Problems of Biological Activity of Natural and Synthetic Pheromones, especially Sex Attractants

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After the discovery and isolation of 10-E,12-Z-hexadecadien-1-ol 'bombycol' by Butenandt et al. (1959, 1961a,b) and the final constitution classification and synthesis by Truscheit & Eiter (1962), not only of bombycol itself, but also of the other theoretically possible 10,12-hexadecadienols-(I), it was possible, initially by applying Butenandt's method of determining the attractant unit in ng/ml, to make a quantitative statement about the biological activity (attractiveness) of a sex attractant on the corresponding insect. The attractant units of 0.0001-0.1 ag/ml which could be well reproduced with bombycol, corresponded mathematically to concentrations of several hundreds to thousands of bombycol molecules/ml, which led to numerous problems at an early stage, particularly with respect to the absolute values of attractant units of, for instance, synthesized geometric isomeric 10,12-hexadecadien-1-ols that are considerably less effective than bombycol itself.

These effects could not only be attributed to properties of the substance, but also to admixtures of bombycol molecules, perhaps originating from spontaneous rearrangement or because the selected methods of synthesis were not specific enough.

Only the development of an analytic technique similar to the tracer method in nuclear chemistry could yield a solution to these problems, as the classical methods of gas chromatography, g.l.c. and use of $^{13}$C spectroscopy or mass spectroscopy did not allow any statements to be made about trace admixtures of geometric isomers.

The electroantennagram method, developed by Schneider & Hecker (1956) and enhanced by Priesner (1973) by taking into consideration the electroantennagram-characteristic curves, permits investigation of the effects of sex attractants at the receptor sites. It has to date been used to determine the concentrations of, e.g. bombycol, in Bombyx mori at the receptor site, and these values were substantially different from those obtained by the original glass-rod method of Butenandt et al. (1959, 1961a,b). With the electroantennagram method, the concentrations exceed, by several powers of ten, those obtained with the AU$_{50}$ method (AU$_{50}$ is the equivalent term to LD$_{50}$ in toxicology). Applications of the electroantennagram method to the discovery of new pheromones have frequently led to spurious results, for example (+)-cis-gyplure, (+)-cis-gyplure, (+)-trans-gyplure, gyptol from Lymantria dispar, propylures from Pectinophora gossypiella S., 2,2-dimethyl-3-isopropylidenecyclopropyl propionate from Periplaneta americana (American cockroach) (Jacobson, 1961), as well as the pheromone from Carpocapsa pomonella, which was detected by Roelofs et al. (1971) as 8-E,10-E-dodecadien-1-ol on the basis of electroantennagram investigations after separation by gas chromatography, not discovered at all by McDonough et al. (1969, 1972) on reinvestigation of the codling moth but determined as active pheromone 7-methyl-3-propyl-2,2,6-E-decadien-1-ol, a constitution that did not correspond in n.m.r. spectra to an attractant synthesized stereospecifically; the correct constitution will therefore probably be 7-methyl-3-propyl-2E,6Z-decadien-1-ol (Cook, 1973).

We are currently engaged in our own investigations into new syntheses of disparlurs and gossypyrurles, taking into account the stereochemistry and the discovery of the erroneous use of inhibitory and masking effects, which were used as arguments in biological quarters at the very time when the first insect-pest pheromones were available for characterization and when these earlier papers proved to be fundamentally incorrect in important respects. These earlier misleading developments are the reason why it is impossible at present to state whether or not sex attractants can be utilized technically as a method of environmentally positive pest control.

The Defence Chemistry of some Water Beetles

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Synthetic Insecticides: A Current Appraisal

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Synthetic insecticides have to meet increasingly stringent requirements in relation to acute and chronic vertebrate toxicity and environmental persistence. At present, the burden of insect control by chemicals rests largely on a declining but indispensable use of chlorinated insecticides and on the continual development of new variants of the organophosphate and carbamate anticholinesterases. Developments in the last two classes must keep pace with the spread of insect resistance to chemicals, which is quite serious in certain disease vectors and in some insects of agricultural and veterinary importance.

The survival rate of compounds entering the complex insecticide-evaluation procedure fell from 1 in 1800 to 1 in 5040 between 1956 and 1969, while the cost of evaluation (excluding that of developing manufacturing processes, marketing, etc.) increased more than threefold. Further, insecticide manufacturers must face the prospect that the value of a successful new compound may be decreased in a very short time by resistance. Nevertheless, insect control by chemicals plays a vital part in producing crop yields unheard of 30 years ago, aside from its value for public-health programmes. Human survival is now quite dependent on this level of food production and chemical control agents of various kinds will be indispensable in the foreseeable future.

Fortunately, resistance to pyrethrins has never reached serious proportions and the synthesis of new derivatives with improved stability and high insecticidal efficiency shows that this area is by no means exhausted. When resistance is due to a modification of the site of action (target), as appears to be the case with organochlorine resistance and resistance of the cattle tick to organophosphates and carbamates anticholinesterases, the search for new targets becomes urgent. The discovery that chlorphenamidine (a monoamine oxidase inhibitor) and its derivatives are effective against cattle tick and that derivatives of 1-(2,6-dichlorobenzoyl)-3-phenylurea interfere with the deposition of insect cuticle (Mulder & Gijswijt, 1973) shows that this requirement can still be met. Further, synthetic compounds mimicking the action of natural juvenile hormone provide the possibility of control by induced selective behavioral changes as well as through morphogenetic effects, although in this area there are many practical problems to be solved.

Chlorinated insecticides

The global production of DDT [1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane] has decreased progressively since 1964, a change undoubtedly accelerated by the appearance