The Thermal Isomerization of Some Trisubstituted Pyrroles[1,2]

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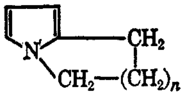
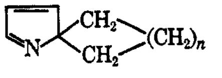
The pyrolysis (at 500–600°) of 1,2,5-trisubstituted pyrroles produces the corresponding 2,3,5-trisubstituted pyrroles as the major products. When the 1 substituent is different from the 2,5 substituents, a mixture of the isomeric 2,3,5-trisubstituted pyrroles is produced. Thus the pyrolysis of 1-phenyl-2,5-dimethylpyrrole yields 2,5-dimethyl-3-phenylpyrrole and 3,5-dimethyl-2-phenylpyrrole in equivalent amounts; 1-methyl-2,5-diphenylpyrrole yields 3-methyl-2,5-diphenylpyrrole and 2-methyl-3,5-diphenylpyrrole in equivalent amounts; and 1-benzyl-2,5-dimethylpyrrole yields 3-benzyl-2,5-dimethylpyrrole and 2-benzyl-3,5-dimethylpyrrole, the 3-benzyl isomer predominating. The pyrolysis of 2-benzyl-2,5-dimethyl-2H-pyrrole produces the same relative yields of isomers that were obtained from the pyrolysis of 1-benzyl-2,5-dimethylpyrrole. These data are regarded as evidence for a pyrrolenine intermediate in the thermal isomerization reaction.

At temperatures of 500–600° 1-substituted pyrroles, where the substituent is alkyl,[3] aryl,[4] and benzyl,[5] isomerize into a mixture of 2- and 3-substituted pyrroles. Asymmetric substituents migrate with about 70–80% retention of configuration.[5b]

Some evidence suggestive of a pyrrolenine intermediate was observed in the pyrolysis of the cycloalkano[*a*]pyrroles[6] I. The yields of the pyrolysis product, the corresponding cycloalkano[*b*]pyrrole, depended upon the size of the cycloalkano ring system. The low yield of the five-membered ring compound could be explained by postulating a pyrrolenine intermediate II, which, in this case, contains a strained four-membered-ring system.



I, $n = 1, 2, 3$



II

The present experiments were carried out to determine the tendency for rearrangement when the 2,5 positions of the pyrrole ring are blocked by substituents and to obtain additional evidence for the existence of the pyrrolenine intermediate.

It has been found that various 1,2,5-trisubstituted pyrroles undergo rearrangement more readily than the 1-substituted pyrroles even though the 2,5 positions are blocked. The greater reactivity of the trisubstituted pyrroles is substantiated by a comparison of the yields of isomeric pyrrole products obtained from pyrolyses run under identical conditions. The results are reported in Tables I and II.

Identification of the pyrolysis products was accomplished by a comparison of the properties of the products with those reported in the literature or with those obtained from synthesized authentic samples. Additional confirmation of structures was obtained from spectral data.

The 2,3,5- and 2,3,4-trimethylpyrroles were identified by a comparison of properties (infrared and nmr spectra, refractive index, and melting point) with those previously reported.[7]

Similarly, the isomeric 2,3,5- and 2,3,4-triphenylpyrroles were characterized by a comparison of melting points and ultraviolet spectra with those reported by Guy and Jones.[8] The infrared and nmr spectra were consistent with the assigned structures.

The structures assigned to the benzyldimethylpyrrole pyrolysis products were confirmed by synthesis. The properties (glpc retention time and infrared and nmr spectra) of 3-benzyl-2,5-dimethylpyrrole were identical with those obtained from the product produced from the reaction of 2,5-dimethylpyrrylmagnesium bromide and benzyl chloride. Likewise, the properties (glpc retention time and infrared and nmr spectra) of 2-benzyl-3,5-dimethylpyrrole were identical with those obtained from the reaction product of 2,4-dimethylpyrrylmagnesium bromide and benzyl chloride. The chemical shifts at 5.42 and 5.45 ppm for each of the isomers confirm the presence of a 3 proton in the pyrrole ring. Examination of the nmr spectra of alkyl and benzylpyrroles shows that alkyl-group protons of substituents attached to the 2 position exhibit larger δ values than alkyl-group protons of substituents attached to the 3 position. The benzyl proton chemical shifts of the 3-benzyl-2,5-dimethylpyrrole and 2-benzyl-3,5-dimethylpyrrole were 3.55 and 3.73 ppm, respectively.

The structures of the isomeric dimethylphenylpyrroles produced on pyrolysis were verified by synthesis. The 3,5-dimethyl-2-phenylpyrrole was synthesized by the procedure of Guy and Jones.[8] The melting point, glpc retention time, and infrared spectrum were in agreement with those obtained from the pyrrole isolated from the pyrolysate, and the nmr and ultraviolet spectra were consistent with the assigned structure. The 2,5-dimethyl-3-phenylpyrrole was synthesized by saponification and decarboxylation of 3-carbethoxy-2,5-dimethyl-4-phenylpyrrole which, in turn, was produced by treatment of an acetic acid solution of ethyl acetoacetate and isonitrosopropiophenone with zinc dust. The glpc retention time, nmr spectrum, and infrared spectrum obtained from the syn-

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(2) Presented before the Division of Organic Chemistry at the 154th National Meeting of the American Chemical Society, Chicago, Ill., 1967.

