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THE STRUCTURES OF SOME 5-PYRAZOLONES AND DERIVED 4-ARYLAZO-5-PYRAZOLONES

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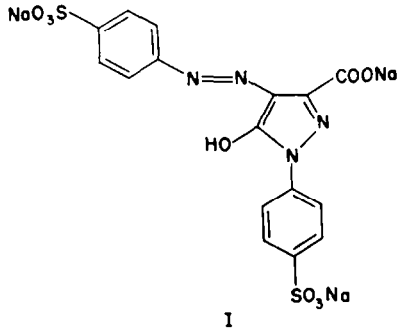
Abstract—Infrared and N.M.R. spectroscopy were used to assign structures to 3,4,4-trimethyl-5-pyrazolone, 3,4-dimethyl-5-pyrazolone, 3-methyl-5-pyrazolone, and their 1-phenyl analogues, 1-(*p*-sulphophenyl)-3-methyl-5-pyrazolone and the corresponding 3-carbethoxy and carboxy derivatives, together with 1-phenyl-3-methyl-4-phenylazo-5-pyrazolone, the corresponding 3-carboxylic acid and its methyl ester, and 1-phenyl-3-carbethoxy-4-(*p*-acetoxyphenylazo)-5-pyrazolone. All the above compounds exist in a keto form and the arylazo derivatives are in the form IX stabilized by strong intramolecular hydrogen bonding.

INTRODUCTION

STUDIES of the metabolism 4-arylazo-5-pyrazolones such as tartrazine (usually formulated as I) have shown that the azo link is remarkably stable to reduction in whole rats,[1,2] a reaction which is considered to be the main metabolic pathway for azo compounds.[3]



I

The reasons for the biochemical inertness of this linkage are important in understanding the metabolism and biochemical effects of this class of compounds, since I is a commonly used food colour. Rapid excretion of unchanged dye has been observed for I and some related compounds,[1,4] but this connot explain the lack of reductive cleavage since prolonged incubation of I with fortified rat-liver homogenate under conditions[5,6] which reduced other dyes, failed to lead to any loss of dye in this case.[7] Water solubility does not account for these results since no cleavage *in vivo* has been observed for the unsulphonated analogue of I when fed to rats.[2]

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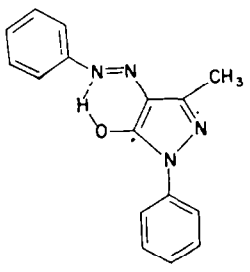
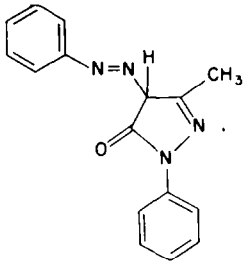
[1] A. J. Ryan and S. E. Wright, *Nature, Lond.* 195 (4845) 1009 (1962).
[2] R. Jones, A. J. Ryan and S. E. Wright, unpublished work.
[3] R. T. Williams, *Detoxication Mechanisms* p. 472. Chapman and Hall, London (1959).
[4] A. J. Ryan and S. E. Wright, *J. Pharm. Pharmacol.* **13**, 492 (1961).
[5] J. R. Fouts, J. J. Kamm and B. B. Brodie, *J. Pharmacol.* **120**, 291 (1957).
[6] P. Manchon, L. Brigant and R. Derache, *C.R. Soc. Biol., Paris* **153**, 1172 (1959).
[7] A. J. Ryan, A. Sivayavirojana and S. E. Wright, unpublished work.

In seeking to rationalize these results in terms of structure the I.R. and N.M.R. spectra of some 5-pyrazolones and their 4-arylazo derivatives have been studied. In particular, it was desired to ascertain whether the simple 5-pyrazolones possessed unique structures or were mixtures of tautomers, as other authors have proposed,[8–10] and to use this information as a guide to formulating the structure of the 4-arylazo-5-pyrazolones either uniquely or in terms of the possible tautomers. Recently two groups of workers have formulated 1-phenyl-3-methyl-4-phenylazo-5-pyrazolone as II[11] and III[12] respectively.



II



III

The present work provides evidence for an alternative structure (IX).

