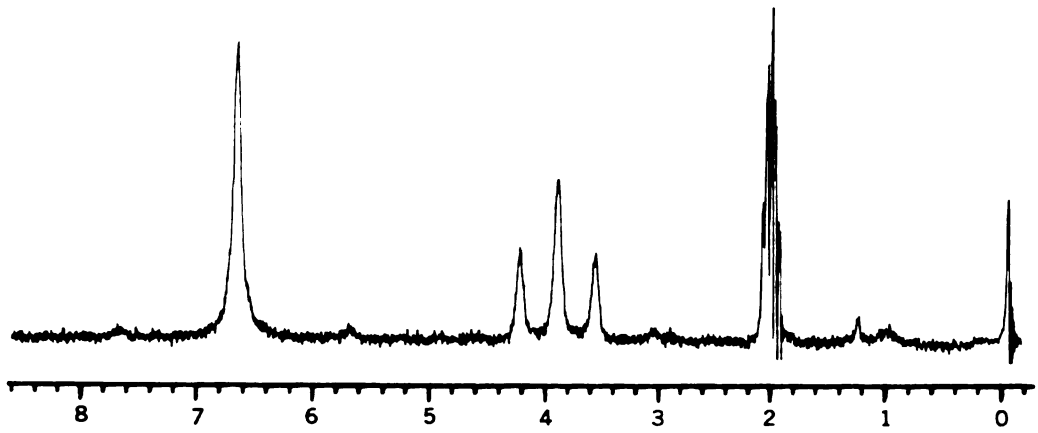


Figure A39. 60 MHz ^{1}H NMR spectrum of 2,5-dicarboxy-3,4-*bis*-(1H,1H-heptafluorobut-1-yl)pyrrole (39c).

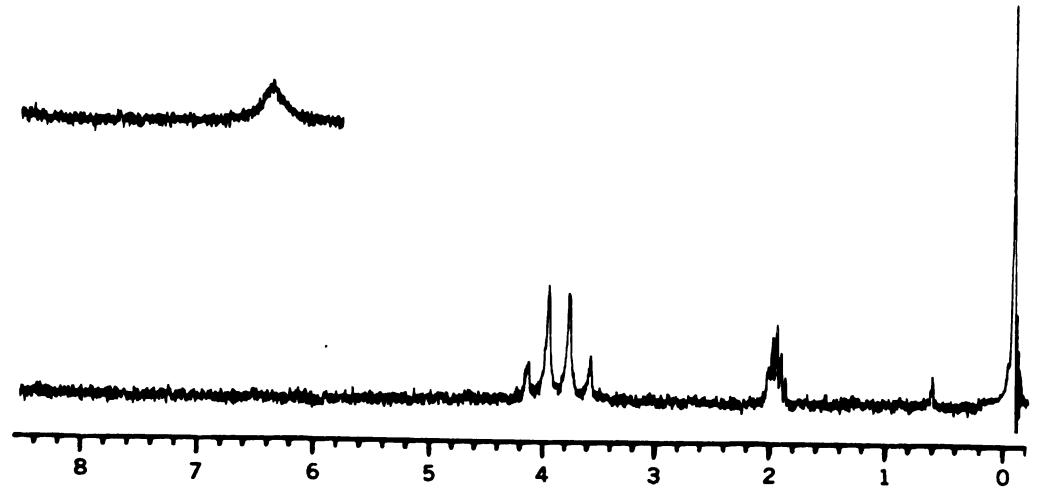


Figure A40. 60 MHz ^{1}H NMR spectrum of 2,5-dicarboxy-3,4-*bis*-(1H,1H-trifluoroeth-1-yl)pyrrole (39d).

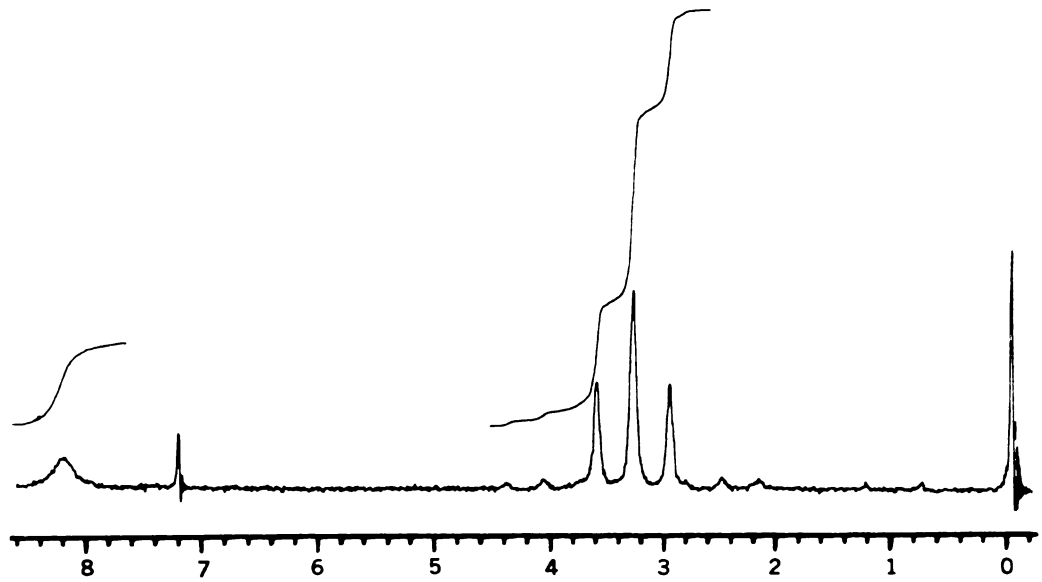


Figure A41. 60 MHz ^{1}H NMR spectrum of 2,5-diiodo-3,4-*bis*-(1H,1H-heptafluorobut-1-yl)pyrrole (40a).

