

petroleum ether (30–60°) afforded colorless prisms, m.p. 70–71.6°, $[\alpha]_D^{25} + 41$ (10% acetone solution).

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.66; H, 10.66.

*Hydrogenation of $\Delta^8(10)$ -*p*-menthene-1,2-diol.* Five grams of $\Delta^8(10)$ -*p*-menthene-1,2-diol was dissolved in 150 ml. of 95% ethanol and hydrogenated at room temperature, using 2 g. of 5% platinum on Darco G-60 catalyst. The hydrogenation was complete in 10 min. The catalyst was removed by filtration and the filtrate concentrated to about 10 ml. Dilution with water afforded colorless crystals which were dried in a vacuum desiccator over concd. H_2SO_4 . The dried product weighed 4.6 g. (92%) and melted at 86.4–88.4°. There was no melting point depression on admixture with a sample of *trans-p*-menthane-1,2-diol (III) (m.p. 86.6–88.6°) prepared by the hydroxylation of Δ^1 -*p*-menthene (II).

Trans-p-menthane-1,2-diol-diacetate (VI). Thirty grams of *trans-p*-menthane-1,2-diol (III) (m.p. 89°) was refluxed for 2 hr. in 150 ml. of acetic anhydride containing 0.5 g. of anhydrous sodium acetate. The solution was poured into water and stirred to decompose excess anhydride. The diester was extracted with three portions of ethyl ether. The combined ether extracts were washed three times with sodium bicarbonate solution, twice with water, and dried over anhydrous sodium sulfate. After removal of the ether under reduced pressure, the residual oil was distilled. At 99° (0.8 mm.) 41 g. (92%) of colorless, slightly viscous oil was collected. The diacetate obtained by distillation was sufficiently pure for analysis $[\alpha]_D^{25} + 93$, n_D^{25} 1.4498.

Anal. Calcd. for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44; Sapon. equiv., 128. Found: C, 65.34; H, 9.70; Sapon. equiv., 135.

Trans-p-menthane-1,2-diol-dipropionate (VII). Thirty grams of *trans-p*-menthane-1,2-diol (III) (m.p. 89°) was refluxed for 2 hr. in 150 ml. of propionic anhydride containing 0.5 g. of anhydrous sodium acetate. Excess anhydride was decomposed by water and the diester was extracted with ether as described in the case of the diacetate ester. After removal of the ether under reduced pressure, the residual oil was distilled. At 114° (0.8 mm.) 46 g. (94%) of colorless, slightly viscous oil was collected. The dipropionate obtained by distillation was sufficiently pure for analysis $[\alpha]_D^{25} + 83$, n_D^{25} 1.4478.

Anal. Calcd. for $C_{16}H_{28}O_4$: C, 67.57; H, 9.92; Sapon. equiv., 142. Found: C, 67.78; H, 9.96; Sapon. equiv., 146.

Trans-p-menthane-1,2-diol-dibutyrate (VIII). Thirty grams of *trans-p*-menthane-1,2-diol (III) (m.p. 89°) was refluxed for 2 hr. in 150 ml. of butyric anhydride containing 0.5 g. of anhydrous sodium acetate. Excess anhydride was decomposed by water and the diester was extracted with ether as described in the case of the diacetate ester. After removal of the ether under reduced pressure, the residual oil was distilled. At 131° (0.8 mm.) 50 g. (92%) of colorless, slightly viscous oil was collected. The dibutyrate obtained by distillation was sufficiently pure for analysis $[\alpha]_D^{25} + 74$, n_D^{25} 1.4486.

Anal. calcd. for $C_{18}H_{32}O_4$: C, 69.19; H, 10.33; Sapon. equiv., 156. Found: C, 69.26; H, 10.47; Sapon. equiv., 154.

