16. R. Wizinger, and H. Wenning, Helv. Chim. Acta, 23, 247 (1940).
17. O. Chaude, Cah. Phys., 50, 17 (1954).
18. K. Friedrich, and H. G. Henning, Ber., 92, 2756 (1959).
19. M. A. Gal'bershtam and N. P. Samoilova, Khim. Geterotsikl. Soedin., No. 9, 1209 (1973).

3-CARBAMIDO-2-INDOLYLURETHANES AND THEIR CYCLIZATION TO PYRIMIDO[4,5-b] INDOLES

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The reaction of isocyanates and isothiocyanates with 2-indolylurethanes takes place primarily in the 3 position of the indole ring to give the corresponding amides and thioamides, which smoothly undergo cyclization when they are heated with sodium ethoxide to give the corresponding quinazoline derivatives.

The high nucleophilicity of the pyrrole ring of the indole grouping makes it possible to directly introduce a carbamido group via the usual scheme of electrophilic substitution. Thus the corresponding amides of indole-3-carboxylic acid are formed by the action of isocyanates on indole and 1- or 2-alkylindoles, and the analogous thioamides are obtained from isothiocyanates under somewhat more severe conditions [1]. Tosyl isocyanate reacts more sluggishly than phenyl isocyanate [2]. The indole anion undergoes carbamidation at the nitrogen atom [1]. Similar processes have been noted in several cases. Thus both the anilide of the acid and 2-methylindole-3-carboxylic acid N,N'-diphenylamidine are formed from 2-methyl-

TABLE 1. 2-(Alkoxycarbonylamino)indole-3-carboxylic Acid Amides

Compound	Reaction time, h	mp, °C*	UV spectrum λ_{max}, nm (log ε)	IR spectrum, ν, cm^{-1}	Found, %			Empirical formula	Calculated, %			Yield, %
					C	H	N		C	H	N	
IIa	2	131—133	237 (4,30), 284 (4,29)	1700, 1720, 3220	67,8	5,9	12,6	$C_{19}H_{19}N_3O_3$	67,6	5,7	12,5	89
IIb	4	101—103	283 (4,28), sh 326 (3,08)	1695, 1710, 3270, 3330	69,7	6,6	11,1	$C_{22}H_{25}N_3O_3$	69,6	6,6	11,1	64
IIc	7	177—178	285 (4,30), 305 (4,26)	1630, 1680, 1720, 3250	71,7	4,8	11,0	$C_{23}H_{19}N_3O_3$	71,7	5,0	10,9	71
IId	5	191—193	285 (4,36), 306 (4,38), sh 313 (4,34), 358 (2,92), 376 (2,76)	1680, 1715, 3320, 3380	65,9	4,5	—	$C_{23}H_{18}ClN_3O_3$ †	65,8	4,3	—	73
IIe	9	187—189	282 (4,36), sh 300 (4,26), 357 (2,65), 375 (2,59)	1630, 1680, 1715, 3330, 3380	72,4	5,4	—	$C_{24}H_{21}N_3O_3$	72,2	5,3	—	62
IIf	8	195—197	sh 242 (4,38), 282 (4,15), 322 (4,21)	1620, 1690, 1750, 3190, 3310, 3340	69,8	4,7	10,2	$C_{24}H_{19}N_3O_4$	69,7	4,6	10,2	21
IIg	6	180—183	244 (4,46), 280 (4,32), 302 (4,25), 385 (3,73)	1650, 1715, 3260, 3380, 3410	64,2	4,4	13,2	$C_{23}H_{18}N_4O_5$	64,2	4,2	13,0	72
IV	5	225—227	283 (4,34), 304 (4,36), sh 312 (4,34), sh 352 (2,08)	1630, 1710, 3380, 3440	66,8	5,4	13,1	$C_{18}H_{17}N_3O_3$	66,9	5,3	13,0	34

*Amides IIa, b, e and IV were recrystallized from benzene—heptane, and the remaining compounds were recrystallized from benzene.
†Found: Cl 8.4%. Calculated: Cl 8.4%.

