[CONTRIBUTION FROM THE WHITMORE LABORATORIES, SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

The Δ^9-12-Keto Steroidal Sapogenins

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Two new steroidal sapogenins, 9-dehydrohecogenin (I) and 9-dehydromanogenin (VII), having the important Δ^9-12-ketone system, have been isolated from *Agave deserti* Engelm. and *Agave huachucensis* Baker, respectively. Their structures have been determined by relating them to other steroidal sapogenins, namely, hecogenin (III), rockogenin (II), agavogenin (V), manogenin (VIII), kammogenin (IX) and gitogenin (IV).

An investigation of the sapogenin fractions from plants which commonly contain hecogenin (III) and manogenin (VIII)[1] reveals that many of these fractions show a strong ultraviolet absorption maximum in the region 238 mμ (in alcohol) typical for an α,β-unsaturated ketone system. These fractions and their acetates appear to be either hecogenin or manogenin from a consideration of the analytical and melting point data. Actually, they may contain from 20 to 80% of an unsaturated ketone based on a molecular extinction coefficient ϵ_{max} of about 11,000 for a pure substance (Table I).[2]

TABLE I

ULTRAVIOLET SPECTRA DATE FOR CERTAIN HECOGENIN AND MANOGENIN FRACTIONS

Plant source	M.p., °C.	ϵ_{max}
(1) Hecogenin Fractions, $C_{27}H_{42}O_4$, λ_{max}^{alc} 238 mμ		
Agave deserti Engelm.	244–247	3050
Agave gracilipes Trel.	254–256	1800
Agave shawii Engelm.	244–246	1650
Agave chrysantha Peebles	255–256	730
Agave americana var.	262–263	500
Agave toumeyana Trel.	265–268	420
Hesperaloë funifera Trel.	263–265	330
(2) Manogenin acetate Fractions, $C_{31}H_{46}O_7$, λ_{max}^{alc} 238 mμ		
Agave huachucensis Baker	245–248	9100[a]
Agave ferox C. Koch	243–245	9000[b]
Agave havardiana Trel.	238–241	6400[a]
Agave chisoensis	242–244	5200[a]
Agave scabra Salm-Dyck	240–242	4400

[a] The unacetylated fraction showed about the same ϵ_{max} value. [b] Data for the free genin.

The fractions from *Agave deserti* Engelm. and *Agave huachucensis* Baker, each showing the highest ultraviolet peak, have been subjected to a chromatographic separation on alumina columns. This procedure resulted in the isolation of two new steroidal sapogenins, 9-dehydrohecogenin (I) and 9-dehydromanogenin (VII). A comparison of the properties of the saturated and unsaturated analogs is given in Table II along with more complete data for other steroidal sapogenins. The melting points of manogenin and its acetate are not depressed appreciably by the corresponding unsaturated compounds; hence the two series of compounds can be reliably differentiated only by some other means such as the rotation and ultraviolet spectra data.

For characterization, 9-dehydrohecogenin (I) is hydrogenated over Adams catalyst followed by acetylation to give 12-dihydrohecogenin diacetate (rockogenin diacetate, II) identical with material similarly prepared from pure hecogenin (III). The recently described conversion of hecogenin to *allo*pregnan-3,12,20-trione fixes its carbonyl oxygen at C-12 and that in the new sapogenin at the same position.[3]

The structure of 9-dehydromanogenin (VII) has been established by relating it to previously described steroidal sapogenins and their derivatives. Sodium and alcohol reduction of VII gives agavogenin (V). Upon catalytic hydrogenation followed by mild chromic acid oxidation, 9-dehydromanogenin diacetate yields manogenin diacetate (VIII), identical with a sample from kammogenin diacetate (IX) prepared by similar treatment. This product (VIII) from 9-dehydromanogenin (VII) has been further characterized by a Wolff–Kishner reduction to furnish gitogenin, identical with gitogenin isolated from *Digitalis*. The presence of further unsaturation in VII seems unlikely since the products from the catalytic hydrogenation and sodium–alcohol reduction yield on mild oxidation the same keto-diacid, manogenic acid (VI).

