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CRLR 490
Project 4-08-03-006
4-08-03-016-01

INTERIM REPORT

PROCESS DEVELOPMENT FOR AGENT Q

by

A. M. Reeves
P. P. Chiesa
S. L. Vail

This is an interim report. It is issued to transmit needed data to authorized personnel as rapidly as possible. Its conclusions are tentative and subject to revision.



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INTERIM REPORT

PROCESS DEVELOPMENT FOR AGENT Q

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ABSTRACT

Object.

The object of project 4-08-03-006 was to conduct prompt investigations of matters pertaining to chemical agents not covered by an active development project and too small to warrant the formal establishment of a project. The object of project 4-08-03-016-01 (4-08-03-001) is to continue research in an effort to find chemical warfare agents that are more effective than the present standard agents.

The object of the work described in this report was to develop a process for the preparation of larger-than-laboratory lots of agent Q.

Results.

The data reported in this work are based on the chlorination of Q glycol with phosphorus trichloride in methylene chloride (dichloromethane) solution. The following table summarizes the data:

Table 1

Preparation of Agent Q

Run	Reactants				Ratio PCl ₃ :Q glycol	Agent Q		
	Q glycol		PCl ₃ (a)			Yield		Melting point
	g.	mole	g.	mole		g.	%	°C.
12	91.0	0.5	92.0	0.67	4:3	92.7	84.7	49.5-53
13	91.0	0.5	92.0	0.67	4:3	94.8	86.6	51.5-54
16	91.0	0.5	92.0	0.67	4:3	102.6	93.7	49.5-52.5
18	91.0 (b)	0.5	92.0	0.67	4:3	94.5	86.3 (c)	46.5-52
17	91.0	0.5	68.5	0.5	1:1	94.7	86.5	50.0-53.5
19	91.0 (d)	0.5	68.5	0.5	1:1	97.6	89.1	48.5-53.5
20	227.5	1.25	171.3	1.25	1:1	250.1	91.4	47.5-51.5

(a) Plant-grade PCl₃ used in all of these runs.

(b) Plant-grade Q glycol, G-45.

(c) Yield 91.8% based on dry glycol.

(d) Plant-grade Q glycol, G-45, air-dried.

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Conclusions.

1. Q glycol of good quality can be prepared from 2-mercaptoethanol and ethylene chloride.
2. Agent Q of good quality can be prepared by the chlorination of Q glycol with phosphorus trichloride in methylene chloride solution.
3. Agent Q can be prepared by this method with a minimum of handling.

Recommendations.

It is recommended that this method be tested on a process-laboratory scale.

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PROCESS DEVELOPMENT FOR AGENT Q

I. INTRODUCTION.

A. Object.

The object of project 4-08-03-006 was to conduct prompt investigations of matters pertaining to chemical agents not covered by an active development project and too small to warrant the formal establishment of a project. The object of project 4-08-03-016-01 (4-08-03-001) is to continue research in an effort to find chemical warfare agents that are more effective than the present standard agents.

The object of the work described in this report was to develop a process for the preparation of larger-than-laboratory lots of agent Q.

B. Authority.

Authority for this work was the 1955 project program, Project 4-08-03-006, Special Problems, Chemical Division (canceled 9 December 1954 (CCTC item 2962)), and 4-08-03-016-01 (4-08-03-001), New Compounds (renumbered 9 December 1954 (CCTC item 2962)).

II. HISTORICAL.

Agent Q has been prepared by several methods. Bennett and Whincop prepared Q by the addition of Q glycol to an excess of thionyl chloride (1). Q was prepared in these Laboratories by the addition of Q glycol to five times the theoretical amount of thionyl chloride (2), and by the photochemical addition of vinyl chloride (chloroethene) to 1,2-ethanedithiol (3,4,5,6,7).

There are several methods reported in the literature by which Q glycol can be synthesized. Bennett and Whincop prepared Q glycol by condensing the sodium salt of 2-mercaptoethanol with ethylene bromide (1,2-dibromoethane) (1). During World War II the same method was used, except that ethylene chloride (1,2-dichloroethane) replaced ethylene bromide (8). Dawson and Hartnett prepared Q glycol from the disodium salt of 1,2-ethanedithiol and ethylene chlorohydrin (2-chloroethanol) (9). This process was later used in the process laboratory by Eckhaus and DeWitt (10).

