

On the Application of p-Carboxyphenylhydrazones in the Identification of Carbonyl Compounds

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Among the different substituted hydrazines proposed for use in the identification of carbonyl compounds no doubt 2,4-dinitrophenylhydrazine has been most widely applied on account of the very slight solubility and the excellent crystallisability of the 2,4-dinitrophenylhydrazones. Allen and Richmond,¹ however, have called attention to some inconveniences in the application, namely the facts that cis-trans-isomerism often most disturbingly has to be dealt with, that dimorphism, too, may produce difficulties in the determination of melting points, and that the 2,4-dinitrophenylhydrazones of different carbonyl compounds are often able to form mixed crystals, thus preventing the isolation by crystallisation of the pure dinitrophenylhydrazones from a mixture of carbonyl compounds.

Moreover, the 2,4-dinitrophenylhydrazones are useful in the *qualitative* determination of the carbonyl compounds only, their applicability in the *quantitative* determination being restricted to nitrogen estimation, *e. g.* after Dumas, but not after Kjeldahl. The present author, therefore, some years ago² proposed the use of p-carboxyphenylhydrazine for identification purposes as it proved possible to use the p-carboxyphenylhydrazones for the quantitative estimation of the molecular weight of carbonyl compounds simply by titrating the ethanolic solution of the p-carboxyphenylhydrazone with standard sodium- or barium hydroxyde solution. Only some few examples were given in the paper mentioned, but later some papers dealing with the applicability of the proposed method have been published in a Danish journal.^{3, 4, 5} The following is a survey of the results given in these papers and the presentation of some results so far unpublished.

The preparation of the reagent p-carboxyphenylhydrazine hydrochloride (I) has previously² been described. In order to prepare the p-carboxyphenylhydrazones the carbonyl compounds are added to 4 % aqueous solutions of (I). If the carbonyl compound is slightly soluble in water, ethanol may be added. Generally the precipitation of the p-carboxyphenylhydrazone starts at once. If no precipitation takes place the solution may be heated on the steam-bath for 1 hour. The precipitation is completed by cooling the mixture in ice water.

It may be added that when amino-groups are present in the carbonyl compound it is necessary to add 1 equivalent of NaOH to the mixture in order to prevent the contamination of the p-carboxyphenylhydrazone with its hydrochloride.

The p-carboxyphenylhydrazones are recrystallised from ethanol or diluted ethanol. Generally one recrystallisation suffices. It is inconvenient that the melting points of the p-carboxyphenylhydrazones are rather high (about 200°, many of them between 250° and 300°) so that the diagnostic value for the qualitative identification is restricted. Their quantitative estimation, on the other hand, is so convenient that they have proved to be of outstanding value, at all events in high school courses of identification of organic substances.

So far we have only met with difficulties caused by more forms of the p-carboxyphenylhydrazone in one case. Salicylic aldehyde p-carboxyphenylhydrazone exists in two forms, m. p. 241—243° or 254—255°. We do not know if it is a case of cis-trans isomerism or a case of dimorphism.

As mentioned above the method of determination of molecular weight is simply a titration with standard base. The p-carboxyphenylhydrazone is dissolved in ethanol, if necessary in hot ethanol, phenolphthalein is added and the solution titrated until it assumes a faint pink colour. The colour fades very soon on account of the fast absorption of CO₂ from the air, but it is not at all difficult to observe the end point of the titration.

In case of aromatic carbonyl compounds with hydroxy groups in the benzene nucleus difficulties may arise. For instance when salicylic aldehyde p-carboxyphenylhydrazone is titrated the molecular weight is found some 2—3 % too low when phenolphthalein is used as indicator, but the correct value is found if methyl red is used instead of phenolphthalein. Presumably the hydroxy group is partly neutralised before the virage of phenolphthalein is reached.

Still worse is it, that when two or more hydroxy groups in o- or vic. position are present the titration becomes impossible because the solution assumes a strong brown or green colour during the addition of alkali which makes an

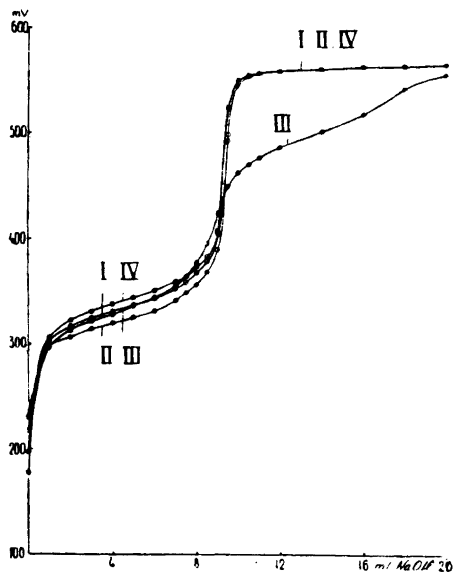


Fig. 1. Potentiometric titration of *p*-carboxyphenylhydrazones of ketones.

Curve I: Acetophenone-*p*-carboxyphenylhydrazone.

Curve II: *o*-Hydroxyacetophenone-*p*-carboxyphenylhydrazone.

Curve III: Gallacetophenone-*p*-carboxyphenylhydrazone.

