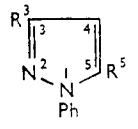
Spectroscopic Studies of Some 1-Phenylpyrazole Derivatives

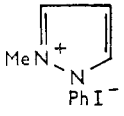
By I. L. Finar * and D. M. Rackham, Northern Polytechnic, Holloway Road, London N.7

1-Phenylpyrazoles have been studied by ultraviolet, nuclear magnetic resonance, and infrared spectroscopy. The steric effects of substituents and the position of protonation in strongly acidic media are discussed in terms of the changes observed in ultraviolet and n.m.r. absorption. A new series of 1-pentafluorophenylpyrazoles has been synthesised, and their spectra are compared with those of the parent pyrazoles. Twenty-five commonly occurring bands in the infrared spectra of 1-phenylpyrazoles are tabulated and assignments have been made.

FURTHER to recent ultraviolet (u.v.)[1-4] and nuclear magnetic resonance (n.m.r.)[5-7] spectroscopic studies, we report an investigation of seventy 1-phenylpyrazole (I) derivatives by u.v., n.m.r., and infrared (i.r.) methods.



	R^3	R^5
(I)	H	H
(II)	Me	Ph
(III)	Ph	Me



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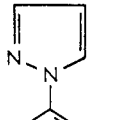

(V)

The steric effect of 5-substitution in 1-phenylpyrazoles is clearly shown by major changes in u.v. and n.m.r. absorption. Grandberg and his co-workers [4] found, in the u.v. spectra of seven isomeric pairs of 3- and 5-substituted 1-phenylpyrazoles, that the absorption maxima for the 5-isomers were hypsochromically shifted (12—44 mμ) and hypochromically changed from those of the 3-isomers. This was attributed to the 5-substituent causing the *N*-phenyl group to twist out of the plane of the pyrazole ring, thereby reducing conjugation between the two rings. Two methyldiphenylpyrazoles, (II) and (III), were also examined. The hypsochromic and hypochromic changes were shown by (II) ($\lambda_{max.}$ 254, ε 17,900), in which both phenyl groups (1- and 5-) are twisted out of the plane of the pyrazole ring, but not by (III) ($\lambda_{max.}$ 265, ε 25,400), in which the 3-phenyl group is coplanar with, and the 1-phenyl group twisted out of the plane of, the pyrazole ring.

N.m.r. spectroscopy [6] is an even more useful guide to 5-substitution. When the two rings are coplanar as in (I), the phenyl resonance appears as a complex multiplet

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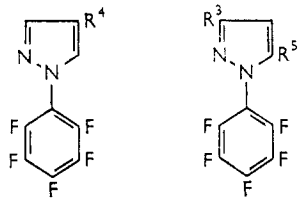
with the signals due to the *ortho*-protons shifted to low field of those due to the *meta*- and *para*-protons by 0·2 p.p.m. Tensmeyer *et al.*[6] attributed this deshielding solely to a ring-current effect of the adjacent pyrazole system, but an important contribution must come from the N:——CH interaction due to the large electric field associated with the lone pair of N-2. Murrell *et al.*[8] used this argument to explain the marked deshielding of *ortho*-protons in the closely similar azabiphenyl series (*e.g.*, 2-phenylpyridine, 2,2-bipyridyl). Furthermore, the existence of this effect of a lone pair on the nitrogen atom in these compounds is supported by the nature of the n.m.r. spectrum of 1-phenylpyrrole. Although a ring current is operable in the pyrrole ring, the pyridine-like nitrogen atom is absent, and the phenyl resonance now no longer shows separate *ortho*-proton signals.

