REACTION OF N-(ACETOXYMETHYL)DIETHYLAMINE WITH SOME DERIVATIVES OF TRIVALENT PHOSPHORUS ACIDS

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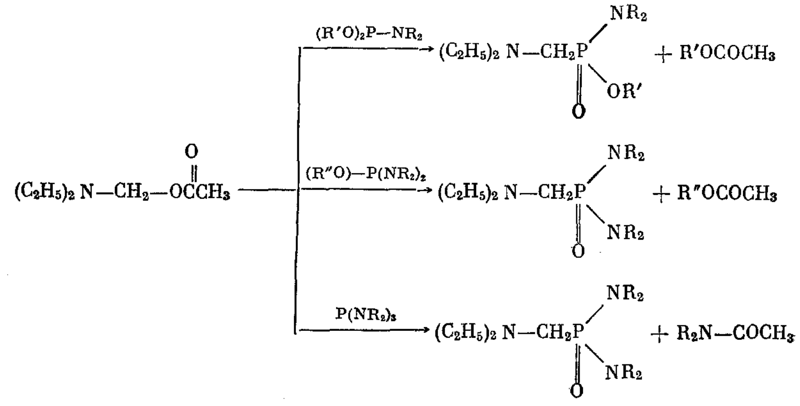
Acetoxymethylamines possess an exceedingly high reactivity in reactions with nucleophiles [1], and in their properties are close to the chloromethylamines. The high reactivity of both classes of compounds is probably explained by the possibility of easily forming the carboimmonium cation. Triethyl phosphite reacts very vigorously with acetoxymethyldimethylamine even at room temperature, with the formation of the diethyl ester of dimethylaminomethylphosphonic acid in 85% yield [2].

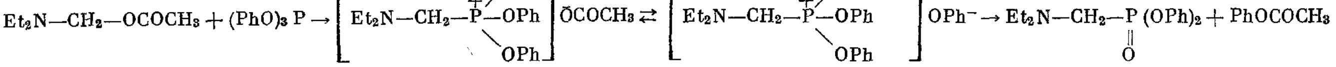
Taking into account the possibility of the acetoxymethyldiethylamines reacting in their ionic form, which opens up additional routes for stabilizing the intermediate quasiphosphonium salts, and in order to ascertain the specificity in the behavior of the acetate anion in the second step of the Arbuzov rearrangement, we studied the reaction of the mono-, di-, and triamidophosphites, and of the triphenyl-, diethylacetyl-, and diethylchlorophosphites with acetoxymethyldiethylamine.

Acetoxymethyldiethylamine reacts with the mono-, di-, and triamidophosphites at room temperature, and the reaction is exothermic and leads to the formation of only one phosphorus-containing product



$R{=}C_2H_5$; $i\text{-}C_4H_9$; $R'{=}C_2H_5$; $R''{=}CH_3$

The corresponding esters of acetic acid were identified by GLC as being the low-boiling products when reaction was with the mono- and diamidophosphites, while diethylacetamide was identified as the low-boiling product when reaction was with the triamidophosphite. The reaction of acetoxymethyldiethylamine with triphenyl phosphite proceeds less vigorously than with the amidophosphites, and heating up to 80° is required for its completion. Phenyl acetate and the diphenyl ester of diethylaminomethylphosphonic acid were isolated when the reaction mixture was subjected to fractional distillation in vacuo. The mild conditions under which the formation of the diphenyl ester of diethylaminomethylphosphonic acid occurs permit making the assumption that the phenoxyl radical in the quasisalt is replaced with relative ease by the acetoxy group, followed by its conversion to the corresponding phosphonate



$$Et_2N{-}CH_2{-}OCOCH_3 + (PhO)_3P \rightarrow \left[Et_2N{-}CH_2{-}\overset{+}{P}(OPh)_3\right]\bar{O}COCH_3 \rightleftarrows \left[Et_2N{-}CH_2{-}\overset{+}{P}(OCOCH_3)(OPh)_2\right]OPh^- \rightarrow Et_2N{-}CH_2{-}\underset{\underset{O}{\|}}{P}(OPh)_2 + PhOCOCH_3$$

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The reaction of acetoxymethyldiethylamine with the triamidophosphite probably proceeds in a similar manner. This is in agreement with [3, 4], in which it was shown that if in a quasiphosphonium salt, containing halogen, the latter is replaced by either the acetate or the nitrate ion, then the decomposition of the formed quasisalt occurs at very low temperatures.

