

## STRUCTURE—ACTIVITY RELATIONSHIP OF INSECTICIDAL STEROIDS. X. ANDROSTANE AND PREGNANE DERIVATIVES

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*The androstane and pregnane steroids 1-10 were verified to have insecticidal activity for larvae of the Colorado beetle *Leptinotarsa decemlineata*. Insect growth and development regulators were found among these compounds.*

**Key words:** insecticidal activity, steroids, Colorado beetle larvae.

We previously screened several synthetic steroids for insecticidal activity [1-8]. The studied compounds were C<sub>27</sub>-C<sub>29</sub>-steroids with structures analogous to ecdysteroids or intermediates in their synthesis. However, it is important to determine if synthetic compounds of simpler structure, e.g., C<sub>19</sub>- or C<sub>21</sub>-steroids belonging to the androstane and pregnane series, respectively, possess insecticidal activity. It should be noted that natural ecdysteroids also include C<sub>19</sub>- and C<sub>21</sub>-steroids, of which the most well known are rubrosterone and poststerone [9]. Significant insecticidal activity has been observed for poststerone [10].

We checked the insecticidal activity of androstane and pregnane steroids **1-10**, which were previously synthesized [11, 12]. The test subjects were Colorado beetle (*Leptinotarsa decemlineata* Say, Coleoptera) larvae, a harmful potato pest. The studied compounds were screened on larvae using a contact-intestinal treatment method consisting of spraying them and their natural feed (potato leaves) with suspensions (0.01%) of the studied compounds in water with OP-10 surfactant. Larvae were grown in the laboratory from egg sacs of Colorado beetle collected under field conditions. The number of dead larvae was counted after one, three, and five days. The standard was the natural insect molting hormone 20-hydroxyecdysone **11**, which in the same test had the highest insecticidal activity for Colorado beetle larvae compared with other ecdysteroids [10]. Then the insecticidal activity of several of the most active compounds was studied at a concentration of 0.001%. Table 1 shows the results for toxicity of the steroids for Colorado beetle larvae. It can be seen that half of the 12 studied steroids exhibited noticeable insecticidal activity. However, most of the compounds are less toxic than the control for larvae. The only exception is **1a**, which at a concentration of 0.01% causes death to all insects and was practically nontoxic at a concentration of 0.001%. Besides **1a**, androstanes **1b** and **4** and pregnanes **2**, **3**, and **7** were also rather active. It should be noted that pregnanes at a concentration of 0.001% were more active compared with androstanes.

It has been found [8] that 3 $\alpha$ ,5-cyclo-6 $\beta$ -hydroxysteroids of the cholestane series and  $\Delta^{22}$ -stigmastane possess significant insecticidal activity. According to Table 1, 3 $\alpha$ ,5-cyclo-6 $\beta$ -hydroxysteroids **4** and **5**, which are structurally similar to them, also have moderate insecticidal activity. The presence of acetoxy groups in these molecules markedly decreases the insecticidal activity. This is especially noticeable in comparing the activities of **1a** and **1b**. Thus, replacing the 3 $\beta$ -hydroxy group in the former by 3 $\beta$ -acetoxy group to form **1b** decreases the insecticidal activity by 50% at a concentration of 0.01%. Steroids **9** and **10**, in which all hydroxyls are protected as acetates, were inactive. The studied androstanes and pregnanes differ significantly from the corresponding C<sub>27</sub>-C<sub>29</sub>-steroids, among which active insect growth regulators containing acetoxy groups are found [7].

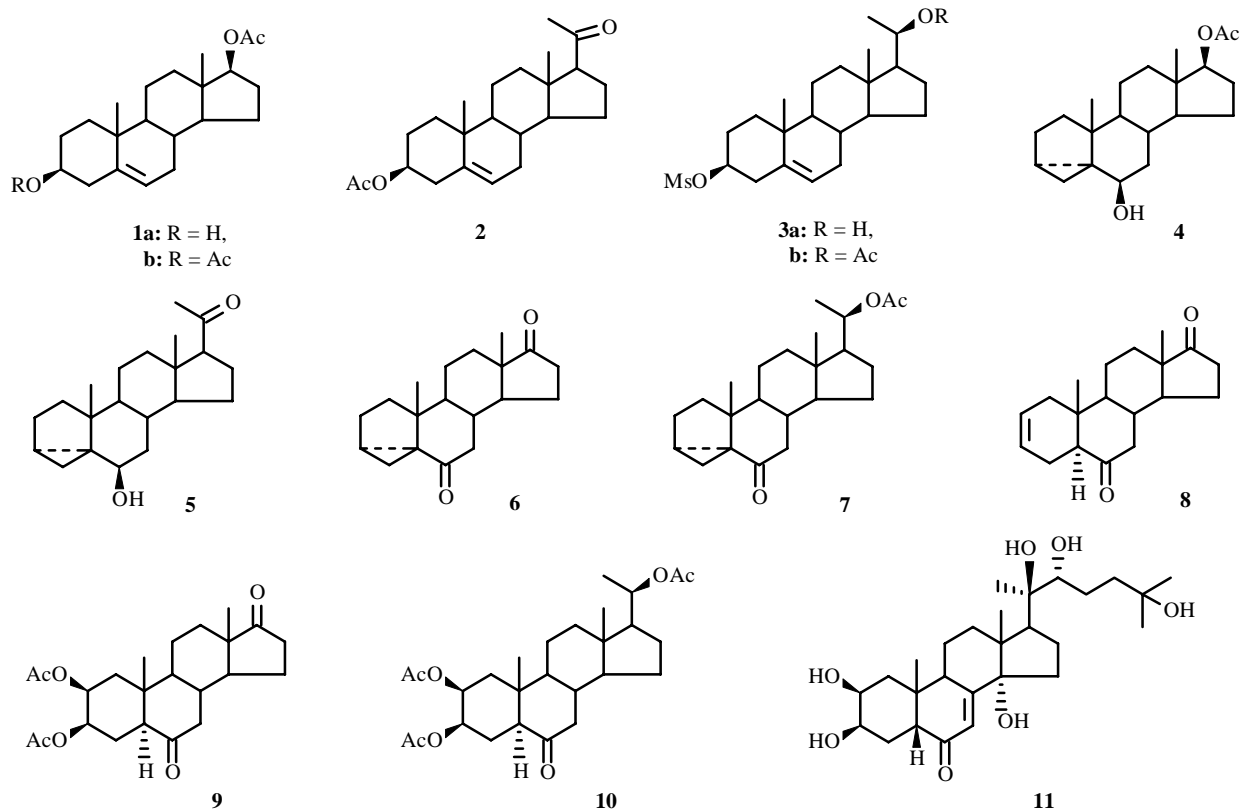
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TABLE 1. Toxicity of Steroids **1-11** for Colorado Beetle Larvae

