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REFERENCES

1. Melnick, D., F. H. Luckman and G. M. Gooding, JAOCS *35,* 271–277 (1958).
2. Keane, K. W., G. A. Jacobson and C. H. Krieger, J. Nutr. *68,* 57–74 (1959).
3. Rice, E. E., C. E. Poling, P. E. Mone and W. D. Warner, JAOCS *37,* 607–613 (1960).
4. Kaunitz, H., C. A. Slanetz, R. C. Johnson, H. B. Knight, R. E. Koos and D. Swern, JAOCS *36,* 611–615 (1959).
5. Crampton, E. W., R. H. Common, F. A. Farmer, A. F. Wells and D. Crawford, J. Nutr. *49,* 333–346 (1953).
6. Perkins, E. G., and F. A. Kummerow, J. Nutr. *68,* 101–108 (1959).
7. Peacock, P. R., and S. Beck, Acta. Unio. Intern. Contra. Cancrum 7, 612–615 (1951).
8. Perkins, E. G., and F. A. Kummerow, JAOCS *36,* 371–375 (1959).
9. Endres, J. G., V. R. Bhalerao and F. A. Kummerow, JAOCS *39,* 159–162 (1962).
10. Ota, Shizuyuki, Naoki Iwata, Akira Mukai and Hitoshi Enei, J. Japan Oil Chem. Soc. *12,* 403–409 (1963).
11. Chang, S. S., JAOCS *38,* 669–671 (1961).
12. Schlenk, H., and J. L. Gellerman, Anal. Chem. *32,* 1412–1414 (1960).
13. Kritchevsky, D., and Shirley A. Tepper, paper reported at the 145th National Meeting of ACS, New York (1963).

Alkaline Cleavage of Hydroxy Unsaturated Fatty Acids.

I. Ricinoleic Acid and Lesquerolic Acid

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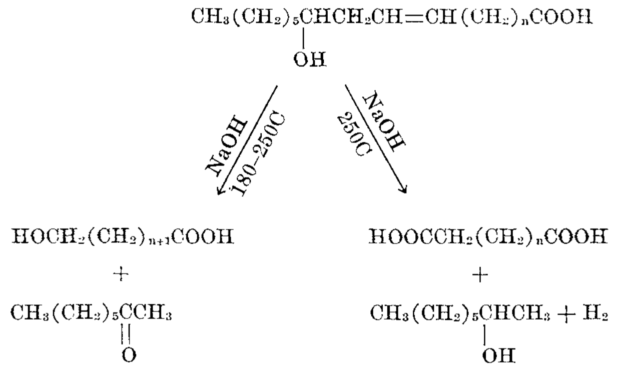
Abstract

The effects of temperature and media on the fusion of ricinoleic and lesquerolic acid derivatives with concentrated aqueous alkali were examined. Improved yields of ω-hydroxy acids were obtained by use of excess 2-octanol. The effect of excess 2-octanol is discussed in relation to a recently proposed reaction mechanism.

Introduction

HIGH TEMPERATURE (above 250C) alkaline fusion of derivatives of ricinoleic acid, 12-hydroxy-*cis*-9-octadecenoic acid, is a commercial method for manufacturing sebacic acid in high yield (1–9). Lower temperature (180–200C) alkaline fusion produces 10-hydroxydecanoic acid (1,5,9–12), but the yield is smaller than for sebacic acid. Analogous compounds are produced from lesquerolic acid, 14-hydroxy-*cis*-11-eicosenoic acid, which is the major fatty acid component of some *Lesquerella* seed oils (13,14). The high temperature alkaline fusion gives dodecanedioic acid (15). The low temperature reaction, which has not been reported previously, yields 12-hydroxydodecanoic acid. The following equations summarize the reactions:



$$CH_3(CH_2)_5\underset{OH}{CH}CH_2CH{=}CH(CH_2)_nCOOH$$

$$\xrightarrow{\text{NaOH, 180–250C}} HOCH_2(CH_2)_{n+1}COOH + CH_3(CH_2)_5\underset{O}{\overset{}{C}}CH_3$$

$$\xrightarrow{\text{NaOH, 250C}} HOOCCH_2(CH_2)_nCOOH + CH_3(CH_2)_5\underset{OH}{CH}CH_3 + H_2$$

n = 7 (ricinoleic acid)
9 (lesquerolic acid)

In this investigation the effects of reaction media, reaction times, and temperatures on the alkaline cleavage of ricinolec acid and lesquerolic acid were examined. A procedure for enhancing yields of ω-hydroxy acids is discussed in relation to possible reaction mechanisms (1,5,16,17).

