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CHEMISTRY OF FURAZANO[3,4-*b*]PYRAZINES
3.* METHOD FOR THE SYNTHESIS OF 5,6-DISUBSTITUTED FURAZANO[3,4-*b*]PYRAZINES

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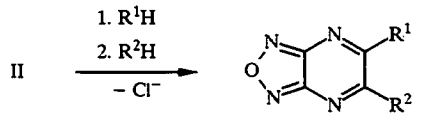
A method was developed for the synthesis of 5,6-dichlorofurazano[3,4-b]pyrazine (a compound with easily removed leaving groups). The optimum conditions for their substitution by various nucleophiles were determined.

The furazano[3,4-*b*]pyrazine heterocyclic system has attracted the attention of researchers in the field of the synthesis of energy-rich polynitrogen compounds. In spite of repeated attempts [2-8], a convenient method had not been found for the synthesis of derivatives of furazano[3,4-*b*]pyrazines until recently.

For the synthesis of derivatives of the type under consideration, it is necessary to have compounds containing reactive groups at positions 5 and 6. With this aim, we studied the substitution of the hydroxyl groups in 5,6-dihydroxyfurazano[3,4-*b*]pyrazine (I), synthesized from diaminofurazan and oxalic acid, by chlorine atoms. 5,6-Dichlorofurazano[3,4-*b*]pyrazine (II) was obtained with yields of 68-69% by the action of thionyl chloride or phosphorus oxychloride in the presence of catalytic amounts of DMFA and also during reaction with phosphorus pentachloride in phosphorus oxychloride.

I II

The realization of nucleophilic substitution reactions for 5,6-dichlorofurazano[3,4-*b*]pyrazine (II) opens up broad possibilities, since the chlorine atoms in this compound are strongly activated and are easily substituted during the action of various nucleophiles [9]:



III–CXIV

R^1 = NR, OR, SR; R^2 = NR′, OR′, SR′, Cl, R^1

The reaction of the dichloro derivative (II) with highly basic amines takes place quickly and under mild conditions (even if the amines are introduced in the form of aqueous solutions), whereas in 2,3-dichloro- and 2,3,5-trichloropyrazines ammonia only substitutes one of the chlorine atoms under severe conditions (15 h at 80°C) [10]. Such high reactivity is clearly explained

*For Communication 2, see [1].

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TABLE 1. Characteristics of the Obtained Compounds

Compound	R^1	R^2	Molecular formula	mp, °C	PMR spectrum (DMSO-d_6), δ, ppm	Basicity of initial amine, pK_aBH^+ (H_2O) [12]	Yield, % (method)
1	2	3	4	5	6	7	8
II	Cl	Cl	$C_4Cl_2N_4O$	170...175 (subl.)	—	—	69
III	Cl	I	C_4ClIN_4O	130...131	—	—	75 (E)
IV	Cl	NH_2	$C_4H_2ClN_5O$	175...177 (decomp.)	8,22 (1H, s, NH); 8,78 (1H, s, NH)	9,3	58 (D)
V	NH_2	NH_2	$C_4H_4N_6O$	320 (decomp.)	7,96 (4H, s, NH_2)	9,3	97 (D)
VI	NHOH	NHOH	$C_4H_4N_6O_3$	320 (decomp.)	10,93 (4H, s, NHOH)	6,0	92 (D)
VII	NHOH	OC_5H_5	$C_6H_7N_5O_3$	270...276	1,42 (3H, t, CH_3); 4,51 (2H, q, CH_2); 11,40 (2H, d, NHOH)	6,0	51 (D)
VIII	$NHCH_3$	$NHCH_3$	$C_6H_8N_6O$	260...262	2,93 (6H, s, CH_3); 8,15 (2H, s, NH)	10,6	85 (D)
IX	NH_2	$NHCH_3$	$C_5H_6N_6O$	210...212 (decomp.)	2,93 (3H, s, CH_3); 7,89 (2H, s, NH_2); 8,25 (1H, s, NH)	9,3	26 (D)
X	NHC_2H_5	NHC_2H_5	$C_8H_{12}N_6O$	234...235	1,26 (6H, t, CH_3); 3,24...3,53 (4H, m, CH_2); 8,13 (2H, t, NH)	10,7	88 (D)
XI	$N(CH_3)_2$	$N(CH_3)_2$	$C_8H_{12}N_6O$	164...165	3,02 (12H, s, CH_3)	10,7	80 (D)

TABLE 1 (continued)

