The phenylurethan derivative was prepared as above, except that diethylene glycol diethyl ether was used as solvent (reaction temperature 165°); small colorless prisms from hexane, m.p. 122–122.5°.

Anal. Calcd. for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 77.74; H, 8.66; N, 4.27.

2,4,6-Triethylphenol was prepared in 86% yield from 2,4,6-triethylaniline[44]; b.p. 104–106° (3 mm.), m.p. 20–21°, n^{25}D 1.5158; λ_{max} 279 mμ, log ϵ 3.28 (95% ethanol); infrared bands at 2.90, 3.50, 5.70w, 6.25m, 6.90, 7.30w, 7.66m, 7.87m, 8.45, 8.75, 9.40m, 10.0w, 11.5 and 12.5 μ.

The phenylurethan derivative was prepared using the procedure developed for XX, above; plates from hexane, m.p. 117–118°.

Anal. Calcd. for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80; N, 4.71. Found: C, 76.60; H, 7.88; N, 5.00.

2,4,6-Triethylphenyl Propionate: Attempted Preparation of 3-Hydroxy-2,4,6-triethylpropiophenone.—To 2,4,6-triethylphenol (8.9 g., 0.05 mole) in 30 ml. of nitrobenzene was slowly added 20 g. (0.15 mole) of aluminum chloride, with stirring (temp. below 20°). After 10 minutes, 9.25 g. (0.10 mole) of propionyl chloride was added during 30 minutes (temp. 15–20°). The mixture was stirred 14 hr. at *ca.* 25°, 0.5 hr. at 90° and then poured into ice and hydrochloric acid. The mixture was worked up in the usual manner and twice distilled to yield 9.0 g. (77%) of 2,4,6-triethylphenyl propionate, b.p. 100° (1 mm.), n^{25}D 1.4920; infrared bands at 3.48, 3.54, 5.72, 6.25m, 6.55w, 6.90, 7.40, 7.90, 8.50, 8.80, 9.48, 10.20, 11.30, 11.50 and 12.45m μ. The ultraviolet absorption was weak; λ_{max} 265 mμ, ϵ 500; 273 mμ, ϵ 380.

Anal. Calcd. for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.93; H, 9.37.

Hydrolysis of the ester (2.32 g.) was effected by refluxing with concd. hydrochloric acid and zinc dust and gave 1.4 g. (78%) of 2,4,6-triethylphenol, b.p. 94–97° (1 mm.); λ_{max} 277 mμ, log ϵ 3.13.

Reaction of the ester with additional propionyl chloride and aluminum chloride in nitrobenzene gave recovered starting material and no acylated product.

NEW BRUNSWICK, N. J.

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(44) 1-Nitro-2,4,6-triethylbenzene, b.p. 99° (1 mm.), n^{22}D 1.510, prepared in 83% yield by nitration of 1,3,5-triethylbenzene, was reduced with iron and water to 2,4,6-triethylaniline in 81% yield, b.p. 106–112° (2 mm.), n^{25}D 1.5330; *cf.* W. B. Dillingham and E. E. Reid, THIS JOURNAL, **60**, 2606 (1938).

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY, THE UNIVERSITY OF IDAHO AND RUTGERS, THE STATE UNIVERSITY]

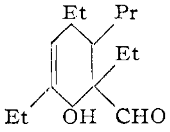
The Base-catalyzed Self-condensation of 2-Ethyl-2-hexenal. II. Formation of a Glycol, $C_{16}H_{30}O_2$, and a Lactone, $C_{16}H_{30}O_3$[1]

BY ARNOLD T. NIELSEN[2]

RECEIVED OCTOBER 22, 1956

The aldol dimer I of 2-ethyl-2-hexenal undergoes an intramolecular disproportionation in the presence of methanolic potassium hydroxide to form 5,7-dihydroxy-3-propyl-2,4,6-triethyl-1,5-heptanolactone (III). In the presence of 2-ethyl-2-hexenal, I also undergoes a Cannizzaro reaction leading to the glycol II, 2-ethyl-2-hexenoic acid and butyric acid. A mechanism for the formation of III in a preferred conformation is discussed.

2-Ethyl-2-hexenal has been shown to self-condense in the presence of aqueous methanolic potassium hydroxide to yield the cyclic dimer I.[3] It has been observed that the yield of I decreases rapidly as the reaction time is increased while, simultaneously, other products are formed, including a C_{16}-lactone III, a C_{16}-glycol II and 2-ethyl-2-hexenoic and butyric acids (Fig. 1).



I

The preparation of compounds I, II and III has been reported previously,[4,5] although no structures were suggested by Anseln and Nickl or Hall and Tuerck.[5] Häusermann[6] also has studied the self-condensation of 2-ethyl-2-hexenal but under more vigorous reaction conditions (25–50% aqueous sodium hydroxide, *ca.* 200°, 22 hr.) than those of the present investigation. He isolated, among other products, butyric and 2-ethyl-2-hexenoic acids, 2,4-diethyl-3-propyl-1,5-pentanolactone and a C_{16}-glycol, to which no structure was assigned. No C_{16}-lactone was reported by him. There are scattered reports in the literature of the formation of high molecular weight glycols and lactones from various saturated and unsaturated aliphatic aldehydes, in the presence of basic catalysts.[4–7] In most cases, however, the structures of these condensation products have not been established.

The glycol II, formed in 10–30% yields, was found to be identical with the lithium aluminum hydride reduction product of the aldol I.[3] It is believed to have been formed by a Cannizzaro reaction involving reduction of I and oxidation, principally of butanal[8] and 2-ethyl-2-hexenal to butanoic and 2-ethyl-2-hexenoic acids.[9] The linear

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(1) Presented, in part, at the 130th American Chemical Society Meeting, Atlantic City, N. J., September, 1956.

(2) School of Chemistry, Rutgers, The State University, New Brunswick, N. J.

(3) A. T. Nielsen, THIS JOURNAL, **79**, 2518 (1957).

(4) A. T. Nielsen, Ph.D. thesis, University of Washington, 1947.

(5) R. H. Hall and K. H. W. Tuerck, (a) British Patent 608,985, Sept. 23, 1948; *C. A.*, **44**, 4493 (1950); (b) U. S. Patent 2,528,592, Nov. 7, 1950; *C. A.*, **45**, 3866 (1951); (c) H. Anseln and E. Nickl, German Patent 752,482, Feb. 23, 1953; *C. A.*, **50**, 2658 (1956).

(6) M. Häusermann, *Helv. Chim. Acta*, **34**, 1482 (1951).

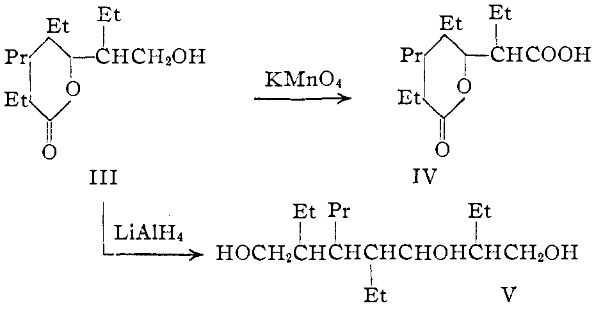
(7) (a) A. Borodin, *Ber.*, **6**, 982 (1873); (b) A. v. Lenz, *Monatsh.*, **24**, 155 (1903); (c) H. Meerwein, *J. prakt. Chem.*, [2] **97**, 225, 257 (1918); (d) H. Meerwein, *Ber.*, **53**, 1829 (1920); (e) J. Ducasse, *Bull. soc. chim. France*, [5] **11**, 333 (1944); (f) W. Hunter, B. I. O. S. Report No. 1053, Item No. 22. German Acetylenic Chemical Industry, Miscellaneous Organic Compounds, October 13, 1947, pp. 239–241.

