INVESTIGATION OF THE COMPOSITIONS AND STRUCTURES OF THE COMPONENTS OF LACTONE $C_{12}H_{22}O_2$ – THE SIDE PRODUCT OF THE CONDENSATION OF n-BUTYL ALCOHOL

I. SEPARATION AND INVESTIGATION OF THE LACTONE

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It was established by gas–liquid chromatography (GLC) that lactone $C_{12}H_{22}O_2$ consists of three components. Two components, which are its isomers, were isolated by rectification and also by means of preparative GLC. A racemic mixture of optical isomers of 2,4-diethyl-3-n-propylpentanedioic acid was isolated from the products of potassium permanganate oxidation of the salts of the hydroxy acids obtained from the isolated lactone isomers in one case, whereas the meso form of this acid was isolated in another case. On the basis of this, it was concluded that one lactone isomer, constituting 60-70% of the mixture, is $2,4_{trans}$-diethyl-3_{cis}-n-propyl-5-pentanolide or $2,4_{trans}$-diethyl-3_{trans}-n-propyl-5-pentanolide, and the other isomer, constituting 20-30% of the mixture, is $2,4_{cis}$-diethyl-3_{cis}-n-propyl-5-pentanolide or $2,4_{cis}$-diethyl-3-$_{trans}$-n-propyl-5-pentanolide.

One of the side products of the Markovnikov–Guerbet condensation [2] of n-butyl alcohol to obtain 2-ethyl-1-hexanol was found to be lactone $C_{12}H_{22}O_2$ [3, 5], to which Machemer [3] assigned the 2,4-diethyl-5-hydroxycaprylic acid lactone structure without proof. The lactone is formed in 3-5% yield with respect to 2-ethyl-1-hexanol [6]. Despite the fact that the lactone is obtained in relatively low yield, because of the large volume of the reduction of 2-ethyl-1-hexanol from n-butyl alcohol [6] the absolute amounts of the lactone produced industrially are considerable. A study of the reactions of the lactone and the gathering of firm proof for its structure are necessary for its skillful utilization.

In order to determine the structure of the lactone, we isolated a sample corresponding to the composition $C_{12}H_{22}O_2$ from the technical product and attempted to oxidize the sodium salt of the hydroxy acid obtained from it with potassium permanganate. If the structure of lactone corresponds to the structure proposed by Machemer [3], one might have expected the appearance of a keto acid or products of its subsequent decomposition in the oxidation products. However, we could not prove either the presence of the keto acid or butyric acid in the oxidation products. Moreover, two dibasic acids $C_{12}H_{22}O_4$, one of which had mp 95°, the other of which had mp 150°, were isolated from the oxidation products. These results constitute adequate proof against the structure assigned to the lactone by Machemer.

A study of the lactone by gas–liquid chromatography (GLC) showed that it consists of at least three components (Fig. 1, chromatogram *a*), which, in conformity with the order of their emergence on the chromatogram, we designate as Nos. 1, 2, and 3. Gas-chromatographic analysis of a number of samples of the lactone obtained both by condensation of n-butyl alcohol in the laboratory and with an industrial apparatus showed that the percentages of these components in the samples vary over small ranges: 20-30% No. 1, 60-70% No. 2, and 5-10% No. 3.

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TABLE 1. Properties of the Investigated Lactone and of Lactone $C_{12}H_{22}O_2$ Described in the Literature and Obtained from 2-Ethyl-2-hexenal

Authors	Sample	bp, °C (mm)	d_4(°C)	n_D(°C)
This paper	Starting I	136 (4)	0,9646 (20)	1,4630 (20)
This paper	Isomer 1 (Ic, d)	123,5 (3)	0,9630 (20)	1,4612 (20)
This paper	Isomer 2 (Ia, b)	124,5 (3)	0,9644 (20)	1,4639 (20)
Häusermann [7]		147—149 (11)	0,9655 (20)	1,4660 (18)
Nielsen [9]		152—156 (10)	—	1,4617 (25)
Blane and Teppa [8]		99—101 (0,2)	0,9601 (19)	1,4642 (19)

