# ETHYL ESTERS OF α-SUBSTITUTED γ-BUTYROLACTONE-α-CARBOXYLIC ACIDS

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A method of preparing (I) (R = $C_4H_9$; $C_6H_5$) in 50% yield by the condensation of the ethyl esters of butyl- and phenylmalonic acid with ethylene dibromide in the presence of sodium, dispersed in xylene, is reported in [1].

We studied the condensation of the ethyl esters of butyl- and phenylmalonic acid with β-chloroethyl acetate in the presence of sodium ethoxide and achieved 10% yields of compounds (I) (R = $C_4H_9$ and $C_6H_5$). Ethyl phenoxymalonate reacted differently with β-chloroethyl acetate. Instead of compound (I) (R = $C_6H_5O$) ethyl α-phenoxy-β-acetoxyethylmalonate is formed. On hydrolysis of this α-phenoxy-γ-butyrolactone-α-carboxylic acid is obtained.

For the preparation of (I) (R = $C_4H_9$ and $C_6H_5CH_2$) we alkylated ethyl γ-butyrolactone-α-carboxylate with the alkyl halides in the presence of sodium ethoxide as reported earlier for the preparation of other compounds of this series [2]. Both compounds (I) (R = $C_4H_9$ and $C_6H_5CH_2$) were obtained in 66% yield.

For the synthesis of the ethyl esters of certain α-substituted γ-butyrolactone-α-carboxylic acids it is possible to use ethyl α-bromo-γ-butyrolactone-α-carboxylate (II). The latter is formed in 80% yield by the bromination of (I) (R = H) in light. On reacting (II) with phenol in the presence of potassium carbonate in acetone medium ethyl α-phenoxy-γ-butyrolactone-α-carboxylate (I, R = $C_6H_5O$) is obtained in 30% yield.

In the IR spectra of the compounds (I) (R = $C_4H_9$; $C_6H_5$; $C_6H_5CH_2$; $C_6H_5O$; Br) mentioned above there are absorption bands for the lactone carbonyl (1760-1785 $cm^{-1}$) and the carbonyl of the ester group (1720 $cm^{-1}$).

The IR spectra were measured on a UR-10 instrument. Crystalline samples were measured as pastes in mineral oil.

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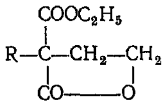
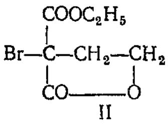


$$\begin{array}{l}\mathrm{COOC_2H_5}\\ \;| \\ \mathrm{R{-}C{-}CH_2{-}CH_2}\\ \quad|\qquad\qquad| \\ \quad\mathrm{CO{-}{-}{-}{-}O}\end{array}$$

R=H; $C_4H_9$; $C_6H_5$; $C_6H_5CH_2$; $C_6H_5O$

I



$$\begin{array}{l}\quad\mathrm{COOC_2H_5}\\ \quad\;| \\ \mathrm{Br{-}C{-}CH_2{-}CH_2}\\ \quad\;|\qquad\qquad| \\ \quad\mathrm{CO{-}{-}{-}{-}O}\end{array}$$

II

## EXPERIMENTAL PART

Ethyl α-Butyl-γ-butyrolactone-α-carboxylate (I; R = $C_4H_9$). Method. 1. To a suspension of 2.2 g (0.095 mole) of sodium in 20 ml of xylene was added with stirring 25 g (0.12 mole) of butylmalonic ester and the mass heated at 110-120°C until complete solution of the sodium. After cooling 12 g (0.1 mole) of β-chloroethyl acetate was added from a dropping funnel over 10 min and the mixture heated at 70-75° for 35-40 h. Then the mass was cooled, 100 ml of water was added, and the oil which separated was extracted with ether (4 × 50 ml). This solution was washed with water and dried with magnesium sulfate, the ether was distilled off and the residue distilled in vacuum and the fraction with bp 120-125° (3 mm) collected. The yield was 4.1 g (11%) with $n_D^{17.5}$ 1.4436 (literature data [1]: $n_D^{20}$ 1.4487).

