ethanol or benzene. This is a direct parallel with the case of saturated fatty acids and esters, and suggests that the fatty acid components of glycerides determine their adsorptive properties.

The order of adsorbability of the mono-, di- and triglycerides depends upon the polarity of the solvent. In the polar solvent, ethanol, the least polar glyceride (triglyceride) is adsorbed most strongly. In the non-polar solvent, benzene, the most polar glyceride (monoglyceride)) is adsorbed most strongly. It should be emphasized that within a homologous glyceride series, increased molecular weight causes increased adsorption, irrespective of solvent.

The possible usefulness of displacement chromatography as a method of separation of glycerides was demonstrated by experiments with model mixtures. It appears that with the systems thus far used, saturated glycerides are more easily handled than are the unsaturated glycerides. Thus, application of these methods to separation of oils containing large proportions of tri-unsaturated glycerides will be limited by the fact that the latter are poorly adsorbed.

The method has been applied to a natural fat in one preliminary experiment. Definitive means of identification of mg. quantities of a series of closely related triglycerides do not exist, but segregation of component triglycerides was demonstrated by means of melting point. Thus beef tallow was displaced by 0.5% tristearin in benzene and the effluent cut into 14 arbitrary portions. The first five fractions were liquid at room temperature, suggesting that they were unsaturated triglycerides. The latter nine portions varied in melting point from 19 to 60° indicating fractionation of less unsaturated glycerides. The analysis was performed on 800 mg. of fat, took 12 hours, and showed the presence of several distinct components. No other method known to the authors could be applied to the analysis of such a small sample of glyceride to yield such information. It is hoped that further study of the method will reduce it to a more routine procedure, and that it can be applied to the characterization of natural glyceride mixtures.

MINNEAPOLIS 14, MINN.
AUSTIN, MINNESOTA

[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES]

Syntheses of DL-α-Lipoic Acid

BY QUENTIN F. SOPER, WALTER E. BUTING, JAMES E. COCHRAN, JR., AND ALBERT POHLAND

RECEIVED MARCH 20, 1954

DL-α-Lipoic acid has been synthesized and its structure confirmed by three new procedures. Tosylation of η-benzylmercapto-ε-hydroxycaprylic acid (IV) followed by replacement of the tosyloxy group by the benzylmercapto group yielded ε,η-dibenzylmercaptocaprylic acid. This substance was reduced and the resulting dimercaptan oxidized to DL-α-lipoic acid. Reduction of the precursors of IV, ethyl 6-oxo-7-octenoate or η-benzylmercapto-ε-oxocaprylic acid by means of hydrogen and hydrogen sulfide in the presence of a cobalt sulfide catalyst also gave the desired product. The third process involved a novel reduction of ε,ε,η-tribenzylmercaptocaprylic acid followed by oxidation yielding the cyclic disulfide of ε,η-dimercaptocaprylic acid. This type of reaction has been shown to yield cyclohexanethiol from cyclohexane dibenzylmercaptol in 18% yield.

DL-α-Lipoic acid has been reported to be synthesized in poor yields[1] as a rearrangement product. In the other reported instance in which this substance is described as 6-thioctic acid,[2] the yields have not been indicated.

It is the purpose of this paper to describe several other methods of synthesis and by these methods also show that DL-α-lipoic acid is the cyclic disulfide derived from ε,η-dimercaptocaprylic acid. The various routes which are followed are shown in the accompanying diagram

By following the synthetic route from I through VI it was hoped that the rearrangements[1,2] met in the other procedures could be avoided. This idea was based on the reports that the replacement of the *p*-toluenesulfonyl group proceeds without rearrangement[3] and that this group can be used as an intermediate in the synthesis of mercaptans.[4] The unsaturated ester I was easily converted to ethyl η-benzylmercapto-ε-oxocaprylate (II) in excellent yields. This ester could not be purified but was identified by oxidation to the sulfone and by hydrolysis to the keto acid III. This acid also yielded a sulfone after oxidation with hydrogen peroxide. Reduction of this keto acid yielded η-benzylmercapto-ε-hydroxycaprylic acid (IV). The *p*-toluenesulfonyl ester of this hydroxy acid was synthesized to be converted to ε,η-dibenzylmercaptocaprylic acid (V). This tosyl ester was never isolated in pure form but was converted directly into the acid V. From this substance DL-α-lipoic acid (VI) was obtained by using the ordinary sodium–liquid ammonia reduction procedure followed by oxidation with iodine to close the disulfide ring.

