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# TAUTOMERISM IN THE 5-PYRAZOLONE SERIES

## 1(H)-5-PYRAZOLONES AND INDAZOLONES

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**Abstract**—Structure (I) is shown to be the correct formulation for the compound hitherto considered to be the "azine" of ethyl acetoacetate; I rearranges to IV. Both IV, 1(H)-3-methyl, and 1(H)-3-phenyl, 5-pyrazolones and related compounds are shown to exist in the enolic form (VII) in the solid state and predominantly so in the solvents in which they are soluble. Similarly the indazolones are found to be represented exclusively by the enolized structure XII. The acetates of both series are reformulated where necessary on the basis of spectroscopic data, and the high frequencies found for the carbonyl groups in the IR are shown to reflect a lack of conjugation with the $\pi$-electrons of the heterocyclic ring.

THE "azine" of ethyl acetoacetate was reported to undergo a facile rearrangement[1,2] and this we have confirmed but a closer examination of the structure of the azine has shown it to be the tautomer I. The rearrangement products, derivatives of 3-methyl-5-pyrazolone, are best formulated in terms of the enolic form for the heterocyclic ring and by extending the study to other derivatives it is possible to show that the N-unsubstituted pyrazolones exist generally as enols.

Structure I may be deduced for Wolffe's azine directly from the NMR assignments shown in Fig. 1 and for comparison, the $\tau$ values obtained for the N-acetylhydrazone of ethyl acetoacetate are included. The tautomerization was not induced by the solvent required for the physical measurement because I was recovered unchanged from the

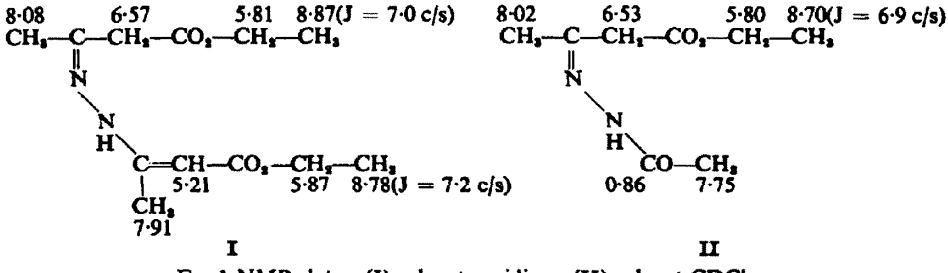



FIG 1 NMR data: (I) solvent pyridine; (II) solvent $CDCl_3$.

sample tube. Compound I rearranges readily to ester IV and this intramolecular cyclization may be understood as proceeding through III followed by ring-opening and rotation about the $C_3$–$C_4$ carbon bond with subsequent recyclization (Fig. 2).

The ester IV is unambiguously formulated on the basis of NMR and IR data which eliminate the alternative[2] structure V. The IR spectrum (KCl disc) shows a

[1] L. Wolffe, *Ber. Dtsch. Chem. Ges.* **37**, 2830 (1904).
[2] L. Wolffe, *Ber. Dtsch. Chem. Ges.* **38**, 3036 (1905).

sharp maximum at 3340 $cm^{-1}$ (NH) and a broad band from 2600 to 2800 $cm^{-1}$, typical of a strongly hydrogen-bonded hydroxyl group. The only carbonyl absorption appears at 1670 $cm^{-1}$ and in the absence of reference compounds would not be inconsistent with an amide band. In examples cited below, however, the cyclic amide group absorbs at a frequency higher than 1700 $cm^{-1}$ and hence the 1670 $cm^{-1}$ absorption is ascribed to the ester carbonyl.

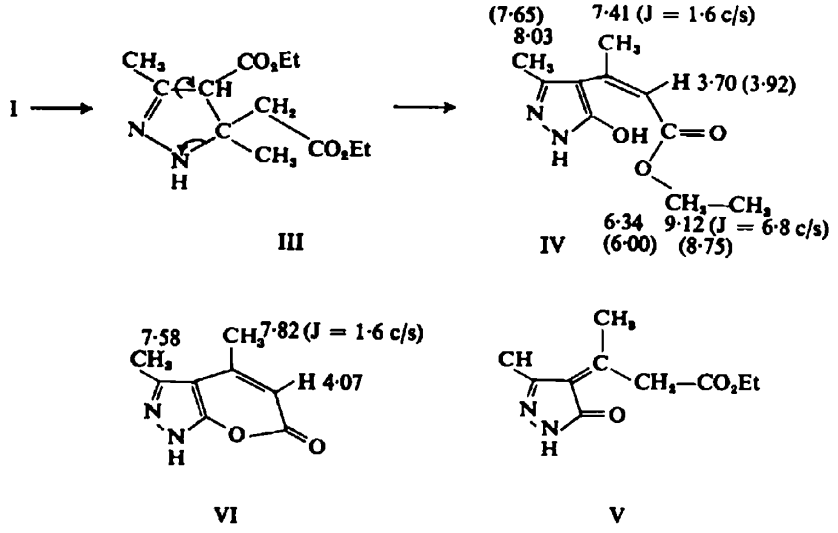



FIG. 2 NMR: (IV) and (VI); Solvent pyridine. Dimethylsulphoxide values are shown in parenthesis.

