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The Diagnostic Value of the Titration-curves of the *p*-Carboxyphenylhydrazones of Hydroxy-substituted Aromatic Aldehydes and Ketones

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In a previous paper [1] one of us mentioned that from the potentiometrical titration-curves of the *p*-carboxyphenylhydrazones of hydroxy-substituted aromatic aldehydes and ketones conclusions may be drawn with regard to the number of phenolic groups present in the carbonyl compound examined. We have now continued the investigation in order to see if, in addition to the number of phenolic groups, also the place of these groups may be determined or discerned from the position of the titration-curve compared with the titration-curve of the *p*-carboxyphenylhydrazone of the unsubstituted carbonyl compound. To some extent this seems to be the case.

The investigation has covered the determination of the titration-curves of alcoholic solutions of benzaldehyde, *o*-, *m*- and *p*-hydroxybenzaldehyde, acetophenone, *o*-, *m*- and *p*-hydroxyacetophenone, 2,4- and 2,5-dihydroxyacetophenone (resacetophenone and chinacetophenone). In addition we have examined the *p*-carboxyphenylhydrazones of 3 aminosubstituted carbonyl compounds, *viz.* *p*-dimethylaminobenzaldehyde and *m*- and *p*-aminoacetophenone, in order to see if the amino-groups have an effect opposite to the effect of the hydroxy-groups.

From Figs. 1—2 it is seen that on the acidic side of the neutral-point a hydroxy-group in *o*-position to the carbonyl group makes the carboxygroup slightly more acid than in the unsubstituted carbonyl compound, whereas hydroxyl groups in *m*- or *p*-positions have practically no effect or, if an effect is discernable, it tends to go in the opposite direction.

Fig. 3 shows that another hydroxy group in position 4 diminishes the effect of the hydroxy group in position 2, whereas the effect is enhanced if the second hydroxy group is introduced in position 5.

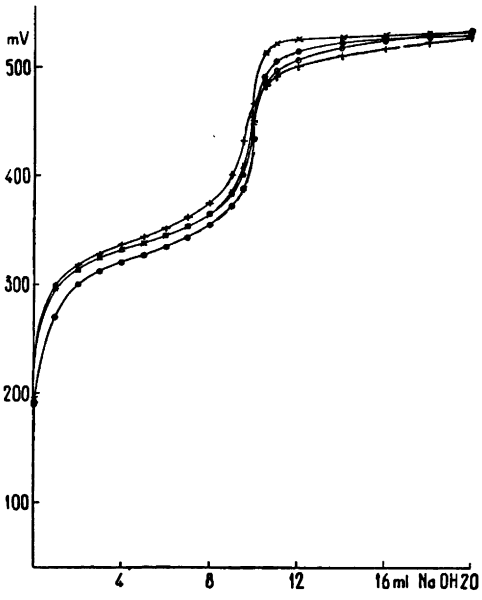

Fig. 1. Titration curves of p-carboxyphenylhydrazones of hydroxy-substituted benzaldehydes.

×——× *Benzaldehyde*
●——● *o-Hydroxybenzaldehyde*
○——○ *m-Hydroxybenzaldehyde*
+——+ *p-Hydroxybenzaldehyde*

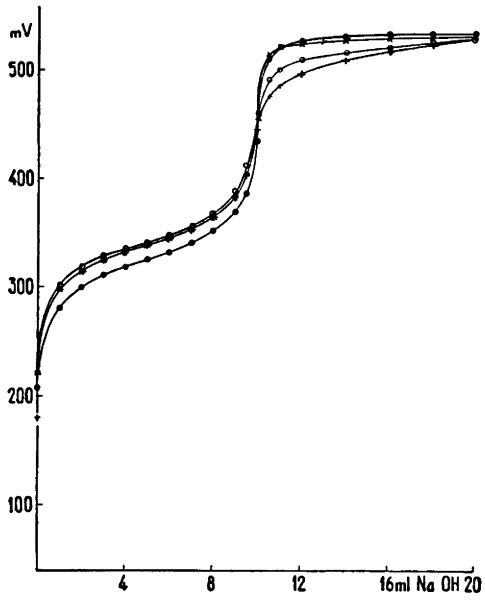

Fig. 2. Titration curves of p-carboxyphenylhydrazones of hydroxy-substituted acetophenones.

