RECYCLIZATION OF 4,5-DIPHENYLOXAZOLIN-2-ONE AND -2-THIONE UNDER THE INFLUENCE OF AMINES

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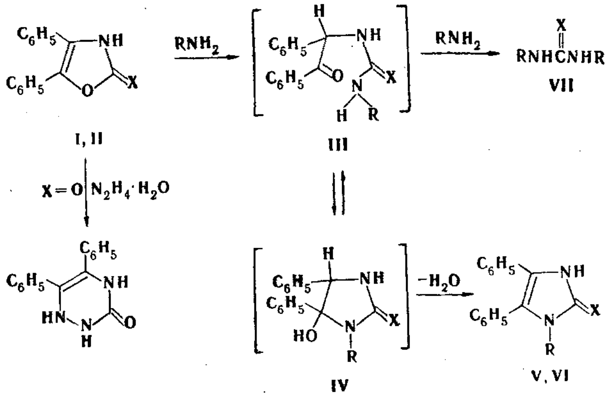
4,5-Diphenyl-4-oxazolin-2-one and -2-thione undergo recyclization to 1-substituted 4,5-diphenyl-4-imidazolin-2-ones and -2-thiones, respectively, under the influence of primary amines. The action of hydrazine hydrate on the oxazolone leads to 5,6-diphenyl-1,2,3,4-tetrahydro-1,2,4-triazin-3-one. The corresponding ureas were isolated from the reaction mixtures in a number of cases.

The nucleophilic reactions of 4-oxazolin-2-ones and -2-thiones (primarily the N-unsubstituted compounds) have been investigated relatively recently. In 1966 it was shown that 3,4-disubstituted oxazolin-2-ones react with primary amines to give 5-hydroxyimidazolidin-2-ones [1], whereas the heteroring is opened under the influence of secondary amines to give β-acylamino enamines [2]. The reactions of 3,4-disubstituted oxazoline-2-thiones with amines also proceed similarly [3]. 5-Phenyloxazolin-2-ones are converted to triazinones under the influence of hydrazine hydrate [4], whereas they are converted to α-anilido ketones under the influence of potassium hydroxide [5].

Since the effect of the substituents attached to the nitrogen atom of the heteroring on the aminolysis of benzoxazolin-2-ones is very substantial [6], a study of the reactions of nitrogen-unsubstituted oxazolin-2-ones and -2-thiones with nucleophilic agents, particularly with amines, is of definite interest. As model compounds we selected 4,5-diphenyl-4-oxazolin-2-one (I) and -2-thione (II), which are isomers of the previously investigated 3,4-diphenyl derivatives. Primary and secondary amines and hydrazine hydrate were used as the reagents.

We found that I and II undergo reaction with primary amines under more severe conditions than the 3,4-diphenyl derivatives to give the corresponding 4,5-diphenyl-4-imidazolin-2-ones (V) and -2-thiones (VI). The structure of Vc was confirmed by alternative synthesis from methylurea and benzoin by the method in [7], while the structure of thione VId was confirmed by the thionation of Vd with phosphorus pentasulfide in xylene (Table 1). The corresponding N,N'-disubstituted ureas (VII), which are evidently formed as a result of transamination of intermediate β-oxourea III, were also isolated from the reaction mixtures in small amounts in the case of benzyl- and cyclohexylamine.



I, V, VII X=O; II, VI X=S; VII $R=C_6H_5CH_2$, C_6H_{11}

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TABLE 1. 4-Imidazolin-2-ones (Va-e) and 4-Imidazoline-2-thiones (VIa-e)

Compound	R	mp, °C	IR spectrum, cm^{-1}		Found, %			Empirical formula	Calc., %			Yield, %
			CO(CS)	NH	C	H	N		C	H	N	
Va	$C_6H_5CH_2$	219—220	1685, 1640*, 1690^6	3470*, 3140, 3050†	81,2	4,9	8,9	$C_{22}H_{18}N_2O$	71,0	5,1	9,0	72
Vb	C_6H_{11}	297—298	1680†	3140†	79,4	7,1	9,0	$C_{21}H_{22}N_2O$	79,2	7,0	8,8	50
Vc	CH_3	271—272 (274—275 [7])	1685†	3140†	76,9	6,0	11,2	$C_{16}H_{11}N_2O_2$	76,8	5,6	11,2	57
Vd	n-C_4H_9	218—219	1685, 1640^a, 1685†	3470*, 3140, 3060†	77,9	7,1	9,5	$C_{19}H_{20}N_2O$	78,1	6,8	9,6	76
Ve	CH_2CH_2O	212—212,5	1690, 1645†	3140†	72,8	5,8	10,0	$C_{17}H_{16}N_2O_2$	72,8	5,8	10,0	62
VIa	$C_2H_5CH_2$	275—276	1180, 1190†	3120, 2750, 2600†			8,0	$C_{22}H_{18}N_2S$			8,2	62
VIb	C_6H_{11}	316—317	1145†	3100, 2745†			8,4	$C_{21}H_{22}N_2S$			8,4	23
VIc	n-C_3H_7	294,5—296	1195*	3480*			9,6	$C_{18}H_{18}N_2S$			9,5	63
VId	n-C_4H_9	237—238 (220 [8])	1170, p. 1190†	3090, 2950*			9,2	$C_{19}H_{20}N_2S$			9,1	59
VIe	n-$CH_3OC_6H_4$	299—300 (297 [9])	1175, 1190†	3080, 2745†			7,8	$C_{22}H_{18}N_2OS$			7,8	38

