SUBSTITUTION IN 1-PHENYLPYRAZOLE

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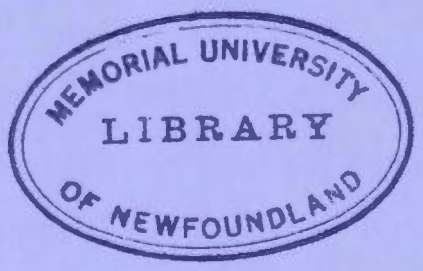

© SUBSTITUTION IN 1-PHENYLPYRAZOLE

by

Misbahul Ain Khan, M. Sc. (Kar.)

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ABSTRACT

A study of the nuclear substitution of 1-phenylpyrazole by the radicals liberated from thermal decomposition of benzoyl peroxide has been undertaken, with the object of testing the predictions of molecular-orbital calculations. Gas-liquid chromatographic analysis of the reaction products showed that the three 1-biphenylylpyrazoles and 1,3-diphenylpyrazole were present, and the isomer ratios were evaluated. There was no evidence for the presence of 1,4- or 1,5-diphenylpyrazole.

Some nuclear benzoyloxylation occurs in addition to phenylation, and a preliminary examination of the reaction products was made. In other preliminary work, the reactions occurring when benzoyl peroxide decomposes in 1-methylpyrazole and in 1-phenylpyrrole were examined.

Certain electrophilic substitutions (bromination and nitration) of 1-phenylpyrazole and 1-p-biphenylylpyrazole have been studied. It has been found possible to effect changes in the orientation of substitution by varying the reaction conditions, and an explanation for this behaviour is suggested.

T A B L E O F C O N T E N T S

Part II

EXPERIMENTAL

PREFACE

Although free radical substitutions of pyridine and quinoline have been examined in detail, and phenylations of some diazines have also been reported, little quantitative work has been done on other nitrogen heterocyclic systems. In view of this fact a study of nuclear substitution of 1-phenylpyrazole by the radicals liberated from thermal decomposition of benzoyl peroxide has been undertaken. Molecular orbital calculations predict the free radical attack at 3-(5-) position of pyrazole ring, but pyrazole did not undergo nuclear substitution, due to direct interaction of -NH- group of pyrazole (Lynch, B. M. Unpublished work.). Since some current views indicate that in the ground state of molecules with linked aromatic nuclei there is little conjugative interaction, 1-phenylpyrazole was chosen for examination, to test the prediction and study the relative reactivity of benzene and pyrazole. All the three 1-biphenylylpyrazoles (o-, m- and p-) were isolated, in addition to 1, 3-diphenylpyrazole. In some preliminary studies 1-methylpyrazole and 1-phenylpyrrole were found to be quite "reactive" towards free radical attack giving products which indicate attack by benzoyloxy radicals and not by phenyl radicals. The results of various other free radical reactions are embodied in this thesis.

Electrophilic substitutions (bromination and nitration) of 1-phenylpyrazole and 1-p-biphenylylpyrazole have also been

studied under various conditions and it has been possible to effect selective changes in the orientation of substitution. An explanation of the results is suggested. Ultraviolet and infrared spectra of various compounds prepared during this study are also discussed.

I am highly indebted to Dr. Brian M. Lynch for his helpful discussions and invaluable guidance throughout this research project. I am also grateful to him for providing a Research assistantship financed by a National Research Council Grant.

I wish to thank the Chemistry Department for a demonstratorship provided during the year 1961-1962, and Misses Dorothy A. Chalker and Joni Murphy for assistance with spectrophotometry.

In the last I owe my thanks to my parents, who have made constant personal sacrifices in connection with my education.

Misbahul Ain Khan

August 20, 1962

PART I

DISCUSSION

Section I

FREE RADICAL SUBSTITUTION IN 1-PHENYLPYRAZOLE AND RELATED COMPOUNDS

A. Introduction

Although free radical arylations of pyridine (1, 8) and quinoline (1, 2) have been examined in considerable detail, and phenylation of some diazines (3) has been reported, little quantitative work has been done on other nitrogen heterocyclic systems. This section of the thesis reports and discusses a study of the nuclear substitution of 1-phenylpyrazole by the radicals liberated by thermal decomposition of benzoyl peroxide.

Molecular orbital calculations (4) have been carried out for pyrazole, and predict the likely site of radical attack to be the 3-(5) position. However, direct observation of the phenylation of pyrazole using benzoyl peroxide is precluded, since a direct reaction involving the -NH- group of pyrazole suppresses the attack in the pyrazole ring (5). 1-Phenylpyrazole was therefore chosen for examination since, current views (6) indicate that in the ground states of molecules with linked aromatic nuclei there is little conjugative interaction. For free radical substitution processes, with typically low activation energies, there would be little electron demand in leading to increased conjugative interaction in the transition states of reactions. Thus 1-phenylpyrazole is regarded to a first

approximation as two weakly interacting nuclei, where the relative amounts of substitution in each ring may be closely related to the intrinsic reactivities of the two separate parent substances.

B. Mechanism of Formation of Products.

Decomposition of aroyl peroxides in various aromatic solvents has been studied extensively (7, 8) and various mechanisms of decomposition and arylation have been proposed explaining the formation of various reaction products (9-13). The kinetics of decomposition were studied in detail by Nozaki and Bartlett (13, 14) and Barnett and Vaughan (15). The reaction in moderately concentrated solution probably follows the course shown below, where ArH is an aromatic substrate.

$$(Ph.CO_2)_2 \longrightarrow 2\ PhCO_2\cdot$$

$$PhCO_2\cdot \longrightarrow Ph\cdot + CO_2$$

$$PhCO_2\cdot + ArH \longrightarrow (PhCO_2ArH)\cdot$$

$$(PhCO_2ArH)\cdot + PhCO_2\cdot \longrightarrow PhCO_2Ar + PhCO_2H$$

$$Ph\cdot + ArH \longrightarrow (PhArH)\cdot$$

$$(PhArH)\cdot + PhCO_2\cdot \longrightarrow PhAr + PhCO_2H$$

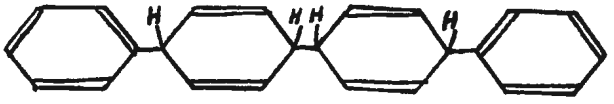
The higher polymerized products may arise from the successive dimerization and hydrogen abstraction of the intermediate radical $(PhArH)\cdot$. The formation of diaryls in the course of reaction was supposed to be due to attack of aryl radicals on the substrate forming an adduct, arylcyclohexadienyl radical, and abstraction of hydrogen from this adduct either by aryloxy

radical (16),(as shown above) or by the aroyl peroxide in an induced decomposition (17):

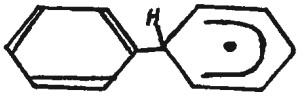
$$Ph\cdot + ArH \longrightarrow (PhArH)\cdot$$

$$(PhArH)\cdot + (PhCO_2)_2 \longrightarrow PhAr + PhCO_2H + PhCO_2\cdot$$

Though the above scheme generally holds good for the decomposition of benzoyl peroxide in concentrated solution, and explains and accounts for all the products isolated, decomposition of benzoyl peroxide in benzene in dilute solution leads to the formation of 1', 4', 1", 4"-tetrahydro-p-quaterphenyl (I) and 1, 4-dihydrobiphenyl (III) (18), in addition to the products noted above.



(I)

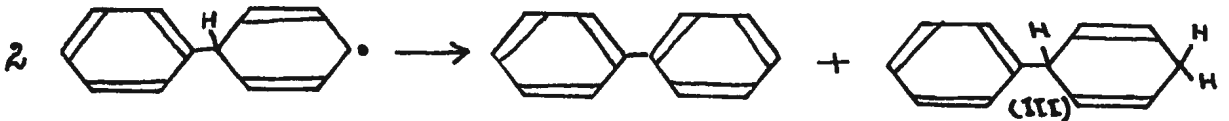


(II)

The isolation of these products from the decomposition in dilute solution confirms the presence of phenylcyclohexadienyl radical (II) as an intermediate, which by dimerization and disproportionation leads to the formation of these products.

This mechanism also explains the formation of biphenyl and quaterphenyl. The di- and tetra-hydro products during the disproportionation of the intermediate radical are dehydrogenated under the experimental conditions usually employed thus no reduced biaryls are detected. Eliel et al. (19) postulated that 1, 4-dihydrobiphenyl (III) formed by the disproportionation of the phenylcyclohexadienyl radical may give rise to further biphenyl through dehydrogenation by benzoyl peroxide.

This has now been established; 1, 4-dihydrobiphenyl is in fact



dehydrogenated to biphenyl by diaroyl peroxides (20). The process requires heat and the dehydrogenating species are thus presumably the carboxy radical ArCOO· rather than the diaroyl peroxide as such.

The various products obtained in the decomposition of benzoyl peroxide in 1-phenylpyrazole can be explained in terms of the above general scheme for the free radical substitution in aromatic substrates. Thus, the various products of reaction are formed in the following manner.

Carbon dioxide. It is generally accepted (10, 11) that carbon dioxide arises from thermal decomposition of benzoyl peroxide.

