Chemistry

1958

SovietRxiv

Abstract

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Chemistry

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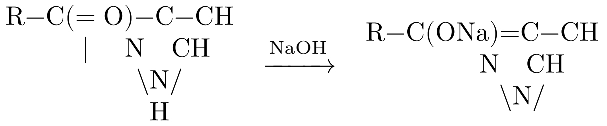
On the Acidic Properties of 3-Acylpyrazoles

(Presented by Academician A. N. Nesmeyanov on 1 VII 1958)

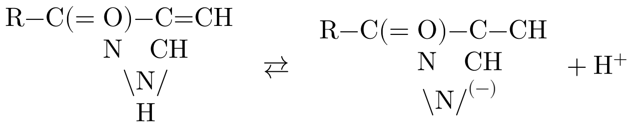
3-Acylpyrazoles, according to A. N. Nesmeyanov and N. K. Kochetkov, who developed a convenient method for the synthesis of these compounds, possess, in contrast to pyrazole and its homologs, the properties of weak acids (^{1}). To explain this phenomenon, it was suggested that salt formation is accompanied by a tautomeric shift of the double bonds, with disruption of the aromatic system of pyrazole and formation of O-metallic derivatives according to the scheme



$$\begin{array}{c}\mathrm{R{-}C(=O){-}C{-}CH}\\ |\quad \mathrm{N}\quad \mathrm{CH}\\ \backslash \mathrm{N}/\\ \mathrm{H}\end{array}\xrightarrow{\mathrm{NaOH}}\begin{array}{c}\mathrm{R{-}C(ONa){=}C{-}CH}\\ \mathrm{N}\quad \mathrm{CH}\\ \backslash \mathrm{N}/\end{array}\qquad \mathrm{(I)}$$

In favor of this supposition was the known fact of the greater electronegativity of the oxygen atom compared with the nitrogen atom, owing to which the negative charge must be concentrated predominantly on the oxygen atom. A number of cases have been described in the literature in which, in compounds containing the system of bonds O=C—C=N—NH (^{2}) or O=C—C=C—NH (^{3}-^{5}), salt formation is associated with a displacement of bonds. A study carried out earlier in our laboratory (^{6}) showed that in the ultraviolet absorption spectra of 3-acylpyrazoles, on passing from neutral to alkaline medium, a considerable bathochromic shift is observed, which seemed to indicate changes in the system of π-electrons of the molecule. At the same time, for 3,5-diphenyl-4-bromopyrazole, which also has acidic properties but is incapable of a tautomeric shift of bonds with disruption of the aromatic pyrazole system, no such noticeable shift in the ultraviolet spectrum was observed (^{7}).

Another possible explanation of the acidic properties of 3-acylpyrazoles is that, under the influence of the electron-acceptor effect of the acyl radical' s carbonyl group conjugated with the ring, the N—H bond in the pyrazole ring is polarized, as a result of which elimination of hydrogen in the form of a proton is possible:



$$\begin{array}{c}\mathrm{R{-}C(=O){-}C{=}CH}\\ \mathrm{N}\quad \mathrm{CH}\\ \backslash \mathrm{N}/\\ \mathrm{H}\end{array}\rightleftarrows\begin{array}{c}\mathrm{R{-}C(=O){-}C{-}CH}\\ \mathrm{N}\quad \mathrm{CH}\\ \backslash \mathrm{N}/^{(-)}\end{array}+\mathrm{H}^{+}\qquad \mathrm{(II)}$$

Fig. 1. Infrared spectra

Figure 1: Fig. 1. Infrared spectra

In favor of this supposition were facts known from the literature, indicating the acidic properties of pyrazole derivatives having negative substituents (^{8}-^{10}).

Initially, on the basis of a study of the UV spectra of acylpyrazoles, we were inclined to give preference to the first of the two possible explanations (^{6}); however, these data did not make it possible to choose definitively between schemes (I) and (II). In order to resolve unambiguously the question of the nature of the acidic properties of acylpyrazoles, we studied the IR spectra of several compounds of this series and of their metallic derivatives. Indeed—

Fig. 1. Infrared spectra of 3-acetylpyrazole (*a*), 3-pivaloylpyrazole (*b*), the sodium salt of 3-acetylpyrazole (*c*), and the silver salt of 3-acetylpyrazole (*d*)

—if, in the IR spectra of the salts, the frequency of the CO group were absent, as is the case for the IR spectra of salts of α- and γ-pyridones (^{11}), one could speak of a tautomeric shift during salt formation according to scheme (I); conversely, retention of the frequency of the carbonyl group in the IR spectra of the salts would unambiguously indicate salt formation according to scheme (II). We recorded the IR spectra of 3-acetyl-, 3-pivaloyl-, and 3-benzoylpyrazoles, as well as of the sodium and silver salts of 3-acetylpyrazole. The indicated 3-acylpyrazoles were synthesized by methods developed earlier in our laboratory (^{1,12}). The sodium salt of 3-acetylpyrazole was obtained in 78% yield by the reaction of sodium ethylate and 3-acetylpyrazole in alcoholic solution, followed by precipitation with ether. The powdered salt contained 10–15% sodium alcoholate, which was of no significance for our purposes.

