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THE TAUTOMERISM OF HETEROAROMATIC COMPOUNDS WITH FIVE-MEMBERED RINGS—IV*[1]

1-SUBSTITUTED PYRAZOLIN-5-ONES

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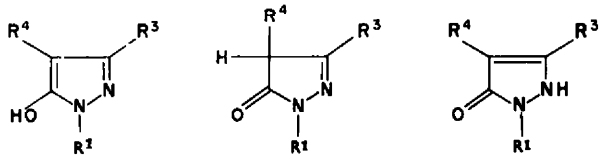
Abstract—The IR, UV, and NMR spectra and p*K* values are discussed of six potentially tautomeric 1-phenyl and 1-methyl-pyrazolin-5-ones. These compounds exist under most conditions in non polar media in the Δ^3-form. In aqueous solution the NH-formis in equilibrium with ca.10% of the OH-form. The effect of substituents, and the relation of the results to those for the corresponding isoxazolin-5-ones is discussed. Previous work is reviewed.

1-SUBSTITUTED pyrazolin-5-ones can exist in three tautomeric forms I, II, and III, which are denoted the OH, CH, and NH forms for brevity. A lot of attention[2–19]



I II III

has been devoted to the tautomerism of compounds of this type, but much of it is, or appeared to be, contradictory. Most of the references quoted do not make adequate

* *Note added in proof, October* 1963. Since submission of the manuscript of this paper, R. Jones, A. J. Ryan, S. Sternhell, and S. E. Wright (*Tetrahedron*, **19**, 1497 (1963)) have published another investigation of the tautomerism of pyrazolin-5-ones. Insufficient data, and errors of interpretation, lead to the false conclusion that "no such tautomerism exists, and a single structure can be written for each compound investigated".

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TABLE 1. SUMMARY OF PREVIOUS INVESTIGATIONS

Ref.	Year	Tautomeric Pyrazolone substituents R^1	R^3	R^4	Method	Phase	Fixed Derivatives Comparison	Conclusion on Tautomerism	Remarks
4.	1941	Ph Ph	Me Me	— Me	UV	EtOH	CMe, NMe	CH + NH	no proportions given. OH not considered.
5,6.	1941	Ph	Me	—	UV	C_6H_{12} EtOH	OMe	"all structures important"	—
7.	1952	Ph	Me	Br	UV	$CHCl_3$ EtOH	CMe	CH OH or NH	Comparison between effect of Br and H made.
8.	1953	Ph	Ph	R	UV pK IR	H_2O H_2O nujol	— — —	OH or NH OH	—
9.	1958	Me Ph	H Me Ph Br	H Me Ph	IR	nujol	CMe	not CH	incidental to another investigation
10.	1958	Ph	Me	—	IR	$CHCl_3$ CH_3CN KBr	— — —	CH CH + OH NH or OH	—
11.	1959	Me Ph Ph	CF_3 — CF_3 $-(CH_2)_4-$		IR	nujol	CR, NMe	NH	zwitterionic structure proposed.
12.	1959	Ph	Me	N_2Ar	IR	KBr	—	CH or 4=N.NHPh	no firm conclusion
13.	1959	Ph Ph	Me Me	 N_2Ph	IR IR	nujol $CHCl_3$	?	? 4=N.NHPh	—
14.	1959	Ph	Me	COR	recrystn^n. $CHCl_3$–etc.			CH or OH	both forms claimed to be isolated.
15.	1959	Ph	MeC.COMe CH_2		IR	KBr		OH	chelated
16.	1960	Ph Ph Ph	Me Me Me	Me H N:NPh	IR IR UV	KBr $CHCl_3$ KBr $CHCl_3$ MeOH	— — C-Me CMe	OH CH OH OH	— chelated OH
17.	1960	Ph	Ar	N_2Ph	IR	KBr	—	CH	OH, NH band reported absent.
18.	1960	2,4-$(NO_2)_2$-C_6H_3	Ph	—	IR NMR	$CHCl_3$ $CDCl_3$	—	CH	suggests that CH always occurs.
19.	1961	Me Ph Ph	Me Ph Me	—	IR p*K*	KBr AcOH	CMe, NMe, OMe CMe, NMe, OMe	OH NH + OH (1:1)	— CH not considered

reference to previous work, and in no single paper is a clear summary of the field presented. Because of the importance of pyrazolinones as pharmaceuticals and dyestuffs,[20] and following work in this laboratory on the related isoxazolin-5-ones[1,21] we have now examined 1-substituted pyrazolin-5-ones. We present in this paper a brief account of previous work, the results of a fresh investigation using a combination of physical methods, and a summary of the overall position.

Previous work. Knorr realised in 1895[2] that isoxazolin-5-ones could give three types of derivative, corresponding to the three tautomeric forms and postulated a mobile equilibrium between them. The tautomerism has frequently been discussed intelligently without definite conclusions being reached (e.g. ref. 3). The results of previous investigations by physical methods[4–19] are summarized in Table 1. The p*K* measurements of Veibel should also be mentioned.[22–24]

Preparation of compounds was carried out by the literature methods noted in the experimental section. Difficulty was encountered in the preparation of 3,4-dimethyl-5-ethoxy-1-phenylpyrazole from ethyl methylacetoacetate: the starting material contained only a small amount of the dimethyl-analogue, but the latter reacted preferentially with phenylhydrazine forming 3,4,4-trimethyl-1-phenylpyrazolin-5-one. The ethoxy-compound was finally separated using a Dowex 50 ion-exchange column.

Preparation of 1-methyl-3,4-tetramethylene pyrazolin-5-one was also attempted; however, although we obtained satisfactory analytical figures, the spectra indicated that this compound had been oxidized to the 4,4′-bis derivative. Easy oxidation of 3,4-dimethyl-1-phenylpyrazolin-5-one was reported,[25] but had not occurred in our case as shown particularly by the UV spectra.