TABLE II

COMPARISON OF THE PROPERTIES OF THE 9-DEHYDROSAPOGENINS AND RELATED SAPOGENINS[a]

	Genin	M.p., °C.	$[\alpha]^{25}D$	Acetate	M.p., °C.	$[\alpha]^{25}D$
9-Dehydrohecogenin (I)	$C_{27}H_{40}O_4$	235	-11^b	$C_{29}H_{42}O_5$	227	-7^b
Hecogenin (III)	$C_{27}H_{42}O_4$	268	$+18^b$	$C_{29}H_{44}O_5$	245	$+4^b$
9-Dehydromanogenin (VII)	$C_{27}H_{40}O_5$	240	-16^b	$C_{31}H_{44}O_7$	263	-62
Manogenin (VIII)	$C_{27}H_{42}O_5$	246	0	$C_{31}H_{46}O_7$	264	-42
Kammogenin (IX)	$C_{27}H_{40}O_5$	242	....	$C_{31}H_{44}O_7$	264	-82
Agavogenin (V)	$C_{27}H_{44}O_5$	240	-62	$C_{33}H_{50}O_8$	230	-98
Gitogenin (IV)	$C_{27}H_{44}O_4$	271	-61	$C_{31}H_{48}O_6$	242	-91
Rockogenin (II)	$C_{27}H_{44}O_4$	220	....	$C_{31}H_{48}O_6$	206	-63
Yuccagenin	$C_{27}H_{42}O_4$	246	-113	$C_{31}H_{46}O_6$	177	-127

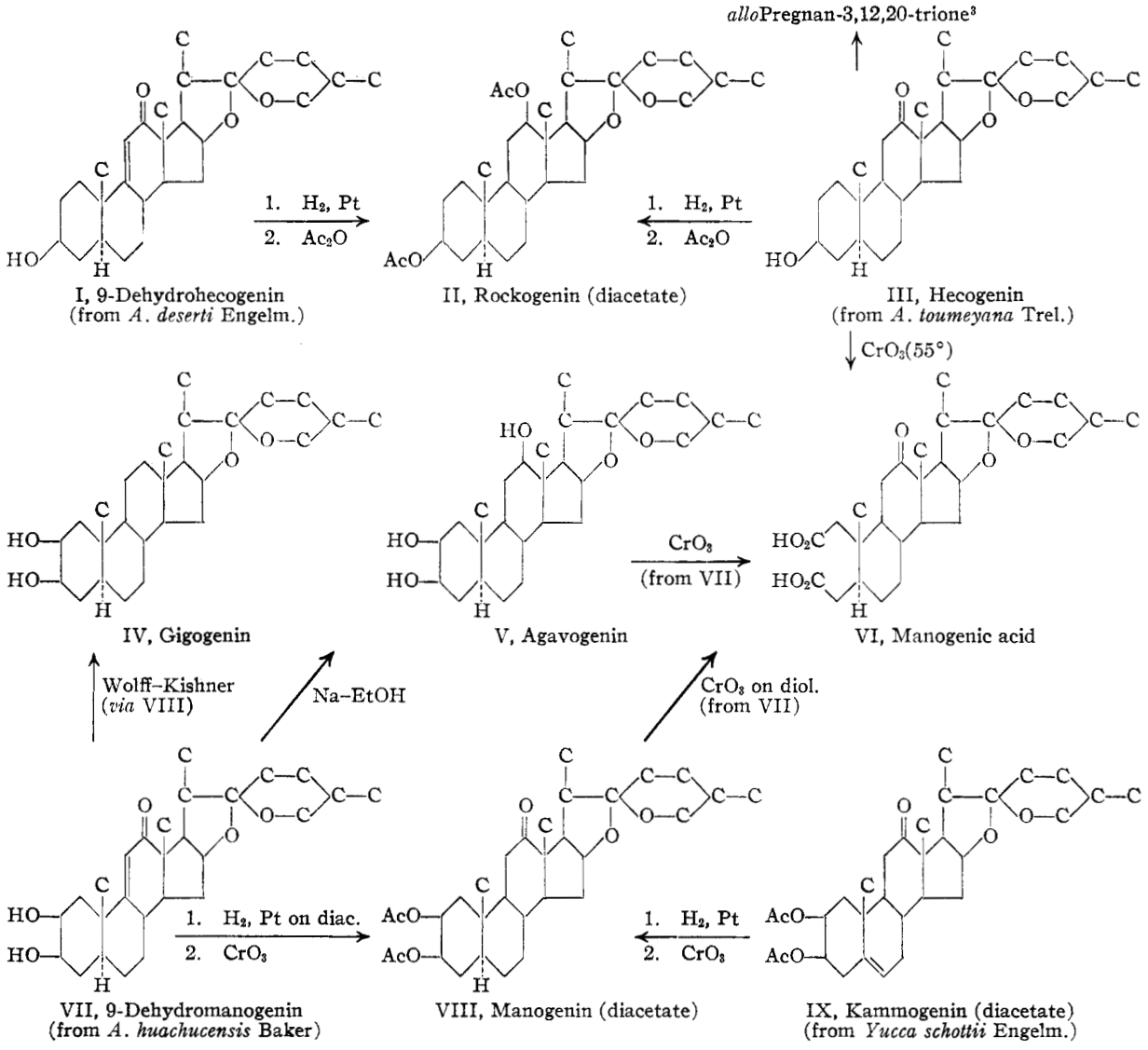
[a] All rotations were observed in dioxane. [b] See Experimental section under Rotations.