By using the procedure of Farlow, Lazier and Signaigo[5] ethyl 6-oxo-7-octenoate (I) or ethyl η-benzylmercapto-ε-oxocaprylate (II) in the presence of hydrogen, hydrogen sulfide and cobalt sulfide at about 200° and 2000 pounds pressure could be converted to DL-α-lipoic acid after working up in the usual manner. This product was contaminated with a polymeric substance from which it was difficult to separate crystalline material.

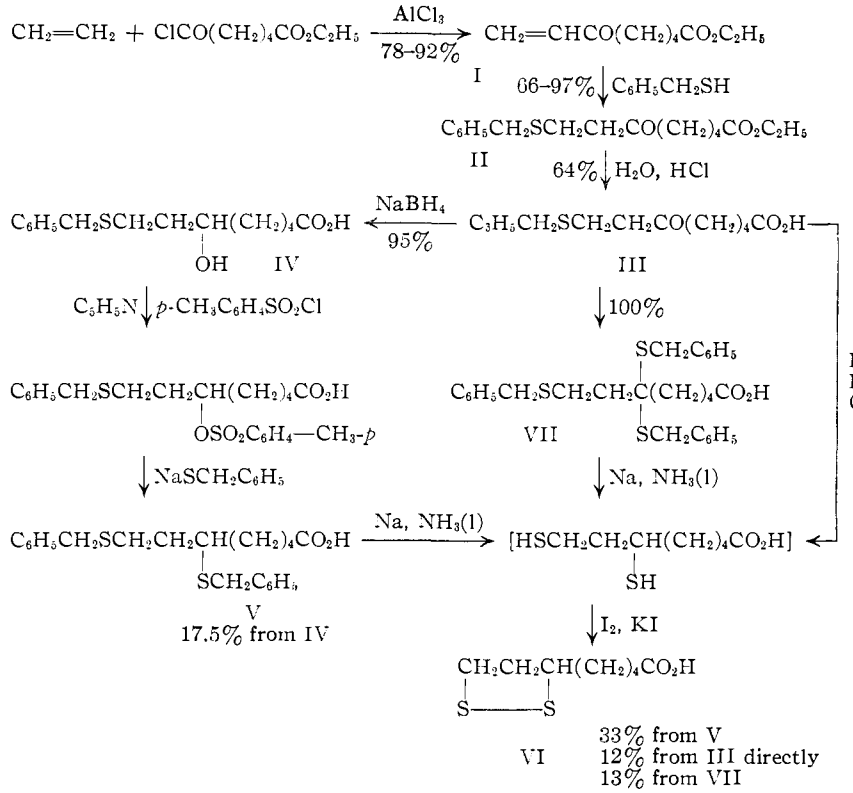
(1) C. S. Hornberger, Jr., R. F. Heitmiller, I. C. Gunsalus, G. H. F. Schnakenberg and L. J. Reed, THIS JOURNAL, **74**, 2382 (1952); **75**, 1273 (1953).

(2) M. W. Bullock, J. A. Brockman, Jr., E. L. Patterson, J. V. Pierce and E. L. R. Stokstad, *ibid.*, **74**, 3455 (1952); reported completely, *cf. ibid.*, **76**, 1828 (1954).

(3) H. Pines, A. Rudin and V. N. Ipatieff, *ibid.*, **74**, 4063 (1952).

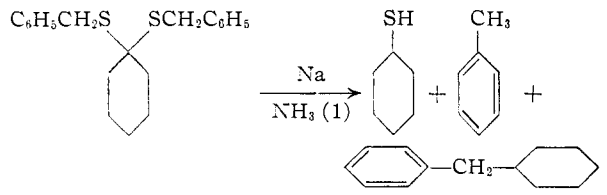
(4) J. H. Chapman and L. N. Owen, *J. Chem. Soc.*, 579 (1950).

(5) M. W. Farlow, W. A. Lazier and F. K. Signaigo, *Ind. Eng. Chem., Ind. Ed.*, **42**, 2547 (1950).



