THE OPTICAL ACTIVITY OF THE CECROPIA JUVENILE HORMONES

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The juvenile hormones isolated from the Cecropia silk moth are not racemic. They exhibit a plain positive optical dispersion curve.

Juvenile hormone (JH) is one of the important growth hormones in insects. Most recently, its regulatory function during postembryonic development has been demonstrated at a molecular level by some effects on the morphology of the puffing pattern in polytene chromosomes of two *Chironomus* species (1) and by experiments leading to the suggestion that JH controls formation of particular tRNAs and their activating enzymes (2).

The fact that JH accumulates in abdominal tissues of the adult male Cecropia moth (3) proved to be a boon for isolation and identification of the active principle. At first only one JH structure, methyl 12,14-dihomojuvenate (I, methyl *cis*-10,11-epoxy-7-ethyl-3,11-dimethyl-*trans*,*trans*-2,6-tridecadienoate), was recognized in this species (4). We were then able to isolate an additional, similarly active JH, methyl 12-homojuvenate (II), that accounted for 13-20% of the endocrine activity of the extracts (5). Structurally, this second compound is a lower homolog of I. The racemic hormones with identical geometry have been synthesized by various routes (I see ref. 6, II see ref. 7).

Because the biological activities of these synthetic substances were found to be equal to the natural hormones, the question arose whether the latter are racemic products instead of single enantiomers (8). In our *Galleria* assay the synthetic substances showed a trend toward lower bioactivity, but it was not possible to distinguish their potency with certainty from those of the natural hormones (9). Hence, even if the natural hormones are single stereoisomers, their unnatural enantiomers may possess considerable biological activity (although it is conceivable that their contribution to the potency of the racemic preparation is caused by a synergistic effect). It may thus be difficult to decide from assay data alone which synthetic enantiomers are identical with the natural hormones.

We therefore wish to report that the natural Cecropia hormones are *not*

racemic. Furthermore, it may aid in the determination of their absolute configuration if it is known that they are dextrorotatory.

Our isolation of the natural hormones was carried out on a scale that permitted measuring the optical rotation of the pure JH preparation. Since the difference between the two JH hormones involves a carbon atom that is relatively distant from the nearest chiral center C-10, we felt it to be unnecessary to separate the preparation into its two components. The measurement was performed with 1.3720 mg of a pure preparation that consisted of 90.2 mol% of I and 9.8 mol% of II (wt. 292.85 dalton) and had been isolated from the fourth batch of silk moths (9). The material was dissolved in chloroform in a calibrated pear-shaped weighing flask ($v = 1.102$ cm^3; $c = 0.1214\%$) and transferred into a tube of 1.000 dm length. Optical rotation was observed at four wavelengths and 28°C by means of a Perkin-Elmer 141 polarimeter with digital readout.

λ	365 nm	436 nm	546 nm	578 nm	S.E.
α	+0.030°	+0.021°	+0.011°	+0.009°	±0.005°
$[\alpha]$	+25°	+17°	+9°	+7.5°	±4°

The rotation at 589 nm was estimated by extrapolation: $[\alpha]_D \simeq +7°$; $[M]_D \simeq +20.5°$. It is evident that the solution was optically active and exhibited a normal positive dispersion curve. Since there is no reason to presume different configurations for the two JHs, the determined values are considered to be representative for the optical dispersion of both hormone structures.

Brewster has elaborated a "conformational dissymmetry" model and derived an empirical relation between the optical rotation of a compound and its absolute configuration (10), but there is some question whether the method is applicable without appropriate qualifications to compounds with distorted bond angles, such as epoxides. According to this method, a positive rotation, $[M]_D = +10°$, can be expected for the Cecropia JHs that have the 10*R*,11*S* configuration. Similarly, an $[M]_D = +5°$ can be computed for (*R*)-(+)-2,3-epoxy-2,5-dimethylhexane for which an $[\alpha]_D^{16} = +8.97°$ (ethanol) (11), $[M]_D^{16} = +11.5°$, had been reported; the absolute configuration of this compound has been deduced from the mode of its synthesis. These results appeared encouraging.

However, in the case of (*R*)-(+)-1,2-epoxypropane (12) as well as (*R*,*R*)-(+)-2,3-epoxybutane (13), the semi-empirical method failed to predict the correct sign. Since this divergence is, at present, not readily explained, we believe that it would be premature to conclude—in spite of the uncanny concordance of the above calculated and observed values—that the configuration of the JHs has been established, and we have initiated experiments that should provide the desired information.

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