743. *The Isomeric Pyruvamide Phenylhydrazones.*

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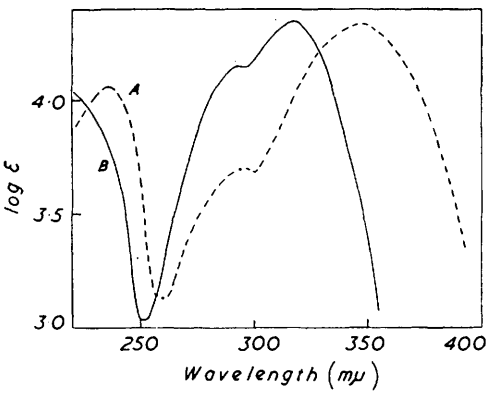
syn- and *anti*-Structures are assigned to the pairs of pyruvamide phenylhydrazones and methyl pyruvate phenylhydrazones on the basis of infrared spectra, hydrogen-bonding occurring in the *syn*-forms.

Pyruvamide phenylhydrazone was first reported by Gastaldi [1] who obtained it as colourless plates, m. p. 144°, by reduction of *N*-hydroxypyruvamide phenylhydrazone with sodium amalgam. The product prepared from pyruvamide and phenylhydrazine in dilute hydrochloric acid [2] was similar to Gastaldi's, whereas that prepared in dilute alcohol [3] was obtained as yellow needles, m. p. 118—119°.

We have now found that the yellow modification is also formed in dilute acetic acid and may be converted into the colourless form by recrystallisation from water containing a trace of alkali, or in the cold by treatment with dilute mineral acid or with chloroform. It has not been possible to effect the reverse transformation; when an aqueous or ethanolic solution of the colourless modification was treated with ammonia or sulphur dioxide [4] a yellow colour appeared immediately, but only the colourless form was recovered. Acid



Methyl pyruvate phenylhydrazones in ether.

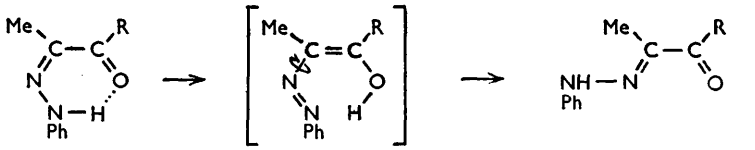
A, syn; *B*, anti.

or alkaline hydrolysis of either amide gave the same pyruvic acid phenylhydrazone, identical in infrared absorption with specimens prepared from pyruvic acid and phenylhydrazine in dilute aqueous hydrochloric or acetic acid, alcohol, or ether. The crude materials from these preparations ranged in colour from orange to colourless and in melting point from 170° to 185°, but on purification all gave the compound, m. p. 189°. The presence of an isomeric form in some of these crude acids could not be detected spectroscopically but was shown indirectly by methylation with diazomethane, whereby two isomeric methyl pyruvate phenylhydrazones were obtained. The colourless modification, m. p. 94—95°, is known; [5] the yellow form, m. p. 56—58°, is new. Two isomeric ethyl pyruvate phenylhydrazones, colourless and yellow, melting at 116—117° and 31—32° respectively, have been reported.[6]

It seemed likely that the isomerism of these hydrazones was geometrical. Instances of such isomerism in similar compounds, *e.g.*, acetaldehyde phenylhydrazone [4] and pyruvic acid 2 : 4-dinitrophenylhydrazone,[7] have been observed. The ultraviolet absorption curves

[1] Gastaldi, *Gazzetta*, 1924, **54**, 212.
[2] Leete, Marion, and Spenser, *Canad. J. Chem.*, 1955, **33**, 405.
[3] Abramovitch, *J.*, 1956, 4593.
[4] Cf. Laws and Sidgwick, *J.*, 1911, **99**, 2085.
[5] Simon and Piaux, *Bull. Soc. Chim. biol.*, 1924, **6**, 412.
[6] Simon, *Compt. rend.*, 1900, **131**, 682.
[7] Isherwood and Lumley-Jones, *Nature*, 1955, **175**, 419.

