(0.0194 g.-atom) of magnesium turnings, and 25 ml. of anhydrous ether. Then a solution of 2.5 g. (0.0085 mole) of crude 1-chloro-4,7,10,13-nonadecatetraene in 20 ml. of anhydrous ether was added over 15 min. to the ethylmagnesium bromide and the remaining magnesium. The reaction mixture was stirred and refluxed for 18 hr., after which time only a small amount of magnesium remained, and then it was poured onto a slurry of 75 g. of powdered Dry Ice in 100 ml. of ether.[21] When the temperature had reached about 10°, 50 ml. of saturated ammonium chloride solution was added, and the mixture was shaken with just enough water to dissolve the solids and give two clear phases. The ether layer was washed with four 30-ml. portions of ice water, dried over sodium sulfate, and stripped *in vacuo*. The product, crude arachidonic acid (XIII), was obtained as an orange, unpleasant-smelling oil.

The crude arachidonic acid, dissolved in 50 ml. of ether, was added to 60 ml. of 0.34*M* diazomethane in ether (0.02 moles of diazomethane) and the solution was allowed to stand at 0° for 20 hr. A small amount of gelatinous matter was filtered, and, after stripping the solvent *in vacuo*, the residue was distilled through a 4-inch Vigreux column at <0.001 mm. pressure. The ester, total yield 1.5 g. (45% based on 1-chloro-4,7,10,13-nonadecatetrayne), was obtained as a series of cuts, which boiled from 113–118°, and had refractive indices which ranged from 1.4797 to 1.4810 at 20°. The tail fraction, consisting of about 10% of the total, distilled at 126° (a reflection of the higher bath temperature) and had n_D^{20} 1.4797. All the cuts were only faintly yellow and had an unpleasant odor.

The cut, b.p. 116–118° (<0.001 mm.), n_D^{20} 1.4806,[22] was selected for microanalysis, spectral examination and hydrogenation with the following results:

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.60; H, 11.17. Infrared (Film): peak at 5.76 μ (ester); peak at 6.05 μ (isolated $-CH{=}CH-$); small peak at 10.3 μ (some *trans* $-CH{=}CH-$). Except for the small peak at 10.3 μ the infrared spectrum of the liquid was essentially identical with that of natural material prepared by Dr. E. Kyburz.[12] Ultraviolet (in isopropyl alcohol): max. at 233–234 mμ (ϵ 815) and poorly defined maxima or inflections at 264–265 mμ (ϵ 235), 273–274 mμ (ϵ 230), and 318 mμ (ϵ 0.60).

Hydrogenation (platinum, methanol): 240 mg. (mol. wt. 318.6) requires 73.6 ml. at 25° (760 mm.) for four double bonds. Actual uptake 74.2 ml. at 25° (760 mm.). M.p. of hydrogenation product (A), 42°. M.p. of methyl arachidate (B),[23] 45°. Mixed m.p. A + B, 42–45°.

Acknowledgment. The authors are indebted to Dr. Al Steyermark and his staff for the microanalyses, to Dr. A. Motchane, Mr. S. Traiman, and Dr. V. Toome for the infrared and ultraviolet spectra, and to Mrs. R. Reardon for technical assistance.

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[21] A. S. Hussey, *J. Am. Chem. Soc.*, **73**, 1364 (1951).

[22] Material isolated from natural sources has been reported to have n_D^{20} 1.47986 (S. F. Herb, R. W. Riemenschneider, and J. Donaldson, footnote 5) and n_D^{20} 1.4786 (Private communication from Dr. E. Kyburz, F. Hoffmann-LaRoche & Co., Basle, Switzerland, footnote 12).

[23] Prepared by esterifying pure synthetic arachidic acid (m.p. 74–75°), purchased from Distillation Products Industries, Rochester, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF BARNARD COLLEGE]

Benzylidenepyruvic Acids. IV.[1a] *o*-Nitrobenzylidenepyruvic Acid and Its Enol-Lactone Tautomer

EMMA DIETZ STECHER AND ERNESTINE GELBLUM[1b]

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Acid-catalyzed condensation of *o*-nitrobenzaldehyde with pyruvic acid produces a stable enol-lactone, 2,4-dihydroxy-4-(*o*-nitrophenyl)crotonic acid, γ-lactone (Ia) which is a weak acid. With diazomethane this forms the lactone ether (III) but with methanolic hydrogen chloride, Ia is methylated and tautomerized to the keto ester (IV). Alkaline hydrolysis of IV forms *o*-nitrobenzylidenepyruvic acid (V), a strong acid. Reactions of Ia and V with bromine and with phenylhydrazine are described.

In a recent publication[2a] we reported the determination of a reaction constant *rho*, for the dissociation of a series of benzylidenepyruvic acids with substituents on the benzene ring. The corresponding methyl esters were used to determine a *rho* value for the hydrolysis reaction in alkaline medium. Rate constants were determined spectrophotometrically in weakly alkaline buffers.

