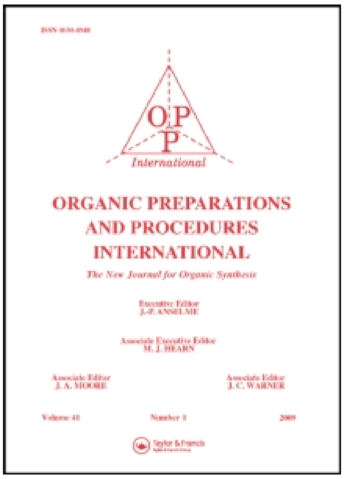

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SURFACE MEDIATED SYNTHESIS OF O-PHOSPHOROTHIOATES

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SURFACE MEDIATED SYNTHESIS OF O-PHOSPHOROTHIOATES

Submitted by
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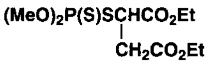
Malathion, parathion, quinalphos, chlorpyrifos, edifenphos, monocrotophos, phosphamidon, and *phorate* are widely used organophosphorus compounds for pest control in India. *Parathion* is manufactured industrially by a laborious procedure involving the treatment of O,O-diethyl thiophosphoryl chloride with *p*-nitrophenol at 10° in a 20% solution of sodium ethoxide in ethanol.[1]

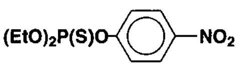
Malathion



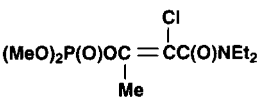
$(MeO)_2P(S)SCH(CH_2CO_2Et)CO_2Et$

Edifenphos $(PhS)_2(P(S)OEt$

Parathion

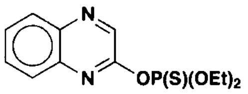


Phosphamidan



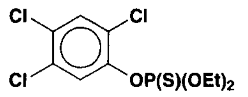
$(MeO)_2P(O)OC(Me){=}C(Cl)C(O)NEt_2$

Quinalphos

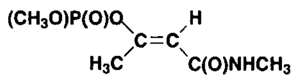


Phorate $(OEt)_2P(S)SCH_2SEt$

Chlorpyrifos



Monocrotophos



Distillation of solvent, followed by dilution with water, filtration and subsequent steam distillation provides the product. Finally the product is dried by heating at 110° under vacuum. Similar aqueous work-up and vacuum distillation are necessary to manufacture *chlorpyrifos*[2] *monocrotophos, phosphamidon* and *malathion.*

The general method of reacting a hydroxy compound with thiophosphoryl chloride at elevated temperatures in the presence of an acid binder in ketones suffers from disadvantages such as (a) liberation of hydrogen chloride gas which leads to corrosion in industrial production, (b) formation of side-products at high temperatures, and (c) hydrolysis of the organophosphorus compounds during aqueous workup.[3-7] Attempts to overcome these difficulties by the use of a two-phase system consisting of toluene and the sodium salt of the hydroxy compounds using tetra-*n*-butyl ammoniumbisulfate (Bu_4NHSO_4) as a phase transfer catalyst,[8] may also lead to possible hydrolysis of the phosphorylated ester in the presence of water and the requirement of another co-catalyst such as 1-methylimidazole to increase the reaction rates. Polymer-supported reagents, such as Amberlyst A-26, have been used to synthesize triaryl phosphates at room temperature. The use of polymer-supported reagent avoids aqueous work-up, and the resin can be processed for re-use.[9] Amberlite IRA-400 was used for the synthesis of thiophosphonates. However, owing to the low exchange capacity of the resin (1g/1 mmol), even an excess of the resin did lead to a good yield of the product. Polyethyleneglycols (PEG) function as efficient phase-transfer catalysts in a variety of reactions.[10-14] Termed as *poor man's PTC*, PEG's are comparable to crown ethers in their ability to complex and transport alkali metal cations from an aqueous medium to the organic phase.[15] Complete solubility in water, ready availability and low cost make PEG an excellent medium for a variety of organic reactions. The present work details the reaction of dialkyl thiophosphoryl chloride with hydroxyaryl compounds in the presence of basic alumina containing PEG-400.

$$\mathrm{ArONa} + \mathrm{ClP(S)(OEt)_2} \xrightarrow[\text{basic alumina}\\ \text{RT}]{\text{PEG-400 on}} \mathrm{ArOP(S)(OEt)_2} + \mathrm{NaCl}$$