The third route involved the reduction of the dibenzylmercaptol VII of η-benzylmercapto-ε-oxocaprylic acid (III). By treatment of this tribenzylmercapto acid with sodium in liquid ammonia, both the sulfide and mercaptol groups were converted to the mercapto group.

This reaction also was demonstrated by the conversion of cyclohexanone dibenzylmercaptol to cyclohexanethiol in a yield of 18%. In this case an interesting by-product was found



The cyclohexylphenylmethane was obtained in about a 38% yield. This reaction is being investigated further.

Experimental

Ethyl 6-Oxo-7-octenoate (I).[2]—To a solution of 63.9 g. (0.33 mole) of ethyl δ-chloroformylvalerate[6] in 400 ml. of carbon tetrachloride, dried over anhydrous calcium chloride, was added 95.8 g. (0.72 mole) of anhydrous aluminum chloride. The temperature was maintained at 25°. The cooling bath was removed and ethylene was passed in with stirring. Within 0.5 hour the temperature rose to 55° and the mixture became gelatinous. After the temperature had begun to fall, the stirring and introduction of gas was continued for 1.5 hours. The mixture was poured on ice and the product extracted with chloroform. The solution was dried over anhydrous magnesium sulfate and distilled *in vacuo*. The yield of product distilling at about 126–136° (8 mm.), $n^{25}D$ 1.4500, varied between 47–55 g. (78–92%). This crude product contained some of the intermediate, ethyl η-chloro-ε-oxocaprylate, as indicated by a Beilstein test and analysis. Redistillation yielded a pure unsaturated ester, b.p. 123–123.5° (8 mm.), $n^{25}D$ 1.4493.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.76. Found: C, 65.21; H, 8.65.

The crude mixture polymerized when heated with dimethylaniline (to remove hydrogen chloride from the contaminating chloro ketone), when heated with aqueous base in an attempt to saponify the ester or sometimes by allowing the mixture to stand. The once-distilled product was used in the following reaction.

Ethyl η-Benzylmercapto-ε-oxocaprylate (II).—A solution of 36.7 g. (0.3 mole) of benzyl mercaptan and 54.4 g. (0.3 mole) of crude ethyl 6-oxo-7-octenoate in 200 ml. of thiophene-free benzene was stirred overnight with sufficient benzyltrimethylammonium hydroxide to maintain basicity (15–25 ml. of a 40% solution). The layers were separated and the benzene solution was washed with 150 ml. of water. After the solution had been dried over anhydrous magnesium sulfate, the benzene was removed under reduced pressure. The residue weighed 60–88 g. (66–97%). Since attempted distillation caused decomposition with evolution of benzyl mercaptan, the crude material was used in the following procedures.

Ethyl η-Benzenesulfonyl-ε-oxocaprylate.—This derivative was prepared from the crude ethyl η-benzylmercapto-ε-oxocaprylate in acetic acid by allowing it to stand 40 hours at room temperature with 30% hydrogen peroxide solution. The solvents were evaporated *in vacuo* and the residue recrystallized several times from ethanol as white needles, m.p. 89.5–90.5°.

Anal. Calcd. for $C_{17}H_{24}O_5S$: C, 59.98; H, 7.11; S, 9.42. Found: C, 59.53; H, 7.31; S, 9.27.

η-Benzylmercapto-ε-oxocaprylic Acid (III).—A solution of 418.4 g. (1.36 moles) of the ester II, 2 l. of acetic acid and 2 l. of 1:1 hydrochloric acid was refluxed 6 hours. The solution was diluted carefully with 5 l. of ice-water and the buff precipitate collected on a filter, m.p. 57–59°. This crude material was dissolved in 1 l. of benzene and the water removed. The organic solution was dried over anhydrous magnesium sulfate and filtered. By heating to boiling and adding petroleum ether (b.p. 60–70°) then cooling, a yield of 240.5 g. (64%) of silvery plates, m.p. 64–65°, resulted. A second crop of 10 g. was obtained but subsequent crops contained too much oily material for use.

Anal. Calcd. for $C_{15}H_{20}O_3S$: C, 64.25; H, 7.03; S, 11.44. Found: C, 64.49; H, 7.29; S, 11.01.

η-Benzylsulfonyl-ε-oxocaprylic Acid.—This sulfone was obtained by oxidation of the preceding sulfide with 30% hydrogen peroxide solution. The material crystallized from isopropyl alcohol, m.p. 143–146°.