of the isomeric methyl esters (see Figure) show marked differences in the intensity of the band at 295 mμ and, since the more elongated of two geometrical isomers generally shows more intense absorption,[8] the colourless ester, m. p. 94—95° (curve *B*), must have the chromophores *trans* to each other. When the chromophores are *cis* to each other (*syn*-form) hydrogen bonding is possible and this leads to increased resonance energy and therefore to a bathochromic shift of the 315 mμ band to 350 mμ (curve *A*), tailing off into the visible region and giving rise to the yellow colour. We were unable to detect such distinct differences in the ultraviolet spectra of the isomeric amides, presumably owing to the ease with which the *syn*-form isomerises to the *anti*-configuration. A differentiation between the *syn*- (I, II) and *anti*-forms (III, IV) should be possible from a study of the infrared spectra, since the carbonyl group is intramolecularly hydrogen-bonded in the *syn*-form. Chloroform isomerised the yellow to the colourless amide, so that the spectra in this solvent were identical. Examination of potassium chloride discs of the isomeric amides showed that the colourless form had the C=O band at 1681 cm.$^{-1}$, whereas the yellow form had the C=O band at 1656 cm.$^{-1}$, indicating that the carbonyl group is hydrogen-bonded in the yellow form, which is then represented by the *syn*-structure (I). Similarly, the ester-carbonyl band of the high-melting methyl ester occurred at 1698 cm.$^{-1}$ (*anti*), while in the low-melting ester it appeared at 1675 cm.$^{-1}$ (*syn*). The isomerisation, which is probably acid- and base-catalysed, presumably takes place in the stages shown, facilitated in the first instance by the proximity of the oxygen and the hydrogen atom:



(I) : R = NH_2
(II): R = OMe

(III) : R = NH_2
(IV) : R = OMe

There are other differences in the infrared absorption spectra of the two amides. The yellow modification is appreciably soluble in Nujol, giving rise to bands for both solution and mull[3] (Table), whereas the colourless form has the expected three bands in the 3 μ region and the amide I band at 1656 cm.$^{-1}$. Of the two bands exhibited by the yellow form in the 6 μ region, one was previously attributed[3] to a C=N stretching motion. It has now

Infrared bands (cm.$^{-1}$).

Pyruvamide phenylhydrazone:		
yellow form	(*a*) 3509 (sh), 3448, 3300, 3226	1656, 1610
	(*b*) 3534, 3484, 3425, 3322, 3247, 3185 (sh)	1667, 1650, 1608
colourless form	(*a*) 3509, 3356 (sh), 3300, 3247	1681, 1672 (sh), 1613
	(*b*) 3425, 3390, 3236	1656, 1616, 1605 (sh)
	(*c*) 3509, 3413, 3378	1681, 1605
Methyl pyruvate phenylhydrazone:		
yellow form	(*b*) 3279	1675
colourless form	(*b*) 3344	1698, 1667 (sh)
Acetaldehyde phenylhydrazone ...	(*b*) 3300	1608

(*a*) Potassium chloride disc. (*b*) Nujol mull. (*c*) Chloroform solution.

been observed that acetaldehyde phenylhydrazone itself shows no separate C=N band in this region, but only one band due to both phenyl and C=N absorptions. The coincidence of phenyl and C=N absorptions is in agreement with the observations of Fabian, Legrand, and Poirier,[9] whereas Kirrmann[10] finds that a *NN*-dialkylhydrazone shows a band at 1650 cm.$^{-1}$. It appears that in phenyl(as opposed to alkyl)hydrazones the aryl group

[8] Koch, *Chem. and Ind.*, 1942, **20**, 273.
[9] Fabian, Legrand, and Poirier, *Bull. Soc. chim. France*, 1956, 1506.
[10] Kirrmann, *ibid.*, p. 1751.

influences considerably the double-bond character of the C=N grouping, perhaps owing to contributions from dipolar canonical forms. It follows that 2 : 3-dioxopiperidine 3-phenylhydrazones should not exhibit the two distinct bands for the amide-carbonyl and the C=N group which were previously expected.[3] The bands at 1667 and 1650 cm.$^{-1}$ in the spectrum of the yellow pyruvamide phenylhydrazone are probably due to C=O absorptions of the compound in solution and in suspension in Nujol.

Experimental

Infrared measurements were carried out on a Grubb–Parsons Model S4 double-beam instrument. Ultraviolet absorption spectra were determined on a Unicam S.P. 500 spectrophotometer.

syn-*Pyruvamide Phenylhydrazone.*—(i) (Cf. ref. 3) Pyruvamide (0·5 g.) in hot water (15 ml.) was treated with phenylhydrazine (0·5 g., 0·46 ml.) in ethanol (2 ml.) and set aside for 15 min. Scratching with a glass rod caused crystallisation of the yellow solid which was collected and recrystallised twice from dilute ethanol, giving yellow needles of the hydrazone, m. p. 118—119° (Found: C, 61·2; H, 6·3; N, 23·4. Calc. for $C_9H_{11}ON_3$: C, 61·0; H, 6·3; N, 23·7%).

