

and heated to 50°. With constant stirring, a solution of 1.5 g. of chromic acid in 75 cc. of 80% acetic acid was added during thirty minutes. The stirring was continued for five hours during which time the temperature was kept at 50°. After addition of 6 g. of zinc dust the solution was heated fifteen minutes on the steam-bath. The mixture was filtered, the filtrate evaporated *in vacuo* and the residue was taken up with ether and water, the ether layer was washed with water, evaporated and the residue boiled with 100 cc. of 2% methanolic potassium hydroxide for thirty minutes. After the addition of water and ether the alkaline layer was separated, acidified, and extracted with ether. Evaporation of the ether gave a residue; m. p. 273–274° after crystallization from dioxane.

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 75.4; H, 9.5. Found: C, 75.1; H, 9.6.

21-Benzal-progesterone.—A solution of 1 g. of 21-benzal-5-pregnen-3(β)-ol-20-one, 1.5 g. of aluminum *t*-butylate 7 cc. of dry acetone and 40 cc. of dry toluene was refluxed for five hours. The solution was poured into dilute hydrochloric acid and steam distilled vigorously to remove acetone polymers and the amorphous product was then taken up in ether, washed free of salts and the ether evaporated. The residue was crystallized from methanol to m. p. 155–158°.

Anal. Calcd. for $C_{28}H_{38}O_2$: C, 83.5; H, 8.5. Found: C, 83.1; H, 8.2.

21-Benzyl-progesterone.—A mixture of 10 g. of 21-benzal-5-pregnen-3(β)-ol-20-one acetate, 10 g. of 3% palladium-barium sulfate catalyst and 150 cc. of dioxane was shaken with hydrogen at room temperature and 3 atm. for ninety minutes. The catalyst was removed by filtering and the filtrate evaporated *in vacuo*. The residue melted at 128–129° (143–145° two forms) on crystallization from methanol.

Anal. Calcd. for $C_{30}H_{40}O_2$: C, 80.3; H, 9.0. Found: C, 80.6; H, 9.3.

A mixture of 4.5 g. of the above acetate, 4.5 g. of potassium bicarbonate and 300 cc. of 70% methanol was refluxed for three hours. Dilution with water gave a crystalline precipitate which was recrystallized from methanol to m. p. 135–136°; mixed m. p. with starting material 90–108°; 3.7 g.

Anal. Calcd. for $C_{28}H_{38}O_2$: C, 82.7; H, 9.4. Found: C, 82.3; H, 9.6.

A mixture of 1 g. of 21-benzyl-5-pregnen-3(β)-ol-20-one, 1.5 g. of aluminum *t*-butoxide, 5 cc. of dry acetone and 30 cc. of dry toluene was refluxed for five hours. The mixture was worked up in the usual manner and the residue from the ether purified by passing a ligroin solution through a short column of alumina. It was crystallized from ether-ligroin to m. p. 86–88°.

Anal. Calcd. for $C_{28}H_{38}O_2$: C, 83.1; H, 8.9. Found: C, 83.2; H, 9.4.

Summary

1. 3(β)-Hydroxy-*etio*-cholic acid has been prepared from 21-benzal-pregnan-3(β)-ol-20-one.

2. *allo*-Pregnan-3(α)-ol-20-one has been converted to 21-benzal-*allo*-pregnan-3(α)-ol-20-one and thence to 3(α)-hydroxy-*etio-allo*-cholic acid.

3. 5-Pregnen-3(β)-ol-20-one has been converted to 21-benzal-5-pregnen-3(β)-ol-20-one which in turn was converted to 3(β)-hydroxy-*etio*-cholic acid, 21-benzal-progesterone and 21-benzyl-progesterone.

STATE COLLEGE, PENNA. RECEIVED JANUARY 17, 1942

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

Sterols. CXLVI. Sapogenins. LX. Some New Sources of Diosgenin

BY RUSSELL E. MARKER, R. B. WAGNER AND PAUL R. ULSHAFFER

In two previous papers^{1,2} we have reported the isolation of diosgenin from *Trillium erectum* (L.), *Dioscorea villosa* and *Aletris formosa*. The only other source of this sapogenin was *Dioscorea tokora*.³ The easy conversion of diosgenin to progesterone⁴ made necessary the investigation of additional plant sources.