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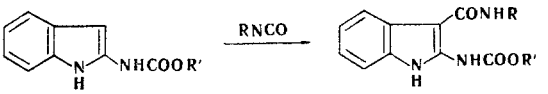
TABLE 2. Intensities of the Characteristic Ions of Amides II*

Compound	W_M	M−RNCO F_1	M−136 F_2	F_1 −44 F_3	F_1 −108 F_4	F_3 −91 F_5	F_2 −28 F_6
IIa	—	9,4	—	3,2	2,0	24,0	—
IIb	—	8,3	—	2,9	1,8	22,1	—
IIc	7,2	5,4	3,7	3,6	1,8	11,1	0,9
IId	7,0	2,8	1,0	1,4	1,9	3,4	1,5
IIe	6,7	2,0	0,8	1,1	1,8	4,0	0,6
IIf	2,5	0,9	0,4	0,4	0,8	1,4	0.4
IIg	5,1	—	—	1,1	1,7	0,9	—

*The intensities in the tables are calculated in percent relative to the total ion current (Σ_{65}).

indole and phenyl isocyanate [3]. The anion of indole-2-carboxylic acid anilide undergoes acylation at the indole nitrogen atom on reaction with phenyl isocyanate and also undergoes cyclization with splitting out of a molecule of diphenylurea to give 2-phenylindolo[1,2-c]-hydantoin [1], i.e., an imidazo [3,4-a]indole derivative is formed. The reaction of indole-2-carboxylic acid esters with methyl isothiocyanate proceeds similarly [4]. Carbamidation at the C_3 atom, the nucleophilicity of which is weakened by an electron-acceptor group in the 2 position, was not observed for such structures. 2-Dimethylaminoindole readily adds both phenyl isocyanate and phenyl isothiocyanate in the 3 position when the reaction components are heated [5]. However, if the amino group is not alkylated, three molecules of phenyl isocyanate are added [6].

We investigated the reaction of isocyanates and isothiocyanates with 2-indolylurethanes, for which one might have expected both carbamidation in the 3 position and reaction with the NH group of the urethane, which is observed in the reaction of isocyanates with amides [7].



III II a-g IV

I, II R′=$CH_2C_6H_5$; III, IV R′=C_2H_5; II a R=C_2H_5; b R=n-C_5H_{11}; c R=C_6H_5; d R=4-ClC_6H_4; e R=4-$CH_3C_6H_4$; f R=C_6H_5CO; g R=2-$NO_2C_6H_4$

It was found that brief heating of 2-benzyloxycarbonylaminoindole (I) with phenyl isocyanate in benzene gives amide IIc, the PMR spectrum of which does not contain the signal of a proton attached to C_3 of the pyrrole ring. Other II amides were similarly obtained (Table 1). The yield of amide IV is considerably lower with the O-ethylurethane (III), since side products, which we did not investigate in detail, are formed.

Molecular-ion peaks (Table 2) were observed in the mass spectra of amides II (except for IIa, b, in which an alkyl group is attached to the nitrogen atom). The principal pathways of their fragmentation were found to be splitting out of RNCO to give ion F_1 or splitting out of benzyl formate to give ion F_2.

The splitting out of RNCO is the primary process in the case of alkylamides IIa, b. The most characteristic peaks for them are the peaks of F_5 ions (more than 20% of the total ion current) due to the successive splitting out of CO_2 and $C_6H_5CH_2$. The maximum peak in the spectra of all of these amides (II) is the ion peak at 91.*

The presence of a molecular ion, which undergoes fragmentation with the splitting out of a C_6H_5NH group (the formation of an ion at 231 with cleavage of an amide C−N bond), elimination of a molecule of alcohol to give an ion at 277 (cleavage of the urethane grouping), and, as in the preceding

*Here and subsequently, the m/e values are presented.