The formulation[2] for VI is confirmed and follows from the NMR assignments. The IR spectrum suggested an NH group ($\nu_{NH}$(KCl) 3225 $cm^{-1}$, broad) which was removed by acetylation,[3] and the product is formulated as the 1-(N)acetyl derivative ($\nu_{CO}$(KCl) 1739 $cm^{-1}$).

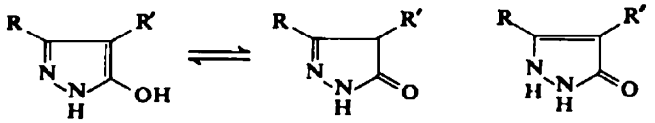
The NMR $\tau$ values found for the 3-methyl substituent in the ester IV and lactone VI appear to reflect differences in electron density in the heterocyclic ring, e.g. the 1-(N)acetyl derivative of VI shows, in the NMR spectrum, the 3-methyl to have a $\tau$ value of 7·12 or 7·28. This moves to $\tau$ 7·58 in VI and $\tau$ 8·03 in IV. In this last case, interaction of the basic solvent pyridine through the lone pair with the NH group or more probably with the OH group will increase the electron density in the ring.

The high $\tau$ values for the ethyl protons in the ester IV observed in pyridine, and taking I and II as standards, may be understood if we assume them to be within the magnetic influence of the lone pairs on the 5-hydroxyl group. The difference observed in dimethylsulphoxide as solvent is consistent with the reduced H-bonding likely to occur in this solvent. These arguments imply the configuration about the double bond shown in Fig. 2.

Spectral data in both solution and the solid state are consistent with the formulation of ester IV in the enolic form of the pyrazolone ring and this suggested that other simpler 1(H)-5-pyrazolones may also be better formulated as the enol rather

[3] L. Wolffe and W. Schreiner, *Ber. Dtsch. Chem. Ges.* **41**, 550 (1908).

than as the lactam. Keto-enol tautomerism in 5-pyrazolones in not a new concept. The 1-phenyl and 1-methyl series have been extensively reviewed[4,5] and investigated with the conclusion that the tautomeric equilibrium is in part, at least, dependent on the polarity of the solvent. Less work has been reported on the N-protonated series presumably because lack of solubility in suitable non-polar solvents reduces the effectiveness of some spectroscopic methods. Nevertheless, this present study provides evidence which shows that a majority of substituted 1(H)-5-pyrazolones may be better formulated as the enol VII rather than as the lactam VIII. Other structures such as IX may be written, in fact a total of five tautomers are possible[6] but initially, we shall discuss the problem in terms of VII and VIII.

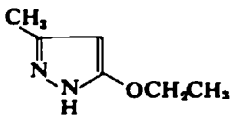



VII VIII IX

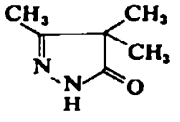
The striking feature of the IR spectrum in the solid state of 3-methyl, 5-pyrazolone (Table 1) is the broad hydrogen-bonded absorption extending from 3500 to 2300 $cm^{-1}$, with the first intense and sharp absorption maximum at 1610 $cm^{-1}$. The remainder of the spectrum is not well resolved. This pattern is changed after crystallization from $D_2O$ when not only the NH proton, but as will be shown later, the proton at position 4 is also exchanged.[7] The deuterated sample shows unresolved maxima centred at about 2700 and 2100 $cm^{-1}$. The maximum at 1610 $cm^{-1}$ is retained. The frequency shift is in good agreement if we assume NH and OH groups in the molecule. A weak shoulder at 1700 $cm^{-1}$ in the NH form is absent in the deuterated compound suggesting that the absorption is due to Fermi resonance rather than to a ketonic tautomer. The 1610 $cm^{-1}$ absorption maximum is interpreted, by analogy with the IR of 3-methyl-5-ethoxypyrazole (X) which shows a maximum at 1577 $cm^{-1}$, as due to either C=N or C=C(OR) absorption. The solid state IR spectra of 3,4-dimethyl, 3-methyl-4-bromo, and 3-phenyl-5-pyrazolone are remarkably similar in the functional group region to 3-methyl-5-pyrazolone with broad NH/OH absorption. In these examples within the series, and where the substitution pattern allows enolization, there is no maximum above 1626 $cm^{-1}$ to be assigned to carbonyl absorption. As a check, 3,4,4-trimethyl-5-pyrazolone (XI) was prepared. In this example tautomerism of the type VII $\rightleftharpoons$ VIII cannot occur. The expected NH absorption appeared at 3460 and 3246 $cm^{-1}$ ($CHCl_3$) and the strong maximum at 1710 $cm^{-1}$ is assigned to the lactam carbonyl. In our hands (cf. Ref. 7) 3-methyl-5-pyrazolone was insufficiently soluble in chloroform to obtain other than a straight line graph after compensation. These IR spectral results agree with other,[6] although less recently published work and provide evidence that in the solid state, tautomer VII best represents these 1(H)-5-pyrazolone systems.

