THE REACTION OF CARBOXAMIDINES WITH OXALYL CHLORIDE

III*. IMIDAZOLINE-4,5-DIONES

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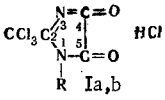
The action of oxalyl chloride on amidines has given imidazoline-4,5-dione hydrochlorides. The reactions of the imidazoline-4,5-diones and their hydrochlorides with water, alcohols, and amines have been studied. In these reactions the imidazoline ring readily opens with the formation of derivatives of oxaminic acid.

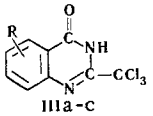
We have found previously that the reaction of amidines with oxalyl chloride gives imidazoline-4,5-dione hydrochlorides [1]. Continuing these investigations, we have obtained new imidazoline-4,5-dione hydrochlorides.



Ia R = 2,4-$(CH_3)_2C_6H_3$;
Ib R = o-$CH_3OC_6H_4$

The action of I of triethylamine in an inert solvent forms the free imidazoline-4,5-diones (II), which are reconverted into I under the action of dry hydrogen chloride.

Like compounds I (see [1]), the bases II containing an aryl radical in position 1, decompose on being heated to ~200°C, giving quinazolin-4-ones.



IIIa R = 5- or 7-CH_3;
IIIb R = 6,8-$(CH_3)_2$;
IIIc R = 8-OCH_3

IIIa-c

The imidazoline-4,5-diones and their hydrochlorides react react readily with water, alcohols, and amines. Some of them are hydrolyzed even by moist air, which shows the strong electrophilic nature of these compounds. It has been shown in many cases that, regardless of the nature of the substituents in positions 1 and 2 of the imidazoline ring, the action of a molecule of water is directed to the electrophilic center C(2). This gives quantitative yields of N-acyl-N'-alkyl(aryl)oxamides (Table 1).

IV

*For Communication II, see [1].

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TABLE 1. Oxamide Derivatives

Compound	R	R′	mp., °C	External form (solvent for crystallization)	Empirical formula	Found, % C	Found, % H	Calculated, % C	Calculated, % H	Yield, %
IVa	CCl3	H	171 (decomp.)	Prisms*	$C_4H_3Cl_3N_2O_3$	20,9	1,5	20,6	1,3	51
IVb	CCl3	CH3	182—183	Prisms (acetone)	$C_5H_5Cl_3N_2O_3$	24,3	2,0	24,3	2,0	78
IVc	CCl3	p-C4H9	159—161	Prisms (methanol + water)	$C_8H_{11}Cl_3N_2O_3$	33,1	3,4	33,2	3,8	87
IVd	CCl3	C6H5(CH2)2	168—170	Needles*	$C_{12}H_{11}Cl_3N_2O_3$	42,6	3,3	42,7	3,3	81
IVe	CCl3	C6H5	170—171	Prisms*	$C_{10}H_7Cl_3N_2O_3$	38,6	2,4	38,8	2,3	78
IVf	C6H5	C6H5	226—228†	Needles (benzene)	$C_{15}H_{12}N_2O_3$	67,0	4,5	67,2	4,5	84
IVg	C6H5	α-C10H7	169—171	Needles (methanol + water)	$C_{19}H_{14}N_2O_3$	71,8	4,6	71,7	4,4	88

*The substance was purified by washing with ether.
†According to the literature [2], mp 230°C (decomp.)

TABLE 2. Methyl N-Oxamoylimidates

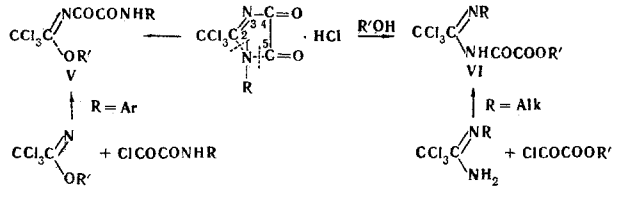
Compound	R	Decomp., °C	External form (solvent for crystallization	Empirical formula	Found, % C	Found, % H	Calculated, % C	Calculated, % H	Yield, %
Va	C6H5	227	Needles (methanol + water)	$C_{11}H_9Cl_3N_2O_3$	40,6	2,8	40,8	2,8	87
Vb	o-CH3OC6H4	229	Prisms (methanol)	$C_{12}H_{11}Cl_3N_2O_4$	40,9	3,2	40,8	3,1	85
Vc	p-CH3OC6H4	247	Prisms (acetone + water)	$C_{12}H_{11}Cl_3N_2O_4$	40,5	3,1	40,8	3,1	96
Vd	p-ClC6H4	270	Prisms (methanol + water)	$C_{11}H_8Cl_4N_2O_3$	36,8	2,3	36,9	2,2	94
Ve	2,4-(CH3)2C6H3	238	Prisms (methanol)	$C_{13}H_{13}Cl_3N_2O_3$	44,1	3,5	44,4	3,7	78

