Notes A department for short papers of immediate interest.

Lead Tetraacetate Oxidation of Some Glutaric Acids. Formation of γ-Lactones

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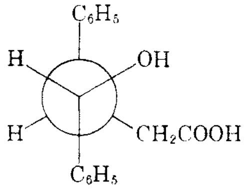
Recently, Grob, Ohta, Renk, and Weiss[1] reported an improved procedure for oxidative bisdecarboxylation of succinic acids to olefins.[2] Because of our interest in three-membered rings, we thought it would be interesting to apply this new method to glutaric acids with the hope that cyclopropanes would be formed. For a test system we prepared the two isomeric 2,3-diphenylglutaric acids, as both isomers can be obtained readily and the hoped for isomeric 1,2-diphenylcyclopropanes are both known.

Lead tetraacetate oxidation[1] of the high melting 2,3-diphenylglutaric acid occurred smoothly, but 1,2-diphenylcyclopropane was not obtained as a product. Instead, a compound (I), m.p. 110–111°, was obtained. The infrared spectrum of this material had a carbonyl band at 1787 cm.$^{-1}$, and the material dissolved slowly in hot, aqueous sodium hydroxide and was reprecipitated unchanged on acidification of the basic solution. This evidence suggests that monodecarboxylation has occurred with formation of a γ-lactone. The same product was obtained when the low melting 2,3-diphenylglutaric acid was oxidized in the same way.

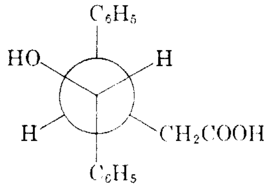
Monodecarboxylation could occur at either of two different positions and the resulting lactones could each exist in two isomeric forms. Of the four possible isomeric lactones two were eliminated as possible structures for I by reducing I with hydriodic acid and red phosphorus to 3,4-diphenylbutyric acid. This showed that decarboxylation occurred at the benzylic position rather than the primary one.

3,4-Diphenylbutyrolactone, m.p. 112–113°, has been reported previously.[3] For comparison we prepared the lactone by reduction of desylacetic acid with either sodium borohydride or sodium amalgam in aqueous solution and then lactonization of the resulting hydroxy acid by warming with dilute aqueous acid or by heating above its melting point. The lactone (II) obtained melts at 109–110°. However, a mixed melting point of I and II was 75–85°. Apparently, the two lactones are stereoisomers.

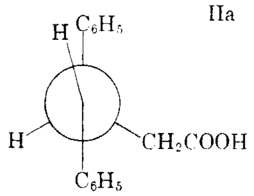
A tentative assignment of configuration may be made by comparing the action of acidifying the sodium salts of the hydroxy acids corresponding to the two lactones. The salt from I gives the lactone spontaneously, while the salt from II gives the hydroxy acid. This suggests that lactone I is the more stable lactone; this isomer would have the two bulky phenyl groups *trans* on the lactone ring. Lactone II would be the less stable *cis* isomer. In the ring-opened hydroxy acids, the stability would be reversed if it is assumed that the bulky phenyl groups are the major control in determining the preferrred conformation, *i.e.*, Ia and IIa corresponding to the lactones with IIa more stable than Ia. Additional evidence is presented by the decarboxylation reaction where both isomers of the diphenylglutaric acid give the same lactone. This means that decarboxylation and lactone formation are not concerted and it suggests that whatever intermediate is formed has sufficient life time to attain the most stable conformation III (radical or carbonium ion). This conformation, III, should lead to the *trans* lactone. Thus, the suggested assignment of configuration is lactone I *trans* and lactone II *cis*.



Ia



IIa



III

The infrared spectra of these two isomers is of some interest. That of the *cis* isomer shows two distinct carbonyl bands of about equal intensity at 1762 cm.$^{-1}$ and 1742 cm.$^{-1}$ and the *trans* isomer although showing a sharp band at 1787 cm.$^{-1}$ has a pronounced shoulder at 1753 cm.$^{-1}$ In both cases, there is a moderately strong band at about one-half the carbonyl frequency, *i.e.*, at 887 cm.$^{-1}$ (*cis*) and 885 cm.$^{-1}$ (*trans*). This possibly represents another example of Fermi

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[1] (a) C. A. Grob, M. Ohta, E. Renk, and A. Weiss, *Helv. Chim. Acta,* **41,** 1191 (1958); (b) C. A. Grob, M. Ohta, and A. Weiss, *Ang. Chem.,* 343 (1958).