IR Spectra

Fixed [1H, 2H,]-*pyrazolin-5-ones.* IR spectra of the three available 1,2-disubstituted pyrazolin-5-ones are summarized in Table 2. The spectra are mutually similar, and comparison with the spectra of corresponding 2H-isoxazol-5-ones[1,21] allows tentative assignments of some of the bands (cf. Table 2). ν C=O occurs at ca. 1655 cm^{-1} for chloroform solutions, and somewhat higher for measurements in carbon tetrachloride.

Fixed [1H, 4H]-*pyrazolin-5-ones.* The spectra of two 1,4,4-trisubstituted pyrazolin-5-ones are included in Table 3, together with a number of potentially tautomeric compounds which exist is this form. The group of spectra show large overall similarity. Tentative assignments are given for some of the bands as suggested by other work on heterocyclic compounds.[26] The carbonyl stretching frequency is found at 1698–1694 for the 1-methyl compounds and at 1712–1705 cm^{-1} for the 1-phenyl analogues.

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TABLE 2. IR SPECTRA OF [1H, 2H] PYRAZOLIN-5-ONES

Substits. 1	2	3	4	Phase	Conc. M	C=O cm⁻¹	ε_A	C=C pyrazolin-one ring cm⁻¹	ε_A	phenyl ring cm⁻¹	ε_A	phenyl + pyrazolin-one ring cm⁻¹	ε_A	Me cm⁻¹	ε_A	? cm⁻¹	ε_A	pyrazolin-one ring cm⁻¹	ε_A	Me cm⁻¹	ε_A
Ph	Me	Me	H	$CHCl_3$	0·2	1658	750	1595	200	1499 1479	220 80	1459	95	1440	60	1424	65	1400	160	1370	70
Ph	Me	Me	Me	$CHCl_3$	0·2	1657	350	1596	180	1499	200	1458	105	1440	70	1426	80	1412	90	1386 1360	50 90
Me	Me	Me	H	CCl_4	sat.	1667	vs	1587	m	—		1465	m	1443	m	—		1406	s	1365	m

pyrazolinone ring and methyl deformation modes														phenyl βCH				?		?		?	
cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A
1339	125	1311	100	—		1175 1169	30 30	1139	90	1103	25	1082	20	1055	20	1031	15	1004	5	983	10	855	20
1344	80	1308	80	1289 1270	80 120	1171*	30	1146	105	1110	25	1082	20	1071	25	1021	15	—		950	25	911	15
—		1315	w	1271	w	1200	m	—		1125	m	1095	m	—		1035	w	1003	w	—		839	w

TABLE 3. INFRARED SPECTRA OF (1H, 4H)-PYRAZOLIN-5-ONES

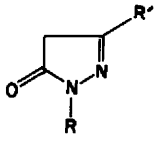
1	Substits. 3	4,4	Phase	Conc. M	C=O cm⁻¹	ε_A	C=N cm⁻¹	ε_A	Ph cm⁻¹	ε_A	Ph cm⁻¹	ε_A	? cm⁻¹	ε_A	3-Me cm⁻¹	ε_A	CH def modes cm⁻¹	ε_A	cm⁻¹	ε_A	N-Ph cm⁻¹	ε_A
Me	Me	Me_2	$CHCl_3$	0.2	1695	390	1610	35	A			A	1471	90	1434	105	{1397 {1392	90 90	1384	90		A
Me	Me	H_2	$CHCl_3$	0.02	1694	430	1605	55	A			A	1472	30	1434	40	1407	40	{1389 {1376	75 240		A
Me	Ph	H_2	$CHCl_3$	sat.	1698	s	1601	m	—		1452	w	—		—		1402	w	1380	w		A
Ph	Me	Me_2	$CHCl_3$	0.2	1705	390	1620	45	1598	165	{1503 {1490*	290 150	1465	85	1434	65	1400	105	1386	100	1365	320
Ph	Me	H_2	$CHCl_3$	0.2	1706	430	1616*	45	{1597 {1566	150 40	{1502 {1485*	350	1461	40	1437	55	1405	70	—		1364	390
Ph	Me	Me,H[a]	$CHCl_3$	0.2	1710	420	1625*	10	1602	190	{1507 {1496*	330	1465	60	1438	75	1399	105	—		{1372 {1333	350 55
Ph	Ph	H_2	$CHCl_3$	0.02	1707	360	(—)		{1598 {1564	130 20	1494 1480*	140	1451	55	—		1399	85	1378	110	1328	215
Ph	—($CH_2)_4$—[a]		$CHCl_3$	0.02	1712	360	1630*	50	1603	230	1494	90	1453	50	—		—		1386	125	1339	130

? cm⁻¹	ε_A	? cm⁻¹	ε_A	pyrazolinone ring cm⁻¹	ε_A	Phenyl β-CH cm⁻¹	ε_A	cm⁻¹	ε_A	pyrazolinone ring cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A
1317	45	1155	45	1054	40		A		A	1017	15	962	35	925	15
1326	100	1132	25	1097	35		A		A	1015	35	962	60	900	10
1350	m	—		1102	w	1076	w	1042	w	—		—		918	m
1309	250	{1174 {1159	45 145	{1102* {1091	25 70	1060	20	1026	15	998	25	955	20	{901 {877	20 35
1319	270	{1193 {1168	65 35	{1110 {1097	65 45	1064	10	1028	25	998	20	955	15	900	45
1297	135	{1180 {1150	50 110	{1120 {1089	70 75	1063	35	1025	30	1003	30	951	5	908	40
{1306* {1290	70 35	1160	40	{1118 {1100	190 70	1067	55	1029	20	1017	20	952	15	{905 {890	30 40
1316	120	1146	80	{1118 {1085	70 60	1056	70	—		1016	30	—		905	25

[a] Spectra of solutions which have stood for one week

1-Substituted 5-alkoxypyrazoles. IR bands of the 5-alkoxypyrazoles are recorded in Table 4. Little is known of the IR spectra of pyrazoles (for ref. see 26); tentative assignments for some of the bands follow from literature data.[26] For the determination of tautomeric structure it is important that strong absorption does not occur above 1600 cm^{-1}.