[4] A. R. Katritzky and J. M. Lagowski, *Advances in Heterocycloic Chemistry*, Vol. 2; p. 27. Academic Press, N.Y. (1963).
[5] A. R. Katritzky and F. W. Maine, *Tetrahedron* **20**, 299 (1964).
[6] S. Refn, *Spectrochim. Acta* **17**, 40 (1961).
[7] R. Jones, A. J. Ryan, S. Sternhell and S. E. Wright, *Tetrahedron* **19**, 1497 (1963).

NMR spectral studies (Table 2) encountered the same difficulties as the IR determinations, viz., lack of solubility in non-polar solvents. Using pyridine as solvent two sharp resonance lines in the NMR spectrum of 3-methyl-5-pyrazolone were assigned to the 3-methyl and 4-vinyl protons on the basis of integrated areas. Structure VII is consistent with the absence of a methylene group. No NH/OH resonance lines were observed in this solvent because of the accelerated rate of proton exchange. Other workers[7] have observed the rapid proton exchange which can occur in this system and this was confirmed by the presence of the methyl resonance only, in the NMR (pyridine as solvent) after 3-methyl-5-pyrazolone was recrystallized from $D_2O$ and dried. Using dimethylsulphoxide as solvent a broad absorption at $\tau$ −0·94, as well as two sharp singlets, was observed for 3-methyl, 5-pyrazolone and this is interpreted as NH and OH group resonances. The vinylic proton line was also present in the spectrum. A similar broad maximum centred at $\tau$ 1·67 was apparent in the spectrum of X and is ascribed to NH resonance.



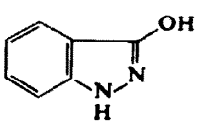

X




XI

The structural study can be taken further. If enolization can occur, acetylation must lead to either an N-acetate or an O-acetate and since vinylic acetates have characteristically high IR frequencies, their formation will be readily detected. This, however, would be no proof of the prior existence of the enol because of the nature of the mechanism of acetate formation. Simple acetylation procedures formed a mono-acetyl derivative of 3-methyl-5-pyrazolone and this was converted to the diacetyl derivative by prolonged reaction. The IR of the mono-acetyl derivative showed absorption at 1600 $cm^{-1}$, i.e., slightly moved from the position found in the parent compound but with a new, intense band at 1709 $cm^{-1}$ assigned to the N-acetyl group. The broad hydrogen-bonded hydroxyl absorption was observed at 2590 $cm^{-1}$ and in the NMR ($CDCl_3$ as solvent), this appeared as a broad resonance at $\tau$ 1·1. The correctness of the interpreptation was confirmed by the spectrum of the diacetyl derivative which showed maxima at 1770 $cm^{-1}$ (vinylic acetate), 1730 $cm^{-1}$ (N-acetyl) and 1587 $cm^{-1}$ (ring unsaturation) in the IR, and in the NMR (Table 2) the sharp resonances expected for the carbon protons. Similar data were obtained for the dibenzoyl derivative viz., 1754 $cm^{-1}$ (vinylic benzoate) and 1706 $cm^{-1}$ (N-benzoyl) confirming the correctness of its earlier formulation[8] as 1-benzoyl,3-methyl,5-benzoyl-oxypyrazole. The isomeric acetates of 3-phenyl-5-pyrazolone are reported in Table 1 and the structures differentiated by the IR data confirm the formulations[9] earlier proposed. The N-acetyl derivatives of both 3-phenyl, and 3-methyl-5-pyrazolone show broad absorptions corresponding to hydrogen-bonded hydroxyls and are formulated in terms of structure VII. More explicitly, the consistency between the IR spectra in the *solid state* of 3-methyl, and 3-phenyl-5-pyrazolones and their derivatives discussed above require the parent compounds to be formulated as enols.

[8] C. A. Rojahn, *Chem. Ber.* **55B**, 293 (1922); *Chem. Abstr.* **16**, 2507 (1922).
[9] A. Weissberger and H. D. Porter, *J. Amer. Chem. Soc.* **65**, 1495 (1943).


XII


XIII

Indazolone (XII) derivatives represent another series in which keto-enol tautomerism may exist. The interpretation in this series is however, readily resolved because, despite the limited application possible for NMR data, both IR and UV spectra are unambiguously in agreement that in the solid state, and the solvent systems used, the predominating, if not exclusive species present is the enol.