[2] (a) W. von E. Doering, M. Farber, and A. Sayigh, *J. Am. Chem. Soc.,* **74,** 4370 (1952); (b) W. von E. Doering and M. Finkelstein, *J. Org. Chem.,* **23,** 141 (1958).

[3] F. R. Japp and G. D. Lander, *J. Chem. Soc.,* **71,** 154 (1897).

resonance similar to that described by Yates and Williams.[4]

Formation of a lactone in good yield in this decarboxylation reaction prompted us to try lead tetraacetate oxidation of two other five-carbon dibasic acids which happened to be available. One of these, glutaric acid, was inert under the conditions used and no butyrolactone was obtained. The other, camphoric acid, decarboxylated smoothly to give crude camphytolactone in 70% yield. This lactone was not purified as such, but was converted to the corresponding hydroxy acid which was readily purified and identified. It should be noted that decarboxylation occurred at the tertiary position in preference to the secondary.

These results are in accord with those reported by Mosher and Kehr[5] for the decomposition of lead IV salts of monocarboxylic acids in the presence of an excess of the acid. That work indicated that the ease of decomposition (decarboxylation) is in the order III>II>I. Although the product mixtures were complex, esters were formed, but usually in low yield. The high yields of lactones in the present work is quite possibly due to the proximity of the second carboxyl group in the same chain.

Although we have not explored the method appreciably, it appears to be a useful method for making some types of γ-lactones (those having tertiary or benzylic positions for the acid group to lactonize with), especially as many methods are available for preparing the requisite glutaric acids.

EXPERIMENTAL[6]

2,3-Diphenylglutaric acid. The high melting isomer was prepared essentially as described by Badger, Campbell and Cook,[7] m.p. 225–227° (lit.,[7] m.p. 230–231°). This isomer was converted to the anhydride,[7] m.p. 124–126° (lit.,[7] m.p. 125–126°), and subsequently to the low melting isomeric glutaric acid, m.p. 207–211° (lit.,[8] m.p. 208–210°), by the method of Avery and Maclay.[8]

Lead tetraacetate oxidation of 2,3-diphenylglutaric acid. The procedure is essentially the same as that given in an example by Grob, Ohta, Renk, and Weiss.[1a]

A. A mixture of high melting 2,3-diphenylglutaric acid (3.0 g., 0.01 mole), pyridine (1.6 ml., 0.02 mole), lead tetraacetate (4.7 g., 0.01 mole; contained a trace of acetic acid) and benzene (15 ml.) was stirred under nitrogen. On warming, a vigorous reaction with gas evolution began when the bath temperature reached about 50°. When the reaction subsided (2–3 min.), the bath temperature was raised and the mixture was maintained at gentle reflux for about 1.5 hr. During the course of the reaction a white precipitate, lead acetate, formed. The mixture was cooled, decanted from the lead acetate, and the lead acetate was washed with a small amount of benzene. The combined reaction solution and wash was washed with 10 ml. portions of water, 2*N* sodium carbonate, and 2*N* hydrochloric acid, and then dried over sodium sulfate. Removal of the benzene left a thick, yellowish material which crystallized readily. This was recrystallized from 50% aqueous ethanol and the resulting white crystals, 1.8 g. (72%), melted at 107–109°. An analytical sample recrystallized from cyclohexane and then sublimed melted at 110–111°.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.47; H, 5.98.

The compound (I) dissolved slowly in hot, aqueous sodium hydroxide and was precipitated by acidification of the cooled basic solution. The infrared spectrum of I had a sharp band at 1787 cm.$^{-1}$ This evidence suggested that I is a lactone.

The carbon skeleton of I was established by reduction of I with hydriodic acid and red phosphorus. The procedure was the same as described for 2,4-diphenylbutyrolactone.[9] 3,4-Diphenylbutyric acid, m.p. 93–95° (recrystallized from cyclohexane and then sublimed) (lit.,[10] m.p. 95–96°), was obtained.

For comparison, 3,4-diphenylbutyrolactone was prepared from desylacetic acid in essentially quantitative yield by reduction with sodium borohydride or sodium amalgam in aqueous solution.[11] The immediate product appeared to be the hydroxy acid, but this was readily converted to the lactone by warming with dilute aqueous acid, or better, by heating slightly above the melting point (*ca.* 115°) for several minutes. The lactone (II) obtained and purified by recrystallization from cyclohexane melted at 109–110° (lit.,[3] m.p. 112–113°). A mixed melting point of I and II was 75–85°. The infrared spectrum of II has two bands of about equal intensity at 1762 cm.$^{-1}$ and 1742 cm.$^{-1}$, and in general, the infrared spectra of I and II are quite different.