(8) Butanal must be formed mainly by hydration of 2-ethyl-2-hexenal to butyraldol, followed by dealdolization. Evidence for formation of butanal from 2-ethyl-2-hexenal (alkaline catalyst) has been reported previously; S. G. Powell and A. T. Nielsen, THIS JOURNAL, **70**, 3627 (1948); Y. Sprinzak, *ibid.*, **74**, 2116 (1952).

(9) The aldol I, itself, is apparently not an important oxidizing agent in this reaction since it was found to be converted solely into lactone III under the milder conditions of the reaction (Fig. 1). However, under more vigorous reaction conditions where the yield of II is higher, some I may be oxidized, leading to a larger amount of

relationship between the mole-per cent. yield of II and these acids supports this view (Table I, Experimental part).

The third major product obtained from the reaction of 2-ethyl-2-hexenal with alkali was shown by elemental analysis, molecular weight and saponification equivalent determinations to be $C_{16}H_{30}O_3$ (40–56% yield). Strong infrared absorption at 2.98 μ, the formation of a monoacetate derivative and the Zerewitinoff determination indicated the presence of one free alcoholic hydroxyl group. Oxidation of III with permanganate led to a monocarboxylic acid lactone, $C_{16}H_{28}O_4$ (IV), in 75% yield, indicating the hydroxyl group to be primary. Compound III was insoluble in hot aqueous *N* sodium hydroxide solution but could be converted into its carboxylate anion with hot aqueous alcoholic *N* sodium hydroxide (saponification equivalent determination). This observation, and the presence of strong infrared absorption at 5.85 μ, support a six-membered lactone structure. Failure of III to react with bromine in carbon tetrachloride or potassium permanganate in acetone and, particularly, failure to absorb hydrogen under conditions favorable for facile hydrogenation of I and II, as well as the empirical formula and spectral data, suggest the absence of olefinic unsaturation in the molecule. Reduction of III with lithium aluminum hydride led to a crystalline triol V, $C_{16}H_{34}O_3$ (58%), m.p. 96.5–97.5°. A Zerewitinoff determination supports the triol assignment as does the intense infrared band at 2.97μ and the absence of carbonyl absorption in the 5.5–6.0μ region; compound V failed to react with lead tetraacetate or periodic acid. On the basis of the above preliminary evidence structure III was proposed for the lactone, IV for the corresponding acid and V for the triol.

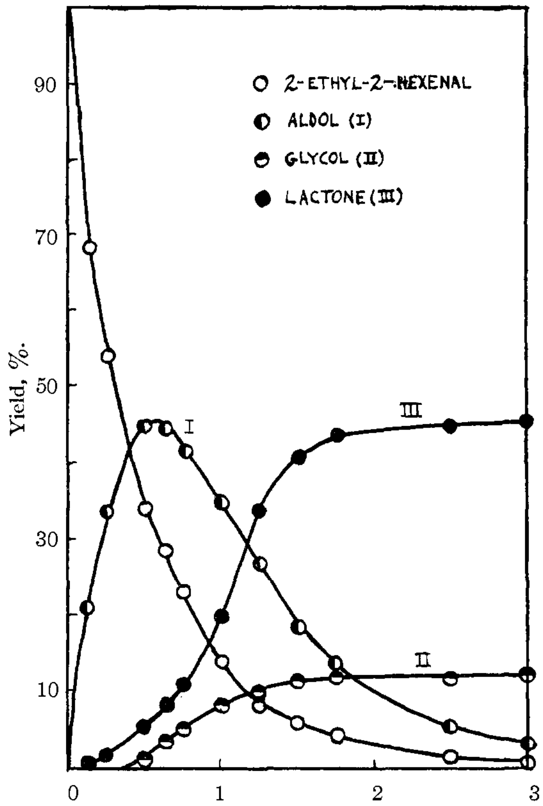


III IV

$HOCH_2\overset{Et}{CH}\overset{Pr}{CH}\underset{Et}{CH}CHOH\overset{Et}{CH}CH_2OH$

V

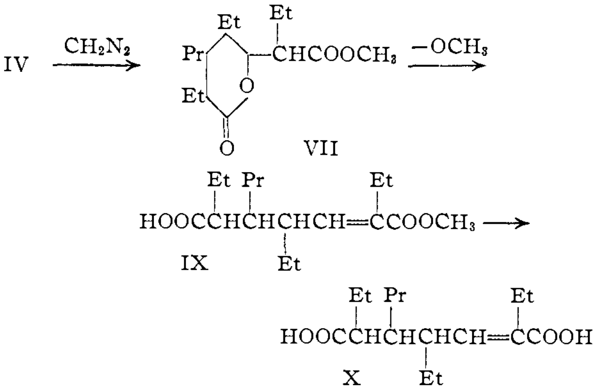
Confirmatory evidence for structure III was obtained when VII, the methyl ester of IV (obtained by reaction of IV with diazomethane or of its monosilver salt VI with methyl iodide),[10] was



Reaction time, hours.

Fig. 1—Percentage yield of reaction products *vs.* reaction time for self-condensation of 2-ethyl-2-hexenal at 25°; for reaction conditions see Experimental part.

treated with one mole-equivalent of sodium methoxide to open the lactone ring and yield the unsaturated monoester IX.[11] Hydrolysis of IX gave the crystalline free acid X (83% yield from VII); α,β-unsaturation was demonstrated in the latter by its ultraviolet[12] (λ_{max} 218 mμ, ϵ 16,300) and infrared[13] (λ_{max} 5.85–5.95, 6.14μ) absorption characteristics.



VII

$HOOC\overset{Et}{C}H\overset{Pr}{C}H\underset{Et}{C}HCH{=}\overset{Et}{C}COOCH_3 \longrightarrow$

IX

$HOOC\overset{Et}{C}H\overset{Pr}{C}H\underset{Et}{C}HCH{=}\overset{Et}{C}COOH$

X

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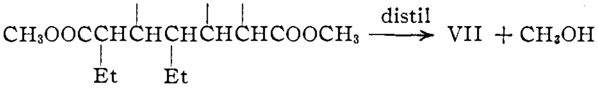
undistillable acid residue (*cf.* Table I) and proportionately less butyric and 2-ethyl-2-hexenoic acids.

(10) Ester VII was also obtained by demethanolation, during distillation, of the dimethyl ester VIII. The latter compound was obtained from the corresponding disilver salt, prepared from IV, and



$CH_3OOC\underset{Et}{CH}\overset{OH}{CH}\underset{Et}{CH}\overset{Pr}{CH}\overset{Et}{CH}COOCH_3 \xrightarrow{distil} VII + CH_3OH$

VIII

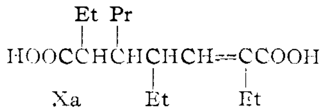
methyl iodide. (*Cf.* E. Oberreit, *Ber.*, **29**, 1998 (1896), for a similar example of thermal demethanolation in the case of methyl 4-hydroxy-2-propylpentanoate.)

(11) Examples of this reaction in five-membered ring systems have been reported; J. A. Elvidge, R. P. Linstead and P. Sims, *J. Chem. Soc.*, 1793 (1953), and earlier papers in this series.