We were able to isolate components 1 and 2 with a purity of 85-90% by rectification of the starting lactone. Chromatographically pure samples of these components were isolated by preparative GLC. The chromatograms of the isolated components are presented in Fig. 1 (chromatograms b-e). The IR spectra for samples isolated by rectification and by means of preparative chromatography were identical over a broad range. The IR spectra of the two components were identical from 1400 to 3600 cm^{-1} and differed substantially at 700-1400 cm^{-1}. The properties of the starting lactone and the components isolated from the reaction mixtures are presented in Table 1. An investigation of components 1 and 2 by PMR spectroscopy showed the presence in both cases of two hydrogen atoms attached to the carbon atom adjacent to the ester oxygen atom. The ratio of their number to the other hydrogen atoms in the molecule was 1 : 10.

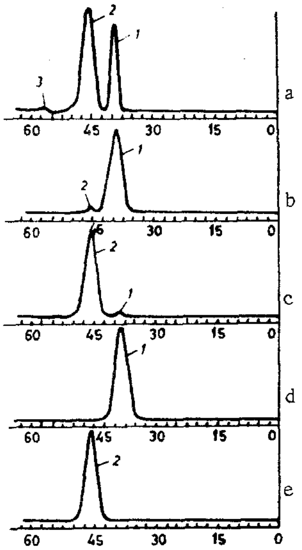
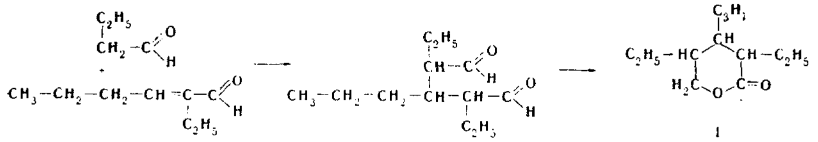


Fig. 1. Gas–liquid chromatograms: a) starting lactone; b) isomers Ic, d isolated by rectification; c) isomers Ia, b isolated by rectification; d) isomers Ic, d isolated by preparative GLC; e) isomers Ia, b isolated by preparative GLC.

Saponification of each of the components with aqueous sodium hydroxide and subsequent acidification showed that both components are isolated in unchanged form. This indicates stereospecificity of closing of the lactone ring. Oxidation of the sodium salt of the hydroxy acid obtained from component 1 by means of potassium permanganate gave dibasic acid $C_{12}H_{22}O_4$ with mp 150°, and an acid with mp 95° was isolated from component 2 in the same way. The acids synthesized by oxidation of the starting lactone were affiliated in this way with each of the components.

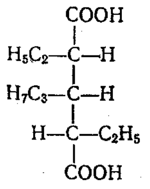
According to the scheme of condensation of alcohols [6], butyraldehyde and 2-ethyl-2-hexenal, which are formed at 130-160° in the presence of alkaline alkoxides and free sodium hydroxide, are present in the products of the condensation of n-butyl alcohol. Häusermann [7] and, later, Blank and Teppa [8] have shown that Michael condensation of the indicated components with subsequent intramolecular Tishchenko reaction of the resulting dialdehyde to give 2,4-diethyl-3-n-propylpentanolide (I) is possible under similar conditions:



I

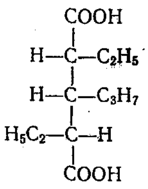
To confirm structure I, Häusermann [7] oxidized the salt of the hydroxy acid obtained by saponification of the lactone that he isolated with potassium permanganate and obtained dibasic acid $C_{12}H_{22}O_4$ with mp 150°, to which he assigned the 2,4-diethyl-3-n-propylpentane-1,5-dioic acid structure (II).

