The observed results have been explained on the basis of a free radical mechanism and some evidence to support this view has been presented.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY, VICTOR CHEMICAL WORKS]

# The Use of Amine and Phosphine Catalysts in the Preparation of Parathion[1]

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## Introduction

Parathion (diethyl *p*-nitrophenyl thionophosphate) has been prepared by the reaction of diethyl chlorothionophosphate and anhydrous sodium *p*-nitrophenolate in chlorobenzene at 130°,[2,3] by the same reactants in a mutual solvent such as ethyl alcohol,[3] or by the reaction of diethyl chlorothionophosphate with an aqueous solution of sodium *p*-nitrophenolate.[3] The chlorobenzene process has the advantage of eventually giving a relatively high yield; however, the reaction itself takes an inconveniently long time in this medium. Cassaday and his co-workers[3] found that this reaction gave a 79% yield after 51 hours at 125°. The alcohol process, a rapid and convenient one, gives a yield of 75%, and the aqueous solution one of 64%.[3]

Without any diluent, diethyl chlorothionophosphate and anhydrous sodium *p*-nitrophenolate undergo a slightly exothermic reaction at about 150–160°. However, the process is difficult to control, and the product is contaminated with tarry impurities. The use of the dihydrate instead of the anhydrous salt in this reaction results in a vigorous hydrolysis of the chloride and the formation of no parathion. If chlorobenzene is present in the proportion of 250 ml. per gram mole of anhydrous sodium salt it was possible to reflux this mixture at 150–155°, at which temperature the reaction was substantially complete in three hours although partial isomerization of the product may have occurred.[4] Because of possible isomerization and the inconvenience of operating at this high a temperature and also because the more readily prepared sodium *p*-nitrophenolate dihydrate cannot be used under these conditions, it was felt that a means of accelerating this reaction at a lower temperature would be desirable.

Our discovery of a unique catalytic effect by certain amines indicated a means of bringing about the reaction under more favorable conditions. Preliminary studies[5] on triethylamine, tributylamine, N-ethylmorpholine, and hexamethylenetetramine showed that these compounds catalyze the reaction to varying degrees. This work has since been extended to cover various types of amines and related compounds. The results are shown in Table I.

TABLE I

| Catalyst | Mole % | Temp., °C. | Time, hr. | Yield, % | $n^{25}$D | Remarks |
|---|---|---|---|---|---|---|
| None | | 105 | 2 | 2.0 | 1.5461 | [b] |
| Triethylamine | 1.4 | 105 | 2 | 87.7 | 1.5387 | |
| Triethylamine | 0.7 | 105 | 2 | 89.3 | 1.5377 | [c] |
| Diethylamine | 1.4 | 105 | 2 | 17.3 | 1.5389 | |
| Tri-*n*-butylamine | 0.8 | 115 | 2 | 92.3 | [a] | |
| N-Ethylmorpholine | 1.0 | 110 | 2 | 88.1 | [a] | |
| Triethanolamine | 1.4 | 105 | 2 | 55.4 | 1.5371 | [d] |
| Hexamethylenetetramine | 1.4 | 130 | 2.5 | 92.7 | [a] | [e] |
| Dimethylaniline | 1.4 | 105 | 4 | 88.4 | 1.5379 | [f] |
| Trimethylamine | 1.4 | 105 | 2 | 87.0 | 1.5374 | |
| Pyridine | 1.4 | 105 | 2 | 85.8 | 1.5380 | |
| Benzyldimethylamine | 1.4 | 105 | 2 | 82.8 | 1.5377 | [g] |
| Phenyldiamylphosphine | 1.4 | 105 | 2 | 89.3 | 1.5382 | |
| Triethyl phosphite | 1.4 | 105 | 2 | 10.8 | 1.5381 | |

[a] Identity established by elementary analysis. [b] Product is highly impure. [c] Less vigorous reaction than preceding. [d] Appeared rather slow. [e] Appeared to be no reaction at 110°. [f] Reaction very slow. [g] Reaction very rapid.

The data in this table show clearly that maximum catalytic activity is limited to tertiary amines and phosphines. The ineffectiveness of diethylamine is without doubt the result of its immediate conversion to an amide. The poor results with triethanolamine can be explained by the fact that besides being a tertiary amine it is a primary alcohol capable of reacting with the chlorophosphate. While hexamethylene tetramine contains tertiary nitrogen atoms, it is chemically a condensed, deammoniated ammonoformaldehyde derivative. In general it will be noted that the best results were obtained with trimethylamine, triethylamine, tributylamine, N-ethylmorpholine, and phenyldiamylphosphine. Less satisfactory results were obtained with dimethylaniline. Triethanolamine was decidedly inferior, and both diethylamine and triethyl phosphite were almost ineffective. Benzyldimethylamine and, to a lesser extent, pyridine have the unusual effects of promoting rapid reaction while giving somewhat inferior yields. It may be significant in all these experiments that the yield falls short of 100% even after making a liberal allowance for losses in handling. It would appear that the catalyst promotes a competing reaction which uses up about 10% of the reactants.

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(1) Presented at the meeting of the American Chemical Society, September 21, 1949, Atlantic City, N. J.