RESULTS

(1) 5-*Pyrazolones*

(*a*) *I.R. spectra.* The I.R. spectra of a number of 5-pyrazolones were examined in Nujol mull, potassium chloride disk, and chloroform solution. In general, the mull and disk spectra were unsatisfactory because important absorption bands were often completely obscured. In particular, the region 2000–1600 cm^{-1} could not be interpreted. These difficulties were removed in solution and under these conditions well-resolved spectra were obtained.

The infrared results are set out in Table 1. All the compounds examined possessed an absorption band typical of a cyclic lactam.[13,14] Pyrazolones lacking a substituent at position 1 have a carbonyl absorption band at 1710–1745 cm^{-1}, visible only in solution. A band at 1610 cm^{-1} present in the spectrum of 3,4,4-trimethyl-5-pyrazolone was assigned to the C=N group since the N.M.R. spectrum (see below) revealed the presence of a vinylic methyl, allowing IV as the only possible structure for this compound. As will be seen in the sequel, this absorption band only appeared in those cases where a carbon-nitrogen double bond was found to be incorporated in the pyrazolone ring.

In the cases of 3,4-dimethyl- and 3-methyl-5-pyrazolone it was not possible to assign with confidence any absorption band as characteristic of the C=N group.

[8] P. E. Gagnon, J. L. Boivin and R. N. Jones, *Canad. J. Res.* Sect. B. **27**, 190 (1949).
[9] P. E. Gagnon, J. L. Boivin and R. J. Paquin, *Canad. J. Chem.* **31**, 1025 (1953).
[10] D. Biquard and M. P. Grammaticakis, *Bull. Soc. Chim.* **8**, 246 (1941).
[11] W. Pelz, W. Puschel, H. Schellenberger and K. Loffler, *Angew. Chem.* **72**, 967 (1960).
[12] F. A. Snavely, W. S. Trahanovsky and F. H. Suydam, *J. Org. Chem.* **27**, (March) 994 (1962).
[13] L. J. Bellamy, *Infrared Spectra of Complex Molecules* (2nd Edition) p. 213. Methuen, London (1958).
[14] A. D. Cross, *Introduction to Practical Infrared Spectroscopy* p. 66. Butterworths, London (1960).

TABLE 1. INFRARED SPECTRA OF 5-PYRAZOLONES

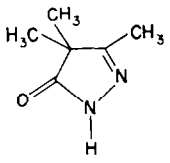
Compound	Phase	ν C=O (cm^{-1})	ν C=N (cm^{-1})	ν Other bands (cm^{-1})
3-Methyl-5-pyrazolone	$CHCl_3$	1725 s 1710 w	—	—
3,4-Dimethyl-5-pyrazolone	$CHCl_3$	1745	—	3580[a]
3,4,4-Trimethyl-5-pyrazolone	$CHCl_3$	1725 s 1710 w	1610 m	3460[a]
1-Phenyl-3-methyl-5-pyrazolone	$CHCl_3$	1710 s	1610 m	—
1-Phenyl-3,4-dimethyl-5-pyrazolone	$CHCl_3$ Nujol Disk	1712 s 1720 s 1720 s	— — —	— — —
1-Phenyl-3,4,4-trimethyl-5-pyrazolone	$CHCl_3$ Nujol Disk	1710 s 1710 s 1710 s	1620 m 1620 m 1620 m	
1-(*p*-Sulphophenyl)-3-methyl-5-pyrazolone	Nujol Disk	— —	1610 m 1610 m	
1-Phenyl-3-carbethoxy-5-pyrazolone	$CHCl_3$ Nujol Disk	1725 s[b] 1685 s 1725 s[b] 1685 s 1725 s[b] 1685 s	1600 m 1600 m 1600 m	
1-(*p*-Sulphophenyl)-3-carbethoxy-5-pyrazolone	Disk	1705 s[b]	1595 m	
1-(*p*-Sulphophenyl)-3-carboxy-5-pyrazolone	Disk	1715 s[c]		
1-Phenyl-3-carboxy-4-phenylazo-5-pyrazolone	Nujol Disk	1680 s[c] 1630 s 1700 s[b] 1635 s	1600 s 1600 s	
1-Phenyl-3-carbomethoxy-4-phenylazo-5-pyrazolone	Nujol Disk	1735 s[b] 1665 s 1735 s[b] 1665 s	1600 m 1600 m	 3440 w[a]
1-Phenyl-3-carbomethoxy-4-(*p*-acetoxyphenylazo)-5-pyrazolone	Nujol	1770 s[d] 1730 s[b] 1675 s	1600 m	
1-Phenyl-3-methyl-4-phenylazo-5-pyrazolone	Disk	1660 s	1595 s	3420 w[a]

[a] NH absorption.
[b] α-β unsaturated ester carbonyl.
[c] α-β unsaturated carboxyl carbonyl.
[d] Phenolic ester carbonyl.

