REACTIONS OF ACYL ISOCYANATES WITH 8-HYDROXY-QUINOLINE AND 2-AMINO DERIVATIVES OF PYRIDINE, THIAZOLE, 4-THIAZOLINONE, AND BENZOTRIAZOLE*

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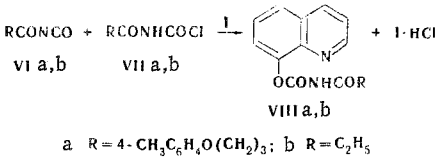
The reaction of acyl isocyanates with 8-hydroxyquinoline and 2-amino derivatives of pyridine, thiazole, 4-thiazolinone, and benzotriazole gave, respectively, 8-quinolyl-N-acylcarbamates, 2-acylcarbamoyl derivatives of pyridine, thiazole, and 4-thiazolinone, and 1-acylcarbamoylbenzotriazoles. It was demonstrated by means of the IR, UV, and PMR spectra that the products of the addition of acyl isocyanates to 2-aminothiazole and 2-aminothiazolinone are tautomeric mixtures of the amine and imine forms.

We have previously established that, in contrast to aryl isocyanates, acyl isocyanates are capable of forming two types of compounds on reaction with the tautomeric N–C = N system of benzamidine [2].

A similar ambiguous reaction also might have been expected in the reaction of acyl isocyanates with tautomeric systems of compounds of the heterocyclic series, and the products obtained in this case might have been of interest, particularly as pesticides.

The aim of the present research was an investigation of the reactions of acyl isocyanates with tautomeric systems – 8-hydroxyquinoline (I) [3] and 2-amino derivatives of pyridine (II) [4], thiazole (III) [5], 4-thiazolinone (IV) [6], and benzotriazole (V) [7]. Acyl isocyanates might have added to the oxygen or nitrogen atom of I, to the exocyclic or endocyclic nitrogen atom of II-IV, and to the 1 or 2 position of V.

The conditions for the synthesis of acyl isocyanates without the possible admixture [8] of acylcarbamoyl chlorides were simultaneously refined.



a R = 4-$CH_3C_6H_4O(CH_2)_3$; b R = C_2H_5

We found that, in the reaction of carboxylic acid amides with oxalyl chloride for more than 2 h, not only does the yield of acyl isocyanates fall, but the resulting acyl isocyanates in a number of cases contain a difficult-to-separate admixture of acylcarbamoyl chlorides. Thus when oxalyl chloride is heated with γ-(4-methylphenoxy)butyramide for 3 h or with propionamide for 50 min with subsequent standing at 20° for 48 h and thermal decomposition of the intermediate reaction products, mixtures that are difficult to separate by distillation are formed. In the first case, one obtains mixture A containing 90% γ-(4-methylphenoxy)butyryl isocyanate (VIa) and 10% γ-(4-methylphenoxy)butyrylcarbamoyl chloride (VIIa), while in the second case, one obtains mixture B containing 26% propionyl isocyanate (VIb) and 74% propionylcarbamoyl

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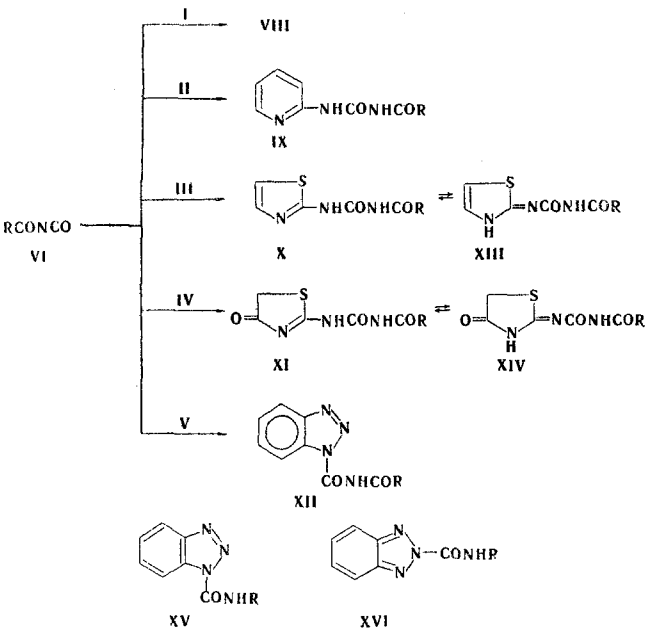

chloride (VIIb), which react with I, for example, to give stoichiometric amounts of carbamates VIIIa,b and the hydrochloride of I. It is interesting that the starting 8-hydroxyquinoline (mp 73.5°) is converted in these reactions to a modification [9] with mp 65-66°. The quantitative analysis of mixtures A and B is also confirmed by their reactions with ammonia (see the Experimental section).

