Identification of the glutamic acid was obtained by preparing the *N*-benzoyl-*dl*-glutamic acid; m.p. 152–154°, reported 155–157°.[10]

Anal. Calcd. for $C_{12}H_{13}NO_5$: N, 5.58. Found: N, 5.73.

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(10) E. Fischer, *Ber.*, **32**, 2451 (1899).

Acknowledgment. The authors wish to express their thanks to Mr. T. Inoue for assistance with the experimental work.

YOKOSUKA, JAPAN

[CONTRIBUTION FROM THE SCIENTIFIC LABORATORY, FORD MOTOR CO.]

Azo Coupling in the Pyrrole System. The Synthesis of Azopyrroles

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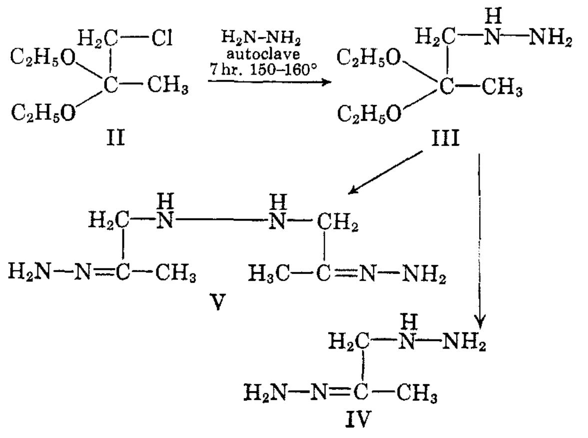
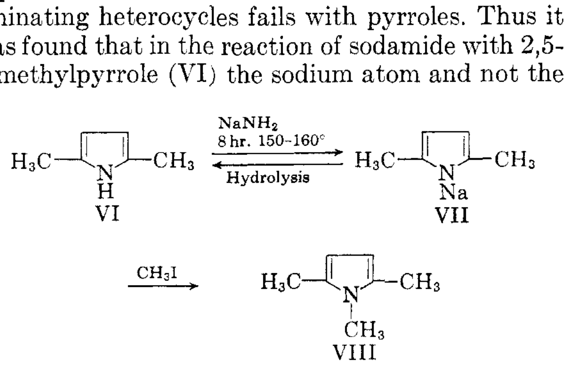
2,5-Diphenylpyrrole-3-diazonium chloride (XIII) has been shown to undergo the azo coupling reaction leading to the new compound class of azopyrroles (I). Coupling of XIII with pyrroles carrying substituents in α-positions furnishes 3,3′-azopyrroles (Ia and Ib), while the coupling products with pyrroles having free α-positions have been assigned the structure of 2,3′-azopyrroles (Ic through Ih). Structure proof of I has been adduced by hydrogenation of the azo group.

Free azotetrazole is not capable of existence,[2] while azotriazoles are more stable and can be isolated.[3] This tendency toward greater stability when proceeding to azo compounds containing heterocycles with less nitrogen, combined with the fact that the pyrrole ring is stabilized by the amount of 31 kcal.[4] of resonance energy per mole, focussed our attention on the hitherto unknown class of azopyrroles (I).

The synthesis of azopyrroles was first attempted by a modified Knorr synthesis using *N*,*N*′-diphenacetylhydrazine[5] as a carbonyl compound with a methylene group in α-position. However, this compound could not be caused to react with α-amino ketones, *e.g.*, ω-aminoacetophenone. On the assumption that the carbonyl group would gain more ketone character if the hydrazino group were attached to the α-carbon, an attempt was made at synthesizing a simple *N*,*N*′-bisacetoalkylhydrazine, *e.g.*, *N*,*N*′ - bisacetonylhydrazine. As hydrazine reacted violently with 1-chloro-2-propanone, the carbonyl group in the latter compound was protected by acetalization. The 1-chloro-2-propanone diethyl acetal (II) thus obtained, however, was inert toward hydrazine even at reflux temperature. When the reactants were forced to react with each other by heating them in an autoclave, the reaction took a different course resulting in a mixture of products which could be separated and identified as 1-hydrazino-2-propanone hydrazone (IV) and *N*,*N*′-bis(2-hydrazonopropyl)hydrazine (V). Based on the fact that, of the two functional groups in 1-chloro-2-propanone, the chlorine atom is first to react with amines,[6] the formation of IV and V may then be explained *via* 1-hydrazino-2-propanone (III).



Because of the unexpected course of the reaction and the rather low yields of pure end products, it appeared to be more promising to close the pyrrole ring first and then connect two rings with each other by an azo bridge. Azo coupling, being the most important method for synthesizing azo compounds, would require availability of diazotizable aminopyrroles. However, simple model compounds of this type are not known and Chichibabin's method[7] of aminating heterocycles fails with pyrroles. Thus it was found that in the reaction of sodamide with 2,5-dimethylpyrrole (VI) the sodium atom and not the



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[1] Presented at the 138th National Meeting of the American Chemical Society in New York, N. Y., September 1960.

[2] J. Thiele, *Ann.*, **303**, 57 (1898).

[3] J. Thiele and W. Manchot, *Ann.*, **303**, 47 (1898).

[4] V. Schomaker and L. Pauling, *J. Am. Chem. Soc.*, **61**, 1769 (1939).

