SYNTHESIS OF HETEROCYCLIC COMPOUNDS ON THE BASIS OF CARBOXYLIC ACID ARYLAMIDES

III.* REACTIONS WITH THE PARTICIPATION OF PHENYLIMINOOXALYL CHLORIDE

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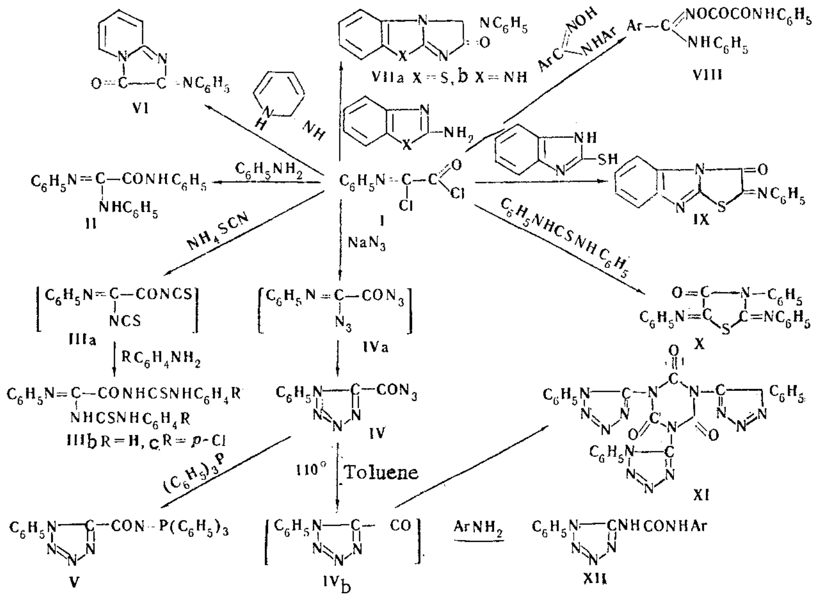
The exchange and cyclization of phenyliminooxalyl chloride with ammonium thiocyanate, sodium azide, aniline, amidoximes, and diphenylthiourea, and with 2-aminopyridine, 2-aminobenzothiazole, and 2-amino- and 2-mercaptobenzimidazole were studied. The cyclization products are derivatives of thiazolidine, imidazo[1,2-a]pyridine, imidazo[2,1-b]benzothiazole, imidazo[1,2-a]benzimidazole, and thiazolo[3,2-a]benzimidazole. A trimer of 1-phenyltetrazole-5-carboxylic acid was obtained when an attempt was made to convert its azide to the corresponding isocyanate.

In a continuation of our previous investigations of exchange and cyclization reactions on the basis of the acid chlorides of oxanilic acids [1, 2] and arylazochloroacetic acids [3] we have studied the reactions of phenyliminooxalyl chloride (I) (which we obtained for the first time) with ammonium thiocyanate, sodium azide, aniline, amidoximes, and diphenylthiourea, as well as with 2-aminopyridine, 2-aminobenzothiazole, and 2-amino- and 2-mercaptobenzimidazole.

Acid chloride I was obtained by the reaction of oxanilic acid with phosphorus pentachloride in benzene.



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*See [1] for communication II.

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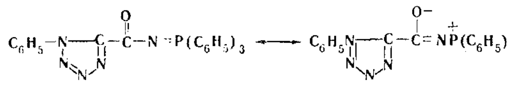
The diphenylamide (II) of phenyliminooxalic acid was isolated by the reaction of I with 5 mole of aniline. The readily polymerized diisothiocyanate (IIIa) was obtained by the reaction of I with ammonium thiocyanate in absolute acetone. Compound IIIa could not be isolated in pure form. It reacts with aromatic amines to form thioureas IIIb and IIIc. The characteristic band of the $N=C=S$ group at 1980-2100 cm^{-1} practically vanishes after prolonged storage, and the polymeric substance apparently formed does not react with aromatic amines and was not investigated in detail. The exchange of I with sodium azide was carried out in acetone at low temperatures. The initial reaction product is probably phenyliminooxalic acid diazide (IVc), which is readily cyclized to 1-phenyl-tetrazole-5-carboxylic acid azide (IV). The literature contains similar data [4-6] which indicate the ease of cyclization of the diazide of the isocyanide to the corresponding 5-azido-1-phenyltetrazole. The structure of IV was also confirmed by its IR spectrum, which contains the characteristic absorption bands of the N_3 group (doublet of bands at 2150-2195 cm^{-1}), $C=O$ (1715 cm^{-1}), and absorption bands at 1280-1320, 1205-1260, 1100-1140, 1020-1080, and 960-990 cm^{-1}, which are usually assumed for the tetrazole ring [5, 7]. An additional confirmation of the structure of IV is the reaction with triphenylphosphine. The IR spectrum of the reaction product (V) does not contain the frequencies of the valence vibrations of the azido group, and the absorption bands of the tetrazole ring are preserved. The frequency of the carbonyl group is lowered by 100 cm^{-1}, probably because of the possible formation of a dipolar structure:



