mmolar D-galactono-1,4-lactone and not by 25 mmolar D-glucono-1,4-lactone. Conversely xylosidase activity was inhibited by the gluconolactone and not by the galactono-lactone¹². The xylosidase and glucosidase activities of rat liver particles (lysosomes) and nasal and ear cartilage could be distinguished by their different pH optima.

The apparent ubiquity of these glycosidases in connective tissues may be of considerable relevance to the turnover of some polysaccharide-protein complexes.

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In vitro Anticholinesterase Activity of Certain N-Methylcarbamate Insecticides compared with their N-Acyl Derivatives

THE insecticidal activity of certain *N*-acyl *N*-methylcarbamate insecticides has been reported recently by Fraser *et al.*¹. Reay and Lewis² showed that the *N*-acetyl derivative of 1-naphthyl *N*-methylcarbamate (carbaryl) was nearly 100 times less inhibitory towards honeybee head cholinesterase (ChE) *in vitro* than the parent compound (see also Table 1). It is the purpose of this communication to report that the *N*-acylation of several other *N*-methylcarbamates leads to a marked reduction in *in vitro* anticholinesterase activity against honeybee head ChE.

The method used for the assay of ChE has already been described in full². The insecticides used were of the general structure I or II, where *R'* is an aromatic nucleus and *R''* is a simple alkyl group.

They were dissolved in 'AnalaR' acetone for addition to the assay mixture, and the activity of ChE in the presence of insecticide was compared with that in the presence of acetone only. The results are summarized in Table 1.

It is clear that *N*-acylation of all the *N*-methylcarbamates tested causes a marked drop in their activity against honeybee head ChE *in vitro*. The fall in activity is, in fact, less in the case of carbaryl, already cited², than for any of the others; the factor involved is nearly a thousand in most instances. It is also apparent, however, that acylation with side chains of increasing length, up to C=6, increases the activity against ChE compared with that of the acetyl derivative, though the activity of the parent carbamate is on no occasion fully restored. *N*-acylation with a dodecanoyl group, however, gives decreased activity against ChE.

Because the lengthening of the nitrogen-attached side-chain from C=2 to C=6 leads to an increase in inhibition

Table 1. *In vitro* ANTICHOLINESTERASE ACTIVITY OF CARBAMATES

Insecticide	IC 50*
1-Naphthyl <i>N</i> -methylcarbamate (carbaryl)	4.75 × 10 ⁻⁸
1-Naphthyl <i>N</i> -acetyl- <i>N</i> -methylcarbamate	4.0 × 10 ⁻⁶
1-Naphthyl <i>N</i> -propionyl- <i>N</i> -methylcarbamate	8.5 × 10 ⁻⁷
1-Naphthyl <i>N</i> -butyryl- <i>N</i> -methylcarbamate	6.0 × 10 ⁻⁷
2-Isopropylphenyl <i>N</i> -methylcarbamate	4.25 × 10 ⁻⁷
2-Isopropylphenyl <i>N</i> -acetyl- <i>N</i> -methylcarbamate	1.4 × 10 ⁻⁴
2-Isopropylphenyl <i>N</i> -hexanoyl- <i>N</i> -methylcarbamate	8.0 × 10 ⁻⁶
2-Isopropylphenyl <i>N</i> -dodecanoyl- <i>N</i> -methylcarbamate	2.2 × 10 ⁻⁴
3-Isopropylphenyl <i>N</i> -methylcarbamate	2.2 × 10 ⁻⁸
3-Isopropylphenyl <i>N</i> -acetyl- <i>N</i> -methylcarbamate	2.0 × 10 ⁻⁵
3-Isopropylphenyl <i>N</i> -butyryl- <i>N</i> -methylcarbamate	8.4 × 10 ⁻⁶
3-Isopropylphenyl <i>N</i> -hexanoyl- <i>N</i> -methylcarbamate	2.3 × 10 ⁻⁶
2-Isopropoxyphenyl <i>N</i> -methylcarbamate	7.5 × 10 ⁻⁷
2-Isopropoxyphenyl <i>N</i> -acetyl- <i>N</i> -methylcarbamate	6.5 × 10 ⁻⁴
2-Isopropoxyphenyl <i>N</i> -butyryl- <i>N</i> -methylcarbamate	3.0 × 10 ⁻⁴
4-Dimethylamino-3,5-xylyl <i>N</i> -methylcarbamate	1.25 × 10 ⁻⁸
4-Dimethylamino-3,5-xylyl <i>N</i> -acetyl- <i>N</i> -methylcarbamate	4.0 × 10 ⁻⁶

* IC 50 = Concentration (moles/l.) for 50 per cent ChE inhibition.

of ChE, it is clearly not possible to postulate that it is steric hindrance which is responsible for the decrease in ChE inhibition on *N*-acetylation. Steric hindrance could, however, be an important reason for the loss of activity of the dodecanoyl derivative. It seems more likely that the decrease of activity on acetylation results from the change of electron distribution brought about by the introduction of the electron-withdrawing acetyl —C=O group. This hypothesis is analogous to those proposed by Kolbezen *et al.*³ and Metcalf *et al.*⁴ to explain the activities of certain other substituted carbamates. The withdrawal of electrons from the —O.CO.N— group of the carbamate will result in the formation of a weaker bond between the inhibitor and ChE, because it is this group that has been found to be the point of attachment to the enzyme⁵⁻⁷. The increased activity of the longer-chain *N*-acylated compounds, however, cannot be explained along these lines, because the alkyl group has little electron-shifting capacity and would, if anything, tend to increase the electron-withdrawing capacity of the acyl group (compare Kolbezen *et al.*³). This means that some factor other than electron density and steric hindrance must be important in determining the affinity of a carbamate inhibitor for ChE.

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Activation of Honeybee Head Cholinesterase by Water-miscible Organic Solvents

COLHOUN¹ showed that many water-miscible organic solvents increased the activity of cholinesterase (ChE) preparations from the cockroach *Periplaneta americana*. Shatoury^{2,3} showed that a similar activation occurred in the case of the housefly *Musca domestica*, though here *n*-butanol only was used as "activator", and the effect was far less marked. It has now been found that an even larger activation than that recorded by Colhoun can be achieved by addition of certain water-miscible organic