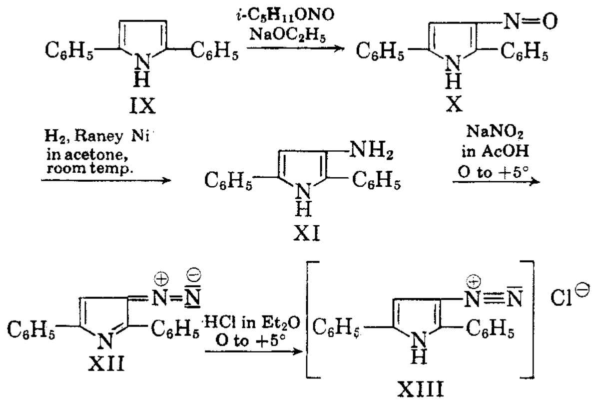
[5] A. Kreutzberger, *J. Org. Chem.*, **22**, 679 (1957).

[6] C. Cloëz, *Ann. chim. et phys.*, (6), **9**, 158 (1886); R. Stoermer and O. Dzimski, *Ber.*, **28**, 2223 (1895).

amino group entered the pyrrole ring. The presence of 1-sodio-2,5-dimethylpyrrole (VII) was proved by reconverting VII to VI through hydrolysis and by converting VII to 1,2,5-trimethylpyrrole (VIII) by means of methyl iodide.

As a simple aromatically substituted aminopyrrole model substance, 3-amino-2,5-diphenylpyrrole (XI) appeared to be suitable for the purpose in mind. This compound is known to react with nitrous acid, but to furnish, unexpectedly, a diazo-2,5-diphenylpyrrole[8] instead of the expected diazonium salt.

Angelico[8] also stated that this diazo-2,5-diphenylpyrrole furnishes a hydrochloride, but that lack of material prevented him from analyzing it. Consequently, this hydrochloride has never been assigned a structure. Since there was a good chance that this hydrochloride could have the structure of 2,5-diphenylpyrrole-3-diazonium chloride (XIII), the methods involved in all intermediate steps of its syntheses were elaborated such as to furnish workable amounts of substance, enabling us to do structure investigations. The hydrochloride was prepared from 2,5-diphenylpyrrole (IX)[9] *via* 3-nitroso-2,5-diphenylpyrrole (X), 3-amino-2,5-diphenylpyrrole (XI) and 3-diazo-2,5-diphenylpyrrole (XII). Thus an 87% yield of X could be obtained when modifying the method of Angelico and Calvello[10] by using a molar ratio of IX: isoamylnitrite:sodium ethoxide = 1:1:3 and by liberating X from its sodium salt by means of solid carbon dioxide without external heating instead of using gaseous carbon dioxide in a boiling aqueous solution. The method of reducing X to XI by zinc dust in a hot alcoholic acetic acid solution[8] was entirely abandoned, because catalytic reduction with Raney nickel in acetone at room temperature and 20 p.s.i. proved to proceed much more smoothly and to furnish a 70% yield of XI. Proper temperature control to maintain the reaction contents between 0 and +5° is the clue to an 89% yield of XII when preparing it from XI by means of sodium nitrite in acetic acid,[8] and to a quantitative conversion of XII to XIII by means of hydrochloric acid in an ethereal suspension.



Through infrared studies, it could be shown that 3-diazo-2,5-diphenylpyrrole in fact is a resonance hybrid receiving major contributions from structure XII, while its hydrochloride has been established as 2,5-diphenylpyrrole-3-diazonium chloride (XIII).[11] If this structure assignment was correct, this compound was expected to undergo the azo coupling reaction. However, when on account of the slightly acidic nature of the pyrrole ring and in accordance with the general coupling rule, XIII was subjected to coupling conditions with pyrrole and simple nonfunctional pyrrole derivatives in alkaline media, no coupling took place. Instead, XII had been regenerated and could be recovered. It was then argued that on the basis of the theoretically secondary nature of the NH group in the pyrrole ring acidic coupling conditions should be applied. On the assumption that XII would form the diazonium acetate when dissolved in acetic acid, the latter was used for the coupling under acidic conditions but also in this case XII was recovered.

Since the reason for this failure of XIII to undergo coupling reactions could not be traced immediately by changing the *p*H of the coupling medium, it was investigated next whether or not the pyrrole ring bearing nonfunctional substituents is capable of being coupled to other diazonium salts. As a matter of fact, it could be shown that pyrroles of the aforementioned type, *e.g.*, 2,5-diphenylpyrrole (IXa), 1-phenylpyrrole (IXb), 1-methylpyrrole (IXc), also pyrrole (IXd) itself, are amenable to coupling with *p*-sulfobenzenediazonium chloride (XIV).

These coupling reactions proceeded excellently under very mild conditions. The coupling medium consisted of an inert solvent such as acetonitrile, ether, hydrocarbons, alcohols, chloroform, carbon tetrachloride, and other halogenated hydrocarbons. During the reaction, the contents had to be well agitated and to be kept at a temperature of 0 to +5°.

The *p*-pyrrolylazobenzenesulfonic acids (XV) thus obtained are red to blue solids with a melting point higher than 400°. They are largely insoluble in most common organic solvents except glacial acetic acid and *N*,*N*-dimethylformamide. Dissolved in the latter solvent, they undergo a color change upon varying the *p*H value. This fact reveals their possible usefulness as indicators in acidimetric and

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(7) A. E. Chichibabin and O. A. Seide, *J. Russ. Phys. Chem. Soc.*, **46**, 1216 (1914); E. Ochiai and M. Karii, *J. Pharm. Soc. Japan*, **59**, 18 (1939).

(8) F. Angelico, *Atti reale accad. Lincei* (5), **14**, II, 167 (1905).

(9) A. Kreutzberger and P. A. Kalter, *J. Org. Chem.*, **25**, 554 (1960).

(10) F. Angelico and E. Calvello, *Gazz. chim. ital.*, **31**, II, 10 (1901).

