REACTION OF N-CHLOROMETHYLDIETHYLAMINE, N-CHLOROMETHYLBENZAMIDE, AND N-CHLOROMETHYLPHTHALIMIDE WITH ESTERS OF TRIVALENT PHOSPHORUS THIOACIDS

B. E. Ivanov, S. S. Krokhina, and T. V. Chichkanova UDC 542.91:547.1'118

Due to the high reactivity of α -substituted amines, in the study of their reactions with trivalent phosphorus derivatives, several important features of these reactions can be shown. Thus, the regularities of a dual reaction in the series of trivalent phosphorus derivatives were first discovered on the example of amidophosphites [1, 2]. However, for a deeper understanding of this problem, the behavior of α -substituted amines was compared with that of amides in systems where the dual reactivity has already been studied. In the series of organophosphorus compounds, this includes esters of trivalent phosphorus thioacids. The dual reactivity of the latter has been shown in reactions with several electrophilic reagents, whose regularities have been generalized in review [3].

The aim of the present work was to study the reactions of N-chloromethyl derivatives R

N.CH2-Cl , N-chloromethyldiethylamine (I), N-chloromethylbenzamide (II) and N-chloro-

methylphthalimide, with S-butyldiphenylthiophosphinite (IV) and S,S-dibutylphenyldithiophosphonite (V). It was also interesting to study the influence of the polarity of the C-Cl bond of an electrophilic reagent on the course of the reaction. In the series (I)-(III), the polarity of the C-Cl bond changes from almost ionic (I) to weakly polar covalent in (III) [4]. In accordance with the conclusions stated in [3], it might have been expected that the contribution of the reaction at the S atom will increase with increase in the polarity of the C-Cl bond.

As an ionic compound, (I) reacts with phosphorous acid esters [6] and amidophosphites [7] at low temperatures to form Arbuzov reaction products. It was expected that both (IV) and (V) will readily react with I to form products at the S atom of the thioester. However, (I) and (IV) practically do not react when heated to 120°C. A noticeable reaction of (I) and (V) was observed in toluene, xylene, DMFA, and without a solvent at 100-120°C. Increase in temperature above the thermal stability of (I) leads to resinification of the reaction mixture. In the ³¹P NMR spectra of the reaction mixture of (I) and (IV), there is a signal of the initial (IV), δ 26 ppm, and in the spectrum of (I) and (V), a signal of the initial (V), δ 74 ppm, and of a product at the S atom, the acid chloride of S-butylphenylthiophosphorous acid (VI), δ 142 ppm (cf. [8]). Distillation in vacuo restored (V) in a mixture with (VI).

N-Chloromethylbenzamide (II) reacts with amidophosphites to form the Arbuzov reaction products [2, 7]. Compound (II) reacts with the monothioester (IV) under mild conditions (20°C), without a solvent or in hexane to form a dense colorless mass, whose ³¹P NMR spectrum shows one single signal at 48 ppm, characteristic of quasiphosphonium salts (VII) [9]. Hydrolysis takes place in contact with air and the odor of a mercaptan is evident. As the result, diphenyl(N-benzaminomethyl)phosphine oxide (VIII) separates, δ 30 ppm (in DMFA).

N-Chloromethylphthalimide, with a weakly polar and covalent C-Cl bond [4], reacts with (IV) under more rigid conditions at 90-110°C in toluene, xylene, and without a solvent. It has been spectrally shown that already at 90°C, a complex mixture of products is formed with signals at 60, 40, and 22 ppm. At the end of the reaction, the same signals are recorded in the spectra, while (IV) is not completely consumed. Diphenyl(N-phthalimidomethyl)-diphenylphosphine sulfide (IX), δ 40 ppm, a direct product of the Arbuzov reaction, and di(N-phthalimidomethyl)diphenylphosphonium chloride (X), δ 22 ppm, were isolated from the

A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan' Branch, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 1, pp. 178-182, January, 1985. Original article submitted October 10, 1983. reaction mixture. Product (XI), with δ 60 ppm, could not be isolated. Compounds (X) and (XI) are probably products of secondary transformations of starting compounds and products formed in the reaction, as described in [3, 10]. Their formation indicates that the reaction proceeds at the P atom (scheme 1).



Compound (III) reacts with dithioester (V) at 120-150°C (4 h), in xylene at 145°C (10 h) and in toluene at 115°C (20 h). The reaction is complex. In the spectra of the reaction mixtures, the formation of the acid chloride (VI) has been recorded, δ 142 ppm (a low-intensity signal) and of products, whose signals lie in the regions characteristic of (XIII), δ 78 ppm, (XIV), δ 50 ppm, (XV), δ 22 ppm, (XVI), δ 62 ppm, and (XVII), δ 42 ppm [9]. Compound (V) is not completely consumed. S-Butyl(N-phthalimidomethyl)phenyldithiophosphinate (XVI), δ 62 ppm, a direct product of reaction at P, and phenyl(di-N-phthalimidomethyl)phosphine sulfide (XVII), δ 42 ppm, a product of secondary transformations, were isolated from the reaction mixture. The formation of products (XIII)-(XV) can be explained by reductive desulfurization processes under fairly rigid reaction conditions, as described in [3] (see Scheme 2). The low intensity of the acid chloride (VI) signal shows that the fraction of the product of the reaction at the S atom is inappreciable, and the main course is the reaction at the P atom.