Substitution at the 5-position of 1-phenylpyrazole (I) prevents ring coplanarity and minimises both the ring-current and electric field deshielding mechanisms, and the phenyl signal collapses to a characteristic singlet. This greatly simplified the identification [9] of 1,5-diphenylpyrazole derivatives; *e.g.*, the spectrum of (II) consisted of four singlets, from the 1- and 5-phenyl groups (τ 2·71 and 2·74), the 3-methyl group (7·61), and the 4-proton (3·68). Formation of methiodide derivatives at N-2 involves an analogous steric effect with the same simplification of the phenyl resonance; *e.g.*, 1-phenylpyrazole methiodide (IV) shows τ_3 1·50, τ_4 2·91, τ_5 0·77, τ_{Ph} 2·25, τ_{Me} 5·72, $J_{34} = J_{45} = 2{\cdot}9$, $J_{35} = 1{\cdot}1$ c./sec. By studying isomeric 1-phenylpyrazoles it was possible to relate the multiplicity of a phenyl proton signal to its coplanarity with the remainder of the molecule. Lynch *et al.*[10] examined the u.v. spectra of three (pyrazol-1-yl)-biphenyls (V) and concluded that the aryl rings of the *ortho*-isomer were twisted through large angles whereas the *meta*- and *para*-isomers were coplanar systems. We have obtained the same result from n.m.r. spectra. The monosubstituted phenyl rings of the *meta*- and *para*-isomers gave rise to complex multiplets whereas the *ortho*-isomer showed a very simple signal, indicating considerable twisting of the rings. A point of particular interest was the chemical shift of the pyrazole 5-proton (τ 2·96) in the *ortho*-isomer, which was at anomalously high field (τ 2·08 and 2·09 in the *meta*- and *para*-isomers). A possible explanation is that the out-of-plane monosubstituted ring is in a favourable position to shield the proton from the magnetic field (cf. ref. 11). Correlations between molecular orbital calculations and angles of twist in 1-phenylpyrazole systems are to be published.[12]

The problem of the protonation of 1-phenylpyrazoles in strongly acidic media has been clarified by u.v. and n.m.r. spectroscopy. N.m.r. has shown that, in heterocycles such as pyridine [13] and quinoline,[14] protonation occurs exclusively at the nitrogen atom, whereas in heterocycles such as pyrrole [15] and indole,[16] it occurs preferentially at a ring carbon atom. For 1-phenylpyrazole in concentrated sulphuric acid solution, a broad, one-proton signal was detected at τ −2·87 to low field of the solvent absorption and in a position characteristic of acidic NH protons (cf. pyrazole in 10% deuteriochloroform for which τ_{NH} is at −2·76). The 3-, 4-, and 5-proton resonances were split by a cross-ring coupling (J = 2·1 c./sec.) to this added proton. However, the 1-methyl resonance of 1-methylpyrazole was not split into a doublet, and thus protonation had occurred at N-2. Further, in the u.v. region 1-phenylpyrazole gave rise to a weak absorption at 323 mμ using ethanol as solvent (341 in hexane); this was absent when concentrated sulphuric acid was solvent. Such behaviour is characteristic of $n \longrightarrow \pi^*$ transitions in azines [17] and supports the conclusions drawn previously regarding the position of protonation.

Five new pyrazole derivatives containing the 1-pentafluorophenyl group (VI)—(X) have been prepared to assist with the interpretation of 1-phenylpyrazole spectra:



(VI) R^4 = H (IX) $R^3 = R^5$ = Me
(VII) R^4 = Br (X) $R^3 = R^5$ = Ph
(VIII) $R^4 = NO_2$

(VI), (IX), and (X) were synthesised by condensation of pentafluorophenylhydrazine with 1,1,3,3-tetraethoxypropane, acetylacetone, or dibenzoylmethane under the same conditions as those used for the unfluorinated analogues; [18,19] (VII) was prepared from (VI) under the conditions used [20] for the 4-monobromination of 1-phenylpyrazole, but those for *para*-mononitration of 1-phenylpyrazole failed with (VI). Use of dinitration conditions (which substitute both the 4- and the *para*-position of 1-phenylpyrazole) gave a good yield of the 4-nitro-derivative (VIII).