Anal. Calcd. for $C_{15}H_{20}O_5S$: C, 57.65; H, 6.45; S, 10.26. Found: C, 57.99; H, 6.36; S, 10.21.

η-Benzylmercapto-ε-hydroxycaprylic Acid (IV).—A solution was prepared from 240.5 g. (0.86 mole) of the keto acid III in 1700 ml. of 5% sodium hydroxide solution. To this was added 34.4 g. of sodium borohydride. The temperature rose to about 45°. The solution was stirred for 2 hours and then was acidified. The product was extracted twice with ether. Evaporation of this ether solution left 230 g. of crude product, m.p. 58–60°. This was recrystallized for analysis from dilute methanol, m.p. 61–63°. A mixed melting point determination with the keto acid melted at 43–50°.

Anal. Calcd. for $C_{15}H_{22}O_3S$: C, 63.80; H, 7.86. Found: C, 63.91; H, 8.05.

(6) H. Bergs, C. Wittfeld and H. Frank, *Ber.*, **67B**, 1622 (1934).

ε,η-Dibenzylmercaptocaprylic Acid (V).—A mixture of 23.5 g. of the hydroxy acid IV, 50 ml. of dry pyridine and 19 g. of *p*-toluenesulfonyl chloride was stirred at 10–20° for 4 hours. The mixture was poured into water acidified with phosphoric acid. The acidic mixture was extracted with ether. The ether layer was washed twice with water, dried over anhydrous magnesium sulfate, and the solvent removed *in vacuo*. The oily residue could not be induced to crystallize nor form a solid sulfone with 30% hydrogen peroxide solution. The crude oily mixture weighed 26.1 g.

A solution of 25.5 g. of this oil, 8.0 g. of benzyl mercaptan and 41 ml. of 15% sodium hydroxide solution was refluxed overnight. The solution was cooled and acidified with phosphoric acid. The oil was then extracted twice with 150-ml. portions of ether. To the ether extract was added 100 ml. of water and sufficient iodoform reagent[7] to give a permanent brown color. This color was discharged by washing with sufficient 1% sodium thiosulfate solution. The acid was removed by extraction with two 100-ml. portions of 5% sodium hydroxide solution. The dibenzyl disulfide left in the ether layer weighed 5.6 g. and melted at 68–70°.

The acids were recovered by acidification with phosphoric acid, extraction with ether and evaporation of the extracts. The crude waxy mixture weighed 17.7 g. Recrystallization of this material from a mixture of benzene and Skelly B (this solvent is essentially *n*-hexane) gave 10.9 g. of an acid, m.p. 53–59°. Several more recrystallizations from the solvent mixture produced a material which melted at 57–59° and whose melting point was not depressed by mixing with the hydroxy acid IV.

From the filtrate of the first recrystallization there was obtained 5.5 g. of a substance by the addition of more Skelly B. This material melted at 63–65° and when mixed with hydroxy acid, the mixture melted at 50–57°. Recrystallizations of this material from the benzene–Skelly B mixture and subsequently dilute ethanol gave a compound whose analysis indicated it was still impure.

Anal. Calcd. for $C_{22}H_{28}O_2S_2$: C, 68.00; H, 7.26; S, 16.56. Found: C, 67.13, 68.31; H, 7.41, 7.46; S, 15.30, 15.97.

DL-α-Lipoic Acid (VI). Method A.—A mixture of 3.88 g. of this crude acid V in 500 ml. of liquid ammonia was treated with solid sodium until a permanent blue color in the solution resulted. This procedure required 2.1 g. of sodium. Ammonium chloride (0.9 g.) was added to discharge the color. The ammonia was allowed to distil off and 200 ml. of benzene was added. The solid residue was dissolved by adding 100 ml. of water. These solutions were shaken well and the organic layer separated. The acid was liberated from the aqueous layer by acidification with phosphoric acid and extraction with two 250-ml. portions of benzene. The benzene solution was treated with iodoform reagent until a permanent color was obtained (about 4 ml. was used). The color was discharged by washing with 1% sodium thiosulfate solution. Evaporation of the benzene solution after washing with water and drying over magnesium sulfate left 0.68 g. of a yellowish solid, m.p. 60.5–61.5°. This material was readily recrystallized from Skelly B, m.p. 62–63°, yield about 33%; biological activity, 100,000 units/mg.[8] It had the characteristic ultraviolet absorption peak of α-lipoic acid at 333 mμ.[9]