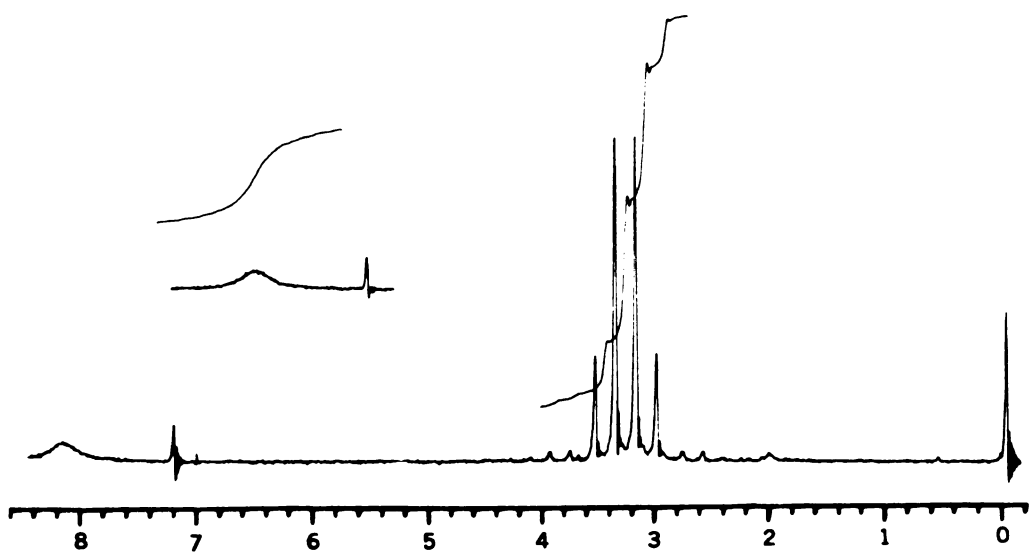


Figure A42. 60 MHz ^{1}H NMR spectrum of 2,5-diiodo-3,4-*bis*-(1H,1H-trifluoroeth-1-yl)pyrrole (40b).

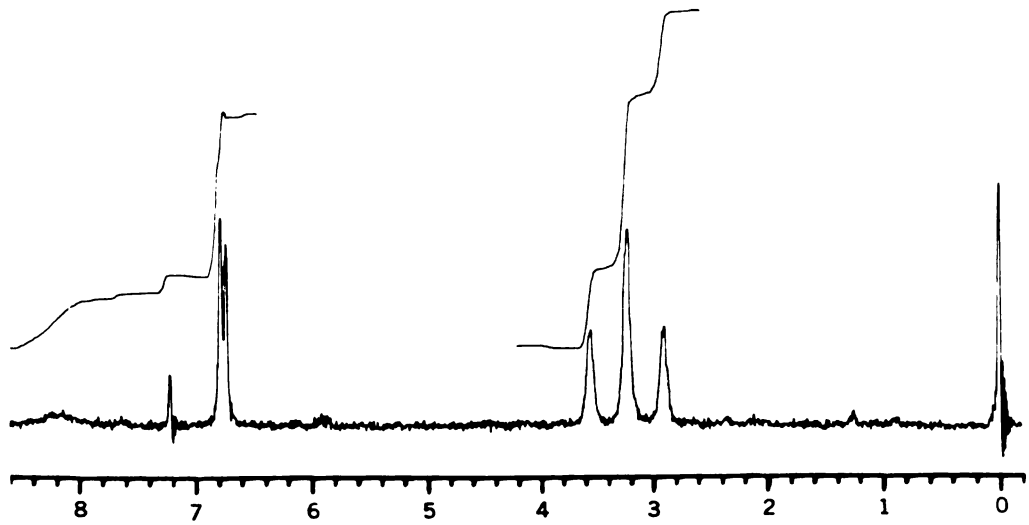


Figure A43. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole (41).

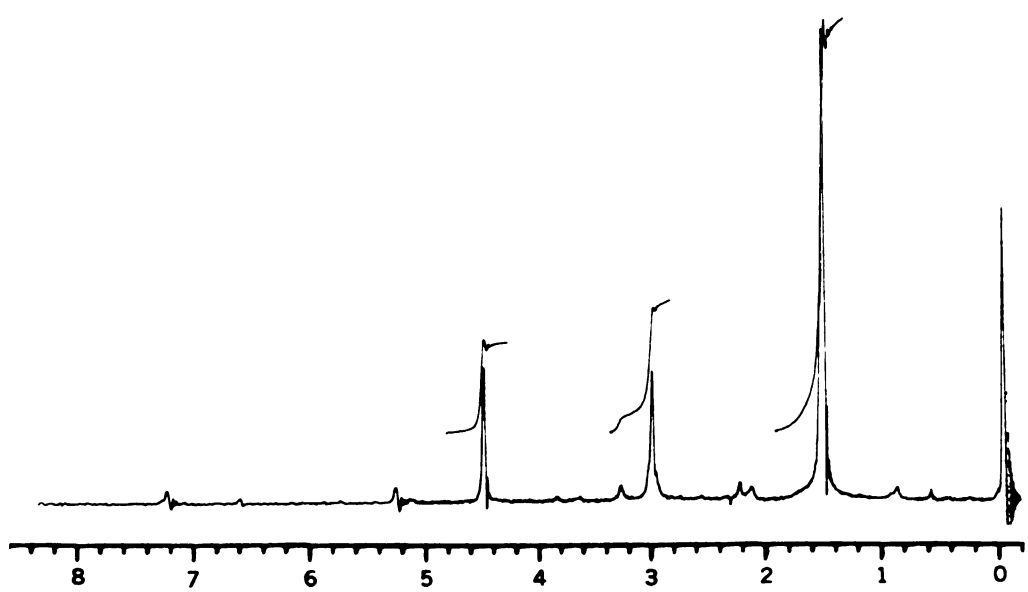


Figure A44. 60 MHz ^{1}H NMR spectrum of 2,5-*bis*(chloromethyl)-3,4-*bis*(2-methyl-2-nitroprop-1-yl)pyrrole (42).