(11) A. Kreutzberger and P. A. Kalter, *J. Phys. Chem.*, **65**, 624 (1961).

TABLE I

p-PYRROLYLAZOBENZENESULFONIC ACIDS (XV)

XV	Position of the Azo Link on the Pyrrole Ring	Color in Solid State	Color in Solution at Lower *p*H	*p*H of Color Change in Solution	Color in Solution at Higher *p*H	Empirical Formula	Carbon, %		Hydrogen, %		Nitrogen, %		Sulfur, %	
							Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
R′ = C_6H_5, R = H (XVa)	3	Reddish brown	Pink	2–3	Green	$C_{22}H_{17}N_3O_3S$	65.49	65.33	4.25	4.31	10.41	10.16	7.95	7.60
R = C_6H_5 (XVb)	2	Maroon	Light beige	Not sharp	Colorless	$C_{16}H_{13}N_3O_3S$	58.70	58.99	4.00	4.29	12.84	12.57	9.80	7.61
R = CH_3 (XVc)	2	Brown	Dark yellow	2–3	Light yellow	$C_{11}H_{11}N_3O_3S$	49.80	49.74	4.18	4.05	15.84	15.61	12.09	11.88
R = H (XVd)	2	Dark blue	Pink	3–4	Colorless	$C_{10}H_9N_3O_3S$	47.80	47.69	3.61	3.75	16.73	16.41	12.76	12.43

TABLE II

3,3′-AZOPYRROLES FROM 2,5-DIPHENYLPYRROLE-3-DIAZONIUM CHLORIDE (XIII)

Pyrrole IX Coupled	3,3′-Azo-pyrrole(I) R	Purification	Yield, %	M.P., (corr.)	Color in Solid State	Empirical Formula	Carbon, %		Hydrogen, %		Nitrogen, %		Chlorine, %	
							Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
2,5-Diphenyl (IXa)	C_6H_5 (Ia)	Recrystallization from dioxane	100	314–315	Brick red	$C_{32}H_{24}N_4$	82.73	82.91	5.21	5.03	12.06	11.88		
2,5-Dimethyl (IXe)	CH_3 (Ib)	Trituration with chloroform	18.7	324–326	Purple	$C_{22}H_{20}N_4 \cdot HCl$	70.11	70.24	5.62	5.41	14.86	14.60	9.41	9.72

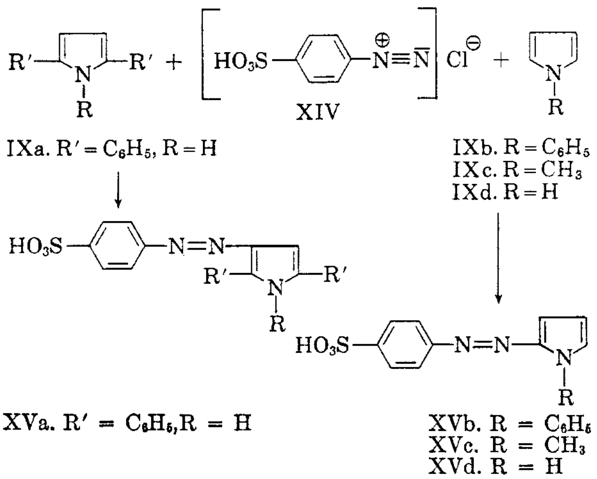
TABLE III

2,3′-AZOPYRROLES FROM 2,5-DIPHENYLPYRROLE-3-DIAZONIUM CHLORIDE (XIII)

Pyrrole IX Coupled	2,3′-Azopyrrole(I)				Purification	Yield, %	M.P., (corr.)	Color in Solid State	Empirical Formula	Carbon, %		Hydrogen, %		Nitrogen, %		Chlorine, %	
	R	R′	R″	R‴						Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
Unsubstituted (IXd)	H	H	H (Ic)	H	Trituration with water	32.2	>400	Bluish black	$C_{20}H_{16}N_4 \cdot HCl$	68.86	68.53	4.91	4.99	16.06	15.86	10.17	9.94
1-Methyl (IXc)	H	H	H (Id)	CH_3	Recrystallization from *N*,*N*-dimethylformamide/water or acetone/petroleum ether	30.8	290–291	Green	$C_{21}H_{18}N_4$	77.27	77.01	5.56	5.31	17.17	17.25		
1-Phenyl (IXb)	H	H	H (Ie)	C_6H_5	Trituration with water, benzene and petroleum ether	71.0	213–215	Brownish black	$C_{26}H_{20}N_4 \cdot HCl$	73.49	73.32	4.98	4.98	13.19	12.90	8.34	8.06
2,4-Diphenyl (IXf)	C_6H_5	H	C_6H_5 (If)	H	Recrystallization from an ethanol water mixture (7:3)	84.9	275–276	Dark red	$C_{32}H_{24}N_4$	82.73	82.51	5.21	5.15	12.06	11.87		
2,4-Dimethyl (IXg)	CH_3	H	CH_3 (Ig)	H	Recrystallization from *n*-Am_2O	37.4	143–145	Dark red	$C_{22}H_{20}N_4 \cdot HCl$	70.11	69.96	5.62	5.92	14.86	14.56	9.41	9.20
2,4-Dimethyl-3-ethyl (IXh)	CH_3	C_2H_5	CH_3 (Ih)	H	Recrystallization from from *n*-Am_2O	44.7	193–195	Brown	$C_{24}H_{24}N_4 \cdot HCl$	71.18	71.37	6.22	6.36	13.84	13.69	8.76	8.51

alkalimetric titrations. Pertinent data referring to XV are given in Table I.