IR spectra of tautomeric pyrazolin-5-ones. The spectra are included in the Tables according to the tautomeric form in which the compounds exist.



IV

Pyrazolin-5-ones in which the 4-position is unsubstituted exist in the CH form (IV) in chloroform solution both for the 1-phenyl series (IV, R = Ph, R' = Me, Ph) and the 1-methyl series (IV, R = Me, R' = Me, Ph). 1,3-Dimethyl-, and 3-methyl-1-phenyl-pyrazolin-5-one were also examined in carbon tetrachloride: the spectra (not reported) are very similar to those in chloroform solution and demonstrate the CH-form: the ν C=O showed hypsochromic shifts of 20 and 14 cm^{-1} to 1714 and 1720 cm^{-1} respectively. Such a shift is expected because hydrogen bonding with the solvent occurs in chloroform but not in carbon tetrachloride solution.

The solution spectra for 4-substituted pyrazolin-5-ones are generally more complicated. The spectrum of a chloroform (or carbon tetrachloride) solution of 3,4-dimethyl-1-phenylpyrazolin-5-one which has stood for several days shows a striking similarity to those of the 3-monomethyl- and 3,4,4-trimethyl-analogues (Fig. 1 and Table 3). However, freshly prepared solutions in chloroform, carbon tetrachloride, bromoform, and tetrachloroethylene, while similar among themselves, are markedly different to the above mentioned spectra: e.g. strong bands occur at ca. 1630 and 1316 cm^{-1} and the relative intensity at 1462 and 952 cm^{-1} is much increased (cf. Fig. 2). Apparent extinction coefficients indicate that only approximately 50% of the compound in the freshly prepared solution exists in the CH-form. The remainder is probably present in the NH-form: although ν C=O for the fixed 2H-pyrazolin-5-ones occurs at 1655 cm^{-1}, intermolecular hydrogen-bonding in the NH-derivatives might well cause a shift of ca. 20 cm^{-1}.

3,4-Tetramethylene-1-phenylpyrazolin-5-one shows very similar behaviour to the 3,4-dimethyl analogue. It is of interest that in the isoxazolin-5-one series, the 4-methyl-3-phenyl derivative exists as ca.40:60 CH:NH in freshly made up chloroform solution, and that this composition changes on standing to ca. 70:30 CH:NH.[21]

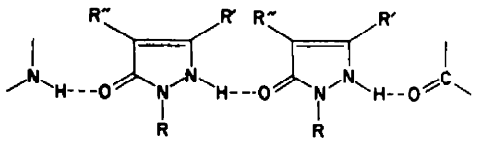
The solid state IR spectra of the tautomeric compounds show mutual similarity (Table 5). The CH-form is easily eliminated by the absence of a normal carbonyl band and evidence of strong hydrogen bonding, but differentiation between the OH and NH form is less simple. Indeed, strong hydrogen bonding blurs the distinction

[26] A. R. Katritzky and A. P. Ambler in *Physical Methods in Heterocyclic Chemistry* Vol. II (edited by A. R. Katritzky) Academic Press, New York (1963).

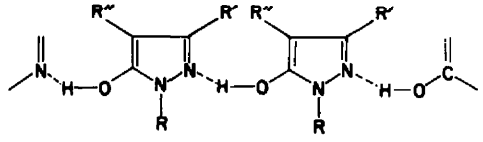
TABLE 4. IR SPECTRA OF 5-ETHOXYPYRAZOLES

Substits. 1	3	4	5	Phase	Conc. *M*	Ph cm⁻¹	ε_A	Ring cm⁻¹	ε_A	Ring cm⁻¹	ε_A	OEt cm⁻¹	ε_A	Ring cm⁻¹	ε_A	Ph cm⁻¹	ε_A	? cm⁻¹	ε_A	OEt cm⁻¹	ε_A
Me	Me	H	OEt	$CHCl_3$	0·2	A		1562	340	1527	120	1486	75	1453	65	A		1425	75	1398	175
Ph	Me	H	OEt	$CHCl_3$	0·2	1591	150	1560	340	1510	310	1474	110	1452	130	1440	130	—		1392	180
Ph	Me	Me	OEt	CCl_4	0·2	1605	180	1564	35	1509	190	1491	85	1457*	65	1439	85	—		1391	150

? cm⁻¹	ε_A	OEt cm⁻¹	ε_A	? cm⁻¹	ε_A	? cm⁻¹	ε_A	? cm⁻¹	ε_A	OEt cm⁻¹	ε_A	OEt & Ph cm⁻¹	ε_A	? cm⁻¹	ε_A	? cm⁻¹	ε_A	OEt? cm⁻¹	A
1369	45	1277	65	1198 1165	100 45	—		1111	30	1092	25	1048	95	1010	55	—		915	25
1360 1311	80 25	1263	40	1174* 1166	70 75	1142	120	1106	40	1087 1069	35 55	1048 1029	160 85	1008	55	975	15	904	50
1372	130	1282	25	—		1137	75	1100	40	1071	20	1026	75	1006*	30	957	20	903 891	17 22



V



VI

between the two forms: the NH form exists as V and the OH as VI. Proton transfer may well occur in the crystal rendering these two designations equivalent. A similar conclusion for the solid state spectra of pyrazolinones has been reached by Refn[19] (cf. Table 1).