In the course of the preparation of the required *o*-nitrobenzylidenepyruvic acid (V) and ester, we found a further example of the lacto-enoic tautomerism recently uncovered for *p*-bromo- and *p*-ethoxy-β-bromobenzylidenepyruvic acids.[2b] When *o*-nitrobenzaldehyde was condensed with pyruvic acid using dry hydrogen chloride as the catalyst, the only product was 2,4-dihydroxy-4-(*o*-nitrophenyl)crotonic acid, γ lactone (Ia), m.p. 138–139°. This is the method described by Baeyer and Drewson,[3] by Heller[4] (m. p. 135–136°) and by Ciusa[4] (m.p. 135–136°). They all believed their product

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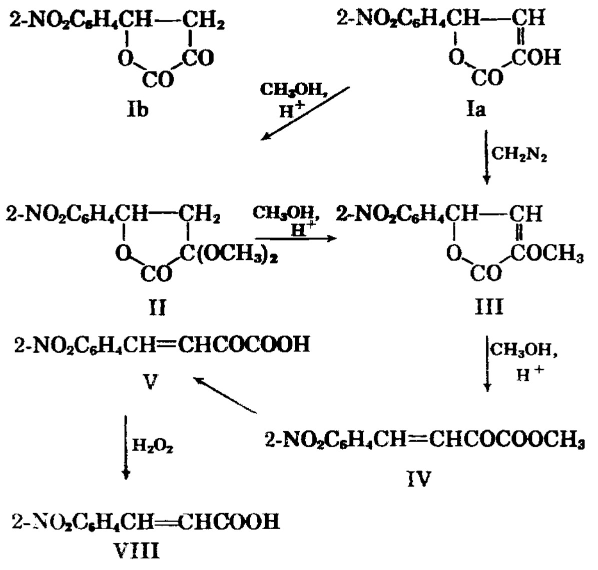
[1] (a) For papers III and II see Ref. 2. (b) Present address: American Cyanamid Laboratory, Stamford, Conn.

[2] (a) E. D. Stecher, F. Dunn, and E. Gelblum, *J. Am. Chem. Soc.*, **79**, 4748 (1957). (b) E. D. Stecher and A. Clements, *J. Am. Chem. Soc.*, **76**, 503 (1954).

[3] A. Baeyer and V. Drewson, *Ber.*, **15**, 2862 (1882); D.R.P. **19768**, Feb. 24, 1882; Frdl. 1, 140.

[4] G. Heller, *Ber.*, **43**, 1924 (1910). R. Ciusa, *Gazz.*, **49**, 168 (1919).



to be the tautomeric *o*-nitrobenzylidenepyruvic acid (V).

We have prepared both of these compounds (Ia and V) and have established their structures by physical and chemical methods. The colorless enol lactone (Ia) is a weak acid (pK' 7.25 in 48% methanol–0.2N lithium chloride). It forms a red complex with alcoholic ferric chloride solution. In methanol it has an absorption peak below 225 mμ, inflection 257 mμ, and in the infrared there is a double peak at 5.67 and 5.71 μ due to the lactone group (potassium bromide spectrum). The yellow keto acid (V) melting at 131° is a much stronger acid than the enol lactone. Its pK' is 2.54 in 48% methanol–0.2N lithium chloride, and it does not react with ferric chloride solution. Absorption takes place at 255 mμ, inflection at 280 mμ (methanol). Sharp bands at 5.67 and 5.95 μ (potassium bromide), correspond to the acid carbonyl and the conjugated carbonyl groups respectively. The keto acid is rapidly oxidized by alkaline hydrogen peroxide to *trans*-*o*-nitrocinnamic acid (VIII), identified by its melting point and that of its methyl ester. The enol lactone is characteristically not oxidized under the same conditions.[2b]

Ia is smoothly methylated with diazomethane to the enol ether (III), which has a sharper lactone band at 5.62 μ. It has lost the bonded hydroxyl band of the free enol at 3.00 μ as well as a weak band at 5.98 μ ascribable to the keto lactone (Ib).

Other enol lactones in this series are unaffected by boiling with methanol containing dry hydrogen chloride.[2b] If however the lactone (Ia) is refluxed with this reagent for various periods, several products are obtained. After fifteen minutes a 42% yield of the dimethyl ketal of the keto lactone II was isolated. After an hour and a half the yield of pure ketal (II) was 22–27% and that of keto ester (IV) was 31–47%. After three to four and a half hours the yield of ester had increased to 47–61%. The ketal was no longer detected, but 8.3% of pure lactone ether (III) was isolated.