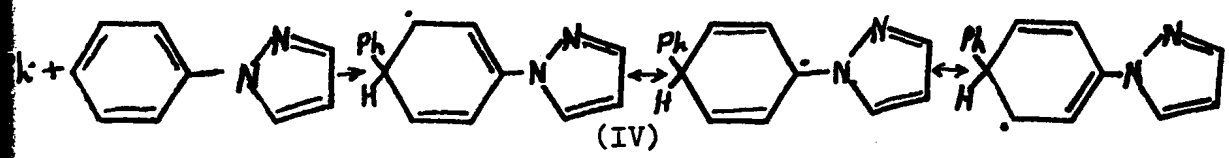
$$(PhCO_2)_2 \longrightarrow 2PhCO_2^{\bullet}$$

$$PhCO_2^{\bullet} \longrightarrow Ph^{\bullet} + CO_2$$

Phenylated pyrazoles and 1st. benzoic acid. If the attack of phenyl radical, derived from benzoyl peroxide is considered to take place in the phenyl ring of 1-phenylpyrazole, adduct (IV) will be formed in the same way as for the attack of phenyl radical on general aromatic substrates. This adduct will, in the same way, give 1-biphenylylpyrazoles, either by successive disproportionation and dehydrogenation of the adduct or by hydrogen abstraction.

$$(PhCO_2)_2 \longrightarrow 2PhCO_2^{\bullet}$$

$$PhCO_2^{\bullet} \longrightarrow Ph^{\bullet} + CO_2$$



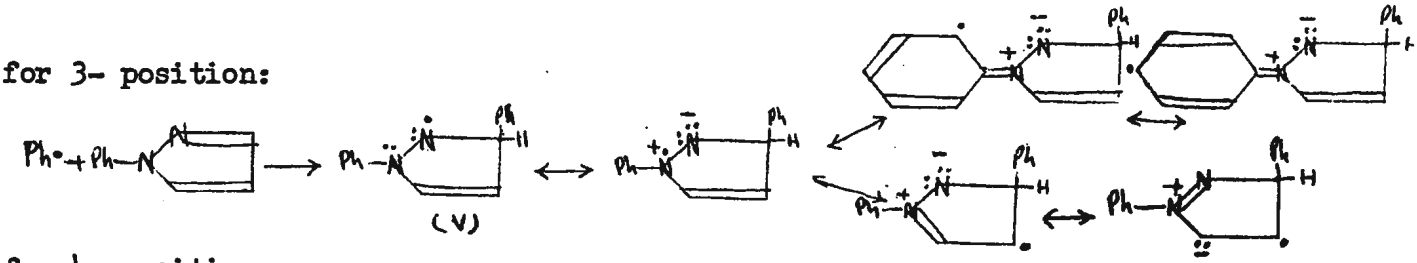
(IV)

Though in the above diagram, attack of phenyl radical has been shown to take place at the p-position, similar structures can be written for the attack at o-, and m- position. Thus all the three isomeric 1-biphenylypyrazoles (o-, m-, and p-) would be formed. The presence of all the three isomers was indicated by infrared spectra and gas-liquid chromatography. The three isomeric 1-biphenylylpyrazoles and 1,4-diphenylpyrazole were prepared from the corresponding amino-phenylpyrazoles by effecting Gomberg arylation on the diazonium salts of these amines (see exptl. page 31, 29). 1, 3- and 1,5- diphenylpyrazoles were synthesized using the standard methods (page 28, 30). 1-p-Biphenylylpyrazole was eluted first when the reaction mixture of phenylated products was subjected to adsorption chromatography on alumina. This was in agreement with the findings of Ward et al. (21, 22) that among all isomeric molecules with same number and kind of functional groups, the sequence of elution is usually the inverse order of dipole moments. The isomer ratio for the substitution in phenyl ring alone was remarkably similar to that of phenylation of anisole by free radicals (o-, 77; m-, 10; and p-, 13%) (23). The ortho isomer predominated in both the cases. The predominance of o- isomer in anisole may probably be due to + R effect of $-OCH_3$ group carrying a lone pair of electrons, which may also be the case in 1-phenylpyrazole where 1-N of 1-pyrazolyl group also carries a lone pair of electrons, which may be sufficiently

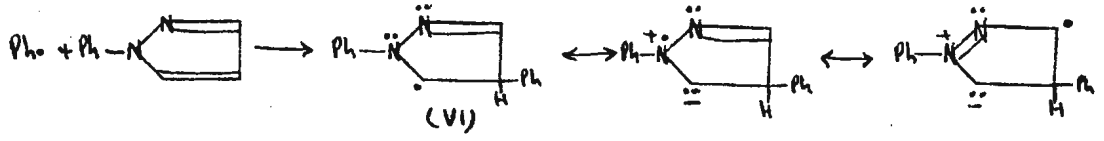
partly localized so as to give +R character to 1-pryazolyl group.

When the attack of phenyl radical takes place in the pyrazole ring, there are three possibilities i.e. at 3-, 4-, or 5- position. The attack of phenyl radical on the pyrazole ring would lead to formation of adducts (V), (VI), and (VII) for 3-, 4-, and 5- position of pyrazole ring respectively, in which resonance stabilization would occur as follows:

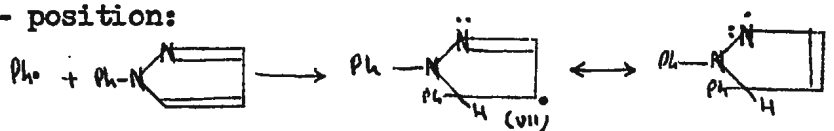
for 3- position:



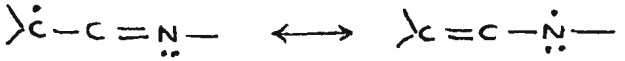
for 4- position:



for 5- position:



There are only two of the possible three resonance-structures involving delocalization of the electrons for 3- substitution, and none for 4- substitution. For attack at 3-, and 4- position, the resonance stabilization involves charge separation (as Wilmarth and Schwartz have shown that resonance stabilization of 1, 1- diphenyl-2-benzoyl hydrazyl radical involves charge separation, the bond between two charged atoms being a three electron bond (24); with the 4- position charge separation leads to a negative carbon atom so would be less significant than for the three position. If the relative resonance stabilization is assumed to control the observed orientation in the pyrazole ring, the most favoured position for the attack would be the 5- position, for in this case the electron can either be localized at 4- position or 2-, in the following manner:



furthermore there is no charge separation involved in this case. However, there was no experimental evidence for the presence of 1, 5-diphenylpyrazole, only 1, 3-diphenylpyrazole could be detected by gas-liquid chromatography. Brown's (4) predictions for the free radical attack on pyrazole ring suggest the 3-(5-) position to be most favoured, where both the positions are equivalent and therefore seem to have some predictive value for 1-phenylpyrazole; however, the preferred formation of 1, 3-diphenylpyrazole cannot be explained in terms of simple resonance theory. From the isomer ratio of the phenylated products it is interesting to note that ortho position of the phenyl ring and 3-position of pyrazole ring are equally reactive towards free radical attack.

Free benzoic acid was formed in the usual manner in the dehydrogenation of the adduct by an attack of free benzoyloxy radicals to give the stable phenylated products and benzoic acid.

Phenolic products and 2nd. benzoic acid. These were produced when benzoyloxyphenylpyrazole was hydrolyzed. Benzoyloxyphenylpyrazoles arise in the same manner as phenylated products, the attack in this case was by free benzoyloxy radicals derived from the decomposition of benzoyl peroxide. The phenols obtained from benzoyloxyphenylpyrazoles hydrolysis were methylated and the infrared absorption spectra markedly resembled those of 1-o-, and 1-p-methoxyphenylpyrazoles. Further work is necessary to evaluate accurate isomer ratios. The 2nd. benzoic acid was obtained from the same hydrolysis.

C. Free Radical Substitution in 1-Phenylpyrrole.

The main products from the decomposition of benzoyl peroxide in 1-phenylpyrrole were a benzoyloxy 1-phenylpyrrole, m.p. 70°, and benzoic acid. No evolution of carbon dioxide was detected and the stoichiometry of the reaction is largely,

$$(PhCO_2)_2 + PhC_4H_4N \longrightarrow PhCO_2\text{-}(PhC_4H_4N) + PhCO_2H$$

These results indicate that 1-phenylpyrrole is highly reactive towards free radicals since the benzoyloxylation-phenylation ratio can be used as an index of reactivity (25). The site of benzoate radical attack is almost certainly in the pyrrole ring, and probably at the 2- position (cf. 1-ethoxycarbonyl pyrrole which is phenylated at the 2- position by the standard sources of free radicals (26)). Radical attack at the 2- position is predicted by molecular orbital calulations (4). The infrared spectra of the benzoyloxy-1-phenylpyrrole shows strong carbonyl stretching absorption at 1749 cm^{-1} (KCl disk) indicating that the benzoate group is linked through its non carbonyl oxygen to a carbon atom having bonds of high order (cf. vinyl esters $>C=C-O-COR$, which shows carbonyl absorption in the region 1770-1800 cm^{-1} (27). Benzoate esters of normal phenols show absorption at lower frequencies (e.g. phenyl benzoate ν_{CO} 1735 cm^{-1} (KCl disk)).

Further supporting evidence for attack in the pyrrole ring is provided by the results of saponification of the ester. Benzoic acid and a tarry residue were obtained. The presumed hydrolysis product (1-phenyl-2-hydroxypyrrole would be expected

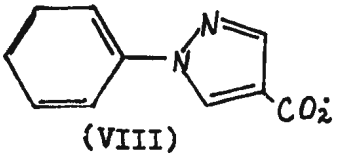
to be unstable to alkali (2-hydroxypyrrole resinifies within 24 hours on keeping (28).

It seems likely therefore that the product of benzoyloxylation of 1-phenylpyrrole is 2-benzoyloxy-1-phenylpyrrole; this system thus resembles the thiophene/benzoyl peroxide reaction where 2-thienyl benzoate is obtained (29).

Synthesis of 2-benzoyloxy-1-phenylpyrrole would offer great difficulty, and proof of structure was therefore attempted using nuclear magnetic resonance spectroscopy. However, the N. M. R. spectrum was very complex, and indicated the possibility that the substance, m. p. 70° was actually a mixture (30).

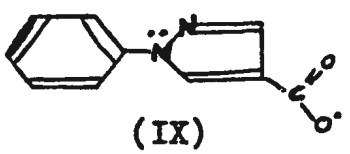
D. Decomposition of Bis (4-Carbonyl-1-Phenylpyrazole)-Peroxide in Benzene and Toluene

The behaviour of the peroxide resembles that noted for other heterocyclic peroxides (29, 31) in that no products of arylation of benzene or toluene were obtained. The high yields of 1-phenylpyrazole-4-carboxylic acid obtained (1.55 moles / mole of peroxide) indicate that the radical (VIII) tends to abstract hydrogen in preference to decarboxylating and thus effecting arylation. In confirmation, bibenzyl was readily formed on reaction of the peroxide with toluene. The presence of an ester m. p. 95-97° in the decomposition of the peroxide in benzene also indicates the nuclear attack by radical (VIII), though the ester was not isolated in significant quantities.

