[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

THE STRUCTURES OF CONVOLVULINOLIC AND JALAPINOLIC ACIDS. SYNTHESIS OF 11-HYDROXYPENTADECANOIC AND 11-HYDROXYHEXADECANOIC ACIDS

BY LETHA A. DAVIES[1] AND ROGER ADAMS

RECEIVED MARCH 12, 1928 PUBLISHED JUNE 5, 1928

The roots of various plants of the *Convolvulaceae* family contain glucosidic resins which have been used medicinally as purgatives for many centuries. The plants are cultivated in Mexico, Jamaica and South America, and also grow wild on the eastern slopes of the Mexican Andes.

Perhaps the most important of the resins are jalap resin, occurring in *Tubera Jalapae*, and the resins obtained from Orizaba root, Scammonium and Tampicojalap. Since the beginning of the nineteenth century these resins have been the subject of many chemical investigations, the earliest of which were concerned chiefly with the extraction of the resins from the tubers.[2] The products of hydrolytic decomposition were studied in Liebig's Laboratory as early as 1844.[3]

The resin from Orizaba root yields on hydrolysis an hydroxyhexadecanoic acid, jalapinolic acid, investigated by Kromer.[4] On reduction of this acid Kromer obtained a hexadecanoic acid which he reported as not identical with palmitic acid. On oxidation the jalapinolic acid gave substances which he believed to be identical with methylethylacetic and sebacic acids. Accordingly Kromer suggested for jalapinolic acid the formula $CH_3CH_2CH(CH_3)CHOH(CH_2)_{10}CO_2H$.

Taverne[5] and Hoehnel[6] worked on the jalap resin, which is now called convolvulin. The chief product of hydrolytic decomposition of convolvulin is an hydroxypentadecanoic acid, convolvulinolic acid. These investigators studied its oxidation and obtained what they assumed to be methylethylacetic acid and an isomer of sebacic acid. As a result of these researches, the structure of convolvulinolic acid was suggested as $CH_3CH_2CH(CH_3)CHOH(CH_2)_9CO_2H$.

Power and Rogerson[7] examined jalap resin and in their investigations reported the isolation of convolvulinolic acid and the preparation of its

---

[1] This communication is an abstract of a portion of a thesis presented by Letha A. Davies in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry at the University of Illinois.

[2] Cadet de Gassicourt, *J. pharm.*, [2] **3**, 495 (1817); Nativelle, *J. pharm. chim.*, [3] 1, 228 (1842).

[3] Kayser, *Ann. Chem. Pharm.*, **51**, 81 (1844). See also Mayer, *ibid.*, **83**, 121 (1852); **92**, 125 (1854); **95**, 129 (1855).

[4] Kromer, *J. prakt. chem.*, [2] **57**, 448 (1898).

[5] Taverne, *Rec. trav. chim.*, **13**, 187 (1894).

[6] Hoehnel, *Arch. Pharm.*, **234**, 647 (1896).

[7] Power and Rogerson, THIS JOURNAL, **32**, 80 (1910).

methyl ester. They assumed the structure assigned by Hoehnel to be correct. A little later the same authors[8] studied scammony root and isolated jalapinolic acid. In this paper the results of a study of the optical rotation of jalapinolic and convolvulinolic acids were reported. Both acids were found to be optically active, a fact which had been overlooked by previous investigators, due possibly to very low values obtained. In a third paper[9] the preparation of methyl jalapinolate and the determination of its optical activity were described.

Y. Asahina[10] and collaborators have recently published the results of their investigations into the structures of convolvulinolic and jalapinolic acids. These acids were reduced with hydriodic acid and red phosphorus and the products obtained were reported by these authors to be *n*-pentadecanoic and *n*-hexadecanoic acids, respectively, identified by melting points of the acids themselves and of their anilides. The hydroxy acids were oxidized to the corresponding keto acids, then converted to the oximes and allowed to undergo the Beckmann rearrangement. The resulting acid amides were decomposed and yielded in the case of convolvulinolic acid, nonanedicarboxylic and 10-aminodecanoic acids and, in the case of jalapinolic acid, nonanedicarboxylic and 10-aminodecanoic acids, along with a small amount of caproic acid. On the basis of these experiments the formulas suggested by these authors were 11-hydroxyhexadecanoic acid (I) for jalapinolic acid and 11-hydroxypentadecanoic acid (II) for convolvulinolic acid.

$$\underset{\text{I}}{CH_3(CH_2)_4CHOH(CH_2)_9CO_2H} \qquad \underset{\text{II}}{CH_3(CH_2)_3CHOH(CH_2)_9CO_2H}$$

The present work was undertaken with the object of synthesizing the two acids having the formulas I and II. These acids have been made by the general procedure developed recently in this Laboratory for synthesizing hydroxy acids.[11] Methyl 10-aldehydodecanoate[11c] was condensed with (a) *n*-amyl magnesium bromide and (b) *n*-butyl magnesium bromide, and the methyl esters of the hydroxy acids thus produced were then saponified.

