Synthesis of the dichloro derivatives (19) and (20) facilitated the isolation of pure *trans* isomers (19a) and (20a). It is interesting to note that in both cases the mixtures (19) and (20) are 100-fold more active than the corresponding *trans* isomers. The mixtures were characterized by nuclear magnetic resonance spectrometry, and were shown to be predominantly the *cis* and *trans* isomers of 7,11-dichloro-7,11-dimethyl-2-dodecenamides. Impurities were detected, however, and they could account for the enhanced activity. The *Cecropia* JH analogue (21) is much less active than the farnesenamide (19); the former is a much more complex mixture of isomers, and has not been as well characterized as (19).

The N-ethyl amides are structually very similar to the esters (1–3). Increased potencies could well be due to the different binding characteristics of the secondary nitrogen (both an electron pair and a hydrogen atom for noncovalent interactions) or to increased stability of the amide over the ester group. The only other nitrogen containing compounds with JH activity are some carbamates reported by Schwarz *et al.*[8] and some peptide derivatives reported by Zaoral and Sláma[12].

During our screening programme combinations of JH agents, or JH agents and insecticide synergists, were examined. In most cases there was little, if any, enhancement of activity, but a 1 : 1 combination of (6) and (19) produced a remarkable potentiation in the *Tenebrio* assay. Pupal characteristics were retained by the test insects at doses as low as 10^{-6} µg.

Compound (6) is effective in preventing maturation of houseflies (*Musca domestica*) when applied topically to final instar larvae. No normal adults are obtained at doses of 0.01 µg. Compound (19) was less active, affording complete control at 0.1 µg per larvae. Only slight potentiation effects are observed on houseflies with combinations of (6) and (19). Adult mosquitoes (*Culex pipiens*) fail to emerge from pupae when larvae are reared in water containing 0.1 p.p.m. of (6).

Incorporation of either (6) or (19) into the diet of the German cockroach (*Blatella germanica*) effectively controls colony growth and most of the adults die within a few days of being given a bait of starch containing 20 p.p.m. of the active ingredient. Gravid females drop their egg sacs prematurely, and the hatch, if any, is very small. Any nymphs which appear fail to survive to adulthood. The baits have retained their effectiveness for more than 6 months against exposure in a test cage.

Although this effect on cockroaches seems to be a general toxic response, it is also highly specific to this species. Other species, such as *Tenebrio molitor* and *Triboloium confusum*, survive as larvae or adults in media containing up to 100 p.p.m. of either (6) or (19). Development of the larvae is arrested (larvae ultimately die long after pupation would normally have occurred) and eggs laid by the adults fail to develop, but no "toxic" deaths are observed. Other species such as the Indian meal moth (*Plodia interpunctella*) seem to be unaffected by either compound. One can only speculate that the *Corpora allata* hormone(s) have some metabolic function in adult insects, and that the German cockroach is particularly susceptible to disruption of this function.

Acute oral toxicity tests have been carried out with both (6) and (19). Massive doses of (6) (3,200 mg/kg) are without effect on laboratory mice. Compound (19) has an observed LD_{50} of 3,980 mg/kg, a value which indicates this material is relatively safe as far as acute toxicity is concerned.

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PHILIP A. CRUICKSHANK
RAYMOND M. PALMERE

Central Research Department,
Chemical Research and Development Center,
FMC Corporation,
Princeton, New Jersey 08540

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Possible Role of the Pituitary/Adrenocortical Axis in Aggressive Behaviour

THE recent finding by Cherkin and Meinecke[1] that aggressive behaviour in previously isolated male rabbits could be suppressed for some weeks by allowing them to recover in pairs from barbiturate anaesthesia, raises an interesting question concerning the action of components of the pituitary/adrenocortical axis on behavioural responses. It is well established that most forms of anaesthesia are "stressful" in that they result in activation of the adrenal cortex, and the possibility thus exists that findings such as those by Cherkin and Meinecke are a consequence of changes in ACTH.

The role of pituitary and adrenocortical hormones on behaviour has been recently reviewed by Levine[2], and evidence has been obtained that ACTH depresses isolation-induced aggressive behaviour in the albino mouse[3,4].

Defeated animals show a pronounced increase in adrenocortical activity[5–7] which is not evident in the victor and it seems likely that this increase in ACTH and/or glucocorticoids may have a cue function in inducing subordinate behaviour by increasing the fear response and reducing the aggressive response. An alternative explanation for the result obtained by Cherkin and Meinecke is thus that the stress of anaesthesia causes both animals to assume subordination on emerging from anaesthesia with a consequent suppression of aggressive behaviour. This subordination could be specific to the animal in whose presence they recovered: dominance could be associated with the visual or olfactory characteristics of the other animal.

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PAUL F. BRAIN

Department of Zoology,
University of Sheffield,
Yorkshire

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