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REACTIONS OF PHENYL-SUBSTITUTED HETEROCYCLIC COMPOUNDS

V. NITRATIONS OF 1,3- AND 1,5-DIPHENYLPYRAZOLES[1]

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ABSTRACT

Dinitration of 1,3- or 1,5-diphenylpyrazole in sulphuric acid yields the corresponding di(*p*-nitrophenyl) compounds, while nitric acid – acetic anhydride yields the 4-nitro-1-*p*-nitrophenyl compounds.

Mononitration at the 4-position occurs when the diphenylpyrazoles and several other 1-phenylpyrazoles are nitrated at 0° by nitric acid – acetic anhydride.

Possible explanations of the dependence of orientation on the nature of the nitrating agent are discussed.

Nuclear magnetic resonance (n.m.r.) spectroscopy was used in demonstrating the structures of many of the nitration products, and a general discussion of the n.m.r. spectra of substituted 1-phenylpyrazoles is given.

INTRODUCTION

In nitrations of aromatic compounds, the stages of successive substitution are usually well defined, since a nitro group is strongly deactivating towards further substitution (1). However, the 1-phenylpyrazole derivatives (IA–IC) are readily *dinitrated* to the 4-nitro-1-*p*-nitrophenyl compounds (IIIA–IIIC), under conditions similar to those employed for *mononitration* of 1-phenylpyrazole (2, 3). In an earlier paper (4), we suggested that 1-phenylpyrazoles (I) will undergo nitration in nitric acid – sulphuric acid as their conjugate acids (II), so that the para-position of the 1-phenyl group is the site of initial nitration. The resulting 1-*p*-nitrophenylpyrazoles (IV) will be far less basic than the parent species (I), and will undergo further nitration as the free bases, in which the 4-position is attacked. Dinitration is thus to be expected, since the various conjugate acids (II) and the 1-*p*-nitrophenylpyrazoles (IV) should be of approximately equal reactivity towards nitronium ion. The generalized conversion I → III is thus to be expected for all 1-phenylpyrazoles with readily accessible 1-para- and 4-positions.

Some assignments of structure to the dinitration products of 1,3- and 1,5-diphenylpyrazoles (ID and IE) conflict with this prediction, although it might be argued that a 3- or 5-phenyl group would shield the 4-position from attack; von Auwers and Mauss (5) suggested that dinitration of 1,3-diphenylpyrazole yielded 1,3-di(*p*-nitrophenyl)pyrazole (VA), while we assigned (4) the dinitro-1,5-diphenylpyrazole, m.p. 185°, obtained by nitric acid – sulphuric acid treatment of 1,5-diphenylpyrazole, as 1,5-di(*p*-nitrophenyl)-pyrazole (VB). In view of these apparent exceptions to the generality of the conversions I → III, we have reexamined the nitrations of 1,3- and 1,5-diphenylpyrazoles in detail. In addition, we have noted several further examples of initial 4-nitration of substituted 1-phenylpyrazoles by nitric acid – acetic anhydride (as predicted in an earlier paper (4)).

The proton nuclear magnetic resonance (n.m.r.) spectra of the various nitration products furnished particularly simple demonstrations of structure, supplementing or replacing classical degradations, syntheses, and conversions into known compounds.

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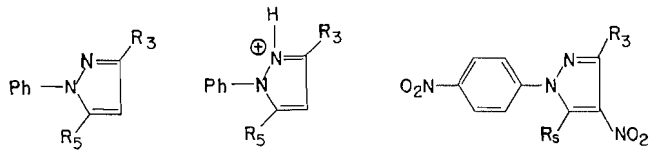
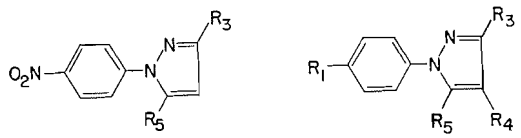
[2]*Graduate Research Assistant: holder of a summer scholarship from the Atlantic Provinces Inter-University Committee on the Sciences, July–August 1963.*