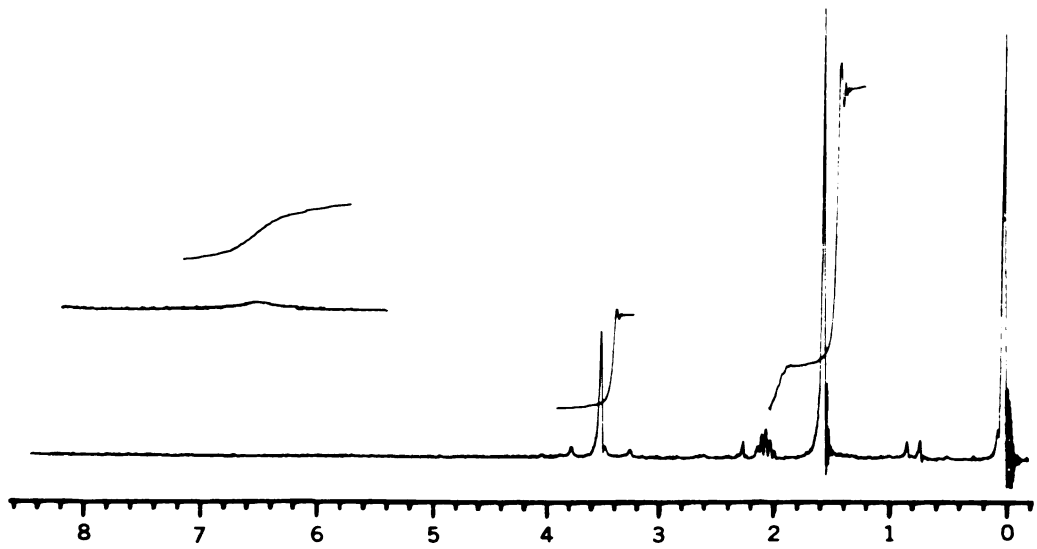


Figure A45. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(2-methyl-2-nitroprop-1-yl)-2,5-dicarboxypyrrole (43).

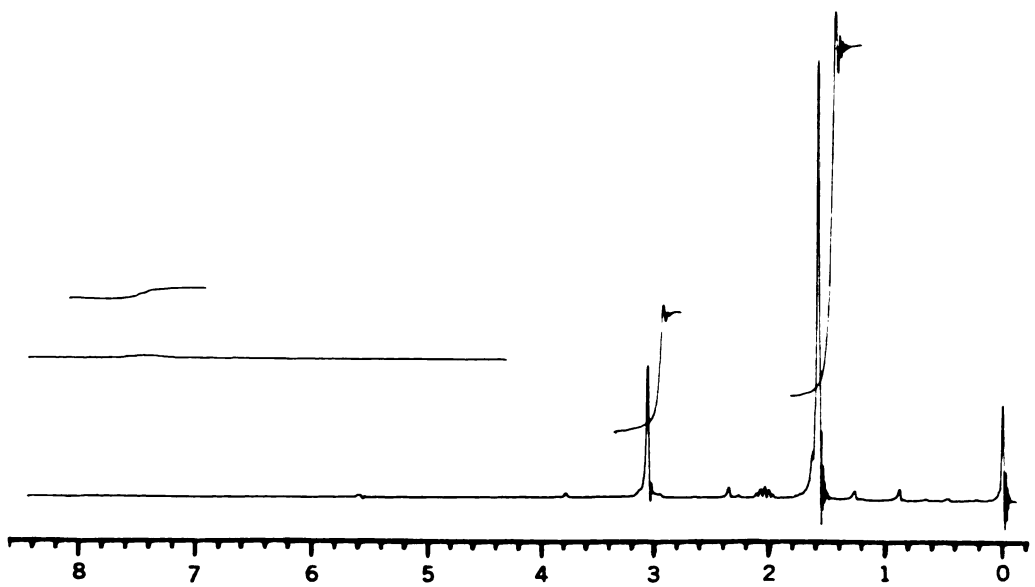


Figure A46. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(2-methyl-2-nitroprop-1-yl)-2,5-diiodopyrrole (44).