We have extracted the undried ground rhizomes of eight plants listed in the accompanying table by a procedure similar to that used in the isolation of sarsasapogenin.⁵ The results and the

geographical location of the plants are given in the table. The identity of the diosgenin was established by analysis of the genin and its acetate along with mixed melting point determinations on both.

Plant	Source	Yield of diosgenin, g. per lb.
1 <i>Chamaelirium carolinianum</i> ^a	Statesville, N. C.	0.1
2 <i>Tofieldia grammifolia</i> ^a	Hartsville, S. C.	0.5
3 <i>Dioscorea quartenata</i> ^a	Hartsville, S. C.	2.0
4 <i>Helonias</i> Root	S. B. Penick and Co.	...
5 <i>Trillium grandiflora</i> ^a	Trylon, N. C.	1.0
6 <i>Trillium sessile</i> ^a	Trylon, N. C.	1.0
7 <i>Clintonia borealis</i>	Southern New Hampshire	0.5
8 <i>Dioscorea hirticaulis</i> ^a	South Carolina	2.0

(1) Marker, Turner and Ulshafer, *THIS JOURNAL*, **62**, 2542 (1940).

(2) Marker, *et al.*, *ibid.*, **62**, 2620 (1940).

(3) Tsukamoto, Ueno and Ohta, *J. Pharm. Soc., Japan*, **56**, 135 (1936).

(4) Marker, Tsukamoto and Turner, *THIS JOURNAL*, **62**, 2525 (1941).

(5) Jacobs and Simpson, *J. Biol. Chem.*, **105**, 501 (1934).

^a We are grateful for the help of Mr. Budd E. Smith, Botany Department of the University of North Carolina, Chapel Hill, N. C., in the collection of these samples.

We thank Parke, Davis and Company for their help.

Experimental Part

The Isolation of Diosgenin from (a) *Dioscorea quartenata*.

--The undried roots weighing four pounds were ground in a food chopper, and the mass was refluxed for four hours with 5 liters of 95% alcohol. The extract was cooled overnight, filtered and the filter cake washed well with alcohol. The solvent was removed by vacuum distillation until a thick sirup remained. This was dissolved in a small amount of alcohol and defatted by stirring with ether. The ethereal layer was decanted from the precipitated gum, and the process repeated twice. The residue was dissolved in a liter of 95% alcohol and treated with 200 cc. of concentrated hydrochloric acid. This was heated under a condenser for two hours on a steam-bath. The mixture was cooled, water added, and the product extracted with ether. The ethereal solution was washed well with water and with dilute sodium hydroxide solution. The solvent was removed and the residue was crystallized from acetone as white needles; m. p. and mixed m. p. with an authentic sample of diosgenin, 206–207°; yield, approximately 2 g. per pound of undried roots.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.0; H, 10.2.

When refluxed with acetic anhydride it gave a product which was crystallized from methanol as white needles; m. p. and mixed m. p. with diosgenin acetate, 202–204°.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7. Found: C, 76.4; H, 9.9.

(b) *Trillium sessile*.—The undried roots were extracted as described under (a). The product was crystallized from acetone as white fine needles; m. p. and mixed m. p. with diosgenin, 205–207°; yield, approximately 1 g. per pound of undried roots.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.3; H, 10.4.

When refluxed with acetic anhydride it gave a product which was crystallized from methanol; m. p. and mixed m. p. with diosgenin acetate, 196–199°.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7. Found: C, 76.4; H, 9.6.

(c) *Tofieldia grammifolia*.—The undried roots were extracted as described in (a). It was crystallized from acetone to give a product melting at 196–200°. When mixed with sarsapogenin there was a 20° depression in melting point. A mixed m. p. with diosgenin gave no depression. The yield was approximately 0.5 g. per pound of undried roots.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.3; H, 10.2.

When refluxed with acetic anhydride it gave an acetate which melted at 196–198°. This gave no depression when mixed with an authentic sample of diosgenin acetate.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7. Found: C, 76.1; H, 9.7.