The criterion of close similarity of UV spectra between the parent compound and alkyl derivative of fixed structure was excellently met in a comparison of indazolone and its O-methyl ether (Table 3). The ether was readily prepared by methylation with diazomethane in contrast to the very sluggish and limited reaction of VII ($R=CH_3$; $R'=H$). The fusion of the benzene and pyrazolone rings enhances the stability of the anion and this explains the very marked acidity of XII over VII. An alkaline solution of XII showed the bathochromic shift associated with the presence of the anion. A similarity in spectra reflecting the structural relationship was observed between 1-acetyl,[10] 1,3-diacetyl,[10a] and 1-acetyl-3-methylindazolone. Similarly, the difference in the UV spectra between 3-tosyl, and 1-acetyl-3-tosylindazolone on one hand and 1-acetyl-2-tosylindazolone on the other, was a confirmation of the IR and chemical basis for determining their structures. The 2-tosyl derivative reported in the literature[11] is in fact 3-tosylindazolone. A similar confusion exists in the identification of 1,2- and 1,3-diacetylindazolones. All[12] except one[10a] of the diacetates previously reported are, in fact, the 1,3-diacetate the structure of which is readily evident from the IR spectrum. Pfannstiel and Janecke[13] have prepared, by heating *o*-hydrazinobenzoic acid with acetic anhydride on a water bath, a different diacetyl derivative to which we assign from the IR spectrum, the 1,2-diacetyl structure. When refluxed with acetic anhydride, it is isomerized to the 1,3-diacetyl isomer; the reverse rearrangement was not observed (cf. Ref. 9).

The IR spectra of XII and its derivatives (Table 3) support the conclusions derived from the UV spectra. The intense maximum at 1621 $cm^{-1}$ ($CHCl_3$) in the O-methyl-ether of indazolone is also found (1616 $cm^{-1}$; KCl disc) for indazolone itself. The maximum at 3413 $cm^{-1}$ (KCl disc) for indazolone is ascribed to NH absorption and the characteristically broad absorption about 2725 $cm^{-1}$ to the enolic hydroxyl.

The physical data conclusively define indazolone as XII in which the heterocyclic ring may be considered as contributing $6\pi$-electrons to the electronic system, delocalization of the $\pi$-electrons being strengthened by fusion with the benzenoid system.

In the 5-pyrazolone series of general formula VII where positions 1 and 2 are

[10a] J. J. Jennen and H. P. Eerdekens, *U.S. Patent* 2,964,402; *Chem. Abstr.* **55**, 9129 (1961);
[b] J. Meisenheimer and A. Diedrich, *Chem. Ber.* **57B**, 1715 (1924);
[c] S. Veibel and H. Lillelund, *Tetrahedron* **1**, 211 (1957).
[11] J. M. Woolley, *U.S. Patent*, 2,872,317; *Chem. Abstr.* **53**, 13853 (1959).
[12a] G. Heller and P. Jacobsohn, *Chem. Ber.* **54**, 1107, (1921);
[b] E. Fischer, *Ann der Chem*, **212**, 336 (1882). See also Ref. 10*b*.
[13] K. Pfannstiel and J. Janecke, *Chem. Ber.* **75B**, 1096 (1942).

unsubstituted, the NMR and IR data suggest that in the solvents of choice, the 3-methyl-5-pyrazolones exist in the enolic form. Within the limits of the sensitivity of the methods no ketonic forms could be detected, but their non-existence is not thereby suggested as is evidenced by deuteration proceeding presumably through the ketonic tautomer. The lack of solubility in non-polar solvents suggests a strongly hydrogen-bonded lattice in the solid state and suggestions have appeared in the literature as to how the enol might be formulated.[6,14]

A more subtle structural feature is the position of the double bonds. Of the several tautomers possible, VII is given the highest weighting. In this structure the aromatic sextet may be invoked as a stabilizing feature and as a corollary, the basic centre becomes position 2. This can be tested, and a comparison of the $\tau$ values (Table 2) found for the methyl groups at position 3 in 3-methyl, and 3,4-dimethyl-pyrazolones in pyridine or neutral solvents with the value determined in trifluoroacetic acid agrees with the view that XIII (R=$CH_3$; H.) is the protonated species. NMR data in dilute acid eliminates structure VIII for 3-methyl-5-pyrazolone in this solvent but points up the limiting feature of the technique in a study such as this, since we are unable to distinguish further between VII and IX. The hypsochromic shift in dilute HCl (Table 4) is common to all the N-unsubstituted pyrazolones. In addition, the UV spectrum observed in dilute HCl for 1,3-dimethyl-5-pyrazolone agrees with that quoted for 20 N $H_2SO_4$ as solvent by Katritzky and Maine[5] in which a protonated form XIII seems not unreasonable. On this basis only can it be concluded that in acid, form VII probably predominates. In basic solution, the spectra suggest that where enolization can occur, VII predominates as the anion. The UV spectra observed in solvents ethanol and water represent a more complex situation and are quoted for completeness, but their interpretation in terms of VII is not unambiguous on the basis of the data presented here.