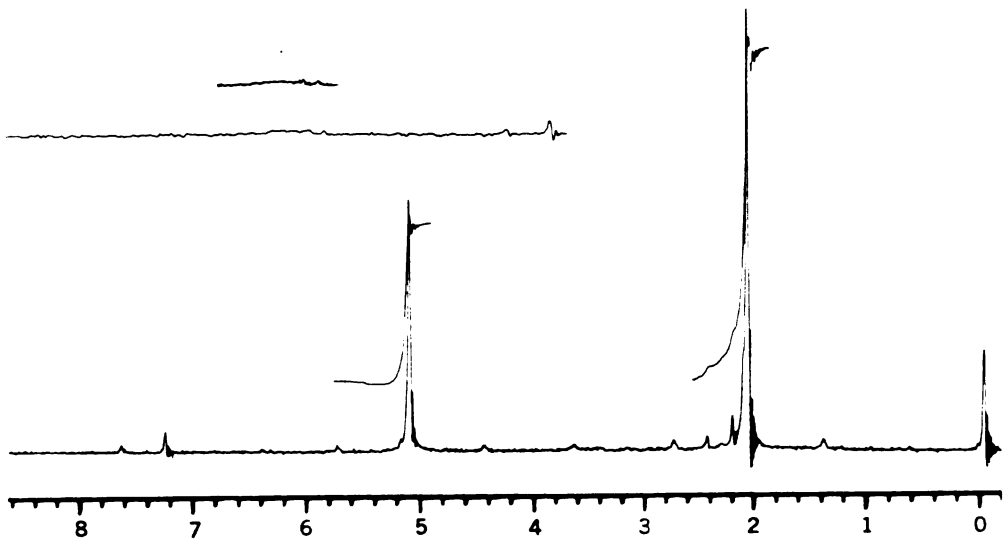


Figure A47. 60 MHz ^{1}H NMR spectrum of 2,5-*bis*(acetoxymethyl)-2,5-diiodopyrrole (46).

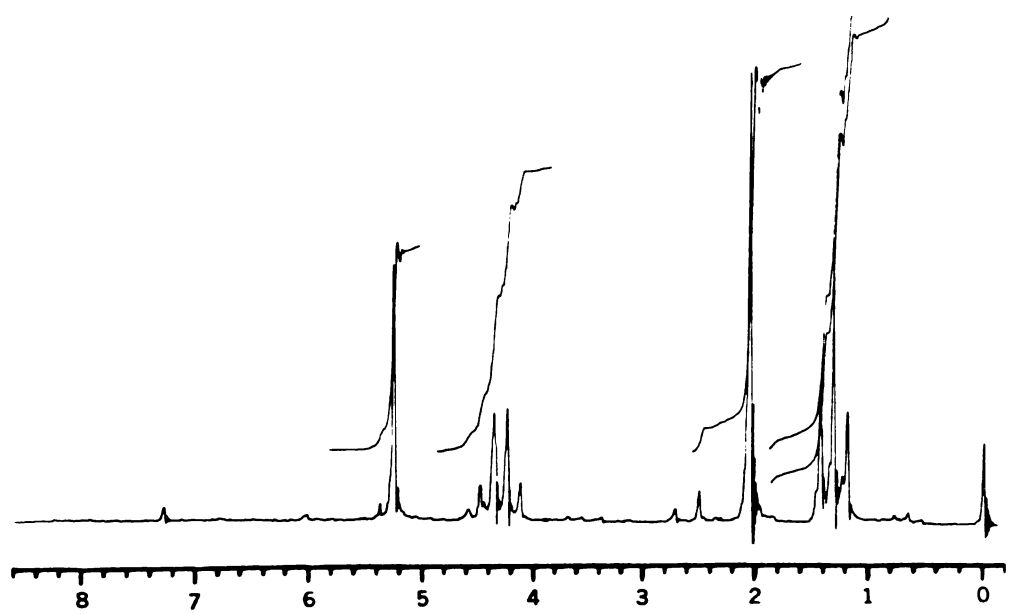


Figure A48. 60 MHz ^{1}H NMR spectrum of 2,5-*bis*(acetoxymethyl)-3,4-*bis*(carbethoxy)pyrrole (49).

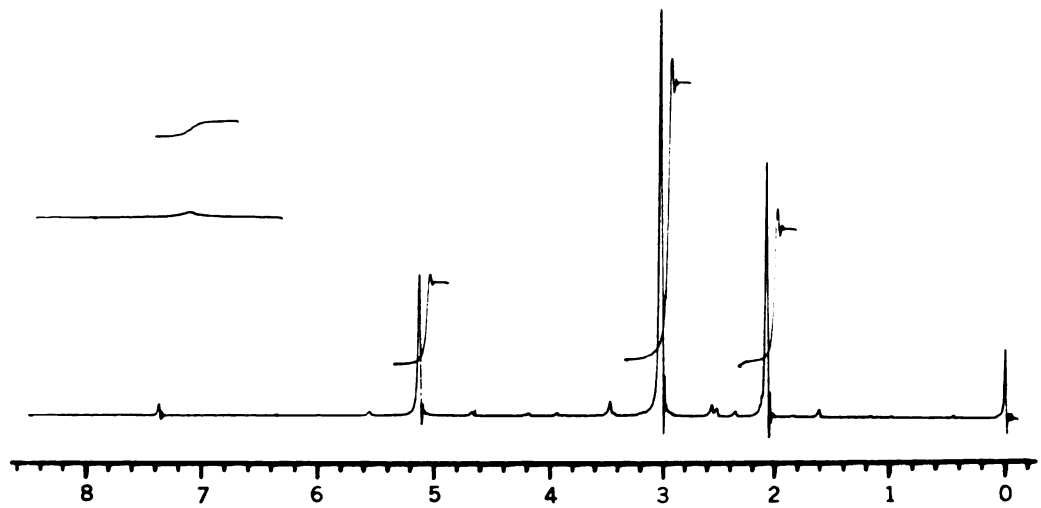


Figure A49. 60 MHz ^{1}H NMR spectrum of 2,5-*bis*(acetoxymethyl)-3,4-*bis*(N,N-dimethylcarboxamide)pyrrole (52).

