tion once with 100 ml. of water, twice with 100 ml. each of 10% sodium bicarbonate solution and once with 100 ml. of water and discarding the aqueous extracts in turn, the organic phase was dried with anhydrous sodium sulfate, filtered through a fluted filter and distilled to dryness on a steam-bath. The yield of product was 60 g. (90%), m.p. 128.5–130°. Recrystallization from aqueous methanol raised the melting point to 131.0–131.2° (reported[5] m.p. 127°).

1-(4'-Chlorophenyl)-3-phenyl-2-propanone.—A mixture of 25 g. (0.093 mole) of crude α-(4-chlorophenyl)-γ-phenylacetoacetonitrile and 75 ml. of 60% sulfuric acid was stirred and refluxed until the evolution of carbon dioxide ceased. After cooling, the mixture was poured into 200 ml. of water and extracted three times with 150-ml. portions of ether. The ether was washed with dilute alkali and water and then dried over anhydrous sodium sulfate. After filtering, the solvent was removed by distillation to yield 16 g. (71%) of product, m.p. 34.5–35.5°. Recrystallization from petroleum ether (b.p. 40–60°) raised the melting point to 35.9–36.5°.

1-(4'-Methylsulfonylphenyl)-3-phenyl-2-propanone.—To a solution of 1.024 g. (4 mmoles) of 1-(4'-methylmercaptophenyl)-3-phenyl-2-propanone in 5 ml. of glacial acetic acid was added 1.4 g. (2 mmoles) of 30% hydrogen peroxide. The solution was refluxed for 20 hours and after cooling a few milliliters of water was added to induce crystallization. The cream-colored crystals were removed by filtration, washed with water and dried to yield 800 mg. (2.78 mmoles, 70%), m.p. 99–101°. Recrystallization from benzene–petroleum ether yielded 400 mg. (1.39 mmoles, 35%), m.p. 104.6–105.2°.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF BARNARD COLLEGE]

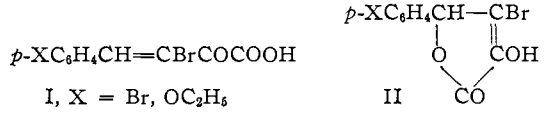
Enol-lactone Tautomers of β-Bromobenzylidenepyruvic Acids

BY EMMA DIETZ STECHER AND ANN CLEMENTS

RECEIVED AUGUST 3, 1953

Previously described isomers of *p*-bromo- and *p*-ethoxy-β-bromobenzylidenepyruvic acid (I) have been shown to be enol-lactone tautomers (II) from which stable acetoxy derivatives have been prepared. The enols, their acetates and ethers all have strong lactone absorption bands at 5.60–5.65 μ in the infrared. Ionization constants determined in 50% methanol–0.2 *M* LiCl are 2.8 and 2.3 × 10^{-6} for the *p*-bromo- and *p*-ethoxyenol lactones, and 5.5 ± 0.3 × 10^{-3} for both keto acids. Ultraviolet absorption spectra in isoöctane solution are reported for all compounds.

In her investigation of β-bromobenzylidenepyruvic acids, Marie Reimer[1,2] reported instances of a type of isomerism which was not easily explained. The *p*-bromo and *p*-ethoxy acids (I) were each obtained in a colorless and a yellow form with different melting points. Corresponding isomeric sodium salts and esters were also reported. Reimer considered the possibility of *cis–trans* isomerism but

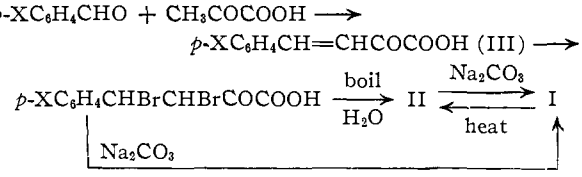


favored hydrogen bond structures for one series of compounds. On the basis of existing evidence Brown[3] suggested that the colorless isomers might be γ-lactones capable of enolization (II).

By a further study of these compounds, chiefly through infrared spectra and the formation of new derivatives, we have been able to show definitely that the yellow isomers are unsaturated keto acids, whereas the colorless compounds are enolized lactones tautomeric with these as suggested by Brown.

