indolizine in 10 ml of dry acetonitrile, and the mixture was allowed to stand at room temperature for 10 min. The acetonitrile was then removed by distillation, and the residue was washed with methanol and recrystallized from DMF to give 0.5 g (71%) of 1,3-bis(triphenylmethyl)-2-phenylindolizine with mp 240-241 deg C. The product did not depress the melting point of a sample of the compound described above.

2,3-Dimethyl-1-(9-acridinyl)indolizine (XVIIa). This compound was obtained by reaction of 10 g (50 mmole) of acridine hydrochloride and 5.8 g (25 mmole) of 2,3-dimethylindolizine in 35 ml of dry DMF at 100 deg C for 8 h. Workup gave 4.8 g (60%) of a product with mp 274-275 deg C (from DMF) and $R_f$ 0.6 (system B). Mass spectrum, m/e (system A): 152 (15.10); 152.5 (2.4); 153 (13.0); 153.5 (8.4); 158.5 (4.2); 159 (3.6); 159.5 (2.4); 160 (8.7); 160.5 (4.9); 161 (9.2); 304 (3.0); 305 (12.4); 306 (6.2); 307 (4.7); 318 (3.0); 319 (4.5); 320 (3.0); 321 (43.8); 322 (100.0); 323 (25.9). Found: C 85.9; H 5.7; N 8.6%. $C_{23}H_{18}N_2$. Calculated: C 85.7; H 5.6; N 8.7%. Compounds XVIIb, c and XVIIIa, b were similarly obtained (see Table 2).

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# REACTION OF α-CYANOMETHYLAZAHETEROCYCLES WITH α-HALO CARBOXYLIC ACID CHLORIDES AND ANHYDRIDES

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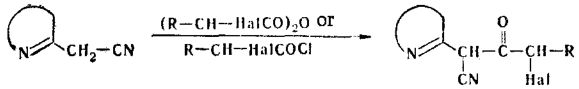
α-Cyanomethylazaheterocycles are acylated by α-halo carboxylic acid chlorides and anhydrides at the methylene carbon atom to give hetaryl-containing halo ketones.

α-Cyanomethylazaheterocycles (I) are acylated at the methylene carbon atom [1-3] to give α-acyl derivatives. However, up until now acyl derivatives that contain a functional group in the acyl residue have not been obtained. In the present research we obtained compounds of this type and studied their properties.



IIa-d; IIIa, b;
IVa, b; V; VI

In the acylation of 2-cyanomethyl derivatives of azaheterocycles of the I type with α-halocarboxylic acid anhydrides and chlorides the reaction may proceed via three pathways: acylation and alkylation of the heteroring nitrogen atom or acylation of the methylene group. In all of the cases that we studied we isolated only C-acylated pyridines (IIa-d), quinolines (IIIa, b), benzimidazoles (IVa, b), 1-methylbenzimidazoles (V), and 4,5-diphenylthiazoles (VI) (see Table 1), the structures of which were confirmed by their chemical properties and spectral data. Three maxima at 240, 295, and 370 nm are observed in the UV spectra of acyl derivatives of 2-cyanomethylpyridine IIa, b, d in ethanol; this is in complete agreement with the data for α-acetyl-2-cyanomethylpyridine [3]. A singlet of protons of a methylene group at 4.5-4.8 ppm is observed in the PMR spectra of the haloacetyl derivatives (IIa, III, IVa, V, and VI). The absorption band in the IR spectra at 2195-2205 $cm^{-1}$ is related to a conjugated nitrile group [2, 3].