The frequencies observed in the IR (Tables 1 and 3) for the ring carbonyls in the 5-pyrazolone and indazolone series where the ketonic forms VIII exist, are high for amides but agree with values expected for cyclic lactams. Presumably ring size, i.e., hybridization changes, determines the position of absorption. A rigidity effect must operate in the indazolones because the increased frequencies observed are the reverse of the expected movement when conjugated with the benzene ring.

The N-acetyl frequencies determined for both series are also sufficiently removed from the normal to warrant further comment. In most of the examples cited in the Tables, steric hindrance is not to be expected and for the indazolones, no special anisotropic effects on the benzenoid protons were observed in the NMR spectra. High amide frequencies have been reported for 4,5-dimethyl,2-benzoyl-3-isoxazolone[15] ($\nu_{benzoyl}$ 1706 $cm^{-1}$ in $CHCl_3$), 2-acetyl,5-phenyl-3-isoxazolone[16] ($\nu_{CH_3CO}$ 1705 $cm^{-1}$ in KBr), N-acetylindole[17] ($\nu_{CO}$ 1711 $cm^{-1}$), N-acetylpyrrole[18] ($\nu_{CO}$ 1732 $cm^{-1}$; film) and N-acetylindazole[19] ($\nu_{CO}$ 1726 $cm^{-1}$). An explanation is that the lone pair on the nitrogen contributes to the $\pi$-electron system and that the acyl carbonyl reflecting the

[14] G. deStevens, A. Halamandaris, P. Wenk and L. Dorfman, *J. Amer. Chem. Soc.* **81**, 6292 (1959).
[15] L. Bauer, C. N. V. Nambury and L. C. Bell, *Tetrahedron* **20**, 169 (1964).
[16] H. D. Stachel, *Chem. Ber.* **96**, 1088 (1963).
[17] H. A. Staab, W. Otting and A. Ueberle, *Z. Electrochem.* **61**, 1000 (1957).
[18] W. Otting, *Chem. Ber.* **89**, 1940 (1956).
[19] J. Derkosch and E. Rieger, *Monatsch. Chem.* **90**, 389 (1959).

TABLE 1. IR SPECTRA OF PYRAZOL-5-ONES

| Substituents | | | | Phase | CH—NH—OH Region | | 1800–1550 $cm^{-1}$ Region | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 3 | 4 | 5 | | | | | | | |
| H | $CH_3$ | H | OH | KCl | 3570 w | 2667 br | 1700 w | 1610 s | 1550 m | |
| | | | | $CH_3CN$ | | | | 1610 s | | |
| D | $CH_3$ | D | OD | KCl | | 2670 br 2100 br | | 1607 m | 1550 s | |
| H | $CH_2$ | $CH_3$ | OH | KCl | | 2700 br | | 1615 s | 1587 s 1545 m | |
| H | $CH_2$ | Br | OH | KCl | | 2667 br | | 1612 s | 1587 s | |
| H | $C_6H_5$ | H | OH | KCl | | 2564 br | | 1626 s | 1600–1592 s | 1550 s |
| H | $CH_3$ | H | OEt | KCl | 3225–3010, | 2900 s | | | 1577 s | |
| | | | | $CCl_4$ | 3475–3072, | 2978, 2884 m | | | 1575 s | |
| H | $CH_3$ | $(CH_2)_2$ | =O | KCl | 3200 | 2950 m | 1704 s | 1610 m | | |
| | | | | $CHCl_3$ | 3460, 3246, | 3021 m | 1710 s | 1612 m | | |
| $CH_3$ | $CH_2$ | $H_2$ | =O | KCl | | 2400 br | 1770 br | | 1557 br | |
| | | | | $CHCl_3$ | 3450 w | 3030 s | 1698 s | 1607 m | 1550 w | |
| Ac | $CH_3$ | H | OH | KCl | 2800 br | 2596 br | 1709 s | 1600 s | | |
| Ac | $CH_3$ | H | OAc | KCl | | 3030 s | 1770 s | 1730 s | 1588 s | |
| Bz | $CH_3$ | H | OBz | KCl | | | 1754 s | 1706 s | 1603 m | 1580 m |
| H | $C_6H_5$ | H | OAc | KCl | | 3280 m | 1740 s | 1692 sh | 1565 w | |
| Ac | $C_6H_5$ | H | OH | KCl | 3106, 2930, | 2850 br | 1712 s 1660 s, 1640 s, 1610 m, 1587, 1545 m | | | |

Ac = acetyl; Bz = benzoyl; br = broad; s = strong; m = medium; w = weak; sh = shoulder.