(3) (a) I. A. Jacobson, Jr., H. H. Heady, and G. V. Dinneen, *J. Phys. Chem.*, **62**, 1563 (1958); (b) I. A. Jacobson, Jr., and H. B. Jensen, *ibid.*, **66**, 1245 (1962); (c) I. A. Jacobson, Jr., and H. B. Jensen, *ibid.*, **68**, 3068 (1964).

(4) J. M. Patterson, unpublished results.

(5) (a) L. A. Pine, *Dissertation Abstr.*, **24**, 522 (1963); (b) J. M. Patterson and L. T. Burka, *J. Amer. Chem. Soc.*, **88**, 3671 (1966).

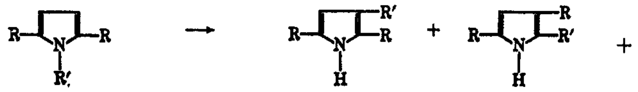
(6) J. M. Patterson and S. Soedigdo, *J. Org. Chem.*, **32**, 2969 (1967).

(7) R. L. Hinman and S. Theodoropulos, *ibid.*, **28**, 3052 (1963).

(8) R. W. Guy and R. A. Jones, *Aust. J. Chem.*, **19**, 1871 (1966).

TABLE I

PYROLYSIS OF THE PYRROLES AS A FUNCTION OF TEMPERATURE



R	R′	%	Temp, °C	%	%	other components
Me	Me	98	525	2	...	
		80	550	17	...	2,3,4 isomer (3%)
		48	575	36	...	2,3,4 isomer (10%); 2,6-Lutidine (2%)
		13	600	48	...	2,3,4 isomer (19%) 2,6-Lutidine (7%)
C_6H_5	C_6H_5	33	535	59	...	2,3,4 isomer (2%) Three unidentified (6% total)
Me	C_6H_5	91	500	5	4	...
		65	550	17	16	One unidentified (1%)
		22	600	36	35	One unidentified (7%)
C_6H_5	Me	55	550	20	21	Two unidentified (4%)
		20	600	35	35	Three unidentified (10%)
Me	$C_6H_5CH_2$	72	500	11	2	Bibenzyl (8%) Four unidentified (6%)
		22	550	24	14	Bibenzyl (16%) Four unidentified (23%)

TABLE II

COMPARISON OF YIELDS OF ISOMERIC PYRROLES FROM PYROLYSIS OF 1-SUBSTITUTED AND 1,3,5-TRISUBSTITUTED PYRROLES

Pyrrole	550° yield, %	600° yield, %
1-Methyl	3	39
1,3,5-Trimethyl	20	67
1-Methyl-2,5-diphenyl	41	70
1-Phenyl	11	42
1,3,5-Triphenyl	59[a]	...
1-Phenyl-2,5-dimethyl	34	71
1-Benzyl	42	...
1-Benzyl-2,5-dimethyl	38[b]	...

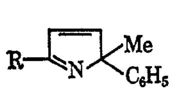
[a] 535°. [b] Bibenzyl (16%) also formed.

thetic material were identical with those obtained from the compound isolated from the pyrolysate.

The structures assigned to the isomers produced on pyrolysis of 1-methyl-2,5-diphenylpyrrole are based upon spectral data. Of the six possible isomeric structures, three can be excluded on the basis of the chemical shift observed for the pyrrole-ring proton. Chemical shift values lower than 6.50 ppm appear to be characteristic of protons in the 3 position of diphenylpyrroles[9] (see Experimental Section). Since the isomers formed on pyrolysis exhibit pyrrole-ring proton shifts of 6.23 and 6.38 ppm, these compounds are unsubstituted in the 3 position. An additional isomer, 5-methyl-2,3-diphenylpyrrole, is known[8] and can be excluded on the basis of its melting point (mp 80°). The isomeric mixture produced on pyrolysis consists of 2-methyl-3,5-diphenylpyrrole and 2-methyl-3,5-diphenylpyrrole. Since a comparison of chemical shifts of the 3 proton in the pyrrole ring shows that the δ value obtained from the 1-methyl-2,4-diphenylpyrrole[9] is larger than that obtained from 1-methyl-2,5-diphenylpyrrole (6.43 and 6.25 ppm, respectively), the pyrolysis isomer exhibiting the larger δ value (6.38 ppm) is assigned the 2-methyl-3,5-diphenylpyrrole structure, and the isomer exhibiting the δ value of 6.23 ppm is assigned the 3-methyl-2,5-diphenylpyrrole structure. The ultraviolet spectra of these compounds confirm these assignments.

It has been reported[8] that 2,5-diphenylpyrrole absorbs at longer wavelengths than 2,4-diphenylpyrrole (λ_{max} 329 and 305 mμ, respectively). The 3-methyl-2,5-diphenylpyrrole shows an absorption band at 326 mμ and the 2-methyl-3,5-diphenylpyrrole shows an absorption band at 311 mμ.