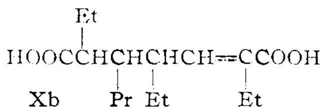
(12) α,β-Dialkylacrylic acids exhibit a maximum absorption in the ultraviolet region at *ca.* 217 mμ, α- or β-monoalkyl substituted acrylic acids at *ca.* 208 mμ; J. Cason, N. L. Allinger and D. E. Williams, *J. Org. Chem.*, **18**, 842 (1953); J. Cason and L. L. Rinehart, *ibid.*, **20**, 1951 (1955).

(13) N. K. Freeman, THIS JOURNAL, **76**, 1859 (1953).

Oxidation of X with either ozone or permanganate yielded, as expected, 2,4-diethyl-3-propylpentanedioic acid (XI) and propionic and formic acids from cleavage of 2-ketobutanoic acid.[3] Acid XI was obtained solely as the racemic form XIa which was resolved through its brucine salts. Heating with aqueous potassium hydroxide at 175–180° partly isomerized XIa into a *meso* isomer XIb, identical with the isomer produced by degradation of the aldol I[3] and with Häusermann's sample, kindly furnished for comparison.[14,15] Since the crystalline unsaturated acid X is homogeneous and gives solely XIa as an oxidation product, its configuration is limited to structures Xa and Xb (excluding *cis* and *trans* forms). In the discussion below certain information is presented leading to Xa as the favored configuration.

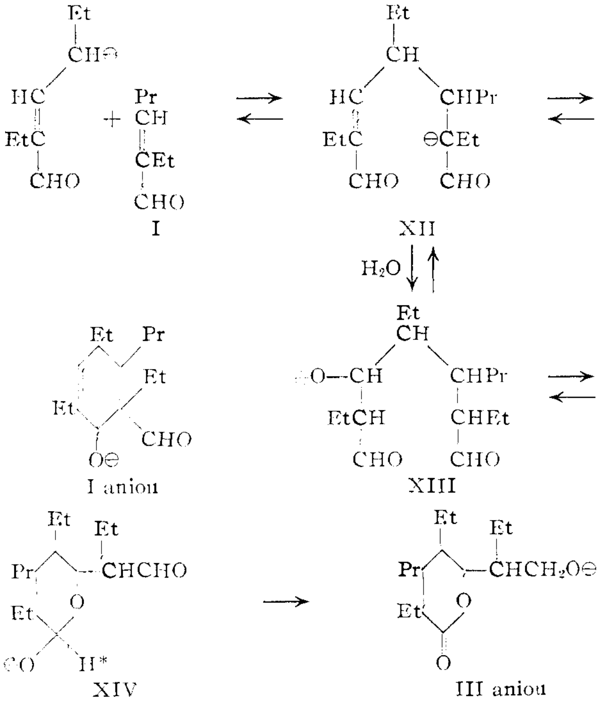

Xa

$$\mathrm{HOOC\overset{Et}{C}H\overset{Pr}{C}H\underset{Et}{C}HCH{=}\underset{Et}{C}COOH}$$

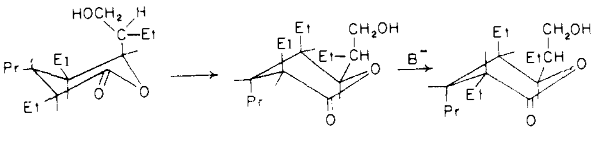

Xb

$$\mathrm{HOOC\overset{Et}{C}H\underset{Pr}{C}H\underset{Et}{C}HCH{=}\underset{Et}{C}COOH}$$

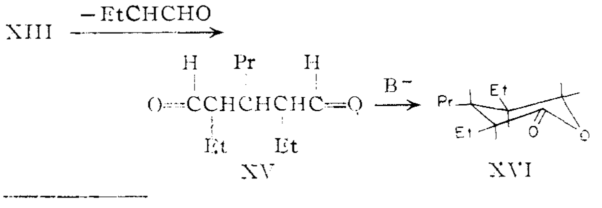
The question arises regarding the mechanism by which III is formed from 2-ethyl-2-hexenal. Figure 1 suggests that the aldol I may be considered as an intermediate, and this is confirmed by experiment, since under the same reaction conditions I is converted exclusively to III in good yield. The mechanism therefore appears to be intramolecular and may reasonably be formulated as shown. In this mechanism the common intermediate precursor of I and III is the anion XII. A hydrated dialdehyde, XIII, is presumed to be the precursor of the cyclic hemiacetal XIV, which undergoes internal disproportionation to III through hydride transfer.



In order for this internal transfer to be sterically possible, both the starred hydrogen and formylpropyl group must be axially rather than equatorially directed; hence the hydroxybutyl group in lactone III must likewise be axial at the time of formation (IIIa). On the assumption that the other three alkyl groups originally occupied the energetically preferred equatorial positions, lactone III should have the conformation IIIa,[16] or more probably the equivalent form IIIb, in which the bulky hydroxybutyl group has become equatorial by a near-strainless ring inversion.[17] However, conformation IIIb would predict the formation of *meso*-XI on degradation of III, whereas the isomer actually isolated was *d,l*-XI. This discrepancy can be accounted for by assuming that the axial ethyl group alpha to the carbonyl of IIIb becomes inverted, in the presence of strong alkali, to the more stable equatorial position (IIIc). Whether all of this inversion occurred before the isolation of III or in the subsequent ring-opening reaction of the ester VII is uncertain.[18]


IIIa IIIb IIIc

In conclusion it may be mentioned that under our conditions, very little, if any, 2,4-diethyl-3-propyl-1,5-pentanolactone (XVI) formed, although under more vigorous conditions (50% aqueous sodium hydroxide at 200° for 24 hr.) Häusermann[6] obtained it from 2-ethyl-2-hexenal in 36% yield. This product presumably arises through dealdolization of XIII, followed by disproportionation of the resulting 2,4-diethyl-3-propylpentanedial (XV).[19]



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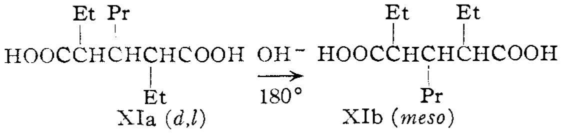
(14) The 150–151° melting *meso* isomer is believed to have the *threo* configuration XIb; *cf.* ref. 3.



$$\mathrm{HOOC\overset{Et}{C}H\overset{Pr}{C}H\underset{Et}{C}HCOOH} \xrightarrow[180^\circ]{OH^-} \mathrm{HOOC\overset{Et}{C}H\underset{Pr}{C}H\overset{Et}{C}HCOOH}$$

XIa (*d,l*) XIb (*meso*)

(15) Numerous attempts to synthesize 2,4-diethyl-3-propylpentanedioic acid (XI) by a variety of approaches failed; Häusermann reports similar failures (private communication).

(16) A favored *threo* arrangement of propyl and α-ethyl groups in XIII would lead to IIIa.

(17) S. Winstein and N. J. Holness, THIS JOURNAL, **77**, 5562 (1955).

(18) The reduction of III with lithium aluminum hydride to the crystalline triol V in 58% yield suggests a favored structure for III, to at least the extent of this yield.

(19) An alternate mechanism involving Michael addition of butanal to 2-ethyl-2-hexenal appears unlikely since this reaction fails in practice (unpublished work, this Laboratory; *cf.* ref. 6).