I II III



IV V

IA, IIA, IIIA, IVA: $R_3 = R_5 = H$
IB, IIB, IIIB, IVB: $R_3 = CH_3$, $R_5 = H$
IC, IIC, IIIC, IVC: $R_3 = H$, $R_5 = CH_3$
ID, IIID: $R_3 = Ph$, $R_5 = H$
IE, IIIE: $R_3 = H$, $R_5 = Ph$
VA: $R_1 = NO_2$, $R_3 = p\text{-}C_6H_4NO_2$, $R_4 = R_5 = H$
VB: $R_1 = NO_2$, $R_3 = R_4 = H$, $R_5 = p\text{-}C_6H_4NO_2$
VC: $R_1 = R_5 = H$, $R_4 = NO_2$, $R_3 = Ph$
VD: $R_1 = R_3 = H$, $R_4 = NO_2$, $R_5 = Ph$

RESULTS

(a) 1,3-Diphenylpyrazole

Nitration by nitric acid – acetic anhydride at 0° yielded 1,3-diphenyl-4-nitropyrazole (VC), m.p. 123°, together with 1-*p*-nitrophenyl-3-phenylpyrazole and 4-nitro-1-*p*-nitrophenyl-3-phenylpyrazole (IIID), m.p. 238–240°: the dinitro compound (IIID) was the sole product of similar nitration at 20°. Nitration by mixed nitrating acids at 0° yielded 1,3-di(*p*-nitrophenyl)pyrazole (VA), m.p. 228–230°, also obtained by similar nitration of 1-*p*-nitrophenyl-3-phenylpyrazole (cf. von Auwers and Mauss (5)).

The structural assignments were confirmed as follows. The mononitro compound of m.p. 123° has structure VC since its n.m.r. spectrum in dimethyl sulphoxide shows a signal at τ 0.20 integrating for a single proton, and a 10-proton envelope between τ 2.0 and 2.5. The low-field signal is typical of a 5-proton adjacent to a 4-nitro group in a 1-phenylpyrazole derivative (see Discussion section for examples). The assignment of structure VC is subject to little doubt in any case, since other likely nitration products are already known (1-*p*-nitrophenyl-3-phenylpyrazole, m.p. 169° (5), and 3-*p*-nitrophenyl-1-phenylpyrazole, m.p. 137° (6)). Structure VA for the dinitro compound of m.p. 228–230° also follows from its n.m.r. spectrum (measured in dimethyl sulphoxide at 50°), which shows two doublets (J, ca. 1 c/s) centered at τ 2.80 and 1.17 assigned to the 4- and 5-protons of the pyrazole ring, and a signal at τ 1.68 corresponding to the 8 (apparently equivalent) protons of the 1- and 3-*p*-nitrophenyl groups (see Discussion section for interpretations of the signal positions). The dinitro compound of m.p. 238–240° has structure IIID since it is obtained by nitration of VC by mixed acids and by nitric acid – acetic anhydride nitration of 1-*p*-nitrophenyl-3-phenylpyrazole, and it differs from the dinitro compound (VA).

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(b) 1,5-Diphenylpyrazole

Our present results confirm previous assignments (4) of structure to the various nitration products of 1,5-diphenylpyrazole, i.e.: 1,5-diphenylpyrazole — (HNO_3/Ac_2O)→VD, m.p. 150°, 1,5-diphenylpyrazole — (HNO_3/H_2SO_4)→VB, m.p. 185°, and confirm that 4-nitro-1-*p*-nitrophenyl-5-phenylpyrazole (IIIE), m.p. 147°, is the product of nitric acid – acetic anhydride nitration of 1-*p*-nitrophenyl-5-phenylpyrazole.

Structure VD for the mononitro-1,5-diphenylpyrazole of m.p. 150° was proved by converting it into 1,4,5-triphenylpyrazole via reduction, diazotization, and Gomberg arylation of benzene (cf. (4)). Furthermore, its n.m.r. spectrum in acetone was consistent with structure VD, in that a single proton signal assignable to the 3-proton, and two five-proton signals at τ 2.56 and 2.63, assignable to the 1- and 5-phenyl groups, are observed. The position of the signal assigned to the 3-proton (at τ 2.77) indicates the presence of some remarkable shielding effect (see Discussion section).