Method 2. 8.15 g (0.35 mole) of sodium was dissolved in 200 ml of absolute ethanol, 56 g (0.35 mole) of ethyl γ-butyrolactone-α-carboxylate [3] was added and after 15 min 50 g (0.36 mole) of butyl bromide. The reaction mixture was boiled with stirring for 20 h, then cooled and worked up as described above. A

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substance with bp 110-111° (1 mm) was obtained. The yield was 50 g (66%), $n_D^{17}$ 1.4490. Found, %: C 61.94; H 8.49; $C_2H_5O$ 20.63. $C_{11}H_{18}O_4$. Calculated, %: C 61.66; H 8.46; $C_2H_5$ 21.01. In the IR spectrum there was an unresolved band 1720-1780 $cm^{-1}$ (lactone carbonyl and the carbonyl of the carbethoxy group).

Ethyl α-Benzyl-γ-butyrolactone-α-carboxylate (I, R = $C_6H_5CH_2$). 2.9 g (0.126 mole) of sodium was dissolved in 40 ml of absolute ethanol and 20 g (0.127 mole) of ethyl γ-butyrolactone-α-carboxylate was added with stirring and after 10 min 16.4 g (0.18 mole) of benzyl chloride. The reaction mixture was heated at 60-65° for 25 h, then cooled and 100 ml of water added and the oil that separated was extracted with ether. The ether solution was washed with water, sodium bicarbonate solution, and water, the ether was evaporated and the residual oil distilled and the fraction with bp 152-154° (2 mm) collected. A colorless slowly crystallizing oil was obtained with mp 52-54° (from ether). The yield was 20.6 g (66%), $n_D^{24}$ 1.5113. Found, %: C 67.51; H 6.61; $C_2H_5O$ 17.60. $C_{14}H_{16}O_4$. Calculated, %: C 67.62; H 6.47; $C_2H_5O$ 17.60. There were bands at 1735 and 1765 $cm^{-1}$ in the IR spectrum.

Ethyl α-Phenyl-γ-butyrolactone-α-carboxylate (I, R = $C_6H_5$). To a suspension of 5 g (0.218 mole) of sodium in 20 ml of xylene was added 47 g (0.5 mole) of phenylmalonic ester and heated with stirring at 130-150° until complete solution of the sodium. The mass was cooled, 51 g (0.418 mole) of β-chloroethyl acetate was added and the mixture heated under reflux at 70-75° for 85 h. On cooling 50 ml of water was added and the oil which separated was extracted with ether. The ether solution was washed with water and dried over magnesium sulfate, the ether was distilled off and the residue distilled in vacuum and the fraction with bp 145-150° (0.5 mm) collected. The yield was 4.7 g (10%) with $n_D^{20}$ 1.5213 [literature data [1]: $n_D^{20}$ 1.5211, bp 145° (1 mm)]. Found, %: C 66.25; H 6.26; $C_2H_5O$ 19.66. $C_{13}H_{14}O_4$. Caculated, %: C 66.70; H 5.98; $C_2H_5O$ 19.20.

Ethyl Phenoxymalonate. In contrast to the method of preparing this compound described in the literature and which consisted of the condensation of ethyl chloromalonate with sodium phenozide [4] we used a somewhat modified method which gave better results.

To 240 ml of acetone was added 16 g (0.478 mole) of finely powdered potassium carbonate, 45 g (0.478 mole) of crystalline phenol, and 93 g (0.478 mole) of chloromalonic ester and the mixture was heated with stirring under reflux for 4 h. The reaction mixture was diluted with 500 ml of water and the oil that separated was extracted with ether (4 × 100 ml). After washing with water and drying with magnesium sulfate, the ether was distilled off and the residue distilled in vacuum and the fraction with bp 121-123° (0.5 mm) collected. The yield was 52 g (46%). The oil crystallized in the receiver, mp 47-49° (from ether). The literature gives mp 51-52° [5] and mp 52-53° [4]. Found, %: C 62.01; H 6.48. $C_{13}H_{16}O_5$. Calculated, %: C 61.90; H 6.38.