(a) $CH_3(CH_2)_4MgBr + CHO(CH_2)_9CO_2CH_3 \longrightarrow CH_3(CH_2)_4CHOH(CH_2)_9CO_2CH_3$

(b) $CH_3(CH_2)_3MgBr + CHO(CH_2)_9CO_2CH_3 \longrightarrow CH_3(CH_2)_3CHOH(CH_2)_9CO_2CH_3$

The acids and esters thus obtained were, of course, racemic and consequently might be expected to have different constants from the corresponding natural acids and esters which are optically active. The identity or non-identity of the general structures of the synthetic molecules

---

[8] Power and Rogerson, *J. Chem. Soc.*, **101**, 1 (1912).

[9] Power and Rogerson, *J. Chem. Soc.*, **101**, 398 (1912).

[10] Asahina, *J. Pharm. Soc. Japan*, **523**, 779 (1925); *C. A.*, **20**, 365, 366 (1926).

[11] (a) Noller with Adams, THIS JOURNAL, **48**, 1074 (1926); (b) Hiers with Adams, *ibid.*, **48**, 1089, 2385 (1926); (c) Tomecko with Adams, *ibid.*, **49**, 522 (1927).

with the natural was, however, readily established. Upon oxidation of the convolvulinolic and jalapinolic acids the corresponding keto acids were produced which, if the structures assigned the natural acids by Asahina are correct, should be optically inactive. The keto acids produced, moreover, should be identical with the keto acids formed by oxidation of synthetic 11-hydroxypentadecanoic acid and 11-hydroxyhexadecanoic acid. Reduction of the keto acids made from the natural acids should yield hydroxy acids identical with the synthetic compounds. The constants of these various compounds are given in Table I.

TABLE I

MELTING POINTS OF NATURAL AND SYNTHETIC COMPOUNDS

	Jalapinolic acid, °C.	11-Hydroxyhexadecanoic acid, °C.	Convolvulinolic acid, °C.	11-Hydroxypentadecanoic acid, °C.
Acid	65.5–66.5	68–69	51–52	63.5–64
Methyl ester	46–47	40.5–41.5	31–32	about 29–32
Ketone by oxidation	74–75	74–75	63–64	70–71
Hydroxy from reduction of ketone	68–69	....	51–52[a]	....

[a] Although the melting point of this substance is the same as that of the original convolvulinolic acid, a mixed melting point proved the two hydroxy acids to be different. The melting point was obtained after three recrystallizations from ethyl acetate. The small quantity of material, however, did not permit further investigation.

It is seen that the keto acids from jalapinolic acid and 11-hydroxyhexadecanoic acid have the same melting point, and a mixed melting point shows them to be identical. Moreover, reduction of the keto acid from jalapinolic acid gives an hydroxy acid identical in melting point with 11-hydroxyhexadecanoic acid, and a mixed melting point shows no depression. It is thus definitely established that jalapinolic acid is the *d*-form of 11-hydroxyhexadecanoic acid.

On the other hand, the keto acids from convolvulinolic acid and from 11-hydroxypentadecanoic acid do not melt at the same point and a mixed melting point gives a marked depression. The reduced keto acid from convolvulinolic acid melts at a different point from 11-hydroxypentadecanoic acid and the mixed melting point is lower than either. It appears, therefore, that convolvulinolic acid is not 11-hydroxypentadecanoic acid. A further study of this substance is now being made.

Worthy of mention is a slight modification of the procedure used in the condensation of aldehyde esters with the Grignard reagent in order to improve the yields of pure product. Where no particular precautions were observed in the condensation of the butylmagnesium or amylmagnesium bromide with methyl 10-aldehydodecanoate, in spite of the fact that the alkyl bromides were pure and the methyl 10-aldehydodecanoate boiled within two degrees, low yields of esters distilling over a wide range were obtained. Upon saponifying, acids were obtained in very low yields. They proved to be the keto acids instead of the expected hydroxy acids. Such formation is extraordinary and unexpected and can only be explained by the presence of acid ester in the aldehyde ester.

$$HO_2C(CH_2)_9CO_2CH_3 + 2RMgBr \longrightarrow BrMgOCO(CH_2)_9CO_2CH_3 \longrightarrow RCO(CH_2)_9CO_2CH_3$$

This would also account for the low yields of product. The lower solubility of the keto acid as compared with the hydroxy acid renders its isolation easy.