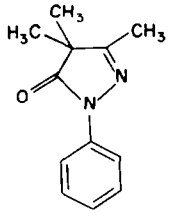
s Strong.
m Medium.
w Weak.

Compound IV and its 3,4-dimethyl analogue possessed bands at 3460 cm^{-1} and 3580 cm^{-1} respectively. These were assigned to NH stretching. Poor resolution obscured this region of the spectrum of 3-methyl-5-pyrazolone.

The spectra of the corresponding 1-phenyl derivatives provided some interesting contrasts. 1-Phenyl-3,4,4-trimethyl-5-pyrazolone possessed absorption bands at 1710 cm^{-1} and 1620 cm^{-1}. This compound can only have structure V (confirmed by the presence of vinylic methyl group in the N.M.R. spectrum), so that these bands may be unequivocally* assigned to the C=O and C=N groups respectively. Similar carbonyl absorptions were found for



IV



V

the analogous 3,4-dimethyl and 3-methyl derivatives. However, only the latter compound possessed a band attributable to a C=N group (at 1620 cm^{-1}). No NH bands were seen in the spectra. Pelz *et al.*[11] have published I.R. spectra of the last two compounds which are in agreement with the spectra obtained in the present work.

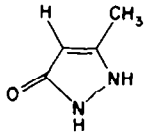
Replacement of the 3-methyl group by carbethoxy or carboxyl did not greatly alter the spectra. 1-Phenyl-3-carbethoxy-5-pyrazolone showed absorption bands at 1725 cm^{-1} (α-β unsaturated ester carbonyl), 1685 cm^{-1} (lactam carbonyl) and 1620 cm^{-1} (C=N).

Compounds containing a sulphonate group in the *para* position of the phenyl ring could only be examined in mull and disk which gave, in general, poorly resolved spectra. The 3-methyl derivative possessed a band at 1610 cm^{-1} (C=N) and the 3-carboxy and 3-carbethoxy derivatives had an α-β unsaturated ester and acid carbonyl absorption with possible C=N absorptions.

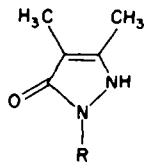
(b) *N.M.R. spectra* (Table 2). Owing to insufficient solubility, some of the N.M.R. spectra (Table 2) were obtained in solvents other than deutero-chloroform and therefore the results cannot always be correlated with certainty with those obtained from I.R. spectra for chloroform solution. However, the 1-(*p*-sulphophenyl) compounds would be expected to be closely analogous to the corresponding 1-phenyl derivatives, whose spectra were obtained in deutero-chloroform, and the spectra of 3-methyl-5-pyrazolone and of 3,4-dimethyl-5-pyrazolone (which were obtained in pyridine and D_2O solutions) show good internal consistency with the structures assigned on the basis of I.R. data.

The N.M.R. spectra of 3-methyl-5-pyrazolone in both D_2O and pyridine showed a signal attributed to a vinylic methyl group. The pyridine spectrum showed additionally another singlet in the region assigned to vinylic protons of relative intensity approximately one-third of the methyl signal. In conjunction with the I.R.

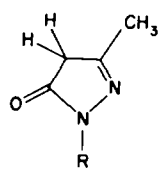
* Aromatic ring vibrations appear in the region 1600–1520 cm^{-1} for all 1-phenyl-5-pyrazolones.



VI



VII



VIII

data (presence of carbonyl and absence of C=N), 3-methyl-5-pyrazolone can be assigned the structure VI.

3,4-dimethyl-5-pyrazolone, whose N.M.R spectrum shows that both methyl groups are vinylic, must have structure (VII; R = H) to accommodate the presence of a carbonyl group (I.R.).

The structure of 3,4,4-trimethyl-5-pyrazolone is confirmed as IV, because its N.M.R. spectrum shows the expected vinylic methyl as well as the gem-dimethyl group.