TABLE 2. NMR SPECTRA OF PYRAZOL-5-ONES

| Solvent | Position 1 | | Position 3 | | Position 4 | | Position 5 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Subst. | τ | Subst. | τ | Subst. | τ | Subst. | τ | |
| Pyridine | H | | $CH_3$ | 7·88 | H | 4·65 | OH | | $(CH_3)_4Si$ as marker unless otherwise noted. |
| $(CH_3)_2SO$ | | −0·94 | | 7·88 | | 4·69 | | | |
| $CF_3CO_2H$ | | | | 7·55 | | 4·11 | | | |
| $H_2O$ | | | | 7·83 | | — | | | Acetone as marker. |
| 1·0 N $HCl/H_2O$ | | | | 7·81 | | 4·25 | | | |
| 1·0 N $NaOH/H_2O$ | | | | 7·92 | | — | | | |
| $SO_2$(liquid) | | | | 7·79 | | 4·61 | | | $H_2O$ τ ca 5·2 |
| $D_2O$ | | | | 7·83 | | | | | Acetone as marker |
| $HCON(CH_3)_2$ | | | | 7·80 | | 4·67 | | | |
| Pyridine | D | | $CH_3$ | 7·80 | D | | D | | |
| Pyridine | H | | $CH_2$ | 7·87 | $CH_2$ | 7·85 | | | |
| $CF_3CO_2H$ | | | | 7·62 | | 7·98 | | | |
| $CDCl_3$ | H | 0·87 | $CH_3$ | 8·02 | $(CH_3)_2$ | 8·90 | =O | | |
| $CDCl_3$ | $CH_3$ | 6·73 | $CH_3$ | 7·91 | H, H | 6·83 | -O | | |
| $CDCl_3$ | Ac | 7·42 | $CH_3$ | 7·42 | H | 4·23 | OH | 1·10 | Integration 1:1:6 |
| $CDCl_3$ | H | 1·67 | $CH_3$ | 7·44 | H | 4·50 | OEt | 5·81, 8·06 | $J_{AX}$ = 7·2 c/s |
| $CDCl_3$ | Ac | 7·39 | $CH_3$ | 7·43 | H | 3·89 | OAc | 7·71 | |

TABLE 3. SPECTRA OF INDAZOLONES

| Solvent | NMR– Methyl resonances | | | | | | IR—Carbonyl region | | UV (ethanol) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Position 1 | | Position 2 | | Position 3 | | Phase | $cm^{-1}$ | $\lambda_{max}$ (m$\mu$) | $\Sigma \times 10^3$ |
| | Substituent | $\tau$ | Substituent | $\tau$ | Substituent | $\tau$ | | | | |
| | H | | | | OH | | KCl | 1642 sh 1616 | 220 | 22·2 |
| | | | | | | | | | 310 | 3·74 |
| | $CH_3CO$ | | | | OH | | KCl | 1701 | 242 | 9·39 |
| | | | | | | | | | 294 | 6·85 |
| | | | | | | | | | 305 | 9·25 |
| $CDCl_3$ | $CH_3CO$ | 7·24 | | | $CH_3CO$ | 7·50 | KCl | 1770, 1730, 1613 | 230 | 17·9 |
| | | | | | | | $CHCl_3$ | 1786, 1715, 1616 | 292 | 6·33 |
| | | | | | | | | | 302 | 7·62 |
| $CDCl_3$ | $CH_3CO$ | 7·27 | $CH_3CO$ | 7·66 | =O | | KCl | 1733 sh, 1712 | 228 | 17·9 |
| | | | | | | | $CHCl_3$ | 1733 br | 322 | 4·67 |
| $CDCl_3$ | H | −0·23 | | | $CH_3C_6H_4SO_3$ | 7·55 | KCl | 1626 | 208 | 37·7 |
| | | | | | | | | | 228 | 14·8 |
| | | | | | | | | | 254 | 5·16 |
| | | | | | | | | | 288 | 5·42 |
| | | | | | | | | | 298 | 4·40 |
| $CDCl_3$ | $CH_3CO$ | 7·44 | | | $CH_3C_6H_4SO_3$ | 7·52 | KCl | 1727 | 230 | 21·1 |
| | | | | | | | $CHCl_3$ | 1721 | 250 infl. | 4·91 |
| | | | | | | | | | 260 | 3·66 |
| | | | | | | | | | 292 | 4·76 |
| | | | | | | | | | 302 | 5·64 |
| $CDCl_3$ | $CH_3CO$ | 7·33 | $CH_3C_6H_4SO_3$ | 7·69 | =O | | KCl | 1742, 1695 | 228 | 22·3 |
| | | | | | | | $CHCl_3$ | 1757, 1721 | 328 | 2·06 |
| $CDCl_3$ | H | 0·67 | | | $CH_3O$ | 5·88 | KCl | 1621 | 216 | 34·0 |
| | | | | | | | $CHCl_3$ | 1621 | 300 | 4·75 |
| $CDCl_3$ | $CH_3CO$ | 7·34 | | | $CH_3O$ | 5·88 | KCl | 1698, 1613 | 242 | 13·6 |
| | | | | | | | $CHCl_3$ | 1701, 1618 | 292 | 8·12 |
| | | | | | | | | | 302 | 13·05 |

