Note

Activity of Stereoisomers of Serricornin, Sex Pheromone of the Cigarette Beetle (Lasioderma serricorne F.)

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Serricornin (4,6-dimethyl-7-hydroxynonan-3-one) is the sex pheromone produced by females of the cigarette beetle (Lasioderma serricorne F.)1 This compound has three chiral carbons at C4, C6, and C7 in the molecule, so that there are eight possible stereoisomers. Recent studies on the synthesis of serricornin stereoisomers have indicated that the absolute structure of natural serricornin is (4S, 6S, 7S) (Fig. 1, 1a).2

In the course of our study on the activity of serricornin isomers, it has been demonstrated that the threo-(6S, 7S) configuration is essential to elicit pheromone activity.3 However the contribution of the C4 chirality to the activity has been remained unknown.

In this paper, we wish to report that the male cigarette beetle requires all three chiralities in the molecule for pheromone recognition.

Four enantiomeric mixtures, (4S, 6S, 7S)- and (4R, 6R, 7R)-serricornin mixture (1) (Fig. 1), (4S, 6S, 7R)- and (4R, 6R, 7S)-mixture (2), (4S, 6R, 7S)- and (4R, 6S, 7R)-mixture (3) and (4S, 6R, 7R)- and (4R, 6S, 7S)-mixture (4) were obtained from a nonstereospecific reaction mixture4 by SiO2 column chromatography, C4 epimerization with tertiary amines and successive preparative GC.5 The purity of these mixtures were estimated from GC-analysis of their acetylated derivatives as follows: 90.6, 99.8, 100.0 and 100.0%, for 1, 2, 3, 4, respectively. Pheromone activity of each enantiomeric mixture was evaluated by a behavioral bioassay3a using 7-10-day-old unmated males and electroantennography (EAG) experiments3b as described before.

The results of the behavioral bioassay are shown in Fig. 2, in which mixture 1 is the most active with respect to all the following parameters3a: attractiveness (the accumulated number of males attracted to the individual serricornin-mixture-impregnated filter paper for 10 min using 10 testing males), 2) sex stimulation (the accumulated number of homosexual couplings for 10 min using 10 testing males) and 3) responding ratio (the maximum number of simultaneous staying males on the filter paper within 10 min for 10 testing males). The EAG response to mixture 1 exhibited greater amplitude than any other enantiomeric mixtures (2, 3 and 4) at every dose level (Fig. 3).

In the previous paper, we reported that the (6,7)-erythro-isomer of serricornin (2 and 3) does not have any activity3a and that only the (4S, 6S, 7S)-isomer (1a) shows high activity in the behavioral bioassay and EAG experiments among three of four (6,7)-threo-isomers examined; (4R, 6R, 7R)- and (4S, 6R, 7R)-isomers do not show any significant activity.3b Thus, the pheromone activity of the remaining isomer (4R, 6S, 7S), which has not been obtained in pure form yet, has remained in question. In this study, the (4R, 6S, 7S)-isomer was obtained as a mixture with (4S, 6R, 7R)-isomer and this

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Fig. 1. Enantiomeric Mixture 1 Composed of (4S, 6S, 7S)-Serricornin (1a) and (4R, 6R, 7R)-Serricornin (1b).

Fig. 2. The Results of Behavioral Bioassay.

See the text.
Fig. 3. The Results of EAG Experiments.

The EAG response to four enantiomeric mixtures at 10⁻³ ~ 10 µg levels were normalized with respect to that of mixture 1 at 10⁻² µg level. 1, -●--; 2, - - - - □---; 3, --- ■---; 4, --○--.

mixture 4 was examined for the pheromone activity. The results indicate that the mixture 4 has no significant activity (Figs. 2 and 3) suggesting that the (4R,6S,7S)-isomer is inactive if the inactive (4S,6R,7R)-isomer is not an inhibitor against the (4R,6S,7S)-isomer. As the mixture 1 has the highest activity (Figs. 2 and 3) and the (4R,6R,7R)-isomer (1b) is inactive, the (4S,6S,7S)-configuration seems to be essential to elicit the pheromone activity. It is concluded that the (4S,6S,7S)-isomer (1a) having the highest activity among the eight possible stereoisomers is just the naturally occurring serricornin.

REFERENCES

d) K. Mori and H. Watanabe, Tetrahedron, in press.