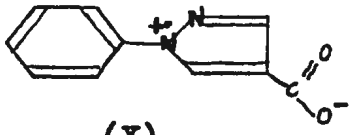


(VIII)

It has been suggested (29, 31) that aroyloxy radicals derived from heterocyclic peroxides owe their stability to a form of zwitterionic resonance, e.g. for the 1-phenylpyrazole-4-carbonyl radical (IX) and (X). This zwitterionic resonance would, however, involve the disruption of the aromatic sextet of the pyrazole ring



(IX)



(X)

B. Decomposition of Benzoyl Peroxide in 1-Methylpyrazole.

Once again, no products of nuclear phenylation were obtained, and the yields of free benzoic acids were >1 mole (1.24 mole/mole of benzoyl peroxide). Low yields of material showing strong infrared absorptions at 1740 and 1770 cm^{-1} (ester ν_{CO}) and bands at 700, and 760 and 800^{-1} (benzoate groups) were obtained. These results indicate that 1-methylpyrazole is benzoyloxylated by benzoyl peroxide and can be therefore classified as a "reactive" substrate, however a more detailed study of the reaction is obviously necessary.

Reaction of benzoyl peroxide with 2-phenyl - 1, 2, 3,-2H triazole has also been studied by Lynch (5), and a benzoyloxylated product isolated. Thus 2-phenyl,-1, 2, 3,-2H triazole can also be classified as a "reactive substrate" in the same way as 1-methylpyrazole and 1-phenylpyrrole.

Section II

NITRATION AND BROMINATION

A. Introduction

The electrophilic substitution reactions of 1-phenylpyrazole (I) have been reviewed in standard treatises (32, 33, 34). Two patterns appear to be followed: attack occurs prefefentially in the 4-position of the pyrazole ring, or in the para position of the phenyl ring. Disubstitution occurs readily, so that apparently the two positions do not differ greatly in reactivity.

(I)

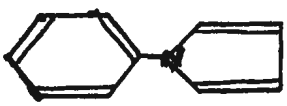
Thus, bromination in inert solvents yields 4-bromo-1-phenylpyrazole and then 4-bromo-1-p-bromophenylpyrazole (35, 36); 3-methyl-1-phenylpyrazole reacts similarly (37). Chlorination follows a similar course (38), while chloromethylation yields 4-chloromethyl-1-phenylpyrazole (39), and formylation with dimethylformamide-$POCl_3$ yields 4-formyl-1-phenylpyrazole (40). Mercuration using mercuric acetate gives 4-acetoxymercuri-1-phenylpyrazole (39), which reacts with lead thiocyanate to give 1-phenyl-4-thiocyanopyrazole. Friedel-Crafts (41), 42) or thermal acylations give 4-aroyl-1-phenylpyrazoles (43).

However, nitration of 1-phenylpyrazole with mixed acids introduces the first nitro group into the benzene ring (44-46); Finar and Hurlock (47) have clarified the course of these reactions, and have shown that the initial product at 0° is 1-p-nitrophenylpyrazole although further substitution occurs readily

to yield 4-nitro-1-p-nitrophenylpyrazole; at 100°, 1-(2, 4-dinitrophenyl)-4-nitropyrazole is formed. Nitration of 4-bromo-3-methyl-1-phenylpyrazole (37) and 5-chloro-3-methyl-1-phenylpyrazole (46) similarly results in attack at the para-position of the phenyl group. Sulphonation of 3-methyl-1-phenyl-5-pyrazolone similarly introduces the substituent into the para-position of the phenyl group (48).

The orientation of nitration can be varied, however; Dal Monte et al (49) report that 1-phenylpyrazole gives 4-nitro-1-phenylpyrazole with nitric acid in acetic anhydride below 5°, although no yields were reported. This behaviour resembles that noted with 1-phenylpyrrole(II) (50).

In the present work, brominations and nitrations of 1-phenylpyrazole have been studied under varying conditions, and it has proved possible to effect selective substitution in either the phenyl group or the pyrazole nucleus, An explanation of the results is suggested, and the selective conditions should be generally applicable to substitution in phenylazoles. In an extension of this work, the structures of the bromination and nitration products of 1-p-biphenylylpyrazole (III) were established.



(II)

(III)

Ultraviolet and infrared absorption spectra of the various compounds are of considerable assistance in establishing and assigning structures, and certain features of these are discussed.

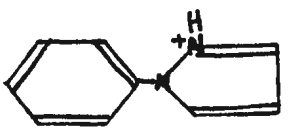
B. Nitration and Bromination of 1-Phenylpyrazole.

The behaviour of 1-phenylpyrazole on nitration in different solvents could be ascribed to differing selectivity of the attacking reagents employed for nitration. In nitric acid/sulphuric acid, nitronium ion (NO_2^+) is the attacking entity (51), while it appears that protonated acetyl nitrate ($CH_3CO.O\overset{+}{H}NO_2$ or $CH_3C(\overset{+}{O}H)ONO_2$) is the reactive species in solution of nitric acid in acetic anhydride (52). Similarly, in bromination, molecular bromine leads to substitution at the 4-position while bromination in sulphuric acid in the presence of silver sulphate (so called positive bromine) leads to substitution in the p- position in 1-phenylpyrazole (see exptl. page 51). Here too, the difference in orientation could be due to different selectivity of reagents. However the electron densities at the 4-position and at the p-position in 1-phenylpyrazole apparently do not differ greatly and are both electron deficient with respect to a benzene ring (relevant pKa values (@ 25° in water): 4-amino-1-phenylpyrazole cation, 3.22±0.05; 1-p-aminophenylpyrazole cation, 3.42±0.20; anilinium ion, 4.58; (@ 25° in 1:1 ethanol/water) 1-phenylpyrazole -4-carboxylic acid, 5.22 ± 0.03; p-1-pyrazolyl benzoic acid, 5.32 ± 0.03; and benzoic acid, 5.67 (53). This is consistent with the facts that further substitution occurs readily both in nitration (47) and bromination (see exptl. page 51).

Since no conjugative interaction involving electron transfer from a phenyl substituent can be written for 1-phenylpyrazole, this compound can therefore be regarded as a pyrazole

substituted by a -I substituent at the 1-position. Brown's (4) calculations of localization energies for attack by an electrophilic reagent at various positions in pyrazole ring predict that the 4-position is the most reactive; furthermore the localization energy at 4-position is lower than any position in benzene or biphenyl. The relevant values are: benzene, -2.54β; 4-biphenyl, -2.44β; pyrazole, h=0.5, approx.-2.1β; h = 2.0, approx.-2.4β.(h is relative electronegativity parameter). The -I effect of the phenyl group would not be expected to alter the values markedly.

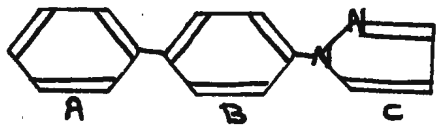
However, the behaviour of 1-phenylpyrazole (I) on nitration with nitric acid/sulphuric acid and bromination in sulphuric acid in the presence of silver sulphate, when substitution takes place on the p-position of phenyl ring can not be explained by localization energy calculations alone. The varying orientation in nitration and bromination under different conditions thus resemble that noted with 1-phenylpyrrole (50). It is very likely that the difference in orientation in strongly acidic medium results from protonation of 1-phenylpyrazole to yield the conjugate acid (IV), in which the pyrazole ring would be deactivated towards electrophilic attack. It is most likely that similar kind of change in orientation can be effected in other aryl azoles and similar behaviour would be expected in the chlorination and iodination of 1-phenylpyrazole as well as other arylazoles.



(IV)

C. Nitration and Bromination of 1-p- Biphenylylpyrazole.

Prediction of the orientation of electrophilic substitution in 1-p-biphenylylpyrazole (V) is not straightforward, the 1-pyrazolyl group could act as a -I, +R deactivating substituent, leading to ortho-, para- substitution in ring (A), similarly to 4-fluorobiphenyl (54); or as an activating substituent of the same type, leading to substitution in the central ring (B) (cf. 4-acetamidobiphenyl (55-58), or substitution in the pyrazole ring (C) may still predominate, as for the attack of electrophils on the neutral molecule of 1-phenylpyrazole.



(V)

Following the same reasoning as for 1-phenylpyrazole, the 4-position of the pyrazole ring (C in IV) will be the most likely site of attack by electrophilic reagents, as the localization energy at the 4-position of pyrazole is less than that of any position in biphenyl. This was in agreement with experiment. Bromination by molecular bromine and nitration by nitric acid in acetic anhydride led to the formation of 4-substituted 1-p-biphenylylpyrazoles. Although the structure was not proved the product of molecular bromination of 1-o-biphenylylpyrazole also indicated the substitution in the 4-position of pyrazole ring. The product obtained from this bromination was found to be identical (infrared and ultraviolet spectra) with one of the products

formed in the decomposition of benzoyl peroxide in 4-bromo-1-phenylpyrazole.

The structure of the monobromo compound obtained in the molecular bromination of 1-p-biphenylylpyrazole was established by an unambiguous synthesis using the route 4-bromo-1-phenylpyrazole ⟶ 4-bromo-1-p-nitrophenylpyrazole ⟶ 1-p-aminophenyl-4-bromopyrazole ⟶ 1-p-biphenylyl-4-bromophenylpyrazole. The product of bromination of 1-p-biphenylylpyrazole was identical with 1-p-biphenylyl-4-bromopyrazole, obtained as above (mixed m.p., ultraviolet and infrared spectra). This compound was also found to be identical with 1-p-biphenylyl-4-bromopyrazole isolated from the decomposition of benzoyl peroxide in 4-bromo -1-phenylpyrazole. 4-Bromo-4'-(1-pyrazolyl)-biphenyl was obtained from the decomposition reaction of bis(-p-bromo benzoyl) peroxide in 1-phenylpyrazole and was found to be different from the bromination product of 1-p-biphenylylpyrazole (mixed m.p., infrared absorption spectrum showed the absence of a pair of strong bands at ca. 690 and 760 cm^{-1}, which are characteristic of an unsubstituted phenyl ring in 1-phenylpyrazole series, but these were present in the bromination product of 1-p-biphenylylpyrazole).

