CLASSIFICATION S-E-C-R-E-T **SECRET**

50X1-HUM

CENTRAL INTELLIGENCE AGENCY
INFORMATION FROM
FOREIGN DOCUMENTS OR RADIO BROADCASTS

REPORT [redacted]
CD NO.

COUNTRY	USSR	DATE OF INFORMATION	1950
SUBJECT	Scientific - Chemicals, organophosphorus compounds	DATE DIST.	19 Jun 1951
HOW PUBLISHED	Bimonthly periodical		
WHERE PUBLISHED	Moscow	NO. OF PAGES	5
DATE PUBLISHED	Jan 1951	SUPPLEMENT TO REPORT NO.	
LANGUAGE	Russian		

THIS IS UNEVALUATED INFORMATION

SOURCE Izvestiya Akademii Nauk SSSR, Otdeleniye Khimicheskikh Nauk, No 1, 1951, pp 95-97.

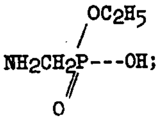
SYNTHESIS OF AMINOMETHYLPHOSPHONIC ACID

M. I. Kabachnik and T. Ya. Medved'
Inst of Org Chem, Acad Sci USSR

/Because aminomethylphosphonic acid is a newly synthesized compound, its physiological action is not known. The Russian authors have not indicated the purpose of the investigation of which this report forms a part. From the viewpoint of potential applications in the field of cholinesterase inhibitors, one may assume that aminomethylphosphonic acid may, under appropriate conditions, serve as a starting material for the preparation of persistent nerve gases in which two phosphonic acid residues are connected by means of a bridge, or some group other than a phosphonic acid residue is introduced into the amino group of the original compound. Because chlorine in the chloromethyl group attached to the phosphorus is extremely unreactive, its replacement with an amino group may conceivably offer better possibilities in that respect./

In a previous communication /1/ we showed that when ammonia acted on the ethyl ester of chloro- and iodomethylphosphonic acid (I) the monoethyl ester of aminomethylphosphonic acid (II) was formed. When II was saponified, free aminomethylphosphonic acid (III) was easily obtained. The total yield of the latter, on the basis of the original ester of the halogen methylphosphonic acid, comprised 25% of theoretical:

$ClCH_2PO(OC_2H_5)_2$; (I)



$NH_2CH_2P(=O)(OC_2H_5)-OH$; (II)

$NH_2CH_2PO(OH)_2$. (III)

CLASSIFICATION S-E-C-R-E-T **SECRET**

STATE	X	NAVY	X	NSRB		DISTRIBUTION
ARMY	X	AIR	X	FBI		

[redacted]

Because aminomethylphosphonic acid is of very great interest to us as the first member of a series of aminophosphonic acids, analogous to the aminocarboxylic acid series, we examined the reaction of its formation from chloromethylphosphonic acid in great detail.

It is well known that the conversion of chloroacetic acid into glycine is easily accomplished by simply dissolving it in a strong aqueous solution of ammonia. Proceeding from the concept that there is an analogy between the carboxylic group COOH and the phosphonic group $PO(OH)_2$ [2], we expected that the effect of a $PO(OH)_2$-group on the mobility of the chlorine atom in chloromethylphosphonic acid would be similar to the effect of the carboxyl in chloroacetic acid. However, we have already noted that chloromethylphosphonic acid is considerably inferior to chloroacetic as far as the reactive capacity of the chlorine atom is concerned. The present paper describes the results obtained by measuring the rate of the reaction of chloromethylphosphonic acid with aqueous and alcoholic ammonia. It was found that its rate of conversion was so far exceeded by that of chloroacetic acid that one can speak of an analogy between them only very conditionally.

Thus, for example, when the ammonium salt of chloromethylphosphonic acid is heated with a saturated anhydrous alcoholic solution of ammonia in a sealed tube in a boiling water bath even for as long as 30 hours, absolutely no splitting off of the chlorine ion occurs. With strong aqueous ammonia, the complete splitting is reached only after 25 hours of heating at a temperature of 100° (cf curve 1 in appended Figure 1; the pseudomolecular reaction constant $K = 0.108$). Moreover, under these conditions the splitting off of chlorine leads chiefly to the formation of oxymethylphosphonic rather than aminomethylphosphonic acid.