Curve IV: *p*-Aminoacetophenone-*p*-carboxyphenylhydrazone.

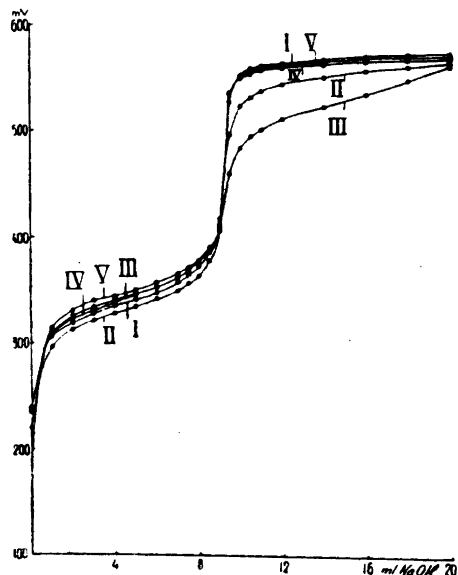


Fig. 2. Potentiometric titration of *p*-carboxyphenylhydrazones of aldehydes.

Curve I: Benzaldehyde-*p*-carboxyphenylhydrazone.

Curve II: Salicylic aldehyde-*p*-carboxyphenylhydrazone.

Curve III: Vanillin-*p*-carboxyphenylhydrazone.

Curve IV: Veratric aldehyde-*p*-carboxyphenylhydrazone.

Curve V: *p*-Dimethylaminobenzaldehyde-*p*-carboxyphenylhydrazone.

observation of the end point of the titration impossible. In such cases the titration may be carried through potentiometrically, using a glass electrode. From the shape of the titration-curve indications of the presence of phenolic groups in the molecule may be obtained. Fig. 1 and fig. 2 show examples of titration curves of unsubstituted and hydroxy- or amino-substituted aromatic carbonyl compounds.

The influence of the hydroxy-group may most clearly be seen from the branch of the titration-curve beyond the neutralisation of the carboxy-group. In fig. 1 the difference between curve I (acetophenone) and curve II (*o*-hydroxyacetophenone) is not great, but when 3 hydroxy-groups are present as in gallacetophenone (curve III) the buffering capacity of the substance

becomes quite obvious. An exact determination of the equivalent weight of the p-carboxyphenylhydrazone is no longer possible but a determination with an exactitude of some 1—2 % can be made. From the shape of the titration-curve it may be concluded that besides the carboxy-group further acid groups, weaker than the first, are present in the molecule.

From fig. 2 the conclusion is drawn that a methoxy-group may also be of influence upon the shape of the curve. A comparison of the curves I, II, and III (benzaldehyde, salicylic aldehyde, and vanilline) shows the increasing buffering capacity of the 3 substances examined. Curve IV (veratric aldehyde) shows that the methylation of the free hydroxy-group in vanillin annihilates the buffering capacity.

Curve IV of fig. 1 and curve V of fig. 2 (p-aminoacetophenone and p-dimethylaminobenzaldehyde) show that amino-groups have no significant influence on the shape of the titration-curves. In both substances the acidic branch of the curve is displaced a little towards potentials indicating lesser acidity than the derivatives of the unsubstituted carbonyl compounds, but the effect is not great enough to be of conclusive diagnostic value as some derivatives of the hydroxy-substituted carbonyl compounds also have the titration-curves displaced in the same direction. An explanation of this somewhat puzzling phenomenon cannot be given so far but the investigation is being continued.

In case of substances with other functional groups than a single carbonyl group complications known from other hydrazine compounds arise. In most cases, however, the quantitative determination is not rendered impossible if due regard is paid to the nature of the condensation product. The following survey may be of some assistance.

Alifatic α -diketones form bis-p-carboxyphenylhydrazones (III) as the normal reaction product. Only if the solution of (I) is added to a great excess of the diketone-solution the mono-p-carboxyphenylhydrazone (II) may be isolated.

Aromatic α -diketones form mono-p-carboxyphenylhydrazones (II) as the normal reaction products, but by prolonged boiling with an excess of (I) the formation of the bis-p-carboxyphenylhydrazone may be obtained.

The titration of the reaction products is normal, the mono-p-carboxyphenylhydrazones requiring 1, the bis-hydrazones 2 equivalents of base. The bis-hydrazones are often so sparingly soluble in ethanol that the titration has to be carried out in a nitrogen atmosphere, the base being added very slowly. For details, see experimental part.