In the acylation of α-halo carboxylic acid chlorides half the amount of starting azaheterocycle is tied up in the form of the hydrochloride, and the yields of acyl derivatives do not even reach 50%. When the reaction

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TABLE 1. Characteristics of the Compounds Obtained

| Compound | R | Hal | mp, °C[a] | Found, % | Empirical formula | Calc., % | Yield, % by method | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | A | B |
| IIa | H | Cl | 157 | Cl 18,1<br>N 14,4 | $C_9H_7ClN_2O$ | 18,2<br>14,4 | 89 | 47 |
| IIb | $CH_3$ | Br | 183 | Br 31,3<br>N 11,2 | $C_{10}H_9BrN_2O$ | 31,6<br>11,1 | 90 | |
| IIc | $C_2H_5$ | Br | 133 | Br 29,8<br>N 10,3 | $C_{11}H_{11}BrN_2O$ | 29,9<br>10,5 | 72 | |
| II d | $C_6H_5$ | Cl | 144 | Cl 13,2<br>N 10,5 | $C_{15}H_{11}ClN_2O$ | 13,1<br>10,4 | | 46 |
| IIIa | H | Cl | 196 197 | Cl 14,3<br>N 11,3 | $C_{13}H_9ClN_2O$ | 14,5<br>11,5 | 99 | 48 |
| IIIb[b] | H | I | 202 203 | N 8,2 | $C_{13}H_9IN_2O$ | 8,3 | | |
| IVa | H | Cl | 278 279 | Cl 15,2<br>N 18,0 | $C_{11}H_8ClN_3O$ | 15,2<br>18,0 | 84 | |
| IVb | $C_2H_5$ | Br | 232 | Br 26,1<br>N 13,7 | $C_{13}H_{12}BrN_3O$ | 26,0<br>13,7 | 60 | |
| V | H | Cl | 236 238 | Cl 14,4<br>N 17,1 | $C_{12}H_{10}ClN_3O$ | 14,3<br>17,0 | 95 | |
| VI | H | Cl | 206 208 | Cl 10,1<br>S 9,3 | $C_{19}H_{13}ClN_2OS$ | 10,0<br>9,1 | 41 | |

[a] The compounds were recrystallized: IIa from benzene, IIb and IIIa from toluene, and V from methyl ethyl ketone. The remaining compounds were recrystallized from n-propyl alcohol. [b] Compound IIIb was obtained from IIIa by halogen exchange.

is carried out in the presence of bases (for example, triethylamine), it gives a resinlike mixture, from which the desired products were isolated in minimal yields. Considerably higher yields (up to 100%) were obtained in the acylation with α-halo carboxylic acid anhydrides. In this case the products isolated from the reaction mixture were practically free of impurities.

The products were crystalline substances that were stable during storage. However, they all decomposed when they were heated to their melting points.

The halogen atom in the products is extremely labile and is readily replaced by various nucleophilic agents. The chlorine atom in 2-(2-quinolyl)-3-keto-4-chlorobutyronitrile (IIIa) is exchanged by iodine via the Finkelstein reaction with sodium iodide. A thiocyanato derivative was obtained when an acetone solution of potassium thiocyanate was refluxed with 2-(2-pyridyl)-3-keto-4-chlorobutyronitrile (IIa), and reaction of IIa and IVa with sodium azide gave the corresponding azides.

## EXPERIMENTAL

The PMR spectra of trifluoroacetic acids solutions of the compounds were recorded with a ZKR-60 spectrometer with tetramethylsilane as the internal standard. The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-10 spectrometer. The UV spectra of ethanol solutions of the compounds were recorded with an SF-4a spectrophotometer.

Acylation of 2-Cyanomethylazaheterocycles. Method A. Acylation with α-Halo Carboxylic Acid Anhydrides. A mixture of 2-cyanomethylazaheterocycle and 10% excess anhydride was refluxed in toluene for 30-60 min, after which it was cooled and treated with a twofold quantity of ether. The resulting precipitate was removed by filtration, washed with ether, and crystallized from a suitable solvent. In the preparation of IV the reaction was carried out in dimethylformamide (DMF).

Method B. Acylation with α-Halo Carboxylic Acid Chlorides. A mixture of 2-cyanomethylazaheterocycle and carboxylic acid chloride in toluene (10 ml per 0.01 mole of reagents) was refluxed for 30 min, after which it was cooled and treated with a twofold quantity of ether. The resulting precipitate was removed by filtration, and water and ammonium hydroxide were added to it until the mixture had pH 8-9. The product was removed by filtration and washed with water and alcohol.