Method B.—A mixture of 28 g. of η-benzylmercapto-ε-oxocaprylic acid (III), 40 g. of sulfur, 100 ml. of benzene and a teaspoon of cobalt sulfide catalyst[5] was hydrogenated at 200° and about 2000 lb. for 4.5 hours. After the mixture had cooled, the catalyst was removed by filtration. The precipitate was washed several times with benzene and the filtrate separated. The benzene solution was evaporated to dryness *in vacuo* to remove hydrogen sulfide. The residue weighed 26.4 g. This material was redissolved in 300 ml. of ether and reduced with sodium in liquid ammonia as before. A further purification step was added in which the acidic material was extracted from the benzene solution with 5% sodium bicarbonate solution. The acid fraction yielded 13.6 g. of a yellow oil after liberation and working up. From this material there was obtained 2.5 g. of crude lipoic acid, m.p. 53–58°. This material was difficult to purify because of an oily impurity that contaminated each crystallization. A product melting at 61–62°, assaying 325,000 units/mg.,[8] was finally obtained.

Anal. Calcd. for $C_8H_{14}O_2S_2$: C, 46.57; H, 6.84; S, 31.08. Found: C, 47.10, 47.01; H, 7.04, 6.86; S, 30.33, 32.22.

A neutral fraction was obtained from the original benzene solution and was shown to be dibenzyl disulfide. The isolation of this product indicated that in the reduction, benzyl mercaptan was liberated and the reaction involved the addition of hydrogen sulfide to the α,β-unsaturated carbonyl system which had formed. Reduction of ethyl 6-oxo-7-octenoate (I) under these conditions followed by saponification gave lipoic acid, further demonstrating the validity of this assumption.

Method C. Ethyl ε,ε,η-Tribenzylmercaptocaprylate.—A mixture of 87.7 g. (0.28 mole) of crude ethyl η-benzylmercapto-ε-oxocaprylate, 73.5 g. (0.59 mole) of benzyl mercaptan and 0.5 g. of anhydrous zinc chloride was cooled in an ice-bath. Gaseous hydrogen chloride was passed through the mixture for about 15 minutes. The mixture was allowed to stand overnight then was poured on ice. The crude product was extracted with ether and the ether solution dried over anhydrous magnesium sulfate. Concentration of the solution *in vacuo* left 161.3 g. of crude mercaptol ester.

Anal. Calcd. for $C_{31}H_{38}O_2S_3$: C, 69.10; H, 7.11; S, 17.85. Found: C, 68.95; H, 7.10; S, 17.96.

ε,ε,η-Tribenzylmercaptocaprylic Acid (VII).—A mixture of 10.4 g. (0.02 mole) of the crude ester, 7.5 g. of sodium hydroxide, 50 ml. of water and 25 ml. of ethanol was refluxed for 3.5 hours. The mixture was diluted with 100 ml. of ice-water and extracted with ether. Three layers formed. The middle layer was undissolved sodium salt in the form of an orange oil. The two lower layers were separated and acidified with hydrochloric acid. This product was extracted with ether. After working up as usual the acid was obtained as an orange oil (7.4 g.) which could not be crystallized under a variety of circumstances. This mercaptol acid could be obtained directly from the keto acid III with comparable yields of product.

The S-benzylisothiuronium salt was prepared in the usual manner.[10] It melted at 101–103°.

Anal. Calcd. for $C_{37}H_{44}N_2O_2S_4$: C, 65.63; H, 6.55; N, 4.14; S, 18.94. Found: C, 65.76; H, 6.33; N, 4.31; S, 18.36.

DL-α-Lipoic Acid.—A well-stirred mixture of 18.1 g. (0.036 mole) of the preceding acid, 600 ml. of liquid ammonia and 300 ml. of dry ether was treated with sodium until the blue color persisted. About 8.0 g. of sodium was used. The color was discharged with 19 g. of ammonium chloride. The product was isolated as before. During these procedures and especially with the use of this method, a yellow, rubber-like polymer was formed as a by-product. The total yield of yellow acid, m.p. 56–59°, was 1.0 g. The material assayed 239,000 units/mg. and had the characteristic ultraviolet absorption.

