1085. *The Properties of a Pyruvic Acid Hydrazone.*

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Pyruvic acid and an equivalent quantity of hydrazine hydrate give two or more products, according to the conditions. One of these products is an ionic compound formed from a molecule of each of the two possible geometrical isomers of the hydrazone.

When, in the course of other work, the preparation of a hydrazone of pyruvic acid was attempted it was found that the product varied with the reaction temperature. At first it was assumed that these products would yield the two geometrical isomers [1] but in fact the situation is more complex. The somewhat unusual nature of one of the products and the instability of both of them, particularly in solution, probably explains why, although the phenylhydrazone of pyruvic acid was first prepared by Fischer and Jourdan [2] and the preparation of the hydrazone was mentioned by Curtius and Lang,[3] no details of this compound appear to have been published.

When the equivalent amount of hydrazine hydrate is added to pyruvic acid in ethanol, at as low a temperature as is consistent with mixing ($\sim -10°$), the product *A* deposited has m. p. 92—100°. Recrystallisation, entirely in the cold, from aqueous ethanol gives white crystals, m. p. 100·5—102°. Recrystallising the product *A* from hot aqueous ethanol, or allowing the original mixture to warm from room temperature, gives a product *B* which, when recrystallised from aqueous ethanol, has m. p. 137—137·5°.

Infrared spectra of different samples of compound *A*, and their titration curves, indicate that it is very difficult, if not impossible, to free it completely from material *B*. This

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[1] Staudinger, *Helv. Chim. Acta*, 1921, **4**, 228.
[2] Fischer and Jourdan, *Ber.*, 1883, **16**, 2243.
[3] Curtius and Lang, *J. prakt. Chem.*, 1891, **44**, 557.

is particularly so since, although dilute solutions are reasonably stable, in concentrated solution the change *A* ⟶ *B* occurs rapidly. For this reason recrystallisation of compound *A* had to be on a very small scale. Its sodium salt also changes to that derived from *B* on recrystallisation. On the other hand, compound *B* can be recrystallised on a reasonable scale to give a constant infrared spectrum and melting point.

The Properties of Hydrazone B.—This product appears to be a hydrazone since it has pK_a 4·35 in water, whereas if it were a hydrazide it would be basic.[4] However, it has a second dissociation constant, pK_a 8·24. The pK_a 4·35, determined by potentiometric titration, corresponds to an equivalent weight of 210; that of 8·24 corresponds to an equivalent of 102.

The theoretical molecular weight of the monomer is 102·1, and that determined cryoscopically in water is 118—128, corresponding to association of up to 21% in concentrations of 30·8—52·9 g./kg.

Potentiometric titration of the acid *B* in 10% formaldehyde solution gives only one end-point, corresponding to pK_a 4·35 and an equivalent of 102. The mechanism of the Sørensen titration has been variously interpreted but effectively involves the blocking of an amino-group. The implication is that in the absence of formaldehyde one of two amino-groups is protonated in aqueous solution.

These facts can be explained in terms of the formation of an internal salt,

$$^{+}\mathrm{NH_3{\cdot}N{=}CMe{\cdot}CO_2H} + \mathrm{NH_2{\cdot}N{:}CMe{\cdot}CO_2^{-}}$$

The high solubility of material *B* in water and its virtual insolubility in organic solvents, except dimethylformamide, supports the salt structure. Its conductance was, therefore, examined. The equivalent conductance was found to be 50% greater than that of acetic acid in 0·001N-solution, but seven times greater in 0·1N-solution (Table 1). The conductance of the material *B* is between that of a weak acid and that of a salt; in the more concentrated solutions it is nearer to that of the salts.

When the acid *B* is titrated conductometrically by adding it to the alkali only one end-point is observed, but if the alkali is added to the acid two end-points are obtained (Fig. 1). The first and the second break in the curve correspond to the neutralisation of the acid and the acid salt, respectively. The slope of the central portion of the curve varies with the alkali cation in the order which might be expected from the mobilities. Here, on the proposed formula the ions present, in a titration with sodium hydroxide solution, would be the *cis*-acid * zwitterion $^{+}\mathrm{H_3N{\cdot}N{:}CMe{\cdot}CO_2^{-}}$, the *trans*-ion $\mathrm{H_2N{\cdot}N{:}CMe{\cdot}CO_2^{-}}$, and $\mathrm{Na^+}$. Of these species, the zwitterion will not carry current. Addition of alkali to the mixture beyond the first break in the curve would be expected to increase the specific conductance;

TABLE 1.

Equivalent conductance of pyruvic acid hydrazone *B* (equiv. 102) at 24·2° and of other substances at 25°.

Primary measurements.

