

Lactone Carboxylic Acids. IV.

Reaction of Ethyl Chloroarylpyruvate with Ethyl Malonate*

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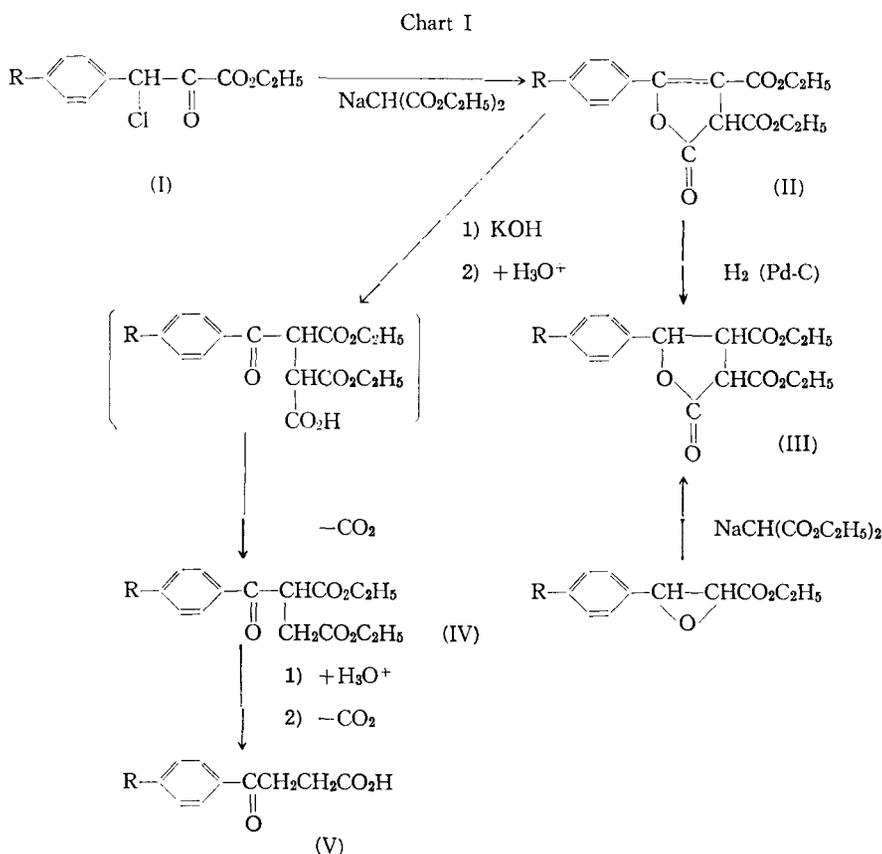
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The condensation of ethyl chloroarylpyruvate (I) with ethyl malonate in the presence of sodium ethoxide afforded γ -aryl- α,β -dicarbethoxy- $\Delta^{\beta,\gamma}$ -butenolide. On the basis of the chemical and spectral evidences, the structure of the product (II) has been elucidated. This reaction provides new routes to α,β -dicarboalkoxy- γ -butyrolactones and/or to γ -ketocarboxylic acids.

It has already been reported that the reaction of ethyl bromopyruvate with β -ketoesters, i. e., ethyl oxalacetate, in the presence of sodium, affords corresponding furancarboxylic acids as a result of O-alkylation¹⁾, whereas the reaction of halogenopyruvic esters with carbanions has not been fully investigated.

The present paper describes and discusses the result of the title reaction attempted for the discovery of a new preparative method of γ -butyrolactones, as is exemplified by the reaction of ethyl chlorophenylpyruvate (I, R=H) with ethyl malonate (Chart I).