β -Diketones, both alifatic and aromatic, yield with (I) as with other hydrazine derivatives pyrazol-derivatives (IV), but these, even when crystallised

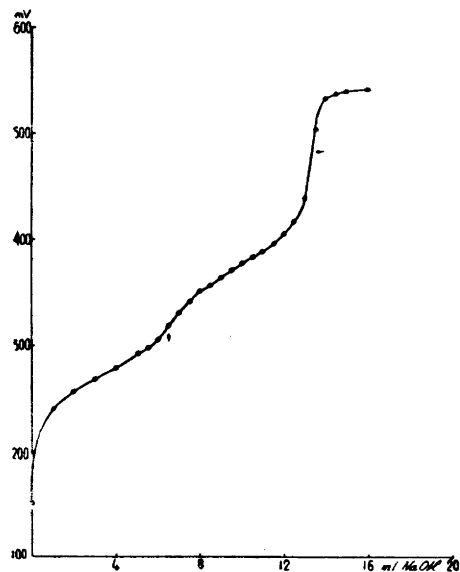


Fig. 3. Potentiometric titration of 1-p-carboxyphenyl-3-methylpyrazolone-(5).

from ethanol, crystallise with 1 mol H_2O . By titration, therefore, a molecular weight corresponding to the p-carboxyphenylhydrazone is found, but by drying the substance at 130° (or in vacuum over P_2O_5 even at ordinary temperature) the anhydrous compounds are obtained.

γ -Diketones give in the cold with an excess of (I) the bis-p-carboxyphenylhydrazone (V), but by recrystallisation from ethanol this compound is disproportionated to p-carboxyphenylhydrazine and a cyclic compound, a pyridazine (VI), which by titration requires 1 equivalent of base.

α -Ketoacids react normally with the reagent, yielding a p-carboxyphenylhydrazone (VII) requiring 2 equivalents of base to its neutralisation as both the carboxyl group of the keto-acid and of the reagent may be titrated.

Esters of β -ketoacids react in the cold with principal formation of p-carboxyphenylhydrazones (VIII) requiring 1 equivalent of base, but if the reaction is carried out on steam-bath, ring-closure to a pyrazolone-derivative (IX) usually occurs. By heating the primary reaction product to 120 – 130° or by boiling it with glacial acetic acid the ring-closure will take place even in cases where it is not completed on steam-bath.

The resulting 5-pyrazolones require by titration, if unsubstituted or mono-substituted in position 4, 2 equivalents of base as the enolised C:O-group in position 5 is completely neutralised before the colour change of the indicator (phenolphthalein). If the β -ketoester is disubstituted the ring-closure meets

with difficulties, and even if it is obtained, no enolisation can possibly take place so that only 1 equivalent of base is required to complete neutralisation.

The potentiometric titration-curve of an unsubstituted 5-pyrazolone (fig. 3) shows that 2 inflexion-points really may be discerned, the one indicating the neutralisation of the carboxy-group allowing only a very approximative determination of the molecular weight, the other indicating the neutralisation of the hydroxy-group formed by enolisation being more pronounced and allowing a fairly exact determination.

Alifatic γ -ketoacids usually form p-carboxyphenylhydrazones (X) requiring 2 equivalents of base to neutralisation, whereas in the case of *aromatic γ -ketoacids* (e. g. o-benzoylbenzoic acid) ring-closure takes place with formation of a phthalazone-derivative (XII). By prolonged heating of the p-carboxyphenylhydrazones of the alifatic γ -ketoacids during their recrystallisation ring-closure to pyridazinone-derivatives (XI) may occur, and by boiling the hydrazones with glacial acetic acid the ring-closure may be obtained even in cases where no ring-closure takes place spontaneously.

The phthalazones and the pyridazinones require only 1 equivalent of base for their neutralisation.

Alifatic α -hydroxyaldehydes or -ketones and *alifatic α -halogenoaldehydes or -ketones* yield bis-p-carboxyphenylhydrazones of the corresponding α -ketoaldehyde or α -diketone (III), whereas the corresponding *aromatic* compounds in the cold react only with 1 mol (I), presumably with formation of a mono-p-carboxyphenylhydrazone (XIII) which then loses 1 mol H₂O or HX (X = the halogen present), giving the substance (XIV) or (XV), cf. Bodfors⁶ and van Alphen.^{6a} If the reaction is carried out on steam-bath the bis-p-carboxyphenylhydrazone of the corresponding di-carbonyl compound is formed.

β -Ketoles form at room temperature p-carboxyphenylhydrazones (XVI) which on heating lose 1 mol H₂O, yielding hydrazones of unsaturated compounds (XVIII) or pyrazoline derivatives (XVII). Both the p-carboxyphenylhydrazones and the pyrazolines require 1 equivalent of base.

α - β unsaturated aldehydes and ketones. The purely alifatic or mixed alifatic-aromatic compounds (e. g. crotonic aldehyde or benzylidene acetone) usually yield the normal p-carboxyphenylhydrazone (XVIII) whereas the p-carboxyphenylhydrazones formed by aromatic compounds (e. g. benzalacetophenone) spontaneously will be transformed into pyrazoline-derivatives (XIX) by ring-closure (cf. v. Auwers and co-workers.^{7, 8, 9} In cases where the ring-closure does not take place spontaneously it may be provoked by boiling the p-carboxyphenylhydrazone with glacial acetic acid.

The solutions of the pyrazolines in ethanol show a brilliant bluish fluorescence which is not shown by the ethanolic solutions of the p-carboxyphenylhydrazones. Both types of derivatives require 1 equivalent of base for their neutralisation, and as the ring-closure in this instance is not accompanied by loss of water but only by the displacement of a hydrogen atom from nitrogen to carbon, the molecular weights of both types are identical.

