Monitoring the Purity of Product in Synthesis or Production of Compounds by Gas Chromatography as Exemplified with Methyl Parathion S-Isomer Production

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The high precision and reliability of gas chromatographic analysis plus its segregative capabilities, normally rapid analysis, capability of use with small samples, and broad applicability to diverse classes of compounds have made this technique extremely useful for both the qualitative and the quantitative evaluations of pesticides, their residues, and their alteration products. Great reliance in glc data can result from the use of columns of differing polarities, of selective detectors, and of certain correlations in homologous series as recently demonstrated by Jaglan and Gunther (1) for substituted p-nitrophenylphosphorothionate and p-nitrophenylphosphate compounds.

The use of glc for monitoring the purity of product in the synthesis of pesticides has not previously come to the notice of the authors, although this technique has been extensively used by workers in the synthesis of other classes of compounds.

Some fundamental concepts in the glc analysis of organophosphorus pesticides and their metabolites, with both practical and theoretical aspects, have been developed in this laboratory (2-5). In this paper is described a simple method for the production of methyl parathion S-isomer and its purification by monitoring its glc behavior. The identity of this compound was substantiated by other methods, thus lending credence to the glc data.

EXPERIMENTAL

Methyl parathion was prepared by the reaction of O,O-dimethyl phosphorothiochloridate with the sodium salt of p-nitrophenol (6); after crystallization, the product (m.p. 35.5°C) gave a single gas chromatographic peak on several columns. O,O-dimethyl phosphorothiochloridate was prepared by bubbling chlorine gas into O,O-dimethyl phosphorodithioic acid (7); distillation yielded a colorless, pungent liquid (b.p. 59-61°C at 5 mm, n_D^{26} 1.4783)

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in 42% yield. O,O-dimethyl phosphorodithioic acid was prepared by reacting phosphorus pentasulfide with dry methanol in benzene (8); after removing the solvent and distilling the residual dithioic acid, a colorless, foul-smelling liquid (b.p. 41-43°C at 0.5 mm, n_D^{26} 1.5312) was obtained in 65.9% yield.

Gas chromatographic analyses were conducted with a Hewlett-Packard 402 high-efficiency gas chromatograph equipped with hydrogen flame detector modified for thermionic detection of phosphorus by mounting a KCl pellet on the hydrogen burner jet. The glc conditions are given in the figure captions.

Thin-layer chromatography of methyl parathion and its reaction products was carried out at room temperature with silica gel (250μ-1 mm thick) on 20x20 cm glass plates with 150 ml each of a 7:3 ether:hexane solvent system.

RESULTS AND DISCUSSION

Triesters of phosphorothioic acid are notorious for their isomerization reactions. This isomerization is probably due to impurities and long storage, and is accelerated by elevated temperatures. Jaglan and Gunther (9) observed that no isomerization of methyl parathion was noticed at temperatures below 60°C, while at very high temperatures (180°C for 4 hours) neither methyl parathion nor its isomeride were recovered; there was a progressive increase in isomeride formation as the temperature approached 150°C, however. It was also seen that good yield of isomeride with fewer side products was obtained when methyl parathion was refluxed even at 58°C in the presence of nucleophilic reagents such as dimethyl sulfide or methyl iodide.

When purified methyl parathion was heated in closed vials at 125°C there was a progressive increase in the production of isomeride up to 7 hours as monitored by glc, when the reaction mixture turned golden yellow. The gas chromatogram of this 7-hour reaction mixture is shown in Figure 1. The predominant product is the S-isomeride (*ca*. 50%), although methyl paraoxon (*ca*. 25%) is also produced and some (*ca*. 25%) of the original methyl parathion remains.