The presence of signals assigned to a vinylic methyl and a methylene group in the N.M.R. spectrum of 1-phenyl-3-methyl-5-pyrazolone, proves structure VIII unequivocally, in agreement with the I.R. data (both C=O and C=N present). The extreme lability of the protons at C_4 is remarkable; usually only protons bound to oxygen or nitrogen exchange under the conditions of the experiment (see footnote *c*, Table 2). This observation is in line with the well-known reactivity of this position towards electrophilic reagents.[15]

The N.M.R. spectrum of 1-phenyl-3,4-dimethyl-5-pyrazolone shows that both methyl groups are vinylic; structure (VII; R = phenyl) is the only one which accommodates this observation in conjunction with the presence of the carbonyl group (I.R. data).

The structure of 1-phenyl-3,4,4-trimethyl-5-pyrazolone is confirmed (see above) as V by the presence of a signal attributed to a vinylic methyl in its N.M.R. spectrum.

The N.M.R. spectra of the three 1-(*p*-sulphophenyl)-3-substituted-5-pyrazolones show that all protons on the pyrazolone ring are labile. With the 3-methyl compound the absence of protons on C_3 is confirmed by the appearance of the signal attributed to the methyl group, which is a singlet. This evidence is consistent with structures analogous to VIII and is supported by the I.R. data available.

(2) *4-Arylazo-5-pyrazolones*

(a) *I.R. spectra.* In the light of the information obtained from the study of the simple pyrazolones it was possible to assign the absorption bands of the 4-phenylazo-5-pyrazolones examined with some confidence. The results are set out in Table 1. The spectra were measured in mull or disk, which, in contrast to the pyrazolones, gave well-resolved spectra. The frequencies of the major bands observed in the present work are in agreement with those found by Snavely *et al.*[12] for chloroform solutions.

Each of the compounds examined was found to have a sharp band in the region 1630–1675 cm^{-1}. This was assigned to the lactam carbonyl group, in agreement with

[15] A. H. Wiley, *Organic Chemistry* (Edited by H. Gilman) Vol. IV, p. 783. John Wiley, New York (1953).

TABLE 2. N.M.R. DATA ON 5-PYRAZOLONES

Compound	Solvent	τ (relative number of protons, multiplicity[a])	Assignment and remarks
3-Methyl-5-pyrazolone	D_2O	7·82 (s)	Vinylic methyl, remaining protons exchange
	Pyridine	8·5 (3, s)	Vinylic methyl
		4·9 (1, s)	Vinylic proton
3,4-Dimethyl-5-pyrazolone	Pyridine	8·60 (1), 8·52 (1)	Two vinylic methyls
	60% Pyridine 40% D_2O	8·62 (1), 8·78 (1)	Two vinylic methyls
3,4,4-Trimethyl-5-pyrazolone	$CDCl_3$	8·88 (6, s)	Gem-dimethyl[b]
		8·07 (3, s)	Vinylic methyl
		0·28 (1, broad s)	NH[c]
1-Phenyl-3-methyl-5-pyrazolone	$CDCl_3$	7·88 (3, s)	Vinylic methyl
		6·63 (2, s)	Methylene at C_4[b,c]
		2·7 (3, m)	Aromatic protons
		2·2 (2, m)	Aromatic protons[d]
1-Phenyl-3,4-dimethyl-5-pyrazolone	$CDCl_3$	8·47 (3, s)	Vinylic methyl
		8·10 (3, s)	Vinylic methyl
		2·7 (3, m)	Aromatic protons
		2·1 (2, m)	Aromatic protons[d]
		−0·6 (1, broad s)	NH[c,e]
1-Phenyl-3,4,4-trimethyl-5-pyrazolone	$CDCl_3$	8·82 (6, s)	Gem-dimethyl[b]
		8·04 (3, s)	Vinylic methyl
		2·8 (3, m)	Aromatic protons
		2·1 (2, m)	Aromatic protons[d]
1-(*p*-Sulphophenyl)-3-carboxy-5-pyrazolone	D_2O	2·18 (m)	Aromatic protons, A_2B_2 J_{AB} is approximately 9 c/s Remaining protons exchange
1-(*p*-Sulphophenyl)-3-carbethoxy-5-pyrazolone	D_2O	8·68 (3, t, J: 7 c/s) 5·72 (2, q, J: 7 c/s)	Ester ethyl
		2·20 (4, m)	Aromatic protons, A_2B_2 J_{AB} is approximately 9 c/s Remaining protons exchange

[a] s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet.