Found, %:	N 18.83; 18.46
$C_5H_5N_2ONa$. Calculated, %:	N 21.21

The silver salt of 3-acetylpyrazole was obtained in 93% yield by reacting 3-acetylpyrazole with an aqueous ammoniacal solution of silver nitrate; it precipitated as a curdy colorless precipitate, which was filtered off and dried.

Found, %:		C 27.97; 27.90;	H 2.48; 2.38;	Ag 49.81; 49.51
$C_5H_5N_2OAg$	Calculated, %:	C 27.67;	H 2.32;	Ag 49.71

The IR spectra of all the substances obtained were recorded on an IKS-11 instrument in crystalline form (as a paste with Vaseline oil); they are shown in Fig. 1. As can be seen, in the IR spectrum of 3-acetylpyrazole (Fig. 1*a*) there is an intense band corresponding to vibrations of the C=O group at 1662 cm^{-1}

and an intense band of stretching vibrations of the bond at 3230 cm^{-1}. It is interesting to note that the shift of the C=O band, as compared with its position in saturated open-chain ketones (1725—1705 cm^{-1}), is greater upon conjugation of the carbonyl group with the pyrazole ring than upon its conjugation with a phenyl nucleus (in acetophenone the frequency of the carbonyl band is 1686 cm^{-1}). A similar and even greater effect is observed, however, for *p*-aminoacetophenone (1634 cm^{-1}) ([13]). Apparently, the reason for such a change in frequency is connected with the electron-donor properties of the amino group, leading to a decrease in the force constant of the C=O bond. In exactly the same way, in our view, one may explain the decrease in the frequency of the C=O band in 3-acetylpyrazole (see scheme (II)). This point of view is supported by the position of the carbonyl band in the IR spectra of 3-pivaloylpyrazole (1650 cm^{-1}, see Fig. 1 b) and 3-benzoylpyrazole (1636 cm^{-1}). The lowering of the frequency in these cases is explained by the fact that, in addition to the electrons supplied to the carbonyl group by the pyrazole ring, electrons are additionally supplied to it by the tert-butyl group (owing to its $+I$ effect) or by the phenyl nucleus (owing to its polarizability).

In the IR spectrum of the sodium salt of 3-acetylpyrazole (Fig. 1 c) there is an intense band of the carbonyl group at 1650 cm^{-1}, while in the region 3000—3500 cm^{-1} (vibrations of the N—H bond) there is a strongly deformed, not very intense band. We attribute the latter to impurities present. The presence of an intense carbonyl band excludes the possibility that the negative charge in the salt anion is concentrated mainly on the oxygen atom. Consequently, in the anion the negative charge is concentrated chiefly on the nitrogen atoms (or on one of them). An argument in favor of this assumption is also the fact that the frequency of the carbonyl group in the spectrum of the salt undergoes an additional shift. This phenomenon can be explained by the fact that the pyrazole ring, in which one of the nitrogen atoms bears a negative charge, is more capable of donating electrons than the "neutral" ring:

$$CH_3{-}C(=O){-}\text{pyrazole ring with } N^{(-)}$$

If one considers the IR spectrum of the silver salt of 3-acetylpyrazole (see Fig. 1 d), the same intense band is observed in it at 1662 cm^{-1} as for free 3-acetylpyrazole. At the same time the band of the N—H bond disappears completely. From this one may conclude that the silver atom replaces the hydrogen atom and that a substance is formed in which the N—Ag bond is covalent. In favor of this assumption is the fact that the vibration frequency of the carbonyl group is exactly the same as in unsubstituted 3-acetylpyrazole and, consequently, the effect observed in the case of the sodium salt of 3-acetylpyrazole and due to the charge on the nitrogen atom is absent here.

Thus, the data presented in this article compel one to reject completely the assumption of salt formation by acylpyrazoles through the formation of O-metal derivatives (scheme (I)); in connection with this, the previously supposed possibility (⁶) of tautomerism of 3-acylpyrazoles also falls away. It is clear that, since a carbonyl group is present in the metallic derivatives of 3-acylpyrazoles, salt formation of these compounds is associated with an enhancement of the polarization of the N—H bond of the pyrazole ring under the influence of the electron-acceptor effect of the acyl group (scheme (II)). Obviously, despite the high electronegativity of the oxygen atom, disruption of the aromaticity of the pyrazole ring in the case of formation of O-derivatives is so strong an obstacle that salt formation at the nitrogen atom is an energetically more favorable process.

As for the above-mentioned bathochromic shift in the UV spectra of 3-acylpyrazoles in alkaline medium, the latter is, in all probability, associated with some deformation of the π-electron system of the pyrazole ring, which is also confirmed by the shift noted above of the band of the $C = O$ group in the IR spectra of salts of 3-acetylpyrazole.

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named after M. V. Lomonosov

Received
25 VI 1958

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Note: Figure translations are in progress. See original paper for figures.