Structure VB for the dinitro-1,5-diphenylpyrazole of m.p. 185° is established, since it is formed by mixed-acid nitration of 1-*p*-nitrophenyl-5-phenylpyrazole, and it yields *p*-nitrobenzoic acid on prolonged oxidation by neutral potassium permanganate. Further confirmation is provided by its n.m.r. spectrum in acetone, which shows two doublets (J, ca. 1 c/s) centered at τ 2.10 and 3.13 assigned to the 3- and 4-protons of the pyrazole ring, together with an A_2B_2 pattern centered at τ 2.05 arising from the two *p*-nitrophenyl groups (which are apparently equivalent: see Discussion section). Similarly, structure IIIE for the dinitro-1,5-diphenylpyrazole of m.p. 147° follows from its n.m.r. spectrum in acetone, which shows a five-proton signal at τ 2.50 due to the 5-phenyl group, an A_2B_2 pattern centered at τ 2.08 arising from the four protons of the 1-*p*-nitrophenyl group, and a single proton signal at τ 1.50 from the 3-proton.

(c) Further Examples of 4-Nitration by Nitric Acid – Acetic Anhydride

Smooth 4-mononitration of the following compounds was effected by nitric acid in acetic anhydride at 0°: 1-*p*-bromo-, 1-*p*-chloro-, 1-*o*-methoxy-, and 1-*p*-phenyl-phenylpyrazoles, and 3-methyl-1-phenylpyrazole. The structures of the first three nitration products were established by comparison with samples synthesized by cyclizing the appropriate arylhydrazine with sodium nitromalonaldehyde hydrate; the structure of 1-*p*-phenylphenyl-4-nitropyrazole (1-*p*-biphenylyl-4-nitropyrazole), m.p. 200° (in previous experiments (4), a polymorphic form, m.p. 170°, having ultraviolet and infrared spectra identical with our present product, was obtained) was proved by synthesis via 1-*p*-aminophenyl-4-nitropyrazole using diazotization and Gomberg arylation (cf. (4)), while our nitro-3-methyl-1-phenylpyrazole had m.p. 110°, identical with that recorded for 3-methyl-4-nitro-1-phenylpyrazole by Finar and Hurlock (3), and its n.m.r. spectrum (see Discussion section) was consistent with the assigned structure.

DISCUSSION

(a) Dependence of Orientation upon the Nitrating Agents

In the dinitrations of both 1,3,- and 1,5-diphenylpyrazoles, the orientations are seen to be reagent-dependent, in the sense that nitration at the para-positions of the N- and C-phenyl groups is favored in sulphuric acid, while 4-nitration is favored when nitric acid – acetic anhydride is used. These results could be rationalized in terms of our previous suggestions (4) if the conjugate acids of the diphenylpyrazoles, and also of the 1-*p*-nitrophenyl-3- and -5-phenylpyrazoles, are the entities undergoing nitration in the strongly acidic solvent, but such a postulate does not appear reasonable. In particular, the

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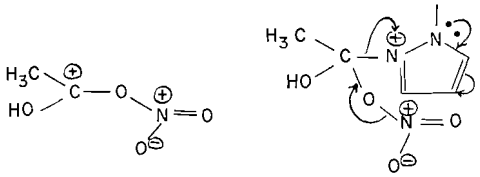
1-*p*-nitrophenyl compounds would surely exist in measurable proportions as the free bases.

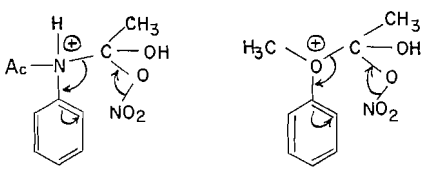
Our present results thus require an interpretation other than deactivation of the pyrazole ring through protonation, with resultant substitution by default in the phenyl rings, to account for the lack of substitution in the pyrazole ring. It is tempting to propose that the adjacent 3- or 5-phenyl group hinders the approach of nitronium ion, but such a suggestion replaces one difficulty by another, since the same factors would operate in the nitric acid – acetic anhydride nitrations, where 4-nitration is favored. However, if a specific interaction occurs between the pyrazole ring and the nitrating agent which is effecting substitution in the nitric acid – acetic anhydride system, such that attack in the pyrazole ring is favored over other sites, then the observed reagent-dependence can be explained.

Since Bordwell and Garbisch (7) have put forward convincing evidence that protonated acetyl nitrate (VI) is the effective species in nitrations by the nitric acid – acetic anhydride reagent, we suggest that the specific interaction suggested above takes the form of an addition of the nucleophilic N_2 of a pyrazole to the electron-deficient carbon of VI, yielding an intermediate (VII). The series of electron shifts shown would then lead to preferred 4-nitration.



