2. H. Böhme and K. Hartke, Chem. Ber., 96, 604 (1963).
3. H. Böhme and A. Sickmüller, Chem. Ber., 110, 208 (1977).
4. H. Böhme and G. Lerche, Chem. Ber., 100, 2125 (1967).
5. R. G. Kostyanovskii and O. A. Pan'shin, Izv. Akad. Nauk SSSR, Ser. Khim., 564 (1965).
6. G. Zinner and W. Kilwing, Chem. Zeitung., 97, 156 (1973).
7. R. G. Kostyanovskii, Yu. I. El'natanov, and Sh. M. Shikhaliev, Izv. Akad. Nauk SSSR, Ser. Khim., 249 (1977); 972 (1978); 1590 (1979).
8. H. Böhme and H. C. Viehe (editors), Advances in Organic Chemistry. Methods and Results, Vol. 9, Iminium Salts in Organic Chemistry, Part 1, Wiley-Interscience, New York–London–Sydney–Toronto (1976).
9. D. Purdela and R. Vilceanu, Chimia Compusilor Organici ai Fosforului si ai Acizilor Lui, Acad. Republicii Socialiste Romania, Bucharest (1965).
10. K. Issleib and R. Rieschel, Chem. Ber., 98, 2086 (1965).
11. V. Mark, C. H. Dungan, M. M. Critchfolld, and J. R. van Wazar, Topics Phosphorus Chem., 5, 227 (1967).
12. R. M. Kren and H. H. Sisler, Inorg. Chem., 9, No. 4, 836 (1970).
13. E. R. Razumova, Yu. I. Él'natanov, Sh. M. Shikhaliev, and R. G. Kostyanovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 97 (1978).
14. I. I. Chervin, M. D. Isobaev, Yu. I. Él'natanov, Sh. M. Shikhaliev, L. V. Bystrov, and R. G. Kostyanovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 1769 (1981).
15. R. G. Kostyanovskii (Kostyanovsky), V. N. Voznesenskii (Voznesensky), G. K. Kadorkina, and Yu. I. El'natanov, Org. Mass Spectrom., 15, 412 (1980).

REACTION OF N-ACETOXYMETHYLACETAMIDE AND N-ACETOXYMETHYLBENZAMIDE WITH ESTER–AMIDES AND AMIDES OF PHOSPHOROUS ACID

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As a continuation of our investigations of the reactions of ester–amides and amides of the acids of trivalent phosphorus we studied the reactions of N-acetoxymethylacetamide (I) and N-acetoxymethylbenzamide (II) with diethyl diethylamidophosphite (III), ethyl tetraethyldiamidophosphite (IV), and hexaethyltriamidophosphite (V) for the purpose of ascertaining the influence of the nature of the substituent on the N atom in the electrophilic reagent on the direction of the substitution reactions. The presence of two nucleophilic centers and the ambidentate nature of the $P^{III}-N$ bond in amidophosphites [1] allows us to expect the formation of products either at the P atom or at an N atom, depending on the structure of the electrophilic reagent.

It has previously been shown that the reactions of mono-, di-, and triamidophosphites III–V with N-hydroxymethyl derivatives of phenol [2] and benzamide [3] result in the simultaneous formation of products of both types, while N-hydroxymethylphthalimide reacts only at the N atom [3]. N-Acetoxy- and chloromethyldiethylamine react with III, IV, and V only at the P atom to form quasi-phosphonium salts or the corresponding phosphonates [4-6]. In ether and other solvents I and II react with triamidophosphites to form the quasi-phosphonium salts tris(deithylamino)(acetamidomethyl)- and tris(diethylamino)(benzamidomethyl)phosphonium acetate, respectively (VI and VII) [7].

In the present work we studied the reactions of I and II with III through V without a solvent upon heating. The composition of the reaction mixtures was monitored by ^{31}P NMR. The samples were held in ampuls under cooling before the spectra were recorded.