While the reaction of XIV with pyrroles carrying substituents in 2,5-position leads to azo compounds of unequivocal structure and furnishes in the case of 2,5-diphenylpyrrole (IXa) the reddish brown azo dyestuff *p*-(2,5-diphenylpyrrol-3-ylazo)benzenesulfonic acid (XVa), there exist two possibilities as regards the position of the sulfobenzeneazo group at the pyrrole nucleus, when XIV is coupled with pyrroles having free α- and β-positions. The same problem has also previously been encountered in connection with structure assignments of azo compounds resulting from coupling of XIV with trisubstituted and carbethoxypyrroles.[12] It was claimed that pyrrol-α-ylazobenzenesulfonic acids could be distinguished from the corresponding β-compounds by a peculiar spot test consisting of the addition of diazotized nitroaniline to a drop of an alkaline solution of the azo dyestuff on filter paper. This paper spot was claimed to turn deep blue, if the azobenzenesulfonic acid group were attached to the α-position of the pyrrole ring, while no color reaction would occur with the corresponding pyrrole-β-derivatives. Unfortunately, it was not recognized immediately that the conclusion was not free of error and subsequently led to some confusion in the elucidation of the blood and plant pigments. A study of typical cases reveals the aforementioned spot test to be of very doubtful value for structure determinations.[13]



IXa. $R' = C_6H_5, R = H$

IXb. $R = C_6H_5$
IXc. $R = CH_3$
IXd. $R = H$

XVa. $R' = C_6H_5, R = H$

XVb. $R = C_6H_5$
XVc. $R = CH_3$
XVd. $R = H$

Therefore, despite the fact that XVb, XVc, and XVd do not develop a blue color with diazotized nitroaniline, we have assigned these structures to the series of *p*-pyrrol-2-ylazobenzenesulfonic acids. This structure assignment is based on the fact that in electrophilic substitution reactions the α-positions in pyrrole rings react first.[17]

Finally, the same conditions found to be most effective in the coupling of XIV with pyrroles were also successful when applied to the coupling reaction of XIII with pyrroles over a reaction period of thirty to thirty-six hours. Coupling of XIII with pyrroles having occupied α-positions led thus to the new compound class of 3,3′-azopyrroles. Representatives of this type compound are 2,2′,5,5′-tetraphenyl-3,3′-azopyrrole (Ia) and 2,5-dimethyl-2′,5′-diphenyl-3,3′-azopyrrole (Ib), pertinent data of which are summarized in Table II. If, however, XIII was coupled with pyrroles having either free α- or free α- and β-positions, the resulting coupling products have been assigned the structure of 2,3′-azopyrroles (Ic through Ih) due to the fact that the α-position of the pyrrole ring is preferred in electrophilic substitutions. The results referring to 2,3′-azopyrroles are given in Table III. Azopyrroles carrying only phenyl groups as substituents were obtained as the free bases, while most of those azopyrroles having also alkyl groups or hydrogen attached to the pyrrole ring were isolated as hydrochlorides. All azopyrroles prepared represent stable colored solids.

Proof of structure I was sought by reducing the azo link to amino groups. Care seemed indicated in the selection of a suitable reducing system as under certain conditions the pyrrole ring itself was likely to be reduced. Reduction of the unsubstituted pyrrole (IXd) to pyrrolidine by means of platinum still takes three to four days,[18] but the rate of reduction is increased with arylpyrroles.[19] Because Raney nickel has previously been shown to reduce preferentially functional groups attached to a pyrrole ring,[20] this catalyst was now applied to Ia, but furnished at ordinary pressure only resinous material along with unchanged Ia. At a pressure of 45 p.s.i., Raney nickel converted Ia into a difficultly separable mixture consisting of Ia, some reduced

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[12] H. Fischer and E. Bartholomäus, *Ber.*, **45**, 1919 (1912).

[13] Thus "phonopyrrole," a degradation product of hemin, gave with XIV an azo dyestuff which, according to its properties including the response to the described spot test, was assigned a pyrrole-3-ylazo structure.[12,14] The immediate precursor of "phonopyrrole" was "phonopyrrole carboxylic acid."[12,15] The latter, however, was shown to contain a pyrrole ring with a free 2- position. No plausible explanation could be given as to why the free 2- position in "phonopyrrole carboxylic acid" during the decarboxylation leading to "phonopyrrole" should rearrange to give a pyrrole ring with a free 3- position. Finally, this contradiction was solved by Piloty *et al.*,[16] who showed that the major constituent of "phonopyrrole" is identical with haemopyrrole 2,3-dimethyl-4-ethylpyrrole.

[14] H. Fischer and E. Bartholomäus, *Z. physiol. Chem., Hoppe-Seyler's*, **77**, 188 (1912).

[15] O. Piloty, *Ann.*, **377**, 320 (1910).

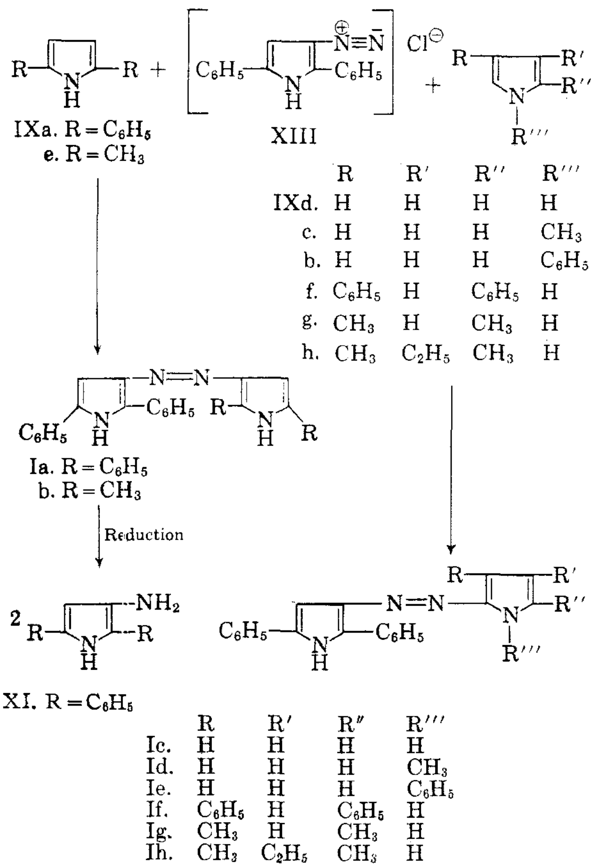
[16] O. Piloty, J. Stock, and E. Dormann, *Ann.*, **406**, 342 (1914).