Although an interpretation along these lines seems to be required to account satisfactorily for the results with the diphenylpyrazoles, the selective 4-nitrations of the simpler species noted in part (*c*) of the Results section, and some previous examples (4), may be accounted for in terms of our previous suggestion, i.e., in a simple 1-phenylpyrazole, where the 1-*para*- or 4-positions are the only probable sites of substitution, 4-substitution is favored for attack on the neutral molecule (4). Supporting evidence for this contention is furnished by the results of Friedel–Crafts nitration of 1-phenylpyrazole using nitronium tetrafluoroborate in tetramethylene sulphone, cf. Olah *et al.* (8(*a*), where 4-nitro-1-phenylpyrazole is the only detectable substitution product (8(*b*)).

Intermediates corresponding to VII account neatly for other selective nitrations effected by the nitric acid – acetic anhydride reagent: thus VIII would lead readily to the observed ortho nitration of acetanilide, and IX to the similar nitration of anisole.



Since previously suggested reaction pathways (9, 10) for these ortho nitrations do not take Bordwell and Garbisch's results into consideration, and the postulated intermediates are consistent with all previous evidence, we are currently engaged in a study (11) seeking to establish VIII as the general intermediate for the selective ortho nitrations of substituted acetanilides.

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(b) Nuclear Magnetic Resonance Spectra

In addition to their value in facilitating and confirming assignments of structure, the n.m.r. spectra of 1-phenylpyrazole derivatives are of interest in their own right: little previous attention has been focussed either on the chemical shifts of ring protons in pyrazoles, or on the effects of heteroaromatic substituents on the chemical shifts of benzenoid protons. Many of the compounds examined by n.m.r. spectroscopy were 1-parasubstituted-phenyl pyrazoles, in which the presence of a readily recognizable A_2B_2 pattern due to the four protons of the substituted phenyl group facilitated identification of the signals from the pyrazole ring protons. Analyses of these A_2B_2 patterns so as to resolve the individual chemical shifts expected for the A and B protons in the absence of spin–spin coupling gave the results in Table I. The analyses employed the simplified approach adopted by Richards and Schaefer (12), in which it is assumed that $J'_{AB} = 0$ and $J_{AA} = J_{BB}$. It is evident from Table I that 1-pyrazolyl substituents usually have a marked deshielding influence on the protons of a parasubstituted-phenyl group. The deshielding is accounted for readily in terms of the effect of the ring current in the pyrazole ring on the adjacent protons of the 1-phenyl group (13). Although the qualitative effects of various substituents in the 1-phenyl group follow the order expected from the chemical shifts of ortho and meta protons in monosubstituted benzenes (14), no constant chemical-shift parameters could be assigned to the 1-pyrazolyl substituent, since the apparent deshielding contribution varies with the nature of the other substituent, and with the solvent. Fortunately, acetone and dimethyl sulphoxide (the most effective solvents for the compounds studied) appear to be closely comparable in their effects on the chemical shifts of the phenyl-group protons (see No. 1 in Table I).

With the 1-*p*-nitrophenyl-5-phenylpyrazole derivatives (Nos. 7–9 in Table I), where coplanarity of the 1-*p*-nitrophenyl and pyrazole rings is highly unlikely, marked changes from the A_2B_2 pattern typical of other 1-*p*-nitrophenylpyrazoles (e.g., Nos. 1, 3, 4–6) are found. The A–B chemical shift separation (δ_{A-B}), and the extracted A and B chemical shifts, are altered in the direction expected for a decreased deshielding contribution accompanying the increased angle between the planes of the 1-*p*-nitrophenyl and pyrazole rings (13). In No. 9, the 1- and 5-*p*-nitrophenyl groups must be magnetically equivalent, since only one A_2B_2 pattern, closely similar to those for Nos. 7 and 8, was resolved. A corresponding situation was observed with 1,3-di(*p*-nitrophenyl)-pyrazole, although in this instance the center of the system is at τ 1.68 (with $J_{AB} \gg \delta_{A-B}$), indicating that the three rings are coplanar in this compound. Further indications that the 5-phenyl groups in Nos. 7 and 8 are not coplanar with the pyrazole ring are provided by the appearance of discrete signals at τ 2.47 and 2.50, rather than the band envelopes between τ 2.0–2.6 observed for No. 4 and for 1,3-diphenyl-4-nitropyrazole (see Results section). Such differences are to be expected if the ortho protons of the 5-phenyl groups are shielded by comparison with the values characteristic of coplanar C-phenyl and pyrazole rings, and such differences are also noted with 1,5-diphenyl-4-nitropyrazole (see Results section).

