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STRUCTURE-ACTIVITY RELATIONSHIP OF INSECTICIDAL STEROIDS. V. 3β-BENZOYLOXYSTIGMASTAN-6-ONES

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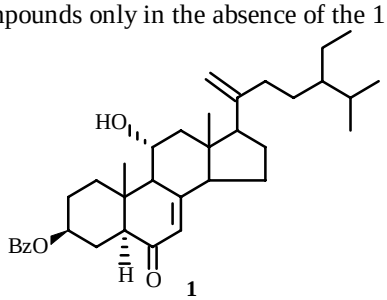
*The toxicity of steroid benzoates **4-10** for Colorado beetle (*Leptinotarsa decemlineata *Say.) larvae was studied by a contact-intestinal method. The most active growth and development regulator for this insect is 3*β*-benzoyloxy-5-hydroxy-Δ^7-6-ketosteroid **9a**.*

Key words: 3β-benzoyloxystigmastan-6-ones, insecticidal activity.

Several compounds with the ecdysteroid benzoate structure have been isolated from various plants. These include, for example, physanols A (**1**) and B (**2**) [1], carpesterol (**3a**) [2-4], 14α-hydroxycarpesterol (**3b**) [5], and 20-hydroxyecdysone and 5α-20-hydroxyecdysone benzoates [6]. It should be noted that the reason these steroids are present in plants and their biological activity have not yet been determined. It could be that these compounds, like other phytosteroids [7], are necessary for protection from harmful insects, in which instance they can be expected to be highly active insecticides. We synthesized previously [8, 9] from β-sitosterol steroid benzoates **7** and **8**, which can be viewed as close structural analogs of physanols A and B. The structural formulas show that **7** and **8** contain most functional groups of physanols A and B. They differ from the natural compounds only in the absence of the 11α-hydroxyl.



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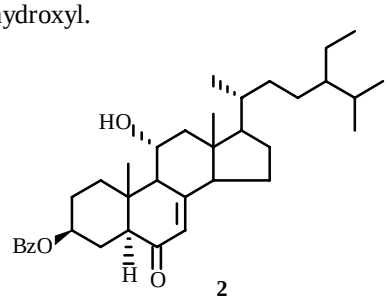

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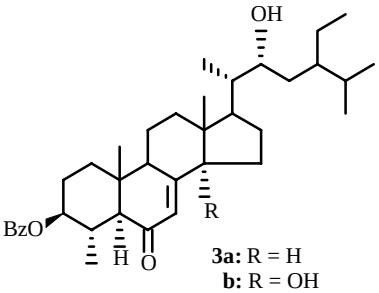
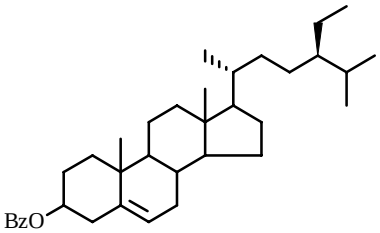


3a: R = H
b: R = OH



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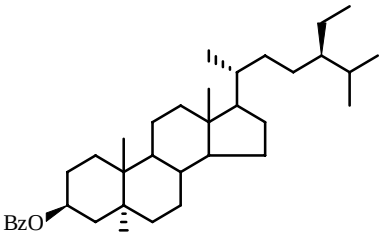

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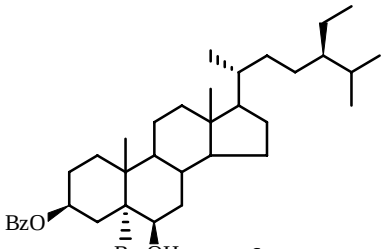

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We investigated the insecticidal activity of the steroid benzoates that we synthesized previously. In addition to Δ^7-6-ketones **7** and **8**, we studied the activity on Colorado beetle (*Leptinotarsa decemlineata* Say., Coleoptera) larvae of **4**-**6**, which are intermediates in their synthesis and also the close structural analog Δ^7-6-ketosteroid **9**. The Colorado beetle larvae were selected as test specimens, like in the previous studies on this topic [10-13], because this insect in Belarus is one of the most harmful potato pests.

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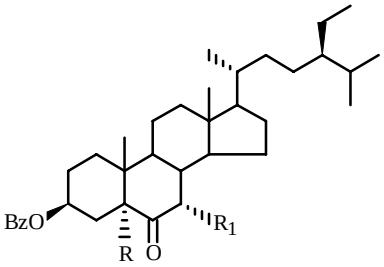
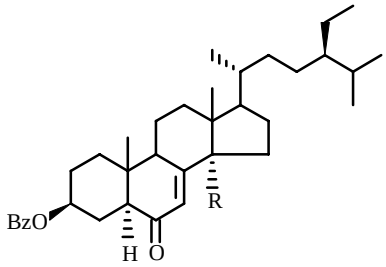
TABLE 1. Toxicity of **4-11** for Colorado Beetle Larvae