In an attempt to convert IV to the corresponding 1-phenyl-5-isocyanatotetrazole (IVb) by means of the Curtius reaction [8] by heating it in absolute toluene we obtained 86% of a high-melting compound (XI) which, from its composition, conformed with the corresponding isocyanate, but its IR spectrum did not contain the characteristic frequencies of the $N=C=O$ group (2240-2270 cm^{-1}), and the substance did not give the characteristic reactions of isocyanates. From cryoscopic data, the molecular weight of the substance is three times the molecular weight of isocyanate IVb. We also observed a similar trimerization in [9]. These results provide a basis for assuming a cyclic trimer structure, viz., 2,4,6-trioxo-1,3,5-tris(1-phenyl-5-tetrazolyl)hexahydro-s-triazine, for XI. We also proved the formation of intermediate isocyanate IVb from IV indirectly by the isolation of 5-(3-phenylureido)-1-phenyltetrazole (XII) by the decomposition of IV in toluene in the presence of aniline. The vibrations of the $N-H$ bonds (3210-3290 cm^{-1}), the $C=O$ bonds (1715 cm^{-1}), and the bands of the tetrazole ring (1280-1320, 1205-1260, 1100-1140, 1020-1080, and 960-990 cm^{-1}) are clearly expressed in the IR spectrum of XII.

Compound VI, the structure of which was confirmed by the IR spectrum, was obtained by the cyclization of I with 2-aminopyridine in absolute benzene in the presence of triethylamine. The IR spectrum of VI contains characteristic bands at 1745 cm^{-1} ($C=O$) and 1695 and 1600 cm^{-1} ($C=N$). The frequencies of the valence vibrations at 1435, 1400, 1340, 1310, 1100, 780, and 695 cm^{-1} are usually taken for the imidazole and pyridine rings [10, 11].

The reaction of I with 2-aminobenzothiazole and 2-amino- and 2-mercaptobenzimidazoles yields condensation products VIIa, b, and IX, the structures of which were proved by the IR spectral data; IX was also hydrolyzed. The IR spectra of VIIa,b and IX contain intense frequencies of the valence vibrations of the $C=O$ group (1710-1770 cm^{-1}) and the $C=N$ group (1660 cm^{-1}). The frequencies of the valence vibrations at 1480-1550, 1270-1390, and 1065-1180 cm^{-1} apparently characterize the vibrations of the imidazo[1,2-b]benzothiazole, thiazolo[2,3-a]benzimidazole, and benzene rings [10].

The O-acylation product (VIII) was obtained by the condensation of I with N-phenyl-p-nitrobenzamideoxime in absolute benzene in the presence of triethylamine. Its structure was confirmed by its IR spectrum, which contains the frequencies of the valence vibrations of $N-H$ bonds (3315 cm^{-1}), $C=O$ bonds (1770 and 1715 cm^{-1}), and $C=N$ bonds (1635-1660 cm^{-1}).

In analogy with [12], a quantitative yield of X was isolated by refluxing I with diphenylthiourea in absolute benzene in the presence of pyridine; the structure was confirmed by the method used for its synthesis [10] and by the presence in the IR spectrum of characteristic frequencies of the $C=O$ group (1775 cm^{-1}) and the $C=N$ group (1660-1670 cm^{-1}).

EXPERIMENTAL

Phenyliminooxalyl Chloride (I). Phosphorus pentachloride [20.8 g (0.1 mole)] was added in small portions in the course of 15 min to a ground suspension of 8.25 g (0.05 mole) of oxanilic acid in 25 ml of dry benzene at room temperature. The mixture was heated at 80° until HCl evolution ceased completely (about 1 h). The phosphorus oxychloride and solvent were removed by distillation, and the residue was vacuum distilled to give a yellow, mobile liquid with lacrimatory properties. It slowly decomposed on distillation with phosgene evolution and the formation of phenylisonitrile. The product [3.9 g (48%)] had bp 114° (12-14 mm), n_D^{20} 1.5840 and d_4^{20} 1.3607. Found %: Cl 35.1, 35.1; MR_D 51.70. $C_8H_5Cl_2NO$. Calculated %: Cl 35.1; MR_D 51.83.