[b] The equivalence of the two methyl groups (or the two hydrogens) on C_4 indicates that the pyrazolone ring is either flat or undergoing inversion at a rapid rate.[37]

[c] Exchange rapidly with D_2O. For the exchange procedure see reference 37, p. 71, and reference 38.

[d] These are most likely the two protons *ortho* to the pyrazolone ring.

[e] Intermolecular hydrogen bonding was indicated by large variation in the chemical shift with concentration.[39] The chemical shift recorded is for a 5% solution.

[37] L. M. Jackman, *Applications of N.M.R. Spectroscopy in Organic Chemistry* pp. 99, 115. Pergamon Press, London (1959).

[38] H. M. Fales and A. V. Robertson, *Tetrahedron Letters* No. 3, 111, (1962).

[39] I. Yamaguchi, *Bull. Chem. Soc., Japan* **34**, (6) 744 (1961).

TABLE 2 (*continued*)

1-(*p*-Sulphophenyl)-3-methyl-5-pyrazolone	D_2O	7·92 (3, s) 2·37 (4, m)	Vinylic methyl Aromatic protons, A_2B_2 J_{AB} is approximately 9 c/s Remaining protons exchange
1-Phenyl-3-methyl-4-phenylazo-5-pyrazolone	$CDCl_3$	7·75 (3, s) 2·7 (8, m) 2·1 (2, m) −3·8 (1, broad)	Vinylic methyl Aromatic protons Aromatic protons[d] Hydrogen-bonded NH[e]
1-Phenyl-3-carbethoxy-4-(*p*-acetoxyphenylazo)-5-pyrazolone	$CDCl_3$	8·53 (3, t, J: 7·2 c/s) 5·50 (2, q, J: 7·2 c/s) 7·70 (3, s) 2·7 (7, m) 2·1 (2, m) −4·2 (1, broad)	Ethyl ester Acetoxy methyl Aromatic protons Aromatic protons[d] Hydrogen-bonded NH[e]
1-Phenyl-3-carbomethoxy-4-phenylazo-5-pyrazolone	$CDCl_3$	6·04 (3, s) 2·7 (8, m) 2·1 (2, m) −3·8 (1, broad)	Methyl ester Aromatic protons Aromatic protons[d] Hydrogen-bonded NH[e]

Snavely *et al.*[12] However, in view of the shift of the absorption band to longer wavelengths than in the simple pyrazolones it seemed likely that the carbonyl group was hydrogen-bonded.[16] The extremely low value of 1630 cm^{-1} for the lactam carbonyl in 1-phenyl-3-carboxyl-4-phenylazo-5-pyrazolone is probably due to intermolecular interaction of the carboxyl and this group. This point, however, was not rigorously examined.

A second sharp band occurring at 1600 cm^{-1} was assigned to the C=N group in the pyrazolone ring. This was not altogether unambiguous, though other authors have assigned it to this grouping.[12] In the present work it has been found that the 1-phenyl-5-pyrazolones have an aromatic absorption in the region of 1600 cm^{-1}, and the C=N absorption appears above 1600 cm^{-1}. However, the N.M.R. spectra (see below) provide considerable support for the presence of a C=N group.

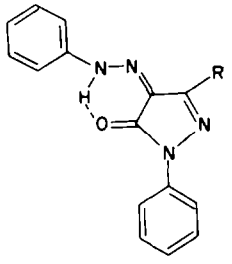
A third band which appears at about 1550 cm^{-1} has been assigned by Snavely *et al.*[12] to the azo group in these compounds. In the present work no firm assignment has been made, though probably it represents an aromatic ring absorption. The N.M.R. spectra (see below) provide strong evidence against the presence of a nitrogen–nitrogen double bond in these compounds.

Several other points of interest arose in these spectra. The carbonyl absorption of the 3-carboxy derivatives and their esters absorbed at wavelengths indicating the presence of α-β unsaturation. Two of the compounds examined (1-phenyl-3-carbomethoxy-4-phenylazo-5-pyrazolone and its 3-methyl analogue) possessed weak absorption bands at 3440 cm^{-1} and 3420 cm^{-1} respectively, which were assigned to NH stretching. In disagreement with Snavely *et al.*[12], no bands corresponding to aliphatic CH stretching were observed. In view of the N.M.R. results (see below), no such bands could be expected to occur.