(I) may react also with other compounds than carbonyl compounds, *e. g.* with *mustard oils*⁴. The reaction product is a thiosemicarbazide (XX) which in ethanolic solution may be titrated with standard base, requiring 1 equivalent of base for its neutralisation (indicator phenolphthalein). When prepared by boiling solutions of (I) and mustard oil on steam bath 1-p-carboxyphenyl-4-alkyl (aryl)-thiosemicarbazides are obtained.

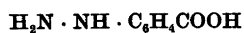
That it is the 1-p-carboxyphenyl-substituted and not the isomeric 2-substituted thiosemicarbazide (*cf.* the papers of Marckwald,¹⁰ of Busch and Holzmann,¹¹ and of Busch, Oppermann and Walther¹²) which is formed at boiling temperature may be seen by treating its ethanolic solution with an ethanolic solution of nickel chloride. Jensen and Rancke Madsen¹³ have shown that 2-substituted thiosemicarbazides but not the 1-substituted ones form intensely coloured complex nickel salts. The thiosemicarbazides prepared by the method mentioned do not give coloured solutions with nickel chloride and consequently they are 1-substituted.

From the *aromatic mustard oils* the 2-substituted thiosemicarbazides may be prepared by reaction between the sodium salt of p-carboxyphenylhydrazine and mustard oil in diluted ethanol at room temperature. After 1—2 hours the 2-p-carboxy-4-aryl-thiosemicarbazide (XXI) is precipitated by addition of hydrochloric acid, filtered off, washed with diluted ethanol and dried at room temperature.

These substances too may be titrated with standard base. Their ethanolic solutions assume by addition of a solution of nickel chloride a deep red colour which with ammonia shifts to dark blue. As the colour of the solution is the same with 3 as with 2 mol thiosemicarbazide per mol NiCl₂ it is to be assumed that the complex is formed of only 2 mol thiosemicarbazide per mol NiCl₂. It has not been possible to isolate the complex salt.

From *alifatic mustard oils* only the 1-p-carboxyphenylthiosemicarbazides are formed, even by reaction at room temperature between the sodium salt of p-carboxyphenylhydrazine and mustard oils.

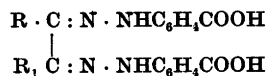
The aromatic 2-p-carboxyphenyl-thiosemicarbazides are transformed into the 1-substituted isomers by recrystallisation from ethanol.



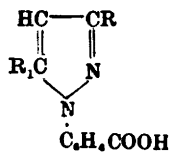
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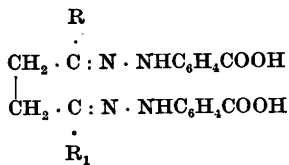
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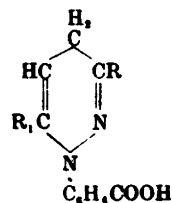
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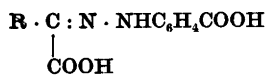
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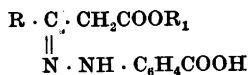
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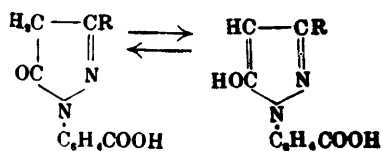
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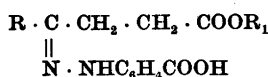
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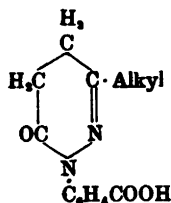
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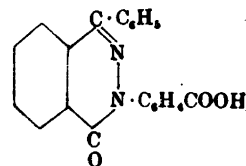
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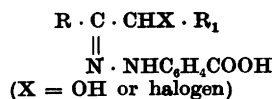
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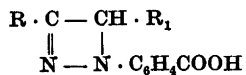
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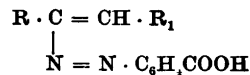
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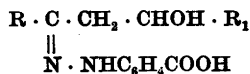
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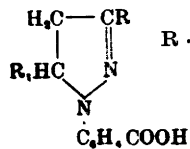
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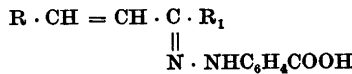
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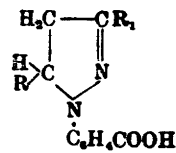
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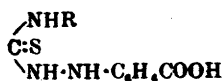
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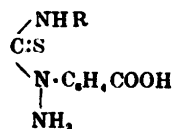
XVIII