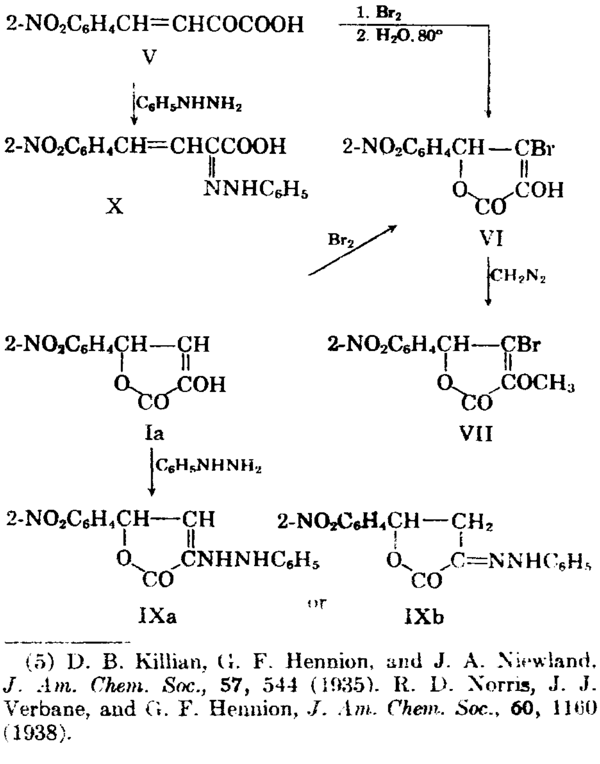
The same reagent converted the pure enol ether (III) to keto ester in 29% yield in thirty minutes. In a qualitative experiment the pure ketal (II) was also changed to keto ester in appreciable amounts in forty-five minutes at 70°.

One may conclude from these results that the enol lactone (Ia) is first converted to the dimethyl ketal of the keto lactone (II), then by loss of methanol to the enol ether (III), then to the keto ester (IV). The acid-catalyzed conversion of dimethyl ketals to enol-ethers has been reported.[5]

Although it is unusual in this series for the enol lactones to react with alcoholic hydrogen chloride,[2b] Ciusa[4] reported a similar formation of an orange ethyl ester, presumably ethyl *o*-nitrobenzylidenepyruvate, from his sample of lactone. Hydrolysis of the keto ester (IV) for a few minutes in 1% sodium bicarbonate solution formed 2-nitrobenzylidenepyruvic acid (V), which was needed for our measurements. This rapid rate of hydrolysis also confirms the keto ester structure.[2a]

It is not practical to condense 2-nitrobenzaldehyde with pyruvic acid in the presence of dilute sodium hydroxide or sodium carbonate, since the chief product is indigo! This was discovered by Baeyer and Drewson[3] who patented the process. Also brief exposure of either the keto acid or the enol lactone to moderately concentrated alkali converts it to indigo. Our only available source of the keto acid (V) was therefore through Ia and IV.

We studied the bromination in chloroform solution of both the enol lactone and the keto acid.



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[5] D. B. Killian, G. F. Hennion, and J. A. Niewland, *J. Am. Chem. Soc.*, **57**, 544 (1935). R. D. Norris, J. J. Verbane, and G. F. Hennion, *J. Am. Chem. Soc.*, **60**, 1160 (1938).

o-Nitrobenzylidenepyruvic acid (V) added bromine rapidly. Evaporation of the solution of the dibromide gave an oil which on boiling with water yielded hydrogen bromide and the expected β-bromolactone (VI), m.p. 183°. (Only rarely are the tautomeric β-bromobenzylidenepyruvic acids stable[2b].) The bromo lactone gives a red color with ferric chloride, and with diazomethane forms the enol ether of the lactone (VII). Neither VI nor VII gave a precipitate with 2,4-dinitrophenylhydrazine solution. They absorb at 255 and 242 mμ respectively in the ultraviolet and at 5.73 and 5.78 μ respectively as the single carbonyl bands in the infrared. These spectra support lactone rather than keto acid or ester structures.

Bromination of the enol lactone (Ia) in chloroform solution immediately formed the same β-bromoenol lactone (VI). Heating with water did not change this product. This was the reaction actually carried out by Ciusa,[4] although he reported a dibromide.

Early investigators studied the products of reaction of benzylidenepyruvic acids, and sometimes inadvertently the tautomeric enol lactones, with phenylhydrazine.[4,6-9] Vaughan *et al.*[10a,b,c] have recently suggested for the phenylhydrazone of benzylidenepyruvic acid, tautomeric structures similar to X for the only form isolated, and a less stable lactone form similar to IXa. In extensive experiments with benzylidenepyruvic acid anils rather than phenylhydrazones, Vaughan found the lactone structures (XII), first reported as pyrrolidinediones,[10d] to be much more stable than the open chain forms (XIII), though both were isolated.

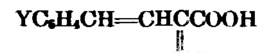
Since in the *o*-nitro series we have available both the keto acid and the stable enol lactone, it seemed of interest to study the reaction of phenylhydrazine on each. Treatment of the enol lactone (Ia) with phenylhydrazine confirmed the findings of Heller.[4] The first product was pale yellow and unstable, possibly an amine salt. It changed rapidly to a stable bright yellow substance, m.p. 223–225° dec. (Heller, m.p. 222° dec.) This still has a lactone absorption band at 5.74 μ (potassium bromide) and is alkali-insoluble. This latter fact rules out a pyrazoline structure (see evidence below proving that the isomeric pyrazolines are acidic). It is probably the phenylhydrazide of the enol form (IXa) or the tautomeric phenylhydrazone of the keto lactone form (IXb).

o-Nitrobenzylidenepyruvic acid (V) on warming with phenylhydrazine in 50% acetic acid readily forms a stable orange-red compound, m.p. 170–171°. This is soluble in dilute alkali, but concentrated base converts it to indigo. The ultraviolet spectrum has a broad peak at 385 mμ (methanol), and in the infrared the first C=O band is found at 6.05 μ (potassium bromide) and is assignable to COO^- of an inner salt structure for the solid. (The first C=O band for potassium benzylidenepyruvate in potassium bromide is at 6.11 μ.) The orange compound is believed to be the true phenylhydrazone (X), probably a dipolar ion in the solid state. It was not sufficiently soluble to permit an infrared spectrum in solution, nor was there enough material for a *p*H titration.