It was shown that the reaction of I with V results in the formation of tris(diethylamino)(acetamidomethyl)-phosphonium acetate (VI) (δ 54 ppm, yield equal to 73.2%) and tetraethyldiamidoacetoxyphosphite (VIII) (δ 126 ppm, yield equal to 12.5%). Their simultaneous formation was detected spectrally. The constants of VIII are

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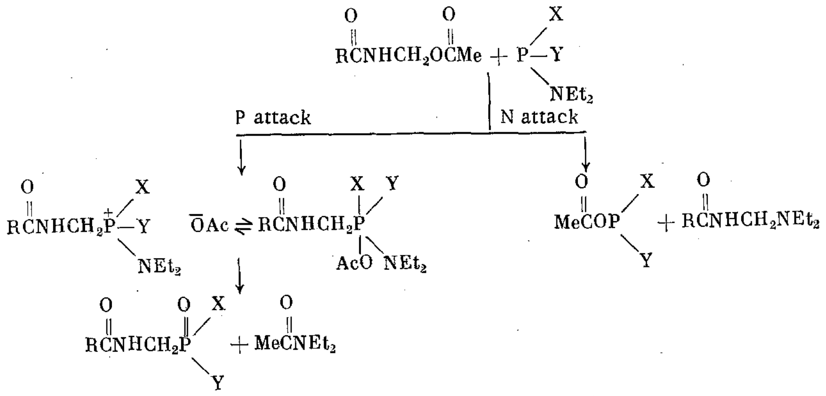
identical to those described in [8]. The reaction of II with V under the same conditions takes place only with the formation of quasi-phosphonium salt VII (δ 54 ppm, yield equal to 91.4%).

The reactions of I and II with IV were carried out under similar conditions. The spectra of the reaction mixtures at 20-30°C showed signals of ethyl diethylamidoacetoxyphosphite (IX) (δ 140 ppm) and a product with a phosphonate structure along with the signal of IV. Tetraethyldiamido(acetamidomethyl)phosphonate (X) (δ 30 ppm) and IX (δ 140 ppm) were recovered with 30 and 40% yields, respectively, from a reaction mixture of I and IV by vacuum distillation, and tetraethyldiamido(benzamidomethyl)phosphonate (XI) (δ 32 ppm, yield equal to 85%) and IX (yield equal to 10%) were recovered from a reaction mixture of II and IV. Because of the lability of IX [9], it could not be isolated in a pure form. When the reaction of II and IV was carried out in benzene, the formation of bis(diethylamino)ethoxy(benzamidomethyl)phosphonium acetate (XII) (δ 54 ppm) and its gradual transformation into phosphonate XI (δ 32 ppm) were detected spectrally.

The reaction of I and II with III without a solvent also takes place at two reaction centers. However, the contribution of the reaction at the N atom is significantly more appreciable. Ethyl diethylamido(acetamidomethyl)phosphonate (XIII) (δ 28 ppm, yield equal to 30%) and diethyl acetoxyphosphite (XIV) (δ 132 ppm, yield equal to 55%) were recovered from a reaction mixture of I and III, and ethyl diethylamino(benzamidomethyl)phosphonate (XV) (δ 28 ppm, yield equal to 45%) and XIV (yield equal to 31%) were recovered from a reaction mixture of II and III. When the reaction was carried out in benzene at 10-30°C, two signals were detected at +54 and −17 ppm. These signals gradually disappeared with the simultaneous appearance of a signal at 28 ppm, which we assigned to XV. In analogy to [7], it may be postulated than an equilibrium between the ionic and pentavalent forms of diethylaminodiethoxy(benzamidomethyl)phosphonium acetate (XVI).



R = Me, Ph; X = Y = OEt; X = Y = NEt$_2$; X = OEt, Y = NEt$_2$

When acyl phosphites (products of the reactions with attack at the N atom) are formed, the formation of N-(diethylaminomethyl)acetamide (XVII) or the analogous compound N-(diethylaminomethyl)benzamide (XVIII) should be expected as a second product. However, they could not be isolated from the reaction mixtures. It may be postulated that they react with I or II or with the acyl phosphites formed. In fact, bis(benzamido)methane was recovered from the reaction mixtures of II and III in a 5% quantity, and diethyl benzamidomethylphosphonate (XIX) was isolated with a 33% yield by vacuum distillation at 65-95°C following the reaction of diethyl acetoxyphosphite (XIV) with N-(diethylaminomethyl)benzamide (XVIII). Apparently, some of XVII and XVIII are consumed in secondary conversions during the reaction.

The data obtained showed that the structure of the electrophilic reagent influences the direction of the reactions of mono-, di-, and triamidophosphites with N-acetoxymethylacetamide and N-acetoxymethylbenzamide.