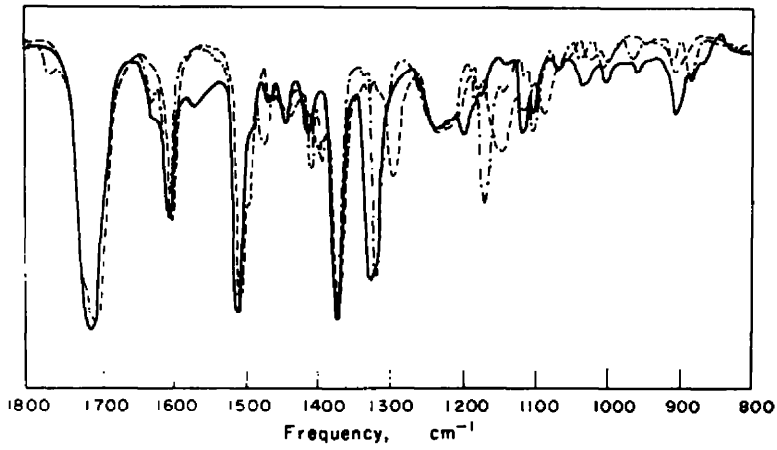


FIG. 1. IR spectra of 3-methyl- ———, 3,4-dimethyl- - - - - - - -, and 3,4,4-trimethyl-1-phenylpyrazolin-5-one ·–·–·–· All spectra are of 0·2 M chloroform solutions and that of the 3,4-dimethyl compound was measured after standing for 1 week.

UV spectra (Table 6)

1-*Phenyl series.* In cyclohexane (Fig. 3a), the 3-methyl- and 3,4-dimethyl-compounds spectrally resemble the 3,4,4-trimethyl analogue, showing that they exist predominantly in the CH form. The shoulders on the high wavelength side of the curves suggest ca. 1% and 10% of the NH form respectively. It is less easy to assess the amount of OH form, but this is probably very small. The 3,4-tetramethylene derivative resembles the 3,4-dimethyl analogue. No conclusion can be drawn as to the structure of the 3-phenyl-compounds as no methyl derivatives are available for comparison.

In aqueous buffers, the UV spectra of the 3-methyl and 3,4-dimethyl compounds (Fig. 3b) are intermediate between those of the fixed N-Me and O-Et derivatives, indicating probably mainly NH with some OH but little CH form. The spectrum of the 3,4-tetramethylene derivative is identical with that of the 3,4-dimethyl analogue.

TABLE 5. SOLID STATE SPECTRA OF TAUTOMERIC PYRAZOLONES

Substits. 1	3	4	Phase	NH/OH bonded cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A
Me	Me	H	Nuj	ca. 2500	vb	ca. 1800	vb	—		1568	s	1550	s	—		1450	m	1426	m	—			
Me	Ph	H	Nuj	ca. 2500	vb	ca. 1800	vb	—		1570	s	1537	s	1518	s	1457	m	1445 1417	m w	1382	m		
Ph	Me	H	Nuj[a]	ca. 2500	vb	ca. 1800	vb	1606	s	1585	m	1525	s	1503	s	1460	m	—		1392 1370 1346	m m m		
Ph	Ph	H	Nuj	ca. 2500	vb	ca. 1800	vb	1595	s	1555	s	1516	s	1497	w	1450	s	—		1380 1341	s s		
Ph	Me	Me	Nuj[a]	ca. 2800	vb	ca. 1950	vb	1605	s	1593	s	---		1503	s	1464	s	1415	s	1367	s		
Ph	$-(CH_2)_4-$		Nuj	ca. 2800	vb	ca. 1950	vb	1615	s	1586	s	—		1477	s	1450*	s	1407	s	1358 1311	m m		

cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A	cm⁻¹	ε_A
1269	s	—		1186	m	—		---		1034	ms	973	w	—		—		830	w	—		740	s	685 680	m m
1273	m	1205	m	1173	m	1107	w	1042	m	1031	w	965	m	910	w	—		830	w	774	m	740	s	683 675	m m
1305 1250	m w	1201	w	1165 1156	m m	—		1075 1047	w w	1029 1017	m w	—		918	m	897	w	846	w	804 777	s m	767 753	m s	709 692	w s
1246	m	1203	w	1182	w	1145 1118	m w	1085 1073	w m	1030 1020	w w	960	m	913	w	—		—		776	m	754	s	687	s
1276	m	1214	w	—		1137	m	1096	m	1033	w	978 954	w m	—		893	m	824	m	776	s	749	s	680	s
1273 1257 1240	w w	—		1183	w	1167 1138	w w	1052	w	—		952	w	917	m	852	w	836 817	w w	776	s	727	m	696	m

[a] KBr disc similar spectra

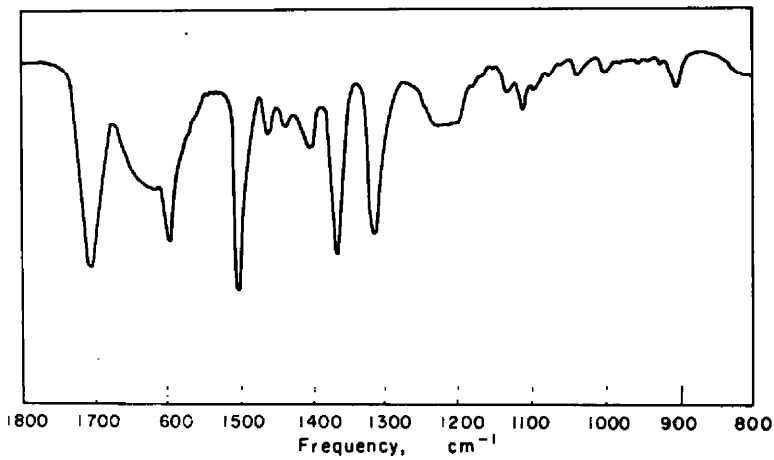
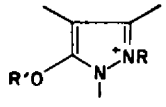


FIG. 2. IR spectra of a freshly made up 0·2 M solution of 3,4-dimethyl-1-phenyl-pyrazolin-5-one in chloroform.

