SYNTHESIS OF DISTEROIDO[3, 2-b:17', 16'-e]PYRILIUM SALTS AND -PYRIDINES BY CONDENSATION OF EPIANDROSTERONE WITH 2-HYDROXYMETHYLENE-3-KETOSTEROIDS

B. M. Savin, L. N. Volovel'skii, and G. N. Dorofeenko

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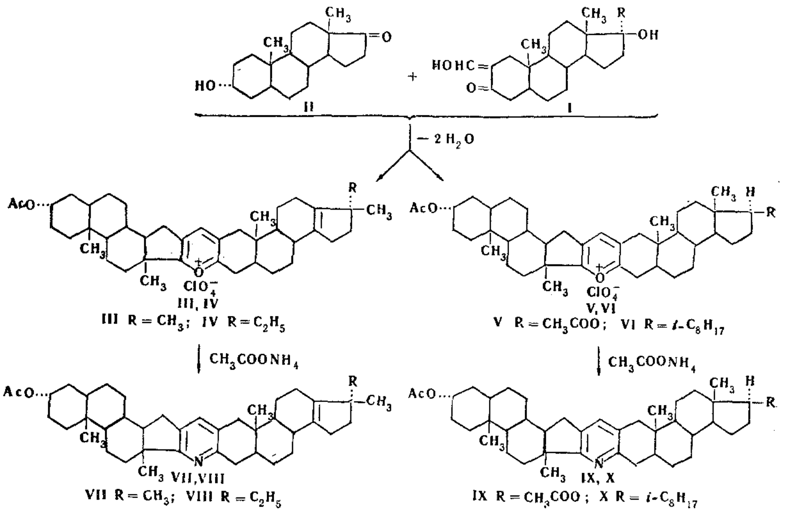
Condensation of 17-ketosteroids with 2-hydroxymethylene-3-ketosteroids of the androstane and cholestane series, under acid conditions, has given some disteroidopyrilium salts and disteroidopyridines.

In previous communications [1–4], we have examined synthetic routes to steroidopyridines via steroidopyrilium compounds, in which the formation of the pyrilium, then the pyridine, rings occurs with participation of ring A of a single steroid, or of rings A and A' of two steroids.

In other to obtain steroidopyrilium perchlorates in which ring D of the steroid molecule participated in the formation of the pyrilium ring, the condensation of 16-hydroxymethylene-17-ketosteroids with methylene ketones in presence of perchloric acid was attempted. Steroidopyrilium salts were not obtained by this route, however, in agreement with the negative results obtained in earlier investigations into the similar condensation of formylcyclopentanone with ketones [5].

Disteroidopyrilium perchlorates involving ring D (see table) were only obtained by condensation of 2-hydroxymethylene-3-ketosteroids (I) with the 17-ketosteroid epiandrosterone (II) in presence of 70% perchloric acid.



Condensation of II with hydroxymethylene steroids containing a tertiary OH group in the 17-position is accompanied, as previously noted [1–3], by a Wagner-Meerwein rearrangement giving the pyrilium salts III and IV, with Δ^{13}-double bond (as shown by IR). Steroids with secondary OH groups (at C_3 and C_{17}) undergo acetylation under the reaction conditions.

The IR spectra of the disteroidopyrilium salts show bands at 1642 (8a), 1446 (19b), and 1090 cm^{-1}, characteristic for the vibrational frequency of the pyrilium ring and the ClO_4^- anion [6, 7].

As in the case of some recently investigated disteroidopyridines [1, 2], the disteroido[3, 2-b:17'-16'-2]pyridines VIII–X (see table) were prepared in high yields, by reaction of the corresponding disteroidopyrilium perchlorates with ammonium acetate in acetic acid.

