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Titration of Pyrazolones with Perchloric Acid in Glacial Acetic Acid

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In 1927 Hall and Conant [1] showed that even very weak bases, *e.g.* amides, may be titrated in non-aqueous solvents, *e.g.* glacial acetic acid, with strong acids, *e.g.* perchloric acid, in the same solvent. Since then a considerable amount of work has been published. Recent summaries have been given by Tomicek and Heyrovsky [2], by Markunas and Riddick [3], and by Riddick [4].

Hall [5] and Tomiček and Heyrovsky [2] showed that by the potentiometrical titration it is possible to determine the pK_B-value of the base examined, as the $pK_{B(HAc)}$-values run parallel to the $pK_{B(H_2O)}$-values at all events for bases with $pK_{B(H_2O)}$-values between 9—10 and 13—14. Lemaire and Lucas [6] have given a theoretical survey of the potentiometrical determination of basic strength in non-aqueous solution, calculating the thermodynamical acid dissociation constant of the ion BH^+ from the apparent dissociation constant.

In previous studies on pyrazolones [7] we have shown that both 5- and 3-pyrazolones may be titrated potentiometrically in ethanolic solution with aqueous sodium hydroxide. From the titration curves it may be concluded that the 5-pyrazolones are stronger acids than the 3-pyrazolones. We have now determined the K_B-values for some 5- and 3-pyrazolones by titrating their glacial acetic acid-solutions with perchloric acid and have found that also as bases the 5-pyrazolones are stronger than the 3-pyrazolones.

The technique employed has been the following:

1 millimol of the pyrazolone is dissolved in 50 ml glacial acetic acid. The solution is titrated potentiometrically with a 0.1000 N solution of perchloric acid in glacial acetic acid, prepared as indicated by Markunas and Riddick [3], using a glass electrode, a saturated calomelelectrode as reference electrode, and a tube potentiometer for determining the potential between the electrodes. Hereby the $pK_{B(HAc)}$-values may be calculated from the potential measured by half-neutralisation of the pyrazolone.

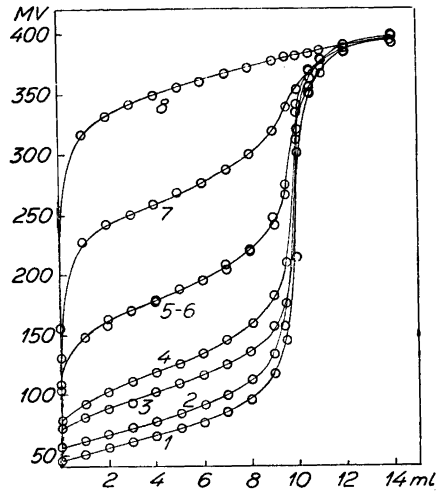


Fig. 1. Titration curves of different amines.

	pK_B
1. *Piperidine*	2.8
2. *Pyridine*	8.7
3. *p-Chloroaniline*	10.1
4. *m-Chloroaniline*	10.5_3
5. *m-Nitroaniline*	11.4
6. *o-Chloroaniline*	11.4_3
7. *p-Nitroaniline*	12.9
8. *o-Nitroaniline*	14.2

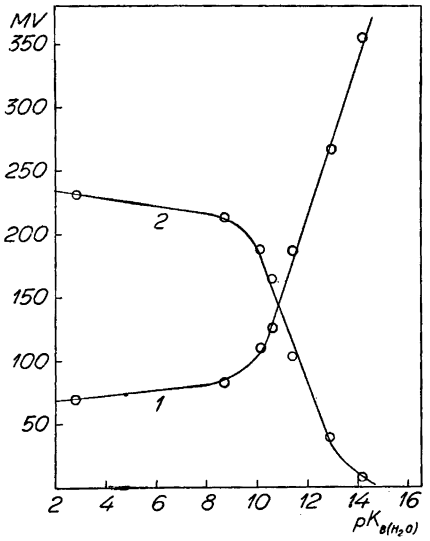


Fig. 2. Dependency of half neutralisation potentials (curve 1) and jump of potential 95 %—110 % neutralisation (curve 2) on $pK_{B(H_2O)}$.