Experimental

Materials

Methyl Ricinoleate. This ester was prepared by alcoholysis of castor oil followed by fractional distillation of the mixed methyl esters under reduced pressure to give a product of $> 98\%$ purity (18).

Methyl Lesquerolate. Lesquerella fendleri oil (13, 19) was alcoholized with methanolic sodium methoxide, and methyl lesquerolate ($\sim 95\%$ purity) was isolated by fractional distillation at 190–195C and 100–275 μ Hg.

2-Octanol. Eastman Kodak 66 (ketone-free) 2-octanol was used as obtained.

Analytical Techniques

Programmed-temperature gas-liquid chromatographic analyses were run on a model 720 F and M Gas Chromatograph. The column was a 3-ft, 0.25-in. stainless steel tube packed with 10% ECNSS-S (Applied Science Laboratories, Inc., State College, Penn.) on 100–120 mesh Gas Chrom P.

Procedures for Alkaline Fusion of Hydroxy Unsaturated Acids

A. Preparation of Sebacic Acid by High Temperature Alkaline Cleavage of Ricinoleic Acid. A one-liter nickel resin kettle and top were fitted with a sealed steel stirrer, heated dropping funnel, and a condenser for collection of volatile by-products. The reaction vessel was charged with 17.8 g of sodium hydroxide, 2.5 g of water, and 3.9 g of lead oxide as catalyst (8), and brought to 250 C with an electrically heated silicone oil bath. Methyl ricinoleate (78 g) was saponified with 20 g of sodium hydroxide in 12 ml of water. The soap was dissolved in 138 ml of hot water, and was

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TABLE I

Alkaline Fusion of Hydroxy Acids

Run No.	Starting materials				Temp, C	Time, hrs	Percent composition of crude reaction mixture[c]			
	Fatty acid,[a] moles	NaOH, moles	H_2O, moles	Diluent,[b] moles			Dibasic acid	ω-Hydroxy acid	Starting acid	Unknowns
1	0.10	0.22	15	0	202	2.3	37	23	40	....
2	0.10	0.85	0.5	0.38	184	6.6	67	19	....	14
3	0.40	3.40	2.0	1.50	183	11.5	11	80	....	9
4	0.10	0.22	13	0	201	2.1	22	20	58	....
5	0.20	1.70	1.5	0.13	192	7.9	53	34	13	....
6	0.10	0.85	0.5	0.82	191	24.8	0	0	98	2
7	0.10	0.85	0.5	0.19	187	10.5	21	63	11	5
8	0.10	0.85	0.5	0.38	183	12.7	14	66	13	7
9	0.10	0.85	0.5	0.57	186	22.5	23	64	5	8
10	0.10	1.70	0.5	0.38	183	12.6	12	66	9	13
11[d]	0.30	2.55	1.5	1.14	185	12.4	19	63	7	11

[a] Run 1: added as aqueous sodium ricinoleate; runs 2 and 3: added as methyl ricinoleate; run 4: added as aqueous potassium lesquerolate; runs 5 to 11: added as methyl lesquerolate.

[b] Run 2: 2-octanone; run 3: 2-octanol; run 5: p-cresol; run 6: glycerol; runs 7 to 11: 2-octanol.

[c] Analyzed as methyl esters by GLC. Not adjusted for nonvolatile products. Compositions reported on the basis of uncorrected areas of peaks.