10^4c (g.-equiv./l.)	1936	968	489	193·6	96·8	19·4	9·68	1·94
Eq. cond. (cm.^{2} mho g.-equiv.$^{-1}$)	35	38	41	44	47	66	75	102

Interpolated or extrapolated values.[5]

Normality	0·2	0·1	0·02	0·01	0·002	0·001
Eq. cond.: subst. *B*	34	37	44	47	66	75
AcOH		5·2		16·2		48·6
$\frac{1}{2}\mathrm{MgSO_4}$	49·8	57·8	79·0	89·9	110·9	117·6
NaCl	101·5	106·6	115·8	118·6	123·0	124·1

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* *cis* and *trans* refer to the relative positions of the amino- and the carboxyl group.

[4] Lindgren and Niemann, *J. Amer. Chem. Soc.*, 1949, **71**, 1504.

[5] Glasstone, "An Introduction to Electrochemistry," Van Nostrand, New York, 1942, p. 51. International Critical Tables, McGraw-Hill, New York, 1929, Vol. **6**.

this is the case with potassium hydroxide, but not with lithium or sodium hydroxide. This behaviour fits qualitatively the idea that the second stage of the neutralisation involves production of a salt in which the metal ion is co-ordinated with a *cis*-isomer, and this view is supported by the molecular weights of the sodium salts in water (Table 2). If the " monosodium " salt were completely dissociated its apparent molecular weight would be 81·4, so at the concentrations used in these experiments (2%) there was up to 10% association. The molecular weight of the " disodium " salt agrees with the view that one anion–cation pair is almost completely undissociated whilst the other is associated to about the same extent as in the " monosodium " salt.

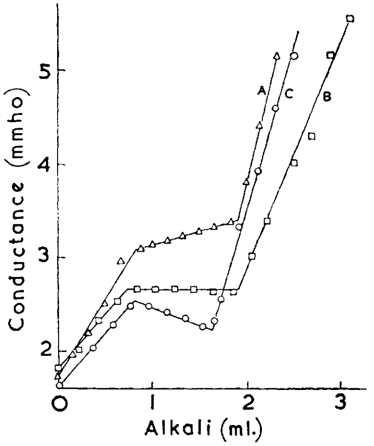

FIG. 1. Titration of 2·5 ml. of pyruvic acid hydrazone *B* solution (46·17 g./l.), made up to about 50 ml., with alkali (corrected to 0·5N): (A) KOH, (B) NaOH, (C) LiOH.

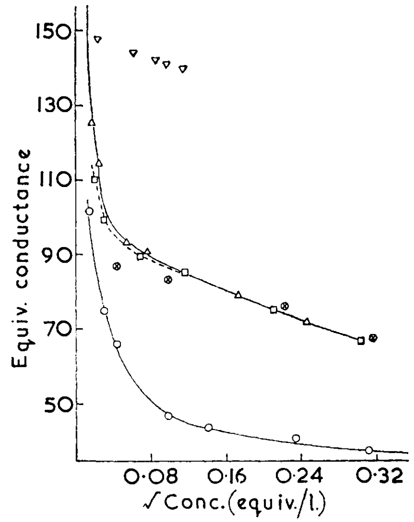

FIG. 2. Equivalent conductance of pyruvic acid hydrazone *B* and its sodium salts (equiv. wts. as in Tables 1 and 3) at 24°. (○) Acid, (□) "monosodium" salt, (△) " disodium " salt, (⊗) sodium acetate at 25°,[5] ▽ potassium chloride at 25°.[6]

TABLE 2.

Apparent molecular weights of pyruvic acid hydrazone *B* and its sodium salts in water.

Free acid		" Monosodium " salt		" Disodium " salt	
c (g./kg.)	*M*	*c* (g./kg.)	*M*	*c* (g./kg.)	*M*
52·89	128·6	13·94	85·7	23·86	96·2
30·81	118·1	17·85	88·6	15·90	82·7
33·21	119·4				

Table 3 shows the equivalent conductances of the " mono- " and " di-sodium " salts at various concentrations. Whilst our experimental conductance techniques were not sophisticated they were adequate in view of the large deviations from " normal " behaviour. The fact that two series of measurements were combined to produce the experimental curve (Fig. 2) suggests that the resistance values of the various solutions are substantially correct. It seems likely from Table 3 that one of the ions has an unusually high conductance since, from molecular weight measurements, one pair of ions in the " disodium "

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[6] Monk, "Electrolytic Dissociation," Academic Press, London and New York, 1961, p. 4.

TABLE 3.

Equivalent conductance of sodium salts of pyruvic acid hydrazone *B* at 24°.