The ethyl ester of chloromethylphosphonic acid reacts even more slowly with strong aqueous ammonia. To achieve a complete splitting off of the chlorine ion requires heating at 100° for more than 40 hours (cf curve II; $K = 0.057$). However, in this case the reaction proceeds chiefly in the direction of replacing the chlorine with an amino group and forming the acid ester of the amino acid II. At 150° the reaction with aqueous ammonia naturally proceeds more rapidly, being completed in one hour with the formation of the acid ester of aminomethylphosphonic acid with a yield of up to 50% of the theoretical (curve III; $K \gg 2.7$). The reaction proceeds more slowly in an absolute ether solution, where at a temperature of 150° 20 hours are required for its completion (curve IV; $K = 0.17$).

A comparison should be made of the above-cited data with the results obtained by measurement of the rate of the reaction of chloroacetic acid with concentrated aqueous ammonia [3]. In the latter reaction, even with a somewhat smaller excess of ammonia and at a temperature of 40°, the complete splitting off of chlorine is attained in only 3 hours, i.e., the reaction proceeds much more rapidly.

Furthermore, data from the literature show that methyl chloride reacts more easily with ammonia in an alcoholic solution that either chloromethylphosphonic acid or its ester. Although in the literature we have found no quantitative data on the rate of reaction of methyl chloride with ammonia in an alcoholic solution, according to the old data of Vincent and Chappuis [4] when saturated solution of ammonia in alcohol stands with methyl chloride in a closed vessel at a low temperature for 24 hours a crystalline precipitate consisting of tetramethylammonium chloride and trimethylamine hydrochloride is formed profusely. Thus, the action of the phosphono group in chloromethylphosphonic acid on the reactive capacity of the chlorine atom can be safely called passivating rather than activating. On the basis of the above-stated results, we considerably improved our method for producing aminomethylphosphonic acid (or its acid ethyl ester), increasing the yield to 48-50% and greatly shortening the duration of the synthesis. The method now consists of heating the ethyl ester of chloromethylphosphonic acid with 25% aqueous ammonia in sealed tubes to 150°, elimination of the ammonium chloride, which is formed at the same time by the action of aqueous silver oxide, and, finally, precipitation of the aniline salt of the acid ethyl ester of aminomethylphosphonic acid $(H_2NCH_2PO(OC_2H_5)OH)_2{:}C_6H_5NH_2$. This salt is extremely unstable and when recrystallized or heated in vacuum, loses aniline to form the inner salt.

DESCRIPTION OF EXPERIMENTS

Determination of Time for Completing Reaction

Portions containing 0.08-0.1 g chloromethylphosphonic acid or its ethyl ester were sealed in tubes with 5 ml aqueous ammonia or saturated ammonia in absolute alcohol. The tubes were heated to 100 or 150° for the stated length of time, then opened. The contents were dissolved in water, acidified with nitric acid, and the ionic chlorine titrated by the Vollhard method. The following results were obtained:

1. $ClCH_2PO(OH)_2$; anhydrous alcoholic ammonia; 100°; from 5 to 30 hours. No ionic chlorine.

2. $ClCH_2PO(OH)_2$; 25% aqueous ammonia; 100° (curve I).

Time (hr)	2	4	6	8	10	14	18	22	25
Cl (%)	17.2	34.8	41.2	62.6	72.0	79.9	86.7	88.2	100

Monomolecular rate constant $K = 0.108$

3. $ClCH_2PO(OC_2H_5)_2$; 25% aqueous ammonia; 100° (curve II).

Time (hr)	2	4	7	10	14	18	28	38
Cl (%)	11.2	20.4	31.6	48.3	55.8	61.3	66.9	89.2

Rate constant $K = 0.057$

4. $ClCH_2PO(OC_2H_5)_2$; 25% aqueous ammonia; 150° (curve III). After only an hour, 92.8% ionic chlorine is obtained. The reaction rate was not determined here, but it is clear that its constant cannot be less than 2.7.