[d] Blanketed with nitrogen.

added dropwise to the stirred hot caustic. Sodium ricinoleate was sufficiently soluble in hot water to permit uniform dropwise addition as a homogeneous aqueous solution. The reaction mixture was then stirred at 250C for 2 hr and the volatile components collected. The mixture remaining in the kettle was cooled to about 90C and dissolved in 90 ml hot water. After filtration of the hot caustic solution, an aliquot of the filtrate was withdrawn for analysis. The aliquot was acidified to pH 1 with 50% aqueous sulfuric acid and extracted with ether. The ether solution was dried with sodium sulfate, and the ether was removed on a rotary evaporator to yield sebacic acid. This was converted to esters in refluxing excess methanol with 0.5% concentrated sulfuric acid as catalyst. The resultant dimethyl sebacate was examined by gas-liquid chromatography (GLC). The GLC pattern showed only one large peak, and no methyl 10-hydroxydecanoate was present. The remaining caustic solution was acidified, and 35.2 g (70%) of >95% pure sebacic acid was obtained; mp 127–131C.

B. Preparation of Dodecanedioic Acid by High Temperature Alkaline Cleavage of Lesquerolic Acid. The equipment and procedures used were identical to those described above except that the less soluble sodium lesquerolate was added in ethanol, or the more soluble potassium lesquerolate was added in water. The yield of crude dodecanedioic acid obtained was 62%; mp 110–122C. One crystallization from ethyl acetate (14:1) gave a 48% yield of dodecanedioic acid; mp 125–128C. A portion of the crude free acid was converted to dimethyl dodecanedioate, and examination by GLC indicated that no methyl 12-hydroxydodecanoate was present in the sample.

C. Preparation of 10-Hydroxydecanoic Acid by Low Temperature Alkaline Cleavage of Ricinoleic Acid. In one experiment without an organic diluent (run 1), the same apparatus and procedures described above were used except a lower temperature was maintained. The quantities of reactants, reaction conditions, and analytical results are shown in Table I.

In all other runs, the apparatus was modified by replacing the take-off arrangement with a reflux condenser. A mixture of concentrated aqueous alkali and an organic diluent such as 2-octanone or 2-octanol was stirred and heated to the desired temperature in the reaction pot. Methyl ricinoleate was added dropwise and the reaction mixture was stirred for the desired time. The mixture was cooled to 90C, water was added, and an aliquot was withdrawn from the vigorously stirred system for analysis. For isolation of the 10-hydroxydecanoic acid in large quantity, the mixture was acidified to pH 1, and the lower aqueous layer was separated from the supernatant organic layer. The hot organic solution was washed with hot water, dried with sodium sulfate, and filtered. Commercial pentane was added, and a copious crop of 10-hydroxydecanoic acid crystals formed. The mixture was stored at —25C overnight, and the crystals were filtered, washed with commercial pentane, and dried. The ω-hydroxy acid was further purified by recrystallization from benzene after decolorization with charcoal. See runs 2 and 3 for quantities of reactants, reaction conditions, and analytical results.

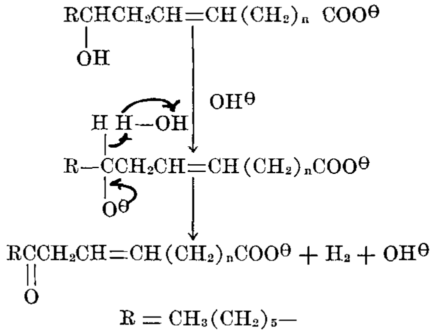
D. Preparation of 12-Hydroxydodecanoic Acid by Low Temperature Alkaline Cleavage of Lesquerolic Acid. In one experiment, the same apparatus and procedure described in (B) were used. The quantities of reactants, reaction conditions, and analytical results are shown in run 4. In all other runs the reaction was performed under reflux and worked up as described in (C). Methyl lesquerolate was added dropwise to a reaction system containing one of the following diluents: p-cresol, glycerol, or 2-octanol. The conditions and results are presented in the table.

Discussion

The nearly exclusive formation of dicarboxylic acids from the alkaline fusion of some hydroxy unsaturated acid derivatives at above 250C has been amply substantiated by numerous earlier investigators (1–9,15), and further confirmed by the results presented here. Manufacturing plants claim greater than 80% yields of sebacic acid from castor oil (3,6–8). Only a 21% yield of dodecanedioic acid from lesquerolic acid was previously reported (15), but by following procedure B, a 48% yield is obtained.