Some lipoic acid could be recovered from the polymeric material. By treatment with ammonium hydroxide solution and evaporation to dryness a brown glass was obtained. A 2.9-g. sample (assaying 5000 units/mg.) was powdered and added to 300 ml. of liquid ammonia. The substance did not appear to dissolve. Sodium was added in portions until the blue color persisted for two hours. The lipoic acid was obtained in the usual manner. The yield of product, m.p. 59–60°, was 0.62 g., assay 308,000 units/mg., X-ray pattern was identical with that of previous samples.

Anal. Calcd. for $C_8H_{14}O_2S_2$: C, 46.57; H, 6.04; S, 31.08. Found: C, 47.10; H, 6.86; S, 30.66.

Lipoic acid also was obtained but with no improvement in yield by the oxidation of the sodium bicarbonate solution of the acid.

Cyclohexanethiol.—Cyclohexanone dibenzylmercaptol was prepared by the method of Hauptmann.[11] The prod-

(7) R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 139.

(8) L. J. Reed, I. C. Gunsalus, G. H. F. Schnakenberg, Q. F. Soper, H. E. Boaz, S. F. Kern and T. V. Parke, THIS JOURNAL, **75**, 1267 (1953). Variances in the biological activity of the crystalline preparations are due to the inability to reproduce biological assay results. This activity would vary mainly with the age of the organism and the level at which the assay was run. In each case the activity of the product corresponded with that of a standard sample.

(9) M. Calvin and J. A. Barltrop, *ibid.*, **74**, 6153 (1952).

(10) Reference 7, p. 159.

(11) H. Hauptmann and M. M. Campos, THIS JOURNAL, **72**, 1406 (1950).

uct, obtained in a 63.5% yield, boiled at 196° (0.15 mm.), $n^{25}D$ 1.6050.[12]

A mixture of 65.6 g. (0.2 mole) of this mercaptol, 500 ml. of liquid ammonia and 200 ml. of dry ether was stirred and treated with small pieces of sodium until a blue color persisted for one hour. The solution became a bright yellow with the addition of the first piece of sodium and gradually changed to a pastel red as more sodium was added. A total of 25 g. of sodium was added with excess being neutralized with 3.5 g. of ammonium chloride. After the ammonia had evaporated, the residue was treated cautiously with 250 ml. of ether and 150 ml. of water. The layers were separated after all of the solid had dissolved and the ether layer extracted with 10% sodium hydroxide solution. The combined aqueous layers were extracted with ether. The ether layer was dried over anhydrous magnesium sulfate and distilled. From this first distillation, 16.3 g. of toluene was recovered as well as three other fractions. Redistillation of these fractions yielded 2.6 g. of crude cyclohexanethiol, b.p. 155–165°, $n^{25}D$ 1.4738 and 11.0 g. of cyclohexylphenylmethane, b.p. 250–255°, 113–115° (5 mm.), $n^{25}D$ 1.5210, d^{25}_4 0.9330. The values of these physical properties vary somewhat in the literature.[13] Oxidation of this material with alkaline permanganate yielded benzoic acid.

Anal. Calcd. for $C_{13}H_{18}$: C, 89.59; H, 10.41; MR_D, 56.45. Found: C, 89.48; H, 10.51; MR_D, 56.85.

The aqueous layer was acidified with 20% sulfuric acid. Considerable gas evolution was noted. Distillation of the liberated oil yielded 1.5 g. of the mercaptan, $n^{25}D$ 1.4747. The total yield of mercaptan amounted to about 18% of the theoretically possible amount. Cyclohexyl 2,4-dinitrophenyl sulfide was prepared from this compound in good yields, m.p. 145–146°. This melting point was not depressed when the substance was mixed with the sulfide prepared in the usual manner[14] from authentic cyclohexanethiol.[15]

Acknowledgment.—We are indebted to Messrs. W. L. Brown, H. L. Hunter and G. M. Maciak for the microanalyses reported and to Dolores M. Rolandson for technical assistance.

(12) This material was prepared by H. R. Sullivan.

(13) *Cf.* R. C. Huston and K. Goodemoot, THIS JOURNAL, **56**, 2433 (1934); N. G. Sidorova and I. P. Tsukervanik, *J. Gen. Chem. (U.S.S.R.)*, **10**, 2073 (1940).