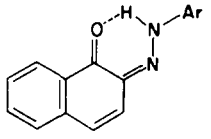
(b) *N.M.R. spectra.* The three 4-arylazo-5-pyrazolones examined all show

[16] I. M. Hunsberger, *J. Amer. Chem. Soc.* **72**, 5626 (1950).

(Table 2) the presence of a highly deshielded (τ −3·8 to −4·2) proton, exchangeable with D_2O, which can be assigned only to an intramolecularly hydrogen-bonded NH or OH. The large width of this signal makes the assignment to NH more attractive, and in view of the I.R. spectroscopic evidence for the presence of a hydrogen-bonded carbonyl group, the 4-arylazo-5-pyrazolones can only have structure IX. Good precedent for the predominance of a tautomeric



IX



X

form which involves the destruction of an aromatic structure exists in the case of arylazonaphthols(X),[17–20] and of Schiff bases derived from 2-acetyl-1-naphthol.[21] The latter were shown to exist in the keto form by (*inter alia*) the assignment of the N.M.R. signal at τ 6·5 to the hydrogen-bonded NH proton. Structure IX requires the presence of a double bond at C_3, and, in confirmation, the methyl group of 1-phenyl-3-methyl-4-phenylazo-5-pyrazolone gives rise to a singlet at τ 7·75 due to a vinylic methyl.

The remaining details (Table 2) of the N.M.R. spectra of the 4-arylazo-5-pyrazolones examined call for no further comment.

DISCUSSION

Previous workers had assumed on the basis of U.V. spectra that 5-pyrazolones were mixtures of tautomers.[8–10] The present work has shown that no such tautomerism exists and that a single structure can be written for each compound studied. A surprising feature was the variable position of the double bond in the pyrazolone ring. This was found to be either 2,3 or 3,4. The compounds without a 1-substituent possessed structure VII, except IV, which cannot have a 3,4 double bond.

In the 1-phenyl series, the position of the double bond depended upon the presence or absence of a 4-substituent. Compounds without a 4-substituent had a 2,3 double bond, whereas those with a substituent in this position had a 3,4 double bond. At present no explanation can be advanced for this.

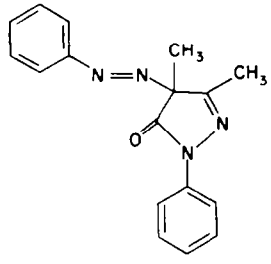
The azo compounds examined can also be written as single structures and are represented as the hydrogen-bonded lactam-hydrazone (IX). This is among the alternatives rejected by Snavely *et al.*[12] However, IX agrees well with the I.R. spectra and is in the only structure compatible with the N.M.R evidence—in particular,

[17] R. Kuhn and F. Bar, *Liebigs Ann.* **516**, 143 (1935).
[18] A. Burawoy and A. R. Thompson, *J. Chem. Soc.* 1443 (1953).
[19] E. Sawicki, *J. Org. Chem.* **22**, 743 (1957).
[20] K. J. Morgan, *J. Chem. Soc.* 2151 (1961).
[21] G. O. Dudek and R. H. Holm, *J. Amer. Chem. Soc.* **83**, 3914 (1961).

accounting for the highly deshielded proton found in the spectra of these compounds. No evidence was found for the hydroxy-azo form (II) proposed by Pelz *et al.*[11]

Structure IX is related to the hydrazone-keto form which is one of the tautomeric forms of the arylazonaphthols.[17–20] The existence of a tautomeric equilibrium in these compounds has been deduced from their U.V.[17–19] and I.R.[20] spectra. The U.V. spectra of these compounds[17–19] show absorption in two regions of the visible spectrum, one at 410–440 mμ (azo form) and the other beyond 450 mμ (hydrazone form). The I.R. spectra[20] reveal the presence of hydroxyl, amino and carbonyl groups. The carbonyl absorption appears at longer wavelengths than usual, being found at 1620–1635 cm^{-1} in mull and at 1630–1650 cm^{-1} in solution. The 1-arylazo-2-naphthols possess a carbonyl absorption showing clear evidence of internal hydrogen bonding.[16,20]