The chemical shifts assigned to the pyrazole ring protons in a series of substituted pyrazoles are listed in Table II. In general the τ values fall in the order $4 > 3 > 5$, which is to be expected since (*a*) the 5-proton should be deshielded most effectively by the ring current of the adjacent 1-phenyl group, and (*b*) the 4-carbon should have a higher electron density than the 3-carbon (which will be influenced electrostatically by the adjacent pyridine-type nitrogen). The assignments are based upon the τ values noted for suitably substituted compounds (Nos. 3 and 6, 10 and 11), and upon the observed multiplicities

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TABLE I

Analyses of A_2B_2 patterns in n.m.r. spectra of parasubstituted 1-phenylpyrazoles

No.	Substituents in *p*-A.C_6H_4.B		Solvent	Center of A_2B_2 system	J_{AB} (c/s)	Chemical shifts (τ scale) for protons ortho to:	
	A	B		(τ scale)		A	B
1	NO_2	1-Pyrazolyl	Dioxane	1.83	10.9	1.66	2.00
			Acetone	1.77	10.1	1.66	1.88
			Dimethyl sulphoxide	1.77	10.4	1.66	1.88
2	1-Pyrazolyl	Cl	CCl_4	2.47	9.2_5	2.34	2.60
			Dimethyl sulphoxide	2.25	9.4_5	2.08	2.42
3	NO_2	1-(4-Nitropyrazolyl)	"	1.75	9.0_5	1.67	1.83
4	"	1-(3-Phenylpyrazolyl)	"	1.70	9.2	1.62	1.78
5	"	1-(4-Bromopyrazolyl)	"	1.75	9.2_5	1.62	1.88
6	"	1-(3-Methyl-4-nitro-pyrazolyl)	"	1.75	10.0	1.67	1.83
7	"	1-(5-Phenylpyrazolyl)	Acetone	2.13	8.1	1.77	2.47
8	"	1-(4-Nitro-5-phenyl-pyrazolyl)	"	2.08	8.4	1.76	2.41
9	"	1-(5-(*p*-Nitrophenyl) pyrazolyl)	"	2.05	11.7	1.74	2.36
10	1-(4-Nitropyrazolyl)	NH_2	"	2.80	12.5	2.41	3.19
11	1-(3-Methyl-4-nitro-pyrazolyl)	NH_2	"	2.83	10.5	2.44	3.22
12	1-(4-Nitropyrazolyl)	Br	Dimethyl sulphoxide	2.18	8.4_5	2.08	2.28

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TABLE II

Chemical shifts of ring protons in pyrazoles

Compound (or No. from Table 1)	Solvent	Chemical shifts (τ scale) for: 3-	4-	5-proton	Other signals (τ scale)
1	Dioxane	2.22	3.45	1.68	
	Acetone	2.22	3.42	1.50	
	Dimethyl sulphoxide	2.13	3.35	1.30	
2	CCl_4	3.03	3.61	2.37	
	Dimethyl sulphoxide	2.13	3.39	1.50	
3	"	1.43	—	0.22	
4	"	—	2.80	1.22	Multiplet from 3-phenyl group at τ 2.00–2.60
5	"	2.00	—	1.00	
6	"	—	—	0.30	3-Methyl group at τ 7.47 (measured in pyridine)
7	Acetone	2.20	3.37	—	5-Phenyl group at τ 2.47
8	"	1.50	—	—	5-Phenyl group at τ 2.50
9	"	2.10	3.13	—	
10	"	1.75	—	1.05	
11	"	—	—	1.17	3-Methyl group at τ 7.37 (measured in $CHCl_3$)
12	Dimethyl sulphoxide	1.50	—	0.38	
3-Methyl-4-nitro-1-phenylpyrazole	Chloroform	—	—	1.40	1-Phenyl group at τ 2.67–2.84, 3-methyl group at τ 7.40
1-Methyl-4-nitropyrazole	Acetone	1.96	—	1.47	1-Methyl group at τ 6.00
p-Di(1-pyrazolyl)benzene	Chloroform	2.05	3.50	1.90	Benzene ring protons at τ 2.20
1-*p*-Bromophenylpyrazole	Dimethyl sulphoxide	2.18	3.42	1.49	A_2B_2 pattern from *p*-bromophenyl group centered at τ 2.22
4-Bromo-1-phenylpyrazole	CCl_4	2.68	—	2.22	1-Phenyl group at τ 2.50–2.83
4-Bromo-1-*p*-bromophenylpyrazole	Dimethyl sulphoxide	2.07	—	1.15	*p*-Bromophenyl group protons (all virtually equivalent) at τ 2.20