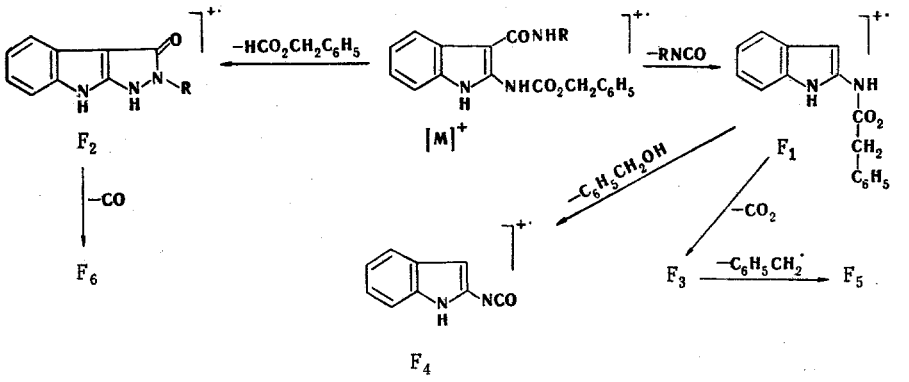
TABLE 3. 2-(Alkoxycarbonylamino)indole-3-carboxylic Acid Thioamides

Compound	Reaction time, h	mp, °C (from alcohol)	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, ν, cm^{-1}	Found, %				Empirical formula	Calculated, %				Yield, %
					C	H	N	S		C	H	N	S	
Va	10	169—171	260 (4,32), 285 (4,28), 343 (4,09)	1630, 1720, 3320, 3380	63,8	5,1	12,3	9,5	$C_{18}H_{17}N_3O_2$	63,7	5,0	12,4	9,4	31
Vb	12	168—170	262 (4,38), 285 (4,34), 343 (4,12)	1630, 1720, 3339, 3390	69,9	5,7	9,8	7,6	$C_{25}H_{23}N_3O_2$	69,9	5,4	9,8	7,5	17
Vc	8	184—186	268 (4,42), 288 (4,43), 355 (4,41)	1630, 1710, 3300, 3360	68,6	4,8	10,8	8,1	$C_{23}H_{19}N_3O_2$	68,8	4,8	10,5	8,0	62
Vd	8	195—197	267 (4,24), 287 (4,28), 360 (4,25)	1625, 1710, 3290, 3360	57,7	3,7	—	—	$C_{23}H_{18}BrN_3O_2$ *	57,7	3,8	—	—	64
Ve	8	175—177	266 (4,32), 286 (4,34), 358 (4,27)	1625, 1710, 3290, 3360	63,5	4,2	—	7,3	$C_{23}H_{18}ClN_3O_2$ †	63,4	4,2	—	7,3	65
Vf	9	181—183	267 (4,34), 287 (4,36), 354 (4,28)	1630, 1710, 3280, 3360	69,5	5,1	—	7,8	$C_{24}H_{21}N_3O_2$	69,4	5,1	—	7,7	60
Vg	10	190—192	265 (4,34), 287 (4,36), 352 (4,27)	1625, 1710, 3290, 3360	66,9	4,8	—	7,8	$C_{24}H_{21}N_3O_3$	66,8	4,9	—	7,4	47
VI	8	196—198	267 (4,28), 287 (4,29), 355 (4,21)	1625, 1700, 3280, 3365	63,8	5,3	—	10,0	$C_{18}H_{17}N_3O_2$	63,7	5,1	—	9,5	27
VIIa	0,5	184—186‡	268 (4,25), 287 (4,32), 393 (4,23)	1670, 1745, 3180, 3220	55,1	5,1	—	10,8	$C_{14}H_{15}N_3O_3$	55,1	4,9	—	10,5	49
VIIb	1	144—147‡	268 (4,20), 287 (4,30), 393 (4,16)	1675, 1735, 3200, 3230	62,2	4,7	—	8,4	$C_{19}H_{17}N_3O_3$	62,1	4,6	—	8,7	58
VIIc	0,2	198—200‡	sh 265 (4,29), 285 (4,34), 410 (4,22)	1630, 1720, 3220, 3360	64,3	4,5	—	7,7	$C_{24}H_{19}N_3O_3$	67,1	4,5	—	7,5	95