1	2	3	4	5	6	7	8
XII	NHC_3H_7	NHC_3H_7	$C_{10}H_{16}N_6O$	144...145	0,86 (6H, t, CH_3); 1,38...1,80 (4H, m, CH_2); 3,18...3,47 (4H, m, CH_2); 8,1 (2H, t, NH)	10,6	48 (D)
XIII	$NHC(CH_3)_3$	$NHC(CH_3)_3$	$C_{12}H_{20}N_6O$	269...270	1,37 (18H, s, CH_3); 7,61 (2H, s, NH)	10,7	81 (D)
XIV	$N(C_4H_9)_2$	$N(C_4H_9)_2$	$C_{20}H_{36}N_6O$	73...75	0,87 (12H, t, CH_3); 0,78...1,64 (1,6H, m, CH_2CH_2); 3,56 (8H, t, CH_2)	10,9	87 (D)
XV	$NHCH_2CH{=}CH_2$	$NHCH_2CH{=}CH_2$	$C_{10}H_{12}N_6O$	122...123	4,14 (4H, t, CH_2); 5,10...5,40 (4H, m, CH_2); 5,71...6,15 (2H, m, CH); 8,39 (2H, t, NH)	9,5	54 (A)
XVI	$NHCH_2C \equiv CH$	$NHCH_2C \equiv CH$	$C_{10}H_8N_6O$	221...223	3,27 (2H, t, CH); 4,24 (4H, t, CH_2); 8,62 (2H, d, NH)	7,9	62 (A)
XVII	$NHCH_2CH_2OH$	$NHCH_2CH_2OH$	$C_8H_{12}N_6O_3$	227...229	3,40...3,71 (8H, m, CH_2); 4,84 (2H, t, OH); 8,36 (2H, t, NH)	9,5	85 (D)
XVIII	$NHCH_2CH(OH)CH_3$	$NHCH_2CH(OH)CH_3$	$C_{10}H_{16}N_6O_3$	173...175	1,11 (6H, d, CH_3); 3,13...3,58 (4H, m, CH_2); 3,78...4,09 (2H, m, CH); 4,82 (2H, d, OH); 8,35 (2H, t, NH)	9,5	38 (D)
XIX	$NHOCH_3$	$NHOCH_3$	$C_6H_8N_6O_3$	280...290	3,82 (6H, s, CH_3); 11,17 (2H, s, NH)	4,6	71 (A)
XX	$NHNH_2$	$NHNH_2$	$C_4H_6N_8O$	260...262	6,95 (6H, s, $NHNH_2$)	8,2	99 (D)
XXI	$NHN(CH_3)_2$	$NHN(CH_3)_2$	$C_8H_{14}N_8O$	254...256	2,64 (12H, s, CH_3); 8,27 (2H, s, NH)	7,5	79 (D)
XXII	Cl	$NHCH_2CH_2Br$	C_6H_5BrClO	258...260	3,48...4,00 (4H, m, CH_2CH_2); 10,15 and 12,27 (1H, s. s., NH)	6,5	71 (A)

TABLE 1 (continued)

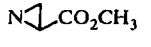
1	2	3	4	5	6	7	8
XXIII	$NHCH_2CH_2Br$	$NHCH_2CH_2Br$	$C_8H_{10}Br_2N_6O$	>250	3,55...3,93 (4H, m, CH_2); 4,06...4,33 (4H, m, CH_2); 7,11 and 9,00 (2H, s, s NH)	6,5	42 (A)
XXIV	$NHCH_2CH_2OCH(CH_3)_2 \cdot 2HBr$	$NHCH_2CH_2OCH(CH_3)_2 \cdot 2HBr$	$C_{14}H_{26}Br_2N_6O_3$	>250	2,93...3,24 (6H, d CH_3); 3,64...3,89 (4H, m, CH_2); 4,04...4,33 (4H, m, CH_2); 5,71 (2H, s, CH); 8,31 and 8,48 (2H, s, s, NH)	—	41 (C)
XXV	$NHCH_2CN$	$NHCH_2CN$	$C_8H_6N_8O$	>220 (decomp.)	4,55 (4H, s, CH_2); 8,82 (2H, s, NH)	5,4	42 (B)
XXVI	$NHCH_2CO_2Bn$	$NHCH_2CO_2Bn$	$C_{22}H_{20}N_6O_5$	160...163	4,20 (4H, s, CH_2); 5,13 (4H, s, CH_2); 6,73 (2H, s, NH); 7,33 (10H, s, C_6H_5)	7,1	57 (A)
XXVII	$NHNHCO_2C_2H_5$	$NHNHCO2C_2H_5$	$C_{10}H_{14}N_8O_5$	205...207	1,15 (6H, t, CH_3); 3,88...4,24 (4H, q, CH_2); 9,49 (2H, s, NH)	3,1	84 (D)
XXVIII	$NHCH_2C(O)C_6H_5 \cdot H_2O$	$NHCH_2C(O)C_6H_5 \cdot H_2O$	$C_{20}H_{18}N_6O_4$	237...239	5,11 (4H, s, CH_2); 7,49...8,13 (10H, m, C_6H_5); 8,89 (2H, s, NH)	—	28 (A)
XXIX	Cl	NHOBn	$C_{11}H_8ClN_5O_2$	154...155	5,22 (2H, s, CH_2); 7,27...7,51 (5H, m, C_6H_5); 11,97 (1H, s, NH)	—	66 (A)
XXX		NHOBn	$C_{15}H_{14}N_6O_4$	153...154	2,71 (2H, m, CH_2); 3,40 (1H, q, CH); 3,62 (3H, s, CH_3); 5,13 (2H, s, CH_2); 7,29...7,53 (5H, m, C_6H_5); 11,60 (1H, s, NH)	—	97 (A)
XXXI	$ON{=}CHC_6H_4NO_2$-*p*	$ON{=}CHC_6H_4NO_2$-*p*	$C_{18}H_{10}N_8O_7$	93...95	8,06...8,51 (8H, q, C_6H_4); 9,29 (2H, s, CH)	—	28 (B)