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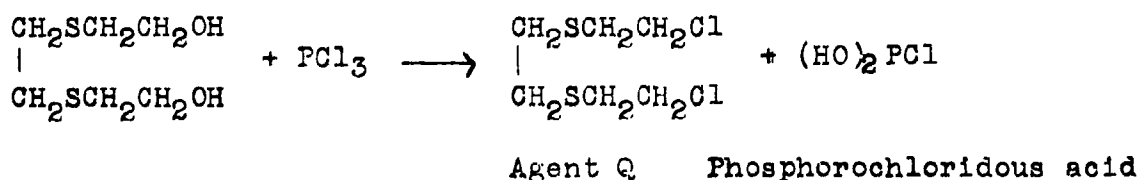
One 5-lb. lot of Q was prepared in eight laboratory runs for use in dispersion studies in 1952. This material was prepared by treating Q glycol with thionyl chloride in ether solution at a temperature below 20°C. The solvent was removed at low temperature, and the resulting solid product was melted, poured into a flat dish to solidify, and broken up into lumps. The average yield of agent Q was 99%. Anal. Calcd. for $C_6H_{12}Cl_2S_2$: Cl, 32.35; S, 29.25. Found: Cl, 31.90; S, 29.53.

III. ANALYSIS OF THE PROBLEM.

The latter method cited above was satisfactory for laboratory-scale preparation. However, when it was tried on a process-laboratory scale, the quality of the product was inferior.

It was decided that a search would be made for a chlorinating agent other than thionyl chloride and for a solvent other than ether.

Phosphorus trichloride, PCl_3 , was one of the chlorinating agents considered. It is assumed that the chlorination reaction is as follows:



IV. EXPERIMENTAL.

A. Preparation of Q Glycol.

Because of the potential availability of large quantities of 1,2-ethanedithiol, the substitution of ethylene oxide (1,2-epoxyethane) for ethylene chlorohydrin in the manufacture of Q glycol was studied. The advantage would be the elimination of salt formation.

Attempts to react 1,2-ethanedithiol with ethylene oxide at atmospheric pressure under the following conditions failed to produce any quantity of Q glycol: no catalyst, a seed charge of Q glycol, ultraviolet radiation, and boron trifluoride or triethylamine as catalyst. In all cases, there apparently

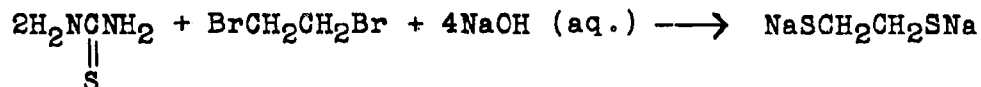
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was no reaction. Ethyl ether was the solvent in those runs where a solvent was used.

Several attempts to react 1,2-ethanedithiol with ethylene oxide in a 75-mm. shell only resulted in traces of Q glycol. No product was formed when the shell was heated in a water bath at 50°C. for 1 hr. When triethylamine was used as a catalyst a small amount of product melting at 50°C. was formed when the shell was heated; in the absence of external heating a trace of product melting at 50°C. was formed. Some heat was evolved when the catalyst was used. The main product was a black spongy mass, apparently a polymer.

An unsuccessful attempt was made to prepare Q glycol according to the following method:



$\text{NaSCH}_2\text{CH}_2\text{SNa} + 2\text{ClCH}_2\text{CH}_2\text{OH} \longrightarrow \text{Q glycol.}$ The product, however, was a tan-colored, waxy solid melting at 83° to 90°C.