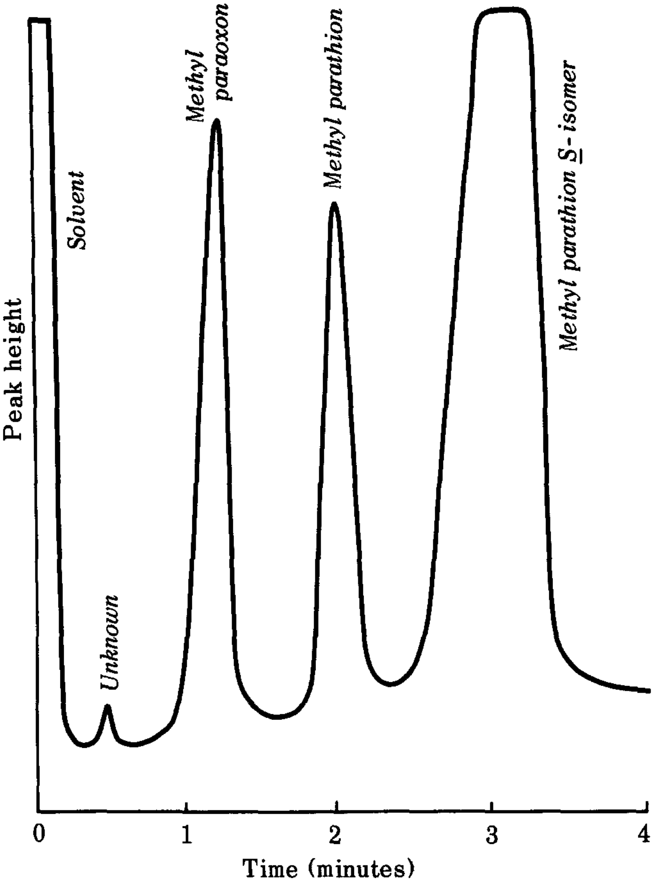

Figure 1. Chromatogram of reaction products from heating one g of methyl parathion at 125°C for 7 hours; column 5% Apiezon L on Gas-Chrom Q 80/100, 2'x4 mm i.d.; temperatures of column, flash heater, and detector 190, 210, and 200°C, respectively; flow rates of nitrogen, hydrogen, and air 40, 21, and 300 ml/min, respectively.

One ml of a benzene solution of this 7-hour reaction mixture was partitioned against 4 ml of benzene-equilibrated water; the gas chromatogram resulting from injection of the benzene layer is shown in Figure 2. From the partitioning behavior it is apparent that the

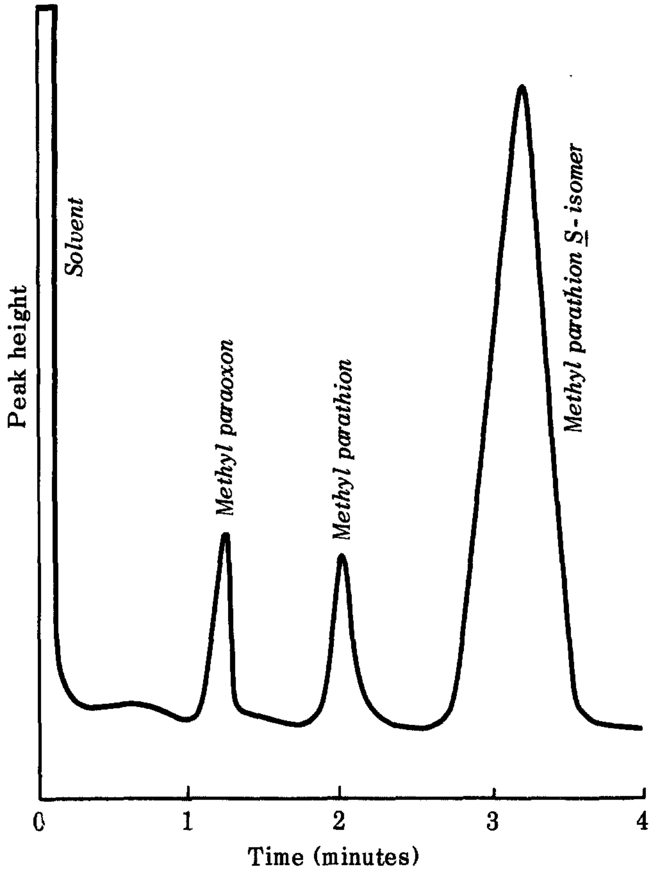

Figure 2. Chromatogram of benzene fraction of benzene:water partitioning (1:4 v/v) or reaction products from heating one g of methyl parathion at 125°C for 7 hours (glc conditions as in Figure 1).