5. $ClCH_2PO(OC_2H_5)_2$; anhydrous alcoholic ammonia; 150° (curve IV).

Time (hr)	5	10	20
Cl (%)	63.2	78.0	96.6

Rate constant $K = 0.17$.

Synthesis of Monoethyl Ester of Aminomethylphosphonic Acid

Fourteen and four tenths grams of the ethyl ester of chloromethylphosphonic acid (bp 89-91° at 4 mm; n_D^{20} 1.4408) and 80 ml of 25% aqueous ammonia were heated in four sealed tubes (the use of a steel autoclave sharply reduces the yield and contaminates the reaction product) at 150° for one hour. To avoid completely the frequent accidental bursting of tubes, it is best to place them in an autoclave in which the required external pressure relative to the tubes can be produced.) Then the contents of the tubes were evaporated in a dish on a water bath to a constant volume. The residue, a syrupy liquid, was dissolved in a small amount of water and shaken up with 9.6 g of freshly prepared, moist silver oxide. The precipitate of silver chloride and the excess of silver oxide were filtered out. The excess of silver was eliminated from the filtrate by hydrogen sulfide, the silver sulfide was filtered out, and the filtrate was evaporated to a constant volume. The residue, a yellowish syrup, was dissolved in a small amount of 95% alcohol, and to this solution was added an alcohol solution of aniline (15.5 g of aninlie was taken, which corresponds to two moles of aniline to one mole of the original substance). On prolonged standing the precipitate was drawn off and washed with alcohol. There was obtained 7.8 g of a white crystalline substance with a melting point of 230° which was a salt of the composition: $(NH_2CH_2PO(OC_2H_5)OH)_2 \cdot C_6H_5NH_2$.

0.1192 g substance; 0.0708 g $Mg_2P_2O_7$
0.1214 g substance; 0.0708 g $Mg_2P_2O_7$
(by melting with soda and saltpeter)

Found P 16.25, 16.54%
$C_{12}H_{27}N_3O_6P_2$. Calculated P 16.70%

The substance can be freed of aniline either by recrystallization from aqueous alcohol or by heating the aniline salt to 100° in a vacuum at 2-4 mm Hg for several hours to a constant weight. Recrystallization of the aniline salt from the aqueous alcohol yielded 4.8 g of the acidic ethyl ester of aminomethylphosphonic acid with a melting point of 240°. The yield was 45% of the theoretical.

By this method in six experiments 87.7 g $(NH_2CH_2PO(OC_2H_5)OH)_2 \cdot C_6H_5NH_2$ were obtained from 183 g $ClCH_2PO(OC_2H_5)_2$, which corresponds on the average to 48% of the theoretical.

BIBLIOGRAPHY

1. M. I. Kabachnik and T. Ya. Medved', Izvestiya AN SSSR, OKhN, No 6, p 635 (1950)
2. A. Ye. Arbuzov, ZhRFKhO, 59, p 243 (1927).
3. G. R. Robertson, J Am Chem Soc, 49, p 2889 (1927).
4. G. Vincent and I. Chappuis, Bl, (2), 45, p 501 (1886).

/Figure follows./

[redacted]

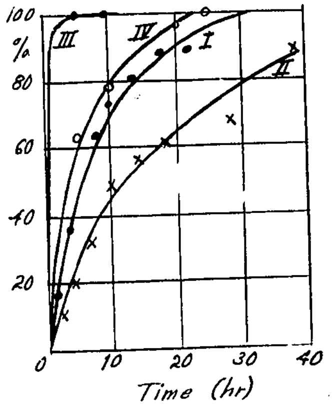


Figure 1. I - $ClCH_2PO(ONH_4)_2$; aqueous ammonia; 100°

II - $ClCH_2PO(OC_2H_5)_2$; aqueous ammonia; 100°

III - $ClCH_2PO(OC_2H_5)_2$; aqueous ammonia; 150°

IV - $ClCH_2PO(OC_2H_5)_2$; alcoholic ammonia; 150°

- E N D -