B. Lead tetraacetate oxidation of the high melting 2,3-diphenylglutaric acid was repeated as in A but with acetonitrile as a solvent.[1a] In the workup, water and petroleum ether were added to the reaction mixture as described,[2a] but the product was insoluble in both phases. After separation of the product, it solidified and was then purified as in A to give 2.0 g. (80%) of the lactone, I. The infrared spectrum was identical with that for the lactone prepared in A.

C. Lead tetraacetate oxidation of the low melting 2,3-diphenylglutaric acid was carried out as in A. The product, 2.0 g. (80%) melted at 108–109° and its infrared spectrum was identical with that for the lactone prepared in A.

Lead tetraacetate oxidation of glutaric acid. Using the same procedure, A, described above did not result in the formation of any detectable amount of γ-butyrolactone from glutaric acid. Even while heating the reaction mixture at gentle reflux, gas evolution was negligible. During the workup with aqueous solutions a large amount of dark brown precipitate, probably lead dioxide, was formed. Apparently, oxidation did not occur.

Lead tetraacetate oxidation of camphoric acid. The same procedure, A, was applied to camphoric acid; the reaction went smoothly, gas evolution commencing with a bath temperature at about 55°. In one run, the gas evolved was measured; 80% of the theoretical amount of monodecar-

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[4] P. Yates and L. L. Williams, *J. Am. Chem. Soc.*, **80**, 5896 (1959).

[5] W. A. Mosher and C. L. Kehr, *J. Am. Chem. Soc.*, **75**, 3172 (1953).

[6] Melting points are not corrected. Infrared spectra were obtained from a Perkin-Elmer Infracord and a Baird Recording Infrared Spectrophotometer; the compounds were prepared as mulls in Nujol. The analysis was done by Micro-Tech Laboratories.

[7] G. M. Badger, J. E. Campbell, and J. W. Cook, *J. Chem. Soc.*, 1084 (1949).

[8] S. Avery and W. D. Maclay, *J. Am. Chem. Soc.*, **51**, 2833 (1929).

[9] F. Bergmann, H. E. Eschinazi, and D. Shapiro, *J. Am. Chem. Soc.*, **64**, 557 (1942).

[10] S. Ruhemann, *J. Chem. Soc.*, **97**, 457 (1910).

[11] The reported preparation of this lactone[3] used desyleneacetic acid and sodium amalagam. A limited amount of sodium amalgam gave a mixture of desyleneacetic acid, desylacetic acid, and lactone, while an excess gave only the lactone. It seems reasonable, therefore, that desylacetic acid is an intermediate and can be used directly to prepare the lactone.

boxylation was obtained. The crude product, a lactone (infrared C = O: 1748 cm.$^{-1}$), was obtained in 70% yield as a liquid which very slowly partially crystallized. By gas phase chromatography this product mixture consisted of a major component (>95%) and two or possibly three trace components. The lactone could be sublimed, but no satisfactory melting point could be obtained.[12] Saponification of the lactone, however, gave the readily purified hydroxy acid, m.p. 118–119° (recrystallized from water) lit.,[12] m.p. 118.5°).

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(12) The melting point range was persistently 5–10° below that reported for camphytolactone. Bicyclic compounds of this sort are notorious for their large cryoscopic constants and difficulty of purification. From a published report [W. A. Noyes and R. S. Potter, *J. Am. Chem. Soc.*, **34**, 1067 (1912)] this lactone is no exception.

The Reaction of Certain Acid-Sensitive Steroid Ketones with Ethanedithiol–Borontrifluoride