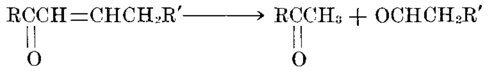
At lower temperature, the yields of dicarboxylic acids decrease and some ω-hydroxy acids form. We find, however, that the dicarboxylic-acid-to-ω-hydroxy-acid ratio favors the former acid even at temperatures as low as 183C (cf. runs 1,2,4, and 5). Hence, lowering the reaction temperature is not adequate to obtain high yields of ω-hydroxy acids. Furthermore, it has been shown that below 180C no appreciable cleavage occurs (5).

In a recent series of investigations, Weedon and co-workers (16,17,20–22) have extensively examined the reactions of fatty acid derivatives with concentrated alkali. The first step in their proposed mechanism for the alkaline cleavage of hydroxy acids is dehydrogenation to give a keto acid. In the case of unsaturated hydroxy acids, e.g., ricinoleic acid or lesquerolic acid, the dehydrogenation process which produces β,γ-unsaturated keto acids may be represented by the following scheme:



$R = CH_3(CH_2)_5—$
$n = 7$ or 9

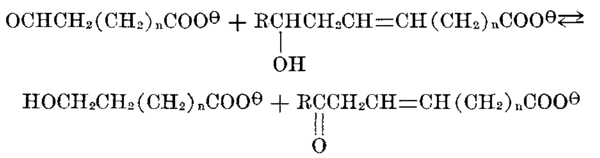
Ellis (23) has shown that in alkaline media β,γ-unsaturated carbonyl compounds readily undergo isomerization to α,β-unsaturated carbonyl compounds. Fission by a reaction of the "retro-aldol" type then should give a saturated ketone and an ω-aldehydo acid:



$$\underset{\underset{\mathrm{O}}{\|}}{\mathrm{RC}}\mathrm{CH{=}CHCH_2R'} \longrightarrow \underset{\underset{\mathrm{O}}{\|}}{\mathrm{RC}}\mathrm{CH_3} + \mathrm{OCHCH_2R'}$$

$R = —(CH_2)_5CH_3$
$R' = —(CH_2)_nCOO^{\ominus}$
$n = 7$, or 9

The isolation of ω-hydroxy acids and failures (16) in attempts to isolate ω-aldehydo acids can be attributed to two factors. Firstly, the aldehyde group may act as a hydrogen acceptor during the dehydrogenation of the unsaturated hydroxy acid:



$$\mathrm{OCHCH_2(CH_2)_nCOO^{\ominus}} + \mathrm{R}\underset{\underset{\mathrm{OH}}{|}}{\mathrm{C}}\mathrm{HCH_2CH{=}CH(CH_2)_nCOO^{\ominus}} \rightleftarrows$$
$$\mathrm{HOCH_2CH_2(CH_2)_nCOO^{\ominus}} + \mathrm{R}\underset{\underset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{CH_2CH{=}CH(CH_2)_nCOO^{\ominus}}$$

The preceding equation represents an equilibrium between a Meerwein-Ponndorf type reduction and an Oppenauer oxidation (16,24). Secondly, in the presence of strong alkali at elevated temperature, aldehydes are irreversibly converted to carboxylic acids with the evolution of hydrogen.

In view of the above scheme, another approach to increasing the formation of ω-hydroxy acid is selection of a suitable reaction medium. If formation of a short-lived, intermediate ω-aldehydo acid does occur, then the presence of excess secondary alcohol should cause the above equilibrium to shift to the right and thus enhance formation of a primary alcohol. The high yields of ω-hydroxy acids in runs 3 and 7 to 11 provide support for the mechanisms proposed by Hargreaves and Owen (5), and Dytham and Weedon (16). Also in accord with the above mechanism, the presence of excess ketone should cause the equilibrium to shift to the left and favor formation of ω-aldehydo acid. Since ω-aldehydo acids irreversibly convert to dicarboxylic acids, the presence of excess ketone should favor formation of dicarboxylic acid. This latter hypothesis is substantiated by the result in run 2 where the fusion is performed in the presence of excess 2-octanone.

Since an excess of a monohydroxy compound, 2-octanol, enhanced the formation of ω-hydroxy acid, an attempt was made to determine whether a polyhydroxy compound, glycerol (run 6), would further improve yields of ω-hydroxy acids. The observation that essentially no cleavage occurred during prolonged fusion with excess glycerol was surprising.