LAKE ALFRED, FLA.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

α -Deoxykojic Acid and Some of Its Derivatives

CHARLES D. HURD AND SWIATOSLAW TROFIMENKO

Received February 17, 1958

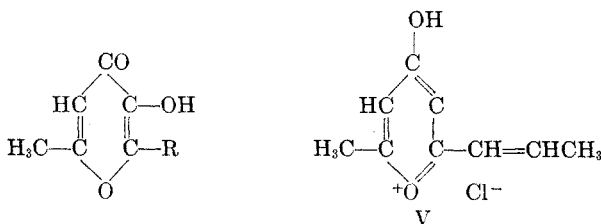
The allyl ether of α -deoxykojic acid was prepared and rearranged to 6-allyl- α -deoxykojic acid, from which the 6-propenyl and 6-propyl analogs were made. 3,5-Dinitrobenzoates were satisfactory derivatives for these compounds.

In connection with studies on kojic acid and related compounds it became of interest to prepare α -deoxykojic acid¹ and certain of its derivatives.

α -Deoxykojic acid (I) was synthesized from kojic acid by halogenation (thionyl chloride) to yield α -chloro- α -deoxykojic acid, followed by catalytic reduction of the latter. The allyl ether of I was prepared from allyl bromide, adapting conditions² employed earlier with kojic acid. The ether was an oil at room temperature that crystallized readily at ice temperature from one run but not from another. It isomerized rapidly to 6-allyl- α -deoxykojic acid (II) at elevated temperatures and gave evidence for slow isomerization at room temperature.

II was a crystalline solid, giving a strong violet color with ferric chloride. When it was treated with dry hydrogen chloride in ethanol it changed to a

salt-like compound (V), the hydrochloride of 6-propenyl- α -deoxykojic acid (III). This compound lost hydrogen chloride on standing but more



- I, R = H
 II, R = $CH_2CH=CH_2$
 III, R = $CH=CHCH_3$
 IV, R = $CH_2CH_2CH_3$

rapidly on heating to yield III. The latter was prepared more readily by treatment with base. V, III, and a mixture thereof all melted at the same temperature which would indicate that hydrogen chloride is lost prior to the attainment of the melting temperature, and that what melts is impure III. The 6-propenylkojic acid hydrochloride of McLamore and co-workers^{2b} also melts a few degrees below the melting point of 6-propenylkojic

(1) The α represents position on the side chain. α -Deoxykojic acid also has been called allomaltol by Yabuta, *J. Chem. Soc.*, 125, 575 (1924).

(2) (a) C. D. Hurd and R. J. Sims, *J. Am. Chem. Soc.*, 71, 2440 (1949); (b) W. M. McLamore, E. Gelblum, and A. Bavey, *J. Am. Chem. Soc.*, 78, 2816 (1956).

acid, but these workers did not report a mixed melting point determination.

It is of interest that the corresponding hydrochloride of I could not be as easily characterized. It was considerably more soluble in alcohol and, although it gave all qualitative tests in agreement with the proposed structure, titration gave consistently high neutralization equivalents. This might be accounted for either by partial loss of hydrogen chloride during isolation or by solvation of this species.

Both II and III could be hydrogenated readily to 6-propyl- α -deoxykojic acid (IV) using palladized charcoal as catalyst.

3,5-Dinitrobenzoates of I, II, III, IV were readily prepared. They proved to be excellent derivatives since the several melting points were widely separated. To prepare these esters, however, low temperatures and short reaction times were desirable to avoid side reactions.

Other reagents tested for derivatives were not satisfactory. From IV and phenyl isocyanate no urethan was obtained. II and IV, on reaction with acetic anhydride and pyridine, yielded oily products; some tar was formed from II as well. Prolonged treatment of II with benzoyl chloride and pyridine resulted in tar. III gave rise to a crystalline acetate but it was not studied further since the other two acetates were oils.

EXPERIMENTAL

α -Chloro- α -deoxykojic acid. Some of this material, m.p. 166–167°, was prepared by reaction of thionyl chloride and kojic acid, but most of it was generously donated by Chas. Pfizer and Co., who supply it under the name "chlorokojic acid." The latter was recrystallized prior to use, otherwise the reduction (below) proceeded very slowly.