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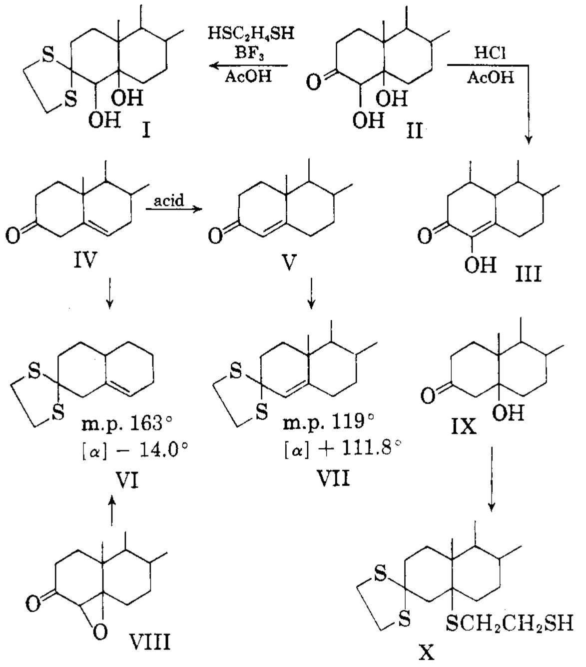
Recently we were successful in obtaining thioketal derivatives (I) from 4,5-dihydroxy-3-keto steroids (II) with ethanedithiol and boron trifluoride in acetic acid.[1] It was somewhat surprising that these strongly acid conditions, originated by Fieser,[2] gave derivative I in good yield, because the diolone II is easily dehydrated by acid to a diosphenol (III).[1] To check these conditions with another acid-sensitive functional arrangement, a thioketal derivative has been prepared from Δ^5-cholesten-3-one (IV), which is easily isomerized by acid to Δ^4-cholestenone (V). The derivative (VI) from the Δ^5-isomer (IV) is distinct from the derivative (VII) obtained[2] from the Δ^4-isomer (V). The negative specific rotation of VI is in accord with the structure assigned.[3]

Attempts to prepare thioketal derivatives of two other acid-sensitive functional arrangements under boron trifluoride catalysis have met with less success. 5-Hydroxycoprostan-3-one (IX) was treated with ethanedithiol and borontrifluoride in acetic acid, as a step in an attempted synthesis of the relatively rare monofunctional 5-hydroxy-steroids. Toward this end, 4,5β-oxidocoprostan-3-one (VIII) was treated with the acidic reagent. The yield of crystalline material from each compound was very slight. The small amount of crystalline product from the epoxide (VIII) proved to be the derivative (VI) from Δ^5-cholesten-3-one. The product from the ol-one (IX) was not fully characterized but has an analysis in agreement with structure X. Although formation of compounds VI and X from VIII and IX respectively is intriguing, further discussion of their formation seems unwarranted until they are obtained in significant yield.



EXPERIMENTAL

Reaction of Δ^5-cholesten-3-one (IV) *with ethanedithiol.* A solution of 1.0 g. of Δ^5-cholesten-3-one in 20 ml. of acetic acid was treated with 1 ml. of ethanedithiol and 1 ml. of boron trifluoride etherate. The solution was stirred for a few minutes and allowed to stand for 3 hr. The crystalline material which precipitated was filtered, washed with water, and recrystallized from ethanol. No additional crystalline material could be isolated from the reaction mixture. After recrystallization the yield of the thioketal (VI) was 0.26 g., m.p. 162–163°, $[\alpha]_D^{26}$ −14.0° (c, in chloroform, 0.895).

Anal. Calcd. for $C_{29}H_{48}S_2$: C, 75.60; H, 10.50. Found: C, 75.48; H, 10.34.

Reaction of 4,5β-oxidocoprostan-3-one (VIII) *with ethanedithiol.* A solution of 1 g. of 4,5β-oxidocoprostan-3-one[4] in 10 ml. of acetic acid was treated with 1 ml. of ethanedithiol and 1 ml. of boron trifluoride etherate. Only a small amount of crystalline material precipitated from the reaction mixture. After recrystallization from ethanol, this material melted at 161–162° and showed no depression with Δ^5-cholesten-3-one ethylene thioketal (VI).

Reaction of 5-hydroxycoprostan-3-one (IX) *with ethanedithiol.* To a solution of 0.38 g. of 5β-hydroxycoprostan-3-one in 5 ml. of acetic acid were added 0.5 ml. of ethanedithiol and 0.5 ml. of boron trifluoride etherate. The solution was stirred and allowed to stand for several hours. The small amount of crystalline material which separated was collected and washed with water. The acetic acid was allowed to evaporate slowly to leave a dark oil which resisted all attempts at crystallization. After the crystalline material

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(1) J. F. Eastham, G. B. Miles, and C. A. Krauth, *J. Am. Chem. Soc.*, **81**, 3114 (1959).

(2) L. F. Fieser, *J. Am. Chem. Soc.*, **76**, 1945 (1954).

(3) *Cf.* W. Klyne in E. A. Braude and F. C. Nachod, *Determination of Organic Structures by Physical Methods*, Academic Press Inc., New York, N. Y., 1955, p. 108 ff.

(4) P. A. Plattner, H. Heusser, and A. B. Kulkarni, *Helv. chim. Acta*, **31**, 1822 (1948).