The pyrolyses of 1-phenyl-2,5-dimethylpyrrole at 550 and 600° produce nearly equivalent amounts of the isomers, 3-phenyl-2,5-dimethylpyrrole and 2-phenyl-3,5-dimethylpyrrole, in which the group ending up in the 3 position had been initially attached to the 1 or 2 position. A prior migration of the methyl group to the 3 position (*i.e.*, before migration from the 1 position occurred) may represent another (although minor) pathway in addition to the pyrrolenine route, since, under identical conditions of reaction (600°), 2,5-dimethylpyrrole gives only 9% of the 2,4-dimethylpyrrole. Likewise, the pyrolyses of 1-methyl-2,5-diphenylpyrrole at 550 and 600° produce the 2- and 3-phenyl isomers in almost equivalent yields. Results are reported in Table III. These observations can be explained in terms of a pyrrolenine intermediate III.



III

Products are produced with the migration of either group and isomer distribution should depend upon the relative migrating abilities of the two groups.

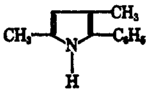
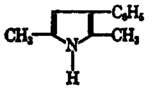
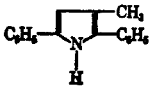
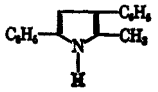
The formation of 3-benzyl-2,5-dimethylpyrrole and 2-benzyl-3,5-dimethylpyrrole (with the 3-benzyl isomer formed in greater amount) on the pyrolysis of 1-benzyl-2,5-dimethylpyrrole (see Table I) lends further support to the pyrrolenine postulate. The 3-benzyl isomer would be expected to be formed in greater yield since a benzyl group migrates more readily than a methyl group (see Table II). The formation of bibenzyl indicates that substitution enhances radical dissociation possibly because of steric hindrance or because of increased stabilization of the alkylpyrrole radical.

Whereas it was not possible to isolate the suspected pyrrolenine intermediate from the pyrolysis mixture, it

[9] R. M. Rodebaugh and N. H. Cromwell, *Tetrahedron Lett.*, **30**, 2859 (1967).

TABLE III

RELATIVE YIELDS OF THE 2,3,5 ISOMERS OBTAINED FROM THE PYROLYSIS OF 1-PHENYL-2,5-DIMETHYL- AND 1-METHYL-2,5-DIPHENYLPYRROLES

Temp, °C				
550	48%	52%	49%	51%
600	49%	51%	50%	50%

could be synthesized by a modification of the method of Booth, Johnson, and Johnson[10] using 2,5-dimethylpyrrylmagnesium bromide and benzyl chloride. The pyrrolenine exhibited nmr and infrared spectra which were consistent with the pyrrolenine structure.

The thermal isomerization of 2-benzyl-2,5-dimethyl-2-H-pyrrole occurs to the extent of 62% at 275° and is complete at 350°. The products of the pyrolyses run at various temperatures are reported in Table IV.

TABLE IV

PYROLYSIS PRODUCTS OF 2-BENZYL-2,5-DIMETHYL-2H-PYRROLE

Temp, °C	3-Benzyl-2,5-dimethylpyrrole, %	2-Benzyl-3,5-dimethylpyrrole, %	Bibenzyl, %	Other components, %
350	90	4	...	6[a]
500	67	15	2	16[b]
550	40	23	8	29[b]

[a] Three components. [b] Four components.

The ratios of the yield of 3-benzyl-2,5-dimethylpyrrole to the yield of 2-benzyl-3,5-dimethylpyrrole obtained at various temperatures from the pyrolyses of 1-benzyl-2,5-dimethylpyrrole and 2-benzyl-2,5-dimethyl-2H-pyrrole are indicated in Table V.

TABLE V

Temp, °C	Ratio of the 3-benzyl to the 2-benzyl isomer: 1-Benzyldimethylpyrrole	2-Benzyldimethyl-2H-pyrrole
500	4.4	4.5
550	1.7	1.7

Since the relative yield of 3-benzyldimethylpyrrole to that of 2-benzyldimethylpyrrole is the same whether the isomeric mixture is produced from the pyrrolenine or from the 1-benzyldimethylpyrrole on pyrolysis, it is concluded that the pyrrolenine is an intermediate in the thermal isomerization.