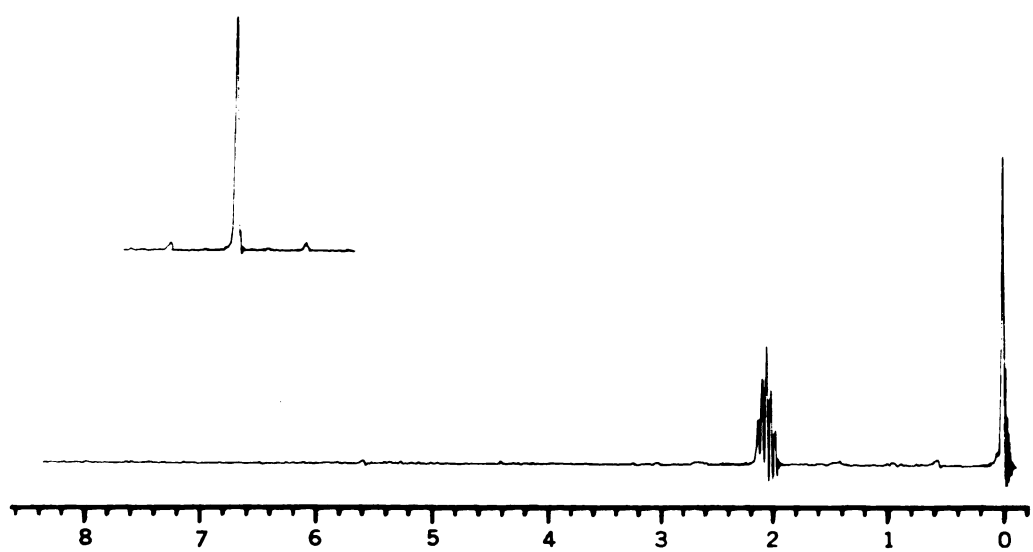


Figure A50. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(trifluoromethyl)-2,5-diformylpyrrole (56).

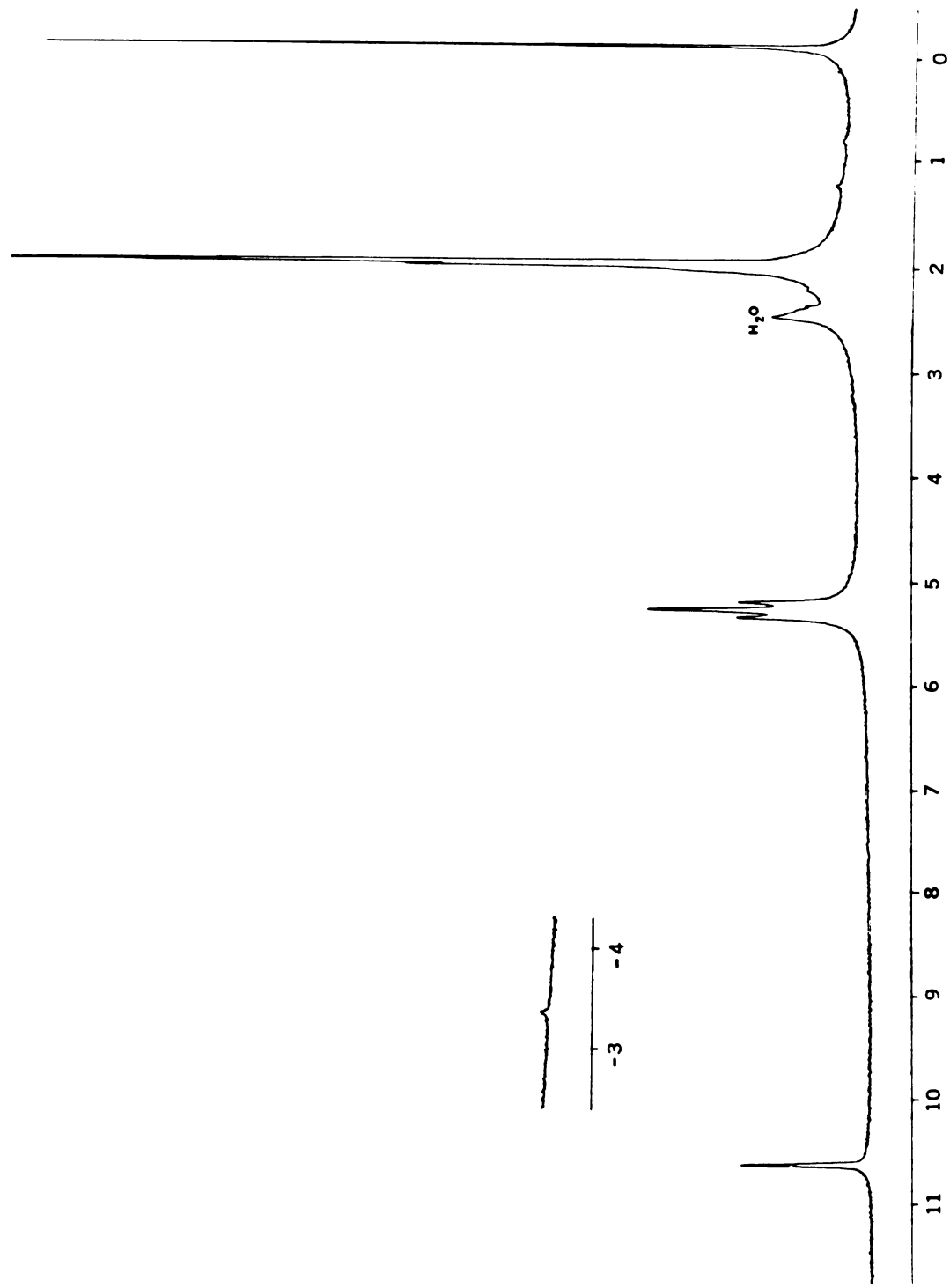


Figure A51. 250 MHz ^{1}H NMR spectrum of octakis(1H,1H-heptafluorobut-1-yl)porphyrin (57).

