genation and direct synthesis. A study of the oxidation potential of the alkylnitronitrosoguanidine system is in progress in comparison and extension of the previously reported studies of the oxidation potential of the nitronitrosoguanidine system.[9]

Summary

The reduction of α-alkyl-γ-nitroguanidines by the method of catalytic hydrogenation has been studied and the preparation of derivatives of α-alkyl-γ-nitroso- and γ-aminoguanidines is described. The structure of the alkylnitroguanidines previously based upon dearrangement and hydrolysis studies has been confirmed by comparison of the alkylaminoguanidines obtained by hydrogenation with those obtained by direct synthesis.

BROOKLYN, N. Y. RECEIVED AUGUST 16, 1937

[9] Smith and Sabetta, THIS JOURNAL, **54**, 1034 (1932).

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

Sterols. XXI. Lanosterol and Agnosterol

BY RUSSELL E. MARKER AND EUGENE L. WITTLE

We have shown recently that α-dihydrolanosterol can be converted into a compound which is identical with α-dihydroagnosterol obtained by the catalytic reduction of agnosterol.[1] Further proof that these two compounds are the same is shown by the fact that they give the same ketone, α-dihydroagnostenone upon dehydrogenation with copper at reduced pressure. Thus lanosterol and agnosterol differ only in the number and position of the double bonds and possess the same carbon structure.

Reduction of α-dihydroagnostenone with sodium in isopropyl alcohol gave the original α-dihydroagnosterol. With aluminum isopropylate in isopropyl alcohol, the ketone gave a mixture of epimers which did not precipitate with digitonin and which could be separated by crystallization of the acetates into α-dihydroagnosteryl acetate and the more soluble *epi*-α-dihydroagnosteryl acetate. These acetates gave a marked depression in melting point when mixed. When *epi*-α-dihydroagnosterol was dehydrogenated with copper, it gave α-dihydroagnostenone, which was identical with the product obtained by the oxidation of α-dihydroagnosterol.

Reduction of α-dihydrolanostenone with aluminum isopropylate in isopropyl alcohol gave a mixture of epimers which upon crystallization of the acetates gave *epi*-α-dihydrolanosteryl acetate, and α-dihydrolanosteryl acetate. Both compounds gave the original ketone upon hydrolysis and oxidation. Neither compound precipitated with digitonin.

The fact that neither of the epimers precipitates with digitonin is of interest in showing that the ring structure differs from other sterols and also from kryptosterol,[2] which is very similar to lanosterol in properties but precipitates with digitonin.

The failure of these epimers to precipitate with digitonin lends support to the conclusion of Schulze[3] that lanosterol and agnosterol are triterpenoid rather than steroid in character.

$$\begin{tikzcd}
\begin{array}{c}\alpha\text{-Dihydrolanosterol}\\149^\circ\end{array} \arrow[r] \arrow[d, shift right=2, "\mathrm{Cu}"'] & \begin{array}{c}\alpha\text{-Dihydroagnosterol}\\152^\circ\end{array} \arrow[d, shift right=2, "\mathrm{Cu}"'] \\
\begin{array}{c}\alpha\text{-Dihydrolanostenone}\\122^\circ\end{array} \arrow[u, shift right=2, "\text{Na in isopropyl alc.}"'] \arrow[d, shift left=2, "\text{Aluminum isopropylate}"] & \begin{array}{c}\alpha\text{-Dihydroagnostenone}\\130^\circ\end{array} \arrow[u, shift right=2, "\text{Na in isopropyl alc.}"'] \arrow[d, shift left=2, "\text{Aluminum isopropylate}"] \\
\begin{array}{c}epi\text{-}\alpha\text{-Dihydrolanosterol}\\139^\circ\end{array} \arrow[u, shift left=2, "\mathrm{Cu}"] \arrow[d, shift right=2, "\mathrm{Ac_2O}"'] & \begin{array}{c}epi\text{-}\alpha\text{-Dihydroagnosterol}\\130^\circ\end{array} \arrow[u, shift left=2, "\mathrm{Cu}"] \arrow[d, shift right=2, "\mathrm{Ac_2O}"'] \\
\begin{array}{c}epi\text{-}\alpha\text{-Dihydrolanosteryl}\\\text{acetate}\\167.5^\circ\end{array} \arrow[u, shift right=2, "\mathrm{KOH}"'] & \begin{array}{c}epi\text{-}\alpha\text{-Dihydroagnosteryl}\\\text{acetate}\\160^\circ\end{array} \arrow[u, shift right=2, "\mathrm{KOH}"']
\end{tikzcd}$$

Experimental

α-Dihydroagnostenone.—A mixture of 0.5 g. of α-dihydroagnosterol, m. p. 152°, and 0.8 g. of finely divided copper was heated at 250° under a pressure of 2 mm. for one hour. The product was then distilled and was crystallized from acetone-methyl alcohol and ethyl acetate giving 0.4 g. of material melting at 130° and crystallizing in large angular plates.

Anal. Calcd. for $C_{30}H_{48}O$: C, 84.8; H, 11.4. Found: C, 84.4; H, 11.5.

This ketone was obtained from α-dihydroagnosterol prepared by the reduction of agnosteryl acetate, and also from α-dihydroagnosterol prepared from α-dihydrolanosterol.[1]

The 2,4-dinitrophenylhydrazone crystallized in fine needles, m. p. 224°.

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[1] Marker, Wittle and Mixon, THIS JOURNAL, **59**, 1368 (1937).