predominant product is not derived from desmethyl methyl parathion, since if it were, the peak from the partitioned material would have been negligible, due to its greater solubility in water. Thin-layer chromatography of this 7-hour reaction mixture shows the presence of *p*-nitrophenol, as well as the other compounds above. Gas chromatography of the acetone-eluted *S*-isomeride TLC spot is shown in Figure 3. The predominant peak

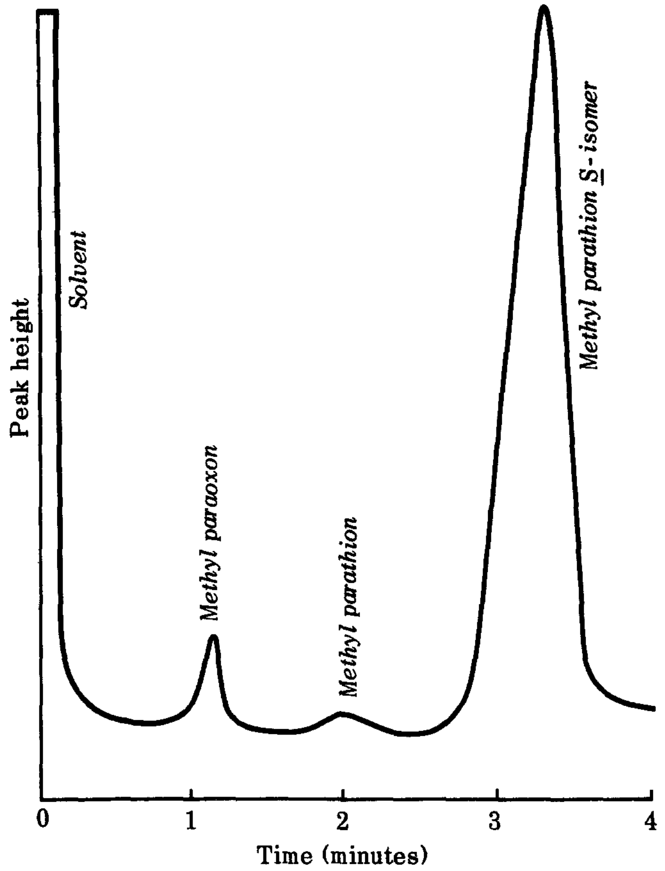

Figure 3. Chromatogram of methyl parathion S-isomer: area extracted from preparative TLC of products from heating one g of methyl parathion at 125°C for 7 hours (glc conditions as in Figure 1).

is methyl parathion S-isomer, although traces of methyl paraoxon and methyl parathion are also present due to unavoidable overlapping of these three compounds on the section scraped from the preparative TLC. Further purification by repeated TLC resulted in a single peak of the S-isomeride.

NMR of the acetone-eluted S-isomeride TLC spot in deuterochloroform with 2% tetramethylsilane showed a doublet at 2.25 and 2.52 ppm for the CH_3S-protons and a doublet at 3.85 and 4.1 ppm for the CH_3O-protons. The areas under these pairs of peaks were equivalent, indicating equal numbers of CH_3S- and CH_3O-protons. Therefore, this compound can only be methyl parathion S-isomer since the NMR spectra of methyl parathion, methyl paraoxon, desmethyl methyl parathion, and desmethyl methyl parathion S-isomer would not yield such results.

Preparation of methyl parathion-S-isomeride by the described procedure is simple and rapid and yields a pure compound. The usual preparation of this S-isomeride by synthesis of mixed ester chloridate for reaction with the sodium salt of p-nitrophenol is both time-consuming and difficult.

It is hoped that this preliminary investigation will accelerate the use of glc for following the course of a reaction (kinetic studies) and for monitoring the purity of product in pesticide synthesis.

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