An attempt was made to brominate 1-p-biphenylylpyrazole in sulphuric acid in the presence of silver sulphate, but a syrupy liquid resulted. This can also be explained if the protonation of pyrazole ring (C) directs attack at biphenyl ring giving a mixture of products.

Bromination of p-di-(1-pyrazolyl)-benzene by bromine in chloroform gave a dibromo product, presumably p-di-(4-bromo-1-pyrazolyl) -benzene.

Nitration of 1-p-biphenylylpyrazole with nitric acid in acetic anhydride gave a mononitro product which is probably 4-nitro-p-biphenylylpyrazole, while nitration with nitric acid/sulphuric acid leads to a mixture of products and polysubstitution from which no single substance could be isolated. The structure of the product obtained from nitric acid/acetic anhydride nitration of 1-p-biphenylylpyrazole (assumed to be 4-substituted) is based on the analogies between the ultraviolet and infrared spectra of the product and of 4-nitro-1-phenylpyrazole.

Similarly p-di-(1-pyrazolyl)-benzene on nitration with nitric acid in acetic anhydride gives a mononitro product (presumably 1-(1-pyrazolyl), 4-(4-nitro-1-pyrazolyl)-benzene). The structure of this product can also be deduced from the infrared studies of this product.

D. Assignment of Structure from Infrared and Ultraviolet Spectra of Nitroarylpyrazoles: the Nitration Product of 1-p-Biphenylylpyrazole in Acetic Anhydride:

The positions of the N-O stretching frequencies, in conjunction with the presence of strong bands at ca. 690 and 760 $cm.^{-1}$ as observed with monosubstituted benzenes (27 Page 77), can be used to characterize the various nitrophenylypyrazoles, and thence to indicate that the structure of the mononitration

product obtained from the nitric acid/acetic anhydride nitration of 1-p-biphenylylpyrazole is 1-p-biphenylyl-4-nitropyrazole. The relevant bands in the infrared spectra are summarized in the Table.

Compound	Absorption between 650-900 cm.$^{-1}$ *	ν_{N-O} sym * cm.$^{-1}$	ν_{N-O} asym * cm.$^{-1}$
1-o-nitrophenylpyrazole	750, 754, 760	1371	1545
1-m-nitrophenylpyrazole	738, 762	1355	1535
1-p-nitrophenylpyrazole	765, 852	1341	1527
4-nitro-1-phenylpyrazole	690, 751, 770, 820	1325	1545
1-(2, 4-dinitrophenyl) Pyrazole	740, 780, 832	1345	1530 1545 1555
4-bromo-1-p-nitrophenyl-pyrazole	750, 855	1340	1527
mononitration product of 1-p-biphenylylpyrazole	692, 748 765, 820	1325	1541
mononitration product of p-di(1-pyrazolyl)benzene	748, 818 832	1324	1542

* All strong bands.

Similarly, the ultraviolet spectra of the various nitrophenyl-pyrazoles are characteristic; 4-nitro-1-phenylpyrazole is the only isomer having two absorption maxima of approximately equal intensity above 220 mμ.

The presumed 1-p-biphenylyl-4-nitropyrazole also exhibits two maxima, displaced bathochromically ca. 30 mμ. The results are shown in the Table:

ULTRAVIOLET ABSORPTION SPECTRA OF NITROPHENYLPYRAZOLES

Solvent: 95% ethanol

Compound	λmax. (mμ)	log ε
1-phenylpyrazole	252	4.13
1-o-nitrophenylpyrazole	238, 300	4.18, 3.27
1-m-nitrophenylpyrazole	250	3.88
1-p-nitrophenylpyrazole	318*	4.29
4-nitro-1-phenylpyrazole	228, 295	4.11, 4.07
4-bromo-1-p-nitrophenyl-pyrazole	315	4.21
1-p-biphenylylpyrazole	280	4.50
mononitration product of 1-p-biphenylylpyrazole	265, 315	4.06, 4.08

* in chloroform solution.

Section III

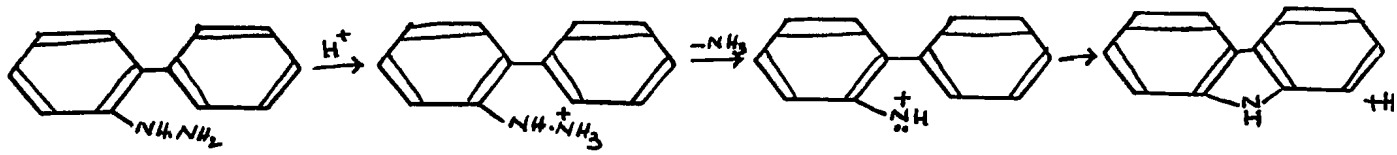
FORMATION OF CARBAZOLE AND BIPHENYL IN CYCLIZATION OF 2-HYDRAZINOBIPHENYL

While attempting to cyclize 2-hydrazinobiphenyl with 1, 1, 3, 3-tetramethoxypropane in the presence of concentrated hydrochloric acid and ethanol, expected 1-o-biphenylylpyrazole was not obtained but instead carbazole and biphenyl were isolated in fair yield. In a similar manner, from 3-hydrazinobiphenylcyclization biphenyl was isolated as a by-product of the reaction.

Carbazoles have been prepared by Fischer Indole synthesis and other processes such as from 2, 2'-diaminobiphenyl, 2-azidobiphenyl, and o-aminophenylenediamine etc. (59). but there seems to be no reference of formation of carbazole through 2-hydrazinobiphenyl. A possible route for the formation of carbazole from 2-hydrazinobiphenyl is suggested below.

It has recently been reported (60) that carbazole is formed in 76% yield when deoxygenation of 2-nitrosobiphenyl by triethyl phosphite is carried out. The formation of carbazole involves an azene radical analogous to that formed during the decomposition of 2-azidobiphenyl (61). In the course of present work the reactions were carried out in the presence of concentrated hydrochloric acid which may protonate the nitrogen, which under the experimental conditions (on heating) will evolve ammonia leaving behind an electron deficient nitrogen $-\overset{+}{N}H$ which

presumably attacks o-position of the other phenyl ring to give carbazole.



The formation of biphenyl is not readily explained and further work is necessary to elucidate the process by which it arises.

REFERENCES

(1) Pausacker, K. H.: Australian J. Chem. 11, 200 (1958).

(2) Hey, D. H. and Walker, E. W.: J. Chem. Soc. 1948, 2213

(3) Atkinson, C. M. and Sharpe, C. J.: J. Chem. Soc. 1959, 3040.

(4) Brown, R. D.: Australian J. Chem. 8, 100 (1955).

(5) Lynch, B. M.: Unpublished results.

(6) Dewar, M. J. S. and Schmeising, H. N.: Tetrahedron. 5, 166 (1959).

(7) Dermer, O. C. and Edmison, M. T.: Chem. Rev. 57, 77 (1957).

(8) Augood, D. R. and Williams, G. H.: Chem. Rev. 57, 123 (1957).

(9) Hey, D. H. and Waters, W. A.: Chem. Rev. 21, 169 (1937).

(10) Waters, W. A.: "The Chemistry of Free Radicals." Oxford. (1946).

(11) Dewar, M. J. S.: "The Electronic Theory of Organic Chemistry." Oxford. (1949).

(12) Walling, C.: "Free Radicals in Solution." Wiley. New York. (1957).

(13) Bartlett, P. D. and Nozaki, K.: J. Am. Chem. Soc. 68, 2299 (1947)

(14) Nozaki, K. and Bartlett, P.D.: J. Am. Chem. Soc. 68, 1686 (1946).

(15) Barnett, B. and Vaughan, W. E.: J. Phys. Chem. 51, 926 (1947).

(16) Szwarc, M.:Discussions. Faraday Soc. 14, 251 (1953).

(17) Pausacker, K. H.: Australian J. Chem. 10, 49 (1957).

(18) DeTar, D. F., and Long, R. A. J.: J. Am. Chem. Soc. 80, 4742 (1958).

(19) Eliel, E. L., Meyerson, S., Welvart, Z. and Wilen, S. H.: J. Am. Chem. Soc. 82, 2936 (1960).

(20) Eliel, E. L. and Eberhardt, M.: J. Org. Chem. 27, 2289 (1962).

(21) Ward, E. R. and Poesche, W. H.: J. Chem. Soc. 1961, 2825.

(22) Ward, E. R., Poesche, W. H., Higgins, D. and Heard, D. D.: J. Chem. Soc. 1962, 2374.

(23) Lynch, B. M. and Moore, R. B.: Can. J. Chem. 40, 1461 (1962).

(24) Wilmarth, W. K. and Schwartz, N.: J. Am. Chem. Soc. 77, 4543; 4551 (1955).

(25) Lynch, B. M. and Pausacker, K. H.: Australian J. Chem. 10, 165 (1957).

(26) Rinkes, I. J.: Rec. Trav. Chim. 62, 116 (1943). Chem. Abstracts. 38, 1741 (1944).

(27) Bellamy, L. J. "The Infrared Spectra of Complex Molecules." Methuen. London (1958).

(28) Grob, C. A. and Ankli, P.: Helv. Chim. Acta. 32, 2010, 2023 (1949).

(29) Ford, M. C. and Mackay, D.: J. Chem. Soc. 1957, 4620.

(30) Stothers, J. B.: Personal Communication.

(31) Ford, M. C. and Mackay, D.: J. Chem. Soc. 1958, 1290.

(32) Elderfield, R. C. ed.: "Heterocyclic Compounds." Vol. V Wiley. New York. (1957).

(33) Rodd, E. H.: "The Chemistry of Carbon Compounds." Vol. IVA. Elseviers. London. (1957).

(34) Gilman, H. ed.: "Organic Chemistry an Advanced Treatise," Vol. IV. Wiley. New York. (1953).

(35) Balbiano, L.: Gazz. Chim. Ital. 19, 128 (1889).

(36) Brain, E. G. and Finar, I. L.: J. Chem. Soc. 1958, 2435.

(37) Finar, I. L. and Miller, B. D.: J. Chem. Soc. 1961, 2769.

(38) Severini.: Gazz. Chim. Ital. 23, I, 284 (1893).

(39) Finar, I. L. and Godfrey, K. E.: J. Chem. Soc. 1954, 2293.