Disteroido[3, 2-b:17', 16'-e] Pyrilium Salts and -Pyridines Prepared*

Compound	Name	Mp, °C	Molecular formula	Found, %				Calculated, %				Yield, %
				C	H	Cl	N	C	H	Cl	N	
IV	Δ^{3}-17α-Ethyl-17β-methylandrosteno-3'β-acetoxyandrostano[3,2-b:17'-16'-e]pyrilium perchlorate	278—279	$C_{43}H_{61}ClO_7$	71.90	8.87	4.71	—	71.27	8.42	4.83	—	13.5
V	17',3'-Diacetoxydiandrostano[3,2-b:17'-16'-e]pyrilium perchlorate	287—289	$C_{43}H_{61}ClO_9$	67.49	7.78	4.12	—	68.25	8.06	4.66	—	26.6
VI	Cholestano-3'β-acetoxyandrostano[3,2-b:17'-16'-e] pyrilium perchlorate	271—272	$C_{49}H_{75}ClO_7$	72.97	9.19	4.61	—	72.59	9.25	4.32	—	5.6
VII	Δ^{13}-17α,17β-Dimethylandrosteno-3'β- acetoxyandrostano [3,2-b:17'-16'-e] pyridine	239—241	$C_{42}H_{59}NO_2$	—	—	—	2.47	—	—	—	2.29	52.0
VIII	Δ^{13}-17α-Ethyl-17β-methylandrosteno- 3'βacetoxyandrostano[3,2-b:17'- 16'-e]pyridine	330	$C_{43}H_{61}NO_2$	—	—	—	2.18	—	—	—	2.24	64.0
IX	17'-3'-Diacetoxyandrostano[3,2-b:17'- 16-e] pyridine	330	$C_{43}H_{61}NO_4$	—	—	—	2.27	—	—	—	2.13	80.0
X	Cholestano-3'β-acetoxyandrostano[3,2-b:17',16'-e]pyridine	235—237	$C_{47}H_{75}NO_2$	—	—	—	2.11	—	—	—	1.97	37.5

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*For properties of compound III, see text.

EXPERIMENTAL

Δ^{13}-17α, 17β-Dimethylandrostano-3'β-acetoxyandrostano[3, 2-b:17'-16'-e]pyrilium perchlorate (III). A mixture of 1.47 g (5 mM) of epiandrosterone [8], 1.66 g (5 mM) of 2-hydroxymethylene-17α-methyldihydrotestosterone (all the 2-hydroxymethylene-3-ketosteroids were obtained by formylation of the 3-ketosteroids with ethyl formate in presence of sodium ethoxide [9]), and 0.5 ml of 70% perchloric acid in 8 ml of glacial acetic acid was heated on the boiling water bath for 30 min, and dilute with 100 ml of ether. The precipitate was filtered off, washed with ether, the dry solid boiled twice with benzene (1: 10), and recrystallized from acetic acid. After drying in vacuo, there was obtained 0.5 g (14%) of the perchlorate III, mp 299–301° C. Found, %: C 71.23; H 8.71; Cl 5.02. Calculated for $C_{42}H_{59}ClO_7$, %: C 70.98; H 8.30; Cl 4.92.

The steroido[3, 2-b:17', 16'-e]pyrilium perchlorates were obtained as yellow crystalline solids which were soluble in chloroform and acetone, but insoluble in benzene and ether.

Steroidopyridines. A mixture of 5 mM of the steroidopyrilium perchlorate and 50 mM of ammonium acetate in 8 ml of glacial acetic acid was boiled for 2 hr, and diluted with 100 ml of water. The resulting precipitate was filtered off, washed with water until neutral, dried to constant weight at 100° C, and recrystallized from ethanol. The steroidopyridines were obtained as yellowish-green crystalline solids, which were soluble in alcohol, benzene, and ether.

REFERENCES

1. G. I. Zhungietu, L. N. Volovel'skii, G. N. Dorofeenko, and G. V. Lazur'evskii, KhPS [Chemistry of Natural Compounds], 318, 1965.
2. G. I. Zhungietu and G. N. Dorofeenko, Usp. khim., **36**, 48, 1967.
3. G. N. Dorofeenko, L. N. Volovel'skii, and B. M. Savin, ZhOKh, **38**, 2686, 1968.
4. G. N. Dorofeenko, L. N. Volovel'skii, and B. M. Savin, ZhOKh, **39**, 656, 1969.
5. G. N. Dorofeenko, Yu. A. Shdanov, G. I. Shungietu, and S. V. Krivun, Tetrah., **22**, 1821, 1966.
6. A. T. Balaban, G. D. Mateescu, and M. Elian, Tetrah., **18**, 1083, 1962.
7. A. D. Semenov, G. N. Dorofeenko, and V. I. Dulenko, KhGS [Chemistry of Heterocyclic Compounds], **14**, 1966.
8. L. N. Volovel'skii, G. V. Knorozova, and M. Ya. Yakovleva, ZhOKh, **37**, 1252, 1967.
9. L. N. Volovel'skii and G. V. Knorozova, ZhOKh, **33**, 676, 1963.

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Rostov State University

Khar'kov Scientific-Research Institute of Endocrinology
and Hormone Chemistry

Khar'kov Plant for Endocrine Preparations