The pure acyl isocyanates, which were obtained by limiting the synthesis time to 2-2.5 h [8, 10], react with I-V to give derivatives VIII-XIV (see Table 1), respectively, in high yields.

The reactions of VI with I-III and V in benzene proceeded readily at both 80° and room temperature. The starting compounds were isolated in all cases in the reaction of IV with VI at 20° even after 48 h.

For a comparative examination of the structures of the products of the reaction of VI with V, we also synthesized XVa-e by reaction of V with alkyl and aryl isocyanates.

The UV spectra of the compounds that we obtained (see Table 1) are similar to the spectra of the starting I-IV. This, in analogy with the studies of 8-hydroxyquinolines [11] and 2-amino derivatives of pyridine [12, 13], thiazole [13], and 4-thiazolinone [14], attests to the addition of the acylcarbamoyl residue to the exocyclic nitrogen atom, i.e., it constitutes evidence in favor of structures VIII-XI. Structures VIIIa-l were confirmed by the absence of ν_{OH} bands and the presence of ν_{CO} bands in their IR spectra (see Table 1). According to [13], the presence or absence in the IR spectra of acyl derivatives of 2-aminopyridine and thiazole (II and III) of a band at 1616-1640 cm^{-1}, assigned to the C(O)N=C group, makes it possible to form an opinion regarding the presence of the imine or amine form. In accordance with this, the absence in the IR spectra (KBr) of IXa-c and Xa,g of a $\nu_{C(O)N=C}$ band and the presence of ν_{CO} bands (see Table 1) is evidence that all of the synthesized 2-acylcarbamoyl derivatives of pyridine (IXa-c) and a portion of the thiazole derivatives (Xa,g) exist exclusively in the amino form in the crystalline state. On the other hand, the presence of a $\nu_{C(O)N=C}$ band in the IR spectra of Xb-f demonstrates that these thiazole derivatives exist partially (Xb,d-f) or completely (Xc) (judging from the presence in the spectra of the first of ν_{CO} bands at 1665-1718 cm^{-1} and in the spectrum of the latter of only one band at 1685 cm^{-1}, which is affiliated with the acyl carbonyl group) in the imino form (XIII). The IR spectrum of the 2-acylcarbamoyl derivative of 4-thiazolinone (XIa) contains carbonyl bands, a C(O)N=C band, and NH bands at 3190 and 3230 cm^{-1}, which are characteristic for an endocyclic and exocyclic NH group [6], while the spectrum of XIb does not contain $\nu_{C(O)N=C}$ bands or bands of an endocyclic NH grouping, but only ν_{CO} bands and an exocyclic NH band (3298 cm^{-1}) (see Table 1). These results demonstrate that amino form XIa prevails over imino form XIVa in the crystalline state in the case of R = 2-CH_3-4-$ClC_6H_3OCH_2$ and is the only form (XIb) in the case of R = C_6H_5. Thus, despite the known [6, 15] intensification of the mesomeric shift of the free pair of electrons of the exocyclic nitrogen atom toward the heterocyclic ring in 2-amino derivatives in the order II < III < IV, the addition of acyl isocyanates to them in all cases proceeds at the exocyclic nitrogen atom. The indicated differences in the electronic fine structures of systems II-IV are reflected (along with the acceptor properties of R) only in an increase in the fraction of the imine tautomeric forms (XIII and XIV) in the order IX < X < XI; this is in agreement with the data in [6, 13, 14].

To prove the position of the substituents in derivatives XIIa-e and XVa-e, we investigated their PMR spectra. It has been shown [16-19] that the proton of the NH group undergoes rapid exchange between the equivalent 1 and 3 positions at room temperature. As a result, the protons of the carbocyclic portion of benzotriazole form an AA'BB' system [20]. The PMR spectra of XIIa-e and XVa-e are unsymmetrical and do not change when the temperature is raised to 95°. This is evidence that (see [16]) the investigated substances have the fixed asymmetrical tautomeric structure of 1-substituted benzotriazoles.