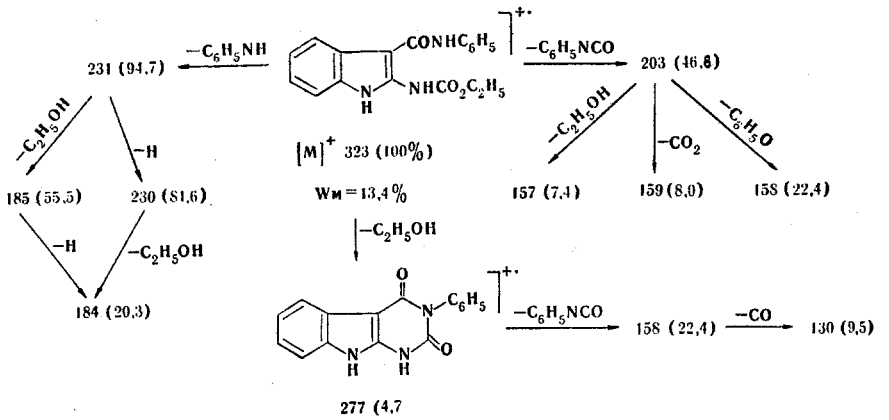
*Found: Br 16.6. Calculated: Br 16.6%.
†Found: Cl 8.1%. Calculated: Cl 8.1%.
‡From benzene.

TABLE 4. Intensities of the Characteristic Ions of Thioamides V

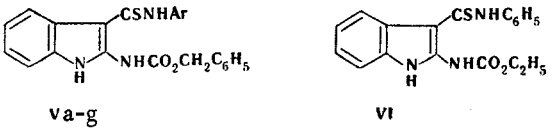
Compound	W_M	M−33 F_7	M−135 F_{10}	M−136 F_2'	F_7-44 F_8	F_8-90 F_9	F_{7-Ar} (234)
Vc	8,3	4,1	3,9	0,6	1,8	5,2	5,2
Ve	7,4	2,5	2,4	1,0	1,4	5,3	11,3
Vf	4,7	2,7	1,4	0,5	0,6	5,5	33,3
Vg	6,2	3,2	2,3	0,6	1,2	5,4	22,1



cases splitting out of C_6H_5NCO to give an ion at 203, is characteristic for the spectrum of amide IV [8, 9].



The reaction with isothiocyanates by refluxing in benzene leads to thioamides Va-g and VI. The yields are poorer with methyl isothiocyanate and α-phenylethyl isothiocyanate than with aryl isothiocyanates. The UV spectra of these thioamides are characterized by absorption maxima at 268, 288, and 355 nm. The presence of substituents in the phenyl group causes only slight changes (Table 3).

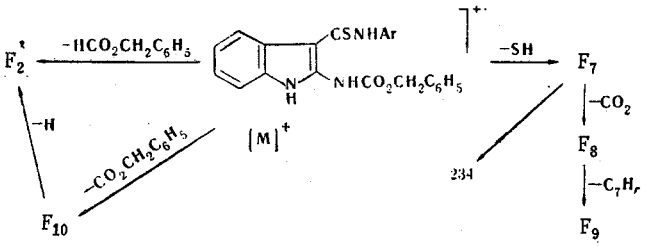


In contrast to the oxygen analogs, thioamides Va-g lose an SH group under the influence of electron impact to give an $[M-33]^+$ ion, which subsequently eliminates CO_2 and C_7H_6 groups successively. In addition to this, peaks of F'_2 ions that are typical for carbobenzoxy derivatives of aminoindole are observed (Table 4).

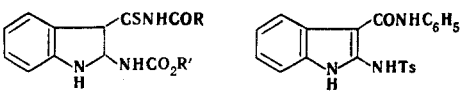
TABLE 5. 1,3-Dioxo-1,2,3,4-tetrahydropyrimido[4,5-b] indoles

Compound	mp, °C (from propyl alcohol)	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, ν, cm^{-1}	Found, % C	H	N	Empirical formula	Calculated, % C	H	N	Yield, %
IXa	255—256*,†	272 (4,21)	1650, 1710, 1750, 3440‡	62,7	4,8	18,5	$C_{12}H_{11}N_3O_2$	62,9	4,8	18,3	86
IXb	248—250*	272 (4,17)	1600, 1640, 1690, 1740	66,4	6,4	15,4	$C_{15}H_{17}N_3O_2$	66,4	6,3	15,5	87
IXc	190—191	285 (4,20), 305 (4,24)	1630, 1720, 3390	69,5	4,2	15,3	$C_{16}H_{11}N_3O_2$	69,3	4,0	15,2	91
IXd	205—207	285 (4,24), 307 (4,27), sh 313 (4,25)	1630, 1716, 3320, 3380	61,8	3,3	—	$C_{16}H_{10}ClN_3O_2$**	61,6	3,2	—	85
IXe	198—200	285 (4,26), 305 (4,29), sh 312 (4,25)	1620, 1710, 3330, 3370	70,1	4,7	—	$C_{17}H_{13}N_3O_2$	70,1	4,5	—	88

*From benzene—heptane.
†With decomposition.
‡The spectrum of the compound in $CHCl_3$ was recorded.
**Found: Cl 11.4%. Calculated: Cl 11.4%.