All the evidence accumulated in the present work indicates that only the hydrazone form (IX) represents the arylazopyrazolones. Structure III, proposed by Snavely *et al.*,[12] is clearly incompatible with the evidence. U.V. spectra also support our conclusions. A structure such as III would not be expected to absorb at wavelengths higher than azo-benzene (320 mμ) unless additional conjugated groups were present.[22] The arylazopyrazolones investigated here, however, gave a fairly intense (ϵ: 13,000–18,000) long-wavelength maximum in the range 400–430 mμ. Pelz *et al.*[11] have published the spectrum of 1-phenyl-3,4-dimethyl-4-phenylazo-5-pyrazolone (XI), which is closely analogous to III, but has an almost featureless spectrum with a weak maximum (log ϵ less than 3) at about 410 mμ

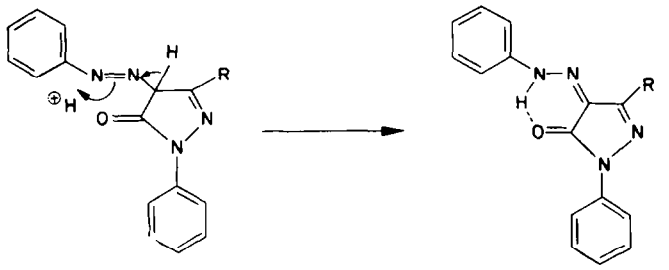


XI

attributed to the group. The U.V. spectra of the pyrazolone dye cannot be interpreted in terms of structures such as III, but evidently they appear compatible with hydrazone structures such as IX by analogy with arylazonaphthols (X), though with considerably less conjugation.

The presence of arylazopyrazolones apparently exclusively in the hydrazone form IX as compared with the tautomeric equilibrium for arylazonaphthols[20] can be explained by a smaller degree of resonance stabilization of the enol form in the former case. The six-membered hydrogen-bonded ring structure in IX would also undoubtedly enhance its relative stability. A further factor in the stabilization of this structure could be the lability of the protons in position 4, noted above, since the initial 4-phenylazo-4-H-5-pyrazolone would probably tend to rearrange as shown on page 1526.

[22] G. E. Lewis, *Tetrahedron* **10**, 129 (1960).



It is possible that the lack of reductive fission *in vivo*, referred to above,[1,2,4,7] is connected with the absence of an azo-link in IX.

EXPERIMENTAL

I.R. spectra were recorded on a Perkin-Elmer infrared spectrometer Model 21 equipped with rock-salt optics. Spectra were measured in Nujol mull, potassium chloride disk, and chloroform solution.

N.M.R. spectra were recorded on a Varian A60 spectrometer. Spectra of compounds in deuterochloroform were calibrated with tetramethylsilane as internal reference and the signal positions are expressed in τ values.[23] Spectra of compounds in deuterium oxide were calibrated from the HDO peak, which was taken to lie at τ 5·30, and the line positions were expressed on the τ scale. The above values are reproducible to within 0·02 p.p.m.[24] The spectra were run in dilute (less than 7% w/v) solutions. Spectra of compounds run in pyridine were calibrated from tetramethylsilane in carbon tetrachloride (5% solution) as external reference; the values thus obtained may be in error of up to 0·2 p.p.m. The probe temperature at which all spectra were run was 32 ± 1°.

The compounds used in this work were prepared by the following methods:

3-*Methyl*-5-*pyrazolone* was prepared from ethyl acetoacetate and hydrazine hydrate according to the method of Curtius and Jay[25] and Knorr.[26] The white prisms were recrystallized from ethanol, m.p. 220–221°, lit.[26] m.p. 219°.

3,4-*Dimethyl*-5-*pyrazolone* was obtained according to Rothenburg[27] from α-methylacetoacetic ester and hydrazine hydrate. The white cubes from ethanol had m.p. 270°, lit. m.p. 269°.

3,4,4-*Trimethyl*-5-*pyrazolone* was prepared from α:α dimethylacetoacetic ester and hydrazine hydrate by the method of Verkade and Dhont.[28] The white prisms were recrystallized from benzene–petrol ether (b.p. 40–60°), m.p. 108–109°, lit. m.p. 109·5°.

1-*Phenyl*-3-*methyl*-5-*pyrazolone* was prepared following the method of Knorr[29] from phenyl hydrazine and ethyl acetoacetate, as white crystals from benzene m.p. 129–130°, lit. m.p. 127°.