$C_6H_{11}N_4O_4Na,H_2O$: equiv. taken as 122·1.

c (10^{-4} g.-equiv./l.)	925·2	462·6	92·52	46·26	9·252	0·925
Eq. cond. (cm.^{2} mho g.-equiv.$^{-1}$)	67	75	85	90	99	110

$C_6H_{10}N_4O_4Na_2,H_2O$: equiv. 133·1.

c	591·3	295·6	59·13	29·56	5·913	2·956	0·591
Eq. cond.	72	79	91	94	115	125	178

salt appears to be undissociated. Further, if 244·2 is used for the equivalent weight of the " monosodium " salt, the figures for its equivalent conductance become very high.

Crystallisation of Salts of Pyruvic Acid Hydrazone B.—The unusual nature of the material *B* could involve its being a compound of the *cis*- and the *trans*-form of pyruvic acid hydrazone. In attempts to recrystallise salts of the acid, brucine and tropine gave complex compounds, and methylamine, diethylamine, and piperidine did not give crystalline derivatives. The reaction with 1-naphthyl isocyanate also gave a complex compound.

The salts of univalent metals such as lithium, sodium, and potassium do not crystallise easily so that they do not provide a ready method of separation. If, however, the initial stages of the crystallisation are followed under a binocular microscope it is possible to detect and prevent any intervening coacervate stage. Crystals were obtained by this method which had a simpler infrared spectrum in the carboxylate ion regions (peaks at 1575, 1425, and 1390 cm.$^{-1}$) in place of the double set usually observed (see below). This spectrum has rather similar features to that obtained from the sodium salt of acid *A* but the relative intensities of the peaks are different, suggesting that one of the salts is impure. Since recrystallisation of the salt from material *A* gives that from *B* it is probably not possible to obtain better evidence of their identity.

Infrared Spectra.—The material *B* and the " monosodium " salt of *B* show broad absorption in the 3000 cm.$^{-1}$ region with smaller peaks at 2600—2800 cm.$^{-1}$, both characteristics associated with hydrogen-bond formation.[7] The " disodium " salt and substance *A* do not show this absorption and thus appear not to be hydrogen-bonded forms. The pure material *A* should then be the *trans*-form, while *B* consists of *cis*- and *trans*-forms combined as a salt.

When the material *B* is converted into either of its sodium salts, strong absorption appears in the carboxylate-ion region (1595, 1560, 1450, and 1410 cm.$^{-1}$), with a shoulder at 1390 cm.$^{-1}$. Compared with those for other sodium salts of organic acids these frequencies appear to be double. A detailed examination of the infrared spectra of these and related compounds will be reported later.

Conclusions.—Potentiometric titrations show pyruvic acid hydrazone *B* to consist of two parts which conductance and solubility measurements indicate are ions in a salt. Whereas it seemed probable that the proton transfer would require the two parts to be dissimilar, a rather similar transfer is involved in the ionic structure of solid phosphorus pentachloride,[8] so this transfer might take place for energetic reasons. The main evidence comes from the infrared spectra. First, the spectrum of the pure material *B* is much " flatter " than that of the impure material *A*, suggesting the presence of more than one component in the latter. Secondly, the unusual complexity of the spectra of the sodium salts in the carboxylate-ion regions confirms the idea that material *B* contains *cis*- and *trans*-isomers. This is supported by the presence of hydrogen-bonded hydroxyl absorption in the " monosodium " salt and its absence in the " disodium " salt. The infrared evidence is thus in accord with that obtained from conductance measurements, which suggests that

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[7] Beaven, Johnson, Willis, and Miller, " Molecular Spectroscopy," Heywood, London, 1961, p. 235.

[8] Clark, Powell, and Wells, *J.*, 1942, 642.

one hydrazone residue chelates much more readily than the other. In general, all the evidence can be fitted together in the view that the hydrazone *B* is a salt composed of a molecule each of the *cis*- and the *trans*-acid, and that the material *A* is the *trans*-acid contaminated with *B*.

It is interesting that the acid *A* and the " mono- " and the " di-sodium " salt of *B* each have half a molecule of water of crystallisation, whereas material *B* is anhydrous.

EXPERIMENTAL

Preparation of Pyruvic Acid Hydrazones.—The acid and its salts generally became coloured on storage and in some cases liquefied. M. p.s were determined on a microscope stage.

(*a*) 99% Hydrazine hydrate (5 g.) was slowly added to fresh or redistilled pyruvic acid (B.D.H.) (8·8 g.) in absolute alcohol (30 ml.), cooled in carbon dioxide–acetone. Crystals of *pyruvic acid hydrazone* A (8·5 g., 85%), m. p. 90—100°, were eventually deposited. When a small quantity was washed with water and rapidly recrystallised from cold aqueous alcohol by evaporation at the pump, they had m. p. 100·5—102° (Found: C, 32·4; H, 6·5; N, 25·8. $C_6H_{12}N_4O_4,H_2O$ requires C, 32·4; H, 6·3; N, 25·2%). Recrystallisation from warm aqueous ethanol gave material *B* (see below).