N-Aryl-N′-trichloroacetyloxamides can be isolated only by the careful hydrolysis of I. With an excess of water, hydrolysis goes further to trichloroacetic acid and the corresponding N-aryloxamides. N-Trichloroacetyloxamides and N-alkoxy-N′-trichloroacetyloxamides hydrolyze only when they are boiled with water.

$$CCl_3CONHCOCONHR \xrightarrow{H_2O} CCl_3COOH + RNHCOCONH_2 \qquad R = H, Alk, Ar$$

Oxamide and the N-alkyl(aryl)oxamides were identified by their melting points in mixtures with authentic known oxamides.

The alcoholysis of I takes place in more complex fashion than hydrolysis. Depending on the nature of the substituent in the position 1 of the imidazoline ring, either the C(2) or the C(5) undergoes nucleophilic attack. In the first case, the products are alkyl N-oxamoylimidates V (Table 2), and in the second case alkyl N-imidoyloxamates VI (Table 3). The same compounds were obtained from alkoxalyl chlorides and amidines and from oxamoyl chlorides and imidic esters.



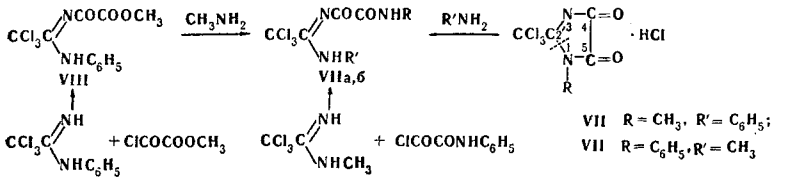
With an excess of methanol, 2-phenylimidazoline-4,5-dione hydrochloride gives benzamidine hydrochloride and dimethyl oxalate. Methyl N-benzimidoyloxamate is probably formed first, and this then undergoes cleavage.

TABLE 3. Alkyl N-Imidoyloxamates

Compound	R	R′	mp., °C	External form (solvent for crystallization)	Empirical formula	Found, % C	Found, % H	Calculated, % C	Calculated, % H	Yield, %
VIa	CH_3	CH_3	186—188*	Prisms (benzene)	—	—	—	—	—	56
VIb	n-C_4H_9	CH_3	127—129	Prisms (methanol + water)	$C_9H_{13}Cl_3N_2O_3$	35,3	4,3	35,6	4,3	73
VIc	$C_6H_5CH_2$	CH_3	129—131*	Prisms (benzene)	—	—	—	—	—	70
VId	$C_6H_5CH_2$	i-C_3H_7	180—181*	Prisms (acetone + water)	—	—	—	—	—	50
VIe	$C_6H_5(CH_2)_2$	CH_3	140—142	Prisms (methanol + water)	$C_{13}H_{13}Cl_3N_2O_3$	44,4	3,9	44,4	3,7	92

*See [3].

The aminolysis of compounds I takes place in a similar manner to their hydrolysis. Regardless of the nature of the substituent R, the action of a molecule of amine is directed only to the electrophilic center C(2). The carbon–nitrogen (2–1) bond is cleaved with the formation of N,N′-disubstituted amidines, the structure of which has been shown by independent syntheses.



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EXPERIMENTAL

Imidazoline-4,5-dione Hydrochlorides (I). With ice-water cooling and stirring, 0.055 mole of oxalyl chloride in 30 ml of carbon tetrachloride was added to a solution or suspension of 0.05 mole of an amidine in 50 ml of anhydrous carbon tetrachloride. With vigorous stirring, the mixture was heated to 50-60°C until the evolution of hydrogen chloride ceased. After cooling, the precipitate of I was separated off in a dry atmosphere, and it was washed with anhydrous carbon tetrachloride and with ether (2 × 15 ml) and dried in vacuum.

1-(2′,4′-Dimethylphenyl)-2-trichloromethylimidazoline-4,5-dione (Ia). Yield 88%, decomp. 201°C. Found, %: Cl 40.3. $C_{12}H_{10}Cl_4N_2O_2$. Calculated, %: Cl 39.8.

1-(o-Methoxyphenyl)-2-trichloromethylimidazoline-4,5-dione (Ib). Yield 91%, decomp. 177°C. Found, %: Cl 40.0. $C_{11}H_8Cl_4N_2O_3$. Calculated, %: Cl 39.6.