[17] For example: O. Fischer and E. Hepp, *Ber.*, **19**, 2251 (1886); I. J. Rinkes, *Rec. trav. chim.*, **53**, 1167 (1934).

[18] R. Willstätter and D. Hatt, *Ber.*, **45**, 1471 (1912); L. H. Andrews and S. M. McElvain, *J. Am. Chem. Soc.*, **51**, 887 (1929).

[19] M. De Jong and J. P. Wibaut, *Rec. trav. chim.*, **49**, 237 (1930).

[20] F. K. Signaigo and H. Adkins, *J. Am. Chem. Soc.*, **58**, 709 (1936).



and some resinous material. Due to these unsatisfactory results, hydrogenation of Ia over Raney nickel was abandoned and different catalysts were investigated instead. Optimum conditions for the hydrogenation of Ia were found with a 10% palladium on charcoal catalyst at room temperature and a pressure of 45 p.s.i. leading to a quantitative yield of 3-amino-2,5-diphenylpyrrole (XI), thus confirming the structure of azopyrroles.

EXPERIMENTAL[21]

1-Chloro-2-propanone diethyl acetal (II) was prepared[22] by treatment of 1-chloro-2-propanone with triethyl orthoformate in ethanol in the presence of a catalytic amount of concd. sulfuric acid. As the boiling point of 38–39° (12 mm.) found in this Laboratory differed somewhat from the reported[22] one (57° at 12 mm.), we have verified the structure of II by analysis and infrared spectrum.

Anal. Calcd. for $C_7H_{15}ClO_2$: C, 50.45; H, 9.07; Cl, 21.28. Found: C, 50.63; H, 9.21; Cl, 21.13. n_D^{20} 1.4238.

The infrared spectrum identifies II clearly as an acetal. It shows thus three strong absorptions at 1140, 1100, and 1060 cm.$^{-1}$ which are the characteristic features of ether bonds[23] and which are missing entirely in the infrared spectrum of 1-chloro-2-propanone. The latter compound in turn exhibits a typical carbonyl absorption at 1725 cm.$^{-1}$ which does not show up in the infrared spectrum of II.

Reaction of 1-chloro-2-propanone diethyl acetal (II) *with hydrazine.* A solution containing 33.3 g. (0.2 mole) of II and 9.6 g. (0.3 mole) of anhydrous hydrazine in 100 ml. of absolute ethanol was heated in a pressure vessel for 7 hr. at 150–160°, the contents reaching thereby a pressure of 140–150 p.s.i. After cooling, the autoclave was opened and the resulting yellowish liquid was put under refrigeration, when white needles crystallized. These amounted to 2.2 g., could be recrystallized from absolute ethanol and melted then at 92–93°. By analysis and comparison with an authentic sample,[24] they were shown to be identical with *hydrazonium chloride.*

Anal. Calcd. for ClH_5N_2: Cl, 51.75; H, 7.36; N, 40.89. Found: Cl, 51.45; H, 7.09; N, 40.63.

The ethanolic filtrate from which the 2.2 g. of hydrazine hydrochloride had been isolated was stripped of solvent and any unchanged starting material II, leaving behind two immiscible oils. Because these two oils formed a clearly distinctive boundary due to different densities, they could be separated by means of a small dropping funnel.

The oil with the greater density crystallized upon standing for a few hours under refrigeration. The crystals amounted to 5.2 g. and were easily soluble in water, ethanol, and acetone and scarcely soluble in ether. By recrystallization from a small amount of hot enthanol, the substance was obtained in a white microcrystalline form melting at 127–128°. The elemental analysis identified this material as *N,N'-bis(2-hydrazonopropyl)hydrazine* (V).

Anal. Calcd. for $C_6H_{16}N_6$: C, 41.84; H, 9.36; N, 48.80. Found: C, 41.60; H, 9.18; N, 49.03.

The lighter oil also crystallized under refrigeration and furnished slightly yellowish leaflets; wt., 3.2 g. They were readily soluble in water, ethanol, acetone, and ether and could best be purified by recrystallization in a highly concentrated ethanolic solution. The white leaflets obtained melted at 104–105° and proved to be *1-hydrazino-2-propanone hydrazone* (IV).

Anal. Calcd. for $C_3H_{10}N_4$: C, 35.28; H, 9.87; N, 54.85. Found: C, 35.45; H, 9.63; N, 54.61.

Reaction of 2,5-dimethylpyrrole (VI) *with sodium amide.* When 7.8 g. (0.2 mole) of sodium amide was added portionwise to 19 g. (0.2 mole) of 2,5-dimethylpyrrole (VI), heat and ammonia were evolved and the mixture became reddish brown. This suspension was heated for 8 hr. at 150–160° in a nitrogen atmosphere. During this heating period, the entire reaction contents solidified forming a bright brown substance which proved to be very sensitive to air and moisture. As it formed a hard cake, it was covered with ether and broken up by means of mortar and pestle. The ether was decanted and the damp powder dried in a vacuum desiccator. The dry powder amounting to 23.3 g. (quantitative yield) had an analysis corresponding to *1-sodio-2,5-dimethylpyrrole* (VII).