Table I lists the acids and esters prepared for this study. The required benzylidenepyruvic acids were synthesized by condensing the substituted benzaldehyde with pyruvic acid in an alkaline medium. Bromination readily produced the dibromides which were converted to the isomers by removal of hydrogen bromide. In an acid medium (boiling with water) the lactone formed readily, whereas shaking with sodium carbonate solution slowly produced the salt of the keto acid.

(1) M. Reimer and E. Tobin, THIS JOURNAL, **62**, 2515 (1940).
(2) M. Reimer and A. L. Morrison, *ibid.*, **63**, 236 (1941).
(3) H. C. Brown, *ibid.*, **63**, 882 (1941).



Yellow *p*-bromo- and *p*-ethoxy-β-bromobenzylidenepyruvic acids and their colorless enolic isomers are all acids which dissolve in very dilute sodium carbonate solution and form stable crystalline sodium salts. Table II summarizes pK' determinations in 50% methanol–0.2 *M* LiCl as a solvent. It was found that the two yellow compounds are very strong acids. K' is 5.5 ± 0.3 × 10^{-3} and is the same for both within the experimental error. These acids are somewhat stronger than the benzylidenepyruvic acids (III) (without the bromine atom) for which the average K' is 3.0 × 10^{-3} as reported in a previous paper.[4] These acid strengths are comparable to that of unsubstituted pyruvic acid (K' in water = 5.6 × 10^{-3},[5] 3.2 × 10^{-3}, [6]). Our results are consistent with the keto acid structure of the yellow acids. Since *p*-ethoxy-β-bromobenzylidenepyruvic acid changes to the colorless isomer on standing, its ionization constant was determined on fresh solutions, or by titrating back the stable sodium salt with acid. It is interesting to note that the β-bromine atom nearly doubles the acid strength. Also, as was previously observed,[4] groups substituted on the benzene ring have little effect on the acidity.

(4) E. D. Stecher and H. F. Ryder, *ibid.*, **74**, 4392 (1952).
(5) A. Hantzsch and A. Moliati, *Z. physik. Chem.*, [A] **10**, 8 (1892).
(6) M. H. Böeseken, L. W. Hansen and S. H. Bertram, *Rec. trav. chim.*, **35**, 313 (1916); E. G. Clair and K. Wiesner, *Nature*, **165**, 202 (1950).

TABLE I

BENZYLIDENEPYRUVIC ACID DERIVATIVES[a]

p-$XC_6H_4CH{=}CBrCOCOOY$

Cmpd.	X	Y	M.p., °C. (cor.)	Lit. m.p., °C.
1	Br	H	141–142.5[b]	141–143[1]
2	Br	CH_3	73–74	75[1]
3	OC_2H_5	CH_3	73–74[c]	75–76[2]

ENOL-LACTONE DERIVATIVES[a]

p-$XC_6H_4CH{-}CBr{=}C(OY)COO$

4	Br	H	144.5–145.5[d]	144–145[1]
5	Br	CH_3	101–101.5	101[1]
6	OC_2H_5	H	150.5–152[e]	148–149[2]
7	OC_2H_5	CH_3	85–86[f]	85–86[2]
8	H	H	131.5–132.5[g]	131–132[6a]
9	H	CH_3	60–61[h]	Oil[6a]
10	Br	$COCH_3$	115.5–116.5 (s. 109–110)[i]	
11	OC_2H_5	$COCH_3$	85–86[j]	
12	H	$COCH_3$	90–91[k]	

