Saturated Keto Esters from Lesquerolic, Dimorphecolic, and Densipolic Acids

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Abstract

The naturally occurring, unsaturated, hydroxy fatty esters, methyl lesquerolate (methyl 14-hydroxy-*cis*-11-eicosenoate), methyl dimorphecolate (methyl 9-hydroxy-*trans, trans*-10,12-octadecadienoate), and methyl densipolate (methyl 12-hydroxy-*cis, cis*-9,15-octadecadienoate) have been converted to the corresponding saturated keto esters by two routes. The unsaturated esters were subjected to a hydrogenation-dehydrogenation reaction in the presence of Raney nickel or their saturated derivatives were dehydrogenated by copper chromite catalysis. Yields of the keto esters are 65–82% in the nickel-catalyzed reactions, and 71–94% by copper chromite-catalyzed dehydrogenation. In the hydrogenation-dehydrogenation system the order of reactivity is: methyl lesquerolate > methyl dimorphecolate > methyl densipolate. Relationships between structure and reactivity of these compounds, methyl 12-hydroxystearate, and methyl ricinoleate are discussed.

Introduction

METHYL 12-KETOSTEARATE can be prepared in ca, 73% yield by Raney nickel-catalyzed hydrogenation-dehydrogenation of methyl ricinoleate (1), and in nearly quantitative yield by copper chromite-catalyzed dehydrogenation of methyl 12-hydroxystearate (2). We have now extended these reactions to methyl lesquerolate, methyl dimorphecolate, and methyl densipolate to determine the effects of structural differences on reactivity and yield. The influence of catalyst type and concentration, reaction scale, and atmosphere (hydrogen vs. nitrogen) was also investigated.

Experimental

Starting Materials

Methyl Lesquerolate. This ester (3,4) was prepared by sodium methoxide-catalyzed methanolysis (6) of *Lesquerella gordonii* seed oil. Distillation at 193–195C/.080 mm separated methyl lesquerolate from nonhydroxy esters, but not from a sterol impurity. The ester was saponified, and lesquerolic acid was separated from the sterol by low temperature crystallization in ether. The pure acid, mp 31.7–32.8C, was esterified in refluxing methanol-1% conc H_2SO_4. Distilled methyl lesquerolate which contained both sterol and nonhydroxy ester impurities was also used.

Methyl Dimorphecolate (5). Base-catalyzed methanolysis of *Dimorphotheca sinuata* seed oil gave mixed methyl esters. Methyl dimorphecolate was concentrated by repeated liquid-liquid extractions using 90% aqueous methanol-commercial pentane (6). Ultraviolet analysis (7) showed that the concentrate contained 93% methyl dimorphecolate.

Methyl Densipolate. This ester (8) was prepared by base-catalyzed alcoholysis of *Lesquerella densipila* seed oil. Distillation at 163–175C/.004 mm gave a fraction that contained methyl densipolate, methyl ricinoleate (9), and a sterol. The sterol was removed by crystallization from acetone at −50C. The filtrate contained 88% methyl densipolate and 12% methyl ricinoleate (GLC). This mixture was not purified further because both compounds should give the same product.

Methyl Ricinoleate. This ester was prepared by base-catalyzed alcoholysis of castor oil and purified by fractional distillation of the mixed methyl esters under reduced pressure (10).

Methyl 14-Hydroxyeicosanoate. Distilled methyl lesquerolate was hydrogenated at 3 atmospheres in methanol containing platinum oxide at 25–30C. The product was purified either by recrystallization from acetone at −20C (88% yield, mp 58.0–61.8C), or recrystallization from Skellysolve B (85% yield, mp 60.4–61.0). Reported mp 56–59C (3). Both products contained ca. 98% methyl 14-hydroxyeicosanoate (GLC).

Methyl 9-Hydroxystearate. Methyl dimorphecolate was hydrogenated, the product was distilled at 197C/.080 mm, and then recrystallized from Skellysolve F (11); mp 51.5–52.8C. Reported mp 49–51C (5). The product contained no impurities detectable by GLC.