Finally, the position of the carbonyl group in 9-dehydromanogenin has been shown to be at C-12 by

(1) R. E. Marker, R. B. Wagner, P. R. Ulshafer, E. L. Wittbecker, D. P. J. Goldsmith and C. H. Ruof, THIS JOURNAL, **65**, 1199 (1943); *ibid.*, **69**, 2167 (1947).

(2) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1949, p. 184.

(3) R. B. Wagner, J. A. Moore and R. F. Forker, THIS JOURNAL, **72**, 1856 (1950).



comparing its derived keto diacid (VI) and the dimethyl ester with the corresponding derivatives obtained by vigorous oxidation of hecogenin (III). It has been necessary to repeat the preparation of manogenic acid (VI) since the original products[1] showed rather large ultraviolet absorption maxima characteristic of the 9-dehydrosapogenins. A comparison of the properties of the dimethyl ester of this new sample with those of other keto dimethyl esters (chlorogenic, digitogenic and 7-ketogitogenic esters) is included. Since all of these keto acids have been converted to gitogenic dimethyl ester, they differ among themselves only in the position of the carbonyl group.

The ring-C-oxygenated sapogenins have been considered as possible starting materials for the synthesis of anti-arthritic compounds. For this reason, the isolation of these 9-dehydrosapogenins is significant in that it raises the possibility of the presence of other sapogenins having this important ring-C structure in plants of this general classification. In this respect, it is noteworthy that many of the sapogenins lacking or having a C-12 oxygen occur in pairs, *i.e.*, tigogenin–hecogenin, gitogenin–manogenin, diosgenin–botogenin, etc. In accord with a possible biogenetic relationship[1] other Δ^9-12-keto analogs should occur and the isolation of a sapogenin having the structure of Δ^9-12-ketodiosgenin (9-dehydrobotogenin) might be anticipated. It would be particularly desirable for the synthesis of cortisone. Of course, a good source of botogenin, hecogenin or 9-dehydrohecogenin would also be desirable. In the present work, only a very small amount of the latter has been isolated. 9-Dehydromanogenin and hecogenin seem to be more widely distributed in plants, particularly the *Agaves*. It should be pointed out, however, that the sapogenin fractions from the *Agaves* are often complex and vary with the age of the plant.[1] For these reasons, the separation and purification of the sapogenins may be difficult. On the other hand, diosgenin which at first was isolated from the more difficultly obtainable species of the *Liliaceae* family is now readily available from the *Dioscoreaceae*. It has found a practical use in the synthesis of certain hormones.

We thank Parke, Davis and Company for their help.

Experimental

All melting points are uncorrected. Ultraviolet spectra data were obtained in a Beckman quartz spectrophotometer using alcohol as the solvent.

Rotations.—All rotations were observed in a 1-dm. tube with 1-cc. volume. Peroxide-free dioxane purified by acid[4] and base[5] treatment and stored under nitrogen was used as the solvent. The steroidal sapogenins are relatively insoluble in many of the usual solvents, but dioxane appears to be the most satisfactory. It is noteworthy that the actual observed rotations for hecogenin and 9-dehydrohecogenin were extremely low (0.03 to 0.15°); consequently, it is felt that the specific rotations for these substances may or may not be accurate.