of signals for the compounds with three adjacent protons (Nos. 1, 2, *p*-di(1-pyrazolyl)-benzene, 1-*p*-bromophenylpyrazole): the 4-protons gave triplets, and the 3- and 5-protons doublets, as expected from simple first-order theory if spin–spin coupling is restricted to adjacent protons. Similarly, doublet signals were observed for compounds with two adjacent protons (Nos. 4, 7, 9, and 1,3-di(*p*-nitrophenyl)pyrazole). The apparent coupling constants between adjacent protons were ca. 1 c/s, and there was no evidence of coupling between non-adjacent protons (the signals from the pyrazole ring protons in Nos. 3, 5, 10, 12, 1-methyl-4-nitropyrazole, 4-bromo-1-phenylpyrazole and 4-bromo-1-*p*-bromophenylpyrazole were singlets). The influence of 4-substituents on the chemical shifts of the 3- and 5-protons qualitatively parallels their influence in monosubstituted benzenes, with one exception.

This exception is 1,5-diphenyl-4-nitropyrazole, where the 3-proton signal falls at τ 2.77 (with most 4-nitro-substituted pyrazoles, the 3-proton signal falls in the range τ 1.4–2.0). The three adjacent groups (the 1- and 5-phenyls, and the 4-nitro group) somehow lead to considerable shielding of the 3-proton. One rationalization of this extraordinary effect is that all three substituents are oriented perpendicularly to the pyrazole ring plane. Circulation of the π-electrons in the nitro group could then produce positive shielding above and below the plane containing the nitro group. Bullock (15) has noted the possibility of such an effect with nitrodurenes and nitromesitylenes, and we find that the n.m.r. spectrum of 3-nitro-*o*-xylene (as the pure liquid), a typical AB_2 system (13, p. 93; 16) may be resolved to give τ 2.67 for the A proton (adjacent to the nitro group) and τ 2.90 for the B protons, while the two methyl groups give a singlet at τ 7.79, thus lending support to the possibility of positive shielding of protons or methyl groups ortho to a nitro group which is in a plane perpendicular to that of an attached aromatic ring.

EXPERIMENTAL

Analyses are by the Schwarzkopf Microanalytical Laboratory, Woodside, N.Y., U.S.A. Melting points were observed using a Fisher–Johns apparatus and are uncorrected. Infrared spectra were recorded using a Beckman IR-8 spectrophotometer: samples were examined as suspensions in potassium chloride disks. Ultraviolet spectra refer to solutions in 95% ethanol, and were recorded using Beckman DK-2 or DK-2A ratio-recording spectrophotometers. Nuclear magnetic resonance spectra were obtained using a Varian A-60 n.m.r. spectrometer. Signal positions are expressed on the τ scale in parts per million from tetramethylsilane, present as an internal reference, and refer to saturated solutions.