Experimental[20]

6-Hydroxymethyl-5-propyl-2,4,6-triethyl-2-cyclohexen-1-ol (II).—To purified 2-ethyl-2-hexenal[3] (113 g., 0.90 mole) was added dropwise, with stirring, during 1.5 hr., a solution of 50 g. (0.76 mole) of potassium hydroxide (86% assay) in 65 ml. of methanol and 16 ml. of water. A nitrogen atmosphere was maintained during the reaction but no external cooling was provided. The temperature gradually rose to 80° during 30 minutes, while one-sixth (17 ml.) of the potassium hydroxide solution was being added gradually. Within the next 60 minutes the addition of the alkali was complete and the temperature had dropped to 40°. Stirring was continued for 1.5 hr., water then added and the mixture separated into acid and neutral parts as described previously.[3]

Distillation of the neutral part gave the following main fractions: (1) 2 g., recovered 2-ethyl-2-hexenal; (2) 37 g. (32%) of the glycol II, b.p. 124–129° (0.25 mm.), $n^{25}\text{D}$ 1.4926; (3) 7.3 g. of residue. A redistilled sample of the glycol was obtained as a pale yellow, extremely viscous liquid, b.p. 135–138° (0.45 mm.), $n^{25}\text{D}$ 1.4935, d^{23}_4 0.921; infrared bands at 3.0, 3.45, 3.53, 5.85w, 6.1w, 6.87, 7.28 and 9.7 μ (chloroform).

Anal. Calcd. for $C_{16}H_{30}O_2$: C, 75.54; H, 11.89; mol. wt., 254.4. Found: C, 75.76; H, 11.48; mol. wt., 252, 256.[21]

Quantitative hydrogenation of a 5.56-millimole sample of the glycol (689 mm., 23°, acetic acid solvent, a few drops of concentrated hydrochloric acid promotor, 5% palladium-charcoal catalyst) resulted in absorption of 1.06 mole-equivalents of hydrogen in 270 minutes, after which time hydrogenation essentially ceased. On quantitative bromination of the glycol with a 5% solution of bromine in carbon tetrachloride, 0.91 mole-equivalent of bromine was absorbed. A Zerewitinoff determination showed 1.90 active hydrogens and no additional methylmagnesium iodide reacted.

The bis-*p*-nitrophenylurethan derivative was obtained as yellow microcrystals from high boiling ligroin, m.p. 74–78°. When mixed with a sample of the bis-*p*-nitrophenylurethan derivative of II obtained previously,[3] m.p. 76.5–78.5°, the melting point was not depressed.

Distillation of the acid part from the above reaction gave (1) *ca.* 3 g., b.p. 50–83° (0.4 mm.), mainly butyric acid; (2) 6.6 g., b.p. 83–138° (0.3 mm.), mainly 2-ethyl-2-hexenoic acid; (3) 37 g. (31%), b.p. 150–157° (0.35 mm.), lactone III, $n^{25}\text{D}$ 1.4740; (4) 13.0 g. of residue.

The butyric acid fraction was redistilled to yield a sample, b.p. 159–162° (760 mm.), $n^{20}\text{D}$ 1.3990, neut. equiv. 90; *p*-phenylphenacyl ester, m.p. 81.5–82.5°, alone and when mixed with an authentic sample.

The 2-ethyl-2-hexenoic acid fraction was dissolved in ether and extracted with sodium hydroxide solution. Acidification of the alkaline extracts gave a sample, b.p. 98–99.5° (2.7 mm.), $n^{20}\text{D}$ 1.455,[22] neut. equiv. 145 (calcd. for $C_8H_{14}O_2$, 142.2). **The** amide derivative, prepared through the acid chloride, melted at 69–69.5°, alone, and when mixed with an authentic sample.[23] *Anal.* Calcd. for $C_8H_{15}NO$: C, 68.04; H, 10.71. Found: C, 68.1; H, 10.7.

The total yield of acids and glycol produced in various runs was calculated by determining the number of moles of each product produced per 100 moles of 2-ethyl-2-hexenal employed (mole-per cent. yield); for purposes of calculation the acid residue was assigned an equivalent weight of 270. In these runs the potassium hydroxide concentration, rate of addition of the catalyst, reaction time and temperature were varied. The glycol yields were proportional to the total mole-per cent. yield of acids produced, as shown in Table I.

TABLE I

YIELDS OF ACIDS AND GLYCOL II FORMED IN VARIOUS RUNS

Run	Mole-per cent. yields[a] II	A	B	C
11	16.0	3.8	5.1	5.4
9	13.5	4.0	4.9	2.5
8	11.5	3.2	3.9	1.9
4	9.5	4.1	3.2	1.6
10	8.3	2.4	3.6	1.7
27	5.5	1.2	1.4	1.6
16	5.0	1.3	1.4	0.8
18	2.5	0.6	0.8	0.3

[a] Actual percentage yield of II from 2-ethyl-2-hexenal is twice the above value: A = butyric acid, B = 2-ethyl-2-hexenoic acid, C = acid residue.

Preparation of 5,7-Dihydroxy-3-propyl-2,4,6-triethyl-1,5-heptanolactone (III). Method A. From 2-Ethyl-2-hexenal.—2-Ethyl-2-hexenal, purified as described previously,[3] was freshly distilled under nitrogen, directly into the reaction flask (128.4 g., 1.02 moles). A solution of 38 g. of potassium hydroxide (85% assay, 0.58 mole) in 18 ml. of water and 64 ml. of methanol was then added during one minute with vigorous stirring while a nitrogen atmosphere was maintained and the temperature held at 25° by ice-bath cooling. The color of the solution quickly became orange while the alkali was being added, and after a total reaction time of 7 hr. (temperature, 25°), 500 ml. of water was added rapidly to the mixture with stirring. The oily layer which formed was separated, the aqueous layer extracted with ether and the extracts combined with the main portion. The ether solution was washed with water and dried over magnesium sulfate.

The aqueous alkaline solution remaining after extraction with ether was acidified with concentrated hydrochloric acid. The oil which formed was separated and the aqueous part extracted with ether. The oil and ether extracts were combined and after distilling the ether, the residue was distilled to give (1) 1 g., b.p. 35–55° (0.7 mm.), mainly butyric acid; (2) 3 g., b.p. 93–114° (0.4 mm.), mainly 2-ethyl-2-hexenoic acid; (3) 1.4 g., b.p. 114–151° (0.3 mm.), forerun; (4) 68.4 g. (49.6%)[24] of lactone III, b.p. 152–157° (0.25 mm.); (5) 10.5 g. of residue. A redistilled sample used for analysis was a colorless, slightly viscous liquid, b.p. 153–155° (0.3 mm.), $n^{25}\text{D}$ 1.4757; infrared bands at 2.98m, 3.46, 3.53, 5.80–5.85, 6.86m, 7.25m, 8.32, 9.05–9.10m and 9.6–9.65m μ.

Anal. Calcd. for $C_{16}H_{30}O_3$: C, 71.07; H, 11.18; mol. wt., 270.4. Found: C, 70.93; H, 11.22; mol. wt., 274, 275[21]; sapn. equiv., 264.

The lactone was found not to decolorize bromine in carbon tetrachloride or dilute potassium permanganate in acetone. No hydrogen was absorbed by the compound in acetic acid in the presence of 5% palladium–charcoal catalyst (695 mm., 27°). A Zerewitinoff determination indicated 1.3 active hydrogens and 1.7 additional mole-equivalents of methylmagnesium iodide reacted.

