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Reaction of Amides of 2,3-Dibromopropionic and 2-Bromoacrylic Acids with Pyridine and Triphenylphosphine

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Abstract—By refluxing pyridine with 2,3-dibromopropionic acid amide in acetonitrile, amide of 3-bromo-2-pyridiniumbromidopropionic acid **I** was synthesized. The latter is inert toward the second molecule of pyridine under the used conditions. Compound **I** was found to react with triphenylphosphine to form a mixture of 3-triphenylphosphoniumbromidopropionitrile **II** and 1-triphenylphosphoniumbromido-2-pyridiniumbromidoethane **III**. Schemes of reactions were suggested involving attack of phosphine on the carbonyl group as the first stage. The reaction of α-bromoacrylic acid amide with triphenylphosphine was shown to yield also compound **II**. Evidently, this reaction proceeds through intermediate formation of enolphosphonium salt.

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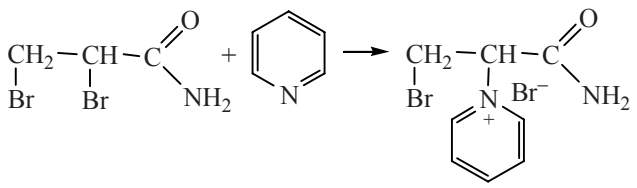
It was established earlier that dibromopropionic acid and its nitrile, esters, and amide react with triphenylphosphine by a common scheme, the first stage of which is debromination [1]. By contrast, reactions of this acid as well as its chlorine analog with aliphatic amines result in dehydrobromination products, and the reaction with pyridine yields vynilpyridinium halides. The latter are formed as a result of the substitution at the α-carbon atom followed by dehydrohalogenation and decarboxylation [1].

In the present work we examined reactions of pyridine with dibromopropionic acid amide. The equimolar mixture refluxed in acetonitrile gave rise to amide of 3-bromo-2-pyridiniumbromidopropionic acid **I** in 87% yield. The situation did not change at the ratio 1:2 indicating that under the used conditions the β-bromine atom is inert relative to the pyridine.



I

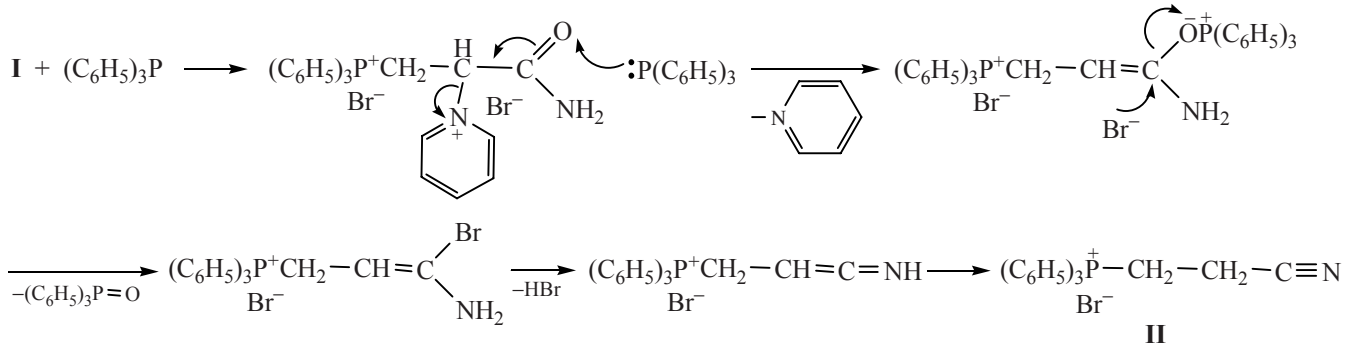
Salt **I** was involved into the reaction with triphenylphosphine in boiling acetonitrile. The results were unexpected. According to the ^{1}H NMR spectral data, a mixture of 3-triphenylphosphoniumbromide-propionitrile **II**, 1-triphenylphosphoniumbromido-2-pyridiniumbromidoethane **III**, and triphenylphosphine oxide was obtained rather than the expected products of dehydrobromination and nucleophilic substitution. In the spectra signals characteristic of the amide moiety are absent. We believe compounds **II** and **III** to form according to Schemes 1 and 2.

The first scheme leading to compound **II** involves substitution of the bromine atom with triphenyl-phosphine followed by the attack of phosphine on the amide oxygen atom, by pyridine elimination and the subsequent stages of nucleophilic substitution with ionic bromine, dehydrobromination, and prototropic isomerization.

According to the second scheme, *O*-betaine under-goes further transformations by successive elimination of triphenylphosphine and ammonia under the action of water (evidently, from solvent) to form compound **III**.