Organic reactions on solid supports have elicited considerable recent interest.[16] The effectiveness of alumina may be due to the combination of several factors such as (a) an increase in the effective surface for the reaction, (b) the presence of pores which contain both substrate and reactant lowers the entropy of activation of reactions, and (c) a synergistic effect resulting from bringing the electrophile and nucleophile into proximity, while at the same time enhancing the nucleophilicy and basicity of the latter.[16] The procedure involves intimate blending of the sodium salt of the hydroxyaryl compound with diethyl thiophosphoryl chloride (DETC) on basic alumina containing PEG-400 for a short duration. The advantage lies in avoiding the usual cumbersome work-up procedure and hydrolysis of the product. This simple methodology which could be exploited effectively for large scale preparations, is envisioned to yield the phosphonochloridothioates in impressive yields. Incidentally, the above strategy provides a facile pathway to *quinalphos*, a commercially important insecticide.

EXPERIMENTAL SECTION

Commercial sample of PEG-400 was obtained from Fischer (India) Chemical Co. The compounds synthesized are known in the literature and their identities were established by IR, ^{1}H NMR, and mass spectra.

Synthesis of O-Phosphorothioates. General Procedure.- Sodium hydroxide (0.48 g, 12 mmol; for entry no **3**, 24 mmol) was added to a stirred mixture of the hydroxyaryl compound (10 mmol) in methanol (8 mL) and water (2 mL). After 30 minutes, the solvent was distilled off under reduced pressure to afford the sodium salt. In the meantime basic alumina (15 g) was added (in 1 g portions) to polyethyleneglycol-400 (5 mL) and mixed throughly. Then 5 g of the above solid mixture of alumina-PEG-400 was added to a mixture of sodium salt of the hydroxyaryl compound (10 mmol) and O,O-diethylthiophosphoryl chloride (1.89g, 10 mmol, 1.57 mL). The resultant mixture was ground up using a mechanical grinder[22] (heavy duty mixer grinder) for an hour up to 300 mesh size. The reaction mixture was then extracted with chloroform (3x25 mL) and dried (sodium sulfate). Chloroform and O,O-diethylthiophosphoryl chloride were removed by distillation under low pressure to leave the pure product (**Table 1**).

Table 1. Solid Surface Mediated Synthesis of Phosphorothioates

Ar-	Yield (%)	PMR (CCl_4/TMS, δ)	mp. (bp.) °C Observed	lit.
p-$NO_2C_6H_4$	79	8.32-8.16 (*d*, *Ar*, 2 H), 7.39-7.28 (*d*, 2 H, *Ar* H), 4.54-3.97 (*q*, 4 H, 2x $-OCH_{2-}$), 1.51-1.25 (*t*, 6 H, 2x $-CH_3$)	mp. 6.0	mp. 6.1 [17]
2-Quinoxalyl	67	8.63(*s*, 1 H, -CH), 7.71 (*m*, 4 H, *Ar* H), 4.46 (*q*, 4 H, 2x $-OCH_2$), 1.41 (*t*, 6 H, 2x $-CH_3$)	mp. 32.0	mp. 31-32 [18]
p-OHC_6H_4	77	7.03 (*m*, 4 H, *Ar* H) 4.20 (*q*, 8 H, 4x $-OCH_2$), 1.31 (*t*, 12 H, 4 x- CH_3)	d_{20} 1.18	d_{20} 1.1822 $bp_{0.08}$ 127-130 n_D^{20} 1.5280 [19]
p-AcC_6H_4	93	8.09-7.94 (*d*, 2 H, *Ar* H), 7.25-7.14 (*d*, 2 H, *Ar* H), 4.25 (*q*, 4 H, 2x $-OCH_2$), 2.30 (*s*, 3 H, $-C(O)CH_3$), 1.33 (*t*, H, -2x $-CH_3$)	d_{20} 1.13	d_{20} 1.1420 bp_4 155-156 n_D^{20} 1.1126 [20]
p-$AcOC_6H_4$	95	8.04-7.91 (*d*, 2 H, *Ar* H), 7.28-7.18 (*d*, 2 H, *Ar* H), 4.26 (*q*, 4 H, 2x $-OCH_2$), 2.51 (*s*, 3 H, $-OC(O)CH_3$), 1.33 (*t*, 6 H, -2 x CH_3)	d_{20} 1.11	n_D^{20} 1.245[21]

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22. PRETT-THeavy duty mixer grinder: Voltage 230 V AC 50 Hz, Power consumption 550 Watts, Speed 20,000 rpm.

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