For the fixed compounds, there are pronounced bathochromic shifts for aqueous → cyclohexane solutions, but the *shape* of the curve remains the same. This is not so for the tautomeric compounds, and this affords further evidence for a change in tautomeric form from predominantly CH → NH. In dioxan and ethanol intermediate behaviour is shown as illustrated in Fig. 4.



VII

The spectra in 10N sulphuric acid (Fig. 3c) show that cations of type VII are formed where possible: all the spectra similar except for the 3,4-trimethyl compound which cannot form such a cation.

TABLE 6. UV ABSORPTION MAXIMA

Substituents					Cyclohexane		Aqueous buffer		Sulphuric acid		0·1N Sodium Hydroxide	
1	2	3	4	5	λ_{max}	ε	λ_{max}	ε	λ_{max}	ε	λ_{max}	ε
Me	Me	Me			257·5	9,310	246·5	9,570	227·5[b]	8,800		—
Me		Me	Me_2		250	4,310	248	3,670	260·5[c]	3,930		—
Me		Me		OEt	—	—[a]	—	—[a]	224[b]	7,800		—
Me		Me			251	4,040	241	7,970	222·5[b]	7,860	233	6,460
Me		Ph			301	12,190	255	16,170	255[b]	20,020	252	17,250
Ph	Me	Me			239	10,020	241	9,100				
					280	9,440	253	8,690	230[d]	12,790		—
Ph	Me	Me	Me		241	10,580	246	8,910				
					278	10,080	265	8,980	236[d]	10,460		—
Ph		Me	Me_2		246	19,070	235	12,550	223·5[c]	10,400		—
Ph		Me		OEt	252	19,360	233·5	12,790	233·5[d]	15,320		—
Ph		Me	Me	OEt	259	16,370	249	11,030	238·5[b]	13,030		—
Ph		Me			245	18,050	239	12,380	231[d]	15,920	246	11,710
Ph		Me	Me		246	16,120	244	13,310	238[d]	14,420	250	12,430
Ph		—$(CH_2)_4$—			247	20,580	246	13,260	239[d]	13,920	252	13,260
Ph		Ph			263	17,850	265·5	20,680	266[d]	22,400	261	21,070

[a] End absorption only
[b] 20N—sulphuric acid
[c] 29N—sulphuric acid
[d] 10N—sulphuric acid

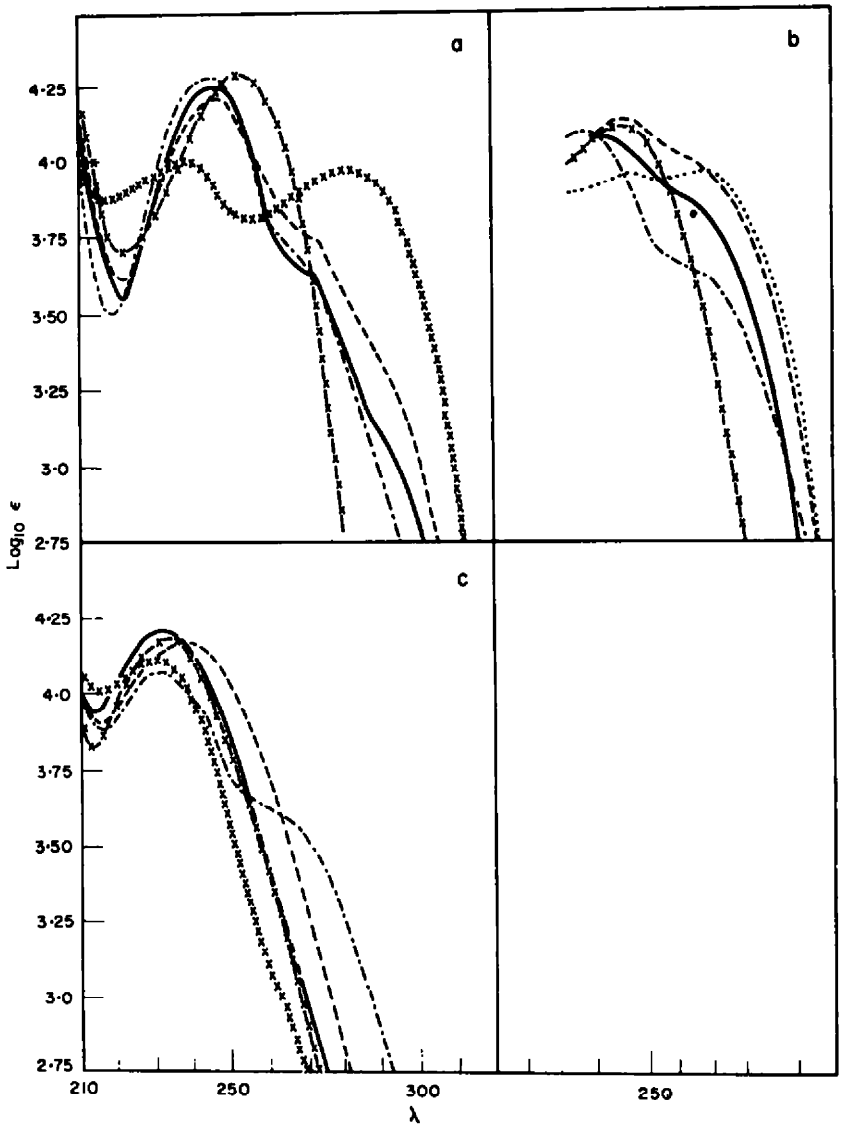


FIG. 3. UV spectra of 3-methyl- ———, 3,4-dimethyl- - - - - - -, 3,4,4-trimethyl- —·—·—·—, and 2,3-dimethyl-1-phenylpyrazolin-5-one × × × × ×, and 5-ethoxy-3-methyl-1-phenylpyrazole –×–×–×–×–×–, 2,3,4-trimethyl-1-phenyl-pyrazolin-5-one . . . . . .