TABLE 1 (continued)

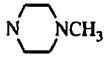
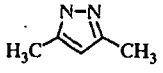
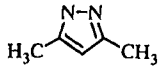
1	2	3	45	6	7	8	9
XXXII	OCH_3	OCH_3	$C_6H_6N_4O_3$	176...177	4,05 (6H, s, CH_3)	-2,1	49 (E)
XXXIII	OC_2H_5	OC_2H_5	$C_8H_{10}N_4O_3$	166...168	1,51 (3H, t, CH_3); 4,67 (2H, q, CH_2)	-2,3	85 (E)
XXXIV	$OC_6H_4\ NO_2$-*p*	$OC_6H_4\ NO_2$-*p*	$C_{16}H_8N_6O_7$	>250	7,69 (4H, d, C_6H_4); 8,44 (4H, d, C_6H_4)	-6,5	94 (E)
XXXV	SH	SH	$C_4H_2N_4OS_2$	>250	3,77 (2H, s, SH)	7,1	73 (E)
XXXVI	SC_6H_5	SC_6H_5	$C_{16}H_{10}N_4OS_2$	217...219	7,51...7,80 (10H, m, C_6H_5)	6,5	95 (A)
XXXVII			$C_{12}H_{16}N_6O$	119...122	3,47...3,71 (8H, m, CH_2); 1,75...1,98 (8H, m, CH_2)	11,8	69 (D)
XXXVIII			$C_{14}H_{20}N_6O$	162...163	1,56 (12H, s, CH_2); 3,57 (8H, s, CH_2)	11,2	68 (D)
XXXIX			$C_{12}H_{16}N_6O_3$	224...225	3,64 (16H, s, CH_2)	8,7	75 (D)
XL			$C_{14}H_{22}N_8O$	225...226	2,12 (6H, s, CH_3); 2,38 (8H, m, CH_2); 3,58 (8H, m, CH_2)	9,3	82 (D)
XLI			$C_{10}H_6N_8O$	237...240	7,13 (2H, s, CH); 8,04 (2H, s, CH); 8,82 (2H, s, CH)	7,1	58 (A)
XLII			$C_{14}H_{14}N_8O$	137...138	1,98 (6H, s, CH_3); 2,49 (6H, s, CH_3); 6,18 (2H, s, CH)	4,3	72 (A)

TABLE 1 (continued)

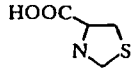
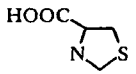
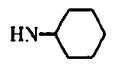
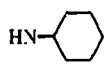
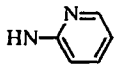
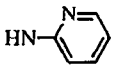
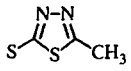
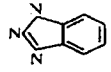
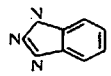
1	2	3	4	5	6	7	8
XLIII			$C_{12}H_{12}N_6O_5S_2$	225...227	2,80...3,69 (4H, m, CH_2); 4,02 (2H, m, CH); 4,37...5,24 (4H, m, CH_2)	6,2	82 (E)
XLIV			$C_8H_4N_{10}O$	210...212	8,38 (2H, s, CH); 9,55 (2H, s, CH)	2,2	61 (B)
XLV			$C_{16}H_{24}N_6O$	180...183	1,00...2,24 (20H, m, CH_2); 3,58 (2H, s, CH); 7,93 (2H, s, NH)	10,8	84 (D)
XLVI			$C_{14}H_{10}N_8O$	235...237	6,44...8,40 (8H, m, C_5H_4N); 8,40 (2H, s, NH)	6,7	13 (D)
XLVII	Cl 		$C_7H_3ClN_6OS_2$	153...155	2,86 (3H, s, CH_3)	—	48 (C)
XLVIII	Cl 		$C_{10}H_4ClN_7O$	205...207	7,67...8,12 (4H, m, C_6H_4)	1,6	41 (C)
XLIX			$C_{14}H_{12}N_8O_2$	210...212	3,33 (4H, m, CH_2); 3,60 (4H, m, CH_2); 7,44...7,89 (2H, m, C_6H_2); 8,04...8,35 (2H, m, C_6H_2)	8,7	74 (D)

TABLE 2. Characteristics of the Aniline Derivatives of 5,6-Furazano[3,4-*b*]pyrazines (L-CXIV)