Compound	Concentration, %	Larvae mortality after							
		1 days		3 days		5 days		Total	
		number	%	number	%	number	%	number	%
<b>1a.</b> Androst-5-en-3 $\beta$ ,17 $\beta$ -diol 17-acetate	0.01	0	0	30	100			30	100
	0.001	0	0	1	3.3	1	3.3	2	6.7
<b>1b.</b> Androst-5-en-3 $\beta$ ,17 $\beta$ -diol 3,17-diacetate	0.01	0	0	15	50.0	0	0	15	50.0
<b>2.</b> Pregn-5-en-3 $\beta$ -ol-20-one acetate	0.01	0	0	21	70.0	0	0	21	70.0
	0.001	1	3.3	3	10.0	4	13.3	8	26.7
<b>3a.</b> Pregn-5-en-3 $\beta$ ,20 $\beta$ -diol 3-mesylate	0.01	0	0	12	40.0	7	23.3	19	63.3
	0.001	0	0	0	0	1	3.3	1	3.3
<b>3b.</b> Pregn-5-en-3 $\beta$ ,20 $\beta$ -diol 3-mesylate 20-acetate	0.01	0	0	0	0	0	0	0	0
<b>4.</b> 3 $\alpha$ ,5-Cyclo-5 $\alpha$ -androstan-6 $\beta$ ,17 $\beta$ -diol 17-acetate	0.01	0	0	9	30.0	8	26.7	17	56.7
<b>5.</b> 3 $\alpha$ ,5-Cyclo-5 $\alpha$ -pregnan-6 $\beta$ -ol-20-one	0.01	0	0	8	26.7	0	0	8	26.7
<b>6.</b> 3 $\alpha$ ,5-Cyclo-5 $\alpha$ -androstan-6,17-dione	0.01	0	0	2	6.7	2	6.7	4	13.3
<b>7.</b> 3 $\alpha$ ,5-Cyclo-5 $\alpha$ -pregnan-20 $\beta$ -ol-6-one acetate	0.01	0	0	20	66.7	3	10.0	23	76.7
	0.001	3	10.0	3	10.0	3	10.0	9	30.0
<b>8.</b> 5 $\alpha$ -Androst-2-en-6,17-dione	0.01	0	0	0	0	1	3.3	1	3.3
<b>9.</b> 2 $\beta$ ,3 $\beta$ -Diacetoxy-5 $\alpha$ -androstan-6,17-dione	0.01	0	0	0	0	0	0	0	0
<b>10.</b> 2 $\beta$ ,3 $\beta$ ,20 $\beta$ -Triacetoxy-5 $\alpha$ -pregnan-6-one	0.01	0	0	0	0	0	0	0	0
<b>11.</b> 20-Hydroxyecdysone	0.01	21	70.0	4	13.3	1	3.3	26	86.7
	0.001	8	26.7	4	13.3	4	13.3	16	53.3
Control		0	0	0	0	0	0	0	0

Number of larvae, 30.



The dynamics of larvae death caused by the studied androstane and pregnane steroids differ markedly from those of 20-hydroxyecdysone. Thus, the maximum death of experimental insects was observed during the first day upon administration of 20-hydroxyecdysone. On the other hand, even the most active androstane and pregnane compounds were not immediately toxic. The most larvae died only on the third day upon their administration. This may be explained by differences in the mechanisms of toxicity of 20-hydroxyecdysone and the studied C<sub>19</sub>- and C<sub>21</sub>-steroids.

Thus, the results indicate that the androstane and pregnane steroids studied by us possess less insecticidal activity than C<sub>27</sub>-C<sub>29</sub>-sterols of analogous structure. Therefore, the presence of the appropriate sterol side chains is important for the production of steroids with high insecticidal activity.

## EXPERIMENTAL

The syntheses of steroids **1-10** have been described [11, 12].

Details of the experiments to determine the insecticidal activity of **1-11** for second-growth Colorado beetle larvae have been published [1].

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