The above ether solution of neutral material was distilled to yield: (1) 2.3 g., b.p. 40–100° (2.7 mm.); (2) 4.9 g., b.p. 100–135° (0.7 mm.), mainly aldol I; (3) 16.6 g. (14%) of the glycol II, b.p. 135–137° (0.5 mm.); (4) 15.4 g. of neutral residue.

Method B. From 6-Formyl-5-propyl-2,4,6-triethyl-2-cyclohexen-1-ol (I).—To 36.9 g. (0.146 mole) of the aldol I was added dropwise, with stirring, during 30 minutes, a solution of 10.9 g. of 85% potassium hydroxide in 18 ml. of methanol and 6 ml. of water. After stirring for 2.5 hr., the mixture was treated with 160 ml. of water and separated into neutral and acid parts as in the condensation procedure described above. Distillation gave the following principal fractions: (1) 19.1 g. (46.8%) of lactone III, b.p. 154–160° (0.55 mm.), $n^{25}\text{D}$ 1.4755; (2) 1.5 g. of acid residue; (3) 6.5 g., b.p. 129–140° (0.56 mm.), $n^{25}\text{D}$ 1.4873, mainly recovered aldol; (4) 6.7 g. neutral residue. Hall and Tuerck[5] reported a similar experiment in which they employed sodium hydroxide and reported a 47.5% yield of III, b.p. 162–163° (3 mm.), $n^{20}\text{D}$ 1.4781.

Influence of Reaction Conditions on the Self-condensation of 2-Ethyl-2-hexenal.—A study was made of the effect of reaction conditions on the yields of the products I, II and III produced from the self-condensation of 2-ethyl-2-

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[20] Melting points are corrected; boiling points are uncorrected.

[21] Procedure of R. E. Kitson, A. N. Oemler and J. Mitchell, *Anal. Chem.*, **21**, 404 (1949).

[22] Reported b.p. 107–108° (3 mm.), $n^{20.5}\text{D}$ 1.4590; J. Lichtenberger and M. Naftali, *Bull. soc. chim. France*, [5] **4**, 325 (1937).

[23] C. Mannich and E. Kniss, *Ber.*, **74**, 1637 (1941), report m.p. 67–68°.

[24] In another run in which 344.2 g. of 2-ethyl-2-hexenal was used (reaction time 16 hr.), the yield of III was 208.2 g., 56.4%, b. p. 172–176° (1 mm.).

hexenal. Factors studied were reaction time, temperature, catalyst concentration and rate of addition of the catalyst. From these experiments optimum procedures were developed for the preparation of the products. Use of freshly purified and distilled 2-ethyl-2-hexenal, in a nitrogen atmosphere, gave the best yields.

The reaction time determined the yields of product obtained, as shown in Fig. 1 (temperature 25°; potassium hydroxide to aldehyde molar ratio, 0.57; catalyst addition time, *ca.* two minutes). Reaction times longer than 3 hr. gave only slightly increased yields of II and III under these conditions.[24]

A reaction temperature of *ca.* 25° was found to give less undistillable residue than did higher temperatures. Product yields also were higher, except in the case of glycol II, where maximum yield was obtained by permitting the reaction mixture to warm spontaneously to 80°. Using a reaction time of 1 hr., a potassium hydroxide–aldehyde molar ratio of 0.85 and a catalyst addition time of 12 minutes, the percentage yields of recovered 2-ethyl-2-hexenal, I, II and III, respectively, at three different temperatures were as follows: (13°) 37% 2-ethyl-2-hexenal, 42% I, 0% II, 3% III; (25°) 5% 2-ethyl-2-hexenal, 21% I, 13% II, 41% III; (40°) 1% 2-ethyl-2-hexenal, 3% I, 12% II, 46% III.

Employing a reaction time of 1 hr., temperature 25°, catalyst addition time 12 minutes, the yields of recovered 2-ethyl-2-hexenal, I, II and III, respectively, were found to vary with potassium hydroxide–aldehyde molar ratios as follows: ratio 0.85, 5% 2-ethyl-2-hexenal, 21% I, 13% II, 41% III; ratio 0.57, 13% 2-ethyl-2-hexenal, 33% I, 3% II, 22% III; ratio 0.29, 65% 2-ethyl-2-hexenal, 21% I, 0% II, 0.5% III.

The addition time of the catalyst when short (*ca.* 1–2 minutes) gave the maximum yields of I and III (see Fig. 1). A longer addition time was required for the best yields of II; in the optimum procedure described above the time was 1.5 hr. (total reaction time, 3 hr.).

5-Propyl-2,4,6-triethyl-1,3,7-heptanetriol (V).—A solution of 28.7 g. (0.106 mole) of the lactone III in 130 ml. of dry ether was added dropwise, with stirring, during 140 minutes to a solution of 4.9 g. (0.129 mole) of lithium aluminum hydride in 200 ml. of ether.[25] The rate of addition of the lactone was adjusted so as to produce gentle refluxing. After addition of the lactone was complete, refluxing by heating was continued for an additional 20 minutes; first 10 ml. of water and then 160 ml. of 10% sulfuric acid were added cautiously with stirring. The ether layer was separated and the aqueous part extracted twice with ether. The combined ether fractions were washed with water and dried. The ether was removed and the residue crystallized from 400 ml. of petroleum ether to yield 16.9 g. (58%) of V as white prisms, m.p. 96–97°; recrystallization did not raise the melting point; infrared bands at 2.77w, 2.97, 3.43, 6.85, 7.01m, 7.26m, 9.31, 9.87, 10.38m, 10.72w, 11.37w and 12.20w μ (chloroform). Repetition of the above experiment, using a 3-fold excess of lithium aluminum hydride and a reflux time of 22 hr., also gave a 58% yield of V.

Anal. Calcd. for $C_{16}H_{34}O_3$: C, 70.02; H, 12.49. Found: 70.22; H, 12.59.

The filtrate obtained above was distilled to yield 2.1 g., b.p. 123–166° (0.5 mm.); 5.7 g., b.p. 166–177° (0.4 mm.), (very viscous); and 1.1 g. of residue; these fractions were not further investigated.

The triol in a Zerewitinoff determination was found to have 3.1 active hydrogens and react with 0.1 mole-equivalent additional methylmagnesium iodide. It did not absorb hydrogen in acetic acid solvent at one atmosphere pressure in the presence of 5% palladium–charcoal catalyst.

3-Propyl-2,4,6-triethyl-5-hydroxy-1,7-heptanedioic Acid-1,5-lactone (IV).—To 37.9 g. (0.14 mole) of lactone III, suspended in a solution of 200 ml. of 10% sulfuric acid and 30 ml. of acetic acid, was added, with stirring during 30 minutes, 31.6 g. of powdered potassium permanganate, keeping the temperature at 25° by external cooling; stirring was then continued for 1.5 hr. Sufficient sodium bisulfite was added to dissolve the manganese dioxide and the mixture extracted with ether. The ether extracts were washed with water and 10% sodium hydroxide solution. The alkaline extracts were extracted several times with ether and then acidified with hydrochloric acid. The oil which separated was extracted with ether, the extract dried and the solution concentrated. All traces of volatile matter were finally removed by heating for 6 hr. at 100° (0.16 mm.) leaving 29.9 g. (75%) of very pure IV, an extremely viscous yellow liquid, n^{25}D 1.4762; molecularly distilled at bath temperature, 135–139° (2–4 μ), n^{25}D 1.4760. The acid could not be crystallized; infrared bands at 3.45, 5.77, 5.84, 6.85, 7.25, 7.9–9.1 and 9.83mμ (chloroform).