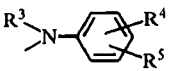
Compound	$R^1, R^2 =$ 						Molecular formula	mp, °C	PMR spectrum (DMSO-d_6), δ, ppm	Basicity of initial amine, $pK_a BH^+$ (H_2O) [12]	Yield, % (method)
	R^1			R^2							
	R^3	R^4	R^5	R^3	R^4	R^5					
1	2	3	4	5	6	7	8	9	10	11	12
L	H	H	H	H	H	H	$C_{16}H_{12}N_6O$	114...115	7,04...7,80 (10H, m, C_6H_5); 9,93 (2H, s, NH)	4,5	72 (D)
LI	H	H	2-CH_3	H	H	2-CH_3	$C_{18}H_{16}N_6O$	228...229	2,24 (6H, s, CH_3); 7,11...7,51 (8H, m, C_6H_4); 9,67 (2H, s, NH)	4,4	75 (A)
LII	H	H	3-CH_3	H	H	3-CH_3	$C_{18}H_{16}N_6O$	205...206	2,36 (6H, s, CH_3); 7,00...7,67 (8H, m, C_6H_4); 9,87 (2H, s, NH)	4,7	72 (A)
LIII	H	H	4-CH_3	H	H	4-CH_3	$C_{18}H_{16}N_6O$	203...204	2,33 (6H, s, CH_3); 7,20...7,73 (8H, m, C_6H_4); 9,87 (2H, s, NH)	5,1	82 (A)
LIV	CH_3	H	H	CH_3	H	H	$C_{18}H_{16}N_6O$	200...201	3,15 (6H, s, CH_3); 6,47...7.09 (18H, m, C_6H_5)	4,7	61 (A)
LV	H	2-CH_3	3-CH_3	H	2-CH_3	3-CH_3	$C_{20}H_{20}N_6O$	195...196	2,13 (6H, s, CH_3); 2,35 (6H, s, CH_3); 7,04...7,33 (6H, m, C_6H_3); 9,69 (2H, s, NH)	4,7	64 (A)
LVI	H	3-CH_3	4-CH_3	H	3-CH_3	4-CH_3	$C_{20}H_{20}N_6O$	230...232	2,15 (6H, s, CH_3); 2,33 (6H, s, CH_3); 7,22 and 7,58 (6H, d,d, C_6H_3); 9,84 (2H, s, NH)	5,1	79 (B)

TABLE 2 (continued)

1	2			5	6	7	8	9	10	11	12
LVII	R^1 = Cl			H	2-CH_3	6-CH_3	$C_{12}H_{10}ClN_5O$	203...204	2,07 (6H, s; CH_3); 7,11 (3H, s, C_6H_3); 9,95 (1H, s, NH)	3,9	53 (D)
LVIII	H	2-CH_3	6-CH_3	H	2-CH_3	6-CH_3	$C_{20}H_{20}N_6O$	261...262	2,22 (12H, s, CH_3); 7,22 (6H, s, C_6H_3); 9,56 (2H, s, NH)	3,9	28 (D)
LIX	H	H	3-OCH_3	H	H	3-OCH_3	$C_{18}H_{16}N_6O_3$	203...204	3,78 (6H, s, CH_3); 6,87...7,44 (8H, m, C_6H_4); 9,91 (2H, s, NH)	4,2	74 (B)
LX	H	H	4-OCH_3	H	H	4-OCH_3	$C_{18}H_{16}N_6O_3$	215...216	3,80 (6H, s, CH_3); 7,04 (4H, d, C_6H_4); 7,73 (4H, d, C_6H_4); 9,84 (2H, s, NH)	5,3	38 (B)
LXI	H	H	2-Cl	H	H	2-Cl	$C_{16}H_{10}Cl_2N_6O$	230...232	7,26...7,64 (8H, m, C_6H_4); 10, 18 and 12, 13 (2H, s, s, NH)	2,6	92 (B)
LXII	H	H	3-Cl	H	H	3-Cl	$C_{16}H_{10}Cl_2N_6O$	234...235	7,22...7,98 (8H, m, C_6H_4); 10,04 (2H, s, NH)	3,5	81 (B)
LXIII	H	H	4-Cl	H	H	4-Cl	$C_{16}H_{10}Cl_2N_6O$	237...238	7,53 and 7,87 (8H, d,d, C_6H_4); 10,00 (2H, s, NH)	4,0	96 (B)
LXIV	R^1 = Cl			H	H	4-Cl	$C_{10}H_5Cl_2N_5O$	198...199	7,44...8,18 (4H, m, C_6H_4); 10,18 and 10,33 (1H, s, s, NH)	4,0	71 (D)
LXV	R^1 = $NHCH_3$			H	H	4-Cl	$C_{11}H_9ClN_6O$	231...232	3,02 (3H, s, CH_3); 7,42 (2H, d, C_6H_4); 7,80 (2H, d, C_6H_4); 8,50 (1H, s, NH); 9,65 (1H, s, NH)	10,6	91 (D)
LXVI	R^1 = NHOH			H	H	4-Cl	$C_{10}H_7ClN_6O_2$	253...255	7,33 (2H, d, C_6H_4); 7,78 (2H, d, C_6H_4); 9,33 (1H, s, NH); 11,13 (1H, s, OH); 11,26 (1H, s, NH)	6,0	83 (D)

TABLE 2 (continued)