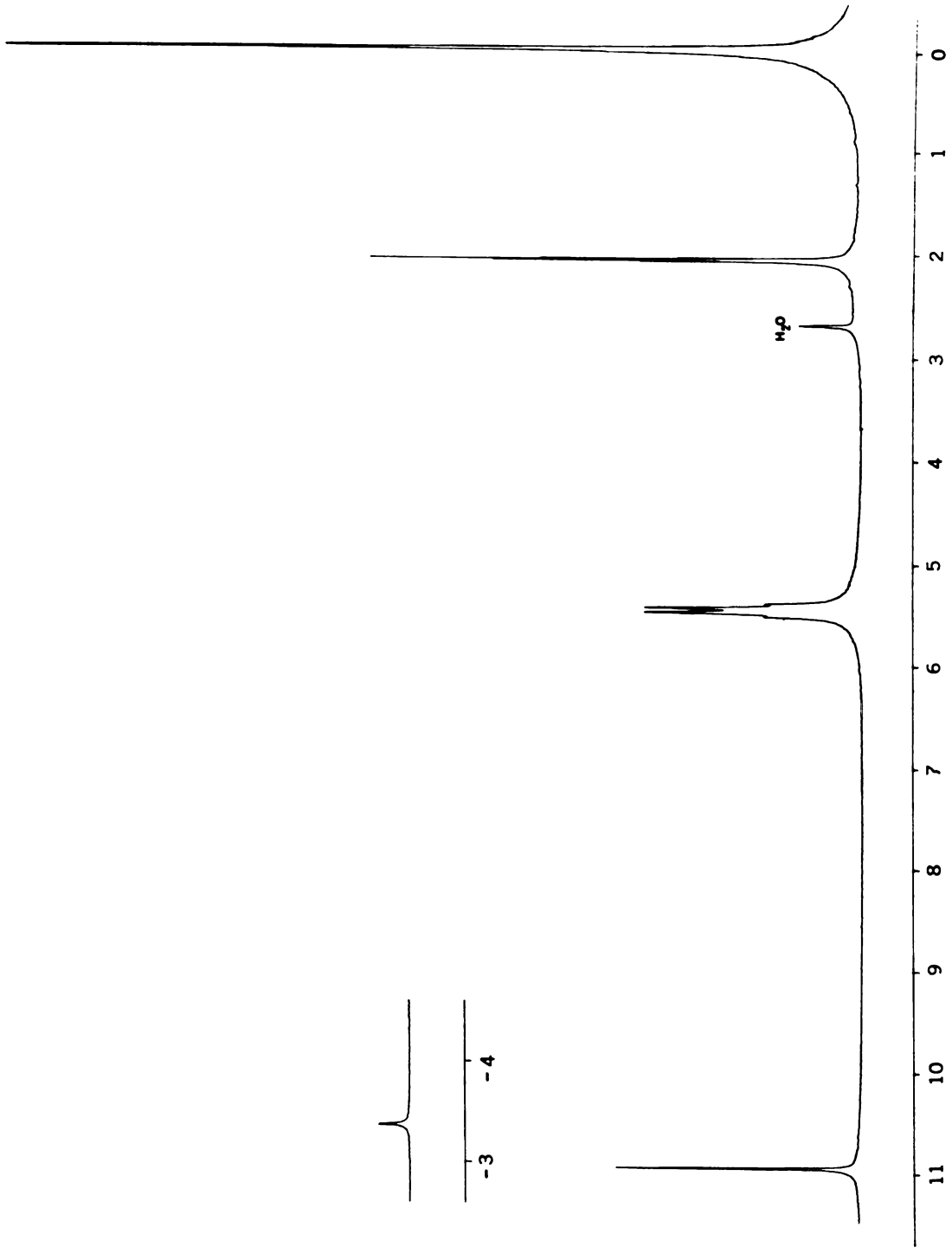


Figure A52. 250 MHz ^{1}H NMR spectrum of octakis(1H,1H-trifluoroeth-1-yl)porphyrin (59).