*In Chloroform. †In mineral oil.

TABLE 2. Effect of Solvents on the Yield of Imidazolone Vd

Solvent	Yield, %
DMF	49
Hexametapol	41
Pyridine	41
n-Butylamine	38
Diethylene glycol	23
Water	20

The weakly basic aniline does not undergo reaction under the conditions described. No reaction is also observed with diethylamine. The reaction of I with piperidine leads unexpectedly to the formation of 4,5-diphenyl-4-imidazolin-2-one (VIII) at 150°C. Oxazolone I does not react with piperidine under milder conditions.

The reaction of oxazolone I with hydrazine hydrate leads to the formation of 5,6-diphenyl-1,2,3,4-tetrahydro-1,2,4-triazin-3-one.

In our study of the effect of solvents on the yield of imidazolone Vd we demonstrated that polar aprotic solvents such as dimethylformamide (DMF) and hexametapol are the optimum solvents; good results are also observed when basic solvents (excess amounts of the amine and pyridine) are used, whereas the yields are lower in solvents with acidic character (diethylene glycol and water) (Table 2).

The experimental data that we obtained show that the oxazolone ring in 4,5-diphenyloxazolin-2-ones and -2-thiones is considerably more stable with respect to nucleophilic reagents than in the case of the 3,4-disubstituted isomer; this may be due to prior deprotonation of the nitrogen atom in these compounds.

EXPERIMENTAL

1-Substituted 4,5-Diphenyl-4-imidazolin-2-ones (Va-e). A mixture of 0.05 mole of I and 0.3 mole of the amine was heated in a sealed ampul at 140°C for 30 h, after which it was cooled, and the resulting crystals were removed by filtration and recrystallized from ethanol. The corresponding 1,3-disubstituted ureas were isolated from the filtrates in 11 and 6% yields, respectively, in experiments with benzylamine and cyclohexylamine.

Synthesis of Imidazolone Vd in Various Solvents. A mixture of 0.05 mole of I, 0.1 mole of n-butylamine, and 2 ml of the solvent was heated in a sealed ampul at 140°C for 20 h, after which the solvent was removed by vacuum distillation, and the residue was recrystallized from ethanol (Table 2).

1-Substituted 4,5-diphenyl-4-imidazoline-2-thiones (VIa-e). A mixture of 0.05 mole of oxazolethione II and 0.3 mole of the amine was heated in a sealed ampul at 160°C for 40 h, after which the excess amine was removed by vacuum distillation, and the residue was recrystallized from ethanol (Table 1).

1-n-Butyl-4,5-diphenyl-4-imidazoline-2-thione (VId) (from Vd). A mixture of 1.4 g (0.005 mole) of imidazolone Vd, 2.3 g (0.015 mole) of phosphorus pentasulfide, and 20 ml of xylene was refluxed for 5 h, after which it was washed to neutrality with water, and the solution was worked up to give 1.17 g (76%) of thione VId.

4,5-Diphenyl-4-imidazolin-2-one. A mixture of 2.4 g (0.01 mole) of I and 5.1 g (0.06 mole) of piperidine was heated in a sealed ampul at 150°C for 30 h, after which the excess piperidine was removed by vacuum distillation, and the residue was recrystallized from ethanol to give 1.1 g (42%) of a product with mp 317°C. Repeated recrystallization from ethanol gave a product with mp 321-321.5°C. IR spectrum (mineral oil): 1685 (CO); 3040, 3145 cm^{-1} (NH). According to the data in [10], this compound had mp 324-325°C.

5,6-Diphenyl-1,2,3,4-tetrahydro-1,2,4-triazin-3-one. A mixture of 1.2 g (0.05 mole) of oxazolone I and 1.2 g (0.025 mole) of hydrazine hydrate was heated in a sealed ampul at 140°C for 30 h, after which the product was recrystallized from ethanol—acetone to give 0.35 g (24%) of a product with mp 263-264°C. IR spectrum (mineral oil): 1700 (CO); 3100, 3220 cm^{-1} (NH). Found: C 72.1; H 5.7; N 16.6%. $C_{15}H_{13}N_3O$. Calculated: C 71.7; H 5.2; N 16.7%.

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