(a) In cyclohexane, (b) in aqueous buffer pH 5, and (c) in 10N sulphuric acid.

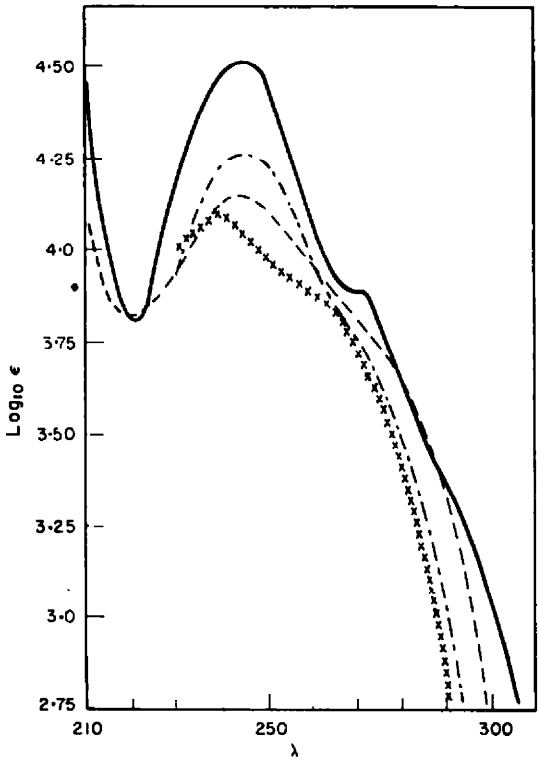
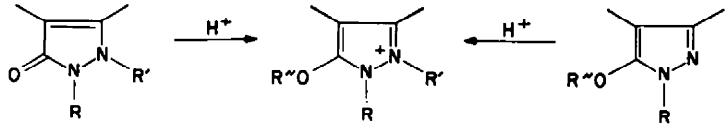


FIG. 4. UV spectra of 3,4-dimethylpyrazolin-5-one, ——— in cyclohexane, –·–·–· in dioxan, – – – – – – in ethanol, × × × × × × in aqueous buffer.

1-*Methyl series.* The results are essentially similar to those in the 1-phenyl series. In cyclohexane (Fig. 5a), the 3-methyl derivative exists in the CH form as its spectrum is similar to the 3,4,4-trimethyl analogue, and not to the other "fixed" derivatives. The curves for the aqueous solutions (Fig. 5b) indicate that in this series also a tautomeric shift to predominantly the NH-form occurs. In sulphuric acid, cations of type VIII are again formed where possible (cf. Fig. 5c).



pK measurements

An estimate of the tautomeric equilibrium between 2H-pyrazolin-5-ones of type VIII and 5-hydroxypyrazoles of type X can be obtained[27] from p*K* data, as a common mesomeric cation of type IX is formed from both.* Values in Table 7 show that, in both the 1-methyl and 1-phenyl series, the NH form predominates by a factor of ca. 10,

* Basicity data cannot give information about the proportion of the CH-form present, as this cannot form a similar cation by simple proton addition.

[27] A. R. Katritzky and J. M. Lagowski in *Advances in Heterocyclic Chemistry* **1**, (1963).

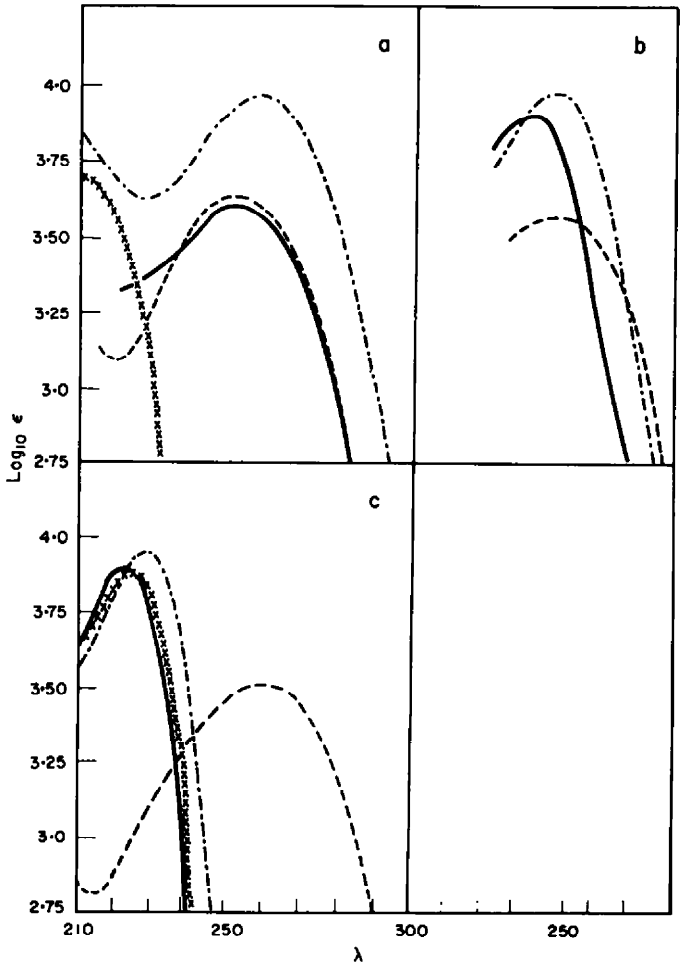


FIG. 5. UV spectra of 1,3-dimethyl- ———, 1,3,4,4-tetramethyl- - - - - - -, and 1,2,3-trimethyl-pyrazolin-5-one -·-·-·-, and 5-ethoxy-1,3-dimethylpyrazole × × × ×. (a) In cyclohexane, (b) in aqueous buffer pH 5, and (c) in 20N sulphuric acid.

