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Pyrazole Studies

IV. Potentiometrical Titrations of 1-Arylpyrazolones *

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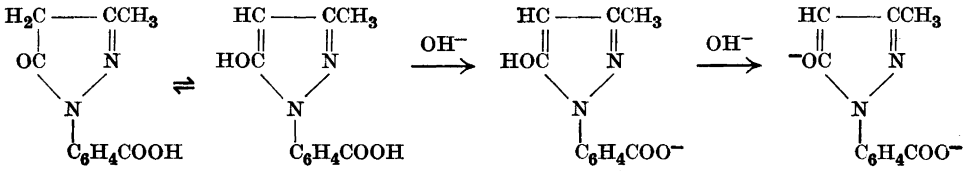
In a previous paper[1] it was shown that 1-*p*-carboxyphenyl-3-methyl-pyrazolone-5 by potentiometrical titration behaved as a dibasic acid, claiming 2 equivalents of base to complete neutralisation. The titration curve does only show an inflexion point when 1 equivalent of base has been added, whereas a real jump of potential is observed after the addition of two equivalents of base.

This means that during the titration complete enolisation of the pyrazolone takes place and that not only the carboxyl group but the hydroxyl group too will give off a proton at the pH at which the jump of potential is observed.



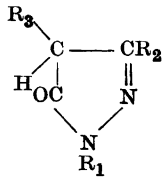
As the titration is carried out in ethanolic solution a definitive pH-value corresponding to the end-point can hardly be indicated without further investigation, but it seems to be about pH 10. The carboxyl group is without doubt more ready to give off a proton than the hydroxyl group, but from the shape of the titration curve it may be concluded that the difference between the dissociation constants cannot be very great.

As the presence of a carboxyl group in the 1-phenyl-group cannot increase the tendency of enolisation of the pyrazolone it is obvious that 1-aryl-3-alkyl-

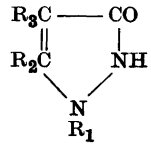
* Preliminary note: *Sjätte nordiska kemistmötet i Lund* (1948) p. 287 *Proc. XI. Intern. Congress Pure and Applied Chemistry. London* (1950) Vol. 2 p. 329.

pyrazolones-5 in general may be titrated in ethanolic solution. The substituents at 1 and 3 in the pyrazolone-nucleus may, however, be able to modify slightly the tendency of enolisation of the pyrazolone group and thus to some extent cause modifications in the shape and position of the titration curves, and to a still greater extent this might be valid for substituents at position 4, whereas substituents at position 2 will prevent the enolisation of the pyrazolone and thus make it untitratable.

In order to investigate the effect of different substituents we prepared a series of 5-pyrazolones (I) with R_1 = phenyl or o-tolyl, R_2 = methyl or



I

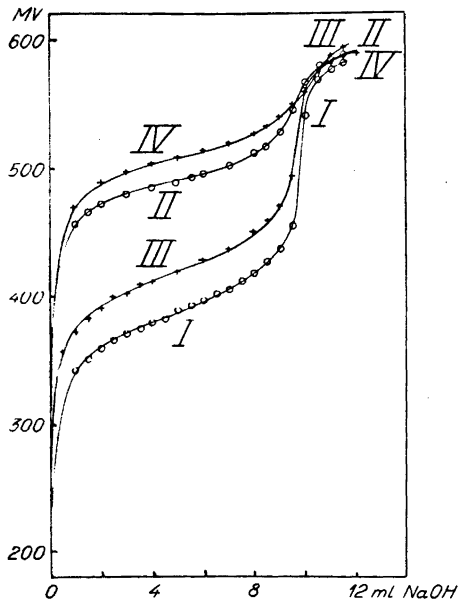


II

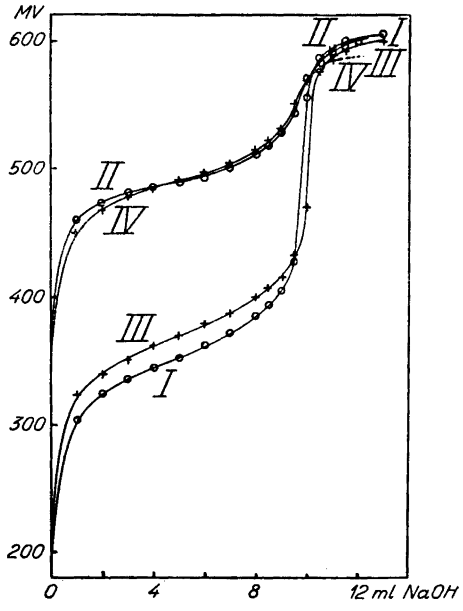
phenyl and R_3 = hydrogen or ethyl and determined the titration curves. As expected, the general shape of the curves is the same but an influence of the nature of the substituents is evident and most pronounced for R_3 = ethyl.