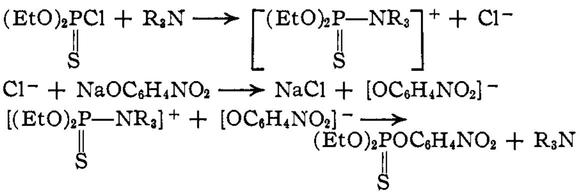
(2) Thurston, FIAT Final Report No. 949, October 14, 1946 (PB-60890).

(3) Fletcher, Hamilton, Hechenbleikner, Hoegberg, Sertl and Cassaday, THIS JOURNAL, **70**, 3943 (1948).

(4) Schrader, P. B. Report 95312 (1947).

(5) Toy and Beck, U. S. Patent 2,471,464 (1949).

Since the catalytic activity of these compounds corresponds qualitatively to the order of their tendencies to form quaternary compounds, it is suggested that an unusual type of quaternary compound serves as an intermediate possibly in accordance with the equations



$$(EtO)_2\underset{\underset{S}{\|}}{P}Cl + R_3N \longrightarrow \left[(EtO)_2\underset{\underset{S}{\|}}{P}-NR_3\right]^+ + Cl^-$$

$$Cl^- + NaOC_6H_4NO_2 \longrightarrow NaCl + [OC_6H_4NO_2]^-$$

$$[(EtO)_2\underset{\underset{S}{\|}}{P}-NR_3]^+ + [OC_6H_4NO_2]^- \longrightarrow (EtO)_2\underset{\underset{S}{\|}}{P}OC_6H_4NO_2 + R_3N$$

If the formation of a quaternary ammonium compound is the immediate step in the catalytic reaction then compounds similar to the tertiary amines, such as tertiary phosphines, should also be capable of forming analogous -onium compounds with the chloride and hence should act as catalysts. The effectiveness of diamylphenylphosphine as a catalyst appears to confirm this hypothesis (Table I). While the hypothetical quaternary ammonium ion shown above is quite unusual, it should be pointed out that diethyl chlorothionophosphate is an unusual acid chloride in that its stability to hydrolysis is comparable to that of an active alkyl halide such as benzyl chloride. Attempts to prepare these hypothetical intermediates have not been successful. Instead, diethyl chlorothionophosphate reacts with triethylamine or pyridine, in a few days at room temperature or a few hours at 100°, to give a complex mixture of reaction products in which only the original amine and ethyl chloride have been definitely identified, and in which the phosphorus–sulfur bond has been broken.

## Experimental

**Preparation of Parathion in Chlorobenzene without Catalyst.**—A mixture of 65 ml. of chlorobenzene, 41 g. (0.254 mole) of anhydrous sodium *p*-nitrophenolate and 48 g. (0.254 mole) of diethyl chlorothionophosphate was stirred under reflux at 150–155° for three hours. On cooling the oil was washed consecutively with 250-ml. portions of water, 5% sodium hydroxide, and twice more with water. The oil was placed in a distilling flask and gradually warmed up under reduced pressure until the temperature reached 130° and the pressure 2 mm. The residue, crude parathion, weighed 68 g. (91.9%).

*Anal.* Calcd. for $C_{10}H_{14}O_5NSP$: P, 10.65; S, 11.00; N, 4.81. Found: P, 10.8; S, 10.5; N, 4.6; $n^{25}D$, 1.5385.

**Preparation of Parathion in Chlorobenzene Using Catalysts.**—A mixture of 85 ml. of chorobenzene, 41 g. (0.254 mole) of anhydrous sodium *p*-nitrophenolate, 48 g. (0.254 mole) of diethyl chlorothionophosphate, and 1 ml. (0.73 g. or 0.0072 mole) of triethylamine was stirred and heated to 90°. A slightly exothermic reaction set in and the temperature rose to 105° without additional heat. The product was stirred at this temperature for two hours; most of the red sodium nitrophenolate disappeared during the first hour. When cool, the product was washed and purified as described above except that a washing with 5% hydrochloric acid was used after treatment with caustic soda; yield, 64.9 g. (87.7%).

*Anal.* Calcd. for $C_{10}H_{14}O_5NPS$: P, 10.65; S, 11.00; N, 4.81. Found: P, 10.7; S, 10.9; N, 4.5.

This procedure was used for measuring the activity of the various catalysts listed in Table I.

A parallel experiment to test the efficacy of the catalyst with the hydrated salt was also carried out. A mixture of 50 g. (0.254 mole) of sodium *p*-nitrophenolate dihydrate, 75 ml. of chlorobenzene, 45.5 g. (0.241 mole) of diethyl chlorothionophosphate, and 0.73 g. of triethylamine (0.0072 mole) was stirred at 105° for three hours. The reaction took place more slowly than with the anhydrous salt. A yield of 56 g. (79.6%) was obtained, after subjecting the reaction mixture to the purification process described above.

**Effect of Alcohol on Catalyst.**—The presence of 1.4% (molar) of triethylamine in the alcohol medium used by Cassaday and co-workers[3] produced no significant improvement in yield or rate over that of these workers. The ineffectiveness of triethylamine in alcohol is probably due to its conversion to the hydrochloride as a by-product of triethyl thionophosphate formation.

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## Summary

Tertiary amines and phosphines were found to be effective catalysts for the reaction between diethyl chlorothionophosphate and sodium *p*-nitrophenolate in chlorobenzene to form parathion. The suggested mechanism of this reaction is that the catalytic activity is due to the formation of an intermediate -onium compound.

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