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Ethyl chloroarylpyruvate (I) as a starting material was prepared from the appropriate aromatic aldehyde and ethyl dichloroacetate following the method of McDonald and Schwab². The reaction of ethyl chlorophenylpyruvate (I, R=H) with ethyl sodiomalonate yielded an oily product, which distilled at 204–208° (2.5 mm.) and gave analytical values corresponding well with the proposed structure (II, R=H). The presence of γ -lactone ring, ester groups and a double bond in the structure of II is confirmed by IR absorption bands at 1780 cm.⁻¹, 1745 cm.⁻¹ and 1645 cm.⁻¹, respectively (Fig. 1b). The UV absorption spectra, which had maxima values at 218 m μ (ϵ 7,600), 275 m μ (ϵ 8,200) and 330 m μ (ϵ 5,100), also support the structure, since the bands at 275 m μ and 330 m μ can be attributable to the conjugated system like II.

The treatment of II (R=H) with ethanolic potassium hydroxide, which was followed by thermal decarboxylation in acidic medium, afforded ethyl benzoylsuccinate (IV), and IV, when heated with dilute sulfuric acid, underwent decarboxylation to form β -benzoylpropionic acid (V).

Thin layer chromatographic study reveals that the degradative hydrogenation of the ozonide derived from II (R=H) yielded ethyl α -oxosuccinate as the neutral component. Benzoic

acid was detected largely in the acid component of the degradation product, while both ethyl benzoylacetate and acetophenone were not by any means. Thus, the possible formation of another butenolide skeleton in an appreciable amount in the title reaction has been excluded from the present consideration.

Catalytic hydrogenation of II (R=H) gave an oil (III, R=H), which solidified readily to afford colorless crystals, m. p. 78–80°, with the empirical formula of C₈H₁₀O₆. The IR spectra observed for III (R=H) agreed to those of γ -phenyl- α , β -dicarbethoxybutyrolactone, which was prepared from ethyl phenylglycidate and diethyl malonate by the procedure reported by Chelintsev et al³. (Fig. 1c).

The structure of γ -phenyl- α , β -dicarbethoxy- $\Delta^{\beta,\gamma}$ -butenolide has now been assigned to the condensation product of the title reaction from the above-mentioned chemical and spectral evidences. Accordingly, it might be assumed as the possible mechanism of the reaction that the attack of the carbanion derived from malonic ester occurred exclusively at the α -position of the chloropyruvic ester (I).

Yields, and physical and analytical data of several γ -aryl- α , β -dicarbethoxy- $\Delta^{\beta,\gamma}$ -butenolides prepared similarly are listed in Table I.

Table I γ -Aryl- α , β -dicarbethoxy- $\Delta^{\beta,\gamma}$ -butenolide (II) ^a

R	B. p., °C. (mm.)	Yield, %	Carbon, %		Hydrogen, %	
			Calcd.	Found	Calcd.	Found
C ₆ H ₅	204–208 (2.5)	32.0	63.15	63.33	5.30	5.59
<i>p</i> -CH ₃ -C ₆ H ₄	210–212 (2.5)	27.7	64.14	63.88	5.70	5.97
<i>p</i> -Cl-C ₆ H ₄	218–220 (5)	29.2	56.73	56.86	4.46	4.79

^a All the compounds listed here are new.

Experimental ***

Ethyl Chlorophenylpyruvate (I, R=H). — To a mixture of 47.0 g. (0.3 mole) of ethyl dichloroacetate and 31.8 g. (0.3 mole) of benzaldehyde dissolved in 150 ml. of anhydrous ether was added with stirring, in small portions, 25.5 g. (0.38 mole) of powdered sodium ethoxide at 0°. The reaction mixture, allowed to warm up

*** All melting points and boiling points are uncorrected.

to room temperature, was refluxed for 1.5 hr. Water was added to dissolve all the deposited salt. The organic layer was washed several times with water and dried over anhydrous magnesium sulfate. After the solvent was removed *in vacuo*, the residue was distilled under reduced pressure to give 34.8 g. (51.1%) of ethyl chlorophenylpyruvate, b. p. 165–167° (18.5 mm.). (IR spectra: Fig. 1a). *Anal.* Calcd. for C₁₁H₁₁ClO₃: C, 58.29; H, 4.85. Found: C,

58.49; H, 5.10.