Considering the high reactivity of acyl isothiocyanates, one might have expected that these reagents would react with our subject compounds without complications, although, as previously demonstrated in [10], the reaction of indolylurethanes with 1,3-diketones or α, β-unsaturated ketones proceeds with the participation of the carbonyl group and leads to the formation of cyclic structures (α-carbolines), during which an ester group is simultaneously split out. It was found that only N-acylated thioamides VII are formed when acyl isothiocyanates are heated with the other reagents in an inert solvent. One might have expected that the quite accessible 2-tosylaminoindole would undergo this reaction, but the tosyl group substantially deactivates the aromatic ring [11]. Correspondingly, the reaction does not take place with phenyl isothiocyanate, whereas carbamidation (in the 3 position) with phenyl isocyanate requires considerably more severe conditions, and amide VIII is obtained in low yield.



VII a-c VIII

VIIa R=CH_3, R'=C_2H_5; b R=CH_3, R'=$CH_2C_6H_5$; c R=C_6H_5, R'=$CH_2C_6H_5$

Having a series of amides and thioamides of this sort at our disposal, we set up exeriments involving closing of a third ring. Amides or thioamides of N-acylated anthranilic

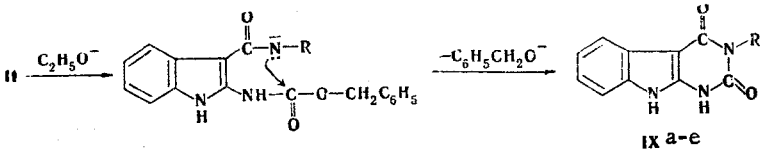
TABLE 6. 2-Aryl-1-thioxo-3-oxo-1,2,3,4-tetrahydropyrimido [4,5-b]indoles

Compound	mp, °C (dec., from propyl alcohol	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, ν, cm^{-1}	Found, % C	Found, % H	Found, % S	Empirical formula	Calculated, % C	Calculated, % H	Calculated, % S	Yield, %
Xa	298—301	262 (4,31), 352 (4,32)	1680, 1620, 3460	65,6	4,1	10,8	$C_{16}H_{11}N_3OS$	65,5	3,8	10,9	90
Xb	324—328	—	1690, 1620, 3490	51,7	2,7	8,9	$C_{16}H_{10}BrN_3OS$*	51,6	2,7	8,6	75
Xc	328	—	1690, 1610, 3370	58,7	3,2	10,1	$C_{16}H_{10}ClN_3OS$	58,6	3,1	9,8	90
Xd	318—321	263 (4,30), sh 300 (3,65), 354 (4,30)	1680, 1620, 3460	66,5	4,2	10,6	$C_{17}H_{13}N_3OS$	66,4	4,3	10,4	97
Xe	309—312	265 (4,17), 287 (4,19), 327 (4,03), sh 345 (4,01)	1680, 1620, 3440	63,1	4,1	9,9	$C_{17}H_{13}N_3O_2S$	63,1	4,0	9,9	97

*Found: Br 21.4%. Calculated: Br 21.5%.

acids, which undergo cyclization to give a pyrimidine ring thermally or under the influence of acidic agents, are used in the well-known Niementowski synthesis of quinazolones [12]. o-Ureidoanthranilates, the cyclization of which proceeds under the influence of both acids and alkalies, have been used for the preparation of dioxo compounds [13]. It has been found that N-substituted amides of o-ureidoanthranilic acid can be cyclized only under the influence of $POCl_3$ [14]. A method for the preparation of N-aminopyrimido[4,5-b]indoles by heating the corresponding hydrazides with carboxylic acids was patented in 1967 [15], but these hydrazides are extremely difficult to obtain.