Anal. Calcd. for C_6H_8NNa: Na, 19.63. Found: Na, 19.89.

The solid VII could be reconverted to 2,5-dimethylpyrrole (VI) in a manner as follows. An 11.7 g. sample (0.1 mole) of VII was dissolved in 150 ml. of water whereby a dark red oil separated. This was extracted with a total of 300 ml. of ether, the ether extract was dried over calcium chloride and then the extract stripped of solvent. The remaining oil was vacuum-fractionated and yielded as main fraction 8.1 g. (90.6%) of a colorless oil which, on the basis of its boiling point (51–53° at 8 mm.), its refractive index (n_D^{22} 1.500) and chemical properties[25] was identified as *2,5-dimethylpyrrole* (VI).

The reactivity of the sodium atom in VII was demonstrated by the reaction with methyl iodide. VII (11.7 g., 0.1 mole) was mixed with 28.4 g. (0.2 mole) of methyl iodide and heated in an autoclave for 5 hr. at 120–125°. After cooling,

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(21) All melting points are corrected. Analyses were carried out by Galbraith Laboratories, Knoxville, Tenn. and Spang Microanalytical Laboratory, Ann Arbor, Mich.

(22) A. Arbusow, *Ber.*, **40**, 3302 (1907).

(23) E. D. Bergmann and S. Pinchas, *Rec. trav. chim.*, **71**, 161 (1952).

(24) T. Curtius and R. Jay, *J. prakt. Chem.* [2], **39**, 38 (1889); E. C. Gilbert and A. W. Cobb, *J. Am. Chem. Soc.*, **57**, 39 (1935).

(25) L. Knorr, *Ber.*, **18**, 1565 (1885); D. M. Young and C. F. H. Allen, *Org. Syntheses*, **Coll. Vol. II**, 219 (1943).

the contents were poured into 150 g. of ice water when a reddish oil separated. Extraction with a total of 300 ml. of ether, drying the ethereal extract over anhydrous calcium sulfate and stripping the extract of solvent furnished a reddish oil. The latter was vacuum-distilled resulting in 9.5 g. (yield 87%) of a colorless oil which was identified as *1,2,5-trimethylpyrrole* (VIII),[26] b.p. 71–72° (12 mm.).

Anal. Calcd. for $C_7H_{11}N$: C, 77.01; H, 10.16; N, 12.83. Found: C, 69.82; H, 9.99; N, 13.02.

3-Nitroso-2,5-diphenylpyrrole (X). To a solution containing 20.4 g. (0.3 mole) of sodium ethoxide in 300 ml. of absolute ethanol was added dropwise a solution of 21.9 g. (0.01 mole) of 2,5-diphenylpyrrole (IX) with good agitation, the mixture assuming there by a greenish color. While the mixture was kept between 0 to +5°, 11.7 g. (0.1 mole) of freshly prepared isoamyl nitrite was added through a dropping funnel over a period of 20–30 min., when the color of the mixture turned yellowish orange. After all of the isoamyl nitrite had been added, the mixture was allowed to assume room temperature and stirring was continued for three more hours. During this time, the mixture had formed a brownish red solution which even prevailed after standing overnight and did not precipitate any solids.

The red solution was concentrated *in vacuo* to dryness and the solid triturated with 125 ml. of water, when an almost clear red solution was formed. Addition of small chunks of Dry Ice to the filtered solution caused precipitation of a brown solid. Solid carbon dioxide was continued to be added until the red color of the sodium salt of X disappeared. The brown solid was vacuum-filtered, washed with water, dried, and identified as X. There was obtained 21.7 g. (87% based on IX), m.p. 204–205°.

Anal. Calcd. for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.29. Found: C, 77.63; H, 5.05; N, 11.25.

3-Amino-2,5-diphenylpyrrole (XI). A 450-ml. hydrogenation bottle was charged with 15 ml. of cold acetone, 15 ml. of cold 2-propanol, 2.5 g. of 3-nitroso-2,5-diphenylpyrrole (X), and one teaspoon of Active Raney Nickel Catalyst. Hydrogen was admitted and the suspension shaken under an initial pressure of 20 p.s.i. Completion of the hydrogenation was indicated by the disappearance of all solid X (15 min). The reaction mixture was separated from the catalyst by filtration at room temperature. The violet fluorescing filtrate was concentrated *in vacuo* to dryness and the solid remainder was collected on a Buchner funnel and washed successively with a 15-, a 10-, and a 5-ml. portion of ice cold ether rendering 1.7 g. (yield 70.7%) of XI as a light yellow microcrystalline solid. In this state, XI melts at 182–183° and can be used for conversion into XII directly. For analysis, a sample was recrystallized from a 7:3 mixture of methanol-water. By this procedure, XI was obtained in the form of pale yellow cubes melting at 186–187°.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 82.04; H, 6.02; N, 11.96. Found: C, 82.14; H, 6.01; N, 11.75.