To clarify further the structure of these nitrogen derivatives, the more readily available unsubstituted benzylidenepyruvic acid phenylhydrazone was prepared in the same way. Its absorption behavior closely resembles that of the *o*-nitrophenylhydrazone (X). In potassium bromide there is no C=O band below 6.06 μ, but in chloroform solution there are bands at 5.73 μ (COOH), 5.90 (shoulder), and 5.98 μ. This spectrum checks that reported by Vaughan and McCane.[10c] A *p*H titration with sodium hydroxide gave a typical S-shaped titration curve, further substantiating the presence of a free carboxyl group in solution. (*p*K′ = 4.4 in 66.7% methanol–0.2*N* lithium chloride; *p*K′ for benzoic acid in the same solvent = 5.4). The phenylhydrazone is therefore more acidic than benzoic acid.

We are currently determining *p*K′ values of other substituted benzylidenepyruvic acid phenylhydrazones and of the corresponding 1,5-diphenyl-Δ^2-pyrazoline-3-carboxylic acids, which are only slightly weaker acids (*p*K′ = 4.7–4.9).

In the light of all the evidence, we have assigned the lactone structure (IXa or b) to the alkali-insoluble compound derived from the enol lactone, and the carboxylic acid structure (X) to the phenylhydrazone from *o*-nitrobenzylidenepyruvic acid. This is a dipolar ion in the solid state, probably XI. Although IX and X are tautomeric structures, the



$$2\text{-}NO_2C_6H_4CH{=}CH\underset{\overset{\|}{+NHNHC_6H_5}}{C}COO^-$$

XI

$$YC_6H_4CH{=}CH\underset{\overset{\|}{NC_6H_4Y}}{C}COOH$$

XII

XIII

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(6) E. Erlenmeyer, Jr., *Ber.*, **36**, 2528 (1903); **38**, 3125 (1905).

(7) R. Ciusa and A. Bernardi, *Gazz.*, **41**, 153 (1911).

(8) S. Bodforss, *Ann.*, **455**, 59 (1927).

(9) K. v. Auwers and P. Heimke, *Ann.*, **458**, 212 (1927).

(10) (a) W. R. Vaughan, *J. Org. Chem.*, **20**, 1619 (1955). (b) W. L. Meyer and W. R. Vaughan, *J. Org. Chem.*, **22**, 1566 (1957). (c) W. R. Vaughan and D. I. McCane, *J. Org. Chem.*, **20**, 148 (1955). (d) W. L. Meyer and W. R. Vaughan, *J. Org. Chem.*, **22**, 98, 1557 (1957). Earlier pyrrolidinedione structures were revised to anilinolactones. (e) W. R. Vaughan and L. R. Peters, *J. Org. Chem.*, **18**, 388 (1953). (f) *J. Org. Chem.*, **18**, 411 (1953).

compounds are both stable and were recrystallized without change.

It is instructive to compare closely the properties of the tautomeric aniline derivatives of benzylidenepyruvic acids, as described by Vaughan and co-workers, with the possibly tautomeric phenylhydrazine derivatives of our *o*-nitrobenzylidenepyruvic acid and its enol-lactone. The acid anils[10e] are yellow compounds readily soluble in base. The exceptionally stable acid (XII. $Y = p\text{-}OCH_3$) gave a normal *p*H titration curve in methanol-dioxane solution.[10f] Recrystallization or even long storage in the solid state, converted the acid anils to colorless, alkali-soluble compounds originally described as pyrrolidinediones, later assigned anilino-lactone structures (XIII).[10d] A solution of XIII ($Y = p\text{-}OCH_3$) could be titrated slowly with base, indicating a rapid tautomerism to the acid form. Indeed interconversion of these two compounds in methanol solution was too rapid for the satisfactory determination of the ultraviolet spectrum of either one.[10f] The anilino-lactones absorb in chloroform solution at 2.93, 5.72, and 6.02 μ.[10c] We can find no clear figures for the acid spectra, which in nujol are described as resembling those of benzylidenepyruvic acid phenylhydrazone. Thus, Vaughan and co-workers have isolated examples of both XII and XIII, the benzylidenepyruvic acid anils and the more stable anilino-lactones derived from them. They have also shown a facile equilibrium between the two tautomers in solution.

Our results with the phenylhydrazine reaction as already described indicate that the only product from treatment of *o*-nitrobenzylidenepyruvic acid (and other acids in the series) is a stable acid phenylhydrazone (X). The only product of reaction of the *o*-nitroenol-lactone (Ia) with phenylhydrazine is insoluble in base and has been tentatively assigned the phenylhydrazinolactone structure (IXa). Although IX and X are tautomeric structures, both are stable and do not in our experience interconvert in solution or in the solid state, as do the corresponding aniline derivatives. Although they isolated only one product Vaughan and his co-workers[10b,c] favor a "readily reversible isomerism" for the phenylhydrazone derivatives. The similarities of behavior in the two series serve to support the postulated structures for Vaughan's anils and for the phenylhydrazones.