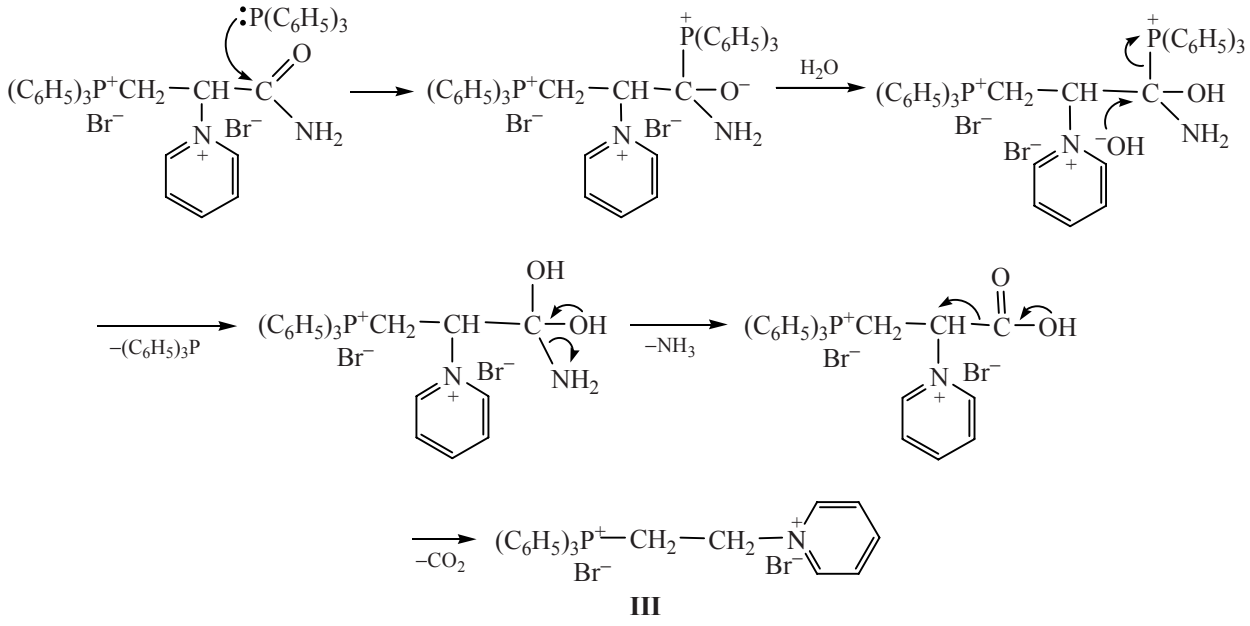
We also carried out a reaction of triphenyl-phosphine with 2-bromoacrylic acid amide **IV** at the

Scheme 1.



II

Scheme 2.

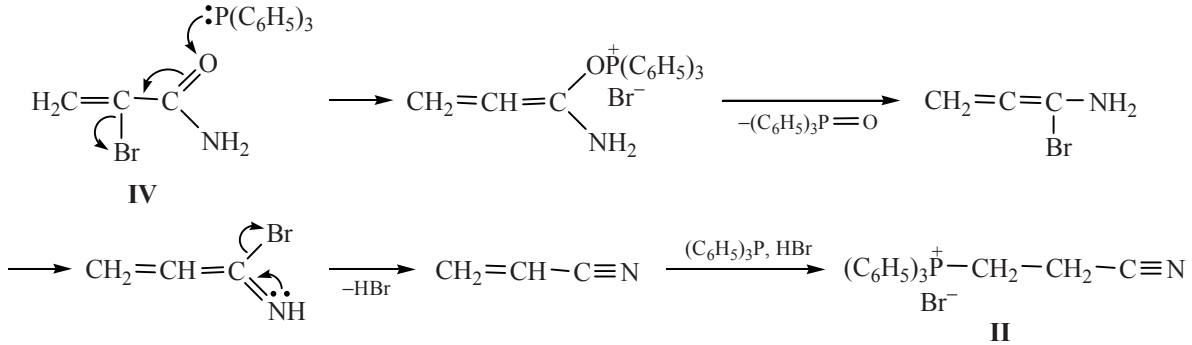


III

component ratio 1:1 under the above conditions. In this case reaction was shown to proceed also through attack of phosphine on carbonyl group yielding compound **II** (Scheme 3).

Amide of 2-bromoacrylic acid **IV** was prepared by the reaction of amide of 2,3-dibomopropionic acid with equimolar amount of triethylamine under heating, yield 83%. Based on the data obtained it may be

Scheme 3.



IV **II**

concluded that aliphatic amines react with the mentioned amide by the dehydrobromination scheme, i.e., similarly to dibromopropionic acid, its esters and nitrile.