Experimental Section

Melting points were taken on a Fisher-Johns melting point block and are uncorrected. Boiling points are uncorrected. Infrared spectra were measured on a Perkin-Elmer Model 21 or on a Beckman IR-8 spectrophotometer; ultraviolet spectra were measured on a Perkin-Elmer Model 202 spectrophotometer; and nmr spectra were obtained on a Varian Associates HA-60-IL spectrometer in carbon tetrachloride solutions (*ca.* 10%) using tetramethylsilane as an internal standard (δ 0). Gas chromatographic analyses and separations were made on an Aerograph Model A-700 gas chromatograph or on an F & M Model 720 gas chromatograph using either SE-30 columns (20 and 30%) or a Carbowax 20M column (30%). Microanalyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

Syntheses of the Pyrroles. 1,2,5-Trimethylpyrrole.—The procedure is a modification of the method of Yanovskaya.[11] A mixture consisting of a 40% solution of methylamine in water (100 g), 2,5-hexanedione (114 g), and benzene (150 ml) was heated slowly to reflux in a flask fitted with a Dean-Stark trap. After the theoretical amount of water was collected (a few hours), the reaction mixture became clear and homogeneous. On distillation, the fraction boiling at 60° (11 mm) was collected (82 g, 75% yield): n^{25}D 1.4890 [lit.[5] bp 49–50° (5 mm), n^{20}D 1.4992]; nmr spectrum, 2.11 (singlet, 6 H), 3.30 (singlet, 3 H), 5.50 ppm (singlet, 2 H) (lit.[7] 2.10, 3.27, 5.52 ppm).

1,2,5-Triphenylpyrrole.—The procedure was adapted from the method of Ghigi and Drusiani.[12] A mixture of dibenzoylethane (1 g), aniline (0.4 g), and 10 ml of acetic acid was refluxed for 2 hr during which time solid material began to separate from the reaction mixture. The crystals which separated on cooling were removed by filtration, washed with acetone, and air dried. The product, colorless needles weighing 1.15 g (93% yield), exhibited the following properties: mp 231–232° (lit.[13] mp 231°); $\lambda_{\max}^{\mathrm{MeOH}}$ 208, 225 (sh), 302 mμ. Thin layer chromatography indicated that the sample was homogeneous.

1-Methyl-2,5-diphenylpyrrole.—The procedure used for 1,2,5-triphenylpyrrole was adapted. A 40% aqueous solution of methylamine (60 ml) was added slowly to a mixture of dibenzoylethane (10 g), benzene (150 ml) and acetic acid (50 ml), and the mixture was refluxed for 24 hr. The water was removed by azeotropic distillation during the heating period. The yellow crystals which separated on cooling were removed by filtration and air dried. The crystals weighed 9 g (96% yield) and showed the following properties: mp 206° (lit.[14] mp 204°); $\lambda_{\max}^{\mathrm{MeOH}}$ 207, 232, 308 mμ; nmr spectrum ($CDCl_3$), 3.54 (singlet, 3 H), 6.25 (singlet, 2 H), 7.35 ppm (multiplet with a sharp peak at 7.35, 10 H).

1-Phenyl-2,5-dimethylpyrrole.—The pyrrole was obtained from Distillation Products Industries and purified by distillation or recrystallization from Skellysolve B. The compound exhibited the following properties: mp 50–51° (lit.[15] mp 51–52°); $\lambda_{\max}^{\mathrm{MeOH}}$ 207, 234 mμ (sh); nmr spectrum, 1.93 (singlet, 6 H), 5.60 (singlet, 2 H), 7.17 ppm (multiplet, 5 H).

1-Benzyl-2,5-dimethylpyrrole.—A mixture of 2,5-hexanedione (1 g), benzylamine (1.2 g), benzene (20 ml), and acetic acid (1 ml) was refluxed overnight. The water which formed in the reaction was removed by azeotropic distillation; the removal of the theoretical quantity required about 2 hr. The solid obtained on cooling (1.2 g, 80% yield) after recrystallization from Skellysolve B exhibited the following properties: mp 43°; nmr spectrum, 2.03 (singlet, 6 H), 4.85 (singlet, 2 H), 5.60 (singlet, 2 H), *ca.* 7.00 ppm (multiplet, 5 H).

Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found: C, 84.51; H, 8.16; N, 7.73.

2,5-Diphenylpyrrole.—The procedure used for 1,2,5-triphenylpyrrole was adapted. A mixture consisting of dibenzoylethane (1 g), ammonium acetate (2 g), and acetic acid (10 ml) was refluxed for 20 hr. After cooling, the reaction mixture was poured into 100 ml of ice water, and the solid which separated was collected by filtration, washed with water, and air dried. The product weighed 0.9 g (98% yield): mp 142–143° (lit.[16] mp 143°); one peak on glpc analysis; $\lambda_{\max}^{\mathrm{MeOH}}$ 208, 231, 329 mμ;

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[10] H. Booth, A. W. Johnson, and F. Johnson, *J. Chem. Soc.*, 98 (1962).

[11] L. A. Yanovskaya, *Akad. Nauk SSSR, Inst. Organ. Khim., Sintezy Organ. Soedin. Sb.*, **1**, 152 (1950); *Chem. Abstr.*, **47**, 8005 (1953).

[12] E. Ghigi and A. Drusiani, *Atti Accad. Sci. Istit. Bologna, Classe Sci. Fis.*, **11**, No. 4, 14 (1957); *Chem. Abstr.*, **52**, 11818 (1958).

[13] J. Baumann, *Ber.*, **20**, 1486 (1887).

[14] R. Lukes and V. Prelog, *Chem. Zentr.*, **1**, 525, 997 (1929).