EXPERIMENTAL

The experiments were carried out in an argon atmosphere with absolute solvents. The amidophosphites were heated before the experiments over Na and then distilled. According to the data from elemental analysis and Bielstein's test, chlorine is absent. The IR spectra were recorded on a UR-20 instrument, and the ^{31}P NMR spectra were recorded on a KGU instrument (10.2 MHz) relative to 85% H_3PO_4.

N-Acetoxymethylacetamide (I). A mixture of acetamide, paraform, and Ac_2O (1 : 1 : 2.5) was heated in 50 ml of AcOH at 90-100°C for 5 h and evaporated in the vacuum of a water-jet pump. The syrupy residue was held in a vacuum with a residual pressure of 0.01 mm Hg and dissolved in ether. The white crystals with mp 180°C, which precipitated in an insignificant quantity were separated, the ether was evaporated, and the oil remaining crystallized at −3 to −10°C. After two recrystallization cycles from ether, I was isolated with mp 51°C. Found:

C, 45.94; H, 6.18; N, 10.9%. Calculated for $C_5H_9NO_3$, %: C, 45.80; H, 6.16; N, 10.68%. IR spectrum, cm^{-1}: ν_{CO-NH} 1680, δ_{NH} 1560, $\nu_{CO\text{-}ether}$ 1745, ν_{NH} 3320.

N-Acetoxymethylbenzamide (II) was obtained in a similar manner after two recrystallization cycles from ethanol and drying in a vacuum desiccator, mp 70-71°C. Found: C, 62.15; H, 5.65; N, 7.40%. Calculated for $C_{10}H_{11}NO_3$; %: C, 61.85; H, 5.67; N, 7.21. IR spectrum, cm^{-1}: ν_{CO-NH} 1660, ν_{NH} 3280, δ_{NH} 1545, $\nu_{CO\text{-}ether}$ 1750 (compare [10]).

Reaction of N-Acetoxymethylacetamide (I) with Hexaethyltriamidophosphite (V). A mixture of 3.93 g (0.03 mole) of I and 7.41 g (0.03 mole) of V was heated with stirring. At 45°C the temperature of the mixture increased to 90°C, and this increase was accompanied by the complete dissolution of the crystals of I. The reaction was carried out at 40-50°C, the disappearance of the original V being monitored according to the ^{31}P NMR spectrum. The mixture was treated with petroleum ether, the undissolved layer was separated and washed five times with ether, and the residue was dried in a vacuum. This yielded 8.3 g (73.2%) of tris(diethylamino)(acetamidomethyl)-phosphonium acetate (VI) in the form of a colorless viscous liquid, δ 54 ppm. Found: C, 53.27; H, 10.30; N, 14.52; P, 7.62%. Calculated for $C_{17}H_{39}O_3N_4P$, %: C, 53.96; H, 10.31; N, 14.81; P, 8.02% (compare [7]). After removal of the petroleum ether, 0.88 g (12.5%) of tetraethyldiamidoacetoxyphosphite (VIII) with bp 84-85°C (10 mm Hg), n_D^{20} 1.4485, and δ 126 ppm (compare [8]) was recovered from the upper layer by distillation.

Reaction of N-Acetoxymethylacetamide (I) with Ethyl Tetraethyldiamidophosphite (IV). When a mixture of 10.5 g (0.08 mole) of I and 17.6 g (0.08 mole) of IV was cautiously heated to 40°C, the temperature of the reaction mixture increased to 98°C, this increase being accompanied by the formation of a transparent mobile liquid. The reaction was carried out at 45-50°C to the disappearance of IV according to the ^{31}P NMR spectrum. The reaction mixture was dissolved in petroleum ether, the white precipitate was separated, the solvent was removed, and the residue was distilled. After two distillation cycles, 7.12 g (40%) of ethyl diethylamidoacetoxyphosphite (IX) with bp 45-47°C (0.03 mm Hg), n_D^{20} 1.4400, and δ 140 ppm were isolated. Found: P, 13.95; N, 6.83%. Calculated for $C_8H_{18}O_3NP$, %: P, 14.98; N, 6.78. Further distillation did not yield an analytically pure product (compare [9]). Then 6.4 g (30%) of tetraethyldiamido(benzamidomethyl)phosphonate (XI) with bp 65-67°C (0.001 mm Hg) and n_D^{20} 1.4555 were obtained. Found: C, 50.65; H, 9.62; N, 15.78; P, 12.2%. Calculated for $C_{11}H_{26}N_3O_2P$, %: C, 50.19; H, 9.98; N, 15.96; P, 11.78%. IR spectrum, cm^{-1}: ν_{CO-NH} 1670, ν_{NH} 3260, δ_{NH} 1560, $\nu_{P=O}$ 1225.