(40) Finar, I. L. and Lord, G. H.: J. Chem. Soc. 1957, 3314.

(41) Michaelis, A. and Rojahn, C. A.:Ber., 50, 737 (1917).

(42) Rojahn, C. A.: Ber. 55, 291 (1922).

(43) Balbiano, L.: Gazz. Chim. Ital. 19, 134 (1889).

(44) Knorr, L. et al.: Ber. 23, 172 (1889); Ann. 279, 217 (1894).

(45) Auwers, V. K. and Mauss, H.: J. Prakt. Chem. (2), 117, 311 (1927).

(46) Michaelis, A. et al.: Ber. 33, 2595, 2607, 2615 (1900); 34, 1300 (1901); Ann. 378, 293 (1910).

(47) Finar, I. L. and Hurlock, R. J.: J. Chem. Soc. 1957, 3024.

(48) Möllenhoff.: Ber. 25, 1941 (1892).

(49) DalMonte, D., Mangini, A. and Passerini, R.: Gazz. Chim. Ital. 86, 797 (1956).

(50) Dhont, J. and Wibaut, J. P.: Rec. Trav. Chim. 62, 177 (1943). Chem. Abstracts. 38, 2336 (1944).

(51) Ingold, C. K.: "Structure and Mechanism in Organic Chemistry." Cornell. Ithaca (1953).

(52) Bordwell, F. G. and Garbisch, E. W.: J. Am. Chem. Soc. 82, 3588 (1960).

(53) Case, J. R., Price, R., Ray, N. H., Roberts, H. L. and Wright, J.: J. Chem. Soc. 1962, 2107.

(54) Vanhore, T.: Bull. Acad. Belgl Ci. Sci. (5), 8, 505 (1922).

(55) Blakey, W. and Scarborough, H. A.: J. Chem. Soc. 1927, 3000.

(56) Grieve, W. S. M. and Hey, D. H.: J. Chem. Soc. 1933, 968.

(57) Scarborough, H. A. and Waters, W. A.: J.Chem. Soc. 1927, 89, 1133.

(58) Bell, F.: J. Chem. Soc. 1928, 2770.

(59) Elderfield, R. C. ed. "Heterocyclic Compounds." Vol. 3. P. 291. Wiley. New York. (1952).

(60) Bunyan, P. J., and Cadogan, J. I. G.: Proc. Chem. Soc. 1962, 78.

(61) Smolinsky, G.: J. Am. Chem. Soc. 82, 4717 (1960); 83, 2489 (1961). J. Org. Chem. 26, 4108 (1961).

PART II

EXPERIMENTAL

EXPERIMENTAL

General

Analyses are by the Schwarzkopf Microanalytical Laboratory, Woodside, N. Y., U. S. A.

Melting points were observed using a Fisher-Johns melting point block, and are uncorrected.

Infrared spectra were recorded for the 650-2150 $cm.^{-1}$ region using a Unicam SP 100 Spectrophotometer equipped with an SP 130 grating accessory; solid samples were examined using the potassium chloride disk technique, and liquids as capillary films between potassium chloride plates.

Ultraviolet spectra were recorded in 95% ethanol using a Beckman DK-2A Ratio-recording Spectrophotometer.

Gas-liquid partition chromatographic analyses were made using a Beckman GC-2A Gas Chromatograph.

Alumina (80-200 mesh; Fisher Scientific Company) was used for adsorption chromatography.

Potentiometric determinations of dissociation constants were made by using a Beckman Zeromatic pH Meter.

Section I

REFERENCE COMPOUNDS

A. 1-Substituted-Phenylpyrazoles by Cyclization:

Certain 1-substituted-phenylpyrazoles were prepared using the method recommended for 1-phenylpyrazole by Finar and Hurlock (1). In each case an equimolar mixture of 1, 1, 3, 3, tetramethoxypropane (Matheson, Coleman, & Bell) and the appropriate substituted hydrazine hydrochloride was heated under reflux in dilute solution in ethanol (2hr.). The ethanol was removed under reduced pressure, and the residue taken up in water and neutralized with sodium carbonate. The reaction mixture was filtered to remove precipitated sodium chloride, and residue and filtrate were thoroughly extracted with ether. The ether extract was dried (Na_2SO_4), the ether was removed, and the residue was distilled.

In the preparations of the isomeric 1-nitrophenylpyrazoles, and of 1-p-tolylpyrazole and 1-p-carboxypyrazole, the reaction mixtures were poured onto ice after completion of heating, and the crude products thus obtained were crystallized from 95% ethanol. The following pyrazoles were obtained:
(Conc. HCl was used only in sufficient amount to convert the hydrazine into hydrochloride and a slight excess of HCl was present in all cyclizations.)

1-Substituent	m.p./b.p.*		Yield (%)[c]	Reference
[Methyl	127°	(127°)	20	(1)]
Phenyl	246°	(107°/7mm.)	78	(1a)
	90°/2mm.	n_D^{25} 1.5957	-	
p-Bromophenyl[a]	70°		70	
p-carboxyphenyl	268°		-	
2, 4-Dinitrophenyl	107°	(109-110)	-	(1)
o-Methoxyphenyl[b]	280°-282°	n_D^{25} 1.58826	-	
o-Nitrophenyl	88-89°	(88-89°)	-	(1)
m-Nitrophenyl	74-75°	(94-95°)	-	(1)
	and 94-95° (polymorphic forms)			
p-Nitrophenyl	169-170°	(169-170°)	-	(1)
p-Tolyl	32-33°	(32-33°)	-	(1a)
	258°			

a. Analysis: Calculated for $C_9H_7N_2Br$ - C, 48.45; H, 3.16%. Found: C, 48.70; H, 3.34%.

b. Analysis: Calculated for $C_{10}H_{10}N_2O$ - C, 68.95; H, 5.79%. Found: C, 69.15; 5.98%.

c. Yields not recorded were nearly theoretical.

* Boiling points are underlined. Literature values are in parentheses.

B. Diphenylpyrazoles:

a. 1, 3-Diphenylpyrazole. Claisen and Fischer's method (2) was found to give 1, 3-diphenylpyrazole. The sodium salt of hydroxymethylene-acetophenone was prepared by reaction of ethyl

formate (112 g.) with acetophenone (120 g.) in ethanolic sodium ethoxide. 108 G. of sodium salt (63%) was collected by filtration.

A portion (20 g.) of the sodium salt was suspended in ether (200 ml.), and hydroxymethylene acetophenone was liberated by acidification with 6N sulphuric acid.

Phenylhydrazine (12.7 g.) was added to the ethereal solution and the mixture heated under reflux (2 hr.). The ether was removed under reduced pressure and the residue vacuum-distilled. The hydrazone was removed at 200°/30 mm., and the residue was crystallized from ethanol giving 1, 3-diphenylpyrazole, m.p. 85° (lit. 84-85°(3)). (Ultraviolet absorption: λ max:280 mμ, 285 mμ; logϵ, 4.36, 4.34 also infrared absorption. See Table Page 38). Although Claisen and Fischer obtained 1, 5-diphenylpyrazole by distillation of the hydrazone at 330° at normal pressure, this isomer was not obtained under the conditions used in the present work.

b. 1, 4-Diphenylpyrazole. 4-Nitro-1-phenylpyrazole (10 g.) (from nitration of 1-phenylpyrazole in acetic anhydride, see page 48) was reduced using tin and hydrochloric acid, yielding 4-amino-1-phenylpyrazole (8.0 g., 95%, m.p. 104-105° (lit. 104-105° (4). The amine was diazotized, and the diazonium salt solution was stirred with benzene at 0°, after buffering to pH5 with sodium acetate (5). The mixture was allowed to reach room temperature and the organic layer was chromatographed on alumina. Evaporation

of the eluate, followed by crystallization of the residure from ethanol, gave 1, 4-diphenylpyrazole (3.5 g., 32%), m.p. 97° (lit, 97° (6). Analyses: Calculated for $C_{15}H_{12}N_2$: C, 81.80; H, 5.50%. Found: C, 81.72; H, 5.50%. Ultraviolet absorption: λ max.: 262 mμ; logξ, 4.28.

c. 1, 5-Diphenylpyrazole. Panizzi and Monti's method (7) was used. To an aqueous solution of the sodium salt of hydroxymethyleneacetophenone (34 g.), aniline acetate (31 g.) was added with stirring. The yellow precipitate was collected, giving the anil m.p. 143° (lit. 140-141°(7) (34.8 g., 78%).

The anil (30 g.), 10N hydrochloric acid (15 ml.), phenylhydrazine (17.4 g.) and ethanol (400 ml.) were heated under reflux (2 hr.). The ethanol was evaporated and the residue diluted with water, acidified to pH3, and extracted with ether. Evaporation of the ether extract yielded an oil, which on distillation at 205-210°/ca 30 mm., solidified to give 1, 5-diphenylpyrazole (10g., 38.3%), m.p. 50°, raised to 55° (lit. 55-56° (8) by crystallization from 1:1 ethanol/water. Ultraviolet absorption: λ max., 240 mμ; logξ, 4.18.

C. 1-Biphenylylpyrazoles.

Two routes were employed in preparing these compounds: (a) Gomberg arylation of benzene using the diazo-compound derived from the 1-aminophenylpyrazoles, and (b) cyclization using the hydrazinobiphenyls and 1, 1, 3, 3-tetramethoxypropane.

Method (a). The various 1-aminophenylpyrazoles were obtained by reduction of the 1-nitrophenylpyrazoles by tin and hydrochloric acid. The amines were diazotized, and the diazo solutions were stirred with excess of benzene at 0°, after buffering to $pH5$ with sodium acetate, and allowed to reach room temperature. After 3 hr., evolution of nitrogen ceased, and the benzene layers were separated and chromatographed on alumina. After evaporation of benzene, the products were isolated by crystallization (para-isomer) or distillation.

The following 1-biphenylpyrazoles were obtained:

1-Substituent	M.p./b.p.*	Yield (%)	Analyses: Found# C	H	N
o-Biphenylyl-	332-334°	33.3	-	-	13.23
m-Biphenylyl-	330-332°	-	81.84	5.72	-
	n_D^{25} 1.65035				
p-Biphenylyl-	125-126°	53	82.00	5.55	13.00

* B.p's are underlined.