TABLE 4. UV SPECTRA OF PYRAZOL-5-ONES

| | Substituents | | Ethanol | | Water | | 0·1 N HCl | | 0·1 N NaOH | |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 3 | 4 | $\lambda_{max}$ | $\Sigma \times 10^3$ | $\lambda_{max}$ | $\Sigma \times 10^3$ | $\lambda_{max}$ | $\Sigma \times 10^3$ | $\lambda_{max}$ | $\Sigma \times 10^3$ |
| | $CH_3$ | H | 221 | 3·39 | | | | | | |
| | | | 243 | 3·32 | 238 | 7·08 | 222 | 5·50 | 230 | 6·17 |
| | $CH_3$ | $CH_3$ | 251 | 5·01 | 245 | 8·32 | 230 | 5·75 | 237 | 7·08 |
| | | | 224 | 5·00 | | | | | | |
| | $CH_3$ | Br | 253 | 3·71 | 248 | 4·16 | 235 | 7·41 | 238 | 7·76 |
| | $CH_3$ | OEt | 216 | 6·60 | 217 | 3·39 | 222 | 10 0 | - - - - | |
| | 1,2,3-Trimethyl | | 255 | 8·73 | 247 | 7·5 | 229 | 8·63 | 248 | 7·45 |
| | $CH_3$ | $(CH_3)_2$ | 242 | 7·8 | 244 | 4·0 | 238 | 7·5 | 263 | 6·3 |
| | | | | | 210 | 4·16 | | | | |
| $CH_3$ | $CH_3$ | $H_2$ | 246 | 7·86 | 240 | 7·4 | 225 | 7·41 | 232 | 5·25 |

diminished conjugation approximates more to the state of a methyl ketone modified by the direct bond to an atom of greater electronegativity. The progressive movement to higher frequencies observed in the solution spectra of the 1-acetyl-indazolones as the 3-substituent increases in electron withdrawing power (OMe < OAc < OTosyl) would appear to support this hypothesis. A similar suggestion has already appeared[18] to account for the increased frequencies observed for N-acyl derivatives of pyrrole, imidazole, triazole and tetrazole.

## EXPERIMENTAL

The compounds were prepared essentially as described in the references given:– Compound I m.p. 46° (Lit.,[1] m.p. 48°); the ester IV m.p. 188° (Lit.,[2] m.p. 186°); The lactone VI m.p. 250° (Lit.,[3] m.p. 246°); and the N-acetyl derivative of lactone VI m.p. 184° (Lit.,[3] m.p. 184°).

*N-Acetylhydrazone of acetoacetic ester.* Ethyl acetoacetate (0·01 mole) and N-acetyhydrazine (0·01 mole) were refluxed together in EtOH for 3 hr. After cooling the solution, II was filtered off, (55% yield), crystallized from ether–pet. ether (1:1) and sublimed for analysis (60°/$10^{-3}$ mm). m.p. 82°. (Found: C, 52·0; H, 7·7; N, 15·05. $C_6H_{14}N_2O_2$ requires: C, 51·6; H, 7·6; N, 15·04%.)

*1-Acetyl-3-methyl-5-pyrazolone.* Acetic anhydride (3·1 g) was added dropwise to a stirred suspension of 3-methyl-5-pyrazolone (3·0 g) in pyridine (10 ml) heated on a steam bath. As soon as solution was effected the reaction mixture was heated for a further 10 min, and then cooled, when water was added until precipitation was complete. The precipitate was filtered off and recrystallized to purity from aqueous alcohol giving a 70% yield of a white mono-acetyl derivative, m.p. 170–172°. (Found: C, 51·3; H, 5·6; N, 19·9. $C_6H_8N_2O_2$ requires: C, 51·4; H, 5·75; N, 19·99%.)

*1-Acetyl,5-acetoxy,3-methyl-5-pyrazole.* 3-Methyl-5-pyrazolone (1 g) was dissolved in acetic anhydride (5 ml) and heated on a steam bath for 1 hr. The solvent was than removed and the residue, the diacetate, sublimed as a glass for analysis, m.p. 38°, yield was 80%. (Found: C, 52·8; H, 5·8; N, 15·65. $C_8H_{10}N_2O_3$ requires: C, 52·7; H, 5·5; N, 15·4%.) Acetylation of the mono-acetate above under the same conditions also formed the diacetate.