In the 5-pyrazolones the enolisation is of the usual type, $-CO-CH_2- \rightleftharpoons -C(OH) = CH-$. For the isomeric 3-pyrazolones (II), on the other hand, there is a possibility of an enolisation of a different type, $-CO-NH- \rightleftharpoons -C(OH) = N-$, but it is not possible to predict whether the tendency of enolisation is great enough to allow the titration of these pyrazolones or not. We therefore prepared a series of 3-pyrazolones isomeric with the 5-pyrazolones investigated. Electrometrical titration of these substances in ethanolic solution with 0.1 n aqueous sodium hydroxide showed that the tendency of enolisation is lesser than for the 5-pyrazolones, but even for the 3-pyrazolones a jump of potential may be observed.

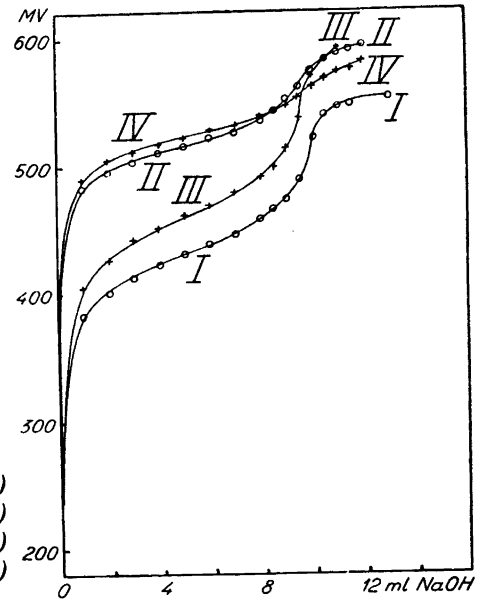
The jump of potential is not great enough to allow an exact determination of the molecular weight of the pyrazolones, the inexactitude being some 3—4 %. But in another way the titration curves seem to be useful. In Figs. 1—3 the titration curves for the pyrazolones examined may be seen, and it is obvious that all curves for 5-pyrazolone are of one type, all curves for the 3-pyrazolones of another type. This means that for an unknown pyrazolone it may be disclosed if it belongs to the 5- or the 3-series simply by determining its titration curve. Till now it has been necessary to establish the structural formula of the substance either by somewhat complicated chemical methods



I 1-Phenyl-3-methyl-pyrazolone-(5)
II 1-Phenyl-5-methyl-pyrazolone-(3)
III 1-o-Tolyl-3-methyl-pyrazolone-(5)
IV 1-o-Tolyl-5-methyl-pyrazolone-(3)



I 1,3-Diphenyl-pyrazolone-(5)
II 1,5-Diphenyl-pyrazolone-(3)
III 1-o-Tolyl-3-phenyl-pyrazolone(5)
IV 1-o-Tolyl-5-phenyl-pyrazolone(3)



I 1-Phenyl-3-methyl-4-ethyl-pyrazolone-(5)
II 1-Phenyl-5-methyl-4-ethyl-pyrazolone-(3)
III 1-o-Tolyl-3-methyl-4-ethyl-pyrazolone-(5)
IV 1-o-Tolyl-5-methyl-4-ethyl-pyrazolone-(3)

Fig. 1—3. Titration curves for different 3- and 5-pyrazolones.

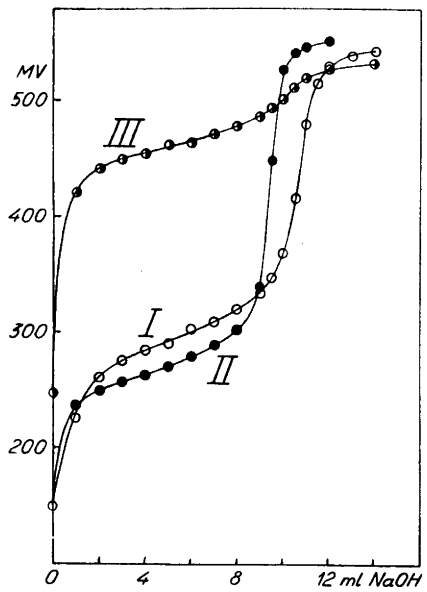


Fig. 4. Titration curves for o-carboxyphenylhydrazine (I), acet-o-carboxyphenylhydrazide (II) and benzopyrazolone (III).

or by determining the ultraviolet absorption spectrum. Biquard and Grammaticakis [2,3] have shown that the absorption spectra of 5- and 3-pyrazolones are sufficiently different to be used for the structural determination, but that the interpretation of the spectra of at all events the 5-pyrazolones is complicated by the enolisation, the absorption of the enolised form being different from that of the ketoform.

Also as a practical means of structural determination the potentiometrical titration is by far more convenient than the determination of the absorption spectrum, and besides it makes possible the calculation of the molecular weight of the substance.