In N-chloromethylbenzamide, the C-Cl bond is more polar than in (III) [4]. The reaction of (II) with (V) proceeds under milder conditions. When the reagents are mixed together, the mixture heats up to 30°C. It has been spectrally recorded that already at 30°C, a product of a reaction at the S atom is formed, the acid chloride (VI), δ 142 ppm. Besides (VI), products with signals at 78, 62, 50, and -18 ppm are also formed. At 80°C, the formation of (VI) is more favorable, the signal at -18 ppm disappears, while the intensity of the remaining signals does not change. After distillation in vacuo, (VI) was isolated in a yield of 51%, and 16% of (V) were recovered. The residue, containing a mixture of products with signals at 78 and 50 ppm, which can be assigned to (XIII) and (XVIII), could not be isolated. Only S-butyl(N-benzamidomethyl)-phenylthiophosphinate (XIX), δ 62 ppm, the normal product of the Arbuzov reaction, and di(N-benzaminomethyl)phenylphosphine oxide (XX), δ 32 ppm, were isolated from the reaction mixture. In analogy with the data in [3], (XIII) and (XVIII) are products of secondary transformations, while (XX) is probably a product of hydrolysis of the intermediately formed quasiphosphonium salt (XVIII) (scheme 2).

The reactions of (I)-(III) with S-butyldiphenylthiophosphinite (IV) thus proceed at the P atom, while with S,S-dibutylphenyldithiophosphonite (V) at the P and S atoms. The course of the reaction is determined by the polarity of the C-Cl bond of the electrophile, while in reactions with (IV) and (V) the chloromethyl derivatives of amines behave like alkyl halides.



EXPERIMENTAL

The experiments were carried out in a dry Ar atomsphere in absolute solvents. The IR spectra were recorded on the UR-20 spectrophotometer, and the ³¹P NMR spectra on the KGU spectrometer (10.2 MHz) with reference to 85% H₃PO₄.

Reaction of N-Chloromethylbenzamide (II) with S-Butyldiphenylthiophosphinite (IV). A mixture of 3.94 g of (II) and 6.38 g of (IV) in 10 ml of hexane and 10 ml of MeCN was stirred for 30 min at 20°C. The crystals of (II) disappear, and a dense colorless liquid is formed in the form of a separate layer. When separated in air, the lower dense layer (δ 48 ppm) crystallizes and a sharp odor of a mercaptan is evident. It was dissolved in 100 ml of acetonitrile, and the solution was boiled for 30 min. When cool, white crystals of diphenyl-(N-benzaminomethyl)phosphine oxide (VIII) separated in yield of 5.5 g (71%), mp 243-245°C, δ 30 ppm (DMFA). Found: C 71.40; H 5.82; N 4.14; P 9.10%. C₂₀H₁₈NO₂P. Calculated: C 71.64; H 5.37; N 4.17; P 9.25%. IR spectrum (ν , cm⁻¹): 1650 (CO-NH), 1550 and 3260 (NH), 1180 (P=0).

<u>Reaction of N-chloromethylphthalimide (III) with S-butyldiphenylthiophosphinite (IV)</u>. A mixture of 7.56 g of (III) and 10.65 g of (IV) was heated at 95-110°C. At 95°C a homogeneous solution is formed, and at 110°C, crystals are formed. After 1.5 h of heating, a dense colorless liquid containing crystals formed in the flask. The crystals were separated, washed with MeCN, and recrystallized from the same solvent (120 ml). Di(N-phthalimido-methyl)diphenylphosphonium chloride (X) was isolated in a yield of 6.2 g, mp 243-244°C, δ 22 ppm (DMFA). Found: C 65.77; H 4.14; P 5.41; Cl 6.56%. C₃₀H₂₂O₄N₂PCl. Calculated: C 66.6; H 4.07; P 5.73; Cl 6.56%. To the dense colorless liquid left after separation of crystals of (X), MeCN was added again, and the mixture was boiled for 3 h. MeCN was removed in vacuo, and the residue crystallized completely. The crystals were soaked in benzene. Crystals of (X) (0.1 g), which are insoluble in benzene, were separated, and after removal of benzene from the benzene mother liquor, diphenyl(N-phthalimidomethyl)phosphine sulfide (IX) was isolated in a yield of 1.5 g (15%), mp 152°C, δ 40 ppm. (DMFA). Found: C 66.86; H 4.68; N 3.59; P 7.77; S 8.56%. C₂₁H₁₆O₂NPS. Calculated: C 66.84; H 4.24; N 3.71; P 8.22; S 8.48%.