XIX



XX



XXI

Table 1. *p*-Carboxyphenylhydrazones of carbonyl compounds

Carbonyl compound	M. p.	Equivalent weight found	Molecular weight calc.
Formaldehyde	ca. 285°	—	164.2
Acetaldehyde	210—211°	179.2	178.2
Propionaldehyde	174—175°	192.2	192.2
<i>n</i> -Butyraldehyde	164—165°	207.8	206.2
Benzaldehyde	234—235°	239.0	240.2
<i>p</i> -Toluyaldehyde	240—242°	253.3	254.3
Hydrocinnamic aldehyde	173—174°	269.6	268.3
Cinnamic aldehyde	236—238°	264.6	266.3
Salicylic aldehyde	241—243°	256.4 ¹	256.3
Salicylic aldehyde	254—255°	257.2 ¹	256.3
Protocatechualdehyde	ca. 265°	—	272.3
Vanillin	244—246°	284.6 ²	286.3
Anisaldehyde	250—251°	271.3	270.3
2,4-Dimethoxybenzaldehyde	211—213°	299.8	300.3
3,4-Dimethoxybenzaldehyde	225—227°	299.6	300.3
Piperonal	244—246°	282.8	284.3
<i>m</i> -Nitrobenzaldehyde	260—262°	283.6	285.3
<i>p</i> -Dimethylaminobenzaldehyde	251—252°	280.9	283.3
<i>o</i> -Carboxybenzaldehyde ³	280—282°	264.9	266.3
Furfural	210—212°	229.4	230.2
Acetone	230—231°	190.8	192.2
Methylethylketone	173—174°	206.8	206.2
Methylpropylketone	149—150°	219.1	220.2
Diethylketone	179—180°	220.4	220.2
Methylisopropylketone	190—192°	219.0	220.2
Methylbutylketone	148—149°	232.8	234.2
Pinacolone	220—222°	233.5	234.2
Methylamylketone	148—150°	248.2	248.3
Methylhexylketone	145—146°	260.9	262.3
Di- <i>n</i> -butylketone	115—116°	278.2	276.3
Cyclopentanone	250—251°	218.6	218.2
Cyclohexanone	240—241°	230.7	232.3
Acetophenone	250—251°	253.5	254.2
<i>p</i> -Methylacetophenone	245—246°	268.6	268.3
<i>o</i> -Hydroxyacetophenone	290—292°	271.3 ⁴	270.3
<i>p</i> -Methoxyacetophenone	246—248°	282.1	284.3
<i>p</i> -Aminoacetophenone	237—238°	268.0	269.3
Propiophenone	193—194°	267.3	268.3
<i>p</i> -Hydroxypropiophenone	143—145°	—	284.3

¹ Indicator methyl red. ² Potentiometrical titration. ³ Phthalazone (XII). ⁴ Pyrazoline (XIX). ⁵ Pyridazinone (XI). ⁶ Pyrazole (IV). ⁷ Pyridazine (VI). ⁸ Pyrazolone (IX). ⁹ Pyrazoline (XVII). ¹⁰ Cyclic or azo-compound (XIV or XV).

Carbonyl compound	M. p.	Equivalent weight found	Molecular weight calc.
Valerophenone	156—157°	295.3	296.3
Gallacetophenone	274—277°	301.3 ¹	302.3
Methyl- α -naphthylketone	230—232°	302.7	304.3
Methyl- β -naphthylketone	279—280°	303.1	304.3
Benzophenone	248—249°	317.9	316.3
Benzalacetophenone ⁴	220—221°	339.4	342.3
p-Bromacetophenone	260—261°	332.2	333.3
Benzalacetone	193—194°	279.0	280.3
Benzalacetone ⁴	249—250°	279.3	280.3
Pyruvic acid	265—266°	111.7	222.2
Levulinic acid	212—213°	125.9	250.3
Levulinic acid ⁵	157—158°	231.0	232.2
β -Benzoylpropionic acid	205—207°	157.2	312.3
β -Benzoylpropionic acid ⁵	194—195°	291.7	294.3
o-Benzoylbenzoic acid ³	273—274°	341.1	342.3
p-Toluylo-benzoic acid ³	269—270°	355.8	356.3
Diacetyl	> 350°	179.0	354.3
Benzil mono-carboxyphenylhydrazone	213—215°	344.6	344.4
Benzil bis-carboxyphenylhydrazone	ca. 320°	237.3	474.6
Acetylacetone ⁶	158—160°	216.0	216.2
Benzoylacetone ⁶	153—154°	276.4	278.3
Dibenzoylmethane ⁶	213—214°	340.7	340.3
Acetylacetone ⁷	234—235°	228.5	230.3
Ethyl acetoacetate ⁸	297—300°	108.9	218.2
Ethyl ethylacetoacetate ⁸	246—247°	122.9	246.3
Ethyl benzoylacetate ⁸	278—280°	139.8	280.3
Acetylpyruvic acid ⁶	288—291°	125.0	246.2
Ethyl acetylpyruvate ⁶	181—182°	272.1	274.3
Form-isobutyraldol ⁹	173—174°	218.9	218.2
Benzoin ¹⁰	151—153°	329.1	328.3

Table 2. Thiosemicarbazides from mustard oils

Mustard oil	M. p.	Equivalent weight found	weight calc.
Methyl	248—250°	224.5	225.3
Allyl	212—214°	250.0	251.3
Phenyl	221—223°	287.7	287.4
p-Tolyl	213—215°	299.8	301.4

EXPERIMENTAL PART

As an example of the preparation of a p-carboxyphenylhydrazone without complications may be quoted methyl- β -naphthylketone-p-carboxyphenylhydrazone. 1.70 g methyl- β -naphthylketone are dissolved in 25 ml ethanol. The solution is added to a solution of

2 g (I) in 50 ml water, the mixture is refluxed for 1 hour on the steam bath and then cooled. The precipitate is filtered off and dried, weight 2 g, m. p. 277—279°. Recrystallised from ethanol the m. p. is raised to 279—280°.