Anal. Calcd. for $C_{16}H_{28}O_4$: C, 67.57; H, 9.93; mol. wt., 284.4. Found: C, 67.26; H, 10.20; neut. equiv., 282 (by direct titration); sapn. equiv., 144.

The *p*-bromophenacyl ester derivative was obtained as white platelets from ethanol, m.p. 114.5–115.5°.

Anal. Calcd. for $C_{24}H_{33}O_5$: C, 59.88; H, 6.91. Found: C, 59.78; H, 7.07.

Disilver 3-Propyl-2,4,6-triethyl-5-hydroxy-1,7-heptanedioate.—The lactone acid IV (31.4 g., 0.1104 mole) was dissolved in 400 ml. of 1.075 *N* sodium hydroxide, the solution heated on the steam-bath for 1 hr. and then allowed to stand overnight at room temperature. After extracting with ether, the aqueous solution was diluted with one l. of ethanol, then neutralized by slowly adding, with vigorous stirring, 176 ml. of 1.109 *N* nitric acid (faint pink color to phenolphthalein). A solution of 40 g. of silver nitrate in 550 ml. of water was then added dropwise with stirring. The precipitate was rapidly filtered, washed thoroughly with water and dried in a vacuum desiccator over calcium chloride, keeping light absent; the yield of white powder was 56 g. (98%), m.p. 134–136° dec. Slowly, on standing in the dark, or rapidly, on exposure to light, the salt darkened and became brown.

Anal. Calcd. for $C_{16}H_{28}O_5Ag_2$: Ag, 41.80. Found: Ag, 41.80.

Dimethyl 3-Propyl-2,4,6-triethyl-5-hydroxy-1,7-heptanedioate (VIII).—To the above disilver salt (28.2 g., 0.0545 mole), suspended in 200 ml. of dry ether and 100 ml. of dry benzene, was added, dropwise, 68 g. of methyl iodide during 30 minutes (temperature 23–25°). Stirring was continued for 40 hr., the mixture filtered and the silver iodide precipitate washed thoroughly with ether. The filtrate was dried over magnesium sulfate and the ether removed to leave a yellow oil (pumped at 1 mm., 24 hr., 25°). The crude diester (14.8 g., 82%, n^{25}D 1.4572), could not be distilled without decomposition (see below); infrared bands at 2.93 m, 3.48, 5.83, 6.90, 7.0, 7.30m, 7.95, 8.45, 8.62, 10.5m, 10.65w and 12.6 m μ.

Anal. Calcd. for $C_{18}H_{34}O_5$: C, 65.42; H, 10.37; mol. wt., 330.45. Found: C, 65.31; H, 10.31; sapn. equiv., 164.

3-Propyl-2,4,6-triethyl-5-hydroxy-1,7-heptanedioic Acid-1,5-lactone Methyl Ester (VII). Method A. Demethanolation of Dimethyl 3-Propyl-2,4,6-triethyl-5-hydroxy-1,7-heptanedioate (VIII).—A 4.95-g. (0.015 mole) sample of the dimethyl ester VIII was heated in a small distilling flask at a bath temperature of 155–160° for 30 minutes. During this time 0.25 g. of methanol was collected, b.p. 65–67°; 3,5-dinitrobenzoate, m.p. 109–110°, alone and when mixed with an authentic sample. Distillation of the residue at 0.5 mm. gave fractions: (1) 0.3 g., b.p. 123–136°; (2) 3.2 g. (71% crude VII), b.p. 136–144°, n^{25}D 1.462–1.465 (65% b.p. 138–142°); (3) 1.0 g. residue and holdup. Redistillation of fraction 2 gave 2.1 g., b.p. 136–144° (0.30 mm.), n^{25}D 1.4640, used for analysis; infrared spectrum was identical with sample prepared by method B.

Anal. Calcd. for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13; mol. wt., 297.4. Found: C, 68.22; H, 9.98; sapn. equiv., 149.

Method B. From 5-Hydroxy-2,4,6-triethyl-1,7-heptanedioic Acid-1,5-lactone (IV) and Diazomethane.—A 13.4-g. (0.047 mole) sample of the lactone acid IV dissolved in 50 ml. of ether was treated with excess diazomethane for 1 hr. The volatile material was evaporated and the residue distilled at 1.5 mm. to yield (1) 1.0 g., b.p. 141–155° (1.5 mm.); (2) 9.8 g. (70%) of VII, b.p. 155–157° (1.5 mm.); and (3) 2.7 g. residue. Redistillation of fraction 2 gave an analytical sample, n^{25}D 1.4643; infrared bands at 3.42, 3.50, 5.75, 6.85, 6.92, 7.25, 7.87, 8.12, 8.35, 9.80, 10.1, 10.45m and 12.55m μ.

Anal. Calcd. for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13. Found: C, 68.31; H, 9.84.

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[25] R. F. Nystrom and W. G. Brown, THIS JOURNAL, **69**, 2548 (1947).

Method C. From Monosilver Salt of 3-Propyl-2,4,6-triethyl-5-hydroxy-1,7-heptanedioic Acid-1,5-lactone and Methyl Iodide.—The acid lactone IV, 11.7 g. (0.0412 mole), in 50 ml. of ethanol was exactly neutralized with 0.1 *N* sodium hydroxide and diluted to 200 ml. with water. A solution of 8.0 g. of silver nitrate in 100 ml. of water was added slowly with vigorous stirring. The white precipitate was filtered, washed with water and dried *in vacuo* in the dark; yield 12.9 g. (80%) of white powder, m.p. 100–110° dec., with sintering at 90°.

Anal. Calcd. for $C_{16}H_{26}O_4Ag$: Ag, 27.6. Found: Ag, 28.2.

To the above silver salt, 12.3 g. (0.315 mole), dissolved in 100 ml. of dry ether was added slowly, with stirring, 22 g. of methyl iodide (temperature 20–25°); stirring was continued for 24 hr. The silver iodide was filtered and washed with ether (7.3 g., 99%). Evaporation of the ether left 8.2 g. of an oil which was distilled to yield the following fractions at 0.4 mm.: (1) 1.9 g., b.p. 83–136°; (2) 4.0 g. (43%) of VII, b.p. 136–146° (80% b.p. 136–144°), n^{25}_D 1.4628; (3) 1.7 g. residue; fraction 2 infrared spectrum identical with sample prepared by method B.

5-Propyl-2,4,6-triethyl-2-heptenedioic Acid (X).—A solution of 14.0 g. (0.0468 mole) of ester VII and 1.2 g. (0.052 mole) of sodium metal in 50 ml. of dry methanol was allowed to stand at room temperature for 45 minutes and then refluxed 17 hr. Sodium hydroxide, 15 g., and 20 ml. of water were then added, and refluxing continued for 23 hr. The solution was diluted with 1500 ml. of water and chilled to 4°. A solution of 30 ml. of acetic acid in 200 ml. of water was then added dropwise, slowly, with vigorous stirring during 30 minutes; after seeding with pure X, stirring was continued at 2° for 4.5 hr. and the mixture then placed in the refrigerator overnight. The precipitate which formed was filtered and washed thoroughly with water; 11.1 g. (83.3%), m.p. 87–95°, white, crystalline powder. In another, similar, run a 78% yield of product, m.p. 90–100°, was obtained. A sample recrystallized from dilute ethanol melted at 99.5–100.5°, small prisms; λ_{max} 218 mμ, ϵ 16,300 (95% ethanol solvent, 10^{-4} *M*); infrared bands at 3.50, 5.85–5.95, 6.14, 6.87, 7.10, 7.28m, 7.80, 8.65w, 9.35w, 10.75 (broad) and 7.8–8.35 μ (broad) (chloroform).

