[CONTRIBUTION OF THE CENTRAL RESEARCH DEPARTMENT, MONSANTO CHEMICAL COMPANY]

Isomerization of Tri-alkyl Phosphites. II. Reaction between Triethyl Phosphite and Trimethylene Bromide

BY GENNADY M. KOSOLAPOFF

In the previous communcation,[1] there were presented some observations on the reaction between triethyl phosphite and ethylene bromide. The present paper deals with the reaction between triethyl phosphite and trimethylene bromide and with some of the compounds derived from the products of this reaction.

Parfent'ev and Shafiev,[2] reported the reaction between triethyl phosphite and trimethylene bromide to yield 3-bromopropane diethyl phosphonate, which, however, could not be distilled for purification. The reaction was conducted with equimolar amounts of the reactants in a sealed tube and the analysis of the residual oil, after removal of the volatile products, indicated it to be the above-named ester. Hydrolysis of this material by concentrated hydrobromic acid in a sealed tube was reported to yield a non-crystallizable oil, which appeared to be the corresponding 3-bromopropanephosphonic acid.

In view of the influence of the reactant ratio on reactions of this type shown in the previous paper on ethylene bromide,[1] it was felt to be highly interesting to investigate the reaction with trimethylene bromide in the same manner. In view of the ready crystallizability of many aliphatic phosphonic acids, it was felt that the oily product obtained by Parfent'ev and Shafiev may have been contaminated by the products of the second possible reaction, *i. e.*, disubstitution. The results obtained with ethylene bromide indicate that both reactions take place and only in the case of a relatively large excess of the dihalide does the monosubstitution predominate.

Experimental

The apparatus and the technique employed were previously described.[1] Triethyl phosphite (16.6 g., 0.1 mole) was treated at 150° with the following amounts of trimethylene bromide: (a) 10.1 g. (0.05 mole), (b) 20.2 g. (0.1 mole) and (c) 101 g. (0.5 mole). In all cases, the reaction mixtures became cloudy within one to two minutes of immersion into the heating bath and ethyl bromide evolution began within seven to ten minutes. The mixture (c) gave a particularly vigorous reaction at this stage. The mixture (a), after a fairly rapid evolution of ethyl bromide during the initial fifty minutes, after that period began to yield gradually decreasing amounts until after three hours of reaction, the evolution was complete with 7.4 cc. of ethyl bromide being collected, which corresponded to nearly the theoretical amount. Distillation of this reaction mixture was accompanied by some decomposition and evolution of small amounts of hydrogen bromide even at the pressure used (2 mm.); however, on redistillation, there was obtained a 75% yield of tetraethyl trimethylenediphosphonate, b. p. 170–172° at 2 mm., b. p. 197–199° at 8 mm., which corresponded in its properties to the product obtained by Nylen in the reaction of trimethylene bromide with sodium diethyl phosphite.[3]

The behavior of the reaction mixtures (b) and (c) was different from that of (a). After rapid ethyl bromide evolution during the initial thirty minutes of the reaction, both mixtures showed decreased ethyl bromide evolution until fifty minutes of total reaction time had elapsed and some 6 cc. of ethyl bromide was collected. At this point both mixtures showed renewed vigor of ethyl bromide evolution, until at eighty minutes reaction time they had yielded, respectively, 8.7 cc. and 8.0 cc. of ethyl bromide. Both amounts were greater than the amount theoretically possible by the normal reaction course. At this point, the evolution appeared to proceed at an increasing rate, indicating, possibly, the initiation of a secondary reaction. Hence, after eighty minutes of elapsed time, the heating was discontinued in both cases. In view of the apparent secondary reaction, the graphical representation of the ethyl bromide evolution was held to be of minor significance in assigning the reaction course. However, the reaction curve for mixture (c) was consistently under that for mixture (b) by 0.5–0.7 cc. ethyl bromide. Parallel experiments showed the impossibility of the distillation of the products of (b) and (c) due to decomposition and HBr evolution even at greatly reduced pressures.

3-Bromopropanephosphonic Acid.—The reaction mixtures (b) and (c) were each treated with 100 cc. of 48% hydrobromic acid and evaporated under an infrared ray lamp until evaporation ceased.

On cooling, the product of (c) readily crystallized to a solid mass of rosets of almost colorless plates. The equivalent weight of this crude product was found to be 97; calcd. for $Br(CH_2)_3PO_3H_2$: 101.5. Recrystallization from water yielded pure 3-bromopropanephosphonic acid as pearly colorless plates, m. p. 107–108°, which were soluble in water and almost insoluble in benzene. Equiv. wt. found, 102; calcd. for $Br(CH_2)_3PO_3H_2$, 101.5. Consistent results for bromine could not be obtained due to difficulty of good combustion, with the best results ranging at 38% Br; calcd. 39.4% Br. The yield of the pure acid ranged in several experiments from 80 to 90%.

On cooling, the product of (b) formed a thick sirup which would not crystallize on prolonged cooling with scratching. Seeding with a crystal of pure bromo-acid induced partial crystallization to a thick mush. The equiv. wt. of a representative sample was 88.2. The solid part of the mixture was filtered off and recrystallized from water to yield 60–70% pure 3-bromopropanephosphonic acid (several experiments). The mother liquors on evaporation and prolonged standing in a desiccator yielded small amounts of the bromo-acid, followed by 0.5 g. of a solid, m. p. 150–160°, which on several crystallizations from water yielded 0.2 g. of trimethylenediphosphonic acid, m. 168–169°. The residue, a thick yellowish sirup, appeared to be allylphosphonic acid, previously reported by Parfent'ev and Shafiev[2]; it decolorized cold dilute potassium permanganate instantly.