Starting and Reference Materials

1-Phenylpyrazole, 1-*p*-biphenylylpyrazole, 4-bromo-1-*p*-bromophenylpyrazole, 4-bromo-1-*p*-nitrophenylpyrazole, 4-bromo-1-phenylpyrazole, 1-*p*-bromophenylpyrazole, 1-*o*-methoxyphenylpyrazole, and 1,5-diphenylpyrazole and its various nitro- and dinitro-derivatives had the properties described previously (4). 1-*p*-Chlorophenylpyrazole, m.p. 51°, 1-methylpyrazole, b.p. 126–127°, and *p*-di(1-pyrazolyl)benzene, m.p. 180° (anal. calc. 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), were prepared by cyclizing the appropriate substituted hydrazine and 1,1,3,3-tetraethoxypropane (4). The 3-methyl-1-phenylpyrazole was purchased from the Aldrich Chemical Co., Inc., Milwaukee, Wisconsin, U.S.A. Authentic samples of 1-*p*-bromophenyl-, 1-*p*-chlorophenyl-, and 1-*o*-methoxyphenyl-4-nitropyrazoles (for melting points, see Table III), and of 1-methyl-4-nitropyrazole, m.p. 88–89° (anal. calc. for $C_4H_5N_3O_2$: C, 37.80; H, 3.96; N, 33.06; found: C, 37.79; H, 4.19; N, 33.11%), were prepared by cyclization using the appropriate substituted hydrazine and sodium nitromalonaldehyde hydrate. 1,3-Diphenylpyrazole, m.p. 85°, and 1-*p*-nitrophenyl-3-phenylpyrazole, m.p. 169° (ultraviolet absorption: λ_{max} 261.5, 337 mμ, log ϵ 4.16, 4.24), were prepared from the appropriate arylhydrazine and hydroxymethyleneacetophenone (5). 4-Nitro-1-*p*-nitrophenylpyrazole, m.p. 146° (ultraviolet absorption: λ_{max} 213.5, 305 mμ, log ϵ 4.22, 4.36), and 3-methyl-4-nitro-1-*p*-nitrophenylpyrazole, m.p. 208–209° (ultraviolet absorption: λ_{max} 216, 312.5 mμ, log ϵ 4.03, 4.30), were prepared by mixed acid nitrations of the parent 1-phenylpyrazoles (2, 3), and 1-*p*-aminophenyl-4-nitropyrazole, m.p. 190° (ultraviolet absorption: λ_{max} 262.5 mμ, log ϵ 4.14), and 1-*p*-aminophenyl-3-methyl-4-nitropyrazole, m.p. 169° (ultraviolet absorption: λ_{max} 261.5 mμ, log ϵ 4.18), were prepared from the corresponding dinitro compounds by partial reduction using ammonium sulphide solution (cf. Finar and Hurlock (3)).

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Nitrations

(a) By Mixed Nitric – Sulphuric Acids

1,3-Diphenylpyrazole (2 g) was dissolved in the minimum volume of sulphuric acid (*d* 1.84), cooled to 0°, and a mixture of nitric acid (4 ml, *d* 1.42) and sulphuric acid (5 ml, *d* 1.84) was added at 0°, and the mixture was kept at 0° overnight, and then poured onto ice. The resulting precipitate was collected and purified by chromatography on alumina and repeated crystallization from methanol, finally yielding 1,3-di(*p*-nitrophenyl)pyrazole (0.7 g, 25%), m.p. 228–230° (anal. calc. for $C_{15}H_{10}N_4O_4$: C, 58.06; H, 3.25; N, 18.06; found: C, 57.85; H, 3.75; N, 18.02%) (ultraviolet absorption: λ_{max} 340 mμ, log ε 4.34; infrared absorption in the 650–1800 cm^{-1} region (cm^{-1}, intensity): 680w, 697w, 746s, 851s, 952m, 1045m, 1105m, 1269w, 1307sh(s), 1333s, 1513s, 1590s). This compound was also obtained in 87% yield by similar nitration of 1-*p*-nitrophenyl-3-phenylpyrazole. Similar nitration of 1,3-diphenyl-4-nitropyrazole yielded 1 g (43%) of 4-nitro-1-*p*-nitrophenyl-3-phenylpyrazole, m.p. 238–240°, after 1 h at 0°. The product was identical (m.p., mixed m.p., superimposable infrared spectra) with that obtained by nitric acid – acetic anhydride nitration of 1,3-diphenylpyrazole or of 1-*p*-nitrophenyl-3-phenylpyrazole (cf. section (*b*) below, and Table III).

(b) By Nitric Acid – Acetic Anhydride

The general procedure used was that adopted in our previous paper (4): A solution of nitric acid (*d* 1.52) in acetic anhydride, prepared at 15–20°, was cooled to 0° and added to the 1-phenylpyrazole derivative (dissolved in the minimum volume of acetic anhydride) over 30 min. The reaction mixture was poured onto ice and the precipitate was collected. Chromatography on alumina, followed by crystallization from methanol or ethanol, yielded the new products listed in Table III. The 4-nitro-1-*p*-nitrophenyl-3-phenylpyrazole (the final entry in Table III) was obtained by nitration of 1,3-diphenylpyrazole at 20°, and showed the following infrared absorption bands in the 650–1800 cm^{-1} region (cm^{-1}, intensity): 680w, 705w, 741s, 826w, 852s, 922w, 952m, 1099m, 1233m, 1307sh(s), 1335s, 1517s, 1590s. This dinitro compound, therefore, differs from 1,3-di(*p*-nitrophenyl)pyrazole (cf. above). 4-Nitro-1-*p*-nitrophenyl-3-phenylpyrazole was also obtained in 40% yield by similar nitration of 1-*p*-nitrophenyl-3-phenylpyrazole at 20°.