[15] L. Knorr and P. Rabe, *Ber.*, **34**, 3491 (1902).

[16] S. Kapf and C. Paal, *ibid.*, **21**, 3053 (1888).

nmr spectrum, 6.40 (doublet, 2 H), 7.25 ppm (multiplet, 10 H); $\nu_{\mathrm{CCl_4}}$ 3480 cm^{-1} (N-H).

2-Benzyl-2,5-dimethyl-2H-pyrrole.—The procedure is a modification of the method used by Booth, *et al.*[10] To a stirred solution of ethylmagnesium bromide (prepared from 2.4 g of magnesium and 10.9 g of ethyl bromide in 250 ml of ether), 10 g of 2,5-dimethylpyrrole was added during a 30-min period. After an additional 20 min, 12.7 g of benzyl chloride in 30 ml of ether was added. The green color of the reaction mixture became dull yellow during the 30-min addition period. When the reaction mixture had been stirred an additional 20 hr, ice-water (150 ml) was added and the mixture was acidified to litmus with 5% HCl. After removal of the ether layer, the acidic aqueous portion was made strongly alkaline with excess cold 25% NaOH solution and then extracted with four 200-ml portions of ether. The combined extracts were dried over anhydrous sodium carbonate and filtered and the ether was distilled. The basic residue thus obtained gave, on distillation at 13 mm, 2 g of colorless liquid boiling at 116°: $n^{25}\mathrm{D}$ 1.5276; $\nu_{\mathrm{CCl_4}}$ 1614 cm^{-1}, ν_{neat} 1614 cm^{-1} (Booth[11] reports absorption at 1613 cm^{-1} for γ-(2,3,4-trimethyl-2H-pyrryl)butyronitrile); nmr spectrum, 1.18 (singlet, 3 H), 2.05 (singlet, 3 H), 2.80 (quartet, 2 H), 5.90 (doublet, 1 H), 7.02 (doublet, 1 H partially buried in phenyl band), 7.02 ppm (singlet, 5 H).

Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found: C, 84.18; N, 8.29; N, 7.42.

The substance formed a yellow crystalline picrate which melted at 124–125° after recrystallization from ethanol.

Anal. Calcd for $C_{19}H_{18}N_4O_7$: C, 55.05; H, 4.35; N, 13.50. Found: C, 55.18; H, 4.51; N, 13.56.

3-Benzyl-2,5-dimethylpyrrole.—The ether solution containing the neutral fraction (from the synthesis of 2-benzyl-2,5-dimethyl-2H-pyrrole) was dried over magnesium sulfate and filtered and the ether was evaporated. The major fraction, 3-benzyl-2,5-dimethylpyrrole, was isolated by preparative glpc using a 10 ft × 0.25 in. 30% Carbowax 20M column at 250°. The glpc retention time and nmr and infrared spectra were identical with those obtained from the 3-benzyl-2,5-dimethylpyrrole produced on pyrolysis.

2-Benzyl-3,5-dimethylpyrrole.—The procedure was the same as that employed in the synthesis of 2-benzyl-2,5-dimethyl-2H-pyrrole. The product was obtained by distillation of the ether solution of the neutral fraction. From 10 g of 2,4-dimethylpyrrole,[17] there was obtained 9.8 g of product, bp 168–170° (22 mm), 95% purity based on glpc analysis. The compound was purified by preparative glpc using a 12 ft × 0.375 in. 20% Apiezon L column at 280°.

Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found: C, 84.11; H, 8.02; N, 7.84.

The glpc retention time and infrared and nmr spectra were identical with those obtained from 2-benzyl-3,5-dimethylpyrrole produced on pyrolysis.

3,5-Dimethyl-2-phenylpyrrole.—3-Carbethoxy-2,4-dimethyl-5-phenylpyrrole was synthesized by the procedure of Guy and Jones[8] from ethyl acetoacetate (26 g, 0.2 mol), isonitrosophenylacetone (27 g, 0.17 mol), zinc dust (50 g, 0.77 g-atom), and acetic acid (100 ml). The solid product obtained on work-up weighed 28.6 g after trituration with Skellysolve B: mp 120–122° (lit.[8] mp 120–121.5°); $\nu_{\mathrm{CHCl_3}}$ 1250, 3440 cm^{-1}; nmr spectrum ($CDCl_3$), 1.28 (triplet, 3 H), 2.32 (singlet, 3 H), 2.48 (singlet, 3 H), 4.22 (quartet, 2 H), 7.32 ppm (multiplet, 6 H).

Saponification and decarboxylation were effected by the bomb procedure of Corwin and Krieble.[18] The solid obtained on evaporation of the ether extract of the reaction mixture was extracted with hot Skellysolve B. The material which dissolved consisted only of decarboxylation product and unreacted starting pyrrole. The mixture was separated by preparative glpc using an 8 ft × 0.375 in. 20% SE-30 column at 240°. The glpc retention time and infrared spectrum were identical with those obtained from the 2,4-dimethyl-5-phenylpyrrole produced on pyrolysis.