Four isomers (IIa-d) correspond to acid II:



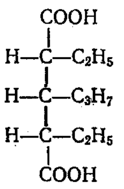
$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{H_5C_2{-}C{-}H}\\ |\\ \mathrm{H_7C_3{-}C{-}H}\\ |\\ \mathrm{H{-}C{-}C_2H_5}\\ |\\ \mathrm{COOH}\end{array}$$

IIa



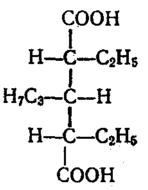
$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{H{-}C{-}C_2H_5}\\ |\\ \mathrm{H{-}C{-}C_3H_7}\\ |\\ \mathrm{H_5C_2{-}C{-}H}\\ |\\ \mathrm{COOH}\end{array}$$

IIb



$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{H{-}C{-}C_2H_5}\\ |\\ \mathrm{H{-}C{-}C_3H_7}\\ |\\ \mathrm{H{-}C{-}C_2H_5}\\ |\\ \mathrm{COOH}\end{array}$$

IIc

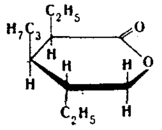


$$\begin{array}{c}\mathrm{COOH}\\ |\\ \mathrm{H{-}C{-}C_2H_5}\\ |\\ \mathrm{H_7C_3{-}C{-}H}\\ |\\ \mathrm{H{-}C{-}C_2H_5}\\ |\\ \mathrm{COOH}\end{array}$$

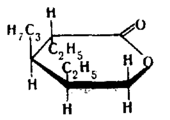
IId

Isomers IIa and IIb are optical antipodes. Isomers IIc and IId are the two meso forms. Our investigation of the isolated acids with mp 150° and 95° by means of PMR spectroscopy confirmed that both of them correspond to structure II. Nielsen [9] obtained an acid with mp 94-96° and showed that it can be separated into optical isomers, i.e., that it is a racemic mixture of isomers IIa and IIb. A choice of structures IIc and IId is presented for the acid with mp 150°.

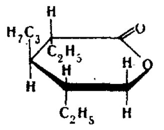
The preparation of the indicated acids and the above-presented quantitative relationships revealed from the PMR spectra of both isomers of the lactones confirm their common structure (I). Thus the isomers are geometrical isomers. On the basis of the structures of the acids, one can conclude that component 2 of the lactone, from which a racemic mixture of acids IIa and IIb was obtained, may have structure Ia or Ib with the corresponding mirror-image isomers:



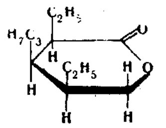
Ia



Ib



Ic



Id

Structure Ic, with a mirror-image isomer corresponding to acid IIc, or structure Id, with a mirror-image isomer corresponding to acid IId, can be considered for component 1 of the lactone from which the meso form of acid II was obtained. Nielsen [10], on examining the possible structures of the Häusermann lactone, considered form Ic to be the most stable form. Thus, on the basis of what was stated above for structures Ia and Ib, a choice between 2,4_{trans}-diethyl-3_{cis}-n-propyl- and 2,4_{trans}-diethyl-3_{trans}-n-propyl-5-pentanolide is possible for structures Ia and Ib, and a choice between 2,4_{cis}-diethyl-3_{cis}-n-propyl- and 2,4_{cis}-diethyl-3_{trans}-n-propyl-5-pentanolide is possible for the meso forms.

In addition to the mechanism for the formation of lactone I proposed by Häusermann, one can also consider the possibility of its formation indicated by Nielsen [9], i.e., dealdolization of the product of condensation of two 2-ethyl-2-hexenal molecules.

Considering the possibility of the common origin of the lactone investigated in this paper and the lactone obtained by reaction of 2-ethyl-2-hexenal with alkali hydroxides [7-9], the properties of the product that we obtained and the literature data are presented in Table 1.

EXPERIMENTAL

Gas–Liquid Chromatography. Gas– liquid chromatography was carried out by three methods. Method A involved the use of a Tsvet-2 chromatograph with a flame-ionization detector, a 3-m long column, a polyethylene glycol-2000 phase on Celite-535, a column temperature of 160°, and a carrier gas (nitrogen) flow rate of 50 ml/min. Method B entailed the use of a model 1-64 Tsvet chromatograph with a catharometer detector, a 3-m long column, 18% diethylene glycol succinate on Chromosorb W, a column temperature of 188°, and a carrier gas (helium) flow rate of 60 ml/min. Method C involved the use of the same apparatus as in method B with a flame-ionization detector, a column length of 5 m, Tridox on Chromatone N-AW, a column temperature of 185°, and carrier gas (helium) flow rate of 50 ml/min.