In Fig. 4 is shown that not only alkyl- or aryl-substituted pyrazolones may be titrated, but that condensed systems as *e. g.* benzopyrazolone-3 as well may be titrated [4]. As this substance may often contaminate preparations of o-carboxyphenylhydrazine or acet-o-carboxyphenylhydrazide it is very convenient to be able to control the purity of the hydrazine derivative by a simple titration method. Fig. 4 gives the titration curves for all three substances. The difference between the three curves is, as might be expected, very great.

EXPERIMENTAL PART

1-Phenyl-3-methyl-pyrazolone-5, 1,3-diphenyl-pyrazolone-5, 1-phenyl-3-methyl-4-ethyl-pyrazolone-5, 1-o-tolyl-3-methyl-pyrazolone-5, 1-phenyl-5-methyl-pyrazolone-3, 1,5-diphenyl-pyrazolone-3, 1-phenyl-4-ethyl-5-methyl-pyrazolone-3 and 1-o-tolyl-5-

methyl-pyrazolone-3 were prepared by current methods and showed the melting points indicated in the litterature.

1-o-Tolyl-3-phenyl-pyrazolone-5 was prepared essentially as indicated by Knorr and Klotz [5] for its lower homologue. It may be recrystallised from 10 parts (by weight) of ethanol. Colourless crystalpowder with m.p. 187°.

$C_{16}H_{14}N_2O$ (250.3) N calc. 11.20, found 11.30 % * M found by titration 251.7

1-o-Tolyl-3-methyl-4-ethyl-pyrazolone-5 was prepared by analogy to lower homologues by heating 14.3 g o-tolylhydrazine (1 mol) with 18.5 g ethyl ethylacetoacetate (1 mol) to 145° for 2 hours. The mixture was then vacuum-distilled. At 222—225° (12 mm) a fraction weighing 12 g was collected. It solidified to a yellowish resinous mass which could not be brought to crystallisation. By titration the equivalent weight was found to 215.2, calc. 216.3.

$C_{13}H_{16}N_2O$ (216.3) N calc. 12.96, found 12.91, 13.05 %

The substance may thus be regarded as pure even if it has not been obtained in the crystalline state. Curve III in Fig. 3 is obtained using this preparation. We are, however, indebted to Mr. Knud Eggersen, M. Sc., for repeating the preparation. He obtained sensibly the same results, but on distilling the substance once more in a high vacuo (< 1 mm Hg) and keeping the distillate for 48 hours in a dry ice acetone bath germs of crystals were formed, which eventually caused crystallisation of the resin after it had been mollified by treatment with ether.

The pyrazolone forms colourless crystals with m.p. 82.5—83.5°. N calc. 12.96, found 12.75 %. M found by titration 215.1. The titration curve obtained with the crystalline compound was identical with the one shown in Fig. 3.

1-o-Tolyl-5-phenyl-pyrazolone-3 was prepared analogously to the method of Michaelis and Willert [6] for the preparation of 1,5-diphenylpyrazolone-3, but with a very poor yield. Recrystallised from ethanol it forms colourless crystals with m.p. 207—208°.

$C_{16}H_{14}N_2O$ (250.3) N calc. 11.20, found 11.12, 11.17 %. M found by titration 250—253.

The shape of the titration curve proves that the substance is a 3-pyrazolone, not a 5-pyrazolone.

1-o-Tolyl-4-ethyl-5-methyl-pyrazolone-3 was prepared analogously from acet-*o*-tolylhydrazide, ethyl ethylacetoacetate and phosphorous oxychloride with slightly better yield than the above mentioned pyrazolone. It forms colourless crystals, m.p. 161.5°.

$C_{13}H_{16}N_2O$ (216.3) N calc. 12.96, found 13.01, 13.07 %. M found by titration 216—220.

Here, too, the shape of the curve was that of a 3-pyrazolone.

Benzopyrazolone was obtained as by-product from the preparation of *acet-o-carboxyphenylhydrazide* (refluxing *o*-carboxyphenylhydrazine with glacial acetic acid for 2 hours). It forms faint yellow crystals with m.p. 247°. The same m.p. is found for both *o*-carboxy-

* All microanalyses by Mr. O. Rosenlund, M. Sc. or by Mr. A. Grossmann. Department of Organic Chemistry, University of Copenhagen.

phenylhydrazine and acet-o-carboxyphenylhydrazide, ring-closure evidently taking place during the heating, comp. Pfannstiel and Janecke [7].

The titrations were carried out potentiometrically, using a glass electrode and a Radiometer-potentiometer, type PHM 3f, measuring the potential between the glass electrode and a calomel electrode with saturated potassium chloride as liquid junction. 0.01 mol substance was dissolved in 50 ml 96 % ethanol. This solution was titrated with 0.1 *N* aqueous NaOH.

SUMMARY

The potentiometric titration of some 1-aryl-5- or 3-pyrazolones with NaOH has been investigated. Two types of titration curves were obtained. One, belonging to the 5-pyrazolones, corresponds to a distinct acidic character of the substance titrated, the other, belonging to the 3-pyrazolones, corresponds to substances, the acidic character of which may only just be observed.

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