(*b*) The above preparation was repeated except that the mixture was allowed to warm from room temperature during the addition. Crystals of *hydrazone* B (6 g., 60%) were deposited. When recrystallised thrice from warm aqueous ethanol these had m. p. 137—137·5° (Found: C, 34·8; H, 6·2; N, 27·1. $C_3H_6N_2O_2$ requires C, 35·3; H, 5·92; N, 27·5%).

Reactions of Pyruvic Acid Hydrazone B.—(*a*) *With brucine.* Pyruvic acid hydrazone *B* (0·5 g.) in water (1 ml.) was added to brucine (2 g.) in alcohol (5 ml.). The deposited crystals (0·9 g.), when recrystallised from absolute ethanol, had m. p. 135—135·5°, $[\alpha]_D$ +38·6° (*c* 1·1 EtOH; *l* = 2) (Found: C, 54·3; H, 6·7; N, 7·6. Calc. for $C_{47}H_{70}N_5O_{18}$: C, 56·8; H, 7·1; N, 7·0%).

(*b*) *With tropine.* The hydrazone *B* (1 g.) in water (0·5 ml.) was added to tropine (1·4 g.) in ethanol (5 ml.). The deposited crystals (0·9 g.), m. p. 118—168°, when recrystallised from water, had m. p. 165·5—167° (Found: C, 69·5; H, 6·9; N, 7·3. Calc. for $C_{11}H_{13}NO_2$: C, 69·1; H, 6·9; N, 7·3%).

(*c*) *With trimethylamine, diethylamine, and piperidine.* Equimolar quantities of the hydrazone *B* in the minimum quantity of water were added to each base in ethanol. Crystallisation could not be induced.

(*d*) *With* 1-*naphthyl isocyanate.* The hydrazone *B* (1·3 g.) was shaken with 1-naphthyl isocyanate (2·1 g.) in light petroleum (b. p. 40—60°; dried by Na) (10 ml.) and left with exclusion of moisture for a week. The white crystals (1·9 g., 70%), m. p. 218—220°, when recrystallised from water and dimethylformamide, had m. p. 222—223° (Found: C, 70·5; H, 5·1; N, 14·3. Calc. for $C_{28}H_{25}N_5O_3$: C, 70·1; H, 5·3; N, 14·6%).

(*e*) *With sodium picrate.* When equimolar amounts of pyruvic acid hydrazone *B* and sodium picrate were mixed in water, hydrazine picrate monohydrate crystallised; it was identified by its infrared spectrum.

(*f*) *With hydrogen chloride.* When hydrogen chloride was passed through saturated aqueous pyruvic acid hydrazone *B* a white solid separated which was identified by its equivalent weight and infrared spectrum as hydrazine dihydrochloride.

Preparation of Salts of Pyruvic Acid Hydrazone B.—" *Monosodium* " *salt.* Water (10 ml.) was added to pyruvic acid hydrazone *B* (2 g.) and ignited sodium carbonate (0·53 g.). The *salt* was then precipitated by addition of ethanol and recrystallised from aqueous ethanol. Carbon and hydrogen analyses were unsatisfactory (Found, by the zinc uranyl acetate method: Na, 9·4. $C_6H_{11}N_4NaO_4,H_2O$ requires Na, 9·4%).

" *Disodium* " *salt.* To pyruvic acid hydrazone *B* (0·84 g.) in water (1 ml.) was added 1·8N-sodium hydroxide (5 ml.). The *salt* was precipitated by ethanol and recrystallised from aqueous ethanol in a saturated alcoholic atmosphere with binocular-microscopic observation of the initial crystallisation (Found, as above: Na, 17·5, 17·6. $C_6H_{10}N_4Na_2O_4,H_2O$ requires 17·3%).

The sodium salt of pyruvic acid hydrazone *A* was made as for the " disodium " salt of *B*.

Conductance Measurements.—An " Advance " signal generator, Kohlrausch bridge, amplifier, and cathode-ray oscillograph were used with Mullard dip-type electrodes with cell constants

~0·5 cm.$^{-1}$. The water was doubly distilled and passed through an Elgastat apparatus; its conductance was not measurable on the apparatus used. The generator was employed at 800 c./sec. and 22 v.

Infrared Spectra.—These were obtained with a Perkin-Elmer Infracord model 137 double-beam spectrometer by the KBr disc technique.

Molecular-weight Determinations.—The usual Beckmann thermometer and cryoscopic apparatus were used.

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