[a] Recrystallized from benzene or benzene–petroleum ether (35–65°) and dried at 5 mm. [b] Equiv. wt. calcd. for $C_{10}H_6O_3Br_2$: 334.0; found: 336.8. [c] The bright yellow acid corresponding to this ester changes rapidly on standing at room temperature to its colorless isomer. Its yellow sodium salt is stable; $\lambda_{max}^{isooctane}$ 240 mμ, ε 76,500, λ_{max} 336.5 mμ, ε 23,950; $\lambda_{max}^{CHCl_3}$ 5.74 μ, 5.95 μ. [d] Equiv. wt. calcd. for $C_{10}H_6O_3Br_2$: 334.0; found: 334.9. [e] Equiv. wt. calcd. for $C_{11}H_{12}O_4Br$: 299.1; found: 302; $\lambda_{max}^{isooctane}$ 231 mμ, ε 19,460; $\lambda_{max}^{CHCl_3}$ 5.65 μ. [f] $\lambda_{max}^{isooctane}$ 230.5 mμ, ε 19.910; $\lambda_{max}^{CHCl_3}$ 5.60 μ. [g] Equiv. wt. calcd. for $C_{10}H_7O_3Br$: 255.1; found: 255.8; $\lambda_{max}^{isooctane}$ 240 mμ, ε 10,480; $\lambda_{max}^{CHCl_3}$ 5.65 μ, 5.90 μ (weak). [h] *Anal.* Calcd. for $C_{11}H_9O_3Br$: C, 49.05; H, 3.37; Br, 29.69. Found: C, 48.75; H, 3.27; Br, 29.58. Previously obtained as an oil by elimination of hydrogen bromide from methyl α,β-dibromobenzylidenepyruvate[1a]; $\lambda_{max}^{isooctane}$ 242 mμ, ε 9,620; $\lambda_{max}^{CHCl_3}$ 5.64 μ. [i] *Anal.* Calcd. for $C_{12}H_8O_4Br_2$: C, 38.33; H, 2.15; Br, 42.50. Found: C, 38.33; H, 2.14; Br, 42.78; $\lambda_{max}^{isooctane}$ 226.5 mμ, ε 23,000; $\lambda_{max}^{CHCl_3}$ 5.60 μ. [j] *Anal.* Calcd. for $C_{14}H_{13}O_5Br$: C, 49.26; H, 3.84; Br, 23.42. Found: C, 49.49; H, 3.96; Br, 23.57; $\lambda_{max}^{isooctane}$ 227.5 mμ, ε 23,320; $\lambda_{max}^{CHCl_3}$ 5.60 μ. [k] *Anal.* Calcd. for $C_{12}H_9O_4Br$: C, 48.51; H, 3.05; Br, 26.90. Found: C, 48.60; H, 3.02; Br, 26.76; $\lambda_{max}^{isooctane}$ < 215 mμ, ε > 15,000; $\lambda_{max}^{CHCl_3}$ 5.60 μ.

The two colorless enolic isomers proved to be much weaker acids with K' values of 2.8×10^{-6} and 2.3×10^{-6} for the p-bromo and p-ethoxy derivatives, respectively. The β-bromine atom probably enhances the acid strength of the enol as it does in acetylacetone ($CH_3COCH_2COCH_3$, $K = 1.0 \times 10^{-9}$; $CH_3COCHBrCOCH_3$, $K = 1 \times 10^{-7}$).[7]

The acid formed by boiling benzylidenepyruvic acid dibromide with water to remove hydrogen bromide is also an enol-lactone (Table I, 8) comparable in acid strength with the two already mentioned ($K' = 2.3 \times 10^{-6}$). Standing in sodium carbonate solution did not convert this to a stable yellow isomer as it does the other two enols.

Reimer isolated methyl esters of the p-bromo and p-ethoxy isomers (Table I, 2, 3, 5, 7). The keto acids were readily methylated with methyl alcohol saturated with dry hydrogen chloride. The enolic isomers, however, were completely resistant to this reagent, but reacted rapidly with diazomethane in ether solution. We used this method to prepare the crystalline enol-ether with no substituent on the benzene ring (Table I, 9) previously reported as an oil.

(6a) M. Reimer, THIS JOURNAL, **48**, 2457 (1926).

(7) R. G. Pearson and R. L. Dillon, THIS JOURNAL, **75**, 2440 (1953).

