PYRYLIUM DERIVATIVES OF STEROID HYDROXYMETHYLENEKETONES

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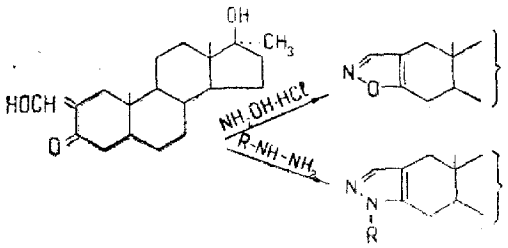
Khimiya Prirodnykh Soedinenii, Vol. 1, No. 5, pp. 318-321, 1965

Recently, great attention has been devoted to heterocyclic compounds of the steroid series. This is explained by the fact that some of these compounds possess valuable physiological properties. For example, some steroid isoxazoles obtained by the condensation of the readily accessible hydroxymethyleneketones of the steroid series [1] with hydroxylamine [2, 3] possess a valuable myotrophic and anabolic action with a low androgenic activity and a complete absence of estrogenic action.

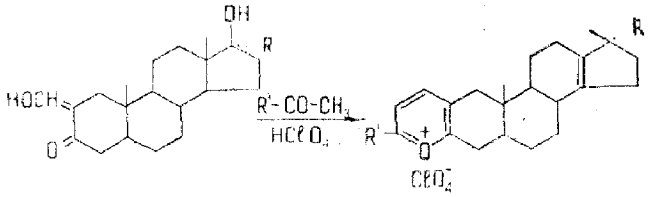
Not less interesting are some pyrazoles obtained by the condensation of steroid hydroxymethylene ketones with hydrazines [4]. Steroid components which have been used are derivatives of androstane, 19-norandrostane, and their saturated analogs.

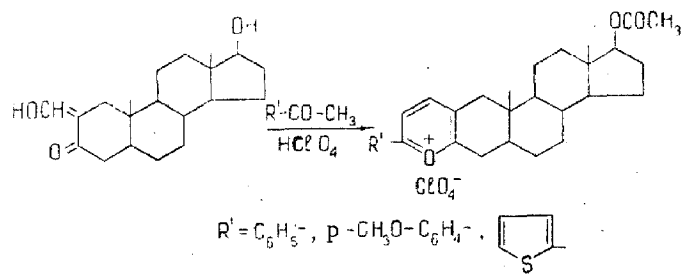


Steroid derivatives containing pyridine, quinoline, pyrimidine, pyrrole, indole, oxazine, triazole, and thiazole rings condensed with ring A have been obtained in a somewhat similar manner [5].

Continuing work on the synthesis of pyrylium salts by the condensation of hydroxymethyleneketones with ketones in the presence of perchloric acid [6], we have obtained a series of pyrylium salts from 2-hydroxymethylenedihydrotestosterone and 17α-ethyl-2-hydroxymethylenedihydrotestosterone, and a number of ketones (acetophenone, p-methoxyacetophenone, dimethoxyacetophenone, and 2-acetylthiophen).

The salts formed are crystalline substances readily soluble in acetic acid and acetone, insoluble in water and nonpolar solvents, crystallizing well from aqueous acetic acid. In solution and on irradiation with UV light, they exhibit an intense fluorescence. The IR spectra of all the compounds synthesized show two intense absorption bands at 1621-1618 and 1563-1556 cm^{-1} characteristic of the stretching vibrations of the C=C bonds of the pyrylium rings. The individuality of all the compounds obtained was confirmed by thin-layer chromatography on gypsum.





When the initial compounds contained a tertiary hydroxyl group, dehydration took place with the formation of a double bond, because, as is known from [7], perchloric acid is a strong dehydrating agent. The absence of the absorption bands of a hydroxyl group, as well as those of di- and tri-substituted double bonds, from the IR spectra of the

substance isolated is apparently explained by the fact that dehydration in an acid medium under similar conditions is accompanied by a Wagner-Meerwein rearrangement and the formation of a Δ^{13}-double bond [8]. The migrating methyl group of the compounds mentioned has a β configuration, because, according to [9], the rearrangement of this group takes place with retention of the configuration at C-17.

If, however, a secondary hydroxyl group is present (2-hydroxymethylenedihydrotestosterone), acetylation takes place under the reaction conditions. This is shown by the results of quantitative analysis and by the IR spectra of the compounds concerned: the spectra of all the pyrylium derivatives of 2-hydroxymethylenedihydrotestosterone contain two strong absorption bands at 1734-1736 and 1135 cm^{-1} which are characteristic for the acetates of steroid alcohols [10].

The pyrylium salts shown on p. 117 were synthesized in this way.