(d) *Dioscorea hirticaulis*.—The undried roots were ground and extracted and the sapogenin isolated as in (a). The product was crystallized from acetone; m. p. and

mixed m. p. with diosgenin, 207–208°; yield, approximately 2 g. per pound of undried roots.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.1; H, 10.2.

When refluxed with acetic anhydride it gave an acetate which was crystallized from methyl alcohol; m. p. and mixed m. p. with an authentic sample of diosgenin acetate, 197–199°.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7. Found: C, 76.2; H, 9.6.

(e) *Clintonia borealis*.—The undried roots were extracted with alcohol and the sapogenin isolated as in (a). The crude sapogenin could not be purified by direct crystallization. It was converted to the acetate and the latter was crystallized slowly from methanol; m. p. and mixed m. p. with diosgenin acetate, 197–199°; yield, approximately 0.5 g. per pound of undried roots.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7. Found: C, 76.4; H, 9.7.

When hydrolyzed with alcoholic potassium hydroxide, the above product gave material from acetone melting at 206–207°. This gave no depression in melting point with an authentic sample of diosgenin.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.5; H, 10.4.

(f) *Trillium grandiflora*.—The undried roots were extracted and the sapogenin isolated as in (a). The product was crystallized from acetone; m. p. and mixed m. p. with an authentic sample of diosgenin, 206–207°.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.4; H, 10.3.

When refluxed with acetic anhydride it gave an acetate which was crystallized from methyl alcohol; m. p. and mixed m. p. with an authentic sample of diosgenin acetate, 197–199°.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7. Found: C, 76.3; H, 9.7.

(g) *Helonias Root*.—The powdered root was extracted with alcohol and the extract concentrated, extracted well with ether and hydrolyzed as in (a). The sapogenin fraction would not crystallize from ordinary solvents. It was hydrolyzed by refluxing for thirty minutes with 5% alcoholic potassium hydroxide solution. Water was added, the product extracted with ether, and the solution washed well with water. The ether was removed, leaving a considerable amount of oil from which no crystalline product could be obtained. This was dissolved in alcohol and a solution of 20 g. of digitonin in 1 liter of 95% alcohol was added. The precipitated digitonide was filtered, dried, and decomposed in the usual way by heating with pyridine for one hour on a steam-bath. Ether was added and the precipitated digitonin was filtered off. The pyridine was removed from the filtrate by shaking with dilute hydrochloric acid. This procedure was repeated several times until no more digitonide formed when the original alcoholic solution of the oil was treated with digitonin. The combined ethereal solution of the sapogenin fraction was evaporated and the residue treated with boiling acetic anhydride for thirty minutes. Upon cooling the crystalline material was filtered and crystallized from ether; m. p.

and mixed m. p. with diosgenin acetate, 198–200°; yield, 1 g. from 15 lb. of dry root.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7. Found: C, 76.1; H, 10.0.

Hydrolysis of the acetate gave a product which was crystallized from acetone; m. p. and mixed m. p. with diosgenin, 208–210°.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.0; H, 10.0.

(h) *Chamaelirium carolinianum*.—Five pounds of the dried roots were pulverized in a mill to a fine powder and the sapogenin was isolated as in (g). The unacetylated product was crystallized from acetone; m. p. and mixed m. p. with diosgenin, 203–205°; yield, 0.4 g.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.0; H, 10.1.

When refluxed with acetic anhydride it gave an acetate which melted at 196–198° and gave no depression in melting point when mixed with an authentic sample of diosgenin acetate.

Anal. Calcd. for $C_{29}H_{44}O_4$: C, 76.3; H, 9.7. Found: C, 76.5; H, 9.9.

Summary

Eight new sources for diosgenin have been reported.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE CITY COLLEGE, THE COLLEGE OF THE CITY OF NEW YORK]

Intermediates of Pentryl Analogs. Chloronitroanilino Alkanols¹

BY CHESTER B. KREMER AND M. MELTSNER

In the course of a study of the condensation of substituted nitrobenzenes with amino alcohols to produce intermediates from which analogs of pentryl can be obtained, the alcohols described below have been prepared and characterized. In these reactions, condensation occurs mainly through the amino group. Condensation through the alcohol group, to produce substituted amino ethers, is found to occur in some cases.