These same conclusions are confirmed by an examination of the IR spectra of XII and XV, which contain the intense bands characteristic for $\nu_{N=N}$ of the benzotriazole ring (1590-1630 cm^{-1}) [21]. The IR spectra of XVa-e differ from the spectra of XII, particularly because of the presence of bands of medium intensity at 1540 cm^{-1}; this is characteristic [21] for the C = N bond of 2-substituted benzotriazoles and consequently means that the crystalline forms of XV apparently contain admixtures of 2-carbamoyl-substituted benzothiazoles (XVI).

TABLE 1. Acylcarbamoyl Derivatives of 8-Hydroxyquinoline (VIIIa-l), 2-Aminopyridine (IXa-c), 2-Aminothiazole (Xa-g), and 2-Amino-4-thiazolinone (XIa,b) and Benzotriazole Derivatives (XIIa-e and XVa-e)

Comp.	R	Mp, °C[a]	Empirical formula	Element	Found, %	Calc., %	IR spect. $\nu_{C=O}$, cm^{-1}	IR spect. $\nu_{C(O)C=N}$, cm^{-1}	UV spectr., λ_{max}, nm	Yield, %
1	2	3	4	5	6	7	8	9	10	11
VIIIa	4-$CH_3C_6H_4O(CH_2)_3$	125—126	$C_{21}H_{20}N_2O_4$	C	69,2	69,2				95
				H	5,4	5,5				
				N	7,6	7,7				
VIIIb	C_2H_5	147—148	$C_{13}H_{12}N_2O_3$	C	63,7	63,9	1695		241	70
				H	5,0	4,9	1785			
				N	11,6	11,5				
VIIIc	CH_3CHCl	119—120	$C_{13}H_{11}ClN_2O_3$	Cl	12,3	12,4	1700			80
				N	10,8	10,0	1780			
VIIId	CH_3CHBr	115—116	$C_{13}H_{11}BrN_2O_3$	N	8,8	8,7	1690			60
							1790			
VIIIe	CH_2Cl	110—111	$C_{12}H_9ClN_2O_3$	N	10,8	10,6	1690			90
							1790			
VIIIf	CH_2F	100—101	$C_{12}H_9FN_2O_3$	C	58,2	58,1	1685			65
				H	3,9	3,6	1785			
VIIIg	$Cl(CH_2)_3$	134—135	$C_{14}H_{13}ClN_2O_3$	N	9,7	9,6	1700			98
							1785			
VIIIh	2-$CH_3C_6H_4OCH_2$	143—144	$C_{19}H_{16}N_2O_4$	C	67,8	67,8			243	100
				H	4,7	4,8				
				N	8,7	8,8				
VIIIi	2-CH_3-4-$ClC_6H_3OCH_2$	143—144	$C_{19}H_{15}ClN_2O_4$	C	61,6	61,5			242	100
				H	4,2	4,0				
				N	7,7	7,6				
VIIIj	2,4-$Cl_2C_6H_3OCH_2$	121—122	$C_{18}H_{12}Cl_2N_2O_4$	Cl	18,2	18,2			242	90
				N	7,2	7,2				
VIIIk	C_6H_5	123—124	$C_{17}H_{12}N_2O_4$	N	9,6	9,6				98
VIIIl	4-ClC_6H_4	139—140	$C_{17}H_{11}ClN_2O_4$	N	8,7	8,6			242	95
IXa	C_2H_5	179—180	$C_9H_{11}N_3O_2$	C	55,7	56,0	1720			86
				H	5,7	5,6	1700			
IXb	2-CH_3-4-$ClC_6H_3OCH_2$	158—159	$C_{15}H_{15}ClN_3O_2$	Cl	11,1	11,1	1725		243	92
				N	13,1	13,1			287	
IXc	C_6H_5	190—191	$C_{13}H_{11}N_3O_2$	C	64,6	64,7	1690		256	90
				H	4,7	4,6	1710		287	
				N	17,4	17,4				
Xa	2-$CH_3C_6H_4OCH_2$	167—168	$C_{13}H_{13}N_3O_3S$	C	53,8	53,5	1718		268	70
				H	4,7	4,5				
Xb	CH_2F	170—172	$C_6H_6FN_3O_2S$	N	21,0	20,7	1695	1645		90
				S	16,0	15,8	1715[b]			
Xc	4-$ClC_6H_4OCH_2$	177—178	$C_{12}H_{10}ClN_3O_3S$	N	13,7	13,5	1685	1640[b]		97
Xd	C_6H_5	193—194	$C_{11}H_9N_3O_2S$	N	17,2	17,2	1685	1645	236	95
							1695		272	
Xe	4-ClC_6H_4	232—233	$C_{11}H_8ClN_3O_2S$	N	15,1	14,9	1665		246	94
							1690		272	
Xf	4-$O_2NC_6H_4OCH_2$	207—208	$C_{12}H_{10}N_4O_5S$	N	17,3	17,4	1680	1640		100
Xg	2,4-$Cl_2C_6H_3OCH_2$	204—205	$C_{12}H_9Cl_2N_3O_2S$	Cl	20,6	20,5	1705			92
XIa	2-CH_3-4-$ClC_6H_3OCH_2$[c]	220 (dec.)	$C_{13}H_{12}ClN_3O_4S$	Cl	10,1	10,4	1680	1643[b]	232	94
				N	11,9	12,3	1750		272	
				S	9,0	9,4				
XIb	C_6H_5	200 (dec.)	$C_{11}H_9N_3O_3S$	C	49,9	50,2	1685[d]		242	95
				H	3,4	3,4	1720		275	
				N	15,7	16,0				
XIIa	$Cl(CH_2)_3$	101—103	$C_{11}H_{11}ClN_4O_2$	N	21,1	21,0				86
XIIb	2-$CH_3C_6H_4OCH_2$[e]	181—182 (dec.)	$C_{16}H_{14}N_4O_3$	C	62,3	61,9				91
				H	4,5	4,5				
				N	17,9	18,1				
XIIc	4-$CH_3C_6H_4O(CH_2)_3$	161—162	$C_{18}H_{18}N_4O_3$	N	16,6	16,6				92
XIId	C_6H_5[e]	139—141 (dec.)	$C_{14}H_{10}N_4O_2$	N	20,8	21,0				89