In order to determine the curve indicating the relation between the $pK_{B(HAc)}$-values and the corresponding $pK_{B(H_2O)}$-values we titrated a series of weak bases with known $pK_{B(H_2O)}$-values. Fig. 1 shows the titration curves for 8 bases with $pK_{B(H_2O)}$-values from 2.8 to 14.2. Instead of calculating the $pK_{B(HAc)}$-values from the half-neutralisation potentials and plotting them against the $pK_{B(H_2O)}$-values we simply plotted the potentials measured after addition of 5 ml of the acid against the $pK_{B(H_2O)}$-values. This may be done because we are using constantly 1 millimol in 50 ml. If other concentrations are used a new series of curves has to be determined, the potential being dependent on the ionic strength of the solution. This has to be done also if the glass electrode is shifted out for another glass electrode.

Fig. 2 curve 1 shows the result. It is seen that both in the region pK_B 2—9 and in the region pK_B 10—14 there is a linear dependence between the half-

neutralisation potentials and the $pK_{B(H_2O)}$-values, but only in the last mentioned region is the slope of the line so that the $pK_{B(H_2O)}$-values may be determined with sufficient accuracy from a half-neutralisation potential found by titration.

In Fig. 2 curve 2 we have plotted the jump of potential from 95 % to 110 % of the theoretical amount of perchloric acid added. It is seen that this jump too is linearly dependent on the $pK_{B(H_2O)}$-value of the base titrated.

It is not strictly necessary to use exactly 1 millimol for the titration, but if other amounts of base are used the curve elaborated with 1 millimol titrations is not exactly valid. Fig. 3 shows the titration curves of 0.70 millimol, 1.00 millimol, and 1.38 millimol m-chloroaniline respectively. The potentials at half neutralisation are 129 MV, 126 MV, and 122 MV, to which correspond the $pK_{B(H_2O)}$-values 10.6, 10.5, and 10.4. The jumps of potential from 95 % to 110 % neutralisation are 166 MV, 168 MV, and 175 MV respectively, to which correspond the $pK_{B(H_2O)}$-values 10.5, 10.4, and 10.3, the value indicated in the litterature being 10.5_3.

We then titrated 1-phenyl-3-methyl-pyrazolone-5, 1-phenyl-3-methyl-4-ethyl-pyrazolone-5, 1,3-diphenyl-pyrazolone-5 and the 3 isomeric 3-pyrazolones. Table 1 summarises the half-neutralisation potentials and the $pK_{B(H_2O)}$ values.

Table 1. Potentiometrical titration of some pyrazolones.

Pyrazolone	Potential at 50 % neutralisation	$pK_{B(H_2O)}$
1-Phenyl-3-methyl-5	176 MV	11.3
1-Phenyl-3-methyl-4-ethyl-5	186 MV	11.5
1,3-Diphenyl-5	228 MV	12.2
1-Phenyl-5-methyl-3	226 MV	12.1
1-Phenyl-4-ethyl-5-methyl-3	236 MV	12.3
1,5-Diphenyl-3	273 MV	12.9

From these figures it is evident that the 5-pyrazolones are stronger bases than the 3-pyrazolones. As might be expected, the substitution of a phenyl group for a methyl group causes a weakening of the basic character of the substance. On the other hand, the substitution of an ethyl group for a hydrogen atom in position 4 has only a minor influence upon the pK_B-value.