3-Anilinopropanephosphonic Acid.—3-Bromopropanephosphonic acid (5 g.) and 15 g. of aniline were heated at 125° for five hours. On cooling a considerable amount of aniline hydrobromide crystallized out. The mixture was made alkaline with 10% sodium hydroxide and excess aniline removed by steam distillation. The residual solution was then neutralized by dilute hydrochloric acid to *p*H 8 and concentrated on a water-bath to *ca.* 50 cc. On cooling, the yellow solution was acidified to congo red by

---

[1] G. M. Kosolapoff, THIS JOURNAL, **66**, 109 (1944).

[2] L. N. Parfent'ev and M. Kh. Shafiev, *Trudy Uzbeksk. Gos. Univ., Sbornik Rabot Khim.*, 87–94 (1939).

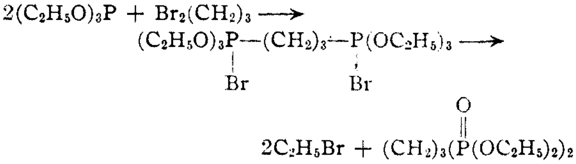
[3] P. Nylen, "Studien über organische Phosphorverbindungen," Upsala, 1930.

careful addition of dilute hydrochloric acid. 3-Anilinopropanephosphonic acid precipitated as a mass of slightly yellow, matted feathery crystals. After recrystallization from water, the pure acid was obtained as colorless prisms, joined in small clusters, m. p. 129–130°. The yield was 75–80%. The acid is poorly soluble in cold water and the usual organic solvents, readily soluble in alkalies and mineral acids and fairly soluble in hot water. Electrometric titration showed three inflection points in the curve, at 4.5 and 7.0, as well as at 9.0 *p*H. Calcd. for $C_6H_5NH(CH_2)_3PO_3H_2$: N, 6.5; P, 14.4. Found: N, 6.5; P, 14.0.

If the reaction mixture, after steam distillation, is neutralized by sodium hydroxide to *p*H 7–8 and concentrated to incipient crystallization, there is formed on cooling an abundant deposit of large colorless plates of the acid sodium salt of 3-anilinopropanephosphonic acid, m. p. 187–189.5°, which is quite readily soluble in water. Analyzed after drying *in vacuo:* Calcd. for $C_6H_5NH(CH_2)_3PO_3NaH$: N, 5.9; P, 13.0. Found: N, 5.9; P, 13.3.

Discussion of the Results.—Although, as was pointed out in the experimental part, it was impossible to use the graphical representation for accurately following the course of the reaction, the combined evidence of the general trend of the rate of ethyl bromide evolution and the nature of the products obtained indicates that the reaction, as might be expected, is greatly affected by the molecular ratio of the reactants.

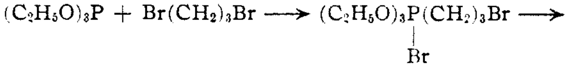
In the case of the 2:1 ratio of the triethyl phosphite–trimethylene bromide, the reaction is predominantly that of disubstitution



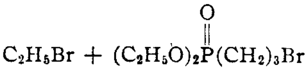
$$2(C_2H_5O)_3P + Br_2(CH_2)_3 \longrightarrow \underset{Br}{(C_2H_5O)_3P}-(CH_2)_3-\underset{Br}{P}(OC_2H_5)_3 \longrightarrow 2C_2H_5Br + (CH_2)_3(\overset{O}{\overset{\|}{P}}(OC_2H_5)_2)_2$$

Evidently, traces of the monosubstitution product caused the slight decomposition at distillation and prevented a higher yield of recoverable tetraethyl trimethylenediphosphonate.

The use of 1:1 and 1:5 reactant ratios leads almost exclusively to the monosubstitution reaction



$$(C_2H_5O)_3P + Br(CH_2)_3Br \longrightarrow (C_2H_5O)_3\underset{Br}{P}(CH_2)_3Br \longrightarrow$$



$$C_2H_5Br + (C_2H_5O)_2\overset{O}{\overset{\|}{P}}(CH_2)_3Br$$

Although the difference between the reaction curves between these two reactant ratios is not as pronounced as it was in the ethylene bromide reaction, nevertheless the 1:5 mixture gave a consistently lower rate of ethyl bromide evolution and the titration values of the hydrolyzed crude products show considerably higher degree of purity for the 1:5 mixture. The isolation of the secondary products from the mixture (b) (1:1) also supports this evidence. The evolution of excessive amounts of ethyl bromide in these two cases is probably due to a secondary reaction of partial decomposition of diethyl bromopropanephosphonate into hydrogen bromide and allylphosphonic acid, with consequent partial de-esterification by the hydrogen bromide, and formation of ethyl bromide from this source. It is interesting to note that the free bromopropanephosphonic acid is relatively more stable to heat than is its ethyl ester.

The 3-bromopropanephosphonic acid has been obtained as a solid of definite physical properties and, apparently, of greater degree of purity than previously reported.[2] It undergoes the usually expected condensation reactions through its reactive bromine atom. Of these products, the anilino compound was described above, being one of the more readily characterized derivatives. It is probable that this acid exists normally in the form of an inner salt.

Summary

The reaction of triethyl phosphite with trimethylene bromide is shown to yield either tetraethyl trimethylenediphosphonate or diethyl bromopropanephosphonate, as governed by the molecular ratio of the reactants.

3-Bromopropanephosphonic acid was isolated as a pure solid.

3-Anilinopropanephosphonic acid, and its acid sodium salt, were prepared and described.

DAYTON, OHIO RECEIVED MAY 22, 1944