1-*Phenyl*-3,4-*dimethyl*-5-*pyrazolone* was prepared from α-methylacetoacetic ester and phenylhydrazine according to Knorr.[30] The white prisms were recrystallized from benzene, m.p. 120–122°, lit. m.p. 117–120°.

1-*Phenyl*-3,4,4-*trimethyl*-5-*pyrazolone* was obtained by Knorr's[31] method from phenyl hydrazine and α:α dimethylacetoacetic ester. The product was distilled to give a colourless liquid boiling at 188–189°/25 mm pressure (lit. b.p. 155–156° at 12 mm). The liquid had n_D^{20} 1·5574. After recrystallization from benzene the white solid had m.p. 55–60°.

[23] G. van D. Tiers, *J. Phys. Chem.* **62**, 1151 (1958).
[24] Varian, N.M.R. *Spectracatalog, Varian Assoc.* Compiled by N. S. Bhacca and J. N. Johnson (1962).
[25] T. Curtius and R. Jay, *J. Pract. Chem.* **39**, 52 (1889).
[26] L. Knorr, *Ber. Dtsch. Chem. Ges.* **29**, 253 (1896).
[27] R. von Rothenburg, *J. Pract. Chem.* **52**, 40 (1895).
[28] P. E. Verkade and J. Dhont, *Rec. Trav. Chim.* **64**, 170 (1945).
[29] L. Knorr, *Ber. Dtsch. Chem. Ges.* **16**, 2597 (1883); *Liebigs Ann.* **238**, 165 (1887).
[30] L. Knorr, *Ber. Dtsch. Chem. Ges.* **17**, 2049 (1884); *Liebigs Ann.* **238**, 147 (1887).
[31] L. Knorr, *Liebigs Ann.* **238**, 166 (1887).

1-(p-*Sulphophenyl*)-3-*methyl*-5-*pyrazolone* was prepared from ethyl acetoacetate and *p*-sulphophenyl-hydrazine by the method of Mollenhoff.[32]

1-(p-*Sulphophenyl*)-3-*carbethoxy*-5-*pyrazolone* was prepared from *p*-sulphophenyl-hydrazine and ethyl oxaloacetate by the method of Anschutz.[33]

1-(p-*Sulphophenyl*)-3-*carboxy*-5-*pyrazolone* was prepared by hydrolysis of the ester according to Anschutz.[33]

1-*Phenyl*-3-*methyl*-4-*phenylazo*-5-*pyrazolone* was prepared from benzene diazonium chloride and 1-phenyl-3-methyl-5-pyrazolone, according to Eibner.[34] The product was recrystallized from glacial acetic acid as red needles, m.p. 156–157°, lit. 155°.

1-*Phenyl*-3-*carboxy*-4-*phenylazo*-5-*pyrazolone* was prepared from phenyl hydrazine and dihydroxy-tartaric acid by the method of Knorr.[35] The product was recrystallized from glacial acetic acid as orange needles, m.p. 230°, lit. m.p. 221–222°.

1-*Phenyl*-3-*carbomethoxy*-4-*phenylazo*-5-*pyrazolone* was obtained in 60% yield by refluxing 1-phenyl-3-carboxy-4-phenylazo-5-pyrazolone (1·4 g) in methanol (50 ml) with conc. sulphuric acid (5 ml) for 4 hr. The resulting red solution was evaporated to low bulk *in vacuo*, and poured into water (250 ml); this was extracted with ether (3 × 100 ml) and the ether layers extracted with saturated sodium bicarbonate solution (2 × 50 ml), washed with water, dried and evaporated to leave an orange-coloured solid. After 2 recrystallizations from ethanol this solid had m.p. 135–136°, lit. m.p. 138°.[36]

1-*Phenyl*-3-*carbethoxy*-4-(p-*acetoxyphenylazo*)-5-*pyrazolone*. Details of the preparation of this compound[2] will be reported later. The compound had m.p. 133–134°.

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[32] C. Mollenhoff, *Ber. Dtsch. Chem. Ges.* **25**, 1941 (1892).
[33] R. Anschutz, *Liebigs Ann.* **294**, 232 (1896).
[34] A. Eibner, *Ber. Dtsch. Chem. Ges.* **36**, 2687 (1903).
[35] L. Knorr, *Ber. Dtsch. Chem. Ges.* **21**, 1201 (1888).
[36] F. D. Chattaway and W. J. Humphrey, *J. Chem. Soc.* 1323 (1927).