2,5-Dimethyl-3-phenylpyrrole.—3-Carbethoxy-2,5-dimethyl-4-phenylpyrrole was synthesized by an adaptation of the procedure of Guy and Jones[8] from ethyl acetoacetate (26 g, 0.2 mol), isonitrosopropiophenone[19] (27 g, 0.17 mol), zinc dust (50 g, 0.77 g-atom), and acetic acid (100 ml). The light yellow solid obtained on work-up was triturated with Skellysolve B and weighed 12.4 g, mp 126.5–128°. The compound was recrystallized from a Skellysolve B-benzene mixture: mp 127–128°; $\nu_{\mathrm{CHCl_3}}$ 1285, 3450 cm^{-1}; nmr spectrum ($CDCl_3$), 1.02 (triplet, 3 H), 2.02 (singlet, 3 H), 2.45 (singlet, 3 H), 4.05 (quartet, 2 H), 7.22 ppm (multiplet, 6 H).

Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.04; H, 7.04; N, 5.76. Found: C, 74.24; H, 7.22; N, 5.90.

Saponification and decarboxylation of the pyrrole were accomplished by the method of Corwin and Krieble.[18] Work-up produced a mixture consisting of decarboxylated pyrrole and starting material which was separated by preparative glpc using an 8 ft × 0.375 in. 20% SE-30 column at 240°. The glpc retention time and infrared and nmr spectra were identical with those obtained from the 2,5-dimethyl-3-phenylpyrrole produced on pyrolysis.

Pyrolyses of the Pyrroles.—The pyrroles were pyrolyzed in the apparatus previously described[20] using, in each experiment, the same sample addition rate of 7.5 ml/hr and the same nitrogen flow rate of 120 cc/min. The pyrolysis reactor contained 40 ml of crushed Berl saddles.

The pyrolysate composition was determined as a function of temperature by carrying out the pyrolyses at several temperatures and by analyzing (glpc) the pyrolysates obtained. Components were identified by comparing the glpc retention times with those obtained from the components isolated from larger scale experiments. The yields of components reported as area per cent are recorded in the tables.

Isolations were accomplished by using preparative glpc or by using conventional column chromatography. The column (25 cm × 4.5 cm) was prepared using Davison commercial grade silica gel (60–200 mesh, Mil-D-3716) and 1:1 benzene–Skellysolve B solvent. Samples in benzene were layered on top of the column and eluded first with benzene–Skellysolve B–Skellysolve A (4:5:2), followed by benzene–Skellysolve B–Skellysolve A (5:5:1).

Thin layer chromatography was employed to determine sample purity and whether or not separation by column chromatography was feasible. The plates were coated (thickness *ca.* 0.25 mm) with a slurry of silica gel G (30 g/60 ml of water) using an applicator, air dried overnight, and activated 1 hr at 115°. The solvent system, benzene–Skellysolve B (1:1), was used for development of the chromatograms.

1,2,5-Trimethylpyrrole.—From 17.9 g of 1,2,5-trimethylpyrrole (pyrolyzed at 600°) 17.0 g of the crude pyrolysate was obtained. The components were separated into basic and neutral fractions by extracting an ether solution of 14 g of the pyrolysate with cold dilute (5%) sulfuric acid. The ether layer (acid-insoluble fraction) was separated, washed once with water, and dried over anhydrous magnesium sulfate, and then the ether was evaporated leaving 9.9 g of dark brown residue. The two major components of the residue were separated by preparative glpc using a 10 ft × 0.375 in. 30% Carbowax 20M column at 175°. The first component, on the basis of its glpc retention time, refractive index, and nmr and infrared spectra, was 1,2,5-trimethylpyrrole. The second component was 2,3,5-trimethylpyrrole: $n^{20}\mathrm{D}$ 1.5055 (lit.[7] $n^{24}\mathrm{D}$ 1.5045); ν_{neat} 3300 cm^{-1}; nmr spectrum, 1.87 (singlet, 3 H), 2.00 (singlet, 3 H), 2.05 (singlet, 3 H), 5.40 (doublet, 1 H), 6.90 ppm (broad, 1 H), (lit.[7] 1.87, 2.02, 2.08, 5.42 ppm).

The acidic aqueous layer was made strongly basic with 25% sodium hydroxide solution, extracted with ether and the ether extract dried over anhydrous sodium carbonate. Removal of the drying agent and ether left 3.2 g of brown residue which had a strong pyridinelike odor. The basic fraction was also separated on the Carbowax 20M column at 175° and contained 2,6- and 2,5-lutidine (based on a comparison of glpc retention times and infrared and nmr spectra with those from authentic samples). The third component was 2,3,4-trimethylpyrrole: mp 36–37°; ν_{neat} 3450 cm^{-1}; nmr spectrum, 1.85 (singlet, 3 H), 1.90 (singlet, 3 H), 2.05 (singlet, 3 H), 6.12 (singlet, 1 H), 6.99 ppm (broad, 1 H) (lit.[7] mp 39.5–40°; nmr spectrum, 1.84, 1.92, 2.08, 6.15 ppm).