$C_{15}H_{12}N_2$ requires: C, 81.80; H, 5.50; N, 12.72%.

ULTRAVIOLET ABSORPTION

1-Substituent	λmax (mμ)	log ε
o-Biphenylyl-	233	4.35
m-Biphenylyl-	250	4.38
p-Biphenylyl-	280	4.50

Method (b): The appropriate aminobiphenyls were diazotized and reduced to the corresponding hydrazinobiphenyls using stannous chloride (9). The hydrazines were then condensed with 1, 1, 3, 3-tetramethoxypropane and worked up in the usual manner (cf. page 27). The meta- and para-hydrazinobiphenyls smoothly gave fairly good yields of the corresponding 1-biphenylylpyrazoles, identical with the products obtained from the Gomberg reactions (cf. above); biphenyl was isolated from the cyclization of m-hydrazinobiphenyl.

However, the reaction with o-hydrazinobiphenyl gave biphenyl and carbazole as the only products. (Identified by m.p.s, mixed m.p.s and IR. and UV. spectra).

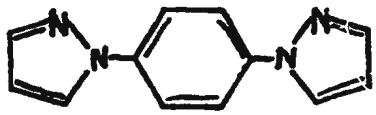
D. 1-p-Methoxyphenylpyrazole.

1-p-Methoxyphenylpyrazole was prepared as follows: 1-p-aminophenylpyrazole (8.5 g. obtained from 1-p-nitrophenylpyrazole by reduction with tin and hydrochloric acid) was diazotized in the usual manner (10). After the diazotization was complete the diazonium salt solution was boiled with excess of water until evolution of nitrogen ceased (3 hr.), 1-p-hydroxyphenylpyrazole (4.1 g., 48.2%) was obtained by standard methods. A portion of hydroxy compound was methylated with dimethyl sulphate and alkali, yielding 1-p-methoxyphenylpyrazole (18.4%), m.p. 33-35°. (Lit. b.p. 138-142° (14).

E. p-Di-(1-pyrazolyl)-benzene.

1-p-aminophenylpyrazole (20 g., from 1-p-nitrophenylpy-

razole) was converted into the corresponding hydrazine, m. p. 83° (17.3 g., 79%) by stannous chloride reduction of the diazonium compound (cf. page 32). 1-p-Hydrazinophenylpyrazole (15 g.) was then condensed with 1, 1, 3, 3-tetramethoxypropane in the usual manner. The product was collected and crystallized from ethanol, giving yellow-orange plates (8.8 g., 50%) of p-di-(1-pyrazolyl)-benzene, (I) m. p. 180-182°. Analysis: Calculated for $C_{12}H_{10}N_4$: C, 68.55; H, 4.79; N, 26.65%. Found: C, 68.76; H, 4.83; N, 26.51. Ultraviolet absorption: λ max. 283 mμ ; log ε 4.37.



(I)

E. Phenylpyrazole Carboxylic Acids and Derivatives.

(a) 1-Phenylpyrazole-4-Carboxylic acid. This compound was prepared from 4-formyl-1-phenylpyrazole (11) by oxidation with alkaline potassium permanganate. The acid obtained had m. p. 220° (lit. 221-222° (11). Analysis: Calculated for $C_{10}H_8N_2O_2$: C, 63.82; H, 4.28%. Found: C, 63.98; H, 4.55%. pKa in 1:1 ethanol/water at 25°: 5.22 ± 0.03.

(b) 1-p-Carboxyphenylpyrazole. This compound was also prepared by alkaline permanganate oxidation of 1-p--tolylpyrazole (see page 28), when the acid, m.p. 268-270° (decomp.) was obtained. Analysis: Calculated for $C_{10}H_8N_2O_2$: C, 63.82; H, 4.28%. Found: C, 63.82; H, 4.47%. pKa in 1:1 ethanol/water at 25°: 5.32 ± 0.03.

(c) Bis-(1-phenylpyrazole-4-carbonyl)-peroxide. The method recommended by Vogel (10) was used. 1-phenylpyrazole-4-carboxylic acid (20 g.) was converted into the acid chloride by thionyl chloride, and reacted with alkaline "30-volume" hydrogen peroxide at 5°. The precipitate was collected and dried, and reprecipitated from solution in chloroform using ice cold methanol. The peroxide (14.7 g. 74%) had m.p. 136-138° (decomp.), infrared absorption due to ν_{CO} 1768 cm.$^{-1}$.

(d) 4-ethoxycarbonyl-1-phenylpyrazole. This compound, m.p. 79-80°, was prepared from 1-phenylpyrazole-4-carbonyl chloride by a standard procedure (9).

Section II

REACTIONS OF AROYL PEROXIDES WITH HETEROCYCLIC SUBSTRATES

General Procedure.

The general procedure adopted was that used by Lynch and Pausacker (12), with slight modifications in some cases. The appropriate peroxide was heated in different substrates at a temperature of ca. 80° for ⩽50 hr. The reactions were carried out in a round bottomed finger flask fitted with an efficient water condenser. After reaction was complete, the reaction mixture was allowed to cool to room temperature and diluted with benzene. The benzene solution was extracted thoroughly with saturated sodium hydrogen carbonate solution. The extract was acidified with 6N hydrochloric acid and extracted with ether; the ether extract was dried (Na_2SO_4), filtered and the ether distilled off yielding benzoic acid (referred to as 1st. Benzoic acid). Benzene and excess of substrate were removed under reduced pressure from the benzene solution, and the residue was heated under reflux overnight with 10% sodium hydroxide in ethanol (100 ml.). Ethanol was removed under reduced pressure and the residue was extracted with ether and with water. The ethereal layer was reserved (extract A), and the aqueous layer was acidified with 6N hydrochloric acid and extracted with ether (extract B). Phenols and an additional quantity of benzoic acid (referred to as 2nd. benzoic acid) were obtained from the extract by standard methods. Extract (A) was dried (Na_2SO_4) and the

ether removed. The residue consisted of arylated products from the decomposition of the peroxides in different substrates.

A number of aroyl peroxides were decomposed in various substrates and the reaction mixtures obtained were worked up as described above. The results of these reactions are in the following pages:

A. Decomposition of Benzoyl Peroxide in 1-Phenylpyrazole.

Benzoyl peroxide was allowed to decompose in 1-phenylpyrazole at 80°. The reaction mixtures were worked up as described above. The following results were obtained:

(The values in parentheses correspond to molar quantities.)

Experiment No.		1	2	3
Benzoyl peroxide	(g.)	20.0	20.0	16.0
1-Phenylpyrazole	(g.)	100.0	100.0	80.0
Reaction time	(hr.)	94	137	140
1st. Benzoic acid	(g.)	10.4 (1.03)	10.8 (1.06)	7.4 0.92
2nd. Benzoic acid	(g.)	2.3 (0.23)	2.2 (0.22)	1.2 (0.15)
Phenols	(g.)	1.5 (0.11)	1.6 (0.12)	1.10 (0.10)
Phenylated products	(g.)	8.1 (0.45)	8.1 (0.45)	6.85 (0.47)
1-p-Biphenylylpyrazole isolated	(g.)	-	0.70	0.65

In separate experiments, benzoyl peroxide (10.0 g.) was

allowed to decompose in 1-phenylpyrazole (100.0 g.) at 84°. Carbon dioxide evolved (610 ml.) was collected in a gas burette at 758 mm pressure and 26°. This was equivalent to 1.10 g., CO_2. (0.61 mole/mole peroxide).

(a) Infrared examination of phenylation products: The infrared absorption spectra of the six possible phenylation products of 1-phenylpyrazole were recorded. The bands in the 650-1650 $cm.^{-1}$ are reproduced in the table, (p. 38-41) together with the infrared spectrum of a typical reaction mixture. It is evident that virtually all the absorption bands in the mixture can be accounted for by the bands due to the 1-o-, 1-m-, and 1-p-biphenylylpyrazoles, and to 1, 3-di-phenylpyrazole. Little indication of the presence of 1, 4- and 1, 5-diphenylpyrazole is given, although the spectra of all the isomers are fairly similar, and the possible presence of these compounds can not be excluded from the spectra alone.

As the infrared spectra were of not much help to calculate the isomer ratio, the phenylation products from the above experiments were subjected to gas chromatography for the calculation of isomer ratios.

INFRARED SPECTRA - PHENYLATED 1-PHENYLPYRAZOLES

1	2	3	4	5	6	7
Reaction mixture	1-o-biphenylylpyrazole	1-m-*	1-p-*	1, 3-diphenylpyrazole	1,4-diphenylpyrazole	1, 5-diphenylpyrazole
660w	660w	655w	660w			
680w	680w	680w				674w
690s				686s	688s	686s
					695vs	
702vs	700s	698s	700s	700w		701s
760vs, br	763vs	760vs	763vs	755vs	755vs, 760s	755vs, 765vs
790w		790m				
					804w	
						834w
845w	845w	840w	840s			
					867w	
886w	885w	890m	887w			880w
				906w	904w	

INFRARED SPECTRA - PHENYLATED 1-PHENYLPYRAZOLES
(continued)

1	2	3	4	5	6	7
Reaction mixture	1-o-biphenylylpyrazole*	1-m-*	1-p-	1, 3-diphenylpyrazole	1, 4-diphenylpyrazole	1, 5-diphenylpyrazole
920w	920w	915w	915m			925m
942s	942s	943s	940s	941m		
955m				956m	959vs	960s
1010w	1013w		1010m			
1025w	1028w	1020w	1022w	1031w		
					1040m	
1054m	1050m	1050s	1052m	1050m		
1065w	1061s			1064w		
			1075w			1070m
1078w	1078w	1080w			1080w	
					1095w	
1108w	1110w		1107w			
		1125m	1123w	1118w		1130m

INFRARED SPECTRA - PHENYLATED 1-PHENYLPYRAZOLES
(continued)

1 Reaction mixture	2 1-o-biphenylylpyrazole*	3 1-m*	4 1-p	5 1, 3-diphenylpyrazole	6 1, 4-diphenylpyrazole	7 1, 5-diphenylpyrazole
1138w			1138w			
1162w	1164w		1163w	1168w	1155w	
				1184w		
1203m	1204m	1200m	1200w		1208m	1226m
1270w	1269w	1273w	1264m	1270m	1265m	
1341m	1340m	1340m	1340m	1337w	1331w	1337w
				1368w	1376m	1382vs
				1392w	1393m	
1405-1410s, br	1410s	1400s	1400s		1414s	
					1469s	
1492s	1490s	1485s	1488vs		1498s	1501vs
1511vs	1510s			1510vs	1514vs	
1527s	1527s	1525s	1533vs	1531m		
	1545sh					

INFRARED SPECTRA - PHENYLATED 1-PHENYLPYRAZOLES
(continued)

1	2	3	4	5	6	7
Reaction mixture	1-o-biphenylylpyrazole	1-m	1-p	1, 3-diphenylpyrazole	1, 4-diphenylpyrazole	1, 5-diphenylpyrazole
1590w	1590w	1580s			1573s	
		1595s				1595, 1600s
1610s	1605s	1610s	1610m	1601s	1606m	..