Isolation of 9-Dehydrohecogenin (I) from *Agave deserti* Engelm.—The hecogenin fraction from *Agave deserti* Engelm.,[1] m.p. 244–247°, 610 mg., λ_{max}^{alc} 238 mμ (log ε 3.5) was dissolved in 110 ml. of dry benzene and the solution was poured onto 18 g. of 80–200-mesh Alcoa activated alumina contained in a tube (10 mm. diameter). The column was eluted successively with benzene, 400 ml. of 8% ether in benzene, 2100 ml. of pentane in ether gradually increasing the ether concentration, then 1600 ml. of ether, and finally 300 ml. of 0.5% methanol in ether. 9-Dehydrohecogenin, 74 mg., was obtained during the elution with methanol–ether, previous elutions yielding impure material. It was recrystallized twice from methanol as needles, m.p. 235, $[\alpha]^{24}D$ −11° (*c*, 1.32), λ_{max}^{alc} 238 mμ (log ε 4.1); estimated yield: 1.5 g./kg. of dry plant.

Anal. Calcd. for $C_{27}H_{40}O_4$: C, 75.7; H, 9.4. Found: C, 75.7; H, 9.5.

The **acetate** was prepared by heating 46 mg. of the above with 1 ml. of acetic anhydride and 1 ml. of pyridine for 90 minutes. The mixture was evaporated to dryness and the residue was crystallized twice from methanol as needles, m.p. 224–227°, $[\alpha]^{25}D$ −7° (*c*, 2.01), wt. 35 mg.

Anal. Calcd. for $C_{29}H_{42}O_5$: C, 74.0; H, 9.0. Found: C, 74.1; H, 9.1.

Rockogenin Diacetate (II) (a) From 9-Dehydrohecogenin Diacetate (I).—A solution of 9-dehydrohecogenin diacetate, 39 mg., in 100 ml. of ether containing five drops of acetic acid was shaken with 0.1 g. of Adams catalyst and hydrogen at room temperature and three atm. for three hours. The mixture was filtered and evaporated. The residue was washed with pentane, wt. 39 mg., and then acetylated as described above. The product was crystallized twice from methanol, m.p. 200–203°, $[\alpha]^{25}D$ −68° (*c*, 1.00), wt. 20 mg. A mixture with rockogenin diacetate prepared in (b) melted at 200–204°.

Anal. Calcd. for $C_{31}H_{48}O_6$: C, 72.1; H, 9.4. Found: C, 72.4; H, 9.5.

(b) **From Hecogenin (III).**—Hecogenin, m.p. 268°, $[\alpha]^{24}D$ +18° (*c*, 0.564), wt. 40 mg., isolated from *Agave toumeyana* Trel. was hydrogenated followed by acetylation as described in (a) to yield rockogenin diacetate, m.p. 204–206°, $[\alpha]^{25}D$ −63° (*c*, 1.28).

Anal. Calcd. for $C_{31}H_{48}O_6$: C, 72,1; H, 9.4. Found: C, 72.2; H, 9.4.

Isolation of 9-Dehydromanogenin (VII) from *Agave huachucensis* Baker.—One of several manogenin diacetate fractions,[1] wt. 0.9 g., m.p. 237°, λ_{max}^{alc} 238 mμ (log ε 3.9) was dissolved in 200 ml. of pentane–benzene (1:1). The solution was poured onto 27 g. of alumina and the column was eluted as described before to give three distinct bands. Elution with pure benzene gave impure 9-dehydromanogenin diacetate. Elution with 1% methanol in ether gave material, m.p. 243–248°, λ_{max}^{alc} 238 mμ (log ε 4.1), wt. 0.1 g., which was not identified but analyzed for the monoacetate. Elution with 7–100% methanol in ether gave pure 9-dehydromanogenin which was crystallized from ether, m.p. 237–240°, $[\alpha]^{24}D$ −16° (*c*, 0.88), λ_{max}^{alc} 238 mμ (log ε 4.1); wt. 0.1 g.; estimated yield: 0.1 g./kg. of dry plant.

Anal. Calcd. for $C_{27}H_{40}O_5$: C, 72.9; H, 9.1. Found: C, 73.1; H, 9.4.

In a similar manner, the unacetylated material was purified by chromatography to give the same product, m.p. and mixed m.p., 237°, λ_{max}^{alc} 238 mμ (log ε 4.1).