α -Deoxykojic acid (I). Directions for this synthesis were essentially those of Brown.³ The catalyst used was palladium (10%) on carbon. The reduction was done in a Parr apparatus on batches of up to 30 g. of α -chloro- α -deoxykojic acid. Methanol was taken as solvent and it was found that addition of up to 15% of water did not affect the yield, but was convenient for better solubilization of the sodium acetate used to neutralize the hydrogen chloride that was formed. The pressures used ranged from 25 to 40 lbs./inch.² and the theoretical amount of hydrogen was usually absorbed within 15–30 min. Yields were good (80–92%). The product melted at 152° after recrystallization from ethyl acetate.

Infrared spectra were taken on a Baird double beam recording spectrophotometer, using potassium bromide pellets. The following bands were observed for I: 3.10, 6.05, 6.18, 6.28, 6.86 (weak), 6.94, 7.23, 7.31, 7.83, 8.00, 8.14, 8.38, 8.67 with shoulder at 8.53, 9.48w, 9.75w, 10.90, 11.28, 11.94, 12.96, 13.34w, and a broad band at about 14.30 μ .

α -Deoxykojic acid hydrochloride. One gram of I was dissolved in 25 cc. of warm absolute ethanol and the solution was saturated with dry hydrogen chloride. Solid separated only after addition of 75 cc. of ether. A total of 0.90 g. was obtained in several crops, m.p. 149° with some darkening above 110°. The material gave an immediate precipitate with silver nitrate, and it responded like an acid of mineral strength with Davidson's A-II indicator.⁴ The ferric chlo-

ride test was positive, giving the same color as that from I. Titration to phenolphthalein end point gave neutralization equivalents of 93 and 95, whereas the calculated value for I is 126, for its hydrochloride 81, and for its monoethanolate 104. On acidification of the solution, crystals were obtained that were identified as I.

α -Deoxykojyl allyl ether. One tenth mole of α -deoxykojic acid was dissolved in 150 cc. of methanol, then 0.1 mole of sodium methoxide was added to the hot solution, followed by water until the salt was completely dissolved. Allyl bromide (0.11 mole) was added and the yellow solution refluxed for 150 min. It was then evaporated in an air stream and the resulting mixture of oil and crystals was extracted with chloroform until the extracts were colorless. The extract was washed with 25-cc. portions of 10% sodium carbonate solution until the chloroform layer gave no ferric chloride test, and then once more (7 washings). The carbonate washings were re-extracted with two 50-cc. portions of chloroform. The combined chloroform solutions were washed with water, dried with sodium sulfate, stirred with Norit and filtered. Chloroform was removed at diminished pressure and the oily residue was dissolved in ether-ligroin. On standing at 5° large crystals separated which melted at room temperature except for a few small crystals which were identified as III. Crystals of the ether which were collected at 5° gave no coloration with ferric chloride solution.

In another run this ether could not be obtained crystalline. When the oil (negative ferric chloride test) was taken up in benzene and refluxed for 11 hr. the benzene layer gave a strong violet color with ferric chloride, indicating some isomerization of the ether even at this relatively low temperature of heating. In this ferric chloride test, one drop of solution was placed on filter paper, the solvent was evaporated, then a drop of the ferric chloride solution was added. Hence, no further attempts were made to purify this ether for analysis, but instead it was rearranged to II.

6-Allyl- α -deoxykojic acid (II). The solution of the above ether was warmed at reduced pressure to remove solvents, then was heated at 180° and 11 mm. for 20 min. The material was dissolved in acetone and methanol, decolorized, and concentrated. There separated 8.9 g. of cream colored crystals in three crops, m.p. 151–153°. The yield, based on I, was 53%. The sample for analysis was sublimed at 20 mm., m.p. 157–158°. In its ultraviolet spectrum, it showed λ_{\max} 275 m μ , log ϵ 3.82. The infrared spectrum had the following characteristic bands: 3.10, 6.04, 6.19, 6.30, shoulder at 6.48, 6.85, 6.97, 7.22, 7.39, 7.72w, 8.10 broad, 8.40, 8.99, 9.54, 9.99, 10.22, 10.85, 11.32, 13.05, 13.70, and a broad band around 14 μ .

Anal. Calcd. for C₉H₁₀O₃: C, 65.05; H, 6.06. Found: C, 65.23; H, 5.86.