Many investigators (4,9,10,11) claim improvement in the alkaline fusion procedure by using an inert diluent such as cresol. In our experience, dicarboxylic acid (run 5) is the predominant product when p-cresol is added to a low temperature reaction. Using a purification procedure involving acetylation, repeated distillation, and saponification, Fray and coworkers (10,11) isolated pure 10-hydroxydecanoic acid in 36% yield following alkaline fusion of castor oil at 180–195C in the presence of excess tricresol. By comparison, approximately 50% of the theoretical yields of both 10-hydroxydecanoic acid and 12-hydroxydodecanoic acid 95% pure are readily isolated, after only one recrystallization in benzene, from the alkaline fusions of methyl ricinoleate and methyl lesquerolate respectively when excess 2-octanol is used. Also, the ω-hydroxy acids are readily precipitated from the 2-octanol solution by adding commercial pentane.

Ansell and Weedon (1) claim that an oxygen-free atmosphere is necessary for obtaining good yields of alkaline cleavage products and performed their experiments under a blanket of nitrogen. When excess 2-octanol was used with or without a nitrogen blanket (compare run 11 to runs 7–10) essentially the same yields of ω-hydroxy acid were obtained. Perhaps oxygen is adequately excluded by the refluxing 2-octanol vapors.

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R. E. Knowles and A. R. Gramps prepared the methyl ricinoleate and methyl lesquerolate.

REFERENCES

1. Ansell, M. F., and B. C. L. Weedon, Ind. Chemist 70–73 (1964).
2. Bourgeois, Y., U. S. 2,935,530 (May 3, 1960).
3. Bruson, H. A., and L. W. Covert, U. S. 2,182,056 (Dec. 5, 1939).
4. Davis, G. D., and B. A. Dombrow, U. S. 2,318,762 (May 11, 1943).
5. Hargreaves, G. H., and L. N. Owen, J. Chem. Soc. 753–756 (1947).
6. Henkel and Cie., Brit. 698,154 (Oct. 7, 1953).
7. Houpt, A. G., U. S. 2,217,516 (Oct. 8, 1940).
8. Naughton, F. C., and P. C. Daidone, U. S. 2,851,491; 2,851,492; 2,851,493 (Sept. 9, 1958).
9. Société Organico, Brit. 675,434 (July 9, 1952).
10. Fray, G. I., R. H. Jaeger, E. D. Morgan, R. Robinson and A. D. B. Sloan, Tetrahedon *15*, 18–25 (1961).
11. Fray, G. I., R. H. Jaeger and E. D. Morgan, U. S. 3,084,178 (Apr. 2, 1963).
12. Houpt, A. G., U. S. 2,217,515 (Oct. 8, 1940); Brit. 534,321 (Mar. 4, 1941).
13. Knowles, R. E., K. W. Taylor, G. O. Kohler and L. A. Goldblatt, J. Agr. Food Chem. *12*, 390–392 (1964).
14. Smith, C. R., Jr., T. L. Wilson, T. K. Miwa, H. Zobel, R. L. Lohmar and I. A. Wolff, J. Org. Chem. *26*, 2903–2905 (1961).
15. Bagby, M. O., J. Org. Chem. *26*, 4735–4737 (1961).
16. Dytham, R. A., and B. C. L. Weedon, Tetrahedron *8*, 246–260 (1960).
17. Weedon, B. C. L., "Techniques of Organic Chemistry," A. Weissberger, ed., XI, pt. II, Interscience, New York, 1963, pp. 671–679.
18. Swern, D., and E. J. Jordan, Jr., Biochem. Prep. *2*, 104–105 (1952).
19. Diamond, M. J., R. E. Knowles, R. G. Binder and L. A. Goldblatt, JAOCS *41*, 430–433 (1964).
20. Ackman, R. G., P. Linstead, B. J. Wakefield and B. C. L. Weedon, Tetrahedron *8*, 221–238 (1960).
21. Ackman, R. G., R. A. Dytham, B. J. Wakefield and B. C. L. Weedon, Tetrahedon *8*, 239–245 (1960).
22. Dytham, R. A., and B. C. L. Weedon, Tetrahedron *9*, 246–253 (1960).
23. Ellis, G. W., J. Chem. Soc. 9–12 (1950).
24. Hargreaves, G. H., and L. N. Owen, J. Chem. Soc. 750–752 (1947).

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