We isolated acetic anhydride (63%) and the diethyl ester of diethylaminomethylphosphonic acid (82%) as the main products when acetoxymethyldiethylamine was reacted with diethyl acetylphosphite. The reaction went very vigorously with spontaneous heating up to 60-65°.

In studying the reaction of diethyl chlorophosphite with acetoxymethyldiethylamine it was interesting to ascertain which properties of the phosphorus atom, namely either nucleophilic or electrophilic, will be manifested in this reaction. The reaction was run in absolute ether at −30 to −40°, with vigorous stirring. The acid chloride of diethylphosphorous acid was added to the acetoxymethyldiethylamine in drops. The formation of a precipitate was observed, which represented a white powder that deliquesced in the air. The precipitate was separated from the reaction mixture and washed with absolute ether. Based on the elemental analysis data and its reaction with triethyl phosphite, which proceeded in the same manner as described in [5], it was established that diethylaminomethyl chloride was obtained. It proved even more difficult to isolate the second intermediate product of this reaction, namely diethyl acetylphosphite, since even a trace amount of the dialkylaminomethyl chloride converted it to the ester of the dialkylaminomethylphosphonic acid. Analysis of the low-boiling products, which were isolated when this reaction was run under various conditions, by GLC disclosed that the acetyl chloride contains only traces of ethyl chloride and the tertiary amine.

As a result, the same as in the case with α-esteramines, acetals and orthoesters [5-9], the reaction of acetoxymethyldiethylamine with the acid chloride of diethylphosphorous acid proceeds in two steps, and the diethyl chlorophosphite is the electrophile. This series of reactions disclosed that replacing the chlorine by the acetate group in an electrophilic reagent substantially expands the possibilities of the Arbuzov rearrangement. In this way can be obtained various phosphonates containing amido and phenoxyl groups attached to the phosphorus atom, which at times is difficult when alkyl halides are used.

EXPERIMENTAL

Reaction of Acetoxymethyldiethylamine with Diethyl Diethylamidophosphite. To 9.65 g of diethyl diethylamidophosphite was added in drops 7.26 g of acetoxymethyldiethylamine in 1 h. The temperature of the reaction mixture rose to 45-50°. Fractional distillation in vacuo gave 3.8 g of low-boiling product, which, based on the GLC data, was ethyl acetate, and 10.8 g (86.4%) of ethyl diethylaminomethyl diethylamidophosphonate with bp 133-134° (10 mm); n_D^{20} 1.4490; d_4^{20} 0.9645. Found: C 53.21; 53.33; H 10.68; 10.95; P 12.07; 12.22%; MR 69.55. $C_{11}H_{27}N_2O_2P$. Calculated: C 52.80; H 10.80; P 12.40%; MR 69.77.

The reaction of acetoxymethyldiethylamine with diethyl diisobutylamidophosphite was run in a similar manner. Ethyl acetate was identified by GLC as being the low-boiling product. Ethyl diethylaminomethyl diisobutylamidophosphonate was obtained in 75.1% yield; bp 100-103° (0.03 mm); n_D^{20} 1.4535; d_4^{20} 0.9427. Found: C 58.51; 58.25; H 11.36; 11.27; P 9.43; 9.59%; MR 87.82. $C_{15}H_{35}N_2O_2P$. Calculated: C 58.82; H 11.43; P 10.13%; MR 88.24.

Reaction of Acetoxymethyldiethylamine with Methyl Bis(diethylamido)phosphite. To 10.3 g of methyl bis(diethylamido)phosphite was added in drops 7.26 g of acetoxymethyldiethylamine in 1 h. Heating up of the reaction mixture to 40° was observed. Fractional distillation of the reaction mixture in vacuo gave 3.1 g of methyl acetate with bp 55.5-56°; n_D^{20} 1.3612; d_4^{20} 0.9329 (from [10]: bp 57.3°; n_D^{20} 1.3593; d_4^{20} 0.9338), and 10 g (72.2%) of diethylaminomethyl tetraethyldiamidophosphonate with bp 150-153° (10 mm); n_D^{20} 1.4660; d_4^{20} 0.9538. Found: C 56.16; 56.23; H 11.79; 12.08; N 15.50; 15.69; P 10.91; 10.71%; MR 80.42. $C_{13}H_{32}N_3OP$. Calculated: C 56.32; H 11.55; N 15.16; P 11.19%; MR 80.98.