6-Propenyl- α -deoxykojic acid hydrochloride (V). One gram of II was dissolved in hot absolute ethanol (20 cc.). Dry hydrogen chloride was bubbled in slowly for an hour. The solution was left at 20° for two days after which time clusters of pale reddish violet needles formed which were filtered off and dried in the air. Later, a second crop of crystals was obtained. Total yield 0.85 g., or 70%; m.p. 148–149°. It gave an intense greenish color with ferric chloride. It was essentially insoluble in ether, but the trace that did dissolve was recognizable by the ferric chloride coloration.

Anal. Calcd. for C₉H₁₁ClO₃: C, 53.33; H, 5.47. Found: C, 53.40; H, 5.65.

Titration of the hydrochloride also was confirmatory: 0.0547 g. of it consumed 2.72 cc. of 0.192*N* sodium hydroxide (phenolphthalein end point), giving a neutralization equivalent of 104. The theoretical value is 101.5, but since the end point for the titration of the enolic hydroxyl was not very sharp the value is satisfactory for the proposed structure.

6-Propenyl- α -deoxykojic acid (III). The solution from the above titration was acidified with acetic acid. Crystals gradually formed which were collected, washed with water and methanol, and dried at 80°; yield, 0.02 g. There was considerable loss during washing since III is soluble in methanol,

(3) M. G. Brown, *J. Chem. Soc.*, 2558 (1956).

(4) D. Davidson, *J. Chem. Ed.*, 19, 221, 532 (1942).

It is also readily soluble in ether, an observation in marked contrast to the insolubility of the hydrochloride. The m.p. was 148–149°. The sample for analysis was purified by sublimation; m.p. 151–152°, mixed m.p. with II was 123–131°. The product gave a green color with ferric chloride.

Anal. Calcd. for $C_9H_{10}O_3$: C, 65.05; H, 6.06. Found: C, 65.26; H, 5.87.

The ultraviolet spectrum of III showed λ_{max} 310 $m\mu$, $\log \epsilon$ 4.17. The important infrared bands were: 3.10, 3.40w, 3.46w, 6.03, 6.12, 6.21, 6.32, 6.84, 6.93, 7.18, 7.39, 7.58, 8.07, 8.20, 8.44, 9.50, 10.00, 10.29, 10.43, 10.90, 11.40, 12.95, and a broad band around 14.70 μ .

6-Propyl- α -deoxykojic acid (IV). To crude II (5.0 g.), dissolved in 150 cc. of methanol, was added 25 mg. of 10% palladium-on-carbon and the suspension was shaken in a Parr apparatus at about 30 lbs./inch.² The uptake of hydrogen ceased after 5 min. The suspension was filtered, the solvent was removed, and the residue was recrystallized from a mixture of methanol and ethyl acetate. The product separated in creamy crystals, yield 3.5 g. (70%), m.p. 128–131°. Sublimation afforded pure IV, m.p. 132.5–133.5°. From the yellow mother liquor 1.5 g. of less pure material was recovered, from which some pure IV could be obtained on sublimation, the rest decomposing.

The product was considerably more soluble in ethyl acetate, acetone, and methanol than I, but it was less soluble in water. It gave a deep violet color with ferric chloride.

When 0.3 g. of crude III was hydrogenated analogously, 0.28 g. of cream colored crystals was obtained, m.p. 131–132.5°. The mixed m.p. with the above crystals also was 132–133.5°. The infrared spectra of the compound from the two sources were identical, with these bands: 3.09, 3.39, 3.41, 3.49, 6.04, 6.18, 6.28, 6.85, 6.97, 7.20, 7.37 with shoulders at 7.43 and 7.48, 7.74, 8.06, 8.18, 8.35, 9.08 with shoulders at 9.11 and 9.20, 9.50 with shoulder at 9.65, 10.19, 10.29, 10.43, 11.35, 11.63, 12.60w, 13.01, and a broad band around 14.20 μ .

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.26; H, 7.19. Found: C, 64.39; H, 7.29.