EXPERIMENTAL

2,4-Dihydroxy-4-(2-nitrophenyl)crotonic acid γ-lactone (Ia), 138–139°, was prepared according to the method of Ciusa[4] who believed it to be the keto acid (V). A mixture of 15.2 g. (0.1 mole) of 2-nitrobenzaldehyde and 18.4 g. (0.21 mole) of pyruvic acid which also serves as solvent, was warmed gently to dissolve, then cooled to 15° while saturating with dry hydrogen chloride. The mixture was left at room temperature for 5 days, when crystals nearly filled the viscous, brown solution. Extraction with small portions of petroleum ether (b.p. 30–60°) removed some aldehyde. The main product was transferred to the filter with 1:1 ether–petroleum ether, and was washed with the same solvent and then with benzene. Yield: 16 g. with 2.2 g. in a second crop (82%). Recrystallized from ether–petroleum ether, the colorless product melted at 138–139°.[11] Yields varied from 60–80% but no other product was isolated.

*p*K′ 7.25 in 48% methanol-0.2*N* lithium chloride; $\lambda_{\max}^{\mathrm{CH_3OH}} < 225$ mμ, $\epsilon > 9400$; inflection 257.5 mμ, ϵ 7,300; $\lambda_{\max}^{\mathrm{KBr}}$ 3.00, broad (bonded hydroxyl) 5.67, 5.71 μ double peak (lactone); 5.98 μ weak (keto lactone Ib?). Both the 3.00 and 5.98 bands are absent in the lactone ether (III). Aqueous ferric chloride solution added to an alcoholic solution produces a clear red color. The addition of 10% sodium hydroxide solution causes indigo to precipitate instantly.[3]

Anal. Calcd. for $C_{10}H_7O_5N$: C, 54.29; H, 3.12; N, 6.33. Found: C, 54.44; H, 3.53; N, 6.30.

2-Methoxy-4-(2-nitrophenyl) crotonic acid, γ-lactone (III) *154.5°*. To 3 g. of lactone (Ia) suspended in 50 ml. of warm ether was added an excess of diazomethane[12] in 200 ml. of ether. A tan powder precipitated rapidly (2.8 g., 88%, m.p. 149–150°). After recrystallization from methanol the colorless crystals melted at 154.5°. Reaction with ferric chloride solution and with 2,4-dinitrophenylhydrazine was negative. $\lambda_{\max}^{\mathrm{CH_3OH}}$ 224 mμ, 14,250; inflection 248 mμ, ϵ 8250. $\lambda_{\max}^{\mathrm{KBr}}$ 5.62 μ (lactone), 6.06 μ (conjugated C=C).

Anal. Calcd. for $C_{11}H_9NO_5$: C, 56.15; H, 3.86; N, 5.96. Found: C, 56.25; H, 3.77; N, 6.20.

Treatment of I with methanolic hydrogen chloride. The following table summarizes individual experiments on 1- to 4-g. samples of lactone (Ia) dissolved in about 15 ml. of methanol saturated with dry hydrogen chloride, per gram of sample. Percentages are based on weights of pure products identified by melting point.

Reflux Time, Hr.	Keto Ester (IV), %	Dimethyl Ketal (II), %	Enol Ether (III), %
0.25	[a]	42	..
1.5	47	27	..
1.5[b]	31	18	..
1.5	54	23	..
4.5	61	..	..
4.5	58	..	8.3[c]
3.0	47	..	

[a] A few yellow crystals separated and the filtrate from II gave an immediate precipitate with 2,4-dinitrophenylhydrazine solution. [b] The usual solution was diluted with an equal volume of methanol. [c] Impure fractions from two experiments were combined and recrystallized to a m.p. of 153–155°; mixture sintered at 153°, melted at 154–155°.

The relative rates of conversion of the pure intermediates, II and III, were followed in a qualitative experiment. Ten-milligram samples of Ia, II, and III were heated at 70° in separate 2-ml. portions of methanolic hydrogen chloride (saturated). One drop of each solution was removed at intervals, cooled, and tested with 2,4-dinitrophenylhydrazine reagent. (Dissolve 1 g. of 2,4-dinitrophenylhydrazine in 15 ml. of concd. sulfuric acid, add 150 ml. of 95% ethanol, dilute to 500 ml. with distilled water, mix and filter.) An

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(11) Melting points were determined with calibrated total immersion thermometers. Ultraviolet spectra were measured on a Beckman DU spectrophotometer; infrared spectra with a Baird instrument using 0.1 mm. sodium chloride cells for solutions. The determination of *p*K′ is described in ref. 2a. Analytical samples were dried for several hours at 3 mm. and 35–55°.