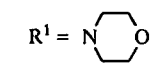
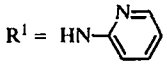
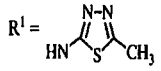
1	2	5	6	7	8	9	10	11	
LXVII		H	H	4-Cl	$C_{14}H_{13}ClN_6O_2$	204...205	3,58...3,84 (8H, m, CH_2); 7,49 (2H, d, C_6H_4); 7,84 (2H, d, C_6H_4); 9,64 (1H, s, NH)	8,7	78 (D)
LXVIII		H	H	4-Cl	$C_{15}H_{10}ClN_7O$	>250	6,40...6,60 (2H, m, C_5H_4N); 7,27...7,51 (2H, m, C_5H_4N); 7,67...8,13 (4H, m, C_6H_4); 8,15 and 8,37 (1H, s, s, NH); 8,75 and 8,93 (1H, s, s, NH)	6,7	38 (A)
LXIX		H	H	4-Cl	$C_{13}H_9ClN_8OS$	>250	2,85 (3H, s, CH_3); 7,52...8,15 (4H, m, C_6H_4); 8,90 and 9,04 (1H, s,s, NH); 9,71 (1H, d, NH)	—	32 (A)
LXX	H H 2-Br	H	H	2-Br	$C_{16}H_{10}Br_2N_6O$	250...251	7,17...7,80 (8H, m, C_6H_4); 10,15 and 12,10 (2H, s,s, NH)	2,5	71 (B)
LXXI	H H 3-Br	H	H	3-Br	$C_{16}H_{10}Br_2N_6O$	234...235	7,33...8,22 (8H, m, C_6H_4); 10,02 (2H, s, NH)	3,5	57 (B)
LXXII	H H 4-Br	H	H	4-Br	$C_{16}H_{10}Br_2N_6O$	252...253	7,60...8,11 (8H, m, C_6H_4); 10,00 (2H, s, NH)	3,8	73 (B)
LXXIII	CH_3 H 4-Cl	CH_3	H	4-Cl	$C_{18}H_{14}Cl_2N_6O$	272...274 (decomp.)	3,20 (6H, s, CH_3); 6,64 (4H, d, C_6H_4); 7,24 (4H, d, C_6H_4)	3,9	82 (B)
LXXIV	H H 4-I	H	H	4-I	$C_{16}H_{10}I_2N_6O$	256...258	7,73 (8H, m, C_6H_4); 9,96 (2H, s, NH)	3,8	88 (B)
LXXV	R^1 = Cl	H	H	2-I	$C_{10}H_5ClIN_5O$	186...187	7,13...8,00 (4H, m, C_6H_4); 10,22 (1H, s, NH)	2,5	75 (B)
LXXVI	H H 2-F	H	H	2-F	$C_{16}H_{10}F_2N_6O$	204...205	7,13...7,71 (8H, m, C_6H_4); 9,93 (2H, s, NH)	3,0	64 (B)
LXXVII	H H 3-F	H	H	3-F	$C_{16}H_{10}F_2N_6O$	240...241	6,93...7,98 (8H, m, C_6H_4); 10,11 (2H, s, NH)	5,0	92 (B)

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9	10	11	12
LXXVIII	H	H	4-F	H	H	4-F	$C_{16}H_{10}F_2N_6O$	269...270	7,22...7,80 (8H, m, C_6H_4); 9,98 (2H, s, NH)	4,6	70 (B)
LXXIX	H	2-CH_3	4-I	H	2-CH_3	4-I	$C_{18}H_{14}I_2N_6O$	>300	2,00 (6H, s, CH_3); 7,18...7,67 (6H, m, C_6H_3); 9,62 (2H, s, NH)	3,6	75 (B)
LXXX	H	3-Cl	4-Cl	H	3-Cl	4-Cl	$C_{16}H_8Cl_4N_6O$	274...276	7,76...8,18 (6H, m, C_6H_3); 10,18 (2H, s, NH)	2,0	80 (B)
LXXXI	H	H	2-NO_2	H	H	2-NO_2	$C_{16}H_{10}N_8O_5$	223...224	7,36...8,27 (8H, m, C_6H_4); 11,62 (2H, s, NH)	-0,2	67 (C)
LXXXII	H	H	3-NO_2	H	H	3-NO_2	$C_{16}H_{10}N_8O_5$	267...269	7,55...8,31 (8H, m, C_6H_4); 10,29 (2H, s, NH)	2,5	90 (B)
LXXXIII	H	H	4-NO_2	H	H	4-NO2	$C_{16}H_{10}N_8O_5$	342...343	7,82...8,44 (8H, m, C_6H_4); 10,44 (2H, s, NH)	1,0	78 (C)
LXXXIV	H	2-CH_3	5-NO_2	H	2-CH3	5-NO_2	$C_{18}H_{14}N_8O_5$	274...275	2,60 (6H, s, CH_3); 7,62...8,02 (6H, m, C_6H_3); 10,04 (2H, s, NH)	2,3	67 (B)
LXXXV	H	2-NO_2	4-CH_3	H	2-NO2	4-CH_3	C18$H_{14}N_8O_5$	>260	2,48 (6H, s, CH_3); 7,55...8,04 (6H, m, C_6H_3); 11,47 (2H, s, NH)	0,4	85 (C)
LXXXVI	H	2-OCH_3	4-NO2	H	2-OCH_3	4-NO2	$C_{18}H_{14}N_8O_7$	190...192	4,11 (6H, s, CH_3); 7,89...8,89 (6H, m, C_6H_3); 9,56 (2H, s, NH)	2,5	61 (B)
LXXXVII	H	2-NO_2	4-OCH3	H	2-NO_2	4-OCH_3	$C_{18}H_{14}N_8O_7$	>260	3,91 (6H, s, CH_3); 7,38...7,80 (6H, m, C_6H_3); 11,22 and 12,18 (2H, s, s, NH)	0,7	65 (B)
LXXXVIII	H	3-NO_2	4-Cl	H	3-NO_2	4-Cl	$C_{16}H_8Cl_2N_8O_5$	>250	7,73...8,24 (6H, m, C_6H_3); 10,44 (2H, s, NH)	1,9	81 (B)
LXXXIX	H	2-Br	4-NO_2	H	2-Br	4-NO_2	$C_{16}H_8Br_2N_8O_5$	>250	8,28...8,82 (6H, m, C_6H_3); 9,83 (2H, s, NH)	-1,0	59 (C)