The diacetate was prepared by the acetic anhydride–pyridine procedure and crystallized from ether and then methanol, m.p. 261–263°, $[\alpha]^{24}D$ −62° (*c*, 1.34), λ_{max}^{alc} 237 mμ (log ε 4.1).

Anal. Calcd. for $C_{31}H_{44}O_7$: C, 70.4; H, 8.3. Found: C, 70.7; H, 8.6.

Agavogenin (V) from 9-Dehydromanogenin (VII).—To a solution of 511 mg. of 9-dehydromanogenin diacetate in 300 ml. of absolute ethanol was added 23 g. of sodium over a period of 40 minutes. After the sodium had reacted the reaction mixture was diluted with water and neutralized with hydrochloric acid. The alcohol was removed by bubbling nitrogen through the hot mixture. The ethereal solution of the product was washed with water and evaporated to give crystals which were recrystallized from aqueous methanol, m.p. 238–240°, $[\alpha]^{25}D$ −62° (*c*, 1.02), no maximum at λ238 mμ; yield 58%.

Anal. Calcd. for $C_{27}H_{44}O_5$: C, 72.3; H, 9.9. Found: C, 72.1; H, 10.1.

The triacetate was prepared by heating the above triol with acetic anhydride–pyridine mixture for eight hours. The product was crystallized from ether, m.p. and mixed m.p. with agavogenin triacetate, 228–230°, $[\alpha]^{26}D$ −98° (*c*, 2.09).

Anal. Calcd. for $C_{33}H_{50}O_8$: C, 68.9; H, 8.8. Found: C, 68.3; H, 9.1.

Manogenin Diacetate (VIII) (a) From 9-Dehydromanogenin Diacetate (VII).—An ethereal solution of 9-dehydromanogenin diacetate, 1.00 g., containing fifteen drops of acetic acid was shaken with hydrogen and 0.6 g. of Adams catalyst for five hours at room temperature and three atm. After filtering and evaporating to a small volume, crystals were obtained, m.p. 248°, wt. 0.85 g. This material was dissolved in 90 ml. of acetic acid and oxidized at room temperature for 3.5 hours with 0.9 g. of chromic anhydride dissolved in 27 ml. of 50% aqueous acetic acid. The excess oxidizing agent was destroyed by methanol and water was added. The product was extracted with ether and the ethereal solution was washed with 5% sodium hydroxide and then water. The solution was dried and evaporated to a small volume to give material melting at 255–258°. Two crystallizations from methanol yielded needles, m.p. 261–264°, $[\alpha]^{26}D$ −42° (*c*, 1.51), no maximum at λ237 mμ; yield 624 mg. A mixture with starting material showed a melting point depression of 10°.

Anal. Calcd. for $C_{31}H_{46}O_7$: C, 70.2; H, 8.7. Found: C, 70.4; H, 9.1.

Manogenin was prepared by hydrolyzing 320 mg. of the diacetate with 5 ml. of 10% alcoholic potassium hydroxide under reflux for 30 minutes. The product was extracted with ether and the ethereal solution was washed with water, dried and then evaporated to a small volume to give crystals, m.p. 243–246°, $[\alpha]^{26}D$ 0° (*c*, 1.7); yield 140 mg.

(b) **From Kammogenin Diacetate (IX).**—Kammogenin diacetate, m.p. 262–264°, $[\alpha]^{25}D$ −82° (*c*, 2.42), no max. at λ238 mμ, 500 mg., isolated from *Yucca schottii* Engelm., was hydrogenated as described above to give material which did not depress the melting point of the intermediate product from above (a). Oxidation was carried out as before to give the product melting at 255–259°, wt. 330 mg. Two recrystallizations from ether gave needles, m.p. and mixed m.p. with material from (a), 259–262°, $[\alpha]^{25}D$ −46° (*c*, 1.92).

Gitogenin (IV) from Manogenin Diacetate (VIII).—Manogenin diacetate, 320 mg., synthesized from 9-dehydromanogenin diacetate was heated with a solution of 3 g. of sodium in 60 ml. of absolute ethanol and 6 ml. of 85% hydrazine hydrate in a sealed tube at 200° for 12 hours. The reaction mixture was poured into water and acidified with 10 ml. of concentrated hydrochloric acid. The alcohol was removed by passing a stream of nitrogen through the hot solution. The precipitate was extracted with ether and crystallized from ether as needles, m.p. and mixed m.p. with an authentic sample of gitogenin from *Digitalis*, 268–271°, $[\alpha]^{24}D$ −61° (*c*, 0.84).