0.2136 g dissolved in 50 ml ethanol require 7.53 ml 0.0936 *N* Ba(OH)₂. Equivalent weight calc. 304.3, found 303.1.

As an example of the potentiometrical titration may be quoted acetophenone-*p*-carboxyphenylhydrazone (m. p. 251—252°). Titrated with Ba(OH)₂ with phenolphthalein as indicator 0.1978 g require 7.91 ml. 0.0986 *N* base. Equivalent weight calc. 254.2, found 253.5.

0.2292 g in 50 ml ethanol were titrated potentiometrically with 0.0971 *N* NaOH. An electronic-tubepotentiometer, type »Radiometer PHM 3 f» and a glass electrode were used, the other half element being a calomel electrode. Curve I on fig. 1 shows the result. 9.30 ml were required for neutralisation. Equivalent weight calc. 254.2, found 253.8.

From all the *p*-carboxyphenylhydrazones, the titration-curves of which are shown in fig. 1 and fig. 2, 0.090 mol are dissolved in 50 ml ethanol, and in all cases 9.3 ml 0.0971 *N* NaOH are required for neutralisation, *i. e.* within the limits of the experiment the amount calculated.

Aliphatic α-diketones. 4 g (I) are dissolved in 100 ml water and a solution of 0.85 g diacetyl in 50 ml ethanol is added. The *p*-carboxyphenylhydrazone is precipitated spontaneously but in order to complete the formation the mixture is refluxed for 2 hours on the steam-bath. The yellow precipitate is filtered off. As it is practically insoluble in all solvents it is purified by boiling it repeatedly with ethanol. It has a m. p. over 350°.

0.1145 g are dredged in 50 ml ethanol in a conical flask. Phenolphthalein is added and the flask is closed with a cork stopper equipped with a glass tube through which a stream of CO₂-free N₂ is conducted into the solution, and another glass tube through which Ba(OH)₂ may be added from a burette. The Ba(OH)₂-solution is added in small quantities, 0.1—0.2 ml, no further amount being added until the red colour has vanished. The titration is very tedious, 6.90 ml being added during some 6 hours. The red colour then persists for many hours. Equivalent weight calc. for diacetyl-bis-*p*-carboxyphenylhydrazone 177.2, found 179.0. By nitrogen determination (micro-Dumas) was found 15.2 % N, calc. 15.8 % N.

If, on the other hand, a solution of (I) in water is added to a solution of excess diacetyl in ethanol at room temperature a yellow precipitate is formed which by recrystallisation from ethanol becomes colourless. M. p. 273—274°. 0.2666 g require 13.66 ml 0.0893 *N* Ba(OH)₂, *i. e.* the substance is diacetyl-mono-*p*-carboxyphenylhydrazone, equivalent weight calc. 220.2, found 219.3.

Aromatic α-diketones. Here the mono-*p*-carboxyphenylhydrazones are the normal reaction products. To a solution of 2 g (I) in 15 ml water + 35 ml ethanol is added a solution of 2 g benzil in 25 ml ethanol. The mixture is refluxed for 1 hour and then cooled. The precipitate is filtered off, recrystallised from ethanol and shows then the m. p. 213—215°. *v. Auwers and Clos*¹⁴ indicate for the monohydrazone m. p. 212°. 0.2084 g require 6.13 ml 0.0986 *N* Ba(OH)₂. Equivalent weight calc. 344.4, found 344.6. By prolonged refluxing the bis-hydrazone may be formed. M. p. 320°.

β-Diketones. A hot solution of 4.6 g dibenzoylmethane in 200 ml ethanol is added to a hot solution of 4 g (I) in 100 ml of water. The mixture is refluxed on the steam-bath

for 4 hours and then cooled. A precipitate is filtered off and recrystallised from ethanol. It shows m. p. 214° and equivalent weight 359.2. For the mono-carboxyphenylhydrazone the calc. equivalent weight is 358.3.

Heated to about 140° for 3 hours or dried *in vacuo* over P₂O₅ for a night the substance loses 1 mol of water. The anhydrous substance shows unaltered m. p. 214° but by titration the equivalent weight is found to 340.7 (0.3327 g, 10.08 ml 0.0969 N Ba(OH)₂), calc. for 1-p-carboxyphenyl-3,5-diphenyl-pyrazole (IV) 340.3.

When the pyrazole-derivative is recrystallised from ethanol the m. p. is not altered but the equivalent weight of the recrystallised product is 359, *i. e.* 1 mol of water is retained, which is lost before the m. p. since identical m. p.'s are found for the anhydrous substance and for the hydrate.

Also with benzoylacetone and with acetylacetone pyrazole-derivatives are formed which heated to 130—140° or dried *in vacuo* over P₂O₅ loose 1 mol of water. It has not yet been established if it is the 3-methyl-5-phenyl- or the 3-phenyl-5-methyl-pyrazole which is formed from benzoylacetone.