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9	10	11	12
XC	H	H	4-OH	H	H	4-OH	$C_{16}H_{12}N_6O_3$	>250	6,67...7,62 (8H, m, C_6H_4); 9,42 (1H, s, OH); 9,69 (1H, s, NH)	5,5	72 (A)
XCI	H	H	3-CH_2OH	H	H	3-CH_2OH	$C_{18}H_{16}N_6O_3$	225...227	4,58 (4H, s, CH_2); 5,29 (2H, s, OH); 7,12...7,82 (8H, m, C_4H_4); 9,96 (2H, s, NH)	—	76 (B)
XCII	H	H	3-CH_2Cl	H	H	3-CH_2Cl	$C_{18}H_{14}Cl_2N_6O$	178...180	4,84 (4H, s, CH_2); 7,22...7,93 (8H, m, C_6H_4); 10,00 (2H s, NH)	—	56 (B)
XCIII	H	H	3-$CONH_2$	H	H	3-$CONH_2$	$C_{18}H_{14}N_8O_3$	>250	7,35...8,04 (8H, m, C_6H_4); 7,93...8,04 (4H, NH_2); 10,09 (2H, s, NH)	3,3	76 (B)
XCIV	H	H	3-CF_3	H	H	3-CF_3	$C_{18}H_{10}F_6N_6O$	242...243	7,53...8,22 (8H, m, C_6H_4); 10,22 (2H, s, NH)	4,0	67 (B)
XCV	H	H	3-CO_2H	H	H	3-CO_2H	$C_{18}H_{12}N_6O_5$	>260	7,49...8,44 (8H, m, C_6H_4); 9,95 (2H, s, NH)	3,1	72 (B)
XCVI	H	H	3-$CO_2C_2H_5$	H	H	3-$CO_2C_2H_5$	$C_{22}H_{20}N_6O_5$	238...240	1,36 (6H, t, CH_3); 4,36 (4H, q, CH_2); 7,51...8,40 (8H, m, C_6H_4); 10,11 (2H, s, NH)	3,6	68 (B)
XCVII	H	H	2-CO_2CH_3	H	H	2-CO_2CH_3	$C_{20}H_{16}N_6O_5$	>300	3,88 (6H, s, CH_3); 7,15...9,00 (8H, m, C_6H_4); 12,00 (2H, s, NH)	2,2	81 (B)
XCVIII	H	H	4-CO_2CH_3	H	H	4-CO2CH_3	$C_{20}H_{16}N_6O_5$	293...294	3,80 (6H, s, CH_3); 8,07 (8H, s, C_6H_4); 10,51 (2H, s, NH)	2,4	77 (B)
XCIX	H	H	2-$NHCOCH_3$	H	H	2-$NHCOCH_3$	$C_{20}H_{18}N_8O_3$	280 (decomp.)	2,07 (6H, s, CH_3); 7,29...7,93 (8H, m, C_6H_4); 9,29 and 9,64 (2H, s, s, NH); 11,80 (2H, s, NH)	3,3	68 (B)

TABLE 2 (continued)

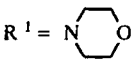
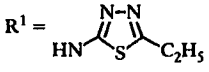
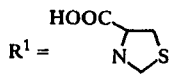
1	2	3	4	5	6	7	8	9	10	11	12
C	H	H	3-$NHCOCH_3$	H	H	3-$NHCOCH_3$	$C_{20}H_{18}N_8O_3$	>300 (decomp.)	2,07 (6H, s, CH_3); 7,33...7,60 (8H, m, C_6H_4); 8,00 (2H, s, NH); 10,20 (2H, s, NH)	3,7	91 (B)
CI	H	H	4-SO_2NH_2	H	H	4-SO_2NH_2	$C_{16}H_{14}N_8O_5S_2$	>310 (decomp.)	3,35 (4H, s, NH_2); 7,80...8,13 (8H, m, C_6H_4); 10,24 (2H, s, NH)	2,1	91 (B)
CII	H	3-OH	4-CO_2H	H	3-OH	4-CO_2H	$C_{18}H_{12}N_6O_7$	>250	6,88...8,13 (6H, m, C_6H_3); 8,45 and 8,63 (each 1H, s, s, OH); 10,27 (2H, s, NH)	1,9	63 (B)
CIII	H	2-CH_3	5-NH_2	H	2-CH_3	5-NH_2	$C_{18}H_{18}N_8O$	>250	2,07 (6H, s, CH_3); 5,00 (4H, s, NH_2); 6,77...7,09 (6H, m, C_6H_3); 9,60 (2H, s, NH)	5,3	82 (B)
CIV	R^1 = Cl			H	H	2-CO_2CH_3	$C_{12}H_8ClN_5O_3$	198...199	3,93 (3H, s, CH_3); 7,20...9,07 (4H, m, C_6H_4); 10,90 and 12,18 (each 1H, s, s, NH)	2,2	61 (B)
CV	R^1 = Cl			H	H	4-CN	$C_{11}H_5ClN_6O$	247...249	7,53 (2H, d, C_6H_4); 7,95 (2H, d, C_6H_4); 9,84 (1H, s, NH)	—	75 (D)
CVI	R^1 = N_3			H	H	4-CN	$C_{11}H_5N_9O$	>300	7,93 (2H, d, C_6H_4); 8,29 (2H, d, C_6H_4); 12,16 (1H, s, NH)	—	81 (E)
CVII	R^1 = 			H	H	4-CN	$C_{15}H_{13}N_7O_2$	128...130	3,71 (8H, s, CH_2); 7,82 (2H, d, C_6H_4); 8,04 (2H, d, C_6H_4); 9,87 (1H, s, NH)	8,7	75 (D)
CVIII	R^1 = Cl			C_2H_5	H	H	$C_{12}H_{10}ClN_5O$	107...108	1,20 (3H, t, CH_3); 4,09 (2H, q, CH_2); 7,44 (5H, s, C_6H_5)	5,6	68 (A)