The diacetate was prepared and crystallized from methanol, m.p. and mixed m.p. with gitogenin diacetate, 242–244°, $[\alpha]^{25}D$ −91° (*c*, 1.56).

(4) K. E. Kavanagh and F. F. Nord, THIS JOURNAL, **65**, 2121 (1943).

(5) G. W. Beste and L. P. Hammett, *ibid.*, **62**, 2481 (1940).

9-Dehydromanogenic Acid.—9-Dehydromanogenin diacetate, 203 mg., was hydrolyzed with 5% alcoholic potassium hydroxide and then oxidized with 210 mg. of chromic anhydride in 18 ml. of acetic acid for one hour at room temperature. Methanol and water was added and the mixture was extracted with ether. The acid fraction was recovered by a 5% aqueous potassium hydroxide wash followed by acidification and extraction with ether. The product, wt. 106 mg., from ether was crystallized from 80% acetic acid and then from glacial acetic acid, m.p. 265–267° (dec.), $[\alpha]^{24}D$ 0° (*c*, 0.99), λ_{max}^{alc} 240 mμ (log ε 4.0); wt. 24 mg.

Anal. Calcd. for $C_{27}H_{38}O_7$: C, 68.2; H, 8.0. Found: C, 67.7; H, 8.3.

The dimethyl ester was prepared by treating the diacid, 80 mg., with an excess of diazomethane in ether at 0° for three hours. The excess diazomethane was destroyed with acetic acid and the ethereal solution was washed with dilute sodium bicarbonate and water and then dried and evaporated. The residue was crystallized four times from methanol to raise the melting point from 171–177° to 178–180°, $[\alpha]^{26}D$ +4° (*c*, 1.10). A mixture with the dimethyl ester of manogenic acid (163°) melted at 170–176°.

Anal. Calcd. for $C_{29}H_{42}O_7$: C, 69.3; H, 8.4. Found: C, 69.0; H, 8.4.

Manogenic Acid (VI) (a) From 9-Dehydromanogenin.—9-Dehydromanogenin, 217 mg., was hydrogenated in ether with a trace of acetic acid as described for the reduction of the diacetate. The intermediate product showed no absorption maximum at λ240 mμ. It was then dissolved in acetic acid and oxidized at room temperature by the procedure described for the preparation of the unsaturated acid to give manogenic acid which was crystallized from acetic acid, m.p. and mixed m.p. with manogenic acid from hecogenin, 266–269° (dec.); wt. 64 mg. A mixture with 9-dehydromanogenic acid showed a melting point depression of 5°.

Anal. Calcd. for $C_{27}H_{40}O_7$: C, 68.0; H, 8.5. Found: C, 67.4; H, 8.4.

The dimethyl ester was prepared with excess diazomethane and crystallized from methanol as needles, m.p. and mixed m.p. with the dimethyl ester of manogenic acid from hecogenin, 161–163°.

Anal. Calcd. for $C_{29}H_{44}O_7$: C, 69.0; H, 8.8. Found: C, 68.9; H, 8.5.

By a similar route, 9-dehydromanogenin was first reduced with sodium and alcohol in a manner described for the preparation of agavogenin and then oxidized at room temperature with chromic anhydride in acetic acid followed by methylation to yield the same dimethyl ester, m.p. and mixed m.p. 163–165°, $[\alpha]^{20}D$ +4 (*c*, 1.40), no maximum at λ240 mμ.

Anal. Calcd. for $C_{29}H_{44}O_7$: C, 69.0; H, 8.8. Found C, 69.5; H, 8.9.

The dimethyl ester of chlorogenic acid (6-ketogitogenic acid) has m.p. 163° and $[\alpha]^{25}D$ −44° (*c*, 1.26). A mixture with the above dimethyl ester (VI) showed a melting point depression of 20°.

The dimethyl ester of digitogenic acid (15-ketogitogenic acid) has m.p. 155° and $[\alpha]^{25}D$ −48° (*c*, 2.07). A mixture with the above ester (VI) showed a melting point depression of 20°.