γ-Diketones. If a cold solution of (I) in 100 ml of water is added to a solution of 1.1 g acetylacetone in 25 ml of water a precipitate is formed which after 1 hour is filtered off, washed with water and ethanol and air-dried, Yield 2 g. Heated slowly the substance begins to decompose at 180°. On bloc Maquenne the instantaneous m. p. (destruction point) is 277—280°. The substance is practically insoluble in cold ethanol. 0.1594 g were dissolved in 50 ml ethanol by addition of 10.05 ml 0.1005 N Ba(OH)₂. The solution is alkaline towards phenolphthalein, the excess base corresponding to 1.82 ml 0.1060 N HCl. Equivalent weight found 194.8, calc. for acetylacetone-bis-p-carboxyphenylhydrazone 191.2.

Heated with ethanol for some time the substance is dissolved. Water precipitates a substance with m. p. 235° (bloc Maquenne) and equivalent weight 228.5 (0.1056 g require 4.60 ml 0.1005 N Ba(OH)₂), calc. for the pyridazine-derivative (VI) 230.3. The filtrate contains p-carboxyphenylhydrazine. By addition of acetone a precipitate of the acetone-p-carboxyphenylhydrazone (m. p. 230—231°) is readily obtained. The bis-p-carboxyphenylhydrazone of acetylacetone first formed is by heating with ethanol disproportionated to a mixture of the pyridazine-derivative and p-carboxyphenylhydrazine.

If the reaction is carried out on the steam-bath only the pyridazine-derivative is formed.

α-Ketoacids. No complications have been met so far. The p-carboxyphenylhydrazones are readily formed and both carboxy-groups are titrated, *e. g.* the p-carboxyphenylhydrazone of pyruvic acid: 0.1167 g require 10.60 ml 0.0986 N Ba(OH)₂ equivalent weight found 111.7, molecular weight calc. 222.2.

Esters of β-ketoacids. If the usual procedure for the preparation of p-carboxyphenylhydrazones is followed, a mixture of p-carboxyphenylhydrazone (VIII) and pyrazolone (IX) is formed. When the precipitation, with ethyl acetoacetate for example, is carried out at room temperature and the product purified by dissolving it in cold ethanol and reprecipitating it by addition of water and refrigerating the mixture in ice, approximately pure (VIII) may be obtained. 0.3832 g require 14.95 ml 0.1048 N Ba(OH)₂. Equivalent weight found 244.5, molecular weight calc. 264.2, *i. e.* the product is a mixture of (VIII) and (IX) with some 13 % (IX). If, on the other hand, the mixture of (I) and ethyl acetoacetate is refluxed for some time, the precipitate filtered off, dissolved by refluxing

it with ethanol and reprecipitated by addition of water after filtration, the pure pyrazolone (IX) is obtained. 0.1764 g require 15.46 ml 0.1048 *N* Ba(OH)₂. Equivalent weight found 108.9, molecular weight calc. 218.2. Obviously, the pyrazolone is titrated as a dibasic acid.

This may be seen too from the potentiometric titration-curve shown in fig. 3. 0.1432 g were titrated with 0.0871 *N* NaOH. The first inflexionpoint is at 6.70 ml, the second at 13.48 ml, the corresponding equivalent weights 220.1 and 109.4. The m. p. of (IX) is 297—300°. For (VIII) no m. p. can be determined. On bloc Maquenne an instantaneous m. p. may be observed at 168—170°, but this only indicates the temperature at which ring-closure to (IX) occurs momentarily.

γ-Ketoacids. If levulinic acid is treated with (I) a p-carboxyphenylhydrazine (X) with m. p. 212—213° and equivalent weight 125.9 is obtained. 0.1446 g require 12.30 ml 0.0936 *N* Ba(OH)₂. Molecular weight calc. 250.3. Evidently the p-carboxyphenylhydrazine is titrated as a dibasic acid. If (X) is heated to 150° for 1—2 hours ring-closure occurs with loss of water. The product (XI) is recrystallised from diluted ethanol and shows the m. p. 157—158° and equivalent weight 231.0. 0.2238 g require 10.35 ml 0.0936 *N* Ba(OH)₂. The molecular weight calc. for (XI) is 232.2, *i. e.* the pyridazinone is titrated as a monobasic acid.

Refluxing of (X) with glacial acetic acid for 15 minutes does not result in ring-closure. (X) may be recovered unaltered.

From β-benzoylpropionic acid a p-carboxyphenylhydrazone with m. p. 205—207° is formed. 0.2065 g require 14.03 ml 0.0936 *N* Ba(OH)₂. Equivalent weight found 157.2, molecular weight calc. 312.3. If this substance is refluxed with glacial acetic acid for 5 minutes or heated to some 160° for 6 hours, ring-closure occurs. The m. p. of the recrystallised product is 194—195°, the equivalent weight found 291.7 (0.2919 g require 10.69 ml 0.0936 *N* Ba(OH)₂). The calc. molecular weight is 294.3. Even boiling of (X) with ethanol for some hours may in this instance provoke ring-closure.

From o-benzoylbenzoic acid (and other *γ*-ketoacids of this type) only the pyridazinones (XII), which are also named phthalazones, are formed. M. p. of the phthalazone from o-benzoylbenzoic acid 273—274°. 0.1619 g require 5.07 ml 0.0936 *N* Ba(OH)₂. Equivalent weight found 341.1, molecular weight calc. 342.3.