Reaction of N-Acetoxymethylacetamide (I) with Diethyl Diethylamidophosphite (III). When a stirred mixture of 9.1 g (0.07 mole) of I and 13.5 g (0.07 mole) of III was heated at 36-40°C for 20 min, a transparent mobile liquid formed. The reaction was carried out until the signal of III in the ^{31}P NMR spectrum disappeared. Two distillation cycles yielded 6.85 g (55%) of diethyl acetoxyphosphite (XIV) with bp 69-70°C (10 mm Hg), n_D^{20} 1.4220, and δ 132 ppm (compare [11]) and 7.3 g (30%) of ethyl diethylamido(acetamidomethyl)phosphonate (XIII) with bp 85-87°C (0.001 mm Hg), n_D^{20} 1.4529, and δ 28 ppm. Found: C, 45.20; H, 8.83; N, 11.72; P, 13.00%. Calculated for $C_9H_{21}N_2O_3P$, %: C, 45.76, H, 8.89; N, 11.86; P, 13.13%.

Reaction of N-Acetoxymethylbenzamide (II) with Hexaethyltriamidophosphite (V). When a mixture of 4.85 g (0.025 mole) of II and 6.17 g (0.025 mole) of V was heated at 30-50°C, a viscous liquid formed. At the conclusion of the reaction, the mixture crystallized. The crystals of VII in a 10.1-g yield (91.4%) were washed with ether and recrystallized from ethyl acetate, mp 76-77°C, δ 54 ppm. Found, %: C, 59.68; H, 9.32; N, 12.35; P, 7.21. Calculated for $C_{22}H_{41}O_3N_4P$, %: C, 60.06; H, 9.32; N, 12.72; P, 7.04 (compare [7]).

Reaction of N-Acetoxymethylbenzamide (II) with Ethyl Tetraethyldiamidophosphite (IV). When 4.82 g (0.025 mole) of II and 5.5 g (0.025 mole) of IV were heated to 40°C with stirring, the temperature increased to 80°C, and a transparent liquid formed and crystallized after 15 min. The crystals were washed with petroleum ether and recrystallized from ethyl acetate. This yielded 6.9 g (85%) of tetraethyldiamido(benzamidomethyl)-phosphonate (XI) with mp 106-107°C. Found: C, 59.36; H, 8.55; N, 12.65; P, 9.38%. Calculated for $C_{16}H_2N_3O_2P$, %: C, 59.07; H, 8.62; N, 12.92; P, 9.53% (compare [7]). After removal of the petroleum ether, 0.8 g (10%) of ethyl diethylamidoacetoxyphosphite (IX) with δ 140 ppm (compare [9]) was recovered from the mother solution.

Reaction of N-Acetoxymethylbenzamide (II) with Diethyl Diethylamidophosphite (III). When 7.75 g (0.04 mole) of II and 7.75 g (0.04 mole) of III were cautiously heated to 50°C, the temperature increased to 67°C. For completion of the reaction, the mixture was heated at 70°C for 15 min. Petroleum ether was added, and a separation of layers was observed in the mixture. A 2.26-g portion (31.4%) of diethylacetoxyphosphite (XIV) with bp 69-70°C (10 mm Hg), n_D^{20} 1.4220, and δ 132 ppm (compare [11]) was isolated from the upper layer. A 0.5-g (5%) portion of crystals of bis(benzamido)methane with mp 240°C was isolated from the lower layer. Found: N, 10.52%. Calculated for $C_{15}H_{14}N_2O_2$, %: N, 11.02% (compare [12]). Crystals of ethyl diethylamino-(benzamidomethyl)phosphonate (XV) precipitated from the residue when it was dissolved in ether. The yield was

5.32 g (45%). After two recrystallization cycles from ether, the mp was 94-95°C. Found: C, 56.68; H, 7.81; N, 9.29; P, 10.41%. Calculated for $C_{14}H_{23}N_2O_3P$: C, 56.37; H, 7.71; N, 9.39; P, 10.10%.