If the aldehyde ester was carefully extracted with 10% sodium carbonate, then worked up and distilled twice in an atmosphere of nitrogen and immediately condensed and carried through to the final product in an atmosphere of nitrogen, the hydroxy esters were obtained readily and in a pure state.

In the course of these investigations, when the exact character of the products obtained from the condensations of the aldehyde ester with Grignard reagents was doubtful, it seemed desirable to prepare the keto acids by some other method. Accordingly, the reaction between an acid chloride and a Grignard reagent was used, and 9-ketohexadecanoic acid was prepared in a trial run by this method. Directions for this condensation were furnished by John R. Johnson.[12]

The authors are deeply indebted to Professor Asahina for his kindness in sending them samples for melting-point determinations, of the compounds used in his investigations, and to Dr. C. G. Tomecko for furnishing generous samples of jalapinolic and convolvulinolic acids.

Experimental Part

Methyl 10-Aldehydodecanoate.—This was prepared in 60% yields by the ozonation of methyl 11,12-dodecenoate according to the general procedure described by Noller and Adams[11a] for preparing aldehyde esters. The methyl 11,12-dodecenoate was synthesized from ethyl undecenoate by the method of Tomecko and Adams.[11c] The aldehyde ester used in these experiments was carefully freed from acid ester by extraction of the ethereal solution with 10% sodium carbonate. The subsequent distillations were carried out in an atmosphere of nitrogen; the product, on second distillation, boiled at 141–143° at 4 mm.

Methyl 11-Hydroxyhexadecanoate, $CH_3(CH_2)_4CHOH(CH_2)_9CO_2CH_3$.—A solution of 50 g. of pure methyl 10-aldehydodecanoate in 500 cc. of anhydrous ether was treated with an equivalent amount (determined by titration of the Grignard solution[13]) of *n*-amyl magnesium bromide, according to the directions of Noller and Adams,[11a] except that the condensation was carried out in an atmosphere of nitrogen. The hydroxy ester obtained was fractionally distilled, also in an atmosphere of nitrogen, and a yield of 22 g. (33%) was obtained; b. p. 183–186° at 3 mm. The ester solidified to a white, crystalline mass; after four recrystallizations from petroleum ether it melted at 40.5–41.5°.

---

[12] Unpublished communication.

[13] Gilman and others, THIS JOURNAL, **45**, 150 (1923).

Anal. Subs., 0.1902: CO_2, 0.4975; H_2O, 0.2026. Calcd. for $C_{17}H_{34}O_3$: C, 71.27; H, 11.97. Found: C, 71.34; H, 11.92.

Several unsuccessful attempts were made to prepare this ester, using methyl 10-aldehydodecanoate which had been worked up and distilled in the ordinary way, that is, with no special precautions to keep the substance absolutely free from acid ester except that it was used immediately after redistillation. In these experiments, the ester obtained from the condensation distilled gradually over a range of 20° (180–200° at 4 mm.) and could not be purified by fractionation; the yield of product was low (18–25%). Upon saponification only about 1 g. of crude acid could be isolated from about 5 g. of ester. Instead of the expected hydroxy acid, the corresponding keto acid was isolated on recrystallization, as was shown by melting point and a mixed melting point with some 11-ketohexadecanoic acid prepared later and described below.

11-Hydroxyhexadecanoic Acid, $CH_3(CH_2)_4CHOH(CH_2)_9CO_2H$.—The methyl 11-hydroxyhexadecanoate was saponified by refluxing for several hours with excess of 10% alcoholic potassium hydroxide. The alcohol was evaporated and the aqueous solution was poured slowly into an excess of hydrochloric acid. The 11-hydroxyhexadecanoic acid was recrystallized four times from ethyl acetate and melted constant at 68–69°.

Anal. Subs., 0.2013: CO_2, 0.5185; H_2O, 0.2125. Calcd. for $C_{16}H_{32}O_3$: C, 70.53; H, 11.84. Found: C, 70.25; H, 11.81.

Mol. wt. Subs., 0.3618: 13.28 cc. of 0.1 *N* NaOH. Calcd. for $C_{16}H_{32}O_3$: mol. wt., 272.3. Found: 272.4.