That really a phthalazone is formed may be proved by heating the substance over free flame to the boiling- (or destruction-) point. After cooling, the reaction-product may be separated into an acid and a neutral part. From the acid part the original substance may be recovered, from the neutral part a substance with m. p. 168°, concordant with the melting-point of 1,3-diphenylphthalazone-(4) formed from the original phthalazone by decarboxylation.

α-Hydroxy-aldehydes or -ketones and α-halogeno-aldehydes or -ketones. When *alifatic* compounds of these types are treated with (I) only the bis-p-carboxyphenylhydrazones of the corresponding diketones (III) are formed, at room temperature as well as on the steam-bath.

The corresponding *aromatic* compounds, too, will on the steam-bath give rise to the bis-p-carboxyphenylhydrazones of the diketones. At room temperature, however, substances of the type (XIV) or (XV) are formed by a very slow reaction (some days), even if an excess of (I) is used. When the reaction mixture is diluted with water an oil is formed which by treatment with benzene is brought to crystallisation. From benzoin and de-

sylchloride identical reaction products, free from chlorine and with m. p. 151—153° when recrystallised from ethanol, were formed. By titration equivalent weights of 328.3 or 329.1 respectively were found. (0.2232 or 0.2451 g require 7.60 or 8.34 ml 0.0893 *N* Ba(OH)₂). The calc. molecular weight is 328.3. When boiled with (I) in diluted ethanol the substance (XIV) or (XV) is transformed into the bis-*p*-carboxyphenylhydrazone of the corresponding diketone.

β-Ketoles. 1.5 g form-isobutyraldol, HCHOH · C(CH₃)₂ · CHO, in 25 ml ethanol and 3 g (I) in 75 ml water were mixed at room temperature and kept over night in the ice-box. Yield 2.5 g of a substance with an instantaneous m. p. on bloc Maquenne about 160°. Slowly heated a m. p. of 173° was found. When boiled for a few minutes with glacial acetic acid, precipitated by 5 volumes of water and recrystallised from ethanol a substance with m. p. 174° without a preceding instantaneous m. p. is obtained. The substance prepared at room temperature has an equivalent weight of 237.4. (0.2189 g require 9.50 ml 0.0971 *N* NaOH), the transformation product an equivalent weight of 218.9. (0.1938 g require 9.12 ml 0.0971 *N* NaOH). The calc. equivalent weights are for the hydrazone (XVI) 236.2, for (XVIII) and the pyrazoline (XVII) 218.2.

α-β unsaturated aldehydes or ketones. When cinnamic aldehyde is treated with (I) a substance with m. p. 236—238° is formed. The equivalent weight found by titration is 264.6. (0.1164 g require 4.70 ml 0.0936 *N* Ba(OH)₂), calc. 266.3. This substance is either (XVIII) or (XIX) (R = C₆H₅, R₁ = H), but from the data obtained no decision can be made. When benzylideneacetone is treated in the same manner a substance with m. p. 194—196° is formed. If refluxed for 1 hour with glacial acetic acid the m. p. is raised to 249—250°. Both substances show by titration the calc. equivalent weight 280.3. (0.3753 or 0.2647 g require 11.05 or 10.62 ml 0.0893 *N* Ba(OH)₂). Equivalent weight found 279.0 or 279.3). The ethanolic solution of the highest melting substance show a blue fluorescence and is, therefore, presumably the pyrazoline (XIX), the other one being the normal *p*-carboxyphenylhydrazone (XVIII).

By condensation of (I) with benzylideneacetophenone only one substance is formed. Its alcoholic solution shows a brilliant blue fluorescence, and the substance is consequently of the type (XIX), *cf.* the condensation of benzylideneacetone with phenylhydrazine, v. Auwers and co-workers.^{7, 8, 9}

Mustard oils. When alcoholic solutions of mustard oils are refluxed for 1—2 hours with aqueous solutions of (I), thiosemicarbazides (XX) separate on cooling. Recrystallised from ethanol the 1-*p*-carboxyphenyl-4-alkyl(aryl)-thiosemicarbazides show sharp melting-points. They may be titrated in ethanolic solution with standard base. 1.6 g phenyl mustard oil yield 2.3 g (XX) (R = C₆H₅) of m. p. 220—222°, which by recrystallisation is raised to 221—223°. 0.1981 g require 7.71 ml 0.0893 *N* Ba(OH)₂. Equivalent weight found 287.7, calc. 287.3.

SUMMARY

The reaction products of *p*-carboxyphenylhydrazine with different types of carbonyl compounds have been described.

The conditions governing ring-closure of the *p*-carboxyphenylhydrazones primarily formed to pyrazole- or pyridazine-derivatives have been established.

It has been stated which derivatives require 1 and which 2 equivalents of base for their neutralisation.

It has been shown that the potentiometrical titration of p-carboxyphenylhydrazones is possible even in cases where the ordinary titration cannot be accomplished. From the shape of the titration curve conclusions as to the presence of weakly acidic or basic groups as substituents in the molecule of the carbonyl-compound may be drawn.

With mustard oils substituted thiosemicarbazides are formed.

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