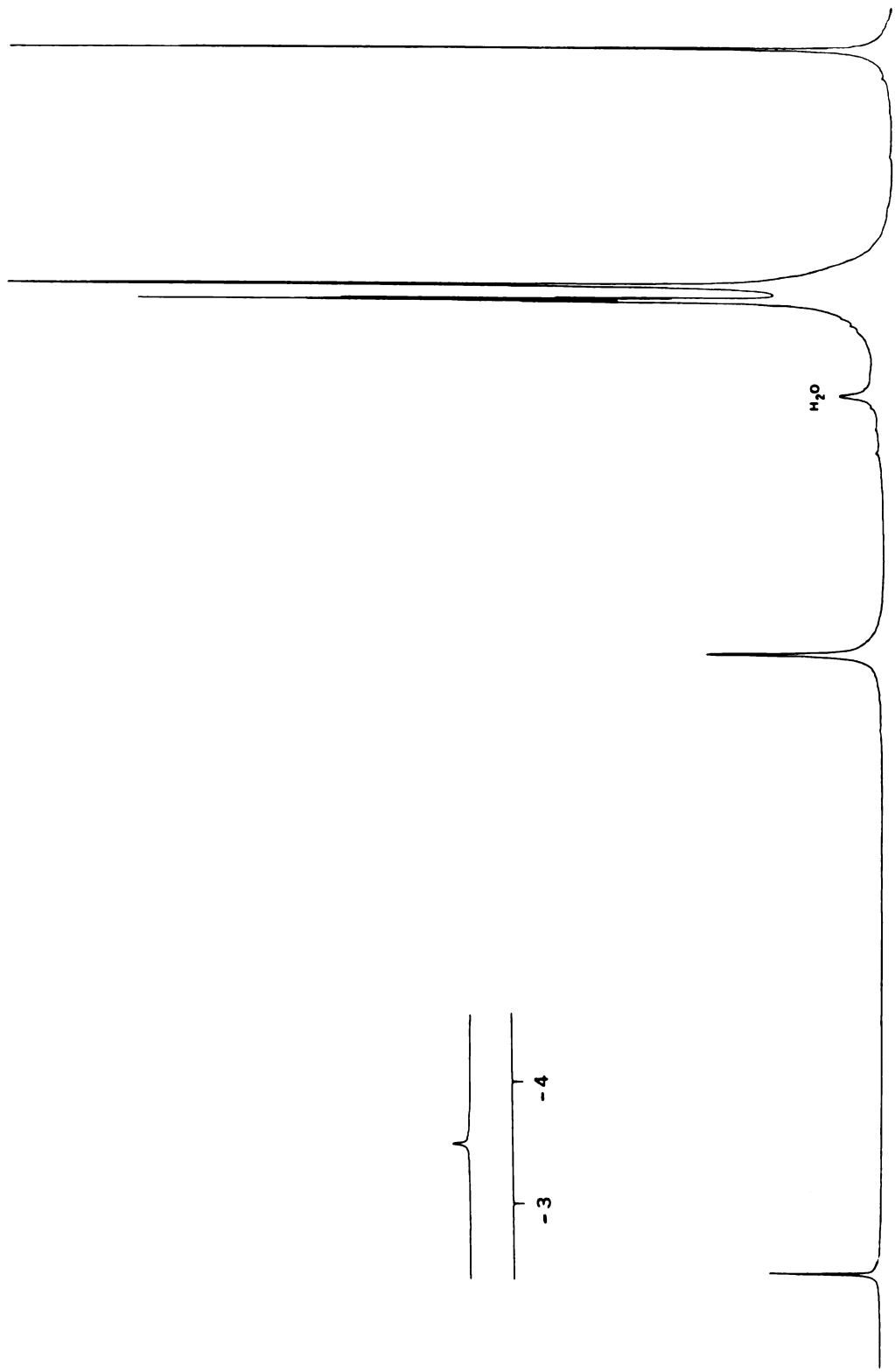


Figure A53. 250 MHz ^{1}H NMR spectrum of octakis(2-methyl-2-nitroprop-1-yl)porphyrin (61).

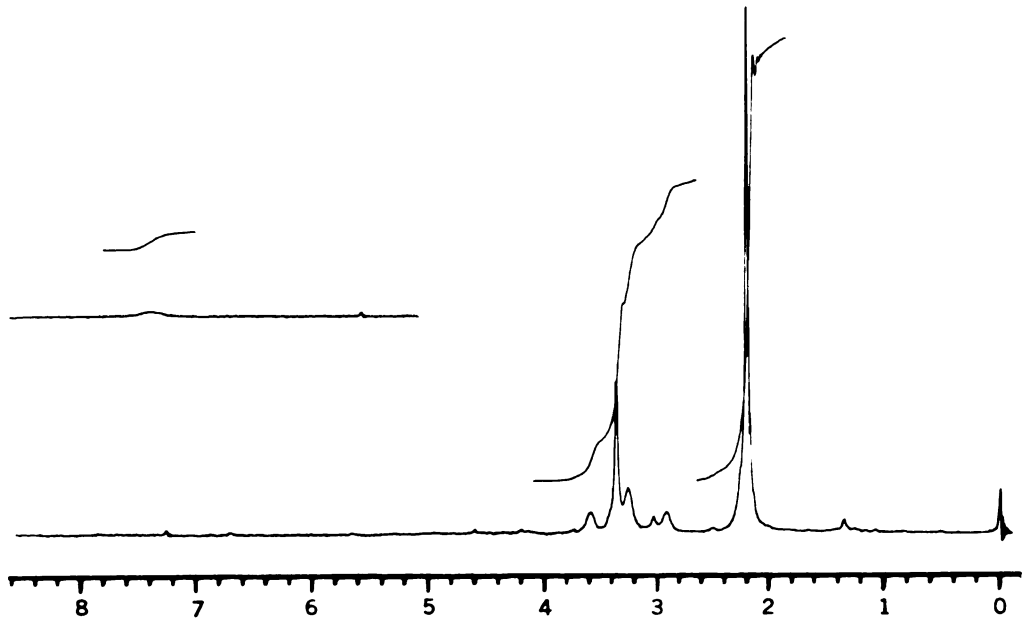


Figure A54. 60 MHz ^{1}H NMR spectrum of 2,3-*bis*(dimethylaminomethyl)-3,4-*bis*(1H,1H-heptafluorobut-1-yl)pyrrole (58).