The dimethyl ester of 7-ketogitogenic melts at 189° and the keto diacid melts at 293° (dec.).[1] No samples were available for direct comparisons.

(b) From Hecogenin.—Hecogenin, m.p. 265–268°, isolated from *Agave toumeyana* Engelm. was oxidized at room temperature with chromic anhydride in acetic acid to give hecogenone, m.p. 237–240°, $[\alpha]^{26}D$ +17° (*c*, 1.30). To 1.6 g. of this material dissolved in 90 ml. of acetic acid was added a solution of 1.1 g. of chromic anhydride in 11 ml. of 90% acetic acid. The temperature was kept at 31° for 90 minutes and then heated at 55° for three hours. The excess oxidizing agent was destroyed with methanol and the mixture was evaporated to a small volume and extracted with ether. The ethereal solution was washed with aqueous sodium bicarbonate and evaporated to give 0.5 g. of unreacted hecogenone. The alkaline extract was partially acidified until a small acid fraction precipitated, wt. 53 mg., which was crystallized twice from acetic acid as white crystals, m.p. 269–272° (dec.).

The dimethyl ester was prepared with excess diazomethane and crystallized three times from methanol, m.p. 160–162°. This material did not exhibit an absorption peak at 240 mμ. A lack of sufficient material prohibited a rotation.

Anal. Calcd. for $C_{29}H_{44}O_7$: C, 69.0; H, 8.8. Found: C, 69.2; H, 8.9.

STATE COLLEGE, PENNA. RECEIVED NOVEMBER 17, 1950

[CONTRIBUTION FROM THE LANKENAU HOSPITAL RESEARCH INSTITUTE AND THE INSTITUTE FOR CANCER RESEARCH, PHILADELPHIA]

The Preparation of the Diastereoisomers of Cystathionine and Homolanthionine[1]

BY SIDNEY WEISS AND JAKOB A. STEKOL

Homoserine or its lactone was resolved with brucine through its N-*p*-nitrobenzoyl derivative. The D- and L-α-amino-γ-butyrolactone hydrobromides were then converted to the corresponding optically active 3,6-bis-(β-hydroxyethyl)-2,5-diketopiperazines which, after chlorination, yielded D- and L-3,6-bis-(β-chloroethyl)-2,5-diketopiperazines. By a suitable choice of the isomers of cysteine or homocysteine, or their S-benzyl derivative, and of the isomers of the dichlorodiketopiperazines, L-cystathionine, L-allocystathionine and the L, D and *meso* forms of homolanthionine were prepared by condensation in liquid ammonia and sodium. This procedure is suitable for the direct preparation of radioactive isomers of methionine, homocystine, cystathionine, homolanthionine or any α-amino-γ-thioether of butyric acid.

Previous studies[2] have established that homolanthionine,[3] the next higher homolog of cystathionine, can be converted to cystine by the rat. The homolanthionine used in these experiments was a mixture of isomers and the question arose as to which of these are active *in vivo*. This paper presents the preparation of the individual isomers of homolanthionine as well as those of cystathionine.

The procedure for the preparation of cystathionine and homolanthionine[3] was based on the use of an extremely useful intermediate, 3,6-bis-(β-chloroethyl)-2,5-diketopiperazine of Snyder and co-workers who have used it for the syntheses of racemic methionine,[4] 3,6-bis-(β-benzylthioethyl)-2,5-diketopiperazine[5] and homocystine.[6]

The separation of mixtures of cystathionine (L- and L-*allo*) and homolanthionine (L, D and *meso*) was attempted by enzymatic resolution with pap-

(1) Aided by grants from the Williams-Waterman fund of the Research Corporation, and from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service. This paper was presented before the Biological Division of the American Chemical Society in Chicago, Illinois, September, 1950.

(2) J. A. Stekol and K. Weiss, *J. Biol. Chem.*, **175**, 405 (1948); **179**, 67 (1949).

(3) J. A. Stekol, *ibid.*, **173**, 153 (1948).

(4) H. R. Snyder, J. H. Andreen, G. W. Cannon and C. F. Peters, THIS JOURNAL, **64**, 2084 (1942).

(5) H. R. Snyder and M. F. Chiddix, *ibid.*, **66**, 1000 (1944).

(6) H. R. Snyder and G. W. Cannon, *ibid.*, **66**, 500 (1944).