Reaction of Acetoxymethyldiethylamine with Tris(diethylamido)phosphite. To 13.4 g of acetoxymethyldiethylamine was added 15 g of tris(diethylamido)phosphite in drops. Heating up of the reaction mixture to 40° was observed. Fractional distillation of the reaction mixture in vacuo gave 7.4 g of diethylacetamide with bp 63.5-65° (8 mm); n_D^{20} 1.4380 (from [11]: bp 38.5-40° (3 mm); n_D^{20} 1.4385), and 12.2 g (72.8%) of diethylaminomethyl tetraethyldiamidophosphonate with bp 98-101° (0.01 mm); n_D^{20} 1.4655; d_4^{20} 0.9516. Found: C 56.41; 56.40; H 11.36; 11.50; P 11.20; 11.22%; MR 80.52. $C_{13}H_{32}N_3OP$. Calculated: C 56.32; H 11.55; P 11.19%; MR 80.98.

Reaction of Acetoxymethyldiethylamine with Triphenyl Phosphite. To 15.5 g of triphenyl phosphite was added 7.25 g of acetoxymethyldiethylamine in drops. A slight warming up of the reaction mixture was observed (by 5°). The mixture was heated at 80° for 1-2 h. Fractional distillation of the reaction mixture in vacuo gave 4.55 g of phenyl acetate with bp 70-72° (8 mm); n_D^{20} 1.4710; d_4^{20} 1.0120. (Found: MR 37.57. $C_8H_8O_2$. Calculated: MR 37.20), and 8.6 g (54%) of the diphenyl ester of diethylaminomethylphosphonic acid with bp 153-154° (0.02 mm); n_D^{20} 1.5535; d_4^{20} 1.1493. Found: P 9.71; 9.69%; MR 88.89. $C_{17}H_{22}NO_3P$. Calculated: P 9.71%; MR 88.31.

Reaction of Acetoxymethyldiethylamine with Diethyl Acetylphosphite. To 9 g of diethyl acetylphosphite was slowly added 7.25 g of acetoxymethyldiethylamine. Heating up of the reaction mixture to 60° was observed. Fractional distillation of the reaction mixture in vacuo gave 3.2 g (63%) of product with bp 137-139°; n_D^{20} 1.3910, which, based on the GLC data, was acetic anhydride, and 9.1 g (81.6%) of the diethyl ester of diethylaminomethylphosphonic acid with bp 111-113° (8 mm); n_D^{20} 1.4340. From [12]: bp 83° (0.04 mm); n_D^{20} 1.4331. Found: P 13.65; 13.80%. $C_9H_{22}NO_3P$. Calculated: P 13.90%.

Reaction of Acetoxymethyldiethylamine with Diethyl Chlorophosphite. The system, composed of an Arbuzov flask, a condenser, and a dropping funnel, was connected through a trap, cooled in a mixture of liquid nitrogen and acetone (temperature −80°), to a vacuum of 0.01 mm. To 6.3 g of the acid chloride of diethylphosphorous acid, placed in the Arbuzov flask, was added 5.9 g of acetoxymethyldiethylamine in drops. Heating up was observed, as well as the formation of a precipitate and its subsequent disappearance. In the trap was condensed 2 g of a low-boiling product, which, based on the GLC data, consisted of acetyl chloride that was contaminated with a small amount of ethyl chloride and diethylmethylamine.

Fractional distillation of the reaction mixture in vacuo gave 3.55 g (40%) of the diethyl ester of diethylaminomethylphosphonic acid, the constants of which coincide with those given above.

To 7.25 g of acetoxymethyldiethylamine in 100 ml of absolute ether was added 7.83 g of diethyl chlorophosphite in drops, with vigorous stirring, at −30 to −40°. The formation of a white precipitate was observed, which quickly deliquesced in the air. The precipitate was washed with absolute ether, and the latter was removed in vacuo. Found: Cl 28.56; 29.05%. $C_5H_{12}ClN$. Calculated: Cl 29.21%.

CONCLUSIONS

1. A study was made of the reaction of acetoxymethyldiethylamine with the mono-, di-, and triamidophosphites, and with triphenyl phosphite, diethyl acetylphosphite and diethyl chlorophosphite.

2. Only one phosphorus-containing product is formed as a reaction result, namely either the corresponding ester or amide of diethylaminomethylphosphonic acid.

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