TABLE 7. pK_a VALUES

Substituents						
1	2	3	4	5	pK_a as base[a]	pK_a (proton loss)
Me	—	Me	Me_2	—	−3·79 ± 0·10	—
Me	Me	Me	—	—	+2·22 ± 0·03	—
Me	—	Me	—	OEt	+3·51 ± 0·03	—
Me	—	Me	—	—	+2·35 ± 0·03	7·94 ± 0·03
Ph	—	Me	Me_2	—	−4·02 ± 0·08	—
Ph	Me	Me	—	—	+1·40 ± 0·02	—
Ph	Me	Me	Me	—	+1·24 ± 0·02	—
Ph	—	Me	—	OEt	+2·34 ± 0·03	—
Ph	—	Me	Me	OEt	+2·55 ± 0·06	—
Ph	—	Me	—	—	+1·42 ± 0·05	7·17 ± 0·03
Ph	—	Me	Me	—	+1·39 ± 0·05	7·38 ± 0·13

[a] Thermodynamic constants. For full details see F. Maine, Thesis, Cambridge, 1963

as the 2-methylpyrazol-5-ones are weaker bases by ca. 1 pK unit than the 5-ethoxypyrazoles. The 4,4-disubstituted pyrazolinones are much weaker bases. Literature pK data have been interpreted as favouring more of the OH form (OH:NH or 1:1) in acetic acid solution.[19]

In all cases, substitution of a 1-phenyl for a 1-methyl group is base weakening (by 0·3 to 1·0 pK unit). Compounds in the isoxazole series[21] are much weaker bases than their analogues of the pyrazole series.

Proton resonance spectra

Proton resonance spectra for 5-ethoxypyrazoles are given in Table 8. Assignment is straightforward, and τ and J values are in the expected ranges. The same applies to the fixed pyrazolinones of the 2H- (Table 9) and 4H-series (Table 10). Direct comparison shows clearly that the four potentially tautomeric compounds with no substituent in the 4-position all exist predominantly in the CH-form in chloroform solution (Table 10).

TABLE 8. NMR SPECTRA (τ) OF 5-ETHOXYPYRAZOLES

Phase	1-Position subst.	τ	3-Position subst.	τ	4-Position subst.	τ	5-Position subst.	τ	(multiplicity)
Liquid	Me	6·54	Me	7·91	H	4·78	OCH_2	6·08	(4, J = 7 c/s)
							CH_3	8·72	(3, J = 7 c/s)
$CHCl_3$	Ph	2·1–3·0[a]	Me	7·74	H	4·50	OCH_2	5·86	(4, J = 7 c/s)
							CH_3	8·59	(3, J = 7 c/s)
CCl_4	Ph	2·1–3·0[a]	Me	7·90	Me	8·13	OCH_2	6·12	(4, J = 7 c/s)
							CH_3	8·82	(3, J = 7 c/s)

[a] Complex peak.

TABLE 9. NMR SPECTRA (τ) OF (1H, 2H) PYRAZOLIN-5-ONES

Phase	1-Position subst.	τ	2-Position subst.	τ	3-Position subst.	τ	4-Position subst.	τ
Liquid	Me	6·71	Me	6·79	Me	7·87	H	4·91
$CHCl_3$	Ph	2·70	Me	6·97	Me	7·80[b]	H	4·63[b]
$CHCl_3$	Ph	2·4–3·0[a]	Me	7·04	Me	7·85	Me	8·15

[a] Complex peak

[b] Spin-spin coupling occurs ca. 1 c/s

TABLE 10. NMR SPECTRA (τ) OF (1H, 4H) PYRAZOLIN-5-ONES

Phase	1-Position subst.	τ	3-Position subst.	τ	4-Position subst.	τ
Liquid	Me	6·86	Me	8·04	Me, Me	8·88
$CHCl_3$	Ph	1·9–2·6[a]	Me	7·93	Me, Me	8·72
$CHCl_3$	Me	6·72	Me	7·91	H_2	6·82
$CHCl_3$	Ph	1·9–2·6[a]	Me	7·84	H_2	6·60
$CHCl_3$	Me	6·59	Ph *ca*	2·7	H_2	6·40
$CHCl_3$	Ph	1·9–2·6[a]	Ph	1·9–2·6[a]	H_2	6·25

[a] Complex peak

CONCLUSIONS

The results are summarized in Table 11. There is good agreement between the results obtained by different methods and the whole forms a logical pattern. Pyrazolin-5-ones exist in non-polar media essentially in the CH- (i.e. 4H-) form, although, in some cases, solutions freshly prepared from the solid contain large quantities of the NH-form. In aqueous solution, little of the CH-form is present, and the compounds exist essentially in the NH-form, with ca. 10% of the OH-form in equilibrium. The solids all consist of the strongly hydrogen bonded NH-form, in which proton transfer (to give the OH-form) probably takes place.