Our experiments showed that the amides and thioamides described above do not undergo thermal cyclization with an o-urethane grouping (decomposition takes place) by refluxing in acetic acid or by heating with mineral acids. A multicomponent mixture that was difficult to separate was obtained in the case of heating with benzaldehyde in the presence of acidic agents. However, splitting out of a molecule of alcohol and ring formation take place smoothly at room temperature in the case of heating with sodium ethoxide (Table 5).



IXa R=C_2H_5; b R=n-C_5H_{11}; c R=C_6H_5; d R=4-ClC_6H_4; e R=4-$CH_3C_6H_4$

The same substance (IXc) as that obtained from amide IIc is obtained from anilide IV, but the reaction proceeds more rapidly and gives the product in better yield. Alkylamides IIa, b require heating the reaction mixture to 40-45°C.

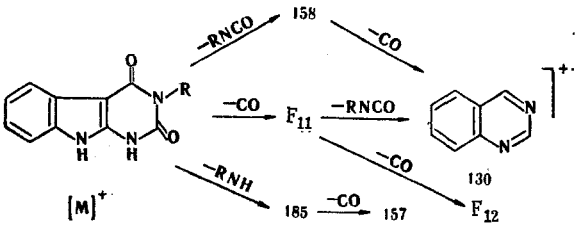
The character of the absorption in the UV spectra of IX depends only slightly on the nature of the solvent. Thus, for example, 2-ethyl-1,3-1,2,3,4-tetrahydropyrimido[4, 5-b]indole (IXa) in chloroform and alcohol has absorption maxima at the same wavelength (272 nm). A considerable bathochromic shift is observed on passing to the anion. Two maxima at 285 and 305 nm appear in the spectra when the alkyl group in the 2 position is replaced by an aryl group (IXc) due to the superimposition of the vibrations of the aromatic ring. The character of the absorption here also depends only slightly on the nature of the solvent. The bathochromic shift on passing to the anion for this model is, of course, greater.

Compounds IX have extremely stable molecular ions (W_M is 28 for IXa, b and 8-9 for IXc, d). Processes similar to those examined for the amides are observed during dissociative ionization in this case. In conformity with a retrodiene fragmentation scheme, an RNCO group is split out to give an ion at 158 (12-13% of the total ion current), which subsequently loses

TABLE 7. Intensities of the Characteristic Ions of Thiones X

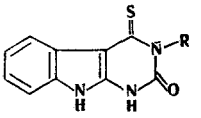
Compound	W_M	M−43 F_{12}	M−ArNCO (174)	M−H F_{13}	M−Ar NH + F_{13} −Ar N (189)
Xa	29,5	1,4	11,7	34,5	1,3
Xb	24,6	1,5	10,9	23,3	2,3
Xc	16,9	1,3	10,2	19,4	1,0
Xd	14,6	1,2	10,4	16,5	1,2
Xe	12,2	2,0	12,3	10,5	1,1

CO to give an ion at 130; the relative stability of the latter is evidently determined by the structure of the cation radical of quinazoline. The second pathway is successive splitting out of RNH and CO, which gives ions at 185 and 157, which are the usual ions for amides II. Successive splitting out of two molecules of CO from the molecular ion (ions with an intensity of 5-10%) is characteristic.



In the case of 2-alkylpyrimido[4, 5-b]indoles (IXa, b), in addition to splitting out of RNCO (ion at 158, intensity 17-21%), there is another fragmentation pathway that involves the splitting out of an olefin via the scheme of the McLafferty rearrangement (ion at 217, intensity 9-11%) and subsequent splitting out of HNCO and CO, as noted for amides [8, 9]. The resulting ions with m/e 158 constitute a large fraction (35-50%) of the total ion current, and this provides evidence for the high selectivity of the process. The examined fragmentation pathways were confirmed by the metastable transitions and the high-resolution spectra.

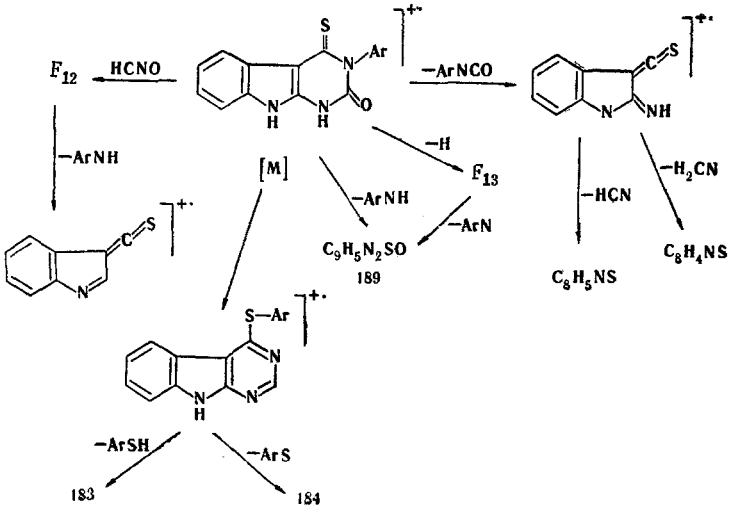
In the case of thioamides of the V type the process could be complicated by the formation of indolothiazoles or indolothiazines, but experiments showed that cyclization to thiones of the pyrimidoindole series (X, Table 6) takes place in this case also.



X a-e

X a R=C_6H_5; b R=4-BrC_6H_4; c R=4-ClC_6H_4; d R=4-$CH_3C_6H_4$; e R=4-$CH_3OC_6H_4$

Their UV spectra are similar to the spectra of IX and have absorption maxima at 262-265 and 327-354 nm. As in the example examined above, one of the most important pathways of dissociative ionization in the mass spectra of X (Table 7) is retrodiene fragmentation with elimination of RNCO (but not RNCS) or HCNO. The appearance of peaks of ions at 183 and 184, which, according to the high-resolution spectrum, do not contain a sulfur atom or aryl residue, is interesting. In this case N-S migration of the aryl group and subsequent splitting out of ArS take place. Similar processes were described in [16].



Thus amides of o-urethanocarboxylic acids were found to be convenient starting substances for the synthesis of quinazoline analogs. A brief communication regarding this has been published [17].

A communication by Sakuma and Yoneda [18], who, by diazotiazation and subsequent photolysis of substituted (at the aniline amino group) 5-amino-3-methyl-6-anilinouracils, obtained substances with mp > 360°C, to which a structure of the IX type (where the pyrrole nitrogen atom is alkylated or arylated) was assigned, appeared somewhat later. The compounds were named indolo [2, 3-d]pyrimidines. Sakuma and Yoneda did not present data that confirm the structure of these substances.

EXPERIMENTAL

The UV spectra of solutions of the compounds in chloroform were recorded with a Cary-15 spectrophotometer. The IR spectra of mineral oil suspensions of the compounds were recorded with IKS-22 or UR-20 spectrometers. The PMR spectra were recorded with Varian T-60 or X-100 spectrometers. The mass spectra were recorded with an MX-1303 spectrometer with direct introduction of the substances into the ionization region (at an energy of 50 eV) with recording on an H-105 loop oscillograph. The high-resolution mass spectra were recorded with a Jeol JMS-01-SQ-2 spectrometer at 75 eV. The synthesis of the starting urethanes was described in [10, 19].

2-(Benzyloxycarbonylamino)indole-3-carboxylic Acid Amides (II). A mixture of 1.06 g (4 mmole) of 2-benzyloxycarbonylaminoindole (I) and 5 mmole of the appropriate isocyanate was refluxed in 25 ml of absolute benzene, after which the mixture was evaporated to half its original volume, the precipitate that formed when the concentrate was cooled was separated, and the solution was evaporated in vacuo. Crystallization was induced by the addition of 10 ml of benzene—heptane (1 : 1). The yields and constants are presented in Table 1.

2-(Ethoxycarbonylamino)indole-3-carboxylic Acid Anilide (IV). As in the preceding experiment, 0.44 g (34%) of amide IV was obtained (after refluxing for 5 h) from 0.82 g (4 mmole) of urethane III and 0.71 g (6 mmole) of phenyl isocyanate. The physical constants are presented in Table 1.

2-(Alkoxycarbonylamino)indole-3-carboxylic Acid Thioamides (VII). Similarly, 4 mmole of urethane I or II was heated with 6 mmole of isocyanate, the crystals that formed after cooling and evaporation were separated, the solution was evaporated, and the residue was crystallized from alcohol. The yields and constants are presented in Table 3.

Reaction of 2-Tosylaminoindole with Phenyl Isocyanate. A mixture of 0.57 g (2 mmole) of 2-tosylaminoindole and 0.71 g (6 mmole) of phenyl isocyanate in 25 ml of absolute tetrahydrofuran was refluxed for 10 h, after which the solvent was evaporated in vacuo, and the residue was purified with a column filled with Al_2O_3 (elution with chloroform). Recrystallization from propyl alcohol gave 0.26 g (32%) of 2-tosylaminoindole-3-carboxylic acid anilide (VIII) with mp 199-202°C. UV spectrum, λ (log ε): shoulder at 240 (4.48), shoulder at 263 (4.14), and 297 nm (3.83), IR spectrum: 1730 cm^{-1}. Found: C 65.2; H 4.7; N 8.0%. $C_{22}H_{19}N_3O_3S$. Calculated: C 65.2; H 4.7; N 7.9%.

2-Substituted 1,3-Dioxo-1,2,3,4-tetrahydropyrimido[4,5-b]indoles (IX) and Their Sulfur Analogs (X). Sodium ethoxide (from 4 g of sodium in 40 ml of alcohol) was added to 2 mmole of amide II, IV, or VII, and the mixture was allowed to stand at room temperature for 2 days. Water (10-15 ml) was then added, and the mixture was neutralized with 5% hydrochloric acid. The precipitate was separated, washed with water and a small amount of aqueous alcohol, and air dried.

In the synthesis of IXa, b the mixture was heated at 40-45°C for 4 h.

LITERATURE CITED

1. E. P. Papandopoulos and S. B. Bedrosian, J. Org. Chem., 33, 4551 (1968).
2. M. Seefelder, Chem. Ber., 96, 3243 (1963).
3. J. M. Weinmann, Diss. Abstr., 25, 1588 (1958).
4. L. Elvidge and F. Spring, J. Chem. Soc., Suppl. Issue No. 1, 135 (1949).
5. A. Deberly and J. Bourdais, Tetrahedron Lett., No. 32, 3049 (1971).
6. R. Pschorr and G. Hoppe, Ber., 43, 2543 (1910).
7. C. W. Whitehead and J. Traverso, J. Am. Chem. Soc., 80, 962 (1958).
8. Yu. S. Nekrasov, P. A. Sharbatyan, R. S. Sagitullin, V. A. Puchkov, A. N. Kost, and N. S. Vul'fson, Izv. Akad. Nauk SSSR, Ser. Khim., No. 10, 2181 (1969).
9. C. P. Lewis, Anal. Chem., 36, 1582 (1964).
10. A. N. Kost, R. S. Sagitullin, T. Jagodzinski, and V. V. Men'shikov, Vestn. Mosk. Gos. Univ. Ser. Khim., 618 (1976).
11. K. Shudo and T. Okamoto, Tetrahedron, 33, 1717 (1977).
12. S. Niementowski, J. Prakt. Chem., 51, 564 (1895).
13. F. Russo and M. Gelardoni, Ann. Chim. (Roma), 56, 839 (1966); Chem. Abstr., 66, 18696 (1967).
14. W. Dymec and B. Lucka-Sobstel, Diss. Pharm., 17, 196 (1965); Chem. Abstr., 63, 16347 (1965).
15. A. J. Frey, G. E. Hardtman, and H. Ott, US Patent No. 3414574 (1967); Chem. Abstr., 70, 47490 (1969).
16. J. H. Bowie, S. O. Lawesson, J. Q. Madson, G. Schroll, and D. H. Williams, J. Chem. Soc., B, No. 10, 951 (1966).
17. A. N. Kost, T. Jagodzinski, and R. S. Sagitullin, Khim. Geterotsikl. Soedin., No. 5, 706 (1977).
18. Y. Sakuma and F. Yoneda, Heterocycles, 6, 1911 (1977).
19. V. I. Gorbunov, A. N. Kost, and R. S. Sagitullin, Khim.-Farm. Zh., No. 9, 12 (1968).