Phenyliminooxalic Acid Diphenylamide (II). A mixture of 0.5 g (0.002 mole) of I and 0.93 g (0.01 mole) of aniline was allowed to stand for 1 h. The resulting precipitate was filtered and washed with water to give 0.56 g (72%) of a product with mp 141-142° (from alcohol). Found %: N 13.6, 13.5. $C_{20}H_{17}N_3O$. Calculated %: N 13.5.

Bis(3-phenylthioureide) of Phenyliminooxalic Acid (IIIb). A solution of 1.0 g (0.05 mole) of I in 10 ml of absolute acetone was added dropwise in the course of 15 min to a solution of 0.76 g (0.1 mole) of ammonium thiocyanate in 25 ml of absolute acetone. The mixture was stirred at 30-40° for 2 h, filtered, 0.93 g (0.1 mole) of aniline was added, and the mixture was stirred at 40° for 2 h. The solvent was evaporated, and the residue was washed with dilute hydrochloric acid and water and dried to give 0.9 g (42%) of a product with mp 172-175° (from alcohol). Found %: S 15.3. $C_{22}H_{19}N_5OS_2$. Calculated %: S 14.8.

Bis[3-(p-chlorophenyl)thioureide] of Phenyliminooxalic Acid (IIIc). This was similarly obtained in 51% yield and had mp 205-206° (from alcohol). Found %: S 12.1. $C_{22}H_{17}Cl_2N_5OS_2$. Calculated %: S 12.7.

Azide of 1-Phenyltetrazole-5-carboxylic Acid (IV). A cooled solution of 1 g (0.005 mole) of I in 10 ml of absolute acetone was added dropwise at 0° to a suspension of 3.3 g (0.05 mole) of sodium azide in 10 ml of absolute acetone. The mixture was stirred in the cold for 3 h and at room temperature for 12 h, water was added to dissolve the precipitate, and the resulting azide was extracted with ether. The solvent was removed in vacuo, and the residue was dried over P_2O_5 to give 0.6 g (60%) of a product with mp 91-91.5° (decomp.). Found %: N 45.1, 45.1. $C_8H_5N_7O$. Calculated %: N 45.6.

1-Phenyl-5-(triphenylphosphazoacyl)tetrazole (V). A cooled solution of 0.52 g (0.002 mole) of triphenylphosphine in 5 ml of ether was added dropwise to a cooled (to 0°) solution of 2.1 g (0.001 mole) of IV in 10 ml of dry ether. The mixture was stirred at 0° for 3 h and at 20° for 96 h. The ether was removed, and the residue was crystallized from alcohol to give 0.35 g (79%) of a product with mp 168-170° (from absolute alcohol). Found %: N 15.5; P 7.0. $C_{26}H_{20}N_5OP$. Calculated %: N 15.6; P 6.9.

2-Phenylimino-3-oxoimidazo[1,2-a]pyridine (VI). A solution of 1 g (0.005 mole) of I in 5 ml of absolute benzene was added dropwise with stirring in the course of 30 min to a solution of 0.47 g (0.005 mole) of 2-aminopyridine and 1.01 g (0.01 mole) of triethylamine in 10 ml of absolute benzene. The mixture was refluxed for 3 h, cooled, and filtered. The solvent was removed, and the residue was treated with dilute (about 1%) hydrochloric acid and water and dried to give 0.72 g (69%) of rose-colored crystals with mp 142-145° (three reprecipitations from benzene with petroleum ether). Found %: C 69.9; H 4.0; N 19.0, 19.1; mol. wt. 223. $C_{13}H_9N_3O$. Calculated %: C 69.9; H 4.0; N 18.9; mol. wt. 238.

3-Phenylimino-2-oxoimidazo[2,1-b]benzothiazole (VIIa). A solution of 0.5 g (0.0025 mole) of I in 5 ml of chloroform was slowly added dropwise to a solution of 0.38 g (0.0025 mole) of 2-aminobenzothiazole and 0.65 g (0.006 mole) of triethylamine in 10 ml of absolute chloroform. The mixture was refluxed for 2 h, and the solvent was removed. The residue was washed with dilute hydrochloric acid and water and dried to give 0.3 g (56%) of a product with mp 150-152° (from aqueous ethanol). Found %: N 14.6, mol. wt. 299, 277. $C_{15}H_9N_3OS$. Calculated %: N 15.0; mol. wt. 279.

