Synthesis of potential pesticide synergists

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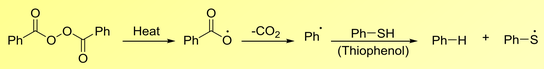
Introduction

Pesticides exterminate various types of insects by inhibiting an important enzyme called CYP 3A4 which is responsible for removing toxins from their system. By inhibiting this enzyme, the insect can no longer remove harmful chemicals from its body and the accumulation of the chemicals will in time kill it.

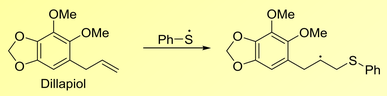
Previous work on this project has shown that any derivatives of dillapiol containing an ester functional group (R-CO_2-R) will have its effect neutralized by another enzyme that most insects possess. The esterase enzymes react with the potent compound and hydrolyze it, turning it into much less potent alcohols. Therefore, new derivatives of dillapiol without any ester groups must be made to successfully inhibit the CYP 3A4 enzyme.

Reaction Mechanism

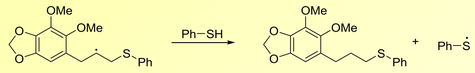
Step 1:



Step 2:

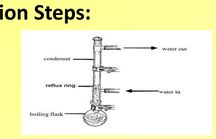


Step 3:

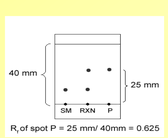


Methods

Reaction Steps:

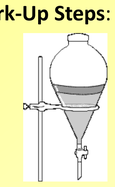


Reflux Condenser



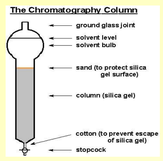
TLC Plate

Work-Up Steps:

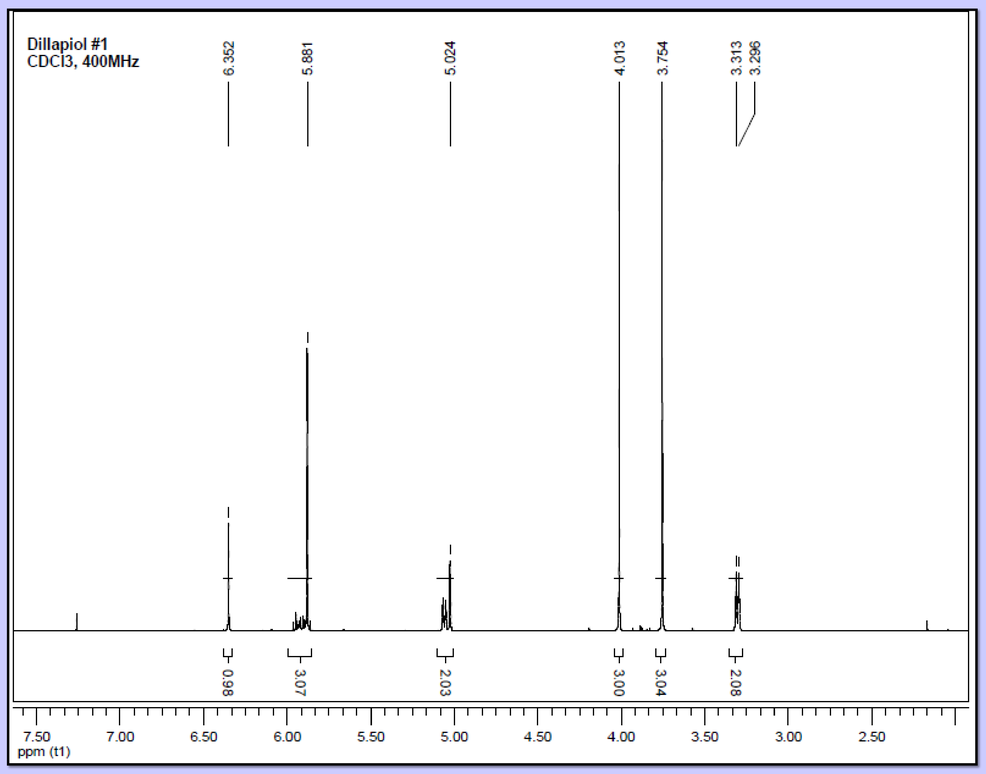


Extraction Funnel

Rotary Evaporator

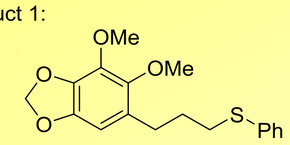


Chromatography Column

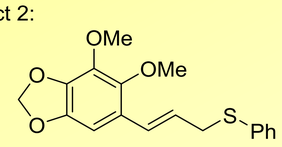


Results

Product 1:

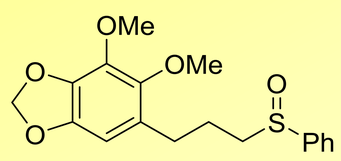


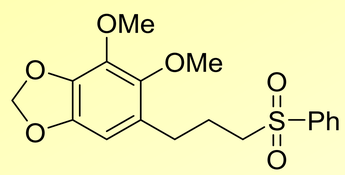
Product 2:



The radical reaction gave two products, several attempts were made to isolate only the first product (the one without the double bond) by running a series of columns as well as trying hydrogenation so as to break the double bond by adding hydrogen atoms to the carbon atoms. All of the attempts were unsuccessful and time constraints prevented any further attempts.

Had the single desired product been isolated, it would have been reacted further via oxidation so as to create two derivatives of the original compound. Oxidation would have been performed with meta-chloroperoxybenzoic acid (mCPBA) which would have created two oxidized products. Afterwards, several steps would have been taken to isolate each individual product. The oxidized products are shown below:





Conclusion

In conclusion, the radical reaction between dillapiol and thiophenol did produce the desired product but what was unexpected was that two products formed. Radical reactions are highly reactive and are hard to control which explains why one of the products had reformed a double bond further down the carbon chain. The two products had very similar chemical properties which made it very difficult to only isolate one.

The isolated desired product would have been used to create another two products via an oxidation reaction. All three synthetic derivatives of dillapiol would have advanced to the next step of testing them on insects. The testing would have been done by ingestion as well as topical application to determine their inhibitory activity of the CYP 3A4 enzyme. Their inhibitory effects would assess their potential as pesticide synergists.

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