The results (Table 1) can be summarized briefly: The high degree of dextrorotation ($[\alpha]_D = 100-150^\circ$) normally characteristic of the alkaline form of poly A in water^{3,4} is, in methanol containing 0.001 *M* sodium acetate, replaced by a small negative rotation.

Furthermore, most of the hypochromism displayed by poly A in water disappears in methanol solution, as Table 1 shows. The absorbancy at 260 m μ increases by more than 40 per cent in the latter medium and becomes independent of temperature. Inasmuch as the absorbancy of the monomer, adenosine monophosphate, was found to be the same in water and in methanol there is a definite implication that the result with poly A reflects some modification in the secondary structure or conformation of the polymer.

The macromolecular properties of poly A underwent an equally dramatic change. A profound increase in the sedimentation coefficient and a decrease in intrinsic viscosity occur in methanol solution, as has already been observed in the case of DNA (refs. 1 and 2).

All these effects were reversible on removal of methanol by dialysis versus water.

The effect of methanol upon the over-all macromolecular properties of poly A is entirely in harmony with the reported results upon DNA. In both cases a dominant factor in the molecular collapse is undoubtedly the largely ion-paired character of the phosphate groups in alcoholic solution². The electrostatic stress, which is important for aqueous solutions of polyelectrolytes at the low ionic strength (0.001) of these investigations, is thus largely relieved.

Thus the apparent helical content of poly A largely disappears in methanol, as judged by both the hypochromism and optical rotation criteria.

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Toxicity of 2-(2-Halogen-4-Chlorophenyl)-2-(4-Chlorophenyl)-1,1,1-Trichloroethanes to Normal and to DDT-Resistant House-Flies

As part of a programme designed to test a free-radical hypothesis of insecticidal action for DDT¹, a series of new DDT compounds substituted by halogen in the ortho-position was synthesized and the toxicity to normal and to DDT-resistant house-flies (*Musca domestica* L.) was determined (Table 1). The results are of unusual significance in regard to: (1) the mechanism of DDT resistance, and (2) the relative toxicity of the positional isomers of DDT.

In the susceptible *S*-strain of the fly, a direct correlation exists between the size of the halogen in the ortho position and the LD_{50} value. A reverse correlation is evident with *in vitro* enzymatic dehydrochlorination. If this detoxication mechanism is indeed the basis for DDT-resistance in the resistant *R*-strain, the toxicity of these compounds to the tolerant strain should be the resultant of these two inverse relationships. Results support this supposition with the maximum insecticidal effectiveness occurring

Table 1. TOXICITY SPECTRA OF DDT ANALOGUES TO SUSCEPTIBLE AND RESISTANT HOUSEFLIES AND CORRELATION WITH DEHYDROCHLORINASE ACTIVITY

LD_{50} ($\mu\text{gm./}\varnothing$ fly)		Relative enzymatic dehydrochlorination (<i>in vitro</i>)
Compound	X	Y	<i>S</i> -strain (CSMA)	<i>R</i> -strain (DDT-45)	<i>R</i> -strain Brel
I	H	Cl	0.1	> 40	+++
II	F	Cl	0.2	14.0	++
III	Cl	Cl	0.4	0.8	+
IV	Br	Cl	1.1	2.0	—
V	H	H	3.3	> 40	+++
VI	Cl	H	6.2	~30	—

LD_{50} values are averages of duplicated tests made on at least two successive generations of 5-day-old flies. Each point on dosage-mortality curve was determined by topical application (in 1 μl . acetone) to 80-100 female flies. Treated flies were held at 75-80° F. and percentage mortality recorded at 24 hr. Enzyme activity was measured on a concentrated homogenate of *R*-strain, assayed by the glass bead procedure (ref. 3).

in the 2-(2,4-dichlorophenyl)-2-(4-chlorophenyl)-1,1,1-trichloroethane (III).

The toxicity spectrum with the *S*-strain indicates that mono-ortho substitution by a chlorine atom reduces toxicity of the parent compound by a small factor. (Compare I with III and V with VI.) When one observes the much greater difference in toxicity between I and V and between III and VI, it becomes evident that the weak activity of VI is primarily the result of the loss of the para-substituent. Hindrance of 'free rotability' of the benzene rings² by a single ortho-chloro-substituent can only be of lesser importance in reducing the insecticidal properties of the molecule. The possibility that samples of VI may contain a small amount of I and thus account for the toxicity of the former compound to *S*-strains may be raised. Barring synergism, the fact that VI is still somewhat toxic to the *R*-strain would appear to preclude this possibility.

Further work is in progress to evaluate these and related compounds against different fly strains, naturally tolerant insects, and species with acquired resistance. Selection experiments are also being conducted to determine if the house fly has the capacity to develop resistance to these new compounds. Data on the methods of synthesis and characterization of these new compounds will be published elsewhere.

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