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CHEMISTRY OF FURAZANO[3,4-*b*]PYRAZINE. 4.* 5,6-DICHLOROFURAZANO[3,4-*b*]PYRAZINE IN CYCLIZATION REACTIONS

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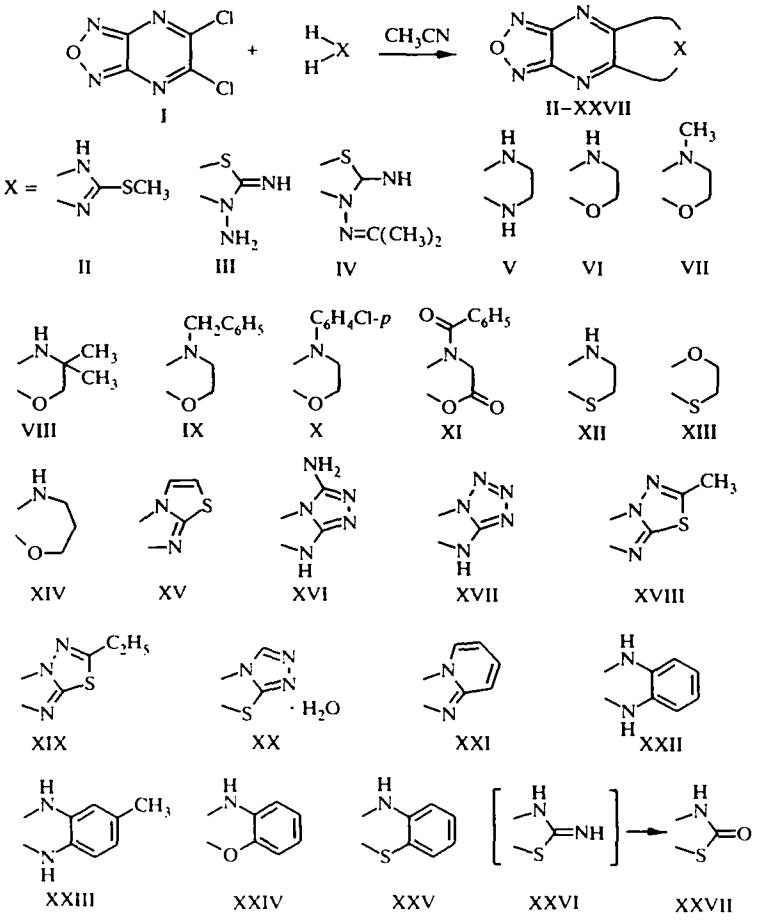
A method was developed for the production of polycyclic compounds containing the furazano[3,4-b]pyrazine fragment by the reaction of difunctional nucleophiles with 5,6-dichlorofurazano[3,4-b]pyrazine. It was shown that the reaction is affected by the hydrogen chloride acceptor (triethylamine).

Furazano[3,4-*b*]pyrazines condensed with heterocycles at positions 5,6 are almost unknown. The only example is 1,4,5,8-tetraazafurazano[3,4-*e*][3,4-*h*]decalin, obtained from diaminofurazan and glyoxal [2]. Within the scope of investigations into the chemistry of furazano[3,4-*b*]pyrazine [1, 3-5] we are reporting on a general method for the production of polycyclic compounds containing the furazano[3,4-*b*]pyrazine fragment.



*For Communication 3, see [1].

