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Pyrazole Studies

X *. The Kinetics of Oxidation by Oxygen of 3,4-Substituted Pyrazol-5-ones in the Presence of Alkanolate Ions

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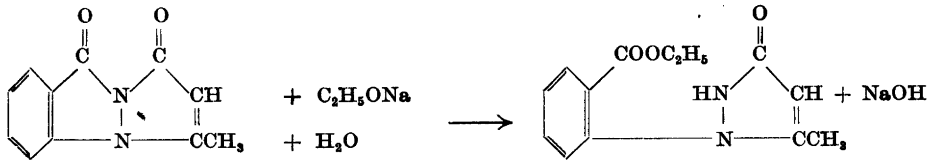
The oxidation by oxygen of pyrazol-5-ones unsubstituted at N_1 leads to unidentified oily oxidation products when water is present. In anhydrous solvents, however, the oxidation, catalysed by alkanolate ions, leads to 4-hydroxysubstituted pyrazol-5-ones, isolable in 80—92 % yield. The kinetics of the reaction is discussed.

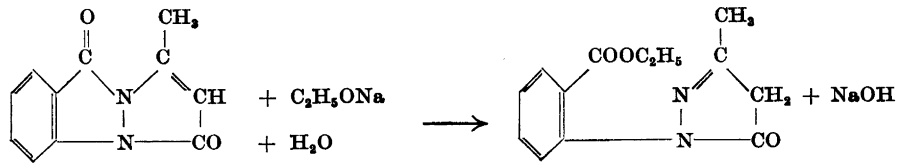
In previous papers was mentioned that the oxidation by oxygen of 3,4-substituted pyrazol-5-ones in the presence of triethylamine[2] or hydroxyl ions[1] cannot be adapted to the scheme followed by 1,3,4-substituted pyrazol-5-ones. In the presence of triethyl amine the absorption of oxygen starts as usual but it comes to an end before 1 mole of oxygen per mole of pyrazolone has been absorbed, and no definite reaction product could be isolated. In the presence of hydroxyl ions (or a mixture of hydroxyl and alkanolate ions) the amount of oxygen absorbed (1/2 mole of oxygen per mole of pyrazolone) is the same as for 1,3,4-substituted pyrazol-5-ones but no crystalline oxidation product can be isolated, only heavy oils which so far have not been identified. By analogy to some pyrazolones examined by Veibel and Lillelund [3] and by Veibel and Plejl [4] a rupture of the amidic linkage of the pyrazolone nucleus may be presumed:

Pyrazolones are usually described as substances resistant to both acid and alkaline hydrolysis. In the two substances mentioned the amidic linkage is weakened by the presence of the benzene nucleus condensed with the pyrazolone nucleus, in the present case the amidic linkage is weakened by the presence of the hydroxyl group. Further evidence is necessary, however, before this hypothesis, which has possibly significance for other 5-membered heterocycles too, can be regarded as proved.

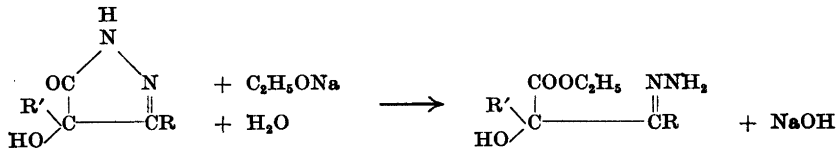
* IX: *Preceding paper.*



(Veibel and Lillelund [3])



(Veibel and Plejl [4])



In the absence of water, on the other hand, the 3,4-substituted 4-hydroxypyrazol-5-ones may be obtained in excellent yield by oxydation with oxygen of the 3,4-substituted pyrazol-5-ones in the presence of alkanolate ions, as they could by oxidation with *tert.* butylhydroperoxide [5]. When the 4-hydroxypyrazolones are treated with sodium hydroxide in ethanolic solution the crystalline substance is converted into oils similar to those isolated when the oxidation is carried out in solvents containing water.

EXPERIMENTAL PART

The pyrazolones investigated here and the resulting 4-hydroxypyrazolones have been described previously [5].

0.01 Mole of the pyrazolone was dissolved in 6 ml of 2 *N* sodium ethanolate and *tert.* butanol added to a total volume of 20 ml. The solution was shaken in an atmosphere of oxygen, the same technique as described previously [1] being applied. The volume of oxygen absorbed was noted at intervals.

After absorption of *ca.* 40 ml of oxygen (*ca.* 1/3 of the volume calculated for complete oxidation of the pyrazolone to a hydroxypyrazolone) the precipitation of a solid started without changing the rate of absorption of oxygen. When no more oxygen was absorbed 20 ml ether was added in order to complete the precipitation of the sodium salt which was isolated by suction, washed on the filter with ether or petroleum ether and dried by passing a stream of air through the filter cake, the salt not being hygroscopic. From the sodium salt the 3,4-substituted 4-hydroxypyrazolone was isolated as described previously [5].

Table 1 gives a summary of the pyrazolones examined and the results obtained. It is seen that whereas the N_1-substituted pyrazolones usually were oxidised following a zero order scheme [3], the N_1-unsubstituted pyrazolones are oxidised following a first order scheme or in a few cases a second order scheme. Figs. 1 and 2 show examples of these types.

Table 1. Oxidation of 3,4-substituted pyrazol-5-ones by oxygen in anhydrous solvents in the presence of ethanolate ions. 6 ml 2 N sodium ethanolate. Tert. butanol added to a total volume of 20 ml. 1.2 mole of base per mole of pyrazolone.