In 1-pentafluorophenylpyrazole (VI) the 4-proton (double doublet) couples to the adjacent 3- and 5-protons, the former appearing as a simple doublet. However, the 5-signal was more complicated and a spin-decoupling

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experiment was carried out to show that this could be explained on the grounds of long-range coupling with the two *ortho*-fluorine atoms. On irradiation of the 4-proton, the doublet (due to the 3-proton) collapsed to a singlet

TABLE 1

^{1}H nuclear magnetic resonance (τ-values)

	3-H	4-H	5-H	
(VI) *	2·14	3·44	2·28	In (VI)—(VIII), $J_{5,\ ortho}$ = 1·0 c./sec.
(VII)	2·21	—	2·31	
(VIII)	1·65	—	1·54	
(IX)	7·83	3·95	7·71	
(X)	2·1—2·75	3·13	2·68	

* J_{34} = 1·8, J_{45} = 2·5 c./sec.

TABLE 2

^{19}F nuclear magnetic resonance (fluorine chemical shifts, ϕ)

	ortho	*meta*	*para*	$J_{o,m}$	$J_{m,p}$
(VI)	147·7	162·5	154·8	16·4	21·2
(VII)	147·2	160·5	152·5	15·8	21·5
(VIII)	146·4	159·2	149·6	15·4	21·5
(IX)	145·3	161·2	152·3	15·6	21·2
(X)	144·2	160·8	151·7	15·8	21·5

but the 5-proton signal simplified only to a triplet, intensity 1 : 2 : 1, with $J_{5,\ ortho}$ = 1·0 c./sec.

The u.v. spectra (Table 3) may be compared with those

TABLE 3

Ultraviolet spectra, $\lambda_{max.}$ in mμ (ε)

(VI)	.....	239 (9100)	(IX)	225 (7500), 240 (7000)
(VII)	.....	249 (8500)	(X)	249 (33,400)
(VIII)	.....	266 (12,400)		

of the corresponding 1-phenylpyrazoles.[1-3] The most marked effect is a hypsochromic shift of the $\pi \longrightarrow \pi^*$ absorption maximum [16 mμ for (VI) and 14 for (VII)]. An increased steric effect due to the *ortho*-fluorine atoms leads to reduced interannular conjugation and thus a

TABLE 4

Infrared absorption (cm.$^{-1}$)

*3120*w	1250w *	830variable
3080w	*1205*m	750vs †
1605m—s	1175w—m	695s
*1530*s	1165w—m	*655*variable
1495s	1075m	*610*m
1460m—s	1040s †	*515*m
*1410*m—s	1000w	460w
*1390*m—s	*950*vs	
1335variable	910m †	

Italicised numbers indicate that the vibration is assigned to a mode of the pyrazole ring.

* Interannular C–N stretch. † Contains absorption from both rings.

lowering of the wavelength and molar extinction coefficient of the $\pi \longrightarrow \pi^*$ band.

Pentafluorination of 1-phenylpyrazole eliminated stretching and bending vibrations due to the phenyl C–H bonds, and a study of the i.r. spectra of pyrazole and simple 1-methyl derivatives [21] gave a guide to the vibrations derived from a pyrazole nucleus. Also, Randle and Whiffen [22] correlated the infrared spectra of some fifty monosubstituted phenyl derivatives. Using this information we observed [23] that the i.r. spectra of 1-phenylpyrazoles (4000—400 cm.$^{-1}$) contain twenty-five commonly occurring bands (Table 4) which were assigned to the pyrazole ring, the phenyl ring, or the interannular bond.

EXPERIMENTAL

Infrared spectra, determined for liquid films or Nujol or hexachlorobutadiene mulls on a Perkin-Elmer 237 grating spectrophotometer, were calibrated by superposition of three strong bands from a polystyrene film. The u.v. spectra were recorded on a Unicam SP 700A spectrophotometer operating between 185 and 400 mμ; samples, of concentration 0·2—0·6mM, were examined in balanced 1-mm. silica gells using analytical grade 99—100% ethanol or 98% sulphuric acid and Spectrosol hexane solvents. N.m.r. spectra were measured at 33·5° on a Perkin-Elmer R.10 instrument at 60·00 (H) or 56·46 Mc./sec. (F). Samples were run at 10% (w/v) concentration in sealed, spinning tubes of o.d. 0·180 ± 0·001 in. Solutions in deuteriochloroform were referred to tetramethylsilane (τ 10·00) and *in* sulphuric acid to tetramethylammonium chloride [15] (τ 6·68). Fluorine shifts were measured as p.p.m. to high field of $CFCl_3$ (ϕ = 0) internal reference.