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TABLE 1. Characteristics of the Synthesized Compounds

Compound	Molecular formula	mp, °C	PMR spectrum, δ, ppm (DMSO)	Yield, % (method)
II	$C_6H_4N_8OS$	168...170	2,64 (3H, s, CH_3); 9,78 (1H, s, NH)	58 (A)
III	$C_5H_5N_7O_2S$	>250 (decomp.)	8,05 (2H, s, NH_2); 10,44 (1H, s, NH)	62 (B)
IV	$C_8H_7N_7OS$	207...208	1,98 (3H, s, CH_3); 2,31 (3H, s, CH_3); 9,84 (1H, s, NH)	73 (A)
V	$C_6H_6N_6O$	270...272 (decomp.)	3,38...3,82 (4H, m, CH_2CH_2); 8,84 (2H, s, NH)	46 (B)
VI	$C_6H_5N_5O_2$	217...219	3,98 (2H, unres. m, CH_2); 4,67 (2H, unres. m, CH_2), 8,73 (1H, s, NH)	72 (A)
VII	$C_7H_7N_5O_2$	231...232	3,18 (3H, s, CH_3); 3,71 (2H, t, CH_2); 4,58 (2H, t, CH_2)	83 (B)
VIII	$C_8H_9N_5O_2$	>250	1,67 (6H, s, CH_3); 4,80 (2H, s, CH_2); 6,76 (1H, s, NH)	32 (A)
IX	$C_{13}H_{11}N_5O_2$	100...103	3,69 (2H, t, CH_2); 4,60 (2H, t, CH_2); 4,93 (2H, s, CH_2); 7,33 (5H, m C_6H_5)	48 (B)
X	$C_{12}H_8ClN_5O_2$	174...175	4,09 (2H, t, CH_2); 4,80 (2H, t, CH_2); 7,33...7,73 (4H, m. C_6H_4)	92 (A)
XI	$C_{13}H_7N_5O_4$	272...274	4,95 (2H, s, CH_2); 7,40...8,07 (5H, m, C_6H_5)	18 (A)
XII	$C_6H_5N_5OS$	212...214	3,47...4,04 (4H, m, CH_2CH_2); 8,51 (1H, s, NH)	80 (A)
XIII	$C_6H_4N_4O_2S$	183...185	3,78 (2H, unres. m, CH_2); 4,82 (2H, unres. m, CH_2)	75 (A)
XIV	$C_7H_7N_5O_2$	235...240 (decomp.)	2,90...3,75 (4H, m, CH_2CH_2); 4,55 (2H, t, CH_2); 8,51 (1H, s, NH)	47 (A)
XV	$C_7H_2N_6OS$	>250	7,40 (1H, d, CH); 8,40 (1H, d, CH)	42 (A)
XVI	$C_6H_5N_9O_2$	>260	5,49 (2H, s, NH_2); 8,40 (1H, s, NH)	66 (A)
XVII	$C_5H_3N_9O$	>260	8,92 (1H, s, NH)	36 (A)
XVIII	$C_7H_3N_7OS$	>300	2,80 (3H, s, CH_3)	62 (A)
XIX	$C_8H_5N_7OS$	218...219	1,33 (3H, t, CH_3); 3,15 (2H, q CH_2)	58 (A)
XX	$C_6H_3N_7O_2S$	200...203 (decomp.)	8,82 (1H, s, CH)	55 (A)
XXI	$C_9H_4N_6O$	329...330	6,33...9,13 (4H, m, C_5H_4N)	81 (B)
XXII	$C_{10}H_6N_6O$	>260	6,84...7,18 (4H, m, C_6H_4); 11,33 (2H, s, NH)	93 (B)
XXIII	$C_{11}H_8N_6O$	>260	2,22 (3H, s, CH_3); 6,77...7,09 (3H, m, C_6H_3); 11,62 (2H, s, NH)	87 (A)
XXIV	$C_{10}H_5N_5O_2$	>300	7,00...7,33 (4H, m, C_6H_4); 12,00 (1H, s, NH)	72 (A)
XXV	$C_{10}H_5N_5OS$	>300	6,93...7,40 (5H, m, C_6H_4); 11,71 (1H, s, NH)	81 (A)
XXVII	$C_5HN_5O_2S$	>250	12,78 (1H, s, NH)	28 (B)

5,6-Dichlorofurazano[3,4-*b*]pyrazine (I) readily reacts by nucleophilic substitution with various compounds containing mobile hydrogen atoms at the γ or δ position [1, 3]. The high reactivity of the chlorine atoms in this compound is explained by the strong electrophilic characteristics of the furazan ring, which makes it possible to conduct the reaction with good yields at room temperature. Heterocyclization was studied for diamines, amino alcohols, thioureas, aminoazoles, aminothiazoles, and N-benzoylglycine.