Other ethyl chloroarylpyruvate (I), obtained similarly, are given in Table II.

Table II Ethyl Chloroarylpyruvate (I) ^a

R	B. p., °C. (mm.)	Yield, %	Carbon, %		Hydrogen, %	
			Calcd.	Fonnd	Calcd.	Found
C ₆ H ₅	165—167 (18.5)	51.1	58.29	58.49	4.85	5.10
<i>p</i> -CH ₃ -C ₆ H ₄	161—162 (10)	43.2	59.88	59.61	5.44	5.78
<i>p</i> -Cl-C ₆ H ₄	186—188 (20)	35.0	50.60	50.74	3.87	4.23

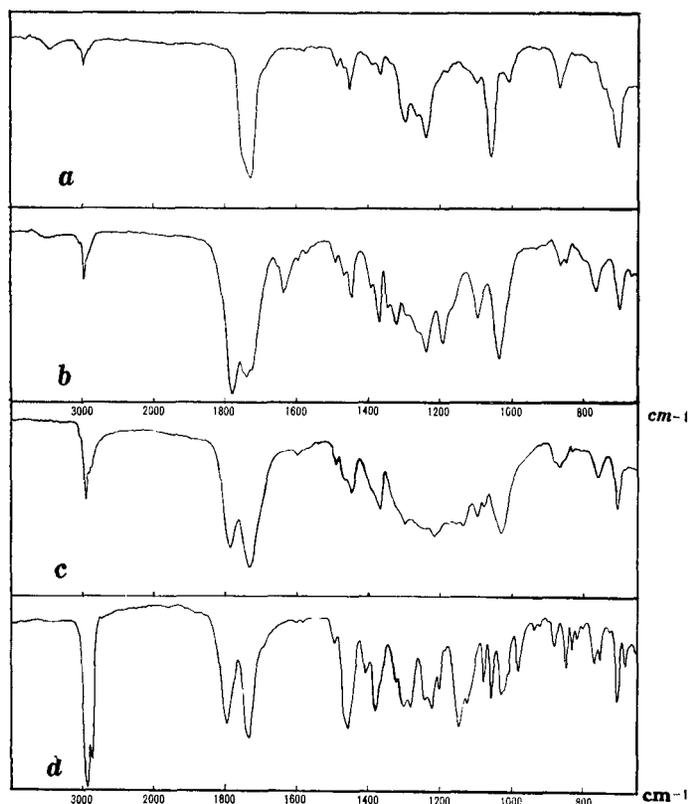
^a All the compounds listed here are new.

Fig. 1. IR spectra of: (a) ethyl chlorophenylpyruvate (I, R=H), liquid film; (b) γ -phenyl- α , β -dicarboxy- $\Delta\beta,\gamma$ -butenolide (II, R=H), liquid film; (c) γ -phenyl- α , β -dicarboxybutyrolactone (III, R=H), liquid film, sampled and measured while it was an oil (see experimental part); (d) γ -phenyl- α , β -dicarboxybutyrolactone (III, R=H), nujol.

Reaction of Ethyl Chlorophenylpyruvate with Ethyl Malonate. — To a solution of sodiummalonate, prepared from 2.3 g. (0.1 mole) of sodium, 20.0 g. (0.125 mole) of diethyl malonate, and 60 ml. of anhydrous ethanol, was added

11.3 g. (0.05 mole) of ethyl chlorophenylpyruvate. The reaction mixture was heated with vigorous stirring for 7 hr. at 60—65°, which, after acidification, was extracted with ether. The ethereal extract, washed with saturated, aqueous sodium bicarbonate, and then with water, dried over anhydrous sodium sulfate, was evaporated under diminished pressure. Distillation of the residue yielded 4.8 g. (32.0%) of yellowish oil (II, R=H), b. p. 218—220° (3.5 mm.); for analysis, and IR and UV measurements, the fraction boiling at 204—208° (2.5 mm.) was collected at the redistillation. *Anal.* Calcd. for C₁₆H₁₆O₆: C, 63.15; H, 5.30. Found: C, 63.33; H, 5.59.