Anal. Calcd. for $C_{16}H_{28}O_4$: C, 67.57; H, 9.93; mol. wt., 284.4. Found: C, 67.17; H, 9.92; neut. equiv., 141.5 (by direct titration).

The bis *p*-phenylphenacyl ester was prepared in the usual manner, recrystallized from ethanol, m.p. 114–115°.

Anal. Calcd. for $C_{44}H_{48}O_6$: C, 78.54; H, 7.19. Found: C, 78.3; H, 7.3.

The unsaturated acid X failed to react with bromine in carbon tetrachloride or with potassium permanganate in acetone. On quantitative hydrogenation of a small sample of the acid, however, 1.0 mole-equivalent of hydrogen was absorbed in 2 hr. (palladium–charcoal catalyst, one atmosphere, 25°, acetic acid solvent), after which time hydrogen uptake ceased. Removal of solvent and catalyst gave a gum which failed to crystallize. The dimethyl ester of X, prepared on a small scale from X and diazomethane, also absorbed one mole-equivalent of hydrogen under the above reaction conditions to yield a saturated dimethyl ester (carbonyl band at 5.81 μ; band at 6.1 μ absent); these esters, prepared on a micro scale, were not distilled. Treatment of the hydrogenated acid with aqueous potassium hydroxide at 160–175° or its dimethyl ester with sodium methoxide in refluxing methanol failed to lead to a crystalline product.

Ozonolysis of 5-Propyl-2,4,6-triethyl-2-heptenedioic Acid (X).—A 500-mg. (1.76 mmole) sample of the acid X in 15 ml. of carbon tetrachloride and 15 ml. of chloroform was ozonized at 0° using a 3-fold molar excess of ozone. The solution was then refluxed 24 hr. with a solution of 10 ml. of *N* sodium hydroxide and 10 ml. of 30% hydrogen peroxide. The solvent layer was separated; the aqueous layer was washed with chloroform and then distilled to remove neutral volatile material. The aqueous residue was acidified with *N* sulfuric acid and extracted with ether. The ether extracts were washed with water (washings added to aqueous part) and saturated sodium bicarbonate solution. The bicarbonate washings were washed with ether, acidified with sulfuric acid and the aqueous part extracted with ether. The ether extracts were washed with water (washings added to aqueous part) and dried. Evaporation of the ether gave 234.6 mg. of a viscous oil (neut. equiv. 130) which crystallized slowly from dilute alcohol to yield 73.5 mg. of crystals, m.p. 97–98°. Recrystallization gave short rectangular prisms, m.p. 98–99°, of racemic 2,4-diethyl-3-propylpentanedioic acid (XIa); when mixed with starting compound X, the melting point was 80–85°; infrared bands: 3.25–3.35 (shoulder), 3.46, 3.50, 3.80m, 5.85, 6.85, 7.10m, 7.25w, 7.85, 8.76w, 8.95w, 9.20w, 9.65, 10.75m (shoulder) and 11.10m μ; broad bands, 3–4, 7.5–8.5 and 10–12 μ (chloroform); this spectrum was practically identical with the uncrystallized oil, above.

Anal. Calcd. for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63; mol. wt., 230.32. Found: C, 62.5; H, 9.5; neut. equiv., 114 (by direct titration).

The combined aqueous portions from the above ozonolysis were made alkaline with sodium hydroxide and distilled to remove volatile neutral material. The aqueous residue was acidified with sulfuric acid and steam distilled to yield 2.15 meq. (1.22 mole-equivalents) of steam volatile water-soluble acidic material. This solution was refluxed with 3 g. of mercuric oxide for 2.5 hr. and distilled to yield 1.50 meq. of acid (0.65 meq. (37%) destroyed formic acid by difference).[3] The remaining distilled water-soluble acid was identified as propionic (85%) by conversion to its *p*-phenylphenacyl ester, m.p. 102–102.5° (melting point not depressed by admixture with authentic sample, m.p. 102–103°).

A 55-mg. sample of the low melting acid, XIa, was dissolved in a solution of 6 g. of potassium hydroxide (85% assay) in 6 ml. of water and heated, with shaking, in a steel bomb at 175–180° for 16 hr. Recovery of the acid in the usual manner gave 45 mg. of an oil which was crystallized from water to yield the crude high melting *meso* isomer, XIb, m.p. 140–145°; one recrystallization raised the melting point to 150–150.5° (rectangular prisms). When mixed with an authentic sample of *meso*-2,4-diethyl-3-propylpentanedioic acid,[26] the melting point was not depressed.

Permanganate Oxidation of 5-Propyl-2,4,6-triethyl-2-heptenedioic Acid. Preparation of Racemic 2,4-Diethyl-3-Propylpentanedioic Acid (XIa).—Permanganate oxidation of X was found to be a more efficient method of securing the racemic dibasic acid, XIa. To a solution of 1.205 g. (4.23 mmoles) of acid X in 40 ml. of saturated sodium bicarbonate solution was added, dropwise, with stirring, during 4.5 hr., a solution of 2.2 g. of potassium permanganate in 100 ml. of water (temperature, 0–5°). Stirring was continued at 0–25° for 17.5 hr. and the mixture warmed on the steam-bath for 30 minutes to remove the pink color. The manganese dioxide was then filtered and washed and the filtrate acidified with dilute hydrochloric acid. The aqueous suspension of the crude acid which separated as an oil was heated to 90° and treated with sufficient ethanol to give a clear solution. The solution on standing several days deposited 521 mg. (51%) of product, m.p. 92–95°, and on further standing 265 mg. of additional crystalline material, m.p. 75–90°; total crude yield, 81%. The crude product could be purified easily by slow crystallization from water or dilute ethanol (seeding); long, needle-like prisms, m.p. 94–96°.

Resolution of Racemic 2,4-Diethyl-3-propylpentanedioic Acid.—A solution of 1.527 g. (6.63 mmoles) of the racemic acid XIa was dissolved in a solution of 40 ml. of ethanol and 150 ml. of water and heated on the steam-bath. A solution of 2.62 g. (6.63 mmoles) of anhydrous brucine in 50 ml. of ethanol was then added slowly to the hot solution. The cooled solution was allowed to evaporate slowly at room temperature and during several days seven successive crops of crystals were removed by alternate filtration and evaporation of the filtrate; 1.70 g. of the crude *l*-acid brucine salt, m.p. 135–144°, and 2.1 g. of the crude *d*-acid brucine salt, m.p. 110–120°, were recovered by this procedure.

Recrystallization of the first crop of crystals, 1.18 g., m.p. 142–144°, from dilute ethanol gave 800 mg. of purified *l*-2,4-diethyl-3-propylpentanedioic acid monobrucine salt, m.p. 142–143°. *Anal.* Calcd. for $C_{35}H_{48}N_2O_8 \cdot 2H_2O$: C, 63.61; H, 7.93; N, 4.24. Found: C, 63.80; H, 7.77; N, 3.94. To the salt, 800 mg., in 50 ml. of hot 10% ethanol, was added dilute ammonium hydroxide dropwise until a slight excess was present. The solution was chilled and the brucine filtered (450 mg.). The filtrate was acidified

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[26] Authentic sample kindly supplied by Dr. Häusermann (ref. 6), m.p. 150–151°.

with dilute hydrochloric acid and the oily acid crystallized on standing to yield 216 mg. of partly active *l*-2,4-diethyl-3-propylpentanedioic acid, m.p. 93–94°, $[\alpha]^{20}\mathrm{D}$ −2.4° (*c* 10); 95% ethanol used as solvent for all rotations measured.