Next we investigated the behaviour of a 4,4-dialkylsubstituted 5-pyrazolone when titrated with perchloric acid. We found that if such a substance has basic properties at all, the pK_B-value is at least > 15, as the potential measured

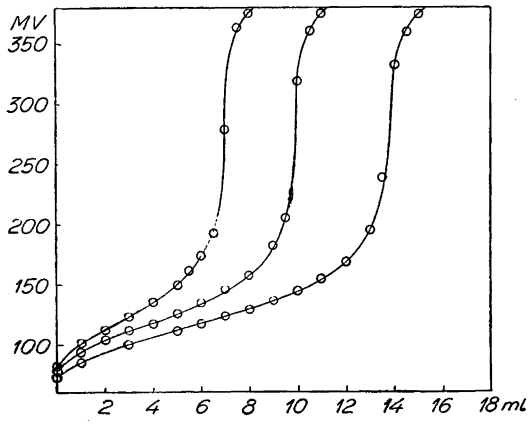
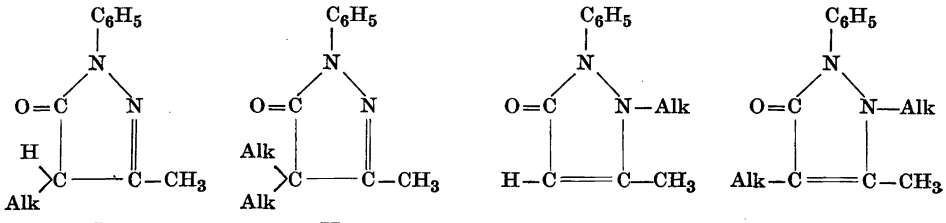


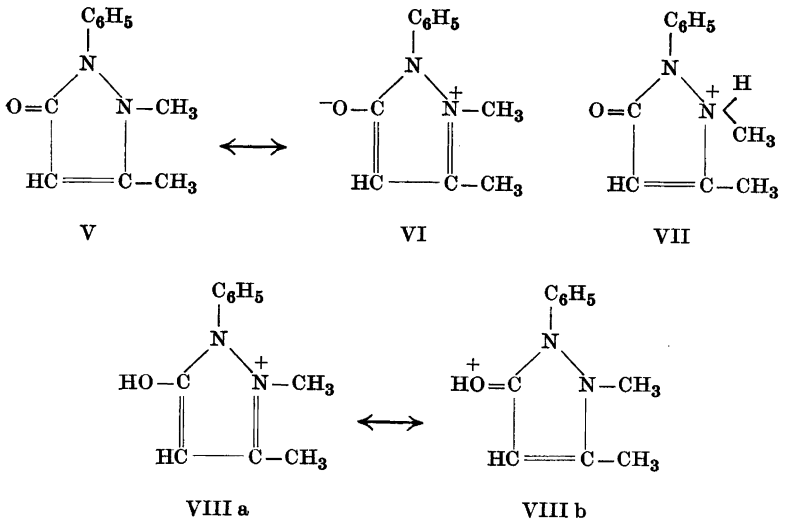
Fig. 3. Titration of 0.70 millimol, 1.00 millimol, and 1.38 millimol m-chloroaniline in 50 ml glacial acetic acid with 0.1000 N $HClO_4$.

after addition of 1—2 ml 0.1 *N* perchloric acid to 1 millimol of the pyrazolone was above 400 MV.

Hall [5] found that it is possible to titrate antipyrine, and we were able to confirm this. We then tried to titrate a 4-substituted antipyrine, *viz.* 4-isopropylantipyrine, which is a dialkylsubstituted 5-pyrazolone. We found it just as titratable as antipyrine itself. This means that it is not the substitution of 2 alkyl groups for 2 hydrogen atoms which abolishes the basic character of the 5-pyrazolone, but the positions in which the alkyl groups are placed determine whether the pyrazolone may be titrated or not.



Looking at the formulas I—IV one might draw the conclusion that the condition for titratability is that the pyrazolone is able to acquire an antipyrine structure. For antipyrine at least two mesomeric formulas V and VI are possible. To formula V corresponds the formulas VII or VIII b for the antipyrinium-



V VI VII

VIII a VIII b

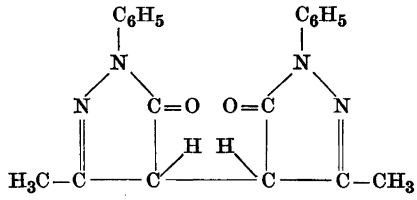
ion, to VI the formula VIII a, mesomeric with VIII b.