3-Amino-propanol-1 and 5-amino-propanol-1 were prepared from the appropriate bromo-alkylphthalimide through Gabriel syntheses.

2,5- and 3,4-dichloronitrobenzenes were commercial products which were further purified by recrystallization from dilute ethanol.

2,3-Dichloronitrobenzene was prepared either by the chlorination of *o*-chloronitrobenzene in the presence of antimony chloride,² or from 2,3-di-

TABLE I

Compound (R = nitroanilino)	NITRO ANILINO ALKANOLS		Molecular formula	Nitrogen, %	
	Cryst. from	M. p., °C.		Calcd.	Found
2-(4-Chloro-2-R)-ethanol	<i>n</i> -BuOH	107.5	$C_8H_9O_3N_2Cl$	12.93	13.04
3-(4-Chloro-2-R)-propanol-1	C_6H_6 -pet. ether	60	$C_9H_{11}O_3N_2Cl$	12.14	12.20
3-(4-Chloro-2-R)-propanol-2	C_6H_6	116.5	$C_9H_{11}O_3N_2Cl$	12.14	12.33
3-(4-Chloro-2-R)-2-methylpropanol-2	C_6H_6	121.5	$C_{10}H_{13}O_3N_2Cl$	11.55	11.32
2-(4-Chloro-2-R)-2,2-dimethylethanol	C_6H_6 -pet. ether	122	$C_{10}H_{13}O_3N_2Cl$	11.55	11.44
2-(6-Chloro-4-R)-ethanol	$C_6H_5CH_3$	120	$C_8H_9O_3N_2Cl$	12.93	13.05
3-(6-Chloro-4-R)-propanol-1	C_6H_6 -pet. ether	73	$C_9H_{11}O_3N_2Cl$	12.14	12.01
3-(6-Chloro-4-R)-propanol-2	EtOH	144	$C_9H_{11}O_3N_2Cl$	12.14	12.31
3-(6-Chloro-4-R)-2-methylpropanol-2	C_6H_6 -pet. ether	71.5	$C_{10}H_{13}O_3N_2Cl$	11.55	11.01
2-(5-Chloro-2-R)-ethanol	Dil. EtOH	116	$C_8H_9O_3N_2Cl$	12.93	13.07
3-(5-Chloro-2-R)-propanol-1	Dil. EtOH	78.5	$C_9H_{11}O_3N_2Cl$	12.14	11.99
3-(5-Chloro-2-R)-propanol-2	Dil. EtOH	109	$C_9H_{11}O_3N_2Cl$	12.14	12.10
3-(5-Chloro-2-R)-2-methylpropanol-2	C_6H_6 -pet. ether	127	$C_{10}H_{13}O_3N_2Cl$	11.55	11.54
2-(3-Chloro-2-R)-ethanol	Dil. EtOH	78.5	$C_8H_9O_3N_2Cl$	12.93	13.15
3-(3-Chloro-2-R)-propanol-2	C_6H_6 -pet. ether	83.5	$C_9H_{11}O_3N_2Cl$	12.14	12.04
3-(3-Chloro-2-R)-2-methylpropanol-2	Dil. EtOH	98.5	$C_{10}H_{13}O_3N_2Cl$	11.55	11.23
2-(6-Chloro-2-R)-ethanol	Oil	155–157 (2 mm.)(b. p.)	$C_8H_9O_3N_2Cl$	12.93	12.87

Materials.—1-Amino-propanol-2, 1-amino-2-methyl-propanol-2 and 2-amino-2-methyl-propanol-1 were commercial products which were purified by redistillation.

(1) The tenth paper in a series dealing with amino alcohols.

nitroaniline by the usual Sandmeyer reaction. The product, purified by vacuum distillation, melted at 61°.

2,4- and 2,6-dichloronitrobenzenes were pre-

(2) Holleman and Reiding, *Rec. trav. chim.*, **23**, 357–359 (1904).