TABLE II

pK' VALUES IN 50% METHANOL[a]–0.2 M LiCl AT 25°

Compound	pK[b] (relative)
p-$BrC_6H_4CH{=}CBrCOCOOH$	2.24
p-$C_2H_5OC_6H_4CH{=}CBrCOCOOH$	2.31[c]
p-$C_2H_5OC_6H_4CH{=}CBrCOCOONa$	2.26
$C_6H_5CH{=}CHCOCOOK$	2.56[d]
p-$BrC_6H_4CHCBr{=}C(OH)COO$	5.55
p-$C_2H_5OC_6H_4CHCBr{=}C(OH)COO$	5.63
$C_6H_5CHCBr{=}C(OH)COO$	5.64
C_6H_5COOH (reference)	5.04

[a] Solutions were $4.5–6.0 \times 10^{-2}$ M. [b] The pK' values in methanol were obtained by substituting pH values as given by the glass electrode, and have only relative validity. Average deviation for benzylidenepyruvic acids, 0.03 pK' unit; for weak acids (enol-lactones and benzoic acid): 0.01 pK' unit. [c] A single determination on this acid in water solution gave a pK' value of 1.72; $K' = 1.9 \times 10^{-2}$. [d] This checks the value of 2.49 ± 0.03 previously determined by the direct titration method.[4]

Further support for these structures is offered by the successful preparation of three crystalline acetates (Table I, 10, 11, 12). This was accomplished by treating the corresponding enols with acetic anhydride containing a trace of concentrated sulfuric acid.

All of the compounds in Table I were subjected to qualitative tests for the carbonyl group and for the enol group. Results were completely consistent with the structures suggested. The two keto acids and their methyl esters formed orange precipitates when alcohol solutions were treated with dinitrophenylhydrazine reagent. The colorless compounds did not react. When the same substances were treated with ferric chloride solution, only 4, 6 and 8 gave rise to color. These are the only ones for which free enol groups have been postulated. The enol acetates and enol ethers did not react.

Figure 1 records the ultraviolet absorption spectra of p-bromo-β-bromobenzylidenepyruvic acid and its methyl ester and of the corresponding enol-lactone and its methyl derivative. Similar curves were found for the three stable ethoxy compounds. The strong absorption band above 300 mμ is characteristic of conjugated carbonyl compounds. For example, p-methoxybenzylideneacetone has a main absorption band at 320 mμ in ethanol.[8] In the enol-lactones the conjugated system is shorter and does not include the benzene ring. As would be expected the compounds absorb light at lower wave lengths (230 mμ). The spectra in isoöctane did not change, indicating that there was no tautomerization in this solvent.

It was found that yellow p-ethoxy-β-bromobenzylidenepyruvic acid changes rapidly and completely to the colorless lactone form when heated,

(8) A. L. Wilds, L. W. Beck, W. J. Close, C. Djerassi, J. A. Johnson, Jr., T. L. Johnson and C. H. Shunk, *ibid.*, **69**, 1985 (1947).

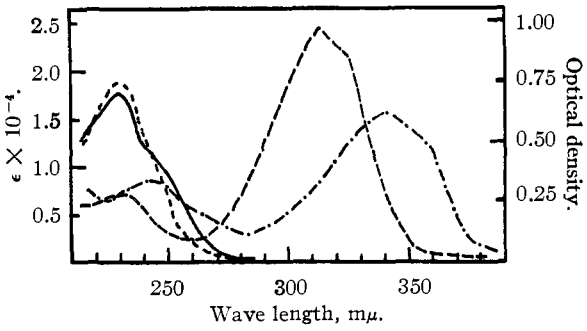


Fig. 1.—Ultraviolet absorption spectra in isoöctane: —·—·, *p*-BrC_6H_4CH=CBrCOCOOH; ——, methyl ester; – – –, *p*-BrC_6H_4CHCBr=C(OH)COO; ——, methyl ether.

or on storage, or when it is dissolved in anhydrous methanol or isoöctane. In aqueous solvents a tautomeric equilibrium is set up. The yellow keto acid is the more stable form in neutral media such as 12% methanol. Figure 2 shows the rapid and nearly complete conversion of the lactone to the keto acid in this solvent. The addition of hydrochloric acid shifts the equilibrium point far to the side of the lactone. Calculation shows that in neutral solutions of this dilution (4×10^{-5} *M*), the keto acids are almost completely ionized while the lactones are only about 50% ionized. In the 0.1 *N* hydrochloric acid solutions the ionization of the keto acids is repressed to 15%, and the lactones are almost completely associated.