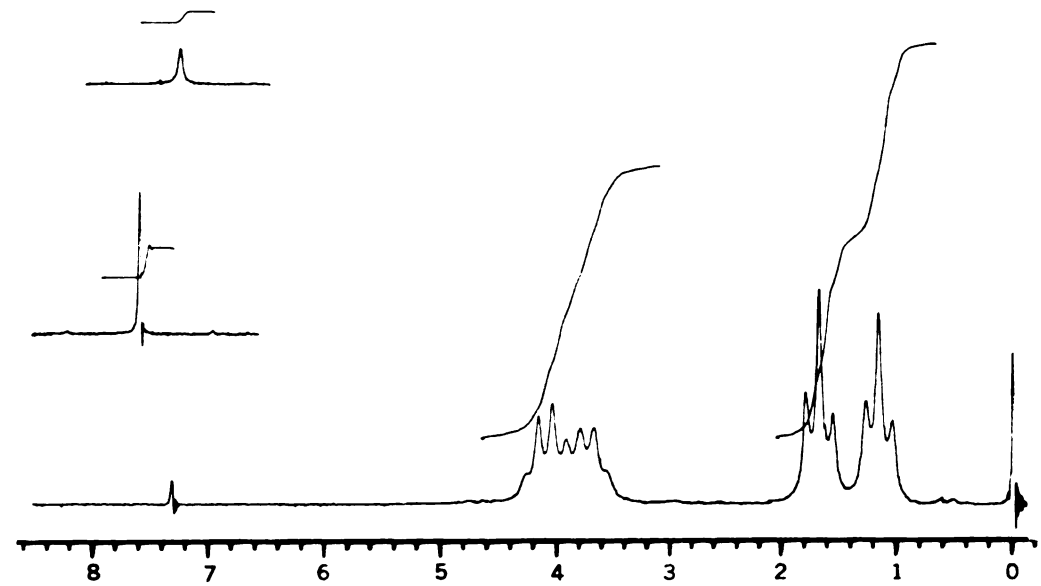


Figure A55. 60 MHz ^{1}H NMR spectrum of octakis(N,N-diethylcarboxamide)porphyrin (62a).

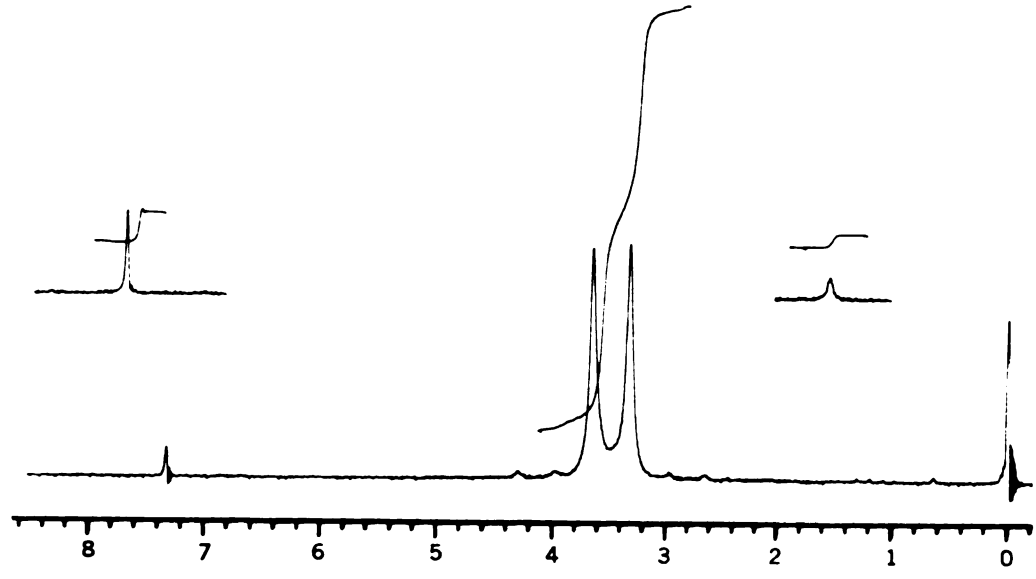


Figure A56. 60 MHz ^{1}H NMR spectrum of octakis(N,N-dimethylcarboxamide)porphyrin (62b).

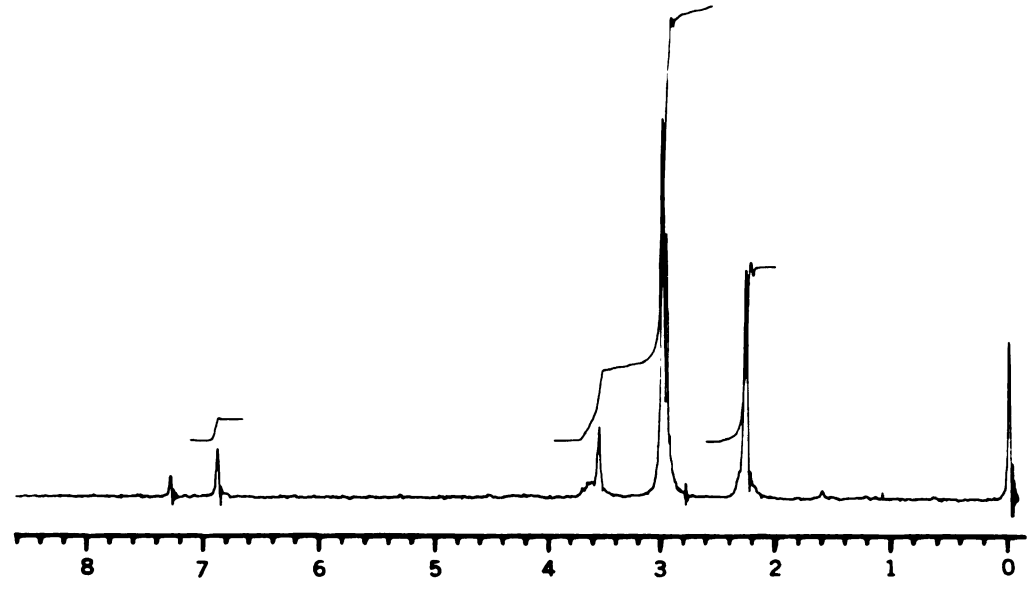


Figure A57. 60 MHz ^{1}H NMR spectrum of 3,4-*bis*(N,N-dimethylcarboxamide)-2-dimethylaminomethylpyrrole (63).

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