11-Ketohexadecanoic Acid, $CH_3(CH_2)_4CO(CH_2)_9CO_2H$.—A solution of 0.5 g. of 11-hydroxyhexadecanoic acid in 10–15 cc. of glacial acetic acid was warmed to 50–60°. It was then treated with a solution of 0.5 g. of chromic acid in 2 cc. of water and 8 cc. of glacial acetic acid, kept warm and shaken for four to five minutes, then heated to 60–70° for three to four minutes longer. The solution was poured into a large volume of ice water, the keto acid filtered off and recrystallized from ethyl acetate. Any trace of color, due to chromium, in the keto acid could be readily removed by converting the acid into its sodium salt, heating the aqueous solution of the salt with a small quantity of Norit, filtering and regenerating the acid. After three crystallizations the keto acid melted constant at 74–75° and when mixed with keto acid prepared from jalapinolic acid there was no change in melting point.

Anal. Subs., 0.0981: CO_2, 0.2548; H_2O, 0.0986. Calcd. for $C_{16}H_{30}O_3$: C, 71.06; H, 11.19. Found: C, 70.82; H, 11.24.

11-Hydroxyhexadecanoic Acid Derived from Jalapinolic Acid.—The keto acid from jalapinolic acid was prepared as described above for 11-ketohexadecanoic acid. It was recrystallized to constant melting point, 74–75°. One gram of the keto acid was dissolved in about 20 cc. of ethyl acetate and shaken for ten hours with hydrogen in the presence of about 0.1 g. of platinum-oxide platinum black prepared according to the method of Adams and Shriner.[14] The solution was filtered from the catalyst, part of the solvent removed by evaporation and the remainder of the solution cooled, whereupon the hydroxy acid crystallized out. On recrystallization from ethyl acetate it melted at 68–69° and was shown by mixed melting point to be identical with the synthetic 11-hydroxyhexadecanoic acid described above. In one or two instances a second addition of catalyst was required before the reduction was accomplished. In still another instance the reduction yielded a product difficult to purify. This may have been due to the presence of small amounts of acid in which the keto was reduced to a methylene group.

Methyl 11-Hydroxypentadecanoate, $CH_3(CH_2)_3CHOH(CH_2)_9CO_2CH_3$.—This ester

---

[14] Adams and Shriner, THIS JOURNAL, **45**, 2171 (1923).

was prepared by condensing methyl 10-aldehydodecanoate with *n*-butyl magnesium bromide under the same conditions as described for the corresponding hexadecanoate. It distilled at 166° at 2 mm., solidified on cooling to white crystals which melted at about 29–32°.

Anal. Subs., 0.1847: CO_2, 0.4786; H_2O, 0.1959. Calcd. for $C_{16}H_{32}O_3$: C, 70.53; H, 11.84. Found: C, 70.66; H, 11.87.

The same difficulty was encountered in the synthesis of this ester as in the case of the corresponding hexadecanoate. The ester distilled at 170–190° at 3 mm. and the keto acid, instead of the expected hydroxy acid, was obtained from the earlier experiments. This was shown by melting point and by mixed melting point with 11-ketopentadecanoic acid, which is described below.

11-Hydroxypentadecanoic Acid, $CH_3(CH_2)_3CHOH(CH_2)_9CO_2H$.—This acid was prepared by saponification of the corresponding ester. It was recrystallized four times from ethyl acetate and melted at 63.5–64°.

Anal. Subs., 0.1543: CO_2, 0.3926; H_2O, 0.1591. Calcd. for $C_{15}H_{30}O_3$: C, 69.70; H, 11.71. Found: C, 69.40; H, 11.53.

Mol. wt. Subs., 0.3563: 13.80 cc. of 0.1 *N* NaOH. Calcd. for $C_{15}H_{30}O_3$: mol. wt., 258.2. Found: 258.1.

11-Ketopentadecanoic Acid, $CH_3(CH_2)_3CO(CH_2)_9CO_2H$.—This acid was prepared by oxidation of the corresponding hydroxy acid in the same manner as described for 11-ketohexadecanoic acid. Upon recrystallization to constant melting point from ethyl acetate, it melted at 70–71°. Mixed with a sample of keto acid, m. p. 63°, prepared from convolvulinolic acid, there was a marked depression of the latter melting point.

Anal. Subs., 0.1882: CO_2, 0.4838; H_2O, 0.1830. Calcd. for $C_{15}H_{28}O_3$: C, 70.28; H, 11.01. Found: C, 70.08; H, 10.87.