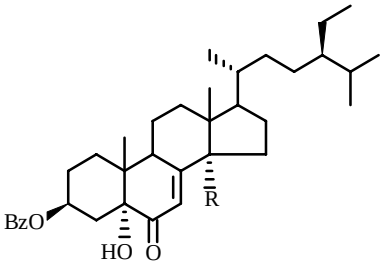
Compound	Number of larvae	Larvae mortality after days							
		1		3		5		Total	
		number	%	number	%	number	%	number	%
4. β-Sitosterol benzoate	30	0	0	1	3.3	2	6.7	3	10.0
5. (24R)-5α-Stigmastan-3β-ol benzoate	30	0	0	0	0	1	3.3	1	3.3
6. (24R)-5-Bromo-5α-stigmastan-3β,6β-diol 3-benzoate	30	0	0	0	0	0	0	0	0
7a. (24R)-3β-Hydroxy-5-bromo-5α-stigmastan-6-one benzoate	30	0	0	0	0	0	0	0	0
7b. (24R)-3β-Hydroxy-5α-bromo-5α-stigmastan-6-one benzoate	30	0	0	0	0	0	0	0	0
7c. (24R)-3β,5-Dihydroxy-7α-bromo-5α-stigmastan-6-one 3- benzoate	30	0	0	0	0	1	3.3	1	3.3
8a. (24R)-3β-Hydroxy-5α-stigmast-7-en-6-one benzoate	30	0	0	0	0	0	0	0	0
8b. (24R)-3β,14α-Dihydroxy-5α-stigmast-7-en-6-one 3-benzoate	30	0	0	0	0	1	3.3	1	3.3
9a. (24R)-3β,5-Dihydroxy-5α-stigmast-7-en-6-one 3-benzoate	30	0	0	3	10.0	7	23.3	10	33.3
9b. (24R)-3β,5,14α-Trihydroxy-5α-stigmast-7-en-6-one 3-benzoate	30	0	0	1	3.3	3	10.0	4	13.3
10. (24R)-3β-Hydroxystigmast-4-en-6-one benzoate	30	0	0	1	3.3	4	13.3	5	16.7
11. 20-Hydroxyecdysone	30	2	6.7	4	13.3	10	33.3	16	53.3
Control	29	0	0	1	3.4	2	6.9	3	10.3



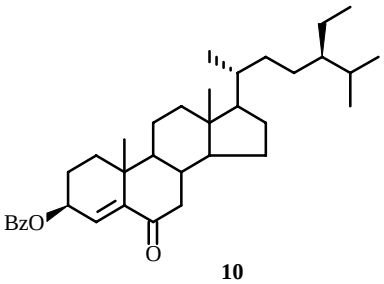
7a: R = Br; R_1 = H
b: R = H; R_1 = Br
c: R = OH; R_1 = Br



8a: R = H
b: R = OH



9a: R = H
b: R = OH



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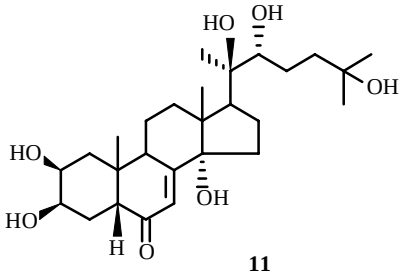

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The insecticidal activity of **4-10** was determined using a contact-intestinal method of administration to second-growth Colorado beetle larvae. This method is most widely used in practice to combat this pest. According to it, insects and their natural food, potato leaves, are sprayed with suspensions (0.01%) of the studied compounds in water in the presence of surfactant OP-10. The treated food is fed to the larvae for one day. Then it is replaced with natural food, potato leaves without steroids. The standard is the natural phytoecdysteroid 20-hydroxyecdysone **11**, which was previously shown to be most active in this test [10]. Control larvae received analogous treatment with the exception that steroids **4-11** were not included in their diet. The mortality of the larvae was calculated on the second, third, and fifth day after administration. Table 1 contains the results for **4-11** on Colorado beetle larvae.

Table 1 shows that steroids absorbed with food are toxic for prolonged periods and cause larvae death even on the fifth

day after administration. The mortality dynamics caused by **4-11** were the same as for phytoecdysteroids [10]. This is probably due to the fact that these compounds have the same mechanism of action.

Thus, only **9a**, **9b**, and **10** among the steroid benzoates have a noticeable insecticidal effect on Colorado beetle larvae. The most active was 3β,5α-dihydroxy-Δ^7-6-ketone 3-benzoate **9a**. Steroids **4-8** in this test were inactive. The lack of any toxicity for Δ^7-6-ketones **8a** and **8b** was especially unexpected because their structures are closest to physanols A and B.

Analysis of the data in Table 1 leads to the conclusion that **4-10** are moderately and slightly toxic for Colorado beetle larvae. In general, they are inferior in activity to previously studied compounds [10-13]. The principal reason for this phenomenon is apparently due to the presence in them of the 3β-benzoate. However, only further research can determine conclusively if the steroid benzoates are slightly toxic for all insect species. It could be that active compounds that are growth and development regulators for harmful agricultural insects will be found.

EXPERIMENTAL

The syntheses of **4-10** have been reported [8, 9]. Experimental details for the determination of the insecticidal activity of **4-11** for Colorado beetle larvae have been published [11].

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