Catalysts. The following catalysts were used: copper chromite (Cu-1106 P) (2), commercial Raney nickel (12), and W-4 Raney nickel (12).

Gas-Liquid Chromatography

Progress of the reactions was followed primarily by GLC. Instrumentation (1) and technique (12) were reported earlier. Stainless-steel columns (3-ft, ⅛-in. O.D.) containing 5% Carbowax 20 M on 60–80 mesh HMDS Chromosorb W, were used at 210–220C with 50 ml/min helium flow.

Reaction Procedures

Saturated hydroxy esters were dehydrogenated in the presence of copper chromite (2), and unsaturated hydroxy esters were converted to saturated ketones by Raney nickel catalysis (1) as previously reported. Methanol was used for all recrystallizations.

Results and Discussion

Dehydrogenation of the Hydroxy Fatty Esters

The dehydrogenation reactions were investigated first, because our earlier studies (1,2) had indicated that the keto esters were obtained in higher yield by dehydrogenation of the saturated hydroxy compounds than by Raney nickel-catalyzed hydrogenation-dehydrogenation of the unsaturated hydroxy compounds. Results are shown in Table I. Methyl 14-hydroxyeicosanoate (12 g) was dehydrogenated to methyl 14-ketoeicosanoate very rapidly; GLC showed reaction was 99% complete in 6 min at 238–260C. The IR spectrum and C-H analysis (Table I) of the product were consistent with the structure of methyl 14-ketoeicosanoate, a new compound. Methyl 9-hydroxystearate was dehydrogenated much more slowly than methyl 14-hydroxyeicosanoate, and re-

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TABLE I

Dehydrogenation of Hydroxy Fatty Esters to Keto Fatty Esters

Starting material					% Compounds (GLC)				
Compound	g	Copper chromite w %	Time, hr	Temp, C	Product	Starting material	By-product [a]	Yield,[b] %	Melting point, C
Me 14-hydroxyeicosanoate	12	1	0.35	238–262	100	0	0	94	54.8–55.0[c]
Me 9-hydroxystearate	9	1	0.62	245–269	80	20	0	....	....
		1	1.00	262–303	92	8	0	71	48.0–48.2
Me 12-hydroxystearate [d]	12	1	0.62	180–263	97	3	0	99	46.1–46.8
Me 14-hydroxyeicosanoate	131	3	2.70	240–299	86	1	13	60[e]	54.2–55.0
								(13)	54.4–54.7
Me 14-hydroxyeicosanoate	131	6	2.03	236–287	97	1	2	67[e]	54.9–55.1

[a] The by-product is probably a mixture of hydrogenolysis and dehydration products (GLC).

[b] The 99% yield was for unrecrystallized product. All other yields are for once-recrystallized products. The 13% yield was for material from the mother liquor.

[c] Calcd. for methyl 14-ketoeicosanoate, $C_{21}H_{40}O_3$:C, 74.06; H, 11.84. Found: C, 74.1; H, 11.9. The pure compound melted at 54.8–55.0C.

[d] This data was previously reported (2).

[e] In the recrystallization step, the products were not cooled below room temperature prior to filtration. The final products were ca. 99% pure (GLC).

quired an additional 1% catalyst to obtain a 92% conversion. The yield of the 9-keto compound compared to the 14-keto was significantly lower. The IR spectrum of this 9-keto compound was identical to authentic methyl 9-ketostearate (7); a mixed melting point showed no depression. The reactivity of methyl 12-hydroxystearate appears to be between that of the 14-hydroxy and 9-hydroxy compounds. These limited observations suggest that the position of the hydroxyl group may affect its reactivity in this system.