Spectra. The IR spectra were recorded with a UR-10 spectrometer with NaCl and LiF prisms, a slit program, and a scanning rate of 150 cm^{-1}/min. The PMR spectra were recorded with a JNM-C-60-HL Jeol spectrometer (Japan) with hexamethyldisiloxane as the internal standard.

Purification of Lactone I. Lactone I, isolated in the usual way [4, 5] from the acidic portion of the products of condensation of n-butyl alcohol, usually contained a certain amount of impurities, mainly higher alcohols. For their removal, 200 g of I was saponified by stirring with 10% aqueous sodium hydroxide at 60-65° until all of the solid had dissolved. The solution was extracted three times (50-ml portions) at room temperature with toluene. The toluene was separated by decantation, and the solution was treated with steam to remove traces of toluene. The solution of the salt of the hydroxy acid was acidified with concentrated HCl, and the lactone was separated and neutralized with vigorous stirring by the addition of 0.1 N NaOH. It was then washed with water and vacuum distilled to give 165 g of a main fraction in the form of of a colorless oily liquid. The properties of the product are given in Table 1. Found: C 71.8; H 11.2%. Ester number 283.0. Acid number 0. $C_{12}H_{22}O_2$. Calculated: C 72.7; H 11.2%. Ester number 282.9. Acid number 0.

Oxidation of Lactone I with Potassium Permanganate. A 5-g (0.025 mole) sample of lactone I was saponified with 15 g of a 10% solution of sodium hydroxide at 60-65°, and a solution of 10 g of potassium permanganate in 160 ml of water was added with stirring at this temperature to the resulting solution in the course of 6-7 h. After all of the permanganate solution had been added, the mixture was heated for another hour at 80°. The precipitated manganese dioxide was removed by filtration and washed with 100 ml of hot water, and the combined filtrates were evaporated to ∼ 30 ml. The concentrated solution was acidified with concentrated hydrochloric acid and extracted with two 15-ml portions of toluene. The toluene was removed from the extract by distillation at reduced pressure, and 30 g of n-hexane was added to the residue (3.6 g). The colorless prismatic crystals that formed after the solution had stood for 24 h were removed by filtration to give 0.8 g (0.0035 mole) of IIc, d with mp 149-150° (from water containing 10% alcohol). Found: C 62.7; H 8.9%. Acid number 485.0 mg KOH/g. $C_{12}H_{22}O_4$. Calculated: C 62.6; H 9.6%. Acid number 487.3 mg KOH/g.

The PMR spectrum of a 17% solution in chloroform was recorded at 90°: t,* 0.9 (CH_3), m, 1.5 (CH_2), m, 2-2.5 (CH), broad s, 9.4 ppm (COOH). The CH_3 : CH_2 : CH : COOH integral intensity ratio was 8.9 : 7.95 : 3 : 2, in agreement with the ratio calculated for structure II (9 : 8 : 3 : 2).

After the crystals of acids IIc, d had been separated, the filtrate, with acid number 40.5 mg KOH/g and ester number 10.3 mg KOH/g, was treated with 0.1 N sodium hydroxide solution (in the cold) in the amount calculated for neutralization of the acid. After the hexane layers had been separated and washed with water, the initially separated aqueous layer was combined with the wash water and evaporated, and the residue was acidified with concentrated HCl and extracted with toluene. The toluene was removed by vacuum distillation, and 2 g of hexane was added to the residue (1.3 g). The mixture was allowed to stand for 24 h to give 1 g (4.5 mmole) of a mixture of IIa, b with mp 95° (from water containing 10% alcohol). Found: C 62.5; H 9.7%. Acid number 485.0 mg KOH/g. $C_{12}H_{22}O_4$. Calculated: C 62.6; H 9.6%. Acid number 487.3 mg KOH/g.