3,5-Dinitrobenzoates of I, II, III, IV. About 0.2 g. of I, II, III, or IV was dissolved in 5 cc. of dry pyridine at room temperature, mixed with 0.35 g. of 3,5-dinitrobenzoyl chlo-

ride, and stirred for 5 min. The solution of I remained clear, that of II turned deep red-brown, that of III became a thick slurry, and that of IV yielded a thin slurry. Each reaction mixture was then heated on a hot plate for 30 sec. and the flasks were then cooled under tap water. Then 10 cc. of ice water was added to each mixture and the resulting precipitate was collected on a filter, washed with water, and dried over calcium chloride at room temperature and 10 mm. Yields were between 0.3 and 0.4 g.

The products were recrystallized from chloroform-ligroin with the use of Norit, and then from benzene-hexane. Fine, colorless crystals were obtained for each product. These melting points were observed for the several dinitrobenzoates: from I, 215–216°; from II, 96.5°; from III, 234–235°; from IV, 125°. The infrared spectra of the derivatives had the following peaks in common: 3.27 (aromatic CH), 5.72 (benzoate carbonyl), 5.97 (pyrone carbonyl), 6.47 and 7.44 (nitro), 12.58 (sym. trisubstituted benzene), and the four spectra were generally similar up to about 9.55 μ . A good region for differentiation of the derivatives was 9.55–11.90 μ where the individual compounds exhibited the following bands: I. 9.75, 9.92, 10.47, 10.73, 10.96, 11.25, 11.90. II. 10.10, 10.34, 10.59, 10.85, 10.94, 11.23, 11.39, 11.90. III. 9.99, 10.23 (shoulder 10.43), 10.66, 10.85, 10.92, 11.30, 11.90. IV. 9.94, 10.49, 10.65, 10.84, 10.92, 11.29, 11.60, 11.90 μ .

Explosions were encountered in analyzing all of the dinitrobenzoates but they seemed not to affect the values for the esters from I, III, IV. The explosion with the dinitrobenzoate of II, however, did make analysis unrealizable, for duplicate analyses (C, H, N) were inconsistent and varied widely. These and other microanalyses were performed by Miss Hilda Beck.

Anal. of dinitrobenzoates.

From I. Calcd. for $C_{13}H_8N_2O_8$: C, 48.76; H, 2.52. Found: C, 48.37; H, 2.54.

From III. Calcd. for $C_{16}H_{12}N_2O_8$: C, 53.33; H, 3.36. Found: C, 53.71; H, 3.10.

From IV. Calcd. for $C_{16}H_{14}N_2O_8$: N, 7.73. Found: N, 7.57.

EVANSTON, ILL.

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

The Structure of 2-Substituted Pyrrolines^{1,2}

J. H. BURCKHALTER AND J. H. SHORT⁴

Received January 24, 1958

Of the five possible structures which may be written for 2-substituted pyrrolines upon the basis of the location of the double bond, only the Δ^1 - and Δ^2 -pyrrolines have been shown conclusively to exist. The present work confirms the existence of the former rather than a Δ^2 structure. An attempt to synthesize 2-phenyl- Δ^4 -pyrroline resulted in failure.

While employing a number of 2-substituted pyrrolines in the synthesis of a group of desired 2-substituted pyrrolidines,⁵ it became apparent from a

survey of the literature that much confusion existed concerning the structures of the intermediate 2-substituted pyrrolines, and a determination of the structures of these pyrrolines became an objective.

Five 2-substituted pyrrolines are structurally possible, depending upon the location of the double bond (I–V). There appears to be no controversy

(1) Based upon a portion of the Ph.D. Thesis of J. H. Short, University of Kansas, 1954.

(2) During the preparation of this manuscript, a recent report on the structure of 2-phenylpyrrolines was noted.³

(3) M. C. Kloetzel, J. Z. Pinkus, and R. M. Washburn, *J. Am. Chem. Soc.*, **79**, 4222 (1957).

(4) Parke, Davis & Co., Fellow. Present address, Abbott Laboratories, North Chicago, Ill.

(5) J. H. Burckhalter and J. H. Short, *J. Org. Chem.*, **23**, 1281 (1958).