* Capillary films

(b) Gas-liquid chromatographic analyses of phenylation products. A Beckman No. 70008 column (1.5 ft., Apiezon "L", 30%, on C-22 firebrick, 42/60 mesh) was used, with helium as carrier gas at an inlet pressure of 30 p.s.i. (outlet pressure, atmospheric), and a column temperature of 220°C.

Under these conditions, the following retention times were observed for the various isomers:

1-o-biphenylylpyrazole	8.20 min.
1-m- "	6.70 "
1-p "	17.00 "
1, 3-diphenylpyrazole	9.80 "
1, 4- "	12.60 "
1, 5- "	12.00 "

Qualitative examination of the phenylation products from the reactions of 1-phenylpyrazole and benzoyl peroxide showed that neither 1, 4-diphenylpyrazole nor 1, 5-diphenylpyrazole was present in detectable amounts. The limit of detectability was 3% under the conditions used.

The major components in the phenylation products were 1-o-biphenylylpyrazole and 1, 3-diphenylpyrazole, with lesser quantities of 1-m-biphenylylpyrazole and 1-p-biphenylylpyrazole. Trial experiments showed that the ratios of peak areas were proportional to the quantities of these isomers present in synthetic mixtures, and the following results were obtained with the mixtures from expts. 1-3.

The values in parentheses are for the phenyl ring only.

Mixture No.	Isomer ratios (%) 1-o-	1-m-	1-p-	1, 3-
1.	54 (77.1)	6 (8.7)	10 (14.2)	30
2.	58 (81.7)	5 (7.0)	8 (11.3)	29
2A. (After removal of 1-p- by chromatography).	58 (82.8)	3* (4.3)	9* (12.9)	30
3.	55 (77.5)	6 (8.5)	10* (14.0)	29

* Separated by adsorption chromatography on alumina and isolated directly before gas-liquid chromatography. Ward et. al. (13) have noted that elution order in a series of isomeric compounds follows the reverse order of dipole moments; in agreement, 1-p-biphenylylpyrazole was eluted first. Expt. 2A shows that there is little concurrent loss of the other components.

It should be noted that the evaluation of accurate peak area for the minor components was difficult in the presence of the major isomers, since some overlapping of peaks occurred with the ortho- and the meta- compounds, while the para- compound was not well resolved, giving a broad peak with some tailing. However, the correspondence between the amount of para- isomer as evaluated by gas-liquid chromatography and by direct isolation from adsorption chromatography (expts. 2 and 2A) is quite satisfactory.

B. Decomposition of Bis-(p-Bromobenzoyl) Peroxide in 1-Phenylpyrazole.

Bis(p-bromo benzoyl) peroxide (10.0 g.) was allowed to decompose in 1-phenylpyrazole (50 g.) at 80° for 50 hr. First p-bromo benzoic acid (6.2 g.) was isolated. Removal of excess of substrate gave p- bromophenylated phenylpyrazoles. Chromatography on alumina and fractional crystallization from ethanol yielded 4-bromo-4'-(1-pyrazolyl)-biphenyl, m.p. 180-182° (Anal. Calc. for $C_{15}H_{11}BrN_2$, Br, 26.72%. Found: Br, 26.84%). Ultraviolet absorption, λmax., 284 mμ; log ε, 4.33. Infrared absorption below 900cm.$^{-1}$: 819 cm.$^{-1}$. No strong absorption below 800 cm.$^{-1}$. Mixed m. p. with 1-p-biphenylyl-4-bromopyrazole, 162°. (cf. page 52).

C. Decomposition of Benzoyl Peroxide in 1-Methylpyrazole.

Benzoyl peroxide (7.0 g.) was allowed to decompose in 1-methylpyrazole (32.7 g.) at 81° for 2 hr. First benzoic acid (4.4 g., 1.24mmole), second benzoic acid (0.5 g.) and neutral material (0.25 g.) was obtained.

In another experiment benzoyl peroxide (5 g.) was decomposed in 1-methyl pyrazole (22.3 g.) at 80° for 70 hr. After this period the reaction mixture was freed of excess of 1-methylpyrazole and the residue chromatographed on alumina with benzene as eluting solvent. The eluate was freed from benzene, the residue thus obtained showed a characteristic infrared absorption at 1740 and 1770 cm.$^{-1}$ (vs) for a >CO group thereby indicating the

presence of an ester in the reaction mixture. The material was not examined further.

D. Decomposition of Benzoyl Peroxide in 4-Bromo-1-Phenylpyrazole.

Benzoyl peroxide (10 g.) was decomposed in 4-bromo-1-phenylpyrazole (40 g.) at 90° for 66 hr. First benzoic acid (4.0 g.) was obtained. Excess of 4-bromo-1-phenylpyrazole was removed by steam distillation followed by distillation under reduced pressure. The residue was chromatographed on alumina with benzene as eluting solvent. This on evaporation of benzene from the eluate yielded the residue (4.6 g.). This residue on twice crystallization from ethanol gave 1-p-biphenylyl-4-bromo pyrazole, m.p. 180°, identical with an authentic sample of 1-p-biphenylyl-4-bromopyrazole. (Mixed m.p., ultraviolet and infrared absorption). The mother liquor on removal of ethanol gave a liquid fraction, which had infrared absorption identical with the brominated 1-o-biphenylylpyrazole, is presumed to be 1-o-biphenylyl-4-bromopyrazole.

E. Decomposition of Benzoyl Peroxide in 1-Phenylpyrrole.

Benzoyl peroxide (15 g.) was heated in 1-phenylpyrrole (50 g. Aldrich Chemical Co.) at 80° for 91 hr. First benzoic acid (9.4 g., 1.24 moles) was obtained in the usual manner. After removal of first benzoic acid the reaction mixture was steam distilled to remove 1-phenylpyrrole. The residue from steam

distillation was chromatographed on alumina using benzene as eluting solvent. The eluted material (5.7 g.) obtained on evaporation of benzene gave crystals m.p. 70° (3.8 g.). Compound m.p. 70° thus obtained was found to be an ester. Strong infrared absorption at 1749 cm.$^{-1}$ due to >CO group. (Anal. Calc. for: $C_{17}H_{13}NO_2$: C, 77.57%; H, 4.9%. Found: 77.55%; H, 5.02%).

A small portion of this ester was hydrolyzed by ethanolic sodium hydroxide solution (25%). A tarry material and an acid was obtained on working up the hydrolysis reaction. The acid was characterized by its infrared absorption and m.p. and was found to be identical with an authentic sample of benzoic acid.

F. Decomposition of Bis-(1-Phenylpyrazole-4-Carbonyl)-Peroxide in benzene.

Bis -(1-phenylpyrazole-4-carbonyl)-peroxide (6 g.) was allowed to decompose in benzene (100 ml.) at 80° for 124 hr. First 1-phenylpyrazole-4-carboxylic acid (4.1 g.) was obtained and the rest of the material was chromatographed on alumina giving material (1.3 g.). This on crystallization from ethanol gave crystals m.p. 95-97° showing infrared absorption at 1730 cm.$^{-1}$ (s) indicative of an ester >CO group. This was perhaps an ester.

In another experiment bis-(1-phenylpyrazole-4-carbonyl)-peroxide (5.0 g.) was decomposed in benzene (100 ml.) at 80° for 65 hr. This yielded 1-phenylpyrazole-4-carboxylic acid (3.9 g.).

G. Decomposition of Bis-(1-Phenylpyrazole-4-Carbonyl)-Peroxide in Toluene.

The peroxide (2.5 g.) on decomposition in toluene (25 ml.) at 80° for 70 hr. gave 1-phenylpyrazole-4-carboxylic acid. Bibenzyl was also obtained from this decomposition reaction.

Section III

NITRATION OF 1-PHENYLPYRAZOLE DERIVATIVES

A. 4-Nitration of 1-Phenylpyrazole.

(cf. Passerini etc. (15)

1-Phenylpyrazole (3g.) in acetic anhydride (ca. 6 ml.) was nitrated by the addition of nitric acid (d 1.52, 1.5ml.) in acetic anhydride (ca. 4 ml.) at -5° over 30 min. The reaction mixture was allowed to reach room temperature, then poured onto ice, collected, and recrystallized from ethanol, yielding 4-nitro-1-phenylpyrazole (2.1 g., 53%), m.p. 124-125° (lit. 126-127° (15). Analysis: Calculated for $C_9H_7N_3O_2$: N, 22.2%. Found: N, 22.0%. Ultraviolet absorption: λmax. 228 and 295 mμ, logϵ 4.11 and 4.07. (Passerini et al (15) find λmax. 229-230 and 293-296 mμ, logϵ 4.11 and 3.99, and also claim a maximum at 255 mμ, logϵ, 4.17). Strong nitro group absorption at 1325 cm.$^{-1}$ and 1545 cm.$^{-1}$ (ν_{N-O}sym, ν_{N-O}asym).

Reactions on a larger scale than the above generally gave lower yields, although unchanged 1-phenylpyrazole was recovered.

B. 4-Nitration of 1-p-Biphenylylpyrazole.

Nitration under the general conditions used for 1-phenylpyrazole, gave with 1-p-biphenylylpyrazole (0.50 g.) and nitric acid (d 1.52, 1ml.) in acetic anhydride (6ml.), the presumed 1-p-biphenylyl-4-nitropyrazole, (0.25 g., 42%) m.p. 170-171°. Analysis: Calculated for $C_{15}H_{11}N_3O_2$: C, 67.91; H, 4.18%.