Experimental

6'-Phenyl-17β-methyl-17α-ethyl-Δ^{13}-androsteno[3,2-b]pyrylium perchlorate. A mixture of 1.730 g (0.005 mole) of 17α-ethyl-2-hydroxymethylenedihydrotestosterone, 1.200 g (0.01 mole) of acetophenone, 0.5 ml of 70% perchloric acid, and 10 ml of glacial acetic acid was heated on a boiling water bath for 30 min and, after cooling, was diluted with a large volume of ether. The precipitate which deposited was filtered off and was carefully washed with ether. This gave 0.840 g (32.8%) of a substance in the form of colorless needles with mp 209°, R_f 0.161 (benzene; purple spot in UV light). IR spectrum: 1621, 1563, 1507 cm^{-1}.

Found, %: C 70.41; H 7.40; Cl 6.40. Calculated for $C_{30}H_{37}ClO_5$, %: C 70.12; H 7.22; Cl 6.91.

6'-(p-Methoxyphenyl)-17β-methyl-17α-ethyl-Δ^{13}-androsteno[3,2-b]pyrylium perchlorate. A mixture of 0.692 g (0.002 mole) of 17α-ethyl-2-hydroxymethylenedihydrotestosterone, 0.600 g (0.004 mole) of p-methoxyacetophenone, 0.2 ml of 70% perchloric acid in 5 ml of glacial acetic acid gave 0.200 g (18.45%) of a substance in the form of bright yellow needles with mp 195-196°, R_f 0.290 (in benzene; green spot in UV light). IR spectrum: 1618, 1606, 1577, 1556, 1523, 1485, 1352, 1276, 1190, 1095, 1020, 838 cm^{-1}.

Found, %: C 68.49; H 7.37; Cl 6.23. Calculated for $C_{31}H_{39}ClO_6$, %: C 68.57; H 7.19, Cl 6.54.

6'-(Dimethoxyphenyl)-17β-methyl-17α-ethyl-Δ^{13}-androsteno[3,2-b]pyrylium perchlorate. A mixture of 1 g (0.0029 mole) of 17α-ethyl-2-hydroxymethylenedihydrotestosterone, 3 g (0.016 mole) of 3, 4-dimethoxyacetophenone, and 0.3 ml of 70% perchloric acid in 10 ml of glacial acetic acid gave 0.810 g (49.6%) of a substance in the form of dark red needles with mp 155-156°, R_f 0.226 [in a mixture of benzene and chloroform (7:8), yellow spot in UV light]. IR spectrum: 1621, 1606, 1557, 1530 cm^{-1}.

Found, %: C 66.56; H 7.29; Cl 6.87. Calculated for $C_{32}H_{41}ClO_7$, %: C 67.07; H 7.16; Cl 6.20.

6'-Phenyl-17-acetoxyandrostano[3,2-b]pyrylium perchlorate. A mixture of 0.636 g (0.002 mole) of 2-hydroxymethylenedihydrotestosterone, 0.480 g (0.004 mole) of acetophenone, and 0.2 ml of 70% perchloric acid in 5 ml of glacial acetic acid gave 0.500 g (45.9%) of a substance in the form of colorless plates with mp 187°, R_f 0.097 [in a mixture of benzene and chloroform (7:8), purple spot in UV light]. IR spectrum: 1734, 1621, 1562, 1509, 1135, 1090 cm^{-1}.

Found, %: C 66.42; H 7.14; Cl 6.11. Calculated for $C_{30}H_{37}ClO_7$, %: C 66.12; H 6.79; Cl 6.51.

6'-(p-Methoxyphenyl)-17-acetoxyandrostano[3,2-b]pyrylium perchlorate. A mixture of 0.636 g (0.002 mole) of 2-hydroxymethylenedihydrotestosterone, 0.600 g (0.004 mole) of p-methoxyacetophenone, and 0.2 ml of 70% perchloric acid in 5 ml of glacial acetic acid gave 0.240 g (20.9%) of a substance in the form of bright yellow needles with mp 188°, R_f 0.032 [in a mixture of benzene and chloroform (7:8), green spot in UV light]. IR spectrum: 1736, 1621, 1605, 1556, 1522, 1496 cm^{-1}.

Found, %: C 64.63; H 7.12; Cl 5.75. Calculated for $C_{31}H_{39}ClO_8$, %: C 64.75; H 6.78; Cl 6.18.

6'-(2-Thienyl)-17-acetoxyandrostano[3,2-b]pyrylium perchlorate. A mixture of 0.636 g (0.002 mole) of 2-hydroxymethylenedihydrotestosterone, 0.504 g (0.004 mole) of 2-acetylthiophene, and 0.2 ml of 70% perchloric acid in 5 ml of glacial acetic acid gave 0.250 g (22.7%) of a substance in the form of bright green needles with mp 259-260°, R_f 0.051 [in a mixture of benzene and chloroform (7:8); light blue spot in UV light]. IR spectrum: 1735, 1621, 1498 cm^{-1}.

Found, %: C 60.84; H 6.42; Cl 6.17. Calculated for $C_{28}H_{35}ClO_7$, %: C 61.04; H 6.36; Cl 6.45.

Summary

A number of derivatives of androstano[3,2-b]pyrylium and androst-13-eno-[3,2-b]pyrylium derivatives forming a new class of heterocyclic steroids has been obtained.

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19 March 1965

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