Reaction of Phenoxymalonic Ester with β-Chloroethyl Acetate. 4.6 g (0.2 mole) of sodium was dissolved in 50 ml of absolute ethanol, 50.4 g (0.2 mole) of molten phenoxymalonic ester was rapidly added, then 24.4 g (0.2 mole) of β-chloroethyl acetate, and the mixture was heated with stirring under reflux at 40-45° for 20 h. On cooling 100 ml of water was added to the mass and the oil extracted with ether. The extract was washed with sodium bicarbonate solution and dried with magnesium sulfate, the ether was distilled off and the residue distilled in vacuum and the fraction with bp 182-192° (0.5 mm) collected. The yield was 14 g (21%). The thick oily liquid was treated with dry ether, the ether was distilled off and the oil distilled in vacuum and the fraction with bp 192-195° (0.5 mm) collected. The yield was 1.2 g (4%).

To 1 g of the substance was added 5 ml of 2 N alcoholic potassium hydroxide solution. After 24 h the precipitate of potassium salt was separated, washed with absolute ethanol, dissolved in 1 ml of water, and acidified with cooling with N hydrochloric acid. The oil which separated was extracted with ether (3 × 5 ml), the solution was washed with water and dried with magnesium sulfate and the ether distilled off at 15-20°. The 0.3 g of oil which remained crystallized on rubbing. The yield was 45%. α-Phenoxy-γ-butyrolactone-α-carboxylic acid had mp 111-116° (decomp.). There was an unresolved band 1715-1778 $cm^{-1}$ in the IR spectrum. Found, %: C 59.62; H 4.96. $C_{11}H_{10}O_5$. Calculated, %: C 59.50; H 4.51.

Ethyl α-Bromo-γ-butyrolactone-α-carboxylate (II). To 10 g (0.063 mole) of ethyl γ-butyrolactone-α-carboxylate at 40-45° and irradiated with an electric lamp pf power 200 W was added 10.1 g (0.063 mole) of bromine over 40 min. The mass was kept at 40° for 2 h and distilled in vacuum and the fraction with bp 107-109° (0.5 mm) collected. The yield was 12 g (80%), $n_D^{18}$ 1.4870. Found, %: C 35.46; H 4.10; Br 35.90. $C_7H_9O_4Br$. Calculated, %: C 35.42; H 3.80; Br 33.70. There were absorption bands in the IR spectrum at 1740 and 1790 $cm^{-1}$.

Ethyl α-Phenoxy-γ-butyrolactone-α-carboxylate (I, R = $C_6H_5O$). To 5.9 g (0.04 mole) of potassium carbonate was added 25 ml of acetone and 4 g (0.04 mole) of molten phenol and the mixture was heated with stirring at 40-45° for 30 min. Then 10 g (0.04 mole) of ethyl α-bromo-γ-butyrolactone-α-carboxylate was added and the mixture kept at 40° for 2 h. The reaction mixture was treated with 50 ml of water, extracted with ether (3 × 30 ml), and dried with magnesium sulfate, the ether was distilled off and the oil that remained distilled and the fraction with bp 143-145° (0.5 mm) collected. The yield was 3.3 g (31%). The colorless oil crystallized rapidly in the air. The mp was 65-66° (from ether). Found, %: C 62.45; H 5.85; $OC_2H_5$ 17.90. $C_{13}H_{14}O_5$. Calculated, %: C 62.50; H 5.60; $OC_2H_5$ 18.00. In the IR spectrum there were absorption bands at 1745 $cm^{-1}$ (carbonyl of the carbethoxy group) and 1778 $cm^{-1}$ (lactone carbonyl).

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