1-Phenyl-2,5-dimethylpyrrole.—A sample (3 g) was pyrolyzed at 600° and, since the glpc retention times of the components were very nearly the same on the SE-30 column, the components were separated by column chromatography on silica gel. The first portion of the eluate on evaporation yielded 1-phenyl-2,5-

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[17] H. Fischer, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p 217.

[18] A. H. Corwin and R. H. Krieble, *J. Amer. Chem. Soc.*, **63**, 1830 (1941).

[19] W. H. Hartung and J. C. Munch, *ibid.*, **51**, 2262 (1929).

[20] J. M. Patterson and P. Drenchko, *J. Org. Chem.*, **27**, 1650 (1962).

dimethylpyrrole (identified on the basis of melting point and infrared and nmr spectra). The second portion of the eluate gave, on evaporation, a viscous residue (3,5-dimethyl-2-phenylpyrrole) which, on purification by preparative glpc, produced a colorless solid: mp 68–70° (lit.[8] mp 71.5–72°); $\lambda_{\max}^{\mathrm{MeOH}}$ 207, 297 mμ; $\nu_{\mathrm{CCl_4}}$ 1250, 3480 cm^{-1}; nmr spectrum, 2.10 (singlet, 3 H), 2.14 (singlet, 3 H), 5.55 (doublet, 1 H), 7.15 ppm (multiplet with a sharp peak at 7.15, 6 H).

Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.40; H, 7.31; N, 8.18.

Evaporation of the solvent from the third portion of the eluent produced 2,5-dimethyl-3-phenylpyrrole as a brown viscous residue. This residue, on purification by glpc, became a colorless liquid which solidified on standing. Recrystallization from carbon tetrachloride gave colorless crystals: mp 82–83°; $\lambda_{\max}^{\mathrm{MeOH}}$ 207, 222 (sh), 278 mμ; $\nu_{\mathrm{CCl_4}}$ 1310, 3482 cm^{-1}; nmr spectrum, 2.08 (singlet, 3 H), 2.12 (singlet, 3 H), 5.75 (doublet, 1 H), 7.15 ppm (multiplet with a sharp peak at 7.15, 6 H).

Anal. Calcd for $C_{12}H_{13}N$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.31; H, 7.43; N, 8.20.

1-Methyl-2,5-diphenylpyrrole.—The solid sample (2.5 g) was pyrolyzed at 600° with an addition rate of 7.5 g/hr. The crude pyrolysate was separated by column chromatography using a silica gel column and a benzene–Skellysolve B (1:1) eluent. The first portion of the eluate, on evaporation, produced 1-methyl-2,5-diphenylpyrrole which was identified by its melting point and ultraviolet and infrared spectra.

The second portion of eluate, on evaporation of the solvent, produced 3-methyl-2,5-diphenylpyrrole. Recrystallization twice from Skellysolve B produced colorless crystals: mp 95°; $\lambda_{\max}^{\mathrm{MeOH}}$ 207, 234, 326 mμ; nmr spectrum, 2.18 (singlet, 3 H), 6.23 (doublet, 1 H), *ca.* 7.25 ppm (multiplet, 10 H).

Anal. Calcd for $C_{17}H_{15}N$: C, 87.51; H, 6.48; N, 6.01. Found: C, 87.43; H, 6.42; N, 6.12.

2-Methyl-3,5-diphenylpyrrole was obtained from the third portion of eluate and gave the following spectral properties after purification by glpc: mp 101–102°; $\lambda_{\max}^{\mathrm{MeOH}}$ 210, 237, 311 mμ; nmr spectrum, 2.24 (singlet, 3 H), 6.38 (doublet, 1 H), 7.30 ppm (multiplet, 10 H).

Anal. Calcd for $C_{17}H_{15}N$: C, 87.51; H, 6.48; N, 6.01. Found: C, 87.57; H, 6.42; N, 6.08.

1-Benzyl-2,5-dimethylpyrrole.—The pyrrole was pyrolyzed at 550° and the pyrolysate separated on a silica gel column using benzene–skellysolve B (1:1) as eluent. The first portion of eluate yielded long yellow needles on evaporation: mp 50–51°; nmr spectrum, 2.82 (singlet, 2 H), 7.07 ppm (singlet, 5 H). The substance showed no N-H absorption in the infrared spectrum and gave a negative Ehrlich test. The properties correspond to those of bibenzyl (lit.[21] mp 51.5–52.5°). The second fraction, on evaporation, produced 1-benzyl-2,5-dimethylpyrrole. The identity was based upon melting point and infrared and nmr spectra. Evaporation of the solvent of the third fraction produced 2-benzyl-3,5-dimethylpyrrole, which (after purification by glpc on 5 ft × 0.25 in. 20% SE-30 column at 168°), mp 51–52°, showed the following spectral properties: $\nu_{\mathrm{CCl_4}}$ 1230, 3470 cm^{-1}; nmr spectrum, 1.92 (singlet, 3 H), 2.03 (singlet, 3 H), 3.73 (singlet, 2 H), 5.45 (doublet, 1 H), 7.08 ppm (multiplet, 6 H).

Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found: C, 84.40; H, 8.19; N, 7.67.

3-Benzyl-2,5-dimethylpyrrole was isolated from the fourth portion of eluate by preparative glpc using the SE-30 column at 168°: mp 65°; $\nu_{\mathrm{CCl_4}}$ 3480 cm^{-1}; nmr spectrum, 2.03 (singlet, 3 H), 2.08 (singlet, 3 H), 3.55 (singlet, 2 H), 5.42 (doublet, 1 H), 7.03 ppm (multiplet, 6 H).

Anal. Calcd for $C_{13}H_{15}N$: C, 84.28; H, 8.16; N, 7.56. Found: C, 84.63; H, 8.15; N, 7.61.

Analysis of the crude pyrolysate by glpc did not separate the starting material from the bibenzyl; however, the quantity of bibenzyl in this fraction could be determined from the ratio of benzyl hydrogens of starting material to bibenzyl obtained from the nmr spectrum of the fraction.

2-Benzyl-2,5-dimethyl-2H-pyrrole.—The major pyrolysis product at 350° was obtained from an acetone solution of the pyrolysate by the addition of water. The solid, 3-benzyl-2,5-dimethylpyrrole, after recrystallization from skellysolve B, exhibited properties (melting point, glpc retention time, and infrared and nmr spectra) which were identical with those obtained from the sample produced on pyrolysis of 1-benzyl-2,5-dimethylpyrrole.

From pyrolysate produced at 550°, 2-benzyl-3,5-dimethylpyrrole was isolated by glpc. The properties of this compound (infrared and nmr spectra) were identical with those obtained from the sample produced on pyrolysis of 1-benzyl-2,5-dimethylpyrrole. Bibenzyl was isolated from the pyrolysate using a silica gel column as previously described. The properties of the bibenzyl were identical with those previously reported.

1,2,5-Triphenylpyrrole.—The pyrolysate produced at 535° was separated using the silica gel column and benzene–Skellysolve B as the eluent. Starting material (1,2,5-triphenylpyrrole) was isolated from the first portion of eluate on evaporation. After recrystallization from benzene, the substance showed properties (melting point and ultraviolet and infrared spectra) which were identical with those obtained from an authentic sample.

Evaporation of the second portion of eluate gave 2,3,5-triphenylpyrrole which, on recrystallization from Skellysolve B, exhibited the following properties: mp 139–140° (lit.[8] mp 142°); $\lambda_{\max}^{\mathrm{MeOH}}$ 208, 237, 258, 320 mμ [lit.[8] $\lambda_{\max}$ 238, 257, 300 (sh), 320 mμ]; $\nu_{\mathrm{CCl_4}}$ 3480 cm^{-1}; nmr spectrum, 6.45 (doublet, 1 H), 7.17 (multiplet, 15 H), 8.08 ppm (broad, 1 H).

Anal. Calcd for $C_{22}H_{17}N$: C, 89.45; H, 5.80; N, 4.74. Found: C, 89.88; H, 5.90; N, 4.55.

From the third portion of eluate, 2,3,4-triphenylpyrrole was obtained and, after recrystallization from 1:1 benzene–Skellysolve B, exhibited the following properties: mp 165–166° (lit.[8] mp 168°); ν_{KBr} 3420 cm^{-1} (N-H); $\lambda_{\max}^{\mathrm{MeOH}}$ 208, 251, 298 mμ [lit.[8] $\lambda_{\max}$ 254, 303 mμ (sh)]; nmr spectrum, 6.85 (doublet), 7.12 ppm (multiplet).

Anal. Calcd for $C_{22}H_{17}N$: C, 89.45; H, 5.80; N, 4.74. Found: C, 89.57; H, 5.89; N, 4.84.

Registry No.—1,2,5-Trimethylpyrrole, 930-87-0; 1-methyl-2,5-diphenylpyrrole, 840-04-0; 1-benzyl-2,5-dimethylpyrrole, 5044-20-2; 2,5-diphenylpyrrole, 838-40-4; 2-benzyl-2,5-dimethyl-2H-pyrrole, 16206-29-4; 2-benzyl-3,5-dimethylpyrrole, 16206-30-7; 3-carbethoxy-2,5-dimethyl-4-phenylpyrrole, 16206-31-8; 2,3,5-trimethylpyrrole, 2199-41-9; 2,3,4-trimethylpyrrole, 3855-78-5; 3,5-dimethyl-2-phenylpyrrole, 3274-53-1; 2,5-dimethyl-3-phenylpyrrole, 3771-60-6; 3-methyl-2,5-diphenylpyrrole, 16206-34-1; 2-methyl-3,5-diphenylpyrrole, 16206-35-2; 3-benzyl-2,5-dimethylpyrrole, 16206-36-3; 2,3,5-triphenylpyrrole, 3274-61-1; 2,3,4-triphenylpyrrole, 3274-59-7.

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(21) S. Cannizzaro and A. Rossi, *Ann. Chem.*, **121**, 251 (1862).