TABLE 11. TAUTOMERIC COMPOSITION OF PYRAZOLIN-5-ONES

Substituents 1	3	4	C_6H_{12} UV	CCl_4 IR	$CHCl_3$ NMR	$CHCl_3$ IR	H_2O pK	H_2O UV	Solid IR
Me	Me	H	CH	CH	CH	CH	90NH + 10.OH	Mainly NH	OH/NH
Me	Ph	H	—	—	CH	CH	—	—	OH/NH
Ph	Me	H	CH	CH	CH	CH	90NH + 10.OH	NH + some OH	OH/NH
Ph	Ph	H	—	—	CH	CH	—	—	OH/NH
Ph	Me	Me	90CH + 10NH	50CH + 50NH → CH	—	50CH + 50NH → CH	90NH + 10.OH	NH + some OH	OH/NH
Ph	—(CH₂)₄—		90CH + 10NH	—	—	50CH + 50NH → CH	—	NH + some OH	OH/NH

The change-over in tautomeric form, from non-polar to polar media, is readily understood: the NH-forms are themselves much more polar and polarizable than the CH-form and the former will be favoured in media of high dielectric constant and hydrogen bonding ability. The OH-form appears to predominate only in special cases—e.g. where chelation can occur, as with 4-phenylazo-compounds (Pelz *et al.*[16]).

Comparison of this overall picture with the corresponding isoxazolin-5-ones[1,21] reveals a large similarity, but the effect of a substituent in the 4-position is less in the present series: isoxazolin-5-ones unsubstituted in the 4-position occur in the CH-form in the solid state, and the CH-form there predominates even in aqueous solution.

EXPERIMENTAL

Preparation of compounds

1-*Methyl series.* 1,3-Dimethyl-,[28] m.p. 122–123·5 (from ether, then sublimed) (lit.,[28] m.p. 117,[29] 106–109,[30] 100–105°; 1,2,3,-trimethyl-,[31] b.p. 104–105°/0·4 mm, (hydrate m.p. 39–41°) (lit.,[31] b.p. 310°, hydrate m.p. 40°); 1,3,4,4-tetramethyl b.p. 76·5°/10 mm (lit.,[32] b.p. 71–72°/24 mm.) (Found: C, 59·6; H, 8·8 Calc. for $C_7H_{12}N_2O$: C, 60·0; H, 8·6%); 1-methyl-3-phenyl-pyrazolin-5-one,[24] m.p. 213–217·5° (from ethanol) (lit.,[24] m.p. 206°) and 1,3-dimethyl-5-ethoxypyrazole,[28] b.p. 80°/15 mm b.p. (lit.,

[28] V. Auwers, *J. Prakt. Chem.* (2), **110**, 182, (1925).
[29] L. Knorr, *Liebig's Ann.*, **279**, 236, (1894).
[30] L. Wolff. *Ber. Dtsch. Chem. Res.* **41**, 555, (1908).
[31] A. Michaelis, *Ber. Dtsch. Chem. Res.* **43**, 2109, (1910).
[32] N. P. Bogunets and V. I. Bliznyukov, *Trudy Khar'kov Politekh Inst. im V. I. Lenina* 26 *Ser. Khim.-Teknol.* No. 6, 207–209, (1959): *Chem. Abstr.* **55**, 15466[h] (1961).

88–89°/10 mm) (Found: C, 60·2; H, 8·8; Calculated for $C_7H_{12}N_2O$; C, 60·0; H, 8·63). were made by the literature methods indicated.

1-*Phenyl series.* 3-Methyl-,[33] m.p. 131–133° (from water) (lit.,[33] m.p. 126°); 2,3-dimethyl- (L. Light and Co.), m.p. 113–116° (from toluene) (lit.,[34] m.p. 113°); 3,4-dimethyl-[35] m.p. 123–124·5° (from ethanol) (lit.,[35] m.p. 120°); 3,4,4-trimethyl-,[34] m.p. 56–59° (from 60–80° pet ether) (lit.,[34] m.p. 55°); 2,3,4-trimethyl-,[34] m.p. 80·5–82·5 (from ether–pet ether) (lit.,[34] m.p. 82°); 3,4-tetramethylene-,[36] m.p. 181·5–183·5 (from ethanol (lit.,[36] m.p. 165°) (Found: C, 72·45; H, 6·8; N, 13·4. Calc. for $C_{13}H_{14}N_2O$: C, 72·9; H, 6·6; N, 13·1%); and 1,3-diphenyl-pyrazolin-5-one,[38] m.p. 137·5–139·5° (lit.,[37] m.p. 137°) were made by the literature methods indicated.

5-Ethoxy-3-methyl-1-phenylpyrazole[38] had m.p. 37–39° (from pet ether) (lit.,[38] m.p. 38·5). The 3,4-dimethyl anologue[39] prepared from ethyl methylacetoacetate and phenylhydrazine was grossly contaminated with 3,4,4-trimethyl-1-phenylpyrazolin-5-one. The mixture (4 g) was placed on a Dowex 50 column (200 g) and the pyrazolinone washed off with water. After washing with dil. HCl, ethanol then eluted the ethoxy-compound. Molecular distillation gave product of b.p. 73°C/2 mm, yield 0·5 g, 12% yield. (Found: C, 72·07; H, 7·82; N, 12·50. Calc. for $C_{13}H_{16}N_2O$: C, 72·19; H, 7·46; N, 12·96%).

[33] L. Knorr, *Ber. Dtsch. Chem. Res.* **16,** 2597, (1883).
[34] L. Knorr, *Liebig's Ann.* **238,** 160, (1887).
[35] L. Knorr, *Ber. Dtsch. Chem. Res.* **17,** 2050, (1884).
[36] W. Dieckmann, *Liebigs Ann.* **317,** 102, (1901).
[37] L. Knorr, *Ber. Dtsch. Chem. Res.* **20,** 2546, (1887).
[38] P. C. Freer, *J. Prakt. Chem.* (2) **47,** 246, (1893).
[39] Fr. Stolz, *J. Prakt. Chem.* (2) **55,** 159, (1897).