G. I. Zhungietu, G. N. Dorofeenko, Academician of the Academy of Sciences of the Moldavian SSR G. V. Lazur’ evskii

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Abstract

Full Text

Chemistry

G. I. Zhungietu, G. N. Dorofeenko, Academician of the Academy of Sciences of the Moldavian SSR G. V. Lazur’ evskii

Synthesis of Derivatives of 17-Methyldihydrotestosterone Condensed with Pyrylium and Pyridine Rings

In recent years there has been a considerable increase of interest in heterocyclic derivatives of steroid compounds possessing enhanced physiological activity. Syntheses of compounds of this type with condensed pyrazole (^{1}) and isoxazole (^{2}) rings are carried out on the basis of the condensation reaction of available oxymethylene ketones of the steroid series (^{3}).

Continuing work on the synthesis of pyrylium salts by the method of acid condensation of oxymethylene ketones with ketones (^{4}), we studied the condensation reaction of 2-oxymethylene-17-α-methyldihydrotestosterone with methyl ketones (acetone, acetophenone, *p*-methoxyacetophenone, α-acetylthiophene) in the presence of 70% perchloric acid. By this method it was possible to obtain, in yields of 24-42%, substituted pyrylium salts condensed in positions 2,3 with the steroid system:

$$\text{[reaction scheme]}$$
$$\text{where } R = \mathrm{CH_3},\ \mathrm{C_6H_5},\ p\text{-}\mathrm{CH_3OC_6H_4},\ \text{2-thienyl.}$$

The reaction proceeds on brief heating (1 h) of oxymethylene ketone (I) with a 1.5-2-fold excess of methyl ketone and 70% perchloric acid (in an equimolecular amount) in acetic acid solution on a boiling water bath. The condensation is accompanied by dehydration of the steroid component and by a Wagner-Meerwein rearrangement occurring as a result of elimination of the tertiary hydroxyl from position 17, since it is known that hydrochloric acid is an effective agent for the dehydration reaction of tertiary alcohols (^{5}).

The pyrylium salts formed are precipitated from the reaction mixture by ether in the form of colorless or brightly colored crystals, readily soluble in polar solvents and fluorescing intensely under irradiation with ultraviolet light. All the synthesized pyrylium salts are individual compounds, as confirmed by thin-layer chromatography on gypsum. The structure of the pyrylium salts was confirmed by the presence in the IR spectrum of intense absorption bands in the regions 1633-1625 and 1567-1565 cm^{-1}, which is characteristic of the C-C bonds of the pyrylium cation (^{6}).

When an alcoholic suspension of pyrylium salts is treated with gaseous ammonia, the corresponding pyridine bases are obtained in quantitative yield:

[structural scheme: pyrylium perchlorate with substituent $R \xrightarrow{NH_3}$ corresponding pyridine base with substitu

(7)

Owing to the high reactivity of the pyrylium ring (7), the synthesized pyrylium salts can evidently be convenient objects for the preparation of various steroid compounds condensed with aromatic and heterocyclic systems.

Experimental Part

Perchlorate of 6′-methyl-13-nor-17-gem-dimethylandrost-13-eno-[3,2b]-pyrylium (II). A mixture of 1.580 g (0.005 g-mole) of 2-oxymethylene-17α-methyldihydrotestosterone, 0.580 g (0.01 g-mole) of acetone, 0.6 ml of 70% hydrochloric acid, and 10 ml of glacial acetic acid is heated on a boiling water bath for one hour; after cooling it is diluted with a large volume of ether, the precipitated solid is filtered off and washed well on the filter with ether. This gives 0.910 g (41.7%) of substance in the form of colorless silky leaflets, m.p. 219°.
IR spectrum: 1633, 1566, 1506 cm^{-1}.

$C_{24}H_{33}ClO_5$.	Found, %:	C 65.39; H 7.52; Cl 8.37
	Calculated, %:	C 65.97; H 7.56; Cl 8.13

6′-Methyl-13-nor-17-gem-dimethylandrost-13-eno-[3,2b]-pyridine (III). Dry ammonia is passed through a suspension of 0.260 g of perchlorate II in 10 ml of methyl alcohol. After a few minutes the perchlorate dissolves; the pyridine is precipitated by several drops of water and crystallized from methyl alcohol. Yield 0.180 g (90%). M.p. 120°.

$C_{24}H_{33}N$.	Found, %:	C 85.22; H 9.61
	Calculated, %:	C 85.97; H 9.85

Perchlorate of 6′-phenyl-13-nor-17-gem-dimethylandrost-13-eno-[3,2b]-pyrylium (IV). From 0.790 g (0.0025 g-mole) of 2-oxymethylene-17α-methyldihydrotestosterone, 0.600 g (0.005 g-mole) of acetophenone, 0.3 ml of 70% $HClO_4$, and 5 ml of glacial acetic acid there is obtained 0.430 g (34.4%) of colorless plates, m.p. 214°, R_f 0.217 (violet spot in UV light, solvent toluene : chloroform = 7 : 8). IR spectrum: 1625, 1567, 1508 cm^{-1}.

$C_{29}H_{35}ClO_5$.	Found, %:	C 69.64; H 7.32; Cl 7.44
	Calculated, %:	C 69.80; H 7.02; Cl 7.12

6-Phenyl-13-nor-17-gem-dimethylandrost-13-eno-[3,2b]-pyridine (V). From 0.300 g of perchlorate IV there is obtained 0.210 g (87.5%) of yellow crystals, m.p. 160°.

$C_{29}H_{35}N$.	Found, %:	C 87.23; H 8.69
	Calculated, %:	C 87.65; H 8.81

Perchlorate of 6′-(p-methoxyphenyl)-13-nor-17-gem-dimethylandrost-13-eno[3,2b]-pyrylium (VI). From 1.580 g (0.005 g-mole) of 2-oxymethylene-17α-methyldihydrotestosterone, 1.5 g (0.01 g-mole) of *p*-methoxyacetophenone, 0.6 ml of 70% $HClO_4$, and 10 ml of glacial acetic acid there is obtained 0.620 g (23.5%) of yellow needles, m.p. 182–

184°, R_f 0.375 (green spot in ultraviolet light). IR spectrum: 1627, 1611, 1489 cm^{-1}.

Found, %: C 68.04; H 7.35; Cl 6.78
$C_{30}H_{37}ClO_6$. Calculated, %: C 68.11; H 7.00; Cl 6.71

6′-(p-Methoxyphenyl)-13-nor-17-hemdimethylandrost-13-eno[3,2b]pyridine (VII). From 0.370 g of perchlorate VI, 0.250 g (83.3%) of red-orange crystals with m.p. 110–112° are obtained.

Found, %: C 83.85; H 8.58
$C_{30}H_{37}ON$. Calculated, %: C 84.30; H 8.66

Perchlorate of 6′-(α-thienyl)-13-nor-17-hemdimethylandrost-13-eno[3,2b]pyrylium (VIII). From 1.580 g (0.005 g-mole) of 2-oxymethylene-17α-methyldihydrotestosterone, 1.260 g (0.01 g-mole) of 2-acetylthiophene, 0.6 ml of 70% $HClO_4$, and 10 ml of glacial acetic acid, 0.720 g (28.5%) of light-yellow needles with m.p. 205–207° are obtained. R_f 0.25 (blue spot). IR spectrum: 1629, 1567, 1531 cm^{-1}.

Found, %: C 63.80; H 6.65
$C_{27}H_{33}ClO_5$. Calculated, %: C 64.22; H 6.54

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Rostov-on-Don State
University

Institute of Chemistry
Academy of Sciences of the MSSR

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