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Synthesis and biological activity of novel anti-juvenile hormone agents

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Abstract:
Ethyl 4-[2-(*tert*-butylcarbonyloxy)butoxy]benzoate (ETB) is a partial juvenile hormone (JH) antagonist which targets larval epidermis. We converted ETB to ethyl 4-(2-substituted alkyloxy)benzoates. These compounds induced precocious metamorphosis in the silkworm, *Bombyx mori*, which is a clear sign of JH deficiency, and their activity was completely counteracted by the simultaneous application of a JH agonist, methoprene. Among these novel compounds, ethyl 4-(2-benzylhexyloxy)benzoate (KF-13) showed high precocious metamorphosis-inducing activity at low doses, but its activity decreased with increasing dose, probably due to their JH-like activity. KF-13 is an enantiomeric compound. The (*S*)-enatiomer of KF-13 was more active than the (*R*)-enantiomer at low doses, but at high doses the activity was reversed (*R*>*S*). Hemolymph JH esterase activity, which is indispensable for the initiation of pupation in normal last-instar larvae, was induced in 4th-instar larvae by treatment with KF-13. 2-(6-Methyl-3-pyridyloxy)hexyl and 2-phenoxyhexyl analogs showed JH activity when topically applied to allatechtomized 4th-instar larvae.

Keywords:
juvenile hormone, anti-juvenile hormone, precocious metamorphosis, juvenile hormone esterase

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