Hydrolysis and Decarboxylation of II (R=H).

— A mixture of 4.2 g. (0.075 mole) of potassium hydroxide dissolved in ethanol containing a small amount of water, and 7.5 g. (0.025 mole) of II (R=H) was kept at room temperature with stirring for 25 hr. The resulted solution, after acidification with dilute sulfuric acid, was extracted with ether. From the ethereal extract, 1.4 g. of acidic material and 3.8 g. of neutral material were separated in the usual manners.

On heating the acidic material in the presence of potassium hydrogen sulfate, it readily underwent decarboxylation and gave ethyl benzoysuccinate (IV) in good yield. By heating with 10% sulfuric acid for several hours under reflux, IV was transformed to β -benzoylpropionic acid (V). The neutral component proved to be the recovery of II (R=H). The identification of these products, i. e. IV and V, was made by the comparison of their IR spectra with those of the authentic samples^{4,5}. (IV: IR, 1735 cm^{-1} (ester ν C=O) and 1685 cm^{-1} (ketone ν C=O); V: IR, 1710 cm^{-1} (ketone ν C=O) and 1675 cm^{-1} (acid ν C=O)).

Ozonolysis of II (R=H).— A solution of 1.0 g. of II (R=H) in 25 ml. of ethyl acetate was treated with ozone at -10° . The ozonide deposited on the wall of vessel was decomposed by hydrogenation in the presence of catalytic amount of Adams' catalyst by the usual procedure. The ethereal extract of the decomposition product was shaken with sodium bicarbonate solution to remove the acidic component. A neutral oil was obtained after the evaporation of the solvent. Thin layer chromatograph of the residual oil admixed with 2,4-dinitrophenylhydrazine showed a prevailing spot at R_f 0.15, when developed by benzene on E. Merck silica-gel G, indicating the presence of ethyl α -oxosuccinate as the major constituent of the ozonolysis product, although the comparisons practiced were only qualitative. The same R_f value as above was observed with the 2,4-dinitrophenylhydrazine of the authentic sample of ethyl α -oxosuccinate under the same condition. Acidification of the alkaline extract gave benzoic acid (identification: by IR spectra).

Hydrogenation of II (R=H).— A solution

of 0.6 g. of II (R=H) in 15 ml. of ethanol was hydrogenated in the presence of 0.6 g. of 5% Palladium-on-carbon under ordinary pressure. After removal of the catalyst and evaporation of the solvent *in vacuo* 0.4 g. of oil (III) was obtained. It solidified to give crystals melting at $78-80^\circ$ after several recrystallizations from *n*-hexane. (IR spectra: Fig. 1d). *Anal.* Calcd. for $\text{C}_{13}\text{H}_{18}\text{O}_6$: C, 62.74; H, 5.92. Found: C, 62.49; H, 6.08.

***r*-Phenyl- α,β -dicarbethoxybutyrolactone.**

— This lactone was prepared by the procedure described in literature³, b. p. $191-192^\circ$ (0.5 mm.), in 33% yield (lit³). b. p. $225-227^\circ/1$ mm.). The product also solidified to white needles while storing at room temperature, m. p. $67-68^\circ$ after recrystallizations from *n*-hexane.

References

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Palladium-on-carbon catalyzed hydrogenation of carbon-carbon double bond in the acidic medium tends to take stereochemical course of *cis* addition [e. g., R. L. Augustine: J. Org. Chem. **23**, (1958) 1853]. One might assume that III (R=H), which was obtained by the hydrogenation of II (R=H), possesses *cis* conformation. There are evidences from the NMR spectra to support the assumption. Discussions and experiments concerning the structural assignment of these products will be published elsewhere.
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