1-(2′,4′-Dimethylphenyl)-2-trichloromethylimidazoline-4,5-dione (II). With stirring and ice-water cooling, 1.01 g (0.01 mole) of triethylamine in 15 ml of ether was added to a suspension of 3.56 g (0.01 mole) of Ia in 40 ml of anhydrous ether. After 2 h, the precipitate of triethylamine hydrochloride was separated off, the filtrate being protected from the access of atmospheric moisture. After the evaporation of the filtrate to 1/3 of its initial volume, a precipitate deposited in the form of yellow prisms, 2.24 g (70%), decomp. 155°C. Found, %: C 45.4; H 2.7. $C_{12}H_9Cl_3N_2O_2$. Calculated, %: C 45.1; H 2.8.

Ia from the "Dione" II. Dry hydrogen chloride was passed through a solution of 1.6 g (0.005 mole) of II in 50 ml of anhydrous benzene. The yellow color gradually disappeared, and after a day the colorless

solution deposited 1.46 g (82%) of Ia with decomp. 201°C. The product gave no depression of the melting point in admixture with an authentic sample of Ia.

Quinazolin-4-ones (III). A compound I or II (0.01 mole) was heated at 200°C (bath temperature) until the evolution of gases ceased. After the end of the reaction, the fused mass solidified. The crystalline residue of III was treated with ether, separated off, and recrystallized.

5- or 7-Methyl-2-trichloromethylquinazolin-4-one (IIIa). Yield 78%, mp 224-226°C (prisms from methanol). Found, %: C 43.7; H 2.4. $C_{10}H_7Cl_3N_2O$. Calculated, %: C 43.3; H 2.5.

6,8-Dimethyl-2-trichloromethylquinazolin-4-one (IIIb). Yield 69%, mp 235-236°C (prisms from acetone). Found, %: C 45.3; H 3.1. $C_{11}H_9Cl_3N_2O$. Calculated, %: C 45.3; H 3.1.

8-Methoxy-2-trichloromethylquinazolin-4-one (IIIc). Yield 47%, mp 251-252°C (prisms from ethanol). Found, %: C 41.0; H 2.2. $C_{10}H_7Cl_3N_2O_2$. Calculated, %: C 40.9; H 2.4.

N'-Substituted N-Acyloxamides (IV). A solution of 0.01 mole of a compound I or II in 30 ml of acetone was treated with 0.01 mole of water. After some time, a crystalline precipitate of IV deposited. In some cases, it was necessary partially to evaporate the solvent.

Hydrolysis of the 1-Aryl-2-trichloromethylimidazoline-4,5-diones and Their Hydrochlorides. A solution of 0.05 mole of a compound I or II in 50 ml of acetone was treated with 2 ml of water. After 1 h, a crystalline precipitate of a N-aryloxamide deposited from the solution, and this was separated off, washed with acetone, and dried. Yield 90-95%. The filtrate was evaporated. The residue contained trichloroacetic acid, which was dried over phosphorus pentoxide and converted into trichloroacetamide. The N-aryloxamides obtained and the trichloroacetamide were identified by determining their melting points in mixtures with authentic samples of the relevant compounds.

Hydrolysis of N-Trichloroacetyloxamide and its N'-Alkyl Derivatives (IVa, b). A suspension of 0.01 mole of IVa or b in 50 ml of water was boiled for 2-5 h. After cooling, the solution deposited a crystalline precipitate of oxamide or a N-alkyloxamide, which was washed with acetone and dried. Yield 60-65%. Mixtures with authentic samples of the corresponding oxamides gave no depression of the melting points.

Alcoholysis of 2-Alkyl(aryl)imidazoline-4,5-dione and Its 1-Alkyl and 1-Aryl Derivatives and Their Hydrochlorides. A solution of 0.01 mole of a compound I or II in 20 ml of an absolute alcohol was left to stand for 2-3 h. The excess of alcohol was evaporated off in vacuum, and the crystalline residue consisted of the product V or VI.

Alcoholysis of 2-Phenylimidazoline-4,5-dione Hydrochloride. A solution of 2.10 g (0.01 mole) of 2-phenylimidazoline-4,5-dione hydrochloride in 15 ml of absolute methanol was left at 20°C for 12 h. Then the methanol was evaporated in vacuum, and the residue was treated with 30 ml of anhydrous ether. The ethereal solution deposited a crystalline precipitate of benzamidine hydrochloride, which was separated off, washed with anhydrous ether, and dried. Yield 1.14 g (73%), mp 167-169°C. The substance gave no depression of the melting point in admixture with an authentic samples of benzamidine hydrochloride. The filtrate after the separation of the benzamidine hydrochloride was evaporated in vacuum, giving 0.75 g (61%) of dimethyl oxalate with mp 54°C. The substance gave no depression of the melting point in admixture with an authentic sample of dimethyl oxalate.

