UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MAR 1 1 1991

MEMORANDUM

SUBJECT: Product Chemistry Review (Supplementary) for Chlorpyrifos (Pyrinex) - EPA Registration No. 11678-45 - Accession No. 416230-01

FROM: Bipin Gandhi, Chemist
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Introduction

This is a supplementary review for chlorpyrifos produced by Makhteshim Chemical Works, Ltd. (MCW), Beer Sheva, Israel. The original review was performed by William L. Anthony of the Residue Chemistry Branch, HED, and assigned RCB No. 698, dated June 3, 1986, and a supplementary review, RCB No. 930, dated July 3, 1986. Additional supplementary review was performed by Bipin Gandhi of Product Chemistry Review Section, Registration Support Branch, RD on April 6, 1989 which reviewed Accession Nos. 404364-02, -03, and -04. This review is in response to the deficiencies of April 6, 1989 review.

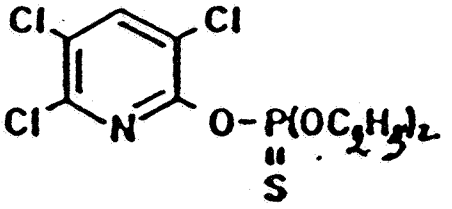
Product Identity

Product Name: Pyrinex chlorpyrifos technical

Common Name: Chlorpyrifos

Molecular Formula: O,O-diethyl O-3,5,6-trichloro-2-pyridyl phosphorothioate

Structural Formula:



Empirical Formula: $C_9H_{11}Cl_3NO_3P_5$

Molecular Weight: 350.6

Deficiencies Reported in the Previous Reviews

The Agency required that the registrant analyze five batches and determine dioxin content. A control should be run to make a quantitative determination and all calculations and analytical data, including graphs, must be submitted.

Series 61-3 (cont'd) - Synthesis and Determination of Dioxin

analog dipyridine analog of 2,3,7,8-Tetrachloro-dibenzo-p-dioxin

Synthesis of 2,3,7,8-Tetrachloro-1,4-dioxino[2,3-b:5,6-b'] dipyridine

The synthesis of 2,3,7,8-tetrachloro-1,4-dioxino [2,3-b:5,6-b'] dipyridine was performed according to the method of C.D. Weis (J. Heterocyclic Chem., 1976, 13(1), 145) (attached). Reagents were purchased from the Aldrich Chemical

Company and were ACS grade or better. The reaction progress and product purity were monitored by infrared spectrometry and mass spectrometry. Due to the potential toxicity of the intermediate and target compounds, all reactions after step 1 were carried out on a microscale and yields were not calculated.

"A 50.0 g sample of 2-methyl-5-hydroxy-pyridine was suspended in 500 mL of concentrated hydrochloric acid. Chlorine gas was introduced slowly at 70 °C for a period of 8 hours. The solution was stirred for 30 hours then concentrated using a rotary evaporator. Upon formation of a heavy suspension, the solution was neutralized with sodium bicarbonate then recrystallized from hot methanol and water. The product was analyzed by direct insertion probe mass spectrometry (MS). Based on the MS data, pure product was obtained.

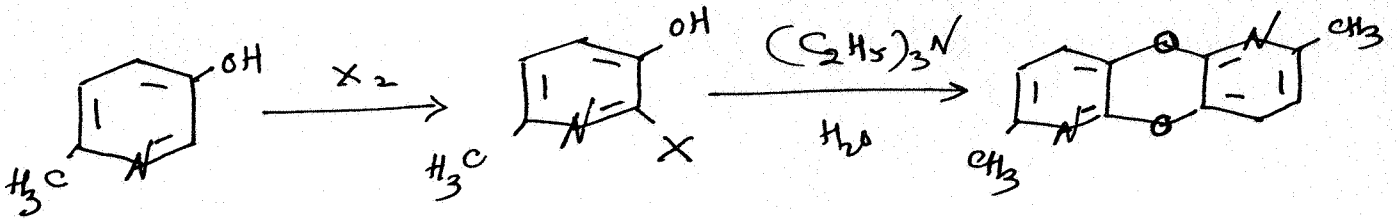
"A 5.0 g aliquot of the recrystallized product was slurried in 25 mL of a 1:1 mixture of triethyl amine and deionized water. This mixture was placed in an evaporating dish and then heated to 160 °C for 72 hours in a sealed vacuum chamber. A complex mixture of products was obtained which required extensive workup. Approximately 0.9 g of crude 2,7-dimethyl-1,4-dioxino [2,3-b:5,6-b']dipyridine was obtained after three iterations of this step of the synthesis.

"A 0.25 g aliquot of the crude 2,7-dimethyl-1,4-dioxino [2,3-b:5,6-b']dipyridine in 10 mL of dimethylformamide (DMF) was treated with chlorine gas. The solution was cooled and filtered. The filtrate was redissolved with hot DMF and cooled to obtain crystalline product (2,7-dimethyl-3,8-dichloro-1,4,dioxino[2,3-b:5,6-b'] dipyridine).

"The product (2,7-dimethyl-3,8-dichloro-1,4,dioxino [2,3-b:5,6-b']dipyridine) from above was slurried in 10 mL of hexachlorobutadiene. Chlorine gas was introduced and irradiated with a low intensity UV source. The solution temperature rose rapidly and gas was evolved. The reaction vessel was cooled to maintain the temperature below 200 °C. The crystalline product (0.0113 g) was isolated by filtration and analyzed by MS. The MS data indicated the product was impure and further cleanup was required.

"The final product was then purified by high performance liquid chromatography (HPLC) using a reverse phase column and 100 percent acetonitrile as the solvent. Five fractions were collected and analyzed by gas chromatography/mass spectrometry (GC/MS) to locate the fraction containing the 2,3,7,8-tetra-

chloro dipyridine analogue (2,3,7,8-TCDPA). This fraction was then chromatographed using normal phase HPLC and concentrated to dryness in a tared vial, resulting in 2.54 mg of pure 2,3,7,8-TCDPA."



X = Cl .

For additional information see Confidential Appendix A.

Recommendations

No additional data are required at the present time and the Agency has no adverse comments at the present time.

Attachment