×——× *Acetophenone*
●——● *o-Hydroxyacetophenone*
○——○ *m-Hydroxyacetophenone*
+——+ *p-Hydroxyacetophenone*

Figs. 4—5 show that an amino group in *m*- or *p*-position to the carbonyl group is without any significant effect (acetophenone) or makes the carboxy group slightly less acidic (benzaldehyde) than in the unsubstituted carbonyl compound.

These results agree tolerably well with the previously known effect of hydroxy substitution on the dissociation constant of benzoic acid:

Table 1. Dissociation constants of hydroxy- and amino-substituted benzoic acids.

	k (25°)	
Benzoic acid	$6.86 \cdot 10^{-5}$	
o-Hydroxybenzoic acid	$1.06 \cdot 10^{-3}$	
m-Hydroxybenzoic acid	$8.3 \cdot 10^{-5}$	
p-Hydroxybenzoic acid	$2.85 \cdot 10^{-5}$	
2,4-Dihydroxybenzoic acid	$5.5 \cdot 10^{-4}$	
2,5-Dihydroxybenzoic acid	$1.08 \cdot 10^{-3}$	k_B (25°)
m-Aminobenzoic acid	$1.67 \cdot 10^{-5}$	$1.22 \cdot 10^{-11}$
p-Aminobenzoic acid	$1.21 \cdot 10^{-5}$	$2.33 \cdot 10^{-11}$

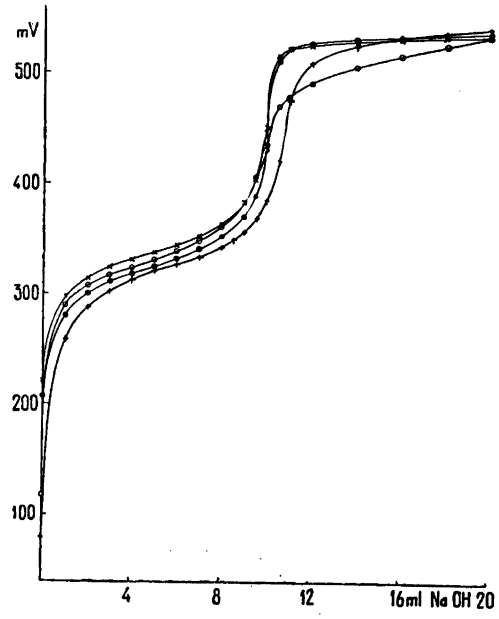

Fig. 3. Titration curves of p-carboxyphenylhydrazones of dihydroxysubstituted acetophenones.

×——× *Acetophenone*
●——● *o-Hydroxyacetophenone*
○——○ *2,4-Dihydroxyacetophenone*
+——+ *2,5-Dihydroxyacetophenone*

When the titration is continued beyond the neutralisation of the carboxyl group the effect becomes more differentiated. In *o*-position the hydroxy group is practically without effect. A hydroxy group in *m*-position displaces the titration curve towards lower potentials and in *p* position the hydroxy group has a still greater effect, *i. e.* the phenolic group in *m*- or *p*-position acts as a very weak acid whereas the acidic character of the hydroxy group in *o*-position is negligible. Here too the effect is in accordance with facts known from the hydroxysubstituted benzoic acids, *e. g.* that salicylic acid may be titrated with phenolphthalein as indicator, whereas the indicator used in the titration of *p*-hydroxybenzoic acid is methyl red.

When two hydroxy groups are present the effect is greater for 2,4-dihydroxyacetophenone than for 2,5-dihydroxyacetophenone, in accordance with the greater effect of a hydroxyl group in *p*-position than in *m*-position.

The effect of amino groups is a displacement of the titration curve towards higher potentials than for the unsubstituted *p*-carboxyphenylhydrazone, *i. e.* the salts of the aminosubstituted *p*-carboxyphenylhydrazones have a somewhat more alkaline reaction than the salts of the correspondant unsubstituted acids (compare the k_B-values of the aminobenzoic acids indicated above).

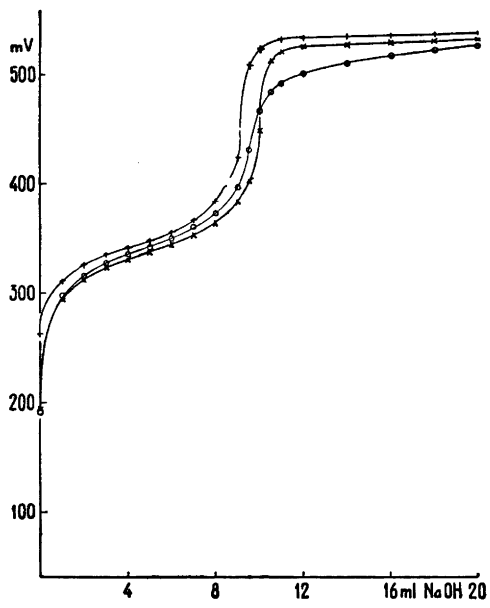

Fig. 4. Titration curves of p-carboxyphenylhydrazones of amino-substituted benzaldehydes.