3-Diazo-2,5-diphenylpyrrole (XII). A solution containing 1.4 g. (0.02 mole) of sodium nitrite in 5 ml. of water was added dropwise to a well agitated solution of 4.7 g. (0.02 mole) of 3-amino-2,5-diphenylpyrrole (XI) in 25 ml. of glacial acetic acid at such a rate as to maintain a temperature of 0 to +5° even during the next step. After a total reaction time of 1 hr., a solution containing 25 g. of anhydrous sodium carbonate in 150 ml. of water was added dropwise over a period of 3 hr. to reach a *p*H of 7 and to precipitate XII as a brownish orange solid. Dried in a vacuum desiccator, the product weighed 4.4 g. (yield 89.5%) and could be recrystallized best from petroleum ether (b.p. 60–110°); bright brown needles, m.p. 122–123° dec.

Anal. Calcd. for $C_{16}H_{11}N_3$: C, 78.35; H, 4.52; N, 17.13. Found: C, 78.43; H, 4.60; N, 16.9 .

2,5-Diphenylpyrrole-3-diazonium chloride (XIII). A 100-ml. round bottomed three-neck flask fitted with a thermometer, gas introduction tube, and a drying tube containing calcium chloride, was charged with 25 ml. of absolute ether. By addition of 4.9 g. (0.02 mole) of 3-diazo-2,5-diphenylpyrrole (XII) a brownish suspension was formed which was agitated by means of a magnetic bar. When gaseous hydrogen chloride was passed into the suspension, heat evolution set in. To avoid resinification, it was found necessary to cool the reaction mixture with ice and to pass in hydrogen chloride at a sufficiently slow rate so that a temperature of +5° was never exceeded. Introduction of hydrogen chloride was discontinued when all of the brown colored XII had been replaced by yellowish green XIII (approximately 45 min.). After the suspension had been allowed to assume room temperature, the yellowish green solid was vacuum-filtered, washed with ether, and dried in a vacuum desiccator, giving 5.6 g. of XIII (quantitative yield). Upon determining the melting point, XIII turned dark brown at 171–173° but did not melt until 209–211 dec.

Anal. Calcd. for $C_{16}H_{12}ClN_3$: C, 68.20; H, 4.29; Cl, 12.59; N, 14.92. Found: C, 68.02; H, 4.19; Cl, 12.48; N, 14.71.

p-(2,5-Diphenylpyrrol-3-ylazo)benzenesulfonic acid (XVa) may be given as an example for the preparation of pyrrolylazobenzenesulfonic acids. A suspension of *p*-sulfobenzenediazonium chloride (XIV) was prepared by bubbling hydrogen chloride gas into a cooled mixture containing 1.9 g. of *p*-diazobenzenesulfonic acid (0.01 mole) in 30 ml. of acetonitrile. The apparatus used for carrying out this reaction was a three necked flask fitted with a thermometer, gas addition tube and a water-cooled condenser which in turn was connected with a calcium chloride drying tube. Agitation was effected by a magnetic bar stirrer. The introduction of hydrogen chloride gas was continued while a solution of 2.1 g. of 2,5-diphenylpyrrole (IXa) in 25 ml. of acetonitrile was added dropwise from a dropping funnel. The reaction contents assumed gradually a blood red color, were allowed to assume room temperature and were vacuum-filtered. The dried reddish brown solid amounted to 4.0 g (quantitative yield), had no melting point up to 400°, was insoluble in all common organic solvents except *N,N*-dimethylformamide and could be purified by successive trituration with water and ether.

The synthesis of 3,3'-azopyrroles may be exemplified by *2,2'5,5'-tetraphenyl-3,3'-azopyrrole* (Ia). While a solution of 2.8 g. of 2,5-diphenylpyrrole-3-diazonium chloride (XIII) (0.01 mole) in 70 ml. of anhydrous chloroform and 20 ml. of absolute ethanol contained in a 500 ml. three necked, round bottomed flask was kept stirring at a temperature of 0 to +5°, a solution containing 2.1 g. of 2,5-diphenylpyrrole (IXa) (0.01 mole) in 50 ml. of dry chloroform was added dropwise at such a rate as not to exceed the indicated temperature range. As the 2,5-diphenylpyrrole was added, the color of the reaction mixture changed to intense blue. After a total of 60 hr., stirring was discontinued and the solvents were stripped in vacuum. The crude material was purified by trituration with water, yielding thus 4.6 g. of dried blue solid (quantitative yield). It was soluble in most common organic solvents. Recrystallization from dioxane furnished Ia in the form of red crystals melting at 314–315°.

3,5-Dimethyl-4-ethyl-2',5'-diphenyl-2,3'-azopyrrole (Ih) may serve as an example of the synthesis of *2,3'-azopyrroles*. Upon the dropwise addition of a solution of 0.6 g. of 2,4-dimethyl-3-ethylpyrrole (IXh) (0.005 mole) in 25 ml. of anhydrous chloroform to an ice-cooled, stirred solution containing 1.4 g. of 2,5-diphenylpyrrole-3-diazonium chloride (XIII) (0.005 mole), 5 ml. of absolute ethanol, and 25 ml. of anhydrous chloroform, azo coupling started immediately as indicated by the development of a brownish purple color of the reaction mixture. Stirring was continued for a total period of 60 hr., after which time the mixture was evaporated in vacuum to dryness. The crude product was purified by trituration with water, when 0.9 g. (44.7% yield) of a brownish solid was obtained. Further purified by recrystallization from *n*-amyl ether, the crystalline material (Ih) melted at 193–195°.