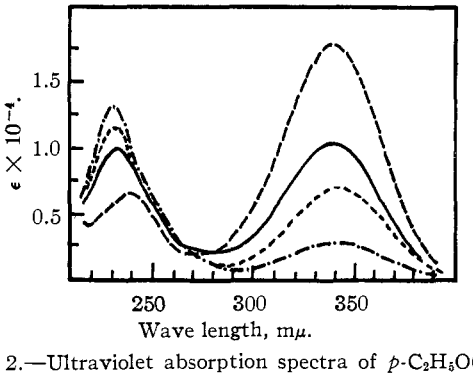
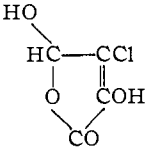


Fig. 2.—Ultraviolet absorption spectra of *p*-$C_2H_5OC_6H_4$-CHBr=C(OH)COO in 12% methanol: ——, after 2 hours; — —, after 1 day; in 12% methanol–0.1 *N* HCl: – – – after 2 hours; —·—, after 1 day.

A similar spectroscopic study showed that *p*-bromo-β-bromobenzylidenepyruvic acid is the stable isomer in 10% methanol but that in acid solution (10% methanol–0.1 *N* HCl) an almost complete conversion to lactone takes place. The interconversion in either direction is much slower in the *p*-bromo series than it is in the *p*-ethoxy series. In alkaline solution (2% sodium carbonate) both lactones are converted to the sodium salts of the corresponding keto acids during the course of several hours.

The infrared spectra of these compounds measured in chloroform solution offer the strongest evidence of their structure. All of the compounds for which lactone groups have been postulated (Table I, 4 through 12) have strong absorption bands at 5.60–5.65 μ. (Figure 3, curves 1 and 2 shows the absorption curves for two of these substances.) There is much evidence in the literature to indicate that this corresponds to a γ-lactone configuration. A close analogy is the enol-lactone form of mucoxychloric acid (IV).[9] This also has a strong band at 5.61–5.65 μ attributed to the lactone group.



IV

Curve 1 in Fig. 3 is that of a free enol-lactone. It contains an hydroxyl band at 2.80 μ and a weak band at 5.90 μ, probably due to a small percentage of keto acid or keto lactone form present in the chloroform solution. As would be expected the yellow keto acids and esters have strong bands at this location (see Fig. 3, curve 3).

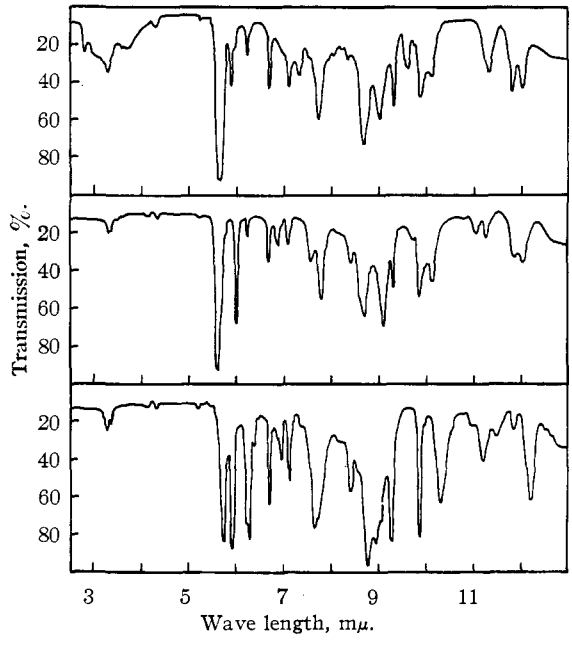


Fig. 3.—Infrared absorption spectra in chloroform: (1) *p*-BrC_6H_4CHCBr=C(OH)COO; (2) *p*-BrC_6H_4-CHCBrC(OCH_3)COO; (3) *p*-BrC_6H_4CH=CBrCOCOOH.