×———× *Benzaldehyde*
○———○ *p-Hydroxybenzaldehyde*
+———+ *p-Dimethylaminobenzaldehyde*

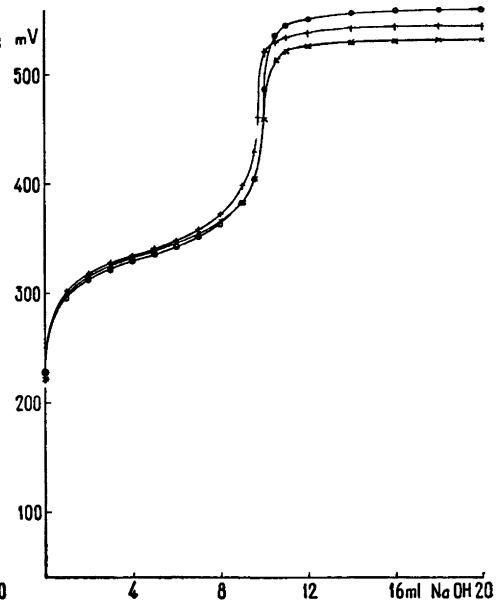

Fig. 5. Titration curves of p-carboxyphenylhydrazones of amino-substituted acetophenones.

×———× *Acetophenone*
●———● *m-Aminoacetophenone*
+———+ *p-Aminoacetophenone*

EXPERIMENTAL PART

The *p*-carboxyphenylhydrazones of benzaldehyde, *o*-hydroxy- and *p*-dimethylaminobenzaldehyde and of acetophenone, *o*-hydroxy- and *p*-aminoacetophenone have been described previously [1].

m-Hydroxybenzaldehyde was prepared from *m*-nitrobenzaldehyde according to the indications of Woodword [2]. The *p*-carboxyphenylhydrazone of the compound was prepared as usually [1]. It contains 1 mol of water which is lost during the determination of the melting point, *i. e.* the m. p. indicated below is that of the anhydrous substance.

The water is lost, too, by heating the substance for 18 hours to 78° in vacuum over P_2O_5. The anhydrous substance regains its water of crystallisation if it is left at room temperature by ordinary degree of humidity for some days.

m-Aminoacetophenone was prepared from *m*-nitroacetophenone by reduction with sodium dithionite [3] and exchange of the amino group for a hydroxygroup by current methods (diazotation).

Resacetophenone and chinacetophenone were prepared by current methods. In the preparation of the *p*-carboxyphenylhydrazones the usual methodique was employed. In case of the aminosubstituted carbonyl compounds it must be remembered that one

equivalent of sodium hydroxyde has to be added to the reaction mixture in order to avoid contamination of the *p*-carboxyphenylhydrazone with its hydrochloride. The *p*-carboxyphenylhydrazones of the dihydroxysubstituted acetophenones are more soluble in water than usual for *p*-carboxyphenylhydrazones.

Table 2. Melting points of p-carboxyphenylhydrazones not previously described.

Carbonyl compound	M. p.	Carbonyl compound	M. p.
m-Hydroxybenzaldehyde	227—228°	*m*-Aminoacetophenone	251—52°
p-Hydroxybenzaldehyde	264—266°	2,4-Dihydroxyacetophenone	304—306°
m-Hydroxyacetophenone	247—248°	2,5-Dihydroxyacetophenone	287—288°
p-Hydroxyacetophenone	288—291°		

SUMMARY

Titration curves of the *p*-carboxyphenylhydrazones of hydroxy- and amino-substituted benzaldehydes and acetophenones have been compared with the titration curves of the *p*-carboxyphenylhydrazones of benzaldehyde and acetophenone. The displacements of the curves, caused by the substituents, seem to agree tolerably well with those predicted from the dissociation constants of the hydroxy- and amino-substituted benzoic acids.

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1. Veibel, S. *Acta Chem. Scand.* **1** (1947) 54.
2. Woodword, R. B. *Org. Synth.* **25** (1945) 55.
3. Comp. D. R. P. 218364 (1910), Friedländer 10 (1913) 162.

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