R	R^1	Order of reaction	Time for 50 % oxidation	Yield of sodium salt of the hydroxypyrazolone, %
CH_3	CH_3	1	8 h	15 *
CH_3	C_2H_5	1	6 h	90
CH_3	*n*-C_3H_7	2	4 h	92
CH_3	*iso*-C_3H_7	1	1 h	80
CH_3	C_3H_5	2	16 h	80
CH_3	*cyclo*-C_6H_{11}	1	1 h	90
CH_3	C_6H_5	2	27 h	85
CH_3	$C_6H_5CH_2$	1	17 h	80
C_6H_5	C_2H_5	1	3 h	80 *
C_6H_5	$C_6H_5CH_2$	1 **	27 h	80
	*Cyclo*hexano	1	6.5 h	80 *

* Yield of pure hydroxypyrazolone.
** Ethanol as solvent instead of *tert.* butanol.

DISCUSSION

Whereas the oxidation of N_1-substituted pyrazolones by oxygen in the presence of hydroxyl or ethanolate ions in many cases proceeded by a chain reaction [2] and the amount of oxygen absorbed often surpassed the calculated volume by 10—20 % [2], we here find no sign of a chain reaction and the absorption of oxygen approaches asymthotically the calculated volume.

In most cases we find $\log \frac{a-x}{a} = k \cdot t$ (a being the total amount of oxygen absorbed, x the volume absorbed at the time t), corresponding to a first order

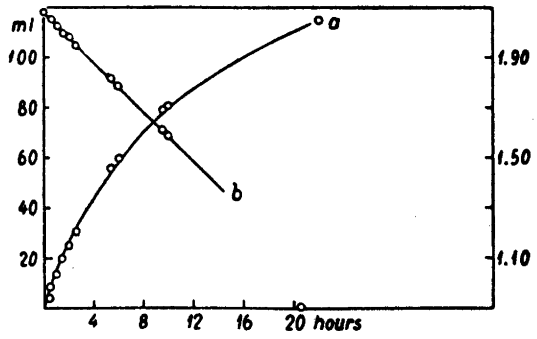


Fig. 1. 3-Methyl-4-ethylpyrazol-5-one. 0.01 mole + 6 ml 2 N $NaOC_2H_5$ diluted to 20 ml with tert. butanol.
a. Absorption of oxygen (Ordinate left)
b. log (c−x)/x (Ordinate right)

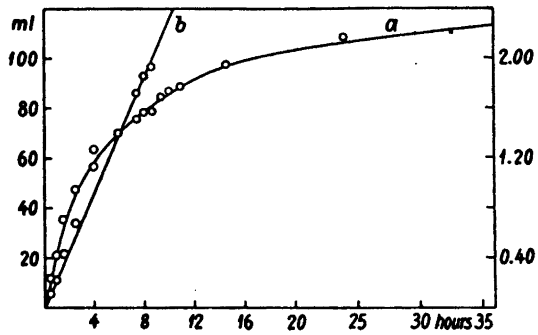


Fig. 2. 3-Methyl-4-propylpyrazol-5-one. 0.01 mole + 6 ml 2 N $NaOC_2H_5$ diluted to 20 ml with tert. butanol.
a. Absorption of oxygen (Ordinate left)
b. $x/(c-x)$ (Ordinate right)

reaction. In other cases we find $\frac{x}{a-x}=k\cdot t$, and this may be shown to correspond to a second order reaction.

When $\frac{x}{a-x}=k\cdot t$ we have:

$$x = a\cdot\frac{k\cdot t}{1+k\cdot t}$$

$$\frac{dx}{dt} = k\cdot a\cdot\frac{1}{(1+k\cdot t)^2} = k\cdot a\cdot\frac{1}{(1+\frac{x}{a-x})^2}$$

$$= k\cdot a\cdot(\frac{a-x}{a})^2$$

As $c_{Py^-} = k_1\cdot c_{Py_o^-}\cdot\frac{a-x}{a}$ we have $k_1\cdot\frac{a-x}{a}=\frac{c_{Py^-}}{c_{Py_o^-}}$

$$\text{or } \frac{dx}{dt} = k_2\cdot a\cdot\frac{(c_{Py^-})^2}{(c_{Py_o^-})^2} = K\cdot(c_{Py^-})^2$$

which is the expression for a second order reaction.

In the preceding paper we indicated a possible sequence of reactions leading to a chain reaction. Another possibility is:

$$PyRH + OR'^- \rightleftharpoons PyR^- + R'OH \quad (a)$$
$$PyR^- + O_2 \rightarrow PyROO^- \text{ or } PyR^- + O_2 \rightarrow (PyR^-, O_2) \quad (b)$$
$$2\ PyROO^- \rightarrow 2\ PyRO^- + O_2 \text{ or } 2\ (PyR^-, O_2) \rightarrow 2\ PyRO^- + O_2 \quad (c_1)$$
$$(PyR^-, O_2) + PyR^- \rightarrow 2\ PyRO^- \quad (c_2)$$
$$PyRO^- + Na^+ \rightarrow PyRONa \quad (d)$$

When (b) is slow as compared with (c) and (d) the result is a reaction following a first order scheme, provided the concentration (*i. e.* the partial pressure) of oxygen is kept constant. When on the other hand any of the reactions

(c_1) or (c_2) is slow as compared with (b) or (d) the result will be a reaction following a second order scheme. Some evidence may be produced in experiments with variation of the partial pressure of oxygen. By diminishing the partial pressure of oxygen it might be possible to change the order of reaction from 1 to 2. Experiments to this effect are planned.

It remains to be explained why a chain reaction will develop in pyrazolones substituted at N_1 but not in pyrazolones unsubstituted at N_1. The initial reaction steps are presumed identical for both types of pyrazolones. No simple explanation presents itself for the fact that in one case a chain reaction will develop, in the other not. An extension of the investigation to other 5-membered heterocycles may possibly throw light on this complicated problem.

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