By analogous methods were prepared 1.1 g of 14 from 1.68 g NaOH, 5 g of 10, and 15 ml Me_2SO_4 in 150 ml H_2O at 60°C.

Also, 1.3 g of 15 from 0.4 g NaOH, 2 g 6, and 5 ml Me_2SO_4 in 100 ml H_2O at 40°C.

Bromination of bis(6-Methyl-4-oxypyrimidinyl-2)amine 6. To 1.7 g of a suspension of 6 in 100 ml n-butanol was added dropwise 2.3 g Br_2 until decolorization of the bromine ceased. The precipitate was filtered off, washed with n-butanol, and recrystallized from H_2O. Yield 2.5 g of 16.

Nitration of bis(6-Methyl-4-oxypyrimidinyl-2)amine 6. To a cooled solution of 2 g of 6 in 12 ml of H_2SO_4 (d 1.8) was added dropwise 7 ml of fuming HNO_3. The temperature was then raised to 50-53°C. The mixture was cooled and poured over ice. The precipitate was filtered off, washed with H_2O, and dried. Yield of 17 was 0.8 g.

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SYNTHESIS OF NOVEL FUNCTIONALIZED 1,2,4-THIADIAZOLES FROM 3,4-DIAMINOFURAZANE AND ISOTHIOCYANATES

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The addition of isothiocyanates to borylated 3,4-diaminofurazane is accompanied by a rearrangement to form compounds of the 1,2,4-thiadiazole series. The derivatives of 3-(5-amino-1,2,4-thiadiazole)carboxamidoxime were prepared and it was suggested to use these reagents in heterocyclic syntheses with 1,2,4-oxadiazole or a second 1,2,4-thiadiazole ring closure.

Keywords: thiadiazoles, furazanes, borylation, isothiocyanates.

In continuation of our investigations of the reactions of aminofurazanes with heterocumulenes [1] the reaction of 3,4-diaminofurazane (1) with isothiocyanates has been studied.

Upon reacting phenylisothiocyanate (PITC) with 3-amino-4-R-furazanes (R = Me, Ph) (3-phenylthioureido)-4-R-furazanes are formed which upon treatment with alkali solution in aqueous alcohol undergo a rearrangement to oximes of 5-anilino-3-acyl-1,2,4-thiadiazoles [2]. Analogous conversions were observed upon reaction of the same furazanes with ethoxycarbonyl isothiocyanate [3].

However, compound (1), which is less active toward electrophiles, does not react with PITC upon heating in DMF or boiling xylene. Earlier we used borylation for activation of (1) in reactions with carbodiimides and phenylisocyanate, i.e., obtaining from (1) its more reactive dialkylboryl derivatives. It is known that borylated amines and α-amino-N-heterocycles easily attack heterocumulenes at the C=N [4] or C=O [5] bond.

In this work it was established that 3,4-bis(dibutylborylamino)furazane (2), obtained upon heating of (1) with excess tributylborane, reacts with PITC or allyl isothiocyanate in DMF under mild conditions. Thus, at ~20°C the N=C=S band (~2100-2180 cm^{-1}) in the IR spectrum of the reaction mixture decreases gradually and disappears after 25-30 days and at 80-

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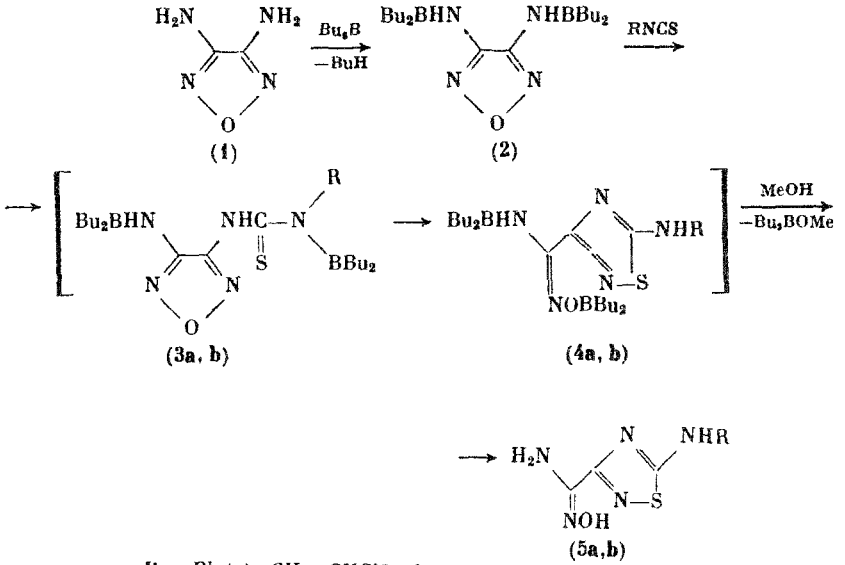
100°C after only 6-8 h. As a result, after treatment of the reaction mixture with methanol the derivatives of 3-(5-amino-1,2,4-thiadiazo)carboxamidoxime (5a, b) are obtained. These conversions can be described by scheme (1).

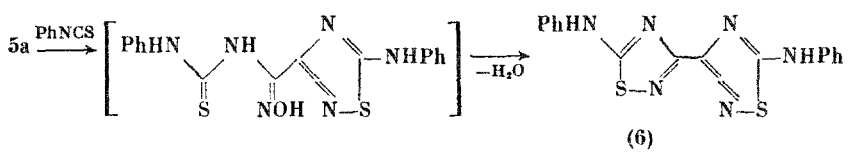


(1)

R = Ph (a), CH_2=$CHCH_2$ (b).

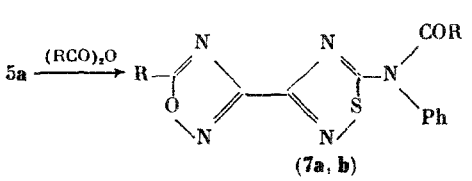
Apparently, thioureidofurazane intermediates 3a, b are formed, which were not isolated since they isomerize easily into derivatives of 1,2,4-thiadiazole 4a, b (the structure with the most probable position of the dibutylboryl groups is shown). It is interesting that rearrangement in this case proceeds in the absence of strong bases (compare with [2, 3]) and it is possible that the presence of the dibutylboryl group on the thiocarbamide fragment (3) promotes this process. Upon alcoholysis of (4a, b) compounds 5a, b are formed, the structure of which was confirmed by the the ^{13}C and ^{15}N NMR spectra. Thus, in the ^{15}N NMR spectra of the synthesized amidoximes there is one NH_2 triplet (δ = −318.5 ppm, $J_{^{15}N-H}$ 88.0 Hz) and one NH doublet {δ = −271.9 ppm, $J_{^{15}N-H}$ 93.1 Hz for (5a) and δ = −293.3 ppm, $J_{^{15}N-H}$ 93.6 Hz for (5b)}, while the corresponding 4-amino-3-thioureidofurazanes ought to give one NH_2 signal and two NH signals.

Amidoximes of the thiadiazole series can be used as reagents for heterocyclic synthesis. Thus, upon action of PITC on (4a) in DMF closing of the second thiadiazole ring takes place and bis(5-anilino-1,2,4-thiadiazol-3-yl) (6) is obtained with 62% yield. In the ^{13}C NMR spectrum of (6) one set of signals is observed for both thiadiazole rings, which confirms the symmetric structure of this compound.



(6)

Reaction of (5a) with excess carboxylic anhydride proceeds also with participation of the amidoxime group and leads to formation