Methyl N-(Oxaniloyl)trichloroacetimidate (Va, independent synthesis). A solution of 1.76 g (0.01 mole) of methyl trichloroacetimidate in 10 ml of dioxane was added to a solution of 1.84 g (0.01 mole) of oxanilic acid hydrochloride in 20 ml of anhydrous dioxane. The solution was heated at 50-60°C for 2 h. The solvent was evaporated off in vacuum, and the residual viscous liquid was treated with 15 ml of ether. The white precipitate formed was separated off and washed with ether to give 1.26 g (39%) of Va in the form of needles, mp 226-227°C (from methanol + water). The substance gave no depression of the melting point in admixture with the Va obtained by the action of methanol on 1-phenyl-2-chloromethylimidazoline-4,5-dione.

Methyl N-Methyltrichloroacetimidoyloxamate (VIa, independent synthesis). A solution of 3.51 g (0.02 mole) of N-methyltrichloroacetamidine in 20 ml of benzene was added to a solution of 1.23 g (0.01 mole) of methoxalyl chloride in 15 ml of anhydrous benzene. The mixture was stirred at 20°C for 1-2 h. Then the precipitate of amidine hydrochloride was separated off and the filtrate was evaporated in vacuum. The residual viscous liquid was treated with 10 ml of ether. The ethereal solution deposited a precipitate which

was separated off and washed with ether to give 1.15 g (44%) of VIa in the form of colorless prisms, mp 186-188°C (from benzene). The substance gave no depression of the melting point in admixture with the VIa obtained by the action of methanol on 1-methyl-2-trichloromethylimidazoline-4,5-dione.

N,N'-Disubstituted Trichloroacetamidines (VII). With stirring and ice-water cooling, 0.1 mole of amine in 15 ml of benzene was added to a solution or suspension of 0.05 mole of a compound I in 20 ml of anhydrous benzene. The mixture was stirred at 20°C for 1-2 h. The solvent was evaporated off in vacuum, and the solid residue was dried and treated with water. The water-insoluble compounds VII were separated off, dried, and recrystallized.

N-(N"-Methyloxamoyl)-N'-phenyltrichloroacetamidine (VIIa). Colorless prisms (from ethanol), decomp. 243°C. Yield 65%. Found, %: C 41.0; H 3.2. $C_{11}H_{10}Cl_3N_3O_2$. Calculated, %: C 40.9; H 3.1.

N-Methyl-N'-oxaniloyltrichloroacetamidine (VIIb). Colorless prisms (from methanol), decomp. 173°C. Yield 73%. Found, %: C 40.6; H 3.2. $C_{11}H_{10}Cl_3N_3O_2$. Calculated, %: C 40.9; H 3.1.

Compound VIIa (independent synthesis). a) With stirring, a solution of 4.75 g (0.02 mole) of N-phenyltrichloroacetamidine in 25 ml of benzene was added to a solution of 1.23 g (0.01 mole) of methoxalyl chloride in 20 ml of anhydrous benzene. The mixture was stirred at 20°C for 1-2 h, and the precipitate of the amidine hydrochloride was separated off. The mother solution was evaporated in vacuum to 1/4 of its original volume and was treated with 3-5 ml of petroleum ether. The precipitate that deposited was separated off to give 1.68 g (52%) of N-methoxalyl-N-phenyltrichloroacetamidine (VIII) in the form of colorless needles, mp 96-98°C (from petroleum ether). Found, %: C 41.0; H 2.8; CH_3O 9.7. $C_{11}H_9Cl_3N_2O_3$. Calculated, %: C 40.8; H 2.8; CH_3O 9.6.

b) A solution of 0.09 g (0.003 mole) of methylamine in 1 ml of methanol was added to a solution of 0.97 g (0.003 mole) of VIII in 20 ml of methanol. The solution was left at 20°C for 10-12 h, and then the solvent was evaporated off in vacuum. The residual viscous oil was treated with 3 ml of ether. The precipitate that deposited was separated off, giving 0.52 g (54%) of VIIa in the form of colorless prisms, decomp. 243°C (from methanol). The substance gave no depression of the melting point in admixture with the VIIa obtained by the action of aniline on 1-methyl-2-chloromethylimidazoline-4,5-dione.

VIIb (independent synthesis). With stirring and ice-water cooling, 1.75 g (0.01 mole) of N-methyltrichloroacetamidine in 20 ml of benzene was added to a solution of 0.92 g (0.005 mole) of oxanilic acid hydrochloride in 20 ml of anhydrous benzene. The mixture was evaporated in vacuum and the residue was treated with 15 ml of petroleum ether. The precipitate that deposited was separated off to give 0.95 g (59%) of VIIb in the form of colorless prisms, decomp. 173°C (from methanol). The substance gave no depression of the melting point in admixture with the VIIb obtained by the action of methylamine on 1-phenyl-2-trichloromethylimidazoline-4,5-dione.

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