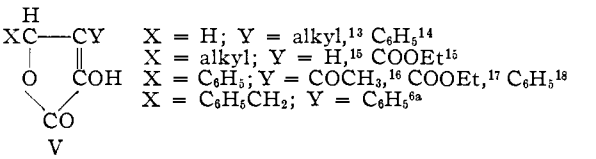
In the series of eight substituted benzylidenepyruvic acids (III) reported by Reimer,[10] the keto acid structure is the only one observed. When a β-bromine atom is introduced into these acids, the enol-lactone structure is the more stable form and the keto acid has been described in a few instances only.[11]

(9) H. H. Wasserman and F. M. Precopio, THIS JOURNAL, **74**, 326 (1952).

(10) M. Reimer, see footnotes, 1, 2, 11, 19; also *ibid.*, **55**, 4643 (1933); **57**, 211 (1935).

(11) Not reinvestigated were 3-bromo-4-methoxy-β-bromobenzylidenepyruvic acid [M. Reimer, *ibid.*, **48**, 2454 (1926)] and 5-bromo-2-methoxy-β-bromobenzylidenepyruvic acid [M. Reimer and M. Howard, *ibid.*, **50**, 2510 (1928)] which probably also have keto acid structures.

There are many other examples of α-keto-β,γ-unsaturated butyric acids, including the parent substance, α-tetronic acid (V, X and Y = H),[12] which exist chiefly in tautomeric γ-lactone forms. These are described as partially or completely enolic and the enol forms are sometimes strong acids.



It will be noted that most of the lactones reported as stable have electrophilic groups at Y. In the keto acid such a group may function by inductive or resonance effects to place a partial positive charge on the carbon atom holding X, so that it is more easily attacked by the acid anion. There may also be a steric factor which stabilizes the lactone. The large X and Y groups may be better accommodated by the ring structure than the open-chain form. We plan in the future to study quantitatively the effect of different types of groups at X and Y on the stability of the lactones and the acid strength of the enols.

Experimental

Preparation of Compounds.—Table I lists the acids and esters prepared for this study. The general method for the preparation of these compounds has been described.[1,2,4]

Acids.—The purity of the acids prepared was checked by *p*H titration in 50% methanol as described later. The acids were synthesized by the Reimer procedures except for the following changes.

***p*-Bromobenzylidenepyruvic Acid Dibromide.**—In the bromination of *p*-bromobenzylidenepyruvic acid (III, X = Br) the following method avoids incomplete reaction. The acid (20.2 g., 0.08 mole) was dissolved by warming in 200 ml. of chloroform (dried over calcium chloride) and was cooled rapidly to 50°. Then 4.5 ml. (0.088 mole) of bromine was added rapidly while shaking the flask by hand. The fine suspension dissolved completely after one-half of the bromine had been added. The solution was cooled to 30° and the addition of the bromine was completed rapidly. After standing another ten minutes, the solution was evaporated in a stream of dry air. The crystalline dibromide was washed with benzene and recrystallized from benzene–petroleum ether; yield 60–70%, m.p. 132–133°.

β-Bromo-γ-(*p*-bromophenyl)-α,γ-dihydroxy-γ-crotonolactone (II, X = Br).—To 500 ml. of mechanically-stirred water at 80° was added 13.0 g. (0.03 mole) of *p*-bromobenzylidenepyruvic acid dibromide. A pale yellow oil formed immediately and after 15 minutes of rapid stirring at this temperature, the mixture was chilled rapidly and the colorless crystalline solid was filtered. The benzene solution of the damp solid was distilled until free of water, using a water-removal tube.[4] The anhydrous acid crystallized from the saturated benzene solution; yield 50%, m.p. 142–143°. When preparing the corresponding ethoxy derivative, a longer heating period in water was required to convert the yellow keto acid which precipitates first, to the lactone form. Further heating in benzene solution completed the change.