Jensen and Friediger [8] have shown that antipyrine has the abnormally high dipole moment of 5.48 D (3-methyl-pyrazolone-5 $\mu = 2.54$ D) and conclude from this that the contribution of formula VI to the constitution of antipyrine amounts to some 30 % (μ calculated for the phenol-betaine VI 18 D).

This being valid the untitrability of II is understandable as the condition for titratability seems to be the possibility of arranging conjugated double bonds in the nucleus, *i.e.* to establish a pyrazole structure VI in stead of the pyrazolone structure V, and with two substituents at C_4 this is impossible.

In order to try the theory of the necessity of an antipyrine-like structure for the titratability of a pyrazolone we investigated the titration of the following substances, the preparation of which will be described elsewhere.

Of these substances X is untitratable. IX and XI are titratable, but IX claims two equivalents of perchloric acid pr. mol, XI only one. This is in accordance with the prediction. XII and XIII, on the other hand, are both titratable, and this cannot be explained if the formulas XII a and XIII a are valid. The two substances may be titrated as acids too, and this means that a displacement of a hydrogen atom from the cyclohexyl ring or from the methylene group in the side chain in position 4 to the carbonyl-oxygen (or to the nitrogen atom 2) is possible so that the formulas XII b and XIII b or the corresponding enol-betainstructures or the mesomeric antipyrine-structures are more likely than the pyrazolone formulas.



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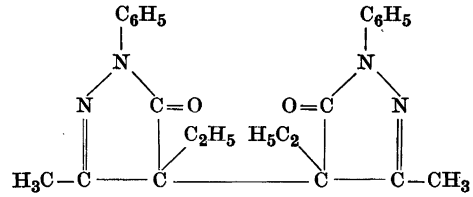
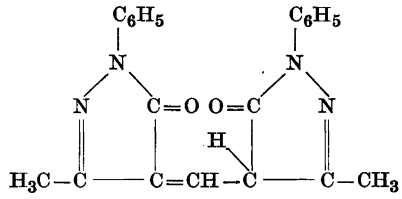
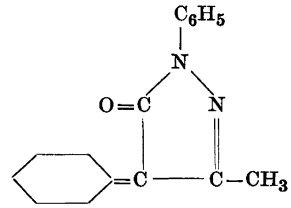


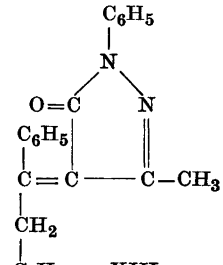
X



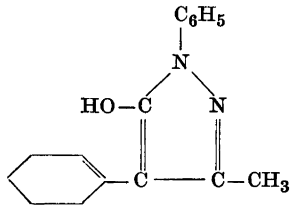
XI



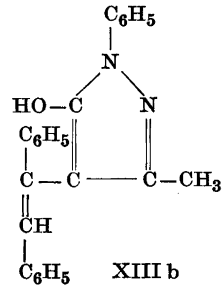
XII a



XIII a



XII b



XIII b

In table 2 we have summarised the half-neutralisation potentials and the $pK_{B(H_2O)}$-values for the pyrazolones investigated and not mentioned in Table 1.

Table 2. Potentiometrical titration of some pyrazolones.

Pyrazolone	Potential at 50% neutralisation	$pK_{B(H_2O)}$
Antipyrine	169 MV	11.2
Isopropylantipyrine	189 MV	11.6
X	> 410 MV	>15
XI	one nucleus 312 MV	13.8
	the other —	> 15
XII	173 MV	11.3
XIII	230 MV	12.2

SUMMARY

It has been shown that pyrazolones may be titrated as bases with perchloric acid in glacial acetic acid. A condition for the titrability of the pyrazolones seems to be that they are able to establish a pyrazole structure by moving a hydrogen from C_4 to N_2 or to O at C_5. From the potentiometrical titration curves of the pyrazolones their $pK_{B(H_2O)}$-values may be estimated.

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