EXPERIMENTAL

The ^{1}H and ^{31}P NMR spectra were recorded on a Varian MERCURY-300 instrument; operating frequency 300 MHz; internal reference TMS**.**

3-Bromo-2-pyridiniumbromidopropionic acid amide (I). A mixture of 1.85 g of 2,3-dibromopropionic acid amide and 0.63 g of pyridine in acetonitrile was refluxed for 20 h. The formed precipitate was filtered off, washed thoroughly with acetonitrile, and dried in a vacuum. Yield 2.15 g (87%), mp 205°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4 1:3), δ, ppm: 5.10–5.38 m (3H, –CH–CH_2–); 7.40 br.s (1H, NH_2); 7.96 br.s (1H, NH_2); 8.20 d. d (2H, *m*-$H_{pyridine}$, J_1 7.8 Hz, J_2 6.4 Hz); 8.70 t. t (1H, *p*-$H_{pyridine}$, J_1 7.8 Hz, J_2 1.2 Hz); 9.35 d. d (2H, *o*-$H_{pyridine}$, J_1 6.4 Hz, J_2 1.1 Hz). Found, %: C 30.87; H 3.60, Br 51.80; N 9.20; $C_8H_{10}Br_2N_2O$. Calculated, %: C 30.97; H 3.20; Br 51.60; N 9.00.

Reaction of salt I with triphenylphosphine: *a.* The components ratio 1:1. A mixture of 0.46 g of **I** and 0.39 g of triphenylphosphine was refluxed in acetonitrile for 20 h. After filtrating of 0.2 g (44%) of the unreacted salt, the filtrate was poured into ether. The precipitate was filtered off, washed thoroughly with ether, and dried in a vacuum. Yield 0.15 g of the mixture of 3-triphenylphosphoniumbromidopropionitrile **II** and 1-triphenylphosphoniumbromido-2-pyridiniumbromidoethane **III** in the ratio 1:1 in an overall yield 22%. ^{1}H NMR spectrum of **II** (DMSO-d_6 + CCl_4 1:3), δ, ppm: 2.60 m (2H, CH_2CN); 3.86 m (2H, CH_2P); 7.74–7.93 m (15H, C_6H_5). ^{31}P NMR spectrum, δ, ppm: 30.65.

^{1}H NMR spectrum of **III** (DMSO-d_6 + CCl_4 1:3), δ, ppm: 2.88 m (2H, NCH_2); 4.30 m (2H, PCH_2); 7.65–7.74 m (15H, C_6H_5); 8.00 d.d (2H, *m*-$H_{pyridine}$, J_1 7.8 Hz, J_2 6.4 Hz); 8.50 t.t (1H, *p*-$H_{pyridine}$, J_1 7.8 Hz, J_2 1.2 Hz); 9.00 d. d (2H, *o*-$H_{pyridine}$, J_1 6.4 Hz, J_2 1.1 Hz). ^{31}P NMR spectrum, δ, ppm: 29.36.

After the solvent was removed from the acetonitrile–ether filtrate, triphenylphosphine oxide was obtained. Yield 0.2 g (50%), mp 154°C (without depression of melting point in the mixture with an authentic sample).

b. The components ratio 1:2. A mixture of 0.46 g of salt **I** and 0.78 g of triphenylphisphine was refluxed in acetonitrile for 20 h. After filtring off 0.1 g (20%) of salt **I** and treating the filtrate as described above, 0.4 g of the mixture of salts **II** and **III** was obtained in the ratio 1:1 in an overall yield 58%. The ^{1}H and ^{31}P NMR spectra were as those given above.

After the solvent was removed from the acetonitrile–ether filtrate, triphenylphosphine oxide was obtained. Yield 0.4 g (50%), mp 154°C (without depression of melting point in the mixture with an authentic sample).

2-Bromoacrylic acid amide (IV). A mixture of 0.5 g of 2,3-dibromopropionic acid amide and 0.2 g of triethylamine in ether was heated for 8 h. The precipitate of 0.35 g of mixture of the unreacted initial amide and the formed triethylamine hydrobromide was filtered off. Then ether was evaporated and residue was dried in a vacuum. Yield 0.25 g (83%), mp above 240°C. ^{1}H NMR spectrum (DMSO-d_6 + CCl_4 1:3), δ, ppm: 6.0 s (1H, CH_2); 6.65 s (1H, CH_2); 7.3 br.s (1H, NH_2); 7.25 br.s (1H, NH_2). Found, %: C 24.45; H 2.81, Br 53.46; N 9.26; C_3H_4BrNO. Calculated, %: C 14.00; H 2.66; Br 53.33; N 9.33.

3-Triphenylphosphoniumbromidopropionitrile (II). A mixture of 0.15 g of **IV** and 0.26 g of triphenylphosphine was refluxed in acetonitrile for 20 h. The acetonitrile filtrate was poured into ether. The precipitate was filtered off, washed thoroughly with ether, and dried in a vacuum. Yield 0.1 g (25.25%), mp 210°C. The ^{1}H and ^{31}P NMR spectra are the same as given above. Found, %: C 63.75; H 4.82; Br 20.42; N 3.62; P 7.92. $C_{21}H_{19}BrNP$. Calculated, %: C 63.64; H 4.79; Br 20.20; N 3.54; P 7.82.

After the solvents were removed from the acetonitrile-ether filtrate and the residue was treated with water, triphenylphosphine oxide was obtained. Yield 0.2 g (70%), mp 154°C (without depression of melting point in the mixture with an authentic sample).

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