Found: C, 67.67; H, 4.41%. Ultraviolet absorption: λmax. 265 and 315 mμ, log ϵ 4.06 and 4.08. Strong nitro-group absorption at 1325 and 1541 cm.$^{-1}$ (ν_{N-O}sym., ν_{N-O}asym.).

C. Attempted Nitration of 1-p-Biphenylpyrazole by Mixed Acids.

Nitration in mixed acids at 0° gave amorphous products, with strong infrared absorption at 1365 and 1530-1560 cm.$^{-1}$ (multiplet) (cf. 1-o-nitrophenylpyrazole, 1373 and 1544 cm.$^{-1}$) and giving a bluish-violet color on addition of aqueous sodium hydroxide to solutions in acetone (Janovsky reaction, cf. Finar and Hurlock (1) indicative of a polynitro compound.

D. Nitration of 4-Bromo-1-Phenylpyrazole.

4-Bromo-1-phenylpyrazole (10 g.) in sulphuric acid (d 1.84, 20 ml.) was nitrated at 0° by addition of sulphuric acid (d 1.84, 20 ml.) and nitric acid (d 1.43, 15 ml.). The mixture was kept overnight at 0°, poured onto ice and collected. After crystallization from ethanol, 4-bromo-1-p-nitrophenylpyrazole (4.8 g., 40%), m.p. 168° (lit. 168-169° (16) was obtained. Analysis: Calculated for $C_9H_6BrN_3O_2$: C, 40.31; H, 2.24; N, 15.69%. Found C, 40.57; H, 2.33; N, 15.90%. Ultraviolet absorption: 315 mμ, logϵ, 4.21 (cf. 1-p-nitrophenylpyrazole λmax. 318 mμ, logϵ4.29 (in chloroform). Strong infrared absorption at 1340 cm.$^{-1}$ and 1527 cm.$^{-1}$ ν_{N-O} sym., ν_{N-O}asym.).

E. (Mononitration) of p-Di(1-Pyrazolyl)benzene

p-Di(1-Pyrazolyl)benzene(1.5 g.) was treated with nitric acid (d 1.42) in acetic anhydride, giving a product, m.p. 210° (decomp.) giving a negative Janovsky reaction. Strong nitro- group absorption at 1324 $cm.^{-1}$ and 1542 $cm.^{-1}$ ($\nu_{N-O}^{sym.}$, $\nu_{N-O}^{asym.}$). This product is probably 1-(1-pyrazolyl), 4-(nitro-1-pyrazolyl)-benzene.

Section IV

BROMINATION OF 1-PHENYLPYRAZOLE DERIVATIVES

A. 4-Bromination of 1-Phenylpyrazole

Bromine (61 g.) was added dropwise to 1-phenylpyrazole (50 g.) in chloroform (1 l.) at 0°. The resultant solution was shaken with excess of sodium carbonate solution and dried over sodium carbonate. Removal of the solvent and crystallization from ethanol gave 4-bromo-1-phenylpyrazole (50 g., 65%), m.p. 83° (lit. 81.5-82.5° (17). Ultraviolet absorption: λmax. 263 mμ log ε 4.24. Infrared Phenyl-group absorption (out-of-plane C-H deformation) at 690 (s) and 760 (vs) cm.$^{-1}$.

Further bromination, under similar conditions to the above, of either 4-bromo-1-phenylpyrazole or 1-*p*-bromophenylpyrazole yielded 4-bromo-1-*p*-bromophenylpyrazole, m.p. 81° (lit. 84.5-85° (17) (mixed m.p. with 4-bromo-1-phenylpyrazole, 72°). Ultraviolet absorption: λmax. 270 mμ, log ε 4.30. No infrared bands in the region 650-800 cm.$^{-1}$.

B. Bromination of 1-Phenylpyrazole in Sulphuric Acid Solvent

1-Phenylpyrazole (10.8g.; 0.075 mole) and bromine (5.2 ml.) were dissolved in a mixture of sulphuric acid (d, 1.84; 90 ml) and water (10 ml). Finely powdered silver sulphate (17 g.; 0.11 equiv. Ag^+) was added and reaction mixture was shaken thoroughly for 3 hr. (18). Silver bromide was filtered off and the filtrate poured onto ice, collected, washed thoroughly with

dilute nitric acid, and crystallized from benzene, yielding 1-p-bromophenylpyrazole (10.5 g.; 69%). This had m.p. 70°; ultraviolet absorption; λ max. 262 mμ, log ε, 4.29. Infrared absorption in C-H out-of-plane region at 752 (vs), 810 (vs) and 824 (s) cm.$^{-1}$, and was identical (mixed m.p., ultraviolet and infrared absorption) with an authentic sample prepared from p-bromophenyl hydrazine hydrochloride and 1, 1, 3, 3-tetramethoxypropane.

C. 4-Bromination of 1-p-Biphenylylpyrazole

(a) Synthesis Bromination in chloroform solution as for 1-phenylpyrazole (see above) using 1-p-biphenylylpyrazole (10 g.), gave 1-p-biphenylyl-4-bromopyrazole (7.5 g., 55%), m.p. 182°. Analysis: Calculated for $C_{15}H_{11}BrN_2$: Br, 26.72%. Found: Br 26.89%. Ultraviolet absorption: λ_{max} 284 mμ, log ε 4.42. Phenyl-group absorption (out-of-plane C-H deformation) at 690 (s) and 760 (vs) cm.$^{-1}$.

(b) Proof of Structure 1-p-biphenylyl-4-bromopyrazole from part (a) was identical (mixed m.p., ultraviolet and infrared absorption spectra) with a sample prepared by the following unambiguous synthesis:-

4-Bromo-1-p-nitrophenylpyrazole (see page 49) was reduced to 1-p-aminophenyl-4-bromopyrazole, m.p. 83° using tin and hydrochloric acid. The amine was diazotized and the diazo-solution was used for Gomberg arylation of benzene (cf. page 31). Chromatography of the reaction mixture yielded 1-p-biphenylyl-4-

bromopyrazole m.p. 182°. Analysis: Calculated for $C_{15}H_{11}BrN_2$: C, 60.22; H, 3.68; Br, 26.72%. Found: C, 60.03; H, 4.04; Br, 26.79%.

D. Dibromination of p-Di(1-pyrazolyl)benzene

Bromination in chloroform solution at 0°, using 2.2 mole bromine, yielded a dibromo-compound, m.p. 258-260°. Analysis calculated for $C_{12}H_8Br_2N_4$: Br, 43.4%. Found: Br, 43.25%. Ultraviolet absorption: λmax. 290 mμ logε, 4.30.

The conditions are those effective in 4-bromination in other systems (see above), so this compound is very probably p-di-(4-bromo-1-pyrazolyl) benzene.

Section V

IONIZATION CONSTANTS OF AMINOPHENYLPYRAZOLES

The pKa values of the cations of 1-p-aminophenylpyrazole and 4-amino-1-phenylpyrazole were determined by differential ultraviolet spectrophotometry of the neutral and cationic species over a pH range covering the pKa of the substances (19).

The ultraviolet absorption of the various species were: 1-p-aminophenylpyrazole--neutral molecule, λ max. 266 mμ, log ε 4.15; cation λmax. 254 mμ log ε 4.18. 4-amino-1-phenylpyrazole--neutral molecule, λ max. 273 mμ, log ε 4.00; cation, λmax. 247 mμ log ε 3.90.

The pKa values for the cations were:

1-p-aminophenylpyrazole: 3.42 ± 0.20

4-amino-1-phenylpyrazole: 3.22 ± 0.05

REFERENCES

(1) Finar, I. L. and Hurlock, R. J.: J. Chem. Soc. 1957, 3024.

(1a) Mangini, A., DalMonte, D., and Passerini, R.: Boll Sci. Fac. Chim. Ind. Bologna. 12, 147 (1954). Chem. Abstracts 49, 8700 (1955).

(2) Claisen, L. and Fischer: Ber. 21, 1139 (1888).

(3) Heilbron, I. and Bunbury, H. M. ed. "Dictionary of Organic Compounds." Eyre and Spottiswoode. London (1946).

(4) Finar, I. L. and Hurlock, R. J.: J. Chem. Soc. 1958, 3259.

(5) Weingarten, H. : J. Org. Chem. 26, 730 (1961).

(6) Rupe, U. H. and Knup, E. : Helv. Chim. Acta. 10, 299 (1927).

(7) Panizzi, L. and Monti, E. : Gazz. Chim. Ital. 77, 556 (1947). Chem. Abstracts 42, 5450 (1948).

(8) Auwers, V. and Mauss, H. : Ann. 452, 182 (1927).

(9) Hickinbottom, W. J. : "Reactions of Organic Compounds." Longmans. London (1948).

(10) Vogel, A. I. : "A Text Book of Practical Organic Chemistry." Longmans. London (1951).

(11) Finar, I. L. and Lord, G. H. : J. Chem Soc. 1957, 3314.

(12) Lynch, B. M. and Pausacker, K. H. : Australian J. Chem. 10, 40 (1957).

(13) Ward, E. R. and Poesche, W. H. : J. Chem. Soc. 1961, 2825.

(14) Kendall, J. D. and Duffin, G. E. : Brit. Patent 797, 144. June 25, 1958. Chem. Abstracts 53, 4984 (1959).

(15) DalMonte, D., Mangini, A. and Passerini, R. : Gazz. Chim. Ital. 86, 797 (1956).

(16) Protopopova, T. V., Klimko, V. T. and Skoldinov, A. P. : Khim. Nauka i Prom. 4, 805 (1959). Chem. Abstracts 54, 11037 (1960).

(17) Brain, E. G. and Finar, I. L. : J. Chem. Soc. 1958, 2435.

(18) DelaMare, P. B. D. and Ridd, J. H. : "Aromatic Substitution, Nitration and Halogenation." P. 110. Butterworths. London (1959).

(19) Lynch, B. M., Robins, R. K. and Cheng, C. C. : J. Chem. Soc. 1958, 2973.