The *p*-ethoxybenzaldehyde required for the preparation of *p*-ethoxybenzylidenepyruvic acid was obtained by treatment of *p*-hydroxybenzaldehyde (Eastman Kodak Co., m.p. 116–117°) in sodium hydroxide solution with diethyl sulfate. The method was similar to that for the preparation of veratraldehyde.[19] A 92% yield of product boiling at 136–139° (19 mm.) was obtained.

Esters and Enol Ethers.—The esters of the yellow (keto) acids were prepared easily and in good yield using methanol containing 10% of dry hydrogen chloride. The colorless enol ethers could not be prepared with this reagent but formed readily with diazomethane in ether solution. All esters were purified by extracting an ether solution with dilute sodium carbonate, and finally crystallizing from benzene–petroleum ether.

Enol Acetates.—In a typical preparation, 1 g. of the enol was dissolved in 5 ml. of acetic anhydride and a drop of concentrated sulfuric acid was added. After several hours the mixture was poured on ice and dilute ammonia was added to *p*H 10. The filtered crystalline precipitate was freed of traces of unchanged enol by extracting an ether solution with dilute sodium carbonate solution. The acetates crystallized readily from benzene–petroleum ether as colorless needles (yield 75–85%).

Ionization Constants.—These were determined at 25° by means of *p*H measurements using a Beckman *p*H meter and an outside glass electrode. Table II summarizes the results. The procedure and method of calculation were described in detail in a previous paper.[4] Since *p*-ethoxy-β-bromobenzylidenepyruvic acid changes completely to its tautomer during the course of several days, determinations on this substance were made on fresh samples without drying. The validity of the results was checked by preparing the pure stable sodium salt of this acid[2] and carrying out a back-titration using a standard acid solution. The two results agree within the limit of error of the method. The K' value obtained by back-titration of potassium benzylidene pyruvate also confirms the previous figure determined on the free acid. As before, the pK' values for the weak acids were read directly as the mid-points of the titration curves. The value for benzoic acid run as a standard substance checks that of 5.03 previously reported.[4]

Although there is possibility of some tautomeric change in the *p*-ethoxy solutions it appears to have been insignificant under our conditions. One argument for this is that pK' values on the free acid and on the sodium salt check. Another is that a period of standing of one hour before titration did not change the result.

Ultraviolet Absorption Spectra.[20]—The ultraviolet absorption spectra of these compounds were measured in isooctane solution (Phillips Petroleum Co. Spectro Grade).[21] A Beckman DU spectrophotometer was used with 1.00-cm. fused quartz absorption cells at room temperature. Duplicate determinations were made for each compound on 4.0×10^{-5} M solutions. The spectra of the *p*-bromo compounds are plotted in Fig. 1. The corresponding ethoxy compounds gave similar curves. Figure 2 shows the tautomeric change in neutral and acid solution of the *p*-ethoxy acids, as determined on a Cary recording spectrophotometer (model 12) at room temperature in 1.00-cm. cells. A position of equilibrium appears to have been reached since there was no further change in 24 hours. Solutions were 8.0×10^{-5} M.

Infrared Spectra.—These were determined with a Baird instrument in 0.1-mm. cells. Solutions were prepared from 25-mg. samples dissolved in 1–2 ml. of chloroform. Figure 3 shows three typical absorption curves. The error in band position is ± 0.03 μ.

NEW YORK, N. Y.

(12) L. Kletz and A. Lapworth, *J. Chem. Soc.*, **107**, 1254 (1915).
(13) H. Schinz and M. Hinder, *Helv. Chim. Acta*, **30**, 1349 (1947).
(14) N. Hall, J. E. Hynes and A. Lapworth, *J. Chem. Soc.*, **107**, 133 (1915).
(15) H. Schinz and A. Rossi, *Helv. Chim. Acta*, **31**, 1953 (1948).
(16) L. Claisen, *Ber.*, **24**, 116 (1891).
(17) W. Wislicenus, *ibid.*, **26**, 2144 (1893).
(18) C. Erlenmeyer, Jr., and N. Knight, *ibid.*, **27**, 2222 (1894).
(19) J. S. Buck, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 619.
(20) Measurements by Marilyn Goldfeder.
(21) Reimer[1,2] reported partial spectra in alcohol solution for four of these compounds.