(12) *Org. Syntheses*, Coll. Vol. II., John Wiley, 1943, p. 165.

immediate orange precipitate indicated appreciable amounts of keto ester (IV). The lactone (Ia) gave a heavy precipitate after 30 min. of heating, the ketal (II) after 45 min., the enol ether (III) after about 20 min. of heating.

Even aqueous hydrochloric acid slowly converted the enol lactone to the tautomeric keto acid. Crystals of Ia suspended in 0.5*N* acid for a week changed to crystals of yellow keto acid identified by mixed melting point.

4-Hydroxy-2,2-dimethoxy-4-(2-nitrophenyl)crotonic acid, γ-lactone (II), 117–118°. In one experiment 2 g. (9 mmoles) of lactone (Ia) was refluxed for 90 min. with 25 ml methanol-2% dry hydrogen chloride. Colorless, cubic crystals separated slowly; 0.65 g. (27%), m.p. 109–112°. Two recrystallizations from acetone–petroleum ether gave a pure product, m.p. 117–118°. The filtrate from this preparation yielded 1 g. of yellow crystals of the keto ester (IV), m.p. 96–97° and 0.4 g., m.p. 79–84° (60%). Recrystallization from acetone–petroleum ether raised the melting point to 97–98° with no depression on admixture with IV.

Although refluxing II with methanolic hydrogen chloride for 30–60 min. converted it to the keto ester (IV), the ketal was unchanged when heated for 1 hr. at 145° in a melting point tube. Reaction with ferric chloride solution and with 2,4-dinitrophenylhydrazine was negative. $\lambda_{max}^{CH_3OH} < 225$, $\epsilon > 5000$; inflection 258, ϵ 5250. λ_{max}^{KBr} 5.58 μ (lactone), next band 6.21 μ; C=C and C=O bands are absent.

Anal. Calcd. for $C_{12}H_{13}O_6N$: C, 53.94; H, 4.90; N, 5.24. Found: C, 54.13; H, 4.82; N, 5.40.

Methyl 2-nitrobenzylidenepyruvate (IV), 97–98°.[13] As described above this yellow ester is the major product of 4.5-hr. refluxing of the enol lactone (Ia) with methanolic hydrogen chloride, with dimethyl ketal (II) and the enol ether of the lactone as intermediates. In another experiment, 200 mg. of the enol ether (III) was refluxed for 30 min. with 15 ml. of methanol-2% hydrogen chloride. The bright yellow solution yielded 70 mg. (28.6%) of keto ester, m.p. 94–95° and 100 mg. of impure, colorless starting material, m.p. 100–123°. The preparation of IV from the readily available lactone (Ia) is fortunate since its synthesis through a base-catalyzed Claisen reaction failed because of indigo formation. The ester in methanol solution forms a pale orange 2,4-dinitrophenylhydrazone. $\lambda_{max}^{CH_3OH}$ 250–260 mμ, ϵ 11,000; inflection 280 mμ, ϵ 9,500. λ_{max}^{KBr} 5.80 μ (ester C=O); 5.98 μ (C=O).

2-Nitrobenzylidenepyruvic acid (V), 131.°[13] Preparation from 2-nitrobenzaldehyde and pyruvic acid using alcoholic potassium hydroxide or sodium carbonate as catalysts failed because of preferential formation of indigo.[3] Hydrolysis of the methyl ester (IV) was achieved in weak alkali without indigo formation. To 2 g. (8.5 mmoles) of IV was added 100 ml. of 1% sodium bicarbonate solution. After 5 min. at 25° the product was acidified to *p*H 2 and extracted with ether. The dried solution was evaporated, benzene was added, and this was distilled off at 15 mm. to remove water of hydration. The total yield in three crops was 1.7 g. (77%). Recrystallization from benzene and drying at 3 mm. and 60° gave pale yellow crystals, m.p. 130.5–131°. A bright yellow hydrate, m.p. 84–85°, crystallized from water solution. On storage this lost water with some increase in melting point. *p*K′ 2.54 in 48% methanol–0.2*N* lithium chloride[2a] supports the keto acid structure. $\lambda_{max}^{CH_3OH}$ 255 mμ, ϵ 14,575, inflection 280 mμ, ϵ 13,250; λ_{max}^{KBr} 3.06 μ broad (bonded hydroxyl), 5.67 μ (COOH), 5.95 μ (C=O).

Anal. Calcd. for monohydrate, $C_{10}H_7O_5N \cdot H_2O$: C, 50.20; H, 3.79. Found: C, 50.77; H, 3.96.

trans-2-Nitrocinnamic acid (VIII), 244–245°. In her extensive investigations, Reimer observed that alkaline solutions of benzylidenepyruvic acids are rapidly converted by hydrogen peroxide to the corresponding cinnamic acids, whereas her colorless "β-bromo acids"[14] which we later proved to be enol lactones,[2b] were unreactive. The rapid oxidation of 2-nitrobenzylidenepyruvic acid further supports its keto acid structure. A solution of 150 mg. of V in 5 ml. dioxane was treated alternately with a total of 7 ml. of 1% sodium carbonate solution and 12 ml. of 3% hydrogen peroxide solution, keeping the *p*H close to 8. After 5 min. the mixture was acidified with hydrochloric acid, precipitating colorless crystals of *o*-nitrocinnamic acid. After recrystallization from ethanol the m.p. was 244–245° (reported:[15] m.p. 240.5–241.5°).