Reaction of N-(Diethylaminomethyl)benzamide (XVIII) with Diethylacetoxyphosphite (XIV). Freshly recrystallized XVIII with mp 63°C (compare [13]) and freshly redistilled XIV with bp 67-68°C (10 mm Hg) and n_D^{20} 1.4207 (compare [11]) were taken in the reaction. When a mixture of 5.15 g (0.025 mole) of XVIII and 4.5 g (0.025 mole) of XIV was heated with stirring at 60-95°C, the crystals of XVIII gradually disappeared, and a mobile, slightly yellowish liquid formed. The composition of the reaction mixture was monitored spectroscopically. At 65°C the ^{31}P NMR spectrum showed two signals at 132 and 25 ppm of equal intensity, at 85°C the intensity of the signal at 25 ppm was sharply increased, and at 95°C only the signal at 25 ppm remained. The reaction mixture was vacuum-distilled. After two distillation cycles, 1.29 g (45.1%) of diethylacetamide with bp 66-67°C (10 mm Hg) and n_D^{20} 1.4372 (compare [7]) and 2.23 g (33%) of diethyl benzamidomethylphosphonate (XIX) with bp 170-172°C (0.006 mm Hg), n_D^{20} 1.5235, and mp 43-45°C were recovered. Found: C, 53.82; H, 6.60; N, 4.98; P, 11.02%. Calculated for $C_{12}H_{18}NO_4P$, %: C, 53.1; H, 6.62; N, 5.17; P, 11.44%. IR spectrum, cm^{-1}: ν_{CO-NH} 1660, ν_{NH} 3280, δ_{NH} 1550, $\nu_{P=O}$ 1225 (compare [10]).

CONCLUSIONS

Mono-, di-, and triamidophosphites react with N-acetoxymethylacetamide and N-acetoxymethylbenzamide at the phosphorus atom and at the nitrogen atom. In the reactions with N-acetoxymethylacetamide the fraction of the product of attack at the nitrogen atom is higher than in the reactions with N-acetoxymethylbenzamide.

LITERATURE CITED

1. L. M. Epshtein, A. N. Zhdanova, N. S. Dolgopyat, D. A. Bochvar, N. P. Gambaryan, and L. A. Kazitsyna, Izv. Akad. Nauk SSSR, Ser. Khim., 2487 (1979).
2. B. E. Ivanov, S. V. Samurina, N. N. Lebedeva, A. B. Ageeva, and É. I. Gol'dfarb, Izv. Akad. Nauk SSSR, Ser. Khim., 1825 (1973).
3. B. E. Ivanov, S. V. Samurina, S. S. Krokhina, and N. P. Anoshina, Izv. Akad. Nauk SSSR, Ser. Khim., 2075 (1974).
4. H. Böhme and K.-H. Meyer-Dulheuer, Liebigs Ann. Chem., 680, 91 (1965).
5. B. E. Ivanov, L. A. Valitova, and S. S. Krokhina, Izv. Akad. Nauk SSSR, Ser. Khim., 1502 (1971).
6. B. E. Ivanov, S. S. Krokhina, L. A. Valitova, and É. F. Gol'dfarb, Izv. Akad. Nauk SSSR, Ser. Khim., 597 (1972).
7. B. E. Ivanov, S. S. Krokhina, T. V. Chichkanova, T. A. Zyablikova, and A. V. Il'yasov, Izv. Akad. Nauk SSSR, Ser. Khim., 2783 (1976).
8. É. E. Nifant'ev, Zh. Obshch. Khim., 38, 1299 (1968).
9. V. P. Evdakov and E. K. Shlepkova, Zh. Obshch. Khim., 35, 739 (1965).
10. K. A. Petrov, É. E. Nifant'ev, I. I. Sonikova, and V. M. Budakov, Zh. Obshch. Khim., 31, 2375 (1961).
11. C. W. Sauer and R. Bruni, J. Am. Chem. Soc., 77, 2559 (1955).
12. H. Hellmann, Angew. Chem., 69, 463 (1957).
13. B. E. Ivanov, S. S. Krokhina, M. S. Skorobogatova, and Ya. A. Levin, Izv. Akad. Nauk SSSR, Ser. Khim., 2768 (1972).