

## A Mild Method for Acylation of *O,S*-Dimethyl Phosphoramidothiolate

*O,S*-Dimethyl phosphoramidothiolate, the insecticide methamidophos, can be acylated under mild conditions with monocarboxylic acids or half-esters of dicarboxylic acids with the aid of dicyclohexylcarbodiimide. The method gives better yields and purer products than acylations of the insecticide with carboxylic acid chlorides or anhydrides.

Acylation of methamidophos (*O,S*-dimethyl phosphoramidothiolate, I) makes it less toxic to certain animals and improves its translocation characteristics in plants. Acetylation, for example, decreases the mammalian toxicity of the parent insecticide 45-fold without lowering insect toxicity to any large degree (Magee, 1973). When acylated with an ethyl malonyl moiety (Crisp et al., 1979), the insecticide is many times more phloem-mobile in plants. Extension of these acylations has been difficult, particularly with the dicarboxylic acid groups. The standard method using acyl chloride or anhydride is harsh and often leads to decomposition of the insecticide and the acylation product. Moreover, the syntheses of half-ester acid chlorides for the acylation are often difficult.

Alternatively, one may acylate with carbodiimide, a method used in peptide synthesis. The method was developed for the half-ester dicarboxylic acylation of *O,S*-dimethyl phosphoramidothiolate in this laboratory and is used routinely for the synthesis of alkyl dicarboxyl *O,S*-dimethyl phosphoramidothiolate (II) (Scheme I).

This method also applies to acylation with monocarboxylic acids. The carbodiimide acylation is considerably milder than the aforementioned methods and gives purer products. The partially hydrolyzed decomposition products of harsher acylation methods are only minor impurities in this synthetic route. The method is currently being developed for acylation of other pesticides.

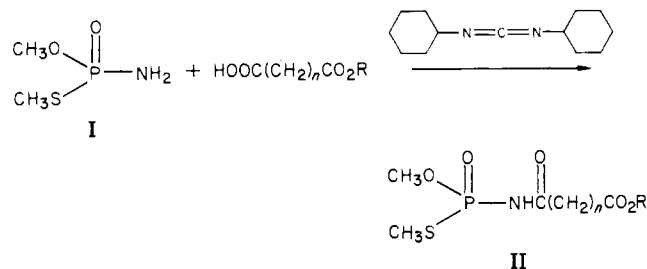
### EXPERIMENTAL SECTION

**Materials.** Dicyclohexylcarbodiimide was purchased from the Aldrich Chemical Co. The *O,S*-dimethyl phosphoramidothiolate was supplied by the Chevron Chemical Co. and was recrystallized to a purity of 95% from methylene chloride. Monoethyl malonate was prepared by partial hydrolysis of the diester.

**Methods.** The following examples are typical procedures for the acylation using dicyclohexylcarbodiimide.

*O,S*-Dimethyl *N*-(Ethyl malonyl)phosphoramidothiolate. Dicyclohexylcarbodiimide (1.05 g, 5.1 mmol) in 10 mL of methylene chloride was added, in one portion, to a stirred solution of 0.6 g (4.25 mmol) of *O,S*-dimethyl phosphoramidothiolate and 0.62 g (4.68 mmol) of monoethyl malonate in 15 mL of methylene chloride chilled in an ice bath. A white precipitate formed almost immediately. Stirring was continued at 0 °C for about 1 h and then at room temperature overnight. The urea precipitate was filtered and washed with 10 mL of methylene chloride. The filtrate was washed once with water and the organic layer was removed by filtration through Whatman phase separator paper. Evaporation of the solvent gave the acylated product with a small amount of urea. The urea was separated by removal of the acylated product with reagent grade acetone. Evaporation of the acetone solution gave 0.87 g of *O,S*-dimethyl *N*-(ethyl malonyl)phosphoramidothiolate of about 90% purity. The product is identical with the product synthesized with acyl chloride (Look et al., 1976). Chromatography on a silica gel column,

Scheme I. Acylation Reaction with Dicyclohexylcarbodiimide



eluting with methylene chloride and then acetone-methylene chloride (1:1), gave even purer material.

*O,S*-Dimethyl *N*-Dodecanoylphosphoramidothiolate. Dicyclohexylcarbodiimide (1.07 g, 5.2 mmol) in 10 mL of methylene chloride was added, in one portion, to a stirred solution of 0.6 g (4.3 mmol) of *O,S*-dimethyl phosphoramidothiolate and 0.94 g (4.7 mmol) of dodecanoic acid in 25 mL of methylene chloride chilled in an ice bath. A precipitation of dicyclohexylurea appeared with 15 min. The reaction was allowed to be stirred at 0 °C for about an hour and then at room temperature overnight. Acetic acid (0.25 mL) was added to decompose the remaining carbodiimide. The urea was filtered and washed with 10 mL of methylene chloride. The filtrate was washed with water and the organic phase was separated by filtration through Whatman phase separator paper. Evaporation of the solvent left a waxy solid contaminated with a small amount of urea. The product was removed from the urea with the aid of cyclohexane. Evaporation of the cyclohexane gave 1.2 g (83%) of *O,S*-dimethyl *N*-dodecanoylphosphoramidothiolate, identical with material synthesized by Magee (1974).

### LITERATURE CITED

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