

2-Cyano-3-(3-indolyl)- Δ^2 -steroids are formed when 2 α -cyano-3-ketosteroids are refluxed with indole and its homologs in acetic acid.

There are compounds among steroid derivatives that have both hormonal activity and psychotropic activity [1]. Hypotensive and coronary-dilating action and the ability to inhibit the action of the adrenal glands and the hypophysis have been observed for 2-cyanosteroids [2]. Considering this and the fact that β -(3-indolyl)acrylic acid derivatives are of biochemical interest [3], we set out to study the possibility of obtaining a number of indolylacrylonitrile derivatives.

We have shown that 2-cyano-3-(3-indolyl)- Δ^2 -steroids (I-IV) are readily formed when indole and its homologs are refluxed with 2 α -cyano-3-ketosteroids in acetic acid. The structure proposed for I-IV is confirmed by the IR and UV spectra (Table 1). In contrast to indole and its derivatives with saturated side chains, the appearance of an intense long-wave band above 300 nm in the UV spectra is characteristic for indolylacrylic acid derivatives. For example, there is a maximum at 325 nm ($\log \epsilon$ 4.38) [4] in the UV spectrum of β -(3-indolyl)acrylonitrile. The absence of this band in the UV spectra of I-V should apparently be explained by the almost complete disruption of the conjugation of the indole portion with the remaining fragment of the molecule, mainly because of the steric hindrance created by the cyclohexene ring.

The condensation of 2-methylindole with 2 α -cyano-17 α -methyl-dihydrotestosterone gives, in addition to nitrile IV in about the same yield, another compound, which, according to the results of elementary analysis, is the product of its dehydration and apparently has the 2-cyano-3-(2-methyl-3-indolyl)-17 α ,17 β -dimethyl-18-norandrostane-2,13-diene (V) structure. Its IR spectrum does not contain hydroxyl group absorption, and the band of the methyl group at 1380 cm^{-1} is split; it must be assumed that this confirms the formation of two geminal methyl groups as a result of dehydration with Wagner-Meerwein rearrangement [5].

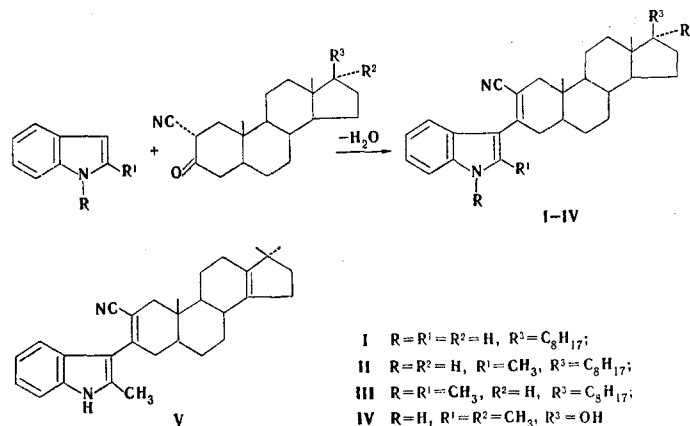
TABLE 1. 2-Cyano-3-(3-indolyl)- Δ^2 -steroids

Compound	mp, °C	[α] _D ²⁵ (pyridine)	IR spectrum ν max, cm^{-1}	UV spec- trum, λ max nm ($\log \epsilon$)	Empirical formula	Found, %			Calc., %			Yield, %
						C	H	N	C	H	N	
I	228— 230 ^c	+40° (c 1,5)	3400—3300 2190, 1610	220 (4,49) 290 (3,95)	C ₃₆ H ₅₀ N ₂	84,9	10,0	5,5	84,7	9,8	5,5	60
II	256 ^d	+93° (c 1,5)	3400, 2220, 1620	225 (4,58) 283 (3,99)	C ₃₇ H ₅₂ N ₂	84,2	9,9	5,3	84,7	9,9	5,3	60
III	244 ^d	+70° (c 1,1)	2220, 1620	227 (4,60) 292 (3,99)	C ₃₈ H ₅₄ N ₂	84,6	10,2	4,9	84,7	10,0	5,2	100
IV	293— 295 ^c	+85° (c 2)	3500, 3420, 3280, 2220, 1620, 1380	224 (4,73) 283 (4,13)	C ₃₀ H ₃₈ N ₂ O	81,1	8,6	6,3	81,4	8,6	6,3	49
V	238— 240 ^c	+62° (c 0,6)	3420, 2220, 1620, 1380	224 (4,50) 282 (3,90)	C ₃₀ H ₃₆ N ₂	84,4	8,5	6,2	84,9	8,5	6,6	51

^aOf KBr pellets with a UR-10 spectrophotometer. ^bOf methanol solutions with a Specord spectrophotometer. ^cFrom acetic acid. ^dFrom ethyl acetate-benzene.

Institute of Chemistry, Academy of Sciences of the Moldavian SSR, Kishinev. Translated from Khimiya Geterotsiklicheskih Soedinenii, No. 2, pp. 222-223, February, 1973. Original article submitted February 28, 1972.

© 1975 Consultants Bureau, a division of Plenum Publishing Corporation, 227 West 17th Street, New York, N. Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$15.00.



EXPERIMENTAL

General Method for the Condensation of Indoles with 2 α -Cyano-3-ketosteroids. A solution of 0.001 mole of a 2 α -cyano-3-cholestanone [6] or 2 α -cyano-17 α -methylidihydrotestosterone [2] and 0.001 mole of indole in 15 ml of acetic acid was refluxed for 5-10 h (the end of the reaction was determined by chromatography on plates with a thin layer of aluminum oxide), after which the mixture was evaporated to half its original volume and allowed to stand for crystallization. A mixture of IV and V, which was readily separated by fractional crystallization, precipitated from the reaction mixture in quantitative yield in the reaction of 2-methylindole with 2 α -cyano-17 α -methylidihydrotestosterone.

LITERATURE CITED

1. M. V. Rubtsov, "Advances in the synthesis of medicinal preparations," Paper Presented at the 9th Mendeleev Congress on General and Applied Chemistry [in Russian], Kiev (1965), p. 41.
2. R. O. Clinton and A. J. Manson, US Patent No. 3,296,255 (1967); Ref. Zh. Khim., 14N476P (1968).
3. M. N. Preobrazhenskaya, L. A. Savel'eva, N. P. Kostyuchenko, and N. N. Suvorov, Zh. Organ. Khim., 6, 1923 (1970).
4. N. N. Suvorov, V. P. Gorbunova, and K. F. Turchin, Khim. Geterotsikl. Soedin., 1029 (1968).
5. E. Caspi and D. M. Piatak, Chem. Ind., 1984 (1962).
6. F. Winternitz, C. Menou, and E. Arnal, Bull. Soc. Chim. France, 505 (1960).