*The following compounds* were prepared essentially as described in the literature references given:– 3-Methyl-5-pyrazolone, m.p. 217° (Lit.,[20] m.p. 219°); 1-Benzoyl, 3-methyl-5-benzoyloxypyrazole-m.p. 128° (Lit.[5] m.p. 126°); 3,4-Dimethyl-5-pyrazolone, m.p. 270° (Lit,[21] m.p. 269°); 1-Acetyl,5. acetoxy, 3,4-dimethyl-5-pyrazole, m.p. 54° (Lit.[22] m.p. 56°); 3,4,4-Trimethyl-5-pyrazolone, m.p. 108° (Lit.[23] 109°); 1,3-Dimethyl-5-pyrazolone, m.p. 117° (Lit.[23] 117°); 3-Indazolone, m.p. 246° (Lit.[24]

[20] T. Curtius and R. Jay, *J. Prakt. Chem.* **39**, 52 (1889).
[21] R. von Rothenburg, *J. Prakt. Chem.* **52**, 40 (1895).
[22] P. E. Verkade and J. Dhont, *Rec. Trav. Chim.* **64**, 165 (1945).
[23] S. Verbel, H. Eggerson and S. Linholt, *Acta Chem. Scand.* **8**, 768 (1954).
[24] E. F. M. Stephenson, *Organic Syntheses* Coll. Vol. 3, p. 470. Wiley, N.Y. (1955).

m.p. 247°); 1-Acetyl-3-indazolone, m.p. 220° (Lit.[10a,b] 211° and 215°[10c]); 1-Acetyl,3-acetoxyindazole m.p. 113° (Lit.[10a] 112°); 3-Phenyl-5-pyrazolone, m.p. 236° (Lit.[9] m.p. 236°); 3-Phenyl-5-acetoxypyrazole, m.p. 148° (Lit.[9] m.p. 148°); 1-Acetyl,3-phenyl-5-pyrazolone, m.p. 126° (Lit.[9] m.p. 128°); 3-Methyl, 5-ethoxypyrazole, m.p. 64° (Lit.[25] m.p. 67°); 3-Methyl,4-bromo-5-pyrazolone, m.p. 182° (Lit.[21] m.p. 178°), and 1,2-Diacetyl-3-indazolone, m.p. 136° (Lit.[18] m.p. 135°). 1,2-Diacetyl-3-indazolone was isomerized to 1-acetyl, 3-acetoxyindazole by refluxing with acetic anhydride for 1 hr.

*3-Tosylindazolone.* Indazolone (0·19 g) and tosylchloride (0·2 g) were refluxed in pyridine (8 ml) for 30 min. The solution was poured into water (60 ml) and the precipitate collected and crystallized from benzene or EtOH. The *tosyl* derivative (0·17 g) had m.p. 147°. (Found: C, 58·3; H, 4·3; N, 9·55; S, 11·3. $C_{14}H_{12}N_2O_3S$ requires: C, 58·3; H, 4·4; N, 9·7; S, 11·1%.)

*1-Acetyl-3-tosylindazolone.* 3-Tosylindazolone was refluxed with acetic anhydride for 2 hr and the reaction solution then stood at 19° overnight. Working up in the usual manner yielded 1-acetyl-3-tosylindazolone as pale brown needles, m.p. 106°. (Found: C, 57·8; H, 4·3; N, 8·3; S, 9·7. $C_{16}H_{14}N_2O_4S$ requires: C, 58·2; H, 4·3; N, 8·5; S, 9·7%.)

*1-Acetyl-2-tosylindazolone.* *o*-Hydrazinobenzoic acid (1·0 g) was refluxed with tosylchloride (1·0 g) in pyridine (10 ml) for 30 min. The solution was poured into water (100 ml) and the precipitate collected, and crystallized from MeOH giving *α-(o-carboxyphenyl),β-tosylhydrazine* (0·73 g) m.p. 187° (dec). (Found: C, 55·1; H, 4·7; N, 9·2. $C_{14}H_{14}N_2O_4S$ requires: C, 54·9; H, 4·6; N, 9·1%.) This compound (0·17 g) was heated on a water bath with acetic anhydride (6 ml) for 2 hr. After working-up the solution in the usual way *1-acetyl-2-tosylindazolone* (0·15 g) was obtained as colourless needles, m.p. 164°. (Found: C, 57·9; H, 4·55; N, 8·45; S, 9·95. $C_{16}H_{14}N_2O_4S$ requires: C, 58·2; H, 4·3; N, 8·5; S, 9·7%.)

*3-Methoxyindazole.* Indazolone was added to a solution of a 3-fold excess of diazomethane in ether–MeOH at 0° and the mixture let stand for 2 hr. The excess diazomethane was destroyed with acetic acid, the solvents removed *in vacuo* and the residue chromatographed on silica gel. Elution with benzene gave the *0-methyl ether* which crystallized from cyclohexane as colourless needles m.p. 104°. (Found C, 64·8; H, 5·5; N, 19·2. $C_8H_8N_2O$ requires: C, 64·85; H, 5·4; N, 18·9%.)

*1-Acetyl-3-methoxyindazole.* The acetyl derivative was prepared from 3-methoxy-indazole in the usual way. Crystallized from pet. ether for analysis, m.p. 89°. (Found: C, 63·0; H, 5·25; N, 14·8. $C_{10}H_{10}N_2O_2$ requires: C, 63·15; H, 5·3; N, 14·7%.)

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[25] H. J. Backer, and W. Meyer, *Rec. Trav. Chim.* **45**, 82 (1926).