11-Hydroxypentadecanoic Acid Derived from Convolvulinolic Acid.—A sample of keto acid prepared by the oxidation of convolvulinolic acid was reduced catalytically to the hydroxy acid. The latter was recrystallized from ethyl acetate and melted at 51–52°. This melting point and a mixed melting point proved it to be different from the synthetic 11-hydroxypentadecanoic acid described above. The quantity of convolvulinolic acid available was small; the hydroxy acid obtained from the reduction was sufficient for three crystallizations, but after this treatment was insufficient for analysis. The melting point reported may be considered as approximately correct.

9-Ketohexadecanoic Acid, $CH_3(CH_2)_6CO(CH_2)_7CO_2H$.—Monomethyl azelate was prepared by the ozonation of methyl oleate and decomposition of the ozonide in the presence of hydrogen peroxide. The ester has been described by Noller and Adams.[11a] It was then converted into monomethyl azelayl chloride by the method of Robinson and Robinson;[15] the acid chloride distilled at 139–141° at 4.5 mm. The methyl ester of 9-ketohexadecanoic acid was prepared from monomethyl azelayl chloride and *n*-heptyl magnesium bromide by a procedure similar to the condensations of aldehyde esters with Grignard reagents previously described. The method is that of John R. Johnson.[12] The methyl ester was saponified and the keto acid, on recrystallization from ethyl acetate, melted at 73.5–74.5°.

Anal. Subs., 0.1857: CO_2, 0.4851; H_2O, 0.1858. Calcd. for $C_{16}H_{30}O_3$: C, 71.06; H, 11.19. Found: C, 71.24; H, 11.19.

Mol. wt. Subs., 0.4213: 15.62 cc. of 0.1 *N* NaOH. Calcd. for $C_{16}H_{30}O_3$: mol. wt., 270.3. Found: 269.9.

---

[15] Robinson and Robinson, *J. Chem. Soc.*, **127**, 175 (1925).

Summary

1. 11-Hydroxyhexadecanoic acid and 11-hydroxypentadecanoic acid have been synthesized by the condensation of methyl 10-aldehydodecanoate with *n*-amyl magnesium bromide and *n*-butyl magnesium bromide, respectively, and subsequent saponification of the esters obtained.

2. Jalapinolic acid has been shown to be the *d*-form of 11-hydroxyhexadecanoic acid. This has been accomplished through oxidation of both substances to the same keto acid, and also by the reduction of the keto acid derived from jalapinolic acid to a substance identical with the synthetic 11-hydroxyhexadecanoic acid.

3. Convolvulinolic acid has been shown to have a structure different from that of 11-hydroxypentadecanoic acid. The procedure used in investigating this substance was identical with that used in the study of jalapinolic acid.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE ROCKEFELLER PHYSICAL AND THE BAKER CHEMICAL LABORATORIES OF CORNELL UNIVERSITY]

THE ABSORPTION SPECTRA OF SULFONEFLUORESCEIN AND SOME OF ITS DERIVATIVES[1]

BY R. C. GIBBS AND C. V. SHAPIRO[2]

RECEIVED MARCH 12, 1928 PUBLISHED JUNE 5, 1928

Sulfonefluorescein[3] is a sulfonic acid derivative of resorcinolbenzein and is analogous in many of its chemical properties to fluorescein. The absorption spectra of resorcinolbenzein[4a] and fluorescein[4b] have already been investigated in this Laboratory. All of the substances used in this study were analytically pure samples prepared by Dr. Vose.[3]

Fig. 1 gives the absorption spectra of neutral alcoholic solutions of sulfonefluorescein, dibromosulfonefluorescein and 2,4-dihydroxybenzoylbenzene-*o*-sulfonic acid, the intermediate product in the formation of sulfonefluorescein from resorcinol and *o*-sulfobenzoic acid anhydride. The absorption of 2,4-dihydroxybenzoylbenzene-*o*-sulfonic acid, Curve C, is characterized by three absorption bands and is entirely similar to the absorption of 2,4-dihydroxybenzoyl-*o*-benzoic acid,[4b] the bands for the former being shifted slightly toward higher frequency numbers. The structure of these intermediate acids has been the subject of considerable

---

[1] The investigations upon which this article is based were supported by grants from the Heckscher Foundation for the Advancement of Research, established by August Heckscher at Cornell University.

[2] Heckscher Research Assistant in Physics and Chemistry, Cornell University, 1923–1928.

[3] Orndorff and Vose, THIS JOURNAL, **46**, 1896 (1924).

[4] Orndorff, Gibbs and Shapiro, *ibid.*, (a) **48**, 1327 (1926); (b) **50**, 819 (1928).