TABLE 2 (continued)

1	2	5	6	7	8	9	10	11	12
CIX	$R^1 = N_3$	C_2H_5	H	H	$C_{12}H_{10}N_8O$	121...123	1,31 (3H, t, CH_3); 4,27 (2H, q, CH_2); 7,33...7,60 (5H, m, C_6H_5)	—	92 (E)
CX	H H 3-NO_2	C_6H_{13}	H	H	$C_{16}H_{18}ClN_5O$	30...32	0,82 (3H, t, CH_3); 1,27 (6H, m, CH_2); 1,65 (2H, m, CH_2); 4,00 (2H, t, CH_2); 7,25...7,63 (5H, m, C_6H_5)	5,4	72 (D)
CXI	H H 3-NO_2	C_6H_{13}	H	H	$C_{22}H_{23}N_7O_3$	127...128	0,84 (3H, t, CH_3); 1,31 (6H, m, CH_2); 1,67 (2H, m, CH_2); 4,02 (2H, t, CH_2); 7,29...7,95 (9H, m, C_6H_4); 8,42 and 8,84 (1H, s, s, NH)	2,5	68 (C)
CXII	$R^1 = Cl$	Bn	H	H	$C_{17}H_{12}ClN_5O$	107...108	5,36 (2H, s, CH_2); 7,20...7,49 (10H, m, C_6H_5)	5,1	77 (D)
CXIII	$R^1 =$ 	Bn	H	H	$C_{21}H_{18}N_8OS$	176...178	1,13 (3H, t, CH_3); 5,28 (2H, s, CH_2); 6,51 (1H, s, NH); 6,80...7,47 (12H, m, C_6H_5)	—	41 (A)
CXIV	$R^1 =$ 	H	H	4-NO_2	$C_{14}H_{11}N_7O_5S$	232...235	4,06 (2H, s, CH_2); 5,18 (1H, s, CH); 5,26 (2H, s, CH_2); 7,02...7,67 (4H, m, C_6H_4); 9,84 (1H, s, NH)	6,2	72 (E)

by the effect of the strong electron-withdrawing furazan ring, leading to strong polarization of the C–Cl bond. For this reason, the dichloro derivative (II) is more reactive in nucleophilic substitution reactions than its sulfur-containing analog — 5,6-dichloro-1,2,5-thiadiazolo[3,4-*b*]pyrazine [11].

Study of the nucleophilic substitution of the dichloro derivative (II) showed that the highest yield of the required reaction products was obtained under conditions where the employed hydrogen chloride acceptor had basicity 1-6 units higher than the amine used in the reaction, i.e., in the case of triethylamine the pK_aBH^+ value of the amines being alkylated must lie in the range of 4.5-9.5 (in water) (method A). The range for the use of N,N-diethylaniline was 0.5-5.5 (method B). The observance of these limiting conditions is essential to reduce the side hydrolysis of the dichloro derivative (II), leading to the dihydroxy derivative (I). The problem of the introduction of such low-basicity amines as 2-nitroaniline ($pK_aBH^+ = -0.2$ in water) [12] or 2-bromo-4-nitroaniline ($pK_aBH^+ = -1.0$ in water) [12] into reaction with the dichloro derivative (II) was solved by omission of the hydrogen chloride acceptor — the reaction mixture was simply fused (method C). Here, hydrogen chloride was released. The use of an excess of the highly basic amines ($pK_aBH^+ > 4$) in the reaction makes it possible to circumvent the hydrogen chloride acceptor, and in this case two equivalents of the amine are used to one chlorine atom (method D). In some cases, the compounds being alkylated were introduced in the form of sodium salts (method E).

By the successive introduction of the compounds being alkylated into the reaction it is possible to synthesize unsymmetrical derivatives. The presence of bulky substituents at the heteroatom and the reduced basicity of the nucleophile increase the yield of the monosubstitution products.

Data from investigation of the biological activity of the synthesized compounds indicate high psychotropic and herbicidal activity in the alkylamino and anilino derivatives respectively.