[2] Wieland, Pasedack and Ballouf, *Ann.*, **529**, 68 (1937).

[3] Schulze, *Z. physiol. Chem.*, **190**, 51 (1936).

Reduction of α-Dihydroagnostenone with Sodium.—To a boiling solution of 0.1 g. of α-dihydroagnostenone in 60 cc. of dry isopropyl alcohol was added 3 g. of sodium over a period of one hour. The solution was poured into water and extracted with ether. The ether solution was washed with water and then was evaporated to dryness. The residue was crystallized from acetone–methyl alcohol mixture, m. p. 151°. This gave no depression in melting point with α-dihydroagnosterol. Conversion to the acetate gave α-dihydroagnosteryl acetate melting at 166° which gave no depression in melting point when mixed with an authentic sample of the acetate.

Reduction of α-Dihydroagnostenone with Aluminum Isopropylate.—A solution of 1.8 g. of α-dihydroagnostenone and 2.0 g. of aluminum isopropylate in 80 cc. of dry isopropyl alcohol was refluxed for six hours on a steam-bath. The alcohol was slowly distilled over a period of six hours. The solution was poured into 300 cc. of water and shaken with 200 cc. of ether. Dilute hydrochloric acid was then added, the ether was separated and evaporated to dryness. The residue was refluxed for one-half hour with 15 cc. of acetic anhydride and the acetate mixture recrystallized fifteen times from ethyl acetate to give 0.3 g. of α-dihydroagnosteryl acetate, m. p. 167.5°. The filtrates from the first five crystallizations were combined and evaporated to dryness. The residue was crystallized from ethyl acetate six times to give 0.1 g. of *epi*-α-dihydroagnosteryl acetate, m. p. 160°. A mixed melting point of the two acetates gave a depression to 130–140°.

Anal. Calcd. for $C_{32}H_{52}O_2$: C, 82.0; H, 11.2. Found: C, 81.8; H, 11.3.

***epi*-α-Dihydroagnosterol.**—A solution of 0.1 g. of *epi*-α-dihydroagnosteryl acetate and 0.3 g. of potassium hydroxide in 50 cc. of ethyl alcohol was refluxed for one-half hour. The solution was poured into water and extracted with ether. The ether solution was washed with water, evaporated to dryness and the product was crystallized from methyl alcohol, m. p. 130°. The compound did not precipitate with digitonin in alcohol.

Anal. Calcd. for $C_{30}H_{50}O$: C, 84.4; H, 11.8. Found: C, 84.3; H, 12.0.

Treatment of this compound with excess acetic anhydride gave the original acetate, m. p. 160°.

Conversion to α-Dihydroagnostenone.—A mixture of 0.2 g. of *epi*-α-dihydroagnosterol and 0.3 g. of precipitated copper was refluxed for one-half hour at 250° and 2 mm. pressure. The product was then distilled and crystallized from ethyl acetate giving α-dihydroagnostenone, m. p. 130°. When mixed with α-dihydroagnostenone prepared from α-dihydroagnosterol, there was no depression in melting point.

Reduction of α-Dihydrolanostenone with Aluminum Isopropylate.—A solution of 1.0 g. of α-dihydrolanostenone and 1.0 g. of aluminum isopropylate in 50 cc. of dry isopropyl alcohol was refluxed for seven hours and then 25 cc. of alcohol was slowly distilled over a period of five hours. The solution was poured into 100 cc. of water and 100 cc. of ether, shaken and acidified with dilute hydrochloric acid. The ether was evaporated to dryness and the residue was converted into the acetates by refluxing with an excess of acetic anhydride. The acetates were crystallized from ethyl acetate to give 0.3 g. of *epi*-α-dihydrolanosteryl acetate as the less soluble acetate, m. p. 167.5°.

Anal. Calcd. for $C_{32}H_{54}O_2$: C, 81.6; H, 11.6. Found: C, 81.5; H, 11.5.

***epi*-α-Dihydrolanosterol.**—A solution of 160 mg. of *epi*-α-dihydrolanosteryl acetate and 300 mg. of potassium hydroxide in 50 cc. of ethyl alcohol was refluxed for one-half hour, poured into water and extracted with ether. The ether was evaporated to dryness and the residue was crystallized from acetone–methyl alcohol and ethyl acetate to give 140 mg. of *epi*-α-dihydrolanosterol in thick needles, m. p. 139°.

Anal. Calcd. for $C_{30}H_{52}O$: C, 84.0; H, 12.1. Found: C, 83.6; H, 12.2.

On treatment with acetic anhydride this compound gave the original acetate, m. p. 167.5°. It did not precipitate with alcoholic digitonin solution.

Conversion of *epi*-α-Dihydrolanosterol to α-Dihydrolanostenone.—A mixture of 0.1 g. of *epi*-α-dihydrolanosterol and 0.2 g. of precipitated copper was heated at 250–300° and 2 mm. pressure for one-half hour and then was distilled. The distillate was crystallized from acetone–methyl alcohol, m. p. 120°. No depression in melting point was obtained when mixed with α-dihydrolanostenone prepared from α-dihydrolanosterol.

Summary

Dehydrogenation of α-dihydroagnosterol with copper gave α-dihydroagnostenone, which upon reduction with aluminum isopropylate gave a mixture of α-dihydroagnosterol and *epi*-α-dihydroagnosterol. These were separated by crystallization of their acetates. Similarly α-dihydrolanostenone gave α-dihydrolanosterol and *epi*-α-dihydrolanosterol. The epimeric compounds gave the original ketones upon oxidation.

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