The PMR spectrum was recorded at room temperature (17% solution in chloroform). The ratio of the areas of the CH_3, (CH_2 + CH), and COOH signals was 9.5 : 10.8 : 2, in agreement with the ratio calculated for structure II (9 : 11 : 2).

The neutralized layer was washed with hexane, and the hexane was removed by distillation to give 1 g (0.005 mole) of starting lactone I. The product was identified by GLC. Ester number 275 mg KOH/g, acid number 0.

The initially obtained acidic aqueous solution was extracted successively with toluene and ether. The ether was removed by distillation to give large crystals of oxalic acid with mp 189° (after drying).

Investigation of the Lactone by GLC. The lactone was investigated by GLC by method A. The chromatogram is presented in Fig. 1 (chromatogram *a*).

Rectification of the Lactone in Order to Isolate the Individual Isomers. Lactone I was subjected to repeated successive fractional rectification in vacuo with a column with an efficiency of nine theoretical plates. The composition of the fraction was monitored by means of GLC (methods B and C).

Isomer Ic, d was isolated with a purity of 90%. Its gas–liquid chromatogram (method A) is presented in Fig. 1 (chromatogram b). Its properties are given in Table 1. Found: C 71.8; H 11.6%. Ester number 284.0 mg KOH/g. $C_{12}H_{22}O_2$. Calculated: C 72.7; H 11.2%. Ester number 282.9 mg KOH/g.

The PMR spectrum without a solvent was recorded at 70°: m 3.8-4.4 (CH_2 group adjacent to the ring oxygen atom, 2H), m from 0.7 to 2.3 (protons of the remaining 20H groups).

Isomer Ia, b was isolated with a purity greater than 85%. Its gas–liquid chromatogram (method A) is presented in Fig. 1 (chromatogram c). Its properties are given in Table 1. Found: C 72.5; H 11.6%.

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*Here and subsequently, s is singlet, t is triplet, and m is multiplet.

Ester number 284.5 mg KOH/g. $C_{12}H_{22}O_2$. Calculated: C 72.7; H 11.2%. Ester number 282.9 mg KOH/g.

The PMR spectrum is similar to the PMR spectrum of lactones Ic, d. One's attention is directed to the certain difference in the asymmetry of the multiplets at 4.1 ppm.

Separation of the Isomers by Preparative GLC. The isomers were separated with an LKhM-7 chromatograph with an 2-m long column with a diameter of 6 mm, 20% PEG-20,000 on Celite-535 (0.2-0.25 mm fraction), a column temperature of 165°, a sensitivity of 1 : 16, and a 50-ml sample. The following components were isolated: component 1 (isomer Ic, d) n_D^{20} 1.4616 [see Fig. 1 (chromatogram d) for its gas−liquid chromatogram (method A)] and component 2 (isomer Ia, b) n_D^{20} 1.4620 [see Fig. 1 (chromatogram e) for its gas−liquid chromatogram (method A)].

The lactone isomers isolated by preparative GLC were chromatographically pure. Their refractive indexes differed somewhat from those of the preparation isolated by rectification (see Table 1). However, the IR spectra of Ic, d isolated by both preparative GLC and rectification were absolutely identical. The same also applies to the IR spectra of Ia, b isolated by these two methods.

Saponification and Reverse Isolation of the Lactone Isomers. Samples (1-g each) of the lactone isomers were saponified with 0.1 N sodium hydroxide solution by stirring at 60-65° until the solid had dissolved completely. The resulting solutions were cooled and acidified with hydrochloric acid. Each of the isomers was isolated quantitatively in the original form (identification by means of GLC).

Oxidation of Isomer Ia, b. A 10-g sample of a mixture of Ia and Ib was oxidized with potassium permanganate via the method described above for lactone I. The mixture was worked up as indicated above to give 1.4 g of acid IIa, b with mp 94-95°; 4.1 g of lactones Ia, b was recovered.

Oxidation of Isomer Ic, d. A 5-g sample of a mixture of Ic, d was treated with potassium permanganate as in the preceding experiment, and workup of the mixture gave 1.1 g of an acid with mp 148-150° (IIc, d); 1.8 g of a mixture of Ic and Id was recovered.

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