Proofs of Structure via Gomberg Reactions

(a) Conversion of 1,5-Diphenyl-4-nitropyrazole into 1,4,5-Triphenylpyrazole

1,5-Diphenyl-4-nitropyrazole (2.3 g) was reduced using tin and hydrochloric acid, and the crude amine thus obtained was diazotized in 10 *N* hydrochloric acid at 0°, and was stirred with benzene for 3 h after basification with sodium hydroxide at 0°. The benzene layer was separated and chromatographed on alumina: evaporation of the eluate followed by crystallization from ethanol yielded 1,4,5-triphenylpyrazole (0.2 g), m.p. 208–211°, undepressed on admixture with an authentic sample, and with infrared absorption identical with that of an authentic sample, showing the following bands in the 650–1800 cm^{-1} region: 654w, 662w, 694s, 718w, 761s, 767s, 773s, 856w, 920w, 952s, 1379s, 1429w, 1439w, 1493s, 1587s.

(b) Synthesis of 1-p-Biphenylyl-4-nitropyrazole

1-*p*-Aminophenyl-4-nitropyrazole (2 g) was diazotized and the basified diazonium salt solution was used to arylate benzene as in (*a*) above. Chromatography on alumina and crystallization from ethanol yielded 1-*p*-biphenylyl-4-nitropyrazole (0.7 g), m.p. 200°, having ultraviolet and infrared absorption identical with the polymorphic form, m.p. 170°, reported previously (4).

Oxidative Degradation of 1,5-Di(p-nitrophenyl)pyrazole

1,5-Di(*p*-nitrophenyl)pyrazole (0.5 g) was heated under reflux with an excess of alkaline potassium permanganate until no further reduction of permanganate occurred (ca. 100 h). Precipitated manganese dioxide was removed using sulphur dioxide, and the reaction mixture was acidified and extracted with hot benzene, re-extracted with sodium hydrogen carbonate, and re-acidified, giving *p*-nitrobenzoic acid (0.1 g), m.p. 237–240°, having infrared absorption identical with that of an authentic sample.

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TABLE III

4-Nitro-derivatives of substituted 1-phenylpyrazoles

R_1	R_2	R_3	R_5	M.p. (obs.)	M.p. (lit.)	Lit. ref. or analysis	Yield of recrystallized product from 2 g substrate (%)	Ultraviolet absorption	
								λ_{max} (mμ)	log ϵ
H	H	H	Ph	150°	150°	*a*	43	245, 280	4.24, 3.85
H	H	Ph	H	123	—	*b*	25[c]	256, 300sh	4.24, 3.95
H	H	CH_3	H	110	110	*d*	60	300	3.95
H	OCH_3	H	H	89	85–87	*e*	65	—	—
Cl	H	H	H	171	—	*f*	60	—	—
Br	H	H	H	154	—	*g*	60	238, 297	4.13, 4.08
Ph	H	H	H	200	170	*a*	42	265, 315	4.06, 4.08
NO_2	H	H	Ph	147	147	*a*	26	285	4.29
NO_2	H	Ph	H	238–240	—	*h*	80	—	—

[a]M. A. Khan, B. M. Lynch, and Y. Hung. Can. J. Chem. 41, 1540 (1963).
[b]Anal. Calc. for $C_{15}H_{11}N_3O_2$: C, 67.92; H, 4.18. Found: C, 68.18; H, 4.33%.
[c]1-*p*-Nitropheuyl-3-phenylpyrazole (25%) and 4-nitro-1-*p*-nitrophenyl-3-phenylpyrazole (25%) were also isolated.
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[e]C. Alberti and C. Tironi. Farmaco Pavia Ed. Sci. 17, 443 (1962).
[f]Anal. Calc. for $C_9H_6ClN_3O_2$: C, 48.34; H, 2.71. Found: C, 48.67; H, 2.77%.
[g]Anal. Calc. for $C_9H_6BrN_3O_2$: C, 40.31; H, 2.24. Found: C, 40.42; H, 2.43%.
[h]Anal. Calc. for $C_{16}H_{10}N_4O_4$: C, 58.06; H, 3.25; N, 18.06. Found: C, 58.06; H, 3.34; N, 17.52%.

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