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Isomerization of Lindane by Reduced Hematin

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The insecticidal activity of technical grade hexachlorocyclohexane (HCH) (also known as benzene hexachloride or BHC) is attributable to its relatively minor (11-18%) γ-isomer component (configuration aaaeee). The α- and β-isomer components (configuration aaeeee and eeeeee, respectively) are more hazardous to mammals than the γ-isomer based on their relative chronic toxicity including oncogenicity and ease of biodegradation. For effectiveness and safety, the purified γ-isomer or lindane is strongly preferred over the isomer mixture (JOHNSON 1976, JOHNSON 1977).

Lindane is reported to isomerize to the α and β isomers under environmental conditions (NEWLAND et al. 1969), in microorganisms (BENEZET and MATSUMURA 1973, MATSUMURA et al. 1976), and rats (KAMADA 1971) and to the α- and δ-isomers on UV irradiation (STEINWANDTER 1976). Some attention was given in these studies to the possibility of trace impurities in the lindane undergoing less rapid metabolism and therefore selective accumulation. On careful reexamination by fat and liver analyses of treated animals it was concluded that bioisomerization to the α or β isomer does not play a significant role in lindane metabolism by rats (COPELAND and CHADWICK 1978).

It is important to evaluate the feasibility of environmental or metabolic isomerization of lindane (JOHNSON 1977). The present investigation establishes that lindane isomerizes to the α- but not the β-isomer on incubation with reduced hematin (SALEH and CASIDA 1978), a biomimetic condition.

MATERIALS AND METHODS

Chemicals. The lindane used was > 99.8% pure (< 0.01% of each of the α, β and δ isomers). Hematin (1.0 g) in 300 ml of glacial acetic acid: N-methylpyrollidone (1:1) under argon was reduced with iron powder (50 mg) then lindane (2 g) was added and the reaction mixture held for 72 hr at 25°C. The products were then

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extracted into hexane which was washed with water, $NaHCO_3$ solution and saturated NaCl solution and dried over $MgSO_4$. The extract was subjected to cleanup by chromatography on a silicic acid column with hexane as the eluting solvent to obtain 107 mg of white solid (5.4% yield) for analysis and identification of some components by GC/MS and TLC. Preparative TLC was appropriate to isolate an individual HCH isomer (0.7% overall yield) for identification by NMR.

GC/MS conditions. The Finnigan 4023 computer system was used with a SP-2100 wall-coated glass capillary column (0.25 mm i.d. x 30 m) and helium as the carrier gas (30 cm/sec linear velocity). Data was acquired at the rate of one scan/sec. Chromatographic conditions were as follows: injection, port and interface temperatures of 260°C; column temperature of 170°C for 3 min then programmed to 270° at 1°C/min.

RESULTS AND DISCUSSION

The hematin reaction gives a product in 0.7% overall yield that cochromatographs with α-HCH (Fig. 1). The MS of this product is identical to an authentic sample of α-HCH but differs from β-, γ- and δ-HCH (Fig. 2). Negative and positive ion CI do not differentiate the HCH isomers. In negative ion CI the only peaks are ion clusters associated with M-Cl (253), Cl_2^-(70) and Cl^-(35), the latter being the base peak. Although negative ion CI is not a useful diagnostic tool, it provides greater detector sensitivity than EI.

The hematin product also cochromatographs with α-HCH on TLC and gives an NMR spectrum identical to α-HCH. These criteria of identity (GLC, TLC, MS, NMR) are adequate to establish unequivocally the conversion of lindane to α-HCH under biomimetic conditions.

No evidence is obtained for formation of any β- or δ-HCH on reacting lindane with reduced hematin. Three other products are formed, however, giving GLC-MS patterns characteristic of lindane metabolites (ENGST et al. 1977), i.e., the dehydrochlorination and reductive dechlorination products.

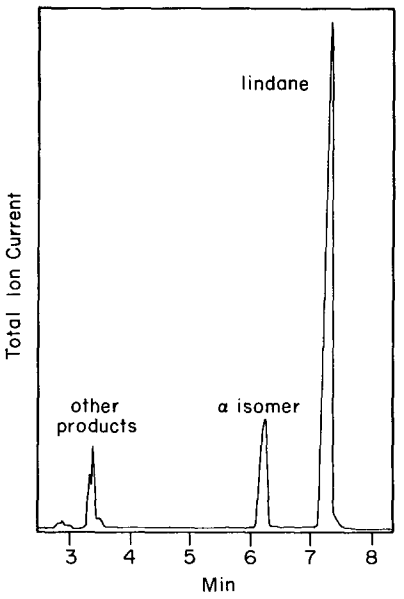


Fig. 1: Total ion current gas chromatogram of the lindane products

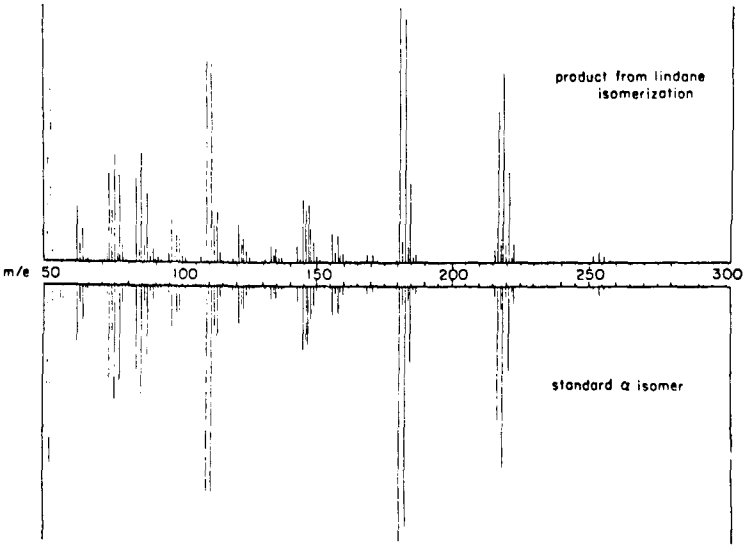
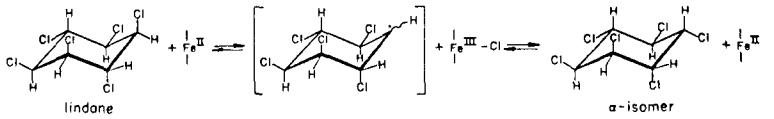


Fig. 2: EI-mass spectrum of product from lindane isomerization and standard ∝-isomer

The hematin system isomerizes lindane to α-HCH possibly via a free radical intermediate.



This study establishes the feasibility of lindane isomerization under biomimetic conditions, however, it does not evaluate the significance of the isomerization under metabolic or environmental conditions.

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