3-Phenylimino-2-oxo-1H-imidazo[1,2-a]benzimidazole (VIIb). A solution of 1 g (0.005 mole) of I in 10 ml of benzene was added dropwise to a suspension of 0.67 g (0.005 mole) of 2-aminobenzimidazole and 1.25 g (0.012 mole) of triethylamine in a mixture of 10 ml of absolute benzene and dioxane (1 : 1). The mixture was refluxed for 3 h, the solvent was removed, and the residue was filtered, washed with water, and dried to give 0.9 g (69%) of a product with mp 218-219° (from alcohol). Found %: N 21.8. $C_{15}H_{10}N_4O$. Calcultated %: N 21.4.

O-[Phenyloxamoyl]-N-phenyl-p-nitrobenzamidoxime (VIII). A solution of 0.5 g (0.002 mole) of I in 5 ml of absolute benzene was added dropwise to a suspension of 0.64 g (0.002 mole) of N-phenyl-p-nitrobenzamidoxime and 0.5 g (0.004 mole) of triethylamine in 10 ml of absolute benzene. The mixture was refluxed for 2 h, the solvent was evaporated, and the residue was treated with water and dried to give 0.66 g (68%) of pale-yellow crystals with mp 152-154° (from alcohol). Found %: C 61.4, 61.6; H 4.0, 4.0; N 13.9, 14.0. $C_{21}H_{16}N_4O_5$. Calculated %: C 62.3; H 4.0; N 13.9.

2-Phenylimino-3-oxothiazolo[3,2-a]benzimidazole (IX). A solution of 0.5 g of I in 5 ml of benzene was carefully added dropwise with stirring to a solution of 0.38 g (0.002 mole) of 2-mercaptobenzimidazole and 0.62 g (0.06 mole) of triethylamine in 10 ml of absolute benzene. The mixture was heated on a water bath for 3 h, cooled, and filtered. The solvent was removed, and the residue was washed with dilute hydrochloric acid and water and dried to give 0.5 g (71%) of a product with mp 163-165° (from 65% alcohol). Found %: C 64.0; H 3.2; N 14.9. $C_{15}H_9N_3OS$. Calculated %: C 64.5; H 3.2; N 15.0.

A mixture of 0.8 g (0.0028 mole) of IX in 30 ml of alcohol and 30 ml of 35% hydrochloric acid was heated on a boiling-water bath for 10-12 h. The mixture was evaporated to dryness, and the residue was treated with water and filtered. The filtrate was cooled to 0° and diazotized at 0-5° with a solution of sodium nitrite. The resulting diazo solution was combined with an alkaline solution of β-naphthol, and the resulting azo dye was recrystallized from methanol to give red plates with a metallic luster with mp 131-132° [14]; this dye was identical to the dye obtained from diazotized aniline and β-naphthol. The secondary hydrolysis product, viz., 2,3-dioxothiazole[3,2-a]benzimidazole, could not be isolated in pure form.

3-Phenyl-2,5-di(phenylimino)thiazolidin-4-one (X). Dry pyridine [1 g (0.012 mole)] was added dropwise to a suspension of 1 g (0.005 mole) of I and 1.14 g (0.005 mole) of symmetrical diphenylthiourea in 15 ml of absolute benzene. The temperature of the reaction mixture went up 6°, and a precipitate formed. The mixture was heated on a water bath for 30 h, evaporated to dryness, and the residue was washed with water and dried to 1 g (98%) of X with mp 205-207° (from benzene). Found %: S 9.0; N 11.2; mol. wt. 338. $C_{21}H_{15}N_3OS$. Calculated %: S 9.0; N 11.7; mol. wt. 357.

2,4,6-Trioxo-1,3,5-tris(1-phenyl-5-tetrazolyl)hexahydro-s-triazine (XI). Compound IV [0.5 g (0.0025 mole)] was heated in 10 ml of absolute toluene until nitrogen evolution ceased and was then cooled to give 0.38 g (86%) of a product with mp 210-212° (from benzene). Found %: N 37.7, 37.5; mol. wt. 580. $C_{27}H_{15}N_{15}O_6$. Calculated %: N 37.4; mol. wt. 561.

5-(3-Phenylureido)-1-phenyltetrazole (XII). A mixture of 0.5 g (0.0025 mole) of IV and 0.22 g (0.002 mole) of aniline in 10 ml of absolute toluene was heated until nitrogen evolution ceased and was then cooled. The resulting precipitate was filtered and washed with dilute hydrochloric acid and water and dried to give 0.6 g (85%) of a product with mp 194-196° (from alcohol). Found %: N 29.8, 29.7. $C_{14}H_{12}N_6O$. Calculated %: N 30.0.

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