TABLE 1 (continued)

Comp.	R	Mp, °C[a]	Empirical formula	Element	Found, %	Calc., %	IR spect.		UV spectr.,	Yield, %
							$\nu_{C=O}$, cm^{-1}	$\nu_{C(O)C=N}$, cm^{-1}	λ_{max}, nm	
1	2	3	4	5	6	7	8	9	10	11
XIIe	4-ClC$_6$H$_4$	175—177 (dec.)	$C_{14}H_9ClN_4O_2$	C	55,9	56,0				88
				H	3,1	3,0				
				Cl	17,9	18,1				
				N	18,9	18,6				
XVa	CH_3e	116—117	$C_8H_8N_4O$	N	31,8	31,8				94
XVb	C_4H_9e	42	$C_{11}H_{14}N_4O$	C	60,6	60,6				99
				H	6,6	6,4				
				N	25,6	25,7				
XVc	2-ClC$_6$H$_4$	160—161	$C_{13}H_9ClN_4O$	C	57,4	57,4	1740[f]			98
				H	3,6	3,3				
				Cl	12,9	13,0				
				N	20,5	20,6				
XVd	3-ClC$_6$H$_4$	180—181	$C_{13}H_9ClN_4O$	N	20,5	20,6				90
XVe	4-ClC$_6$H$_4$	194—195	$C_{13}H_9ClN_4O$	C	57,5	57,4				97
				H	3,3	3,3				
				Cl	13,0	13,0				
				N	20,6	20,6				

[a]Purified by recrystallization from benzene (VIIIa-l, IXa-c, Xa,d, XIIa,c, and XVa,c), from nitromethane (Xb), from ethanol (Xc,g), from benzene-isooctane (Xe,f), from toluene (XIIb,d and XVd,e), from toluene-isooctane (XIId), from isooctane (XVb), and by washing with hot benzene, ether, and isooctane (XIa,b). [b]Inflection. [c]IR spectrum: 3190 and 3230 cm^{-1} (NH). [d]IR spectrum: 3298 cm^{-1} (NH). [e]The IR spectra contain bands characteristic for $\nu_{N=N}$ at 1600 cm^{-1} (XIIb,d) and 1590 cm^{-1} (XVa,b) and for $\nu_{C=N}$ at 1540 cm^{-1} (XVa). [f]IR spectrum: 3600 cm^{-1} (NH).