Reduction of 2,2',5,5'-tetraphenyl-3,3'-azopyrrole (Ia). Hydrogen (45 p.s.i.) was admitted to a hydrogenation bottle

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(26) L. Knorr, *Ann.*, **236**, 304 (1886).

containing a mixture of 1.4 g. (0.003 mole) of Ia and 0.1 g. of 10% palladium on charcoal catalyst in 25 ml. of absolute ethanol. The mixture was shaken for 1 hr. at room temperature (22°) during which time the theoretical amount of hydrogen required for the cleavage of the azo link (0.006 mole) was absorbed. The catalyst was then removed by heating the mixture to the boiling point and filtering hot. The transparent beige colored filtrate was evaporated to dryness rendering 1.4 g. of 3-amino-2,5-diphenylpyrrole (XI) (quantitative yield). Recrystallization from a methanol-water mixture furnished XI as silver-gray crystals melting at 186–187°. The authenticity of XI was established by an undepressed mixed melting point of a mixture with a specimen of XII obtained by an independent route (see above). The infrared spectrum was identical with that of an authentic sample.[11]

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Pyridine 1-Oxides. IX. Further Oxidative Dimerizations of 4-Nitro-3-picolines[1a,b]

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Further experiments are described which verify the structure of the oxidative dimerization product of 4-nitro-3-picoline 1-oxide (I) as 1,2-di(1′-oxy-4′-nitro-3′-pyridyl)ethane (II) and elucidate its mode of formation. It is shown that II may be formed by treatment of I with sodium ethoxide *in the absence of external oxidizing agents;* since 4-nitro-3-picoline (VII) is recovered unchanged under similar conditions, it is concluded that the *N*-oxide grouping rather than the 4-nitro group is the effective oxidizing agent in the conversion of I to II. However, treatment of VII with 30% potassium hydroxide in ethanol in the presence of oxygen of 0° yields 1,2-di(4′-nitro-3′-pyridyl)ethane (VIII), identical with the product of phosphorus trichloride deoxygenation of II. Treatment of VII with 30% potassium hydroxide in ethanol in the presence of oxygen at room temperature yields 1,2-di(4′-ethoxy-3′-pyridyl)ethylene (X. R = C_2H_5), and it is shown that 1,2-di(4′-nitro-3′-pyridyl)ethane (VIII) is an intermediate in this conversion. Under similar conditions, 4-nitro-3-picoline 1-oxide (I) can be converted with sodium ethoxide in ethanol to 1,2-di(1′-oxy-4′-methoxy-3′-pyridyl)ethylene (XI. R = C_2H_5), which on deoxygenation gives X (R = C_2H_5). A similar series of reactions is described with the corresponding 4-methoxy derivatives. Catalytic reduction of XI (R = CH_3) yields 1,2-di(4′-methoxy-3′-pyridyl)ethane (XII. R = CH_3), identical with the reduction product of X (R = CH_3). Oxidation of XII (R = C_2H_5) with peracetic acid yields 1,2-di(1′-oxy-4′-ethoxy-3′-pyridyl)ethane (III. R = C_2H_5) which is identical with the product of the action of sodium ethoxide on 1,2-di(1′-oxy-4′-chloro-3′-pyridyl)ethane (IV). Compound II can be converted to XI (R = C_2H_5) with sodium ethoxide.

Previous work from this laboratory[2] had shown that treatment of 4-nitro-3-picoline 1-oxide (I) with *n*-butyl nitrite in the presence of sodium ethoxide resulted in oxidative dimerization to yield 1,2-(1′-oxy-4′-nitro-3′-pyridyl)ethane (II). The present investigation was undertaken in an effort to provide further evidence for the structure of II and to elucidate its mode of formation.

It has now been found that the oxidative dimerization product II is formed in moderate yield (20–35%) by treatment of 4-nitro-3-picoline 1-oxide (I) with sodium ethoxide alone. The same product is formed in comparable yield even when the reaction is run in a nitrogen atmosphere. This result can only mean that either the *N*-oxide group or the 4-nitro group is functioning as the oxidizing agent in the conversion of I to II, and that the *n*-butyl nitrite originally employed was presumably not essential for the conversion but merely served as an additional and perhaps more efficient oxidizing agent. As one would predict, deliberate addition of a better oxidizing agent such as sodium hypochlorite resulted in considerably increased yields of II.

In order to resolve the question of whether the *N*-oxide group or the nitro group was the active oxidizing agent, 4-nitro-3-picoline (VII),[3] prepared by deoxygenation of I with phosphorus trichloride in chloroform at 0°, was treated with sodium ethoxide in ethanol under nitrogen. No reaction took place and starting material was recovered. Thus, the *N*-oxide group is apparently serving as the oxidizing agent in the conversion of I to II. Activation of the 3-methyl group by the 4-nitro group is presumably also important, however, for 4-ethoxy-3-picoline 1-oxide could not be dimerized with sodium ethoxide, even when external oxidizing agents were also employed. This conclusion is further emphasized by the observation that 4-nitro-3-picoline (VII) with 30% potassium hydroxide in ethanol solution at 0° in the presence of oxygen gave an oxidative coupling product, 1,2-di(4′-nitro-3′-pyridyl)ethane (VIII), in 79% yield. This compound proved to be identical with the

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[1] (a) This work was supported in part by a research grant (C-2551) to Princeton University from the National Cancer Institute, National Institutes of Health, Public Health Service. (b) For the previous paper in this series, see E. C. Taylor and J. S. Driscoll, *J. Org. Chem.*, **26**, 3001 (1961). (c) Parke, Davis and Co. Fellow in Chemistry, 1957–1958: Monsanto Chemical Co. Fellow, 1958–1959.

[2] E. C. Taylor, A. J. Crovetti, and N. E. Boyer, *J. Am. Chem. Soc.*, **79**, 3549 (1957).

[3] This compound is rapidly converted to a mixture of 3-methyl-4-pyridone and 1-(3′-methyl-4′-pyridyl)-3-methyl-4-pyridone by moisture and care must be exercised to maintain anhydrous conditions in handling it. For details see ref. 1b.