Methyl 14-hydroxyeicosanoate was also dehydrogenated on a 131-g scale using 3 and 6% catalysts (Table I). The 60% yield of product with 3% catalyst compared to the 94% yield with 1% catalyst (12-g scale) may have resulted from insufficient mixing during the large scale reaction. Product yield was lower with 6% than 1% catalyst, because the crude products were recrystallized differently (see footnote e, Table I). Because conversion to product was almost complete with 6% catalyst, a much higher yield of methyl 14-ketoeicosanoate could have been obtained by eliminating the recrystallization step. The purity of methyl 14-ketoeicosanoate from these experiments was 99% or greater (GLC).

Keto Esters from Unsaturated Hydroxy Esters

Hydrogen vs. Nitrogen. Conversion of methyl ricinoleate to methyl 12-ketostearate in a nitrogen atmosphere requires a minimum of 50 weight per cent Raney nickel, because the catalyst supplies the hydrogen for the reaction (1). It seemed possible that by using a hydrogen rather than nitrogen atmosphere, methyl ricinoleate might be converted to product more rapidly and completely, and the amount of Raney nickel required might be reduced. In run I (Table II) conducted in a nitrogen atmosphere, the product yield was 74%. When a hydrogen atmosphere was used (run 2A), the 60% methyl 12-ketostearate which formed initially was partially hydrogenated back to methyl 12-hydroxystearate. The concentration of these two compounds soon became almost equal. Formation of methyl 12-ketostearate was favored only by changing to a nitrogen atmosphere (run 2B). Because the use of hydrogen followed by nitrogen gave a lower yield of product than with nitrogen alone, runs 3–8 were conducted in nitrogen.

Results with Commercial Raney Nickel. In runs 3–5, commercial Raney nickel was used to convert the methyl esters of lesquerolic, dimorphecolic and densipolic acids to the corresponding saturated keto esters. Product yield from methyl lesquerolate was somewhat higher than from methyl ricinoleate. A mixed melting point of this methyl 14-ketoeicosanoate and methyl 14-ketoeicosanoate prepared by dehydrogenation showed no depression.

Methyl dimorphecolate is readily dehydrated to the conjugated triene by heat (6,14), and acidic catalysts (5). It also dehydrates during GLC analysis (13,15). The latter problem was eliminated by use of the trimethylsilyl ether of methyl dimorphecolate, which, unlike the hydroxy ester, is stable during analysis (13).

In an attempt to provide sufficient hydrogen to rapidly convert methyl dimorphecolate to product before extensive dehydration occurred, the weight ratio of Raney nickel to methyl dimorphecolate used was 2:1. Although this ratio of catalyst was more than adequate to saturate the one double bond of methyl ricinoleate, there was no certainty that it would be sufficient to saturate both double bonds of methyl dimorphecolate.

After methyl dimorphecolate and catalyst had been heated for only 17 min at 33 to 124C, analysis of the reaction mixture showed the absence of methyl dimorphecolate. It had thus reacted about as rapidly as methyl ricinoleate. This analysis also showed only 5% by-product was present. Apparently, the quick conversion of methyl dimorphecolate to more stable compounds at relatively low temperatures minimized by-product formation. The overall reaction (run 4, Table II), compared to runs 1 and 3, was slower and gave product (methyl 9-ketostearate) in lower yield. The infrared spectra of this 9-ketostearate and authentic methyl 9-ketostearate were identical; a mixed melting point was not depressed.

The reaction with methyl densipolate (run 5) differed from that with methyl dimorphecolate in several respects: 1) The overall reaction was much slower, by-product formation was higher, and product yield was much lower. 2) Under comparable conditions, methyl densipolate was hydrogenated much slower than methyl dimorphecolate (GLC). The conjugated *trans* bonds of methyl dimorphecolate must therefore be easier to hydrogenate than the nonconjugated *cis* bonds of methyl densipolate. Supporting this conclusion are the observations that methyl dimorphecolate was hydrogenated much faster than methyl densipolate in glacial acetic acid with PtO_2 (16); with a nickel catalyst, a similar conjugated system was hydrogenated much more readily than a nonconjugated system (17). 3) During the methyl densipolate conversion, an unexpected intermediate was detected by GLC. It contained no hydroxyl group (did not form a trifluoroacetate), its GLC peak eluted between methyl 12-ketostearate and methyl ricinoleate (Carbowax col-