Reaction of N-Chloromethylphthalimide (III) with S,S-Dibutylphenyldithiophosphonite (V). A mixture of 6.59 g of (III) and 9.65 g of (V) was heated at 150°C for 4 h. When cool, crystals were separated from the dense colorless mass, and washed with benzene. From the benzene solution, 0.8 g of (III), mp 135°C, were isolated. Found: Cl 18.8%. C₉H₆O₂NCl. Calculated: Cl 18.15%. The crystals of phenyl(di-N-phthalimidomethyl)phosphine sulfide (XVII) (3.5 g (40%)), insoluble in benzene, were recrystallized from MeCN, mp 235-236°C. Found: C 62.47; H 4.00; N 6.36; P 6.57; S 6.95%. C₂4H₁₇O₄N₂PS. Calculated: C 62.60; H 3.69; N 6.08; P 6.73; S 6.95%. The dense mass left after separation of the crystals (III) and (XVII) crystallized on standing to yield 1.5 g (20%) of S-butyl(N-phthalimidomethyl)phenyl-dithiophosphinate (XVI), mp 65-67°C (from benzene), δ 62 ppm. Found: N 3.73; P 7.83; S 16.20%. C1₉H₂₀O₂NPS₂. Calculated: N 3.59; P 7.96; S 16.45%.

Reaction of N-Chloromethylbenzamide (II) with S,S-Dibutylphenyldithiophosphonate (V). A 7.42-g portion of (V) was added dropwise to 4.4 g of (II) in 25 ml of toluene. The mixture heated up to 30°C, and crystals of (II) disappeared. The mixture was heated for 45 min at 80°C. At the end of the reaction, the mixture stratified. Toluene was removed in vacuo from the upper liquid layer. The residue was washed four times from hexane. After removal of hexane, the residue was fractionated to yield 3.2 g (51%) of acid chloride of S-butylphenylthiophosphonous acid (VI), bp 65-70°C (0.04 mm), δ 142 ppm (cf. [8]). Found: P 12.94; S 13.72%. C10H14PSC1. Calculated: P 13.30; S 14.15%. Then, 1.2 g of (V), δ 74 ppm, was recovered. After distillation, the residue was a mobile liquid (δ 78 and 50 ppm), insoluble in hexane, which crystallized on standing. The viscous greasy crystals are a mixture of S-butyl ester of N-benzaminomethylphenyldithiophosphonic acid (XIX) (δ 62 ppm) and N-benzaminomethyl butyl sulfide. The δ 62 ppm signal was assigned to (XIX) in analogy with (XVI). IR spectrum (ν , cm⁻¹): 1670 (CO-NH), 1540 and 3080-3300 (NH). Found: S 16.20; P 5.20%.

The dense colorless liquid formed in the reaction (the lower layer), crystallized when left in air, and had the odor of a mercaptan. The crystals were dissolved, with heating, in MeCN. When cool, crystals of phenyl(di-N-benzaminomethyl)phosphine oxide (XX) precipitated in a yield of 1.5 g (14.9%), δ 32 ppm. Found: P 7.93; N 7.20%. C₂₂H₂₁N₂O₃P. Calculated: P 7.91; N 7.14%. IR spectrum (ν , cm⁻¹): 1640, 1690 (CO-NH), 1540, 1560, and 3200-3220 (NH), 1180 (P=O); mp 210-212°C.

CONCLUSIONS

N-Chloromethylbenzamide and N-chloromethylphthalimide react with S-butyldiphenylthiophosphinite at the P atom. The reaction of S,S-dibutylphenyldithiophosphonite with N-chloromethylphthalimide proceeds preferentially at the P atom, and with N-chloromethylbenzamide at the S atom. With increase in the polarity of the C-Cl bond in the N-chloromethyldiethylamine > N-chloromethylbenzamide > N-chloromethylphthalimide series, the tendency to react at the S atom increases.

LITERATURE CITED

- B. E. Ivanov, S. V. Samurina, S. S. Krokhina, and L. A. Valitova, Chemistry and Use of Organophosphorus Compounds. Proceedings of V-th Conference [in Russian], Nauka, Moscow (1974), p. 119.
- B. E. Ivanov, S. S. Korkhina, T. V. Chichkanova, and S. V. Samurina, VII-th All-Union Conference on Chemistry of Organophosphorus Compounds. Summaries of Lectures [in Russian], Leningrad (1982), p. 28.
- 3. E. A. Krasil'nikova, Usp. Khim., 46, 1638 (1977).
- B. A. Arbuzov, D. M. Nasyrov, and A. N. Vereshchagin, Izv. Akad. Nauk SSSR, Ser. Khim., 1537 (1982).
- 5. P. A. Kollman, J. M. Mc Kelvey, and P. Gund, J. Am. Chem. Soc., 97, 1640 (1975).
- 6. H. Böhme, L. Koch, and E. Köhler, Chem. Ber., <u>95</u>, 1849 (1962).
- 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 (1979).
- 8. L. N. Shitov and B. M. Gladshtein, Zh. Obshch, Khim., <u>39</u>, 1251 (1969).
- 9. M. M. Crutchfield, C. H. Dungan, J. H. Letcher, V. Mark, and J. R. Van Wazer, Topics in Phosphorus Chemistry, Vol. 5, Int. Publ., N.Y.-London-Sydney (1967), p. 242.
- A. E. Arbuzov, Selected Transactions of Academy of Sciences of the USSR [in Russian], Moscow (1952), p. 226.