(14) R. W. Bost, J. O. Turner and M. W. Conn, THIS JOURNAL, **55**, 4956 (1933).

(15) J. Staněk, *Chem. Listy*, **46**, 383 (1952); *C. A.*, **47**, 4296*i* (1953).

INDIANAPOLIS, INDIANA

CONTRIBUTION FROM THE LABORATORY OF PHARMACEUTICAL CHEMISTRY, UNIVERSITY OF KANSAS SCHOOL OF PHARMACY]

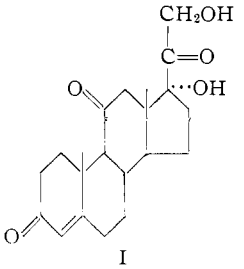
Steroidal Hormone Relatives. II.[1] The Synthesis of 4-(*m*-Carboxyphenyl)-3-(*p*-hydroxyphenyl)-2-hexanone

BY J. H. BURCKHALTER, PETER H. JACKSON, JOSEPH SAM AND HANS R. MEYER

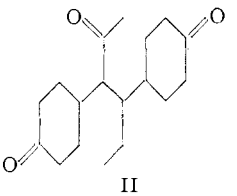
RECEIVED OCTOBER 10, 1953

4-(*m*-Carboxyphenyl)-3-(*p*-hydroxyphenyl)-2-hexanone (IIIa) and 4-(*m*-acetoxyacetylphenyl)-3-(*p*-methoxyphenyl)-2-hexanone (IV), designed as intermediates in the synthesis of open chain models of cortisone (*e.g.*, V), have been prepared in good yields. Attempts to reduce the benzene rings of IIIa to alicyclic rings have not yet been successful, as in the preparation of II. Compound IIIa showed considerable estrogenic effect, while IV lacked the effects of cortisone.

A previous report describes the synthesis of 3,4-bis-(4-oxocyclohexyl)-2-hexanone (II),[1] which is an open chain triketone holding carbonyl groups in positions corresponding to 3 and 11 of cortisone (I). We wish now to describe the preparation of



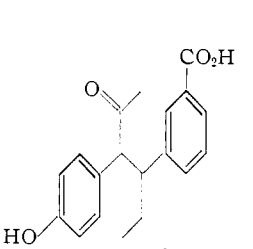
I



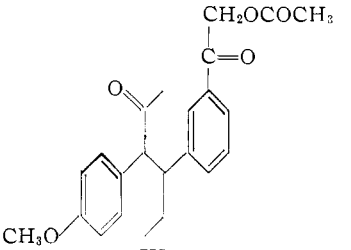
II

other open model compounds (III and IV) which may be considered to bear a closer structural relationship to the hormones of the adrenal cortex and which might serve as intermediates leading to V.

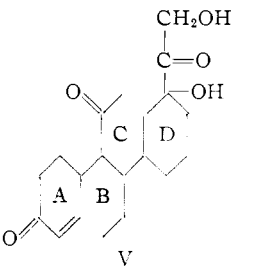
It can be seen that these structures contain a six-membered ring in a position corresponding to the five-membered D ring of the steroids. The observation that the androgenic effect of 17α-methyltestosterone is doubled by an enlargement of ring D[2] offers encouragement to the incorporation of a 6-membered D ring in the cortical steroids. Further, it is apparent that proposed compound V would not possess angular methyl groups. That the C-19 methyl between rings A and B of testosterone, progesterone and desoxycorticosterone can be omitted without loss of the specific activities of these hormones has recently been demonstrated.[3,4] An



IIIa, 236°
b, 160°



IV



V

(1) Paper I: J. H. Burckhalter and J. Sam, THIS JOURNAL, **74**, 187 (1952).

(2) L. Ruzicka, N. Wahba, P. T. Herzig and H. Heusser, *Chem. Ber.*, **85**, 491 (1952).

(3) A. J. Birch and H. Smith, *J. Chem. Soc.*, 1882 (1951).

(4) (a) L. Miramontes, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **73**, 3540 (1951); (b) A. Sandoval, L. Miramontes, G. Rosenkranz, C. Djerassi and F. Sondheimer, *ibid.*, **75**, 4117 (1953).