Nucleophilic substitution takes place in stages, and in cases where the second reaction center is insufficiently reactive a mixture of linear and cyclic or predominantly linear products is formed. For example, the reaction of the dichloro derivative (I) with 2-aminoethanol leads to 5,6-di(2-hydroxyethylamino)furazano[3,4-*b*]pyrazine [1, 3] with a yield of 85%, whereas the addition of triethylamine to the reaction mixture leads to cyclization of the active intermediate formed at the first stage into

1,4-oxazino[2,3-*e*]furazano[3,4-*b*]pyrazine (VI) with a yield of 72% (method A). The introduction of nucleophiles with bulky substituents into the reaction leads to a side reaction with the formation of linear derivatives, and good yields of the products are obtained in the absence of triethylamine.

The reaction of the dichloro derivative (I) with thiosemicarbazide and acetone thiosemicarbazone can lead both to the iminothiazoles (III) and (IV) respectively and to imidazolidinethiones with an exocyclic sulfur atom. The structure of the iminothiazole (IV) was confirmed unambiguously by x-ray crystallographic analysis. The cyclization of compound (I) with thiourea takes place in a well-defined manner. The thiazolidone (XXVII), which is clearly the product from hydrolysis of the iminothiazolidine (XXVI), was isolated from the reaction mixture with a yield of 28%.

The synthesized products (II-XXVII) were high-melting compounds, poorly soluble in water and organic solvents, and had high density.

EXPERIMENTAL

The PMR spectra were recorded in DMSO-d_6 on a Bruker WH 90/DS spectrometer (90 MHz) with TMS as internal standard. The mass spectra were obtained on a VS-50AET spectrometer at 70 eV. The purity of the products was monitored by TLC on Silufol UV-254 plates and also by HPLC on a Du Pont 850 chromatograph with Zorbax SIL (4.6 × 250 mm). Elemental analysis for C, H, N, and S was performed on a Carlo-Erba instrument.

The analytical data agreed with the calculated data.

Method A

7,8-Dihydro-1,4-oxazino[2,3-*e*]furazano[3,4-*b*]pyrazine (VI). We added 1.22 g (0.02 mole) of 2-aminoethanol to a stirred and cooled suspension of 3.82 g (0.02 mole) of 5,6-dichlorofurazano[3,4-*b*]pyrazine (I) [1, 3] in 15 ml of acetonitrile. Without cooling we then added with stirring over 10 min 5.56 ml (0.04 mole) of triethylamine. After 1 h 20 ml of water was added to the reaction mixture, and the mixture was cooled in the refrigerator. The crystals were filtered off, washed with water (3 × 30 ml), and crystallized from acetic acid. After drying we obtained colorless crystals of the amine (VI). Found %: C 39.83; H 2.92; N 38.71. $C_6H_5N_5O_2$. Calculated %: C 40.24; H 2.81; N 39.10. Mass spectrum (*m/z*): 179 (M^+).

Method B

7,8-Dihydro-5-methyl-1,4-oxazino[2,3-*e*]furazano[3,4-*b*]pyrazine (VII). We added 2.25 g (0.03 mole) of N-methylaminoethanol to a stirred and cooled suspension of 1.91 g (0.01 mole) of the dichloro derivative (Ic) in 7 ml of acetonitrile. After 3 h 10 ml of water was added to the reaction mixture, and the mixture was cooled in the refrigerator. The product was filtered off, washed with water (2 × 15 ml), and crystallized from aqueous acetone. After drying we obtained light-yellow crystals of compound (VII). Found %: C 43.21; H 3.54; N 35.89. $C_7H_7N_5O_2$. Calculated %: C 43.53; H 3.65; N 36.25.

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