The following compounds were synthesised as described in the literature: pyrazole;[24] 1-methylpyrazole;[24] 1-phenylpyrazole (I);[18] 1-phenylpyrazole methiodide (IV);[25] *o*-, *m*-, and *p*-(pyrazol-1-yl)biphenyls (V);[26] 5-methyl-1,3-diphenylpyrazole (III);[19] 3-methyl-1,5-diphenylpyrazole (II).[19]

1-*Pentafluorophenylpyrazole* (VI).—Pentafluorophenylhydrazine (5·0 g., 0·025 mole) was added to a mixture of 1,1,3,3-tetraethoxypropane (5·6 g., 0·025 mole), conc. hydrochloric acid (4 ml.), and ethanol (95%; 25 ml.), and the mixture refluxed for 2¼ hr. The *product* was obtained, as for 1-phenylpyrazole,[18] as a colourless viscous liquid (3·75 g., 64%), b. p. 55°/0·2 mm. (Found: C, 46·1; H, 1·55; N, 11·7. $C_9H_3F_5N_2$ requires C, 46·15; H, 1·3; N, 11·95%).

3,5-*Dimethyl*-1-*pentafluorophenylpyrazole* (IX).—Pentafluorophenylhydrazine (5·0 g., 0·025 mole) was added to a solution of acetylacetone (2·6 g., 0·026 mole) in glacial acetic acid (4 ml.), and the mixture heated on a steam-bath for 1 hr. Working up as for the corresponding pyrazole [19] gave the *product* (4·09 g., 62%), b. p. 75°/0·7 mm. (Found: C, 50·7; H, 2·5; N, 10·7. $C_{11}H_7F_5N_2$ requires C, 50·4; H, 2·7; N, 10·7%).

3,5-*Diphenyl*-1-*pentafluorophenylpyrazole* (X).—Pentafluorophenylpyrazole (5·0 g., 0·025 mole) was added to a solution of dibenzoylmethane (5·84 g., 0·026 mole) in glacial acetic acid (13 ml.), and the mixture heated on a steam-bath for 3½ hr. Working up [19] gave the *product* (7·1 g., 73%), m. p. 156—157° (Found: C, 65·25; H, 2·75; N, 7·2. $C_{21}H_{11}F_5N_2$ requires C, 65·3; H, 2·85; N, 7·25%).

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4-*Bromo*-1-*pentafluorophenylpyrazole* (VII).—1-Pentafluorophenylpyrazole (2·25 g., 0·0096 mole) was dissolved in glacial acetic acid (10 ml.) and cooled in ice. A solution of bromine (1·84 g., 0·0115 mole) in glacial acetic acid (10 ml.) was added slowly, and the mixture heated on a steam-bath for 12 min. and poured on ice. The pale yellow solid was recrystallised twice from ethanol to give the *product*, long rhomboids (2·15 g., 71·5%), m. p. 81—82° (Found: C, 34·8; H, 0·5; Br, 25·5; N, 8·8. $C_9H_2BrF_5N_2$ requires C, 34·5; H, 0·6; Br, 25·5; N, 8·95%).

4-*Nitro*-1-*pentafluorophenylpyrazole* (VIII).—1-Pentafluorophenylpyrazole (0·5 g., 0·00215 mole) was dissolved in cold concentrated sulphuric acid (5 ml.), and a chilled 1 : 1 mixture (6 ml.) of concentrated nitric and sulphuric acids was added dropwise during ¼ hr. The resulting mixture was left for 18½ hr. at 21° and poured on ice. The precipitate was washed with iced water, dried, and recrystallised from aqueous ethanol, to give the *product* (0·44 g., 73·5%), m. p. 60—61° (Found: C, 38·8; H, 1·0; N, 15·15. $C_9H_2F_5N_3O_2$ requires C, 38·7; H, 0·7; N, 15·05%).

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