TABLE II

Conversion of Unsaturated Hydroxy Fatty Esters to Saturated Keto Fatty Esters [a]

				% compounds (GLC)				
Run no.	Starting material	Time, hr	Temp, C	Product	Saturated hydroxy ester	Hydrogenolysis products	Yield,[b] %	Melting point, C
1	Me Ricinoleate N_2 atmp	1.70	126–205	93	3	4	74	46.0–46.5
2A	Me Ricinoleate H_2 atmp	0.17	131–145	60	35	5	....	....
		0.50	131–151	47	44	9	....	....
		0.28	147–155	47	44	9	....	....
2B	N_2 atmp	0.33	142–159	83	11	6	....	....
		0.72	153–205	91	0	9	66	46.0–46.1
3	Me Lesquerolate	2.33	133–192	94	1	5	82	54.1–54.6
4	Me Dimorphecolate	2.77	124–224	90	0	10	54	46.2–47.0
5	Me Densipolate	3.57	128–213	78	0	22	23	45.6–46.1
6	Me Dimorphecolate	2.43	122–200	94	0	6	73	47.1–47.5
7	Me Densipolate	2.50	124–192	94	2	4	65	46.5–46.9
8	Me Lesquerolate [c]	3.13	109–221	91	4	5	59	54.5–55.6

[a] Fifty g of methyl lesquerolate was used with 50 g moist commercial Raney nickel in run 8. In all other runs 12.0 g starting material was used with 24.0 g moist Raney nickel. Commercial Raney nickel was used in runs 1–5, W-4 Raney nickel in runs 6 and 7.

[b] Yields are for once-recrystallized products.

[c] The methyl lesquerolate content is ca. 92% by infrared analysis.

umn), and it slowly disappeared as the reaction progressed. The compound thus appeared to be methyl 12-keto-9(15)-octadecenoate. Its presence suggests that methyl 12-hydroxy-9(15)-octadecenoate not only undergoes hydrogenation followed by dehydrogenation, but concurrently undergoes dehydrogenation as well to give the ketomonoene. In the reactions of the other unsaturated hydroxy esters studied, hydrogenation seems to occur so much faster than dehydrogenation that only saturated hydroxy intermediates are dehydrogenated.

Results with W-4 Raney Nickel. We had previously shown that methyl ricinoleate was converted to methyl 12-ketostearate in higher yield by using W-4 rather than commercial Raney nickel (1). Methyl dimorphecolate and methyl densipolate were similarly converted to the corresponding ketostearates in much higher yield in the presence of W-4 (runs 6 and 7) than by use of commercial Raney nickel (runs 4 and 5). W-4 thus appears to be superior to the commercial catalyst for this hydrogenation-dehydrogenation reaction. The commercial catalyst, however, is superior to W-4 for dehydrognation of methyl 12-hydroxystearate (12).

Methyl lesquerolate was converted to methyl 14-ketoeicosanoate in lower yield on a 50-g scale (run 8) than on a 12-g scale (run 3). The lower yield in run 8 may have resulted from the use of a lower weight ratio of catalyst to starting material (1:1). In addition, impurities present in the methyl lesquerolate of run 8 may have decreased the activity of the nickel catalyst, causing by-products to form which were not detectable by GLC.

In summary, the method for converting the methyl esters of lesquerolic, dimorphecolic and densipolic acids to the corresponding saturated keto esters by separate hydrogenation and dehydrogenation steps gives high overall conversion at low catalyst concentrations. The keto esters are also obtained in good yields from the Raney nickel catalyzed hydrogenation-dehydrogenation reaction. This latter process is convenient because it is conducted at atmospheric pressure in a single operation.

ACKNOWLEDGMENT

Aid in the preparation of starting material provided by Gwen Piersee, R. E. Knowles and A. R. Gramps. Carbon-hydrogen analysis by G. Secor.

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[Received February 16, 1966]