Methyl o-nitrocinnamate. The acid (VIII) was esterified with diazomethane in ether solution. On evaporation and addition of petroleum ether, the pure methyl ester separated, m.p. 71–72° (reported[16] m.p. 72–73°).

3-Bromo-2,4-dihydroxy-4-(2-nitrophenyl)crotonic acid, γ-lactone (VI) 183°. Ciusa[4] reported colorless needles, m.p. 182°, from the addition of two bromine atoms to what he believed was the keto acid (V). Actually as we have shown, his original compound was the enol lactone (Ia) from which we obtained only a monobromide. To a solution of 2 g. (9 mmoles) lactone (Ia) in 80 ml. chloroform (dried over calcium chloride) was added 157 ml. of 0.05*M* solution of bromine in chloroform, when an excess of yellow color was observed. After 15 min. at 25°, the solvent was distilled at 15 mm. in a nitrogen atmosphere. Several crops of colorless crystals weighed 2.6 g. (78%). After recrystallization from benzene, the m.p. was 183° dec. There was no loss of hydrogen bromide on boiling with water. A red color resulted with ferric chloride solution and the 2,4-dinitrophenylhydrazine test was negative.

$\lambda_{max}^{CH_3OH}$ 255 mμ, ϵ 8,750; min. 230 mμ, ϵ 5,375; λ_{max}^{KBr} 3.2 μ (bonded hydroxyl), 5.73 μ (lactone), 5.98 μ weak (keto form?).

Anal. Calcd. for $C_{10}H_6O_5NBr$: C, 40.02; H, 2.01; Br, 26.63. Found: C, 39.82; H, 2.20; Br, 26.22.

The same β-bromo enol lactone (VI) was obtained in the usual manner[2b] by treating the keto acid with bromine, and boiling the isolated dibromide with water to remove hydrogen bromide. To a solution of 330 mg. (1.5 mmoles) of 2-nitrobenzylidenepyruvic acid (V) in 15 ml. dry chloroform at 25° was added 17 ml. of a solution of bromine in chloroform (approximately 0.05*M*) to a permanent orange color. The solvent was removed at 12 mm. in a nitrogen atmosphere, but the dibromide did not crystallize readily so the oil was stirred with water at 85° for 30 min. A few crystals separated on cooling but the main product in small yield was extracted from the filtrate with ether, and recrystallized from benzene; m.p. 178–180°. A mixture m.p. with VI gave no depression. A red color was obtained with ferric chloride solution.

3-Bromo-2-methoxy-4-hydroxy-4-(2-nitrophenyl)crotonic acid, γ-lactone (VII), 136–137°. To 470 mg. (1.6 mmoles) of β-bromolactone (VI).in 40 ml. of ether was added 25 ml. of a solution of diazomethane in ether (excess). Shiny, colorless crystals separated on cooling (360 mg., 72%); m.p. 136–137°.

Both ferric chloride and 2,4-dinitrophenylhydrazine tests were negative. $\lambda_{max}^{CH_3OH}$ 242 mμ, ϵ 11,125; min. 230 mμ, ϵ 9250. λ_{max}^{KBr} 5.78, (lactone), 6.09 μ strong. (3.2 and 5.98 bands of the enol (VI) are missing).

Anal. Calcd. for $C_{11}H_8O_5NBr$: C, 42.06; H, 2.56; Br, 25.44. Found: C, 41.90; H, 2.72; Br, 25.35.

4-Hydroxy-2-phenylhydrazino-4-(2-nitrophenyl)crotonic acid, γ-lactone (IX), 224–225°. Following Heller's procedure closely,[4] 150 mg. (0.7 mmole) of *o*-nitrolactone (Ia) was dissolved in 2 ml. of warm ethanol, and treated with 10 drops of phenylhydrazine. Cooling precipitated 150 mg. (71%) of pale yellow crystals. When heated with 10% sodium

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[13] Analytical figures are given in Ref. 2a.

[14] M. Reimer and E. Tobin, *J. Am. Chem. Soc.*, **62**, 2515 (1940); M. Reimer and A. L. Morrison, *J. Am. Chem. Soc.*, **63**, 236 (1941).

[15] F. Tiemann and J. Opperman, *Ber.*, **13**, 2060 (1880).

[16] F. Beilstein and A. Kuhlberg, *Ann.*, **163**, 1311 (1872).

hydroxide solution this forms indigo. Even on heating in a melting point tube or in acetone solution, or on storage in a desiccator for several hours, it changes to a deep yellow product, m.p. 218°. If 2 ml. of glacial acetic acid is added in the above preparation and the mixture is warmed, the deep yellow product forms immediately. Recrystallized from ethanol, it melts at 224–225° (red melt). Heller reported m.p. 222° dec. and believed he had *cis* and *trans* forms of the keto acid phenylhydrazone. The deep yellow product is alkali insoluble and no longer forms indigo with 10% sodium hydroxide. The absorption at 5.74 μ indicates that the lactone structure is still present. It may be the hydrazide (IXa) of the enol lactone or the true phenylhydrazone (IXb) of the keto lactone (Ib). It gives a purple color in the Knorr pyrazoline test (90% sulfuric acid with ferric chloride[17]).

