References and Notes

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n-Butyl 5-Chloro-2-pyrimidoxyacetate—a Plant Growth Regulator Analog

Since the first demonstration of plant growth stimulation by substituted phenoxyacetic acids (*1*), much attention has been directed toward this series of compounds in an attempt to correlate the position and type of substituent with observed growth promotion. The results of the many investigations aimed at the elucidation of the mechanism of growth-regulator action have been resolved into three general theories.

One of these theories (*2*) supposes that there is a chemical reaction between the regulator and appropriate groups, probably nucleophilic, on some plant substrate, resulting in the formation of new convalent bonds. It has been shown that the most likely point of attack on the ring is at the positions *ortho* to the ether oxygen. Another theory (*3*) gives major importance to the shape of the regulator molecule and the specificity of its "fit" onto some receptor within the plant. In this case, the benzene nucleus with its substituents acts as a whole at the locus or point of attachment, and chemical reactions at the ring are considered unlikely. The third and most recent theory, unlike the other two, is not concerned with the relations of the regulator with an "active site," but suggests that the growth-regulating activity of a compound is primarily associated with its ability to chelate metal ions, such as Mg^{++} (*4*).

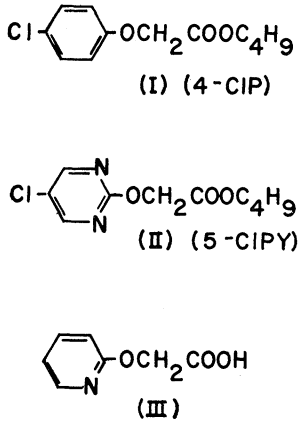

Fig. 1. Structural formulas.

In order to make a comparative test of these theories, we have prepared the butyl ester of 5-chloro-2-pyrimidoxyacetic acid (Fig. 1, II) (*5*). This compound is almost identical with the very active growth regulator, butyl *p*-chlorophenoxyacetate (Fig. 1, I) in its size, shape, ring planarity, molecular weight, halogen and ester reactivity, and also in those physical constants which were measured. However, the pyrimidine offers no possibility of nucleophilic reaction in the positions *ortho* to the ether oxygen (positions 1 and 3), and an aromatic type of substitution has never been observed to occur in positions 4 or 6 of the pyrimidine nucleus.

The plant growth regulatory activity of compounds I and II (Fig. 1) was measured by use of the oat coleoptile, wheat coleoptile, oat first-internode, and slit-pea curvature bioassays. In each case, the phenoxy ester was shown to be a highly active growth stimulator, while the pyrimidoxy ester was completely inactive.

An example of this difference in activity is shown in Fig. 2. For these tests, 4-mm sections of first internodes of dark-grown oat seedlings were rotated at *p*H 5.0 in citrate-phosphate buffer containing 2 percent sucrose and the compound under investigation at concentrations of 10^{-3} to $10^{-7}M$ (*6*). After about 20 hours, the oat sections were removed, their length was measured, and the data were subjected to statistical analysis. Results similar to those presented in Fig. 1 were obtained at *p*H 7.5 in 0.067*M* phosphate buffer, but were less clearly defined because of a diminished difference in growth between the treated sections and controls under alkaline conditions (*6*).

Consideration of the structure of compound II (Fig. 1) shows that it should be a chelating agent in the ways proposed for indole-3-acetic ester and for derivatives of phenoxyacetic acid. In addition, chelation could occur through the two nitrogens as it does in similar

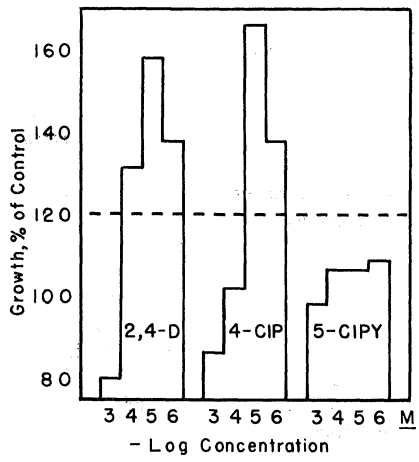

Fig. 2. Growth of oat first-internode sections at *p*H 5.0. Values above the broken line represent statistically significant promotion.

ureas and pyrimidines. Regarding the specificity of its "fit" onto a receptor, the molecule is spatially almost indistinguishable from that of compound I (Fig. 1) and while the pyrimidine ring would be expected to be more hydrophilic than the benzene ring, the recent descriptions of the high degree of plant growth stimulation by 2-pyridoxyacetic acid (Fig. 1, III) (*7*) indicate that lipophilic character may not be as important as previously suggested. Consequently, the inactivity of compound II (Fig. 1) does not substantiate two of the current theories, and it leads us to conclude that the *ortho* positions may indeed bear an important relation to biological activity in the phenoxy acid series (*8*).

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