The preferred method of preparing Q glycol was by reacting ethylene chloride with 2-mercaptoethanol in the presence of sodium hydroxide, following the procedure outlined in OSRD 67, Serial No. 4 (8). The method described below gave satisfactory results:

A solution of 485 g. (12 moles) of NaOH in 2.5 l. of water was placed in a 5-l., three-necked flask equipped with a dropping funnel, reflux condenser, and an efficient stirrer. Then 945 g. (12 moles) of 2-mercaptoethanol was added slowly, with stirring, to the cooled alkaline solution. As the mercaptan was added, the solution first turned green, faded as the neutral point was approached, and then turned pink as the last of the 2-mercaptoethanol was added. The mixture was heated to 65°C., and 620 g. (6.1 moles) of ethylene chloride was added slowly, so as to keep the ethylene chloride refluxing (1 to 2 hr. was required). After heating at 85° to 90°C. for 1 hr. to insure completion of the reaction, the mixture was transferred to beakers and cooled. The precipitate was collected on a filter and dried. A large amount of salt was present. The pure Q glycol was isolated by crystallization from ethyl acetate or acetone. Yield, 80% to 85%; m.p., 64° to 65°C.

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B. Preparation of Agent Q.

Approximately twenty runs were made to determine the optimum conditions for the preparation of Q by treating Q glycol with phosphorus trichloride.

In a typical run, solid Q glycol (91.0 g., 0.5 mole) was suspended in methylene chloride (dichloromethane) (500 ml.) in a 1,000-ml. round-bottom, three-necked flask having a short glass draw-off tube and stopcock at the bottom and fitted with a reflux condenser, mercury-sealed stirrer and dropping funnel. While stirring, PCl_3 (92.0 g., 0.67 mole) was added dropwise over approx. 30 min. After the PCl_3 was added, stirring was continued for 30 min. A small amount of heat was evolved, and the reaction remained under control as the solvent refluxed moderately. Two layers formed in the reaction flask, a fairly clear upper layer (Q) and a heavy, syrupy lower layer (by-product). In order to hydrolyze the excess PCl_3 and to dilute the heavy by-product layer, water was carefully added, a drop at a time, while stirring vigorously. The reflux rate of the solvent determined the addition of the water. Extreme care was taken to avoid a buildup of water in the mixture, which would cause, upon sudden reaction, violent bubbling, flooding of the condenser, and possible overflowing. After hydrolysis was completed, more water was added to wash the solvent layer (to a total of 200 ml. for the average run). After stirring for several minutes, the mixture was allowed to stand while the layers separated. The solution of Q in methylene chloride, which is heavier than the diluted by-product layer, was drawn off at the bottom of the flask. Without further washing or drying the solvent was removed at reduced pressure; the dry solid product was melted on a hot water bath, kept below $80^\circ\text{C}.$; and the liquid was poured into an open evaporating dish, where it was allowed to solidify before being broken into lumps for storage. Yield, 85% to 90% (average); a pure-white, dry product; m.p., up to $54^\circ\text{C}.$

In the typical run above a 4:3 molar ratio of PCl_3 to Q glycol was used, but equally good results were obtained in runs employing a 1:1 ratio. Such a ratio is preferred since less PCl_3 is required with a corresponding reduction in the quantity to be hydrolyzed at the end of the reaction. The results of the runs made are summarized in table 2.