(ii) Pyruvamide (0·545 g.) in water (10 ml.) was added to a filtered solution of redistilled phenylhydrazine (0·675 g.) in water (5 ml.) containing acetic acid (0·5 ml.). The mixture became yellow instantly and crystallisation was completed by keeping it at 0° for 2 hr.; the product was collected and recrystallised from dilute alcohol, giving the *syn*-amide phenylhydrazone (0·75 g.), m. p. 117—118°. Concentration of the mother-liquors in the cold at 10^{-3} mm. gave the *anti*-amide phenylhydrazone (0·055 g.), m. p. 143—144°. In more dilute solution a smaller first crop of the *syn*-amide and a larger second crop of the *anti*-amide are obtained.

anti-*Pyruvamide Phenylhydrazone* (cf. Leete, Marion, and Spenser [2]).—Pyruvamide (0·261 g.) in water (2·5 ml.) was added to a warm solution of redistilled phenylhydrazine (0·324 g.) in N-hydrochloric acid (3·5 ml.). The mixture became momentarily yellow, and colourless product separated immediately. After 2 hr. at 0° the product was collected and recrystallised from hot water, giving colourless *anti*-pyruvamide phenylhydrazone (0·435 g.), m. p. 143—144°, $\lambda_{max.}$ 225, 295, 325, mμ (log ε 4·10, 4·05, 4·30) in EtOH (Found: C, 61·1; H, 6·4; N, 23·3%; *M*, 181. Calc. for $C_9H_{11}ON_3$: C, 61·0; H, 6·3; N, 23·7%; *M*, 177). Gastaldi [1] gives m. p. 144°.

Conversion of syn- *into* anti-*Amide.*—Recrystallisation of the *syn*-isomer from water containing 1 or 2 drops of 5N-sodium hydroxide gave the colourless *anti*-isomer, m. p. 143—144°. The same conversion was effected by treating the yellow phenylhydrazone with dilute hydrochloric acid at room temperature or dissolving it in chloroform. A crude sample of the yellow isomer changed to the colourless modification when kept in a specimen tube for a few months.

Treatment of the *anti*-form in aqueous alcohol with sulphur dioxide gave an immediate yellow colour. Evaporation of the solvent gave a yellow product, m. p. 130—135°, but pure low-melting isomer could not be obtained.

Hydrolysis of the Isomeric Amides.—(i) *Acid hydrolysis.* Either amide (0·20 g.) in water (10 ml.) containing a trace of methanol was heated at 100° for 10 min. with 3N-hydrochloric acid (4 ml.); there separated pyruvic acid phenylhydrazone (85%), m. p. 178—179° (decomp.), $\lambda_{max.}$ (log ε in parentheses) 230 (4·05), 295 (4·05) (sh), 320 mμ (4·35) in 0·1N-HCl in aq. EtOH; 290 (4·27), 310 mμ (4·26) in 0·1N-NaOH in aq. EtOH. The infrared spectra of the acids obtained from the *syn*- and the *anti*-amide were identical. If a large excess of hydrochloric acid was used the solution became red and only intractable material was obtained, probably owing to formation of indole compounds.

(ii) *Alkaline hydrolysis.* Either amide (0·3 g.) in hot methanol (4 ml.) was refluxed with 5N-sodium hydroxide (10 ml.). Ammonia was liberated after a few minutes and hydrolysis was complete in 2 hr. The cold solution was acidified with acetic acid, giving pyruvic acid phenylhydrazone, m. p. 180—181° (decomp.), quantitatively. The infrared spectra of the acids obtained were identical with those of the acid hydrolysis products.

Isomeric Methyl Pyruvate Phenylhydrazones.—Redistilled phenylhydrazine (2·7 g.) in ether (30 ml.) was added to pyruvic acid (2·2 g.) in ether (30 ml.) and the phenylhydrazone (2·7 g.), m. p. 178—180° (fraction A), which crystallised almost immediately, was filtered off after the mixture had been kept for 3 days at 0°. The filtrate was taken to dryness and yielded a red solid which was extracted with boiling water (300 ml.), leaving an undissolved residue (0·3 g.), m. p.

173—174° (fraction B). The aqueous extract gave a further crop of product (0·9 g.), m. p. 179—180°.

(i) anti-*Methyl pyruvate phenylhydrazone.* A suspension of pyruvic acid phenylhydrazone (1 g. of fraction A) in ether was treated with excess of diazomethane in ether. After removal of the solvent the *anti*-ester (0·92 g.) crystallised slowly. It was dissolved in boiling water, filtered from some oily drops, and crystallised in long colourless needles, m. p. 94—95° (Found: C, 62·5; H, 6·5; N, 14·6. Calc. for $C_{10}H_{12}O_2N_2$: C, 62·5; H, 6·3; N, 14·6%). (ii) syn-*Methyl pyruvate phenylhydrazone.* Fraction B was suspended in ether and treated with ethereal diazomethane, the solvent evaporated, and the red oily residue extracted with boiling water. The water-insoluble oil was dissolved in ether, dried (Na_2SO_4), and recovered. The product sublimed at 70°/10^{-3} mm., to give prisms of yellow syn-*methyl pyruvate phenylhydrazone* (0·2 g.), m. p. 56—58° (Found: C, 62·4; H, 6·4; N, 14·5%). At 90°/10^{-3} mm. colourless needles of the *anti*-ester, m. p. 94—95°, sublimed.

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