Fractional crystallization of the crude *d*-acid monobrucine salt gave 929 mg. of the purified salt as rectangular prisms, m.p. 114–121°. Regeneration of the *d*-acid from this sample in the manner used above for the *l*-acid gave 180 mg. of partly active *d*-2,4-diethyl-3-propylpentanedioic acid, m.p. 85–93°, $[\alpha]^{20}\mathrm{D}$ 5.4° (*c* 11), and a second crop, 71 mg., m.p. 86–91°, somewhat more active, $[\alpha]^{20}\mathrm{D}$ 11.0° (*c* 5).

Dehydration of 5,7-Dihydroxy-3-propyl-2,4,6-triethyl-1,5-heptanolactone.—A 41.9-g. (0.155 mole) sample of the lactone III was slowly distilled with a few crystals of iodine in a nitrogen atmosphere to yield 2.14 g. (0.119 mole) of water. The remaining residue was diluted with ether and washed with potassium hydroxide solution and water. After drying and distilling the ether, the following main fractions were obtained: (1) 3.5 g. of forerun, b.p. 60–134° (4.0 mm.); (2) 10.5 g. (27%) of crude C_{16}-unsaturated lactone mixture, b.p. 134–142° (4.0 mm.); (3) 1.0 g. of recovered III, b.p. 150–158° (1.3 mm.); and (4) 21 g. of residue. The crude lactone mixture was purified by extraction with *N* sodium hydroxide; b.p. 125–127° (0.5 mm.), $n^{25}\mathrm{D}$ 1.4728; infrared bands at 3.37, 3.47, 5.64, 5.76, 6.84, 7.25m, 8.38, 8.85m, 9.25m, 10.40m and 11.1w μ.

Anal. Calcd. for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.03; H, 11.31.

On quantitative hydrogenation the unsaturated lactone mixture absorbed 1.0 mole-equivalent of hydrogen (platinum catalyst, one atm., 25°). On quantitative bromination (bromine in acetic acid), 0.68 mole-equivalent of bromine was absorbed. A Zerewitinoff determination showed 0.19 active hydrogen and 1.92 additional moles of methylmagnesium iodide reacted. Other acidic catalysts (sulfuric and phosphoric acids, aluminum oxide at 400°) were used to dehydrate III, but iodine distillation gave the best results.

A 4.83 g. (0.0192 mole) sample of the lactones in chloroform was ozonized using a slight excess of ozone. After removing the chloroform, the ozonide solution was decomposed with water, first at room temperature, then at reflux temperature while air was aspirated through the mixture. The exit vapors were passed through 2,4-dinitrophenylhydrazine reagent to yield 1.26 g. of precipitate, m.p. 85–150°. Fractional crystallization of this material gave (1) 0.74 g., m.p. 112–125°, and (2) 0.28 g., m.p. 135–140°. Recrystallization of the first fraction gave orange needles, m.p. 116–117°; melting point not depressed when mixed with an authentic sample of 2-butanone 2,4-dinitrophenylhydrazone, m.p. 117°. Several recrystallizations of the smaller second fraction gave orange platelets, m.p. 155–157°, identified as acetaldehyde 2,4-dinitrophenylhydrazone (mixture melting point with authentic sample, m.p. 157°, undepressed). Water-soluble, steam-volatile acidic material was isolated; 0.0108 equivalent total. By refluxing with mercuric oxide, 0.0036 equivalent of this acid was destroyed (formic acid, 19%).[3] The remainder of the acid, 0.072 equivalent (37.5%), gave Duclaux numbers, 8.5, 7.5 and 6.8 and a *p*-phenylphenacyl ester derivative, m.p. 106–114°, which could not be recrystallized to constant melting point. Acetic acid is believed to be the main constituent of this portion, with a small amount of higher molecular weight acid(s). Of the 1.26 g. of 2,4-dinitrophenylhydrazone derivative which precipitated, it is estimated from the above fractionation data that 0.0034 equivalent (18%) of 2-butanone and 0.015 equivalent of acetaldehyde (7.5%) were formed. Other ozonolysis products isolated were water insoluble and included 1.1 g. of a steam-volatile neutral oil, 0.37 g. of a neutral non-steam-volatile gum and 0.41 g. of an oily non-steam-volatile acid; none of these fractions could be crystallized, and they were not investigated further.[27]

7-Acetoxy-5-hydroxy-3-propyl-2,4,6-triethyl-1,5-heptanolactone.—A solution of 70.7 g. (0.0262 mole) of the lactone III in 150 ml. of acetic anhydride was treated with one drop of concentrated sulfuric acid and allowed to stand 15 hr. at room temperature, then heated on the steam-bath for 8 hr. After standing overnight and then treating with 2 g. of barium hydroxide, the material was distilled *in vacuo* to remove acetic acid and acetic anhydride. The residue was then filtered and the filtrate distilled twice to yield 63 g. (77%) of the colorless acetate, b.p. 158–162° (0.5 mm.), $n^{25}\mathrm{D}$ 1.4662. By slowly distilling the acetate through a glass tube packed with glass wool (450°), low yields (10–20%) of unsaturated lactone were obtained.

Anal. Calcd. for $C_{18}H_{32}O_4$: C, 69.19; H, 10.33. Found: C, 69.57; H, 10.65.

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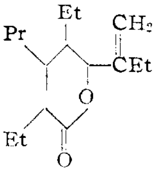
(27) The above data suggest the unsaturated lactone mixture to consist mainly of the isomers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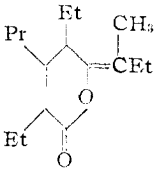
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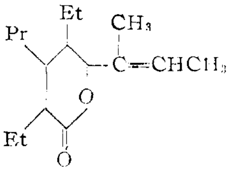
XIX

NEW BRUNSWICK, N. J.

[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Steric Effects in Hydrolysis of Hindered Amides and Nitriles[1]

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The relative extent of alkaline hydrolysis in ethylene glycol at 190–192° of seven hindered aliphatic amides has been determined. The results are reasonably well correlated by the Rule of Six. Alkaline hydrolysis of hindered aromatic amides leads to the formation of nitriles. The acidic hydrolysis of hindered aliphatic nitriles to amides and the conversion of these amides to acids by sulfuric acid–sodium nitrite treatment is described.

Perhaps the most inclusive study of steric hindrance to carbonyl addition reactions in the aliphatic series is that involving the acid-catalyzed esterification. In this work the effect of structure on the rate of esterification with methanol of 26 saturated aliphatic acids was reported and discussed in terms of the Rule of Six and other variables.[5] However, the rates of esterification of highly sterically hindered acids could not be measured because the side reaction between the catalyst, hydrogen chloride and methanol became too important a factor when longer times and higher temperatures were needed for esterification. For example, diisopropylacetic acid esterified too slowly to measure under the general conditions used for the other acids. Accord-

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(5) K. L. Loening, A. B. Garrett and M. S. Newman, THIS JOURNAL, **74**, 3929 (1952).