EXPERIMENTAL

The PMR spectra were recorded 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 a Zorbax SIL column (4.6 × 250 mm). Elemental analysis for C, H, N, and S was performed on a Carlo Erba instrument.

The elemental analyses agreed with the calculated data. The characteristics of the synthesized compounds (II-XLIX) are given in Table 1, and those of the arylamino derivatives (L-CXIV) are given in Table 2.

5,6-Dichlorofurazano[3,4-*b*]pyrazine (II). In a 4-liter flask we placed 500 ml of phosphorus oxychloride, 1040 g (4.75 moles) of phosphorus pentachloride, and 350 g (2.27 moles) of 5,6-dihydroxyfurazano[3,4-*b*]pyrazine (I) [2], and we distilled off 600 ml of phosphorus oxychloride by heating. The heat was replaced by an ice bath, and 2 liters of cold water was added with cooling to 5-10°C. The precipitate was filtered off and washed with cold water (3 × 150 ml). The moist product was crystallized from a mixture of 650 ml of acetone and 1400 ml of water. After washing with water and drying over alkali, we obtained colorless crystals of (II). Mass spectrum (m/z): 190 (M^+), 160 (M–NO), 108 ($M-C_2NCl_2$). Found %: C 25.17; N 29.03; Cl 37.72. $C_4Cl_2N_4O$. Calculated %: C 25.26; N 29.47; Cl 37.37.

Method A. 5,6-Di(N-allylamino)furazano[3,4-*b*]pyrazine (XV). We added 4.3 ml (0.057 mole) of allylamine to a stirred and cooled suspension of 5.13 g (0.027 mole) of 5,6-dichlorofurazano[3,4-*b*]pyrazine (II) in 30 ml of acetonitrile. While stirring and cooling, we added 7.93 ml (0.057 mole) of triethylamine. After 30 min the triethylamine hydrochloride was filtered off, the mother solution was evaporated, the remaining oil was dissolved in 50 ml of chloroform, and the solution was washed with water. After drying with sodium sulfate, the product (XV) was crystallized in the refrigerator. Found %: C 51.60; H 5.07; N 36.02. $C_{10}H_{12}N_6O$. Calculated %: C 51.72; H 5.21; N 36.18.

Method B. 5,6-Di(3-nitroanilino)furazano[3,4-*b*]pyrazine (LXXXII). We added 12.76 ml (0.08 mole) of N,N-diethylaniline to a mixture of 7.64 g (0.04 mole) of the dichloro derivative (II) and 10.05 g (0.08 mole) of 3-nitroaniline in 40 ml of acetonitrile. The mixture was heated to boiling and slowly cooled. The crystals were filtered off and washed with acetonitrile and water. The crude product was crystallized from a mixture of 100 ml of acetone and 30 ml of water. Found %: C 48.43; H 2.54; N 28.07. $C_{16}H_{10}N_8O_5$. Calculated %: C 48.74; H 2.56; N 28.42.

Method C. 5,6-Di(2-nitroanilino)furazano[3,4-*b*]pyrazine (LXXXI). We heated 7.64 g (0.04 mole) of the dichloro derivative (II) and 10.05 g (0.08 mole) of 2-nitroaniline at 130°C for 10 min in an open beaker with stirring. The mass was then crystallized from 120 ml of acetone. Found %: C 48.93; H 2.71; N 28.04. $C_{16}H_{10}N_8O_5$. Calculated %: C 48.74; H 2.56; N 28.42.

Method D. 5,6-Diaminofurazano[3,4-*b*]pyrazine (V). We added, with stirring, 7.64 g (0.04 mole) of the dichloro derivative (II) to a mixture of 20 ml of 25% aqueous ammonia solution and 5 ml of acetonitrile, cooled to 5-10°C. After 2 h the precipitate was filtered off, washed with water (2 × 15 ml), and dried. The diamine can be recrystallized from acetic acid or dimethylformamide. Mass spectrum (m/z): 152 (M^+), 122 (M−NO), 95 (M−NO−CHN), 68 (M−NO−CHN−CHN). Found %: C 31.50; H 2.47; N 54.97. $C_4H_4N_6O$. Calculated %: C 31.58; H 2.65; N 55.24.

Method E. 5,6-Diethoxyfurazano[3,4-*b*]pyrazine (XXXIII). While stirring, we added 0.95 g (0.005 mole) of the dichloro derivative (II) to a solution of 0.62 g (0.011 mole) of potassium hydroxide in 7 ml of ethanol, cooled to 5-10°C. After 2 h the precipitate was filtered off, washed with water (2 × 10 ml), and dried. The product was dissolved in 15 ml of hot acetone, the insoluble salts were filtered off, and 20 ml of water was added to the solution. After cooling, the crystals of (XXXIII) were filtered off. Mass spectrum (m/z): 210 (M^+), 195 ($M-CH_3$), 182 ($M-C_2H_4$), 167 ($M-C_2H_4-CH_3$), 166 ($M-C_2H_5-CH_3$), 154 ($M-C_2H_4-NO$). Found %: C 45.67; H 4.76; N 26.76. $C_8H_{10}N_4O_3$. Calculated %: C 45.71; H 4.76; N 26.65.

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