$\lambda_{\max}^{\mathrm{CH_3OH}}$ 335 mμ, ε 22,500; inflection 235 mμ, ε 14,000. $\lambda_{\max}^{\mathrm{KBr}}$ 3.08 μ (NH), 5.74 μ (lactone), next band 6.28 μ (not present in lactone Ia spectrum).

Anal. Calcd. for $C_{16}H_{13}N_3O_4$: C, 61.73; H, 4.21; N, 13.51. Found: C, 61.70; H, 3.99; N, 13.46.

2-Nitrobenzylidenepyruvic acid phenylhydrazone (X), 169.5–170.5°. To a solution of 100 mg. (0.45 mmole) of keto acid in 3 ml. of warm 50% acetic acid was added 5 drops of phenylhydrazine. After heating at 70° for 2 min. the mixture was cooled. The red precipitate weighed 150 mg. (100%), m.p. 146–147°. After two recrystallizations from 50% ethanol it melted at 169.5–170.5° dec. The compound is soluble in dilute alkali and does not change to indigo. There was not enough available for titration but its ultraviolet and infrared spectra are characteristic of other phenylhydrazones in the benzylidenepyruvic acid series. Since there is no band between 5 and 6 μ, a lactone structure is ruled out, and this is believed to be a true phenylhydrazone in solution or its dipolar ion in the solid state. Potassium benzylidenepyruvate in potassium bromide has no C═O band below 6.11 μ so this is assigned to the COO^- group.

$\lambda_{\max}^{\mathrm{CH_3OH}}$ 250 mμ, ε 15,000; 385 mμ, ε 17,800; inflection 280 mμ, ε 11,750 $\lambda_{\max}^{\mathrm{KBr}}$ 6.05 μ (COO^-), next band 6.25.

Anal. Calcd. for $C_{16}H_{13}N_3O_4$: C, 61.73; H, 4.21; N, 13.51. Found: C, 61.99; H, 4.28; N, 13.54.

Benzylidenepyruvic acid phenylhydrazone.[18] This was prepared as a model compound to study further the structure of phenylhydrazones in this series. To 10 g. (0.048 mole) potassium benzylidenepyruvate in 200 ml. 50% acetic acid at 55°, was added 12 ml. (0.12 mole) phenylhydrazine. Orange crystals precipitated immediately. After 3 min. at 55° the solution was chilled briefly and then filtered and air dried (10.3 g., 83%, m.p. 157–158° dec.). On recrystallization from acetone–petroleum ether it melted at 158–159° dec. After drying at 65° and 3 mm. for 2 hr. the m.p. was 162–163° dec. Reported m.p.s are 158°,[9] 154–155° uncorr.,[10a] 162°,[6] 163–165°.[7] Higher melting points were obtained by introducing the tube into the bath only 5° below the melting point and heating 2° per min.

The alkaline solution is orange; there is no color with alcoholic ferric chloride solution, and the Knorr test is negative. Infrared spectra indicate a free acid group in chloroform solution and an inner salt structure in the solid state.

$\lambda_{\max}^{\mathrm{CH_3OH}}$ 245 mμ, ε 12,700; 275 mμ, ε 15,700; 380 mμ, ε 26,400. $\lambda_{\max}^{\mathrm{KBr}}$ 3.18 μ (NH), 3.38 wide (bonded hydrogen); 6.06 (COO^- of inner salt?). The next band is at 6.25 μ.

$\lambda_{\max}^{\mathrm{CHCl_3}}$ 2.85 μ (OH), 3.08 μ (NH), 3.32 μ wide (hydrogen bonding); 5.73 μ (COOH); 5.90 μ shoulder, 5.98 μ. A solvent cell was used in this determination.

Conversion to the yellow 1,5-diphenyl-Δ^2-pyrazoline-3-carboxylic acid takes place readily in acetic acid (m.p. 199–200° dec.; v. Auwers and Heimke[9] report 192–193°).

pK′ Determinations. These were carried out in 66.7% methanol–0.2*N* lithium chloride using a procedure similar to that described for 50% methanol solutions.[2a] The sample (170 mg.) of phenylhydrazone was dissolved in 150 ml. of methanol and 75 ml. of 0.6*N* lithium chloride was added. Nitrogen was bubbled into the stirred solution, and it was titrated using a *p*H meter and outside glass and calomel electrodes. The alkali was 0.0657*N* sodium hydroxide prepared in 66.7% methanol–0.2*N* lithium chloride. A typical S-shaped curve was obtained with a *p*K′ of 4.4 (from the midpoint of the curve) for benzylidenepyruvic acid phenylhydrazone and *p*K′ = 5.5 for benzoic acid in the same solvent. The corresponding 1,5-diphenyl-Δ^2-pyrazoline-3-carboxylic acid[9] had a *p*K′ value of 4.7.

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(17) L. Knorr., *Ber.*, **26**, 100 (1893). See also Ref. 10a.

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