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Table 2

Chlorination of Q Glycol With Phosphorus Trichloride

Run	Reactants				Solvent	Agent Q		
	Q glycol		PCl ₃			Yield	Melting point	
	g.	mole	g.	mole		g.	%	°C.
1	18.2	0.1	27.5	0.2	Ether	7.5	-	52.0-53.5
2	91.0	0.5	48.2	0.35	Ether	50.0	45.7	50.0-52.5
3	91.0	0.5	48.2	0.35	Ether	52.5	47.9	49.0-53.0
4	91.0	0.5	92.0	0.67	Ether	62.5	59.8	48.5-52.0
5	91.0	0.5	92.0	0.67	CCl ₄	69.5	63.5	49.0-52.0
6	91.0	0.5	92.0	0.67	Benzene	88.8	81.1	50.0-53.0
7	91.0	0.5	68.5	0.5	Benzene	77.6	70.9	48.5-51.5
8	91.0	0.5	92.0	0.67	Benzene	99.6	91.0	47.0-52.0
10	91.0	0.5	92.0	0.67	Benzene	95.1	86.8	47.0-52.0
11	91.0	0.5	92.0	0.67	Benzene	63.4	57.9	47.0-51.5
	(a)							
12	91.0	0.5	92.0	0.67	Benzene	92.7	84.7	49.5-53.0
13	91.0	0.5	92.0	0.67	Methylene chloride	94.8	86.6	51.5-54.0
14	91.0	0.5	76.5	0.5	Methylene chloride	55.3	50.5	36.0-44.0
			(b)					
15	91.0	0.5	102.0	0.67	Methylene chloride	71.8	65.6	42.0-48.0
			(b)					
16	91.0	0.5	92.0	0.67	Methylene chloride	102.6	93.7	49.5-52.5
17	91.0	0.5	68.5	0.5	Methylene chloride	94.7	86.5	50.0-53.5
18	91.0	0.5	92.0	0.67	Methylene chloride	94.5	86.3	46.5-52.0
	(a)							
19	91.0	0.5	68.5	0.5	Methylene chloride	97.6	89.1	48.5-53.5
	(c)							
20	227.5	1.25	171.3	1.25	Methylene chloride	250.1	91.4	47.5-51.5

(a) Plant-grade Q glycol, G-45.

(b) POCl₃.

(c) Plant-grade Q glycol, G-45, air-dried.

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Anal. (run 7): Calcd. for $C_6H_{12}Cl_2S_2$: Cl, 32.35; S, 29.25. Found: Cl, 32.76; S, 29.50; P (impurity), 0.12%.

Run 20 was made using 2-1/2 times the quantities of glycol and PCl_3 in the same amount of methylene chloride. Results were satisfactory, except that at first a very thick suspension which was quite difficult to stir resulted from the relatively low solubility of Q glycol.

When ethyl ether, benzene, or carbon tetrachloride was used as a solvent, a flocculent white solid dispersed at the interface of the two liquid layers, making clean separation impossible. With methylene chloride no solid formed and separation was good. Moreover, the high density of methylene chloride allowed it to be drawn off from the bottom of the reactor.

In several runs the syrupy by-product layer was drawn off before washing the product solution with water, but the by-product layer was so viscous that it barely flowed through the stopcock. The addition of water before this separation diluted the syrupy layer and reduced its density so that it rose to the top and allowed the product to be removed below it.

In runs 14 and 15 phosphoryl chloride, rather than phosphorus trichloride, was the chlorinating agent. Poor results were obtained with low yields of low-melting product.

In runs 11 and 18, where impure Q glycol was used, poor results also occurred, indicating that purification of the glycol is important in the production of high-quality Q.

Other chlorinating agents were tested. With phosgene a product which appeared to be a chlorocarbonic ester was obtained. With zinc chloride and hydrochloric acid only a polymeric product was obtained.

V. DISCUSSION.

After phosphorus trichloride had been found to be a suitable chlorinating agent for Q glycol, there were two problems to solve: (1) the separation of the product solution from the thick, syrupy by-product layer at the bottom of the reactor, and (2) the clean separation of the two layers after the wash water was added. With ether, benzene, or carbon tetrachloride as solvents, the reaction proceeded normally, but when water was added to hydrolyze the excess PCl_3 , a white flocculent precipitate appeared at the interface of the two layers. This made a clean separation difficult and the procedure unsuitable on a process-laboratory scale. Both problems were solved by using methylene chloride as the solvent. The heavier methylene chloride layer

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was clear, and the absence of any flocculent material at the interface allowed its clean separation from the cloudy aqueous layer.

Another problem was to dry the solvent layer containing agent Q. To do this without handling, the separated solvent layer was distilled at a moderate reduced pressure. With both benzene and methylene chloride the water was removed with the solvent, thus making a separate drying operation unnecessary.

VI. CONCLUSIONS.

1. Q glycol of good quality can be prepared from 2-mercaptoethanol and ethylene chloride.
2. Agent Q of good quality can be prepared by the chlorination of Q glycol with phosphorus trichloride in methylene chloride solution.
3. Agent Q can be prepared by this method with a minimum of handling.

VII. RECOMMENDATIONS.

It is recommended that this method be tested on a process-laboratory scale.

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