EXPERIMENTAL

The IR spectra were recorded with a UR-10 spectrophotometer, and the UV spectra of ethanol solutions were recorded with a Specord spectrophotometer. Thin-layer chromatography was realized on Silufol UV254 with benzene–methanol (19:1) and development with $FeCl_3$ solution.

2-Imino-4-thiazolidinone (IV) was obtained by the method in [22]. Benzotriazole (V) was obtained by the action of nitrous acid on o-phenylenediamine [23].

Mixture of γ-(4-Methylphenoxy)butyryl Isocyanate (VIa) and γ-(4-Methylphenoxy)butyrylcarbamoyl Chloride (VIIa) (A). The reactions of 5.0 g (26 mmole) of γ-(4-methylphenoxy)butyramide and 2.3 ml (26 mmole) of oxalyl chloride via the method in [8] for 3 h gave 4.08 g of a mixture of A containing 90% VIa (65% yield) and 10% VIIa (6% yield) with bp 126-128° (0.3 mm). IR spectrum (in CCl_4): 2256 (N=C=O), 1740 (C=O), and 1815 cm^{-1} (ClC=O). Found,%: Cl 1.4; 1.5. $C_{12}H_{13}NO_3$ (90%) + $C_{12}H_{14}ClNO_3$ (10%). Calculated,%: Cl 1.4.

Mixture of Propionyl Isocyanate (VIb) and Propionylcarbamoyl Chloride (VIIb) (B). Similarly, but with heating for 50 min and subsequent standing at 20° for 48 h, the reaction of 5.0 g of propionamide and 6.0 ml of oxalyl chloride gave 3.0 g of mixture B containing 26% VIb (11.5% yield) and 74% VIIb (24% yield) with bp 50-60° (100-110 mm). IR spectrum (in CCl_4): 2249 (N=C=O), 1740 (C=O), and 1800 cm^{-1} (ClC=O). Found,%: Cl 19.4, 19.7. $C_4H_5NO_2$ (26%) + $C_4H_6ClNO_2$ (74%). Calculated,%: Cl 19.4.

Reaction of Mixture B with Ammonia. A solution of 2.0 g of mixture B in 40 ml of dry benzene was saturated with ammonia at room temperature. The resulting precipitate (2.5 g) was removed by filtration, washed thoroughly with water, and dried to give 1.85 g (95%) of N-propionylurea with mp 207° [24]. Evaporation of the wash water gave 0.55 g (95%) of ammonium chloride.

Reaction of Mixture A with 8-Hydroxyquinoline (I). A 2.19-g sample of mixture A in 20 ml of benzene was added at room temperature to a solution of 1.8 g of I in 15 ml of dry benzene, and the mixture was stirred for 3 h. The precipitate (3.5 g) was removed by filtration, washed with benzene, and extracted with 50 ml of hot benzene to give 0.15 g (99%) of the hydrochloride of I with mp 220-221° (from nitromethane) [9] and R_f 0.4. The action of ammonium hydroxide on the hydrochloride of I gave I with mp 65-66° (from isooctane) [9]. The physical constants and IR spectra of the products and known samples of I and its hydro-

chloride were identical. The benzene solutions were concentrated, and the precipitate was removed by filtration to give 3.2 g (89%) of 8-quinolyl-N-[γ-(4-methylphenoxy)butyryl]carbamate (VIIIa) with mp 125-126° (from benzene) and R_f 0.18.

Reaction of Mixture B with I. Under conditions similar to those in the preceding experiment, 1.0 g of mixture B and 2.0 g of I in 40 ml of benzene gave 2.3 g of a precipitate. Extraction with 40 ml of hot benzene left a residue of 0.94 g (95%) of the hydrochloride of I. The benzene solutions yielded 1.95 g (95%) of 8-quinolyl-N-propionylcarbamate (VIIIb).

N-(2-Pyridyl)-N'-benzoylurea (IXc). A solution of 1.47 g (10 mmole) of benzoyl isocyanate was added at room temperature to a solution of 0.94 g (10 mmole) of II in 15 ml of benzene, and the mixture was stirred for 1 h. The precipitate was removed by filtration, washed with benzene, and recrystallized to give 2.17 g (90%) of IXc.

The characteristics of the above-indicated compounds and of similarly prepared compounds are presented in Table 1.

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