2-(2-Quinolyl)-3-keto-4-iodobutyronitrile (IIIb). A solution of 0.57 g (3.8 mmole) of sodium iodide in 5 ml of acetone was added to a heated solution of 0.61 g (2.5 mmole) of 2-(2-quinolyl)-3-keto-4-chlorobutyronitrile in 40 ml of acetone, after which the mixture was refluxed for 5 min and allowed to stand overnight. The resulting precipitate was removed by filtration and washed with water and acetone to give 0.7 g (83.3%) of IIIb.

2-(2-Pyridyl)-3-keto-4-thiocyanatobutyronitrile (VII). A mixture of 0.97 g (5 mmole) of 2-(2-pyridyl)-3-keto-4-chlorobutyronitrile and 0.74 g (7.5 mmole) of potassium thiocyanate in 20 ml of acetone was refluxed for 2 h, after which it was cooled, and the resulting precipitate was removed by filtration and washed with 12 ml of water and acetone to give 0.96 g (88%) of VII with mp 184 deg C (from n-propyl alcohol). IR spectrum: 2200 (CN) and 2155 $cm^{-1}$ (SCN). Found: N 19.5; S 15.0%. $C_{10}H_7N_3OS$. Calculated: N 19.3; S 14.8%.

2-(2-Pyridyl)-3-keto-4-azidobutyronitrile (VIII). A mixture of 5.82 g (30 mmole) of 2-(2-pyridyl)-3-keto-4-chlorobutyronitrile, 2.16 g (33 mmole) of finely ground sodium azide, 25 ml of DMF, and 2 ml of water was heated at 50-60 deg C for 20 min, after which it was allowed to stand at room temperature for 12-15 h. Cold water (25 ml) was added to the reaction mixture, and the precipitate was removed by filtration and washed with water to give 5 g (83%) of a product with mp 158-159 deg C (dec., from n-propyl alcohol). IR spectrum: 2195 (CN) and 2122 $cm^{-1}$ ($N_3$). Found: N 34.8%. $C_9H_7N_5O$. Calculated: N 34.8%.

2-(2-Benzimidazolyl)-3-keto-4-azidobutyronitrile (IX). A 0.72-g (11 mmole) sample of finely ground sodium azide was added to a solution of 2.34 g (10 mmole) of 2-(2-benzimidazolyl)-3-keto-4-chlorobutyronitrile in a refluxing mixture of 20 ml of DMF and 4 ml of water, after which heating was discontinued. After 2 h, 30 ml of water was added, and the resulting precipitate was removed by filtration and washed with water and alcohol to give 2.4 g (99%) of a product with mp > 320 deg C (from n-propyl alcohol). IR spectrum: 2200 (CN) and 2120 $cm^{-1}$ ($N_3$). Found: N 35.2%. $C_{11}H_8N_6O$. Calculated: N 35.0%.

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# ACETALS OF LACTAMS AND ACID AMIDES

## XXII.* REACTION OF AMIDE AND LACTAM ACETALS WITH ENAMINO ESTERS. SYNTHESIS OF BENZENE, PYRIDINE, INDOLE, QUINOLINE, AND BENZAZEPINE DERIVATIVES

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It is shown that acetals of acid amides and lactams undergo condensation at the α-$CH_3$ (or $CH_2$) groups of enamino esters to give dienediamines, the cyclization of which led to benzene, pyridine, indole, quinoline, and benzazepine derivatives.

The chemical and physicochemical properties of enamines (for example, of the I type) are determined to a great extent by the electron-acceptor effect of the β substituents and the electron-donor effect of the tertiary amino group.

In the case of the reaction of enamine I with dimethylformamide diethylacetal (II), as a result of which 1-carbethoxy-1-cyano-2,4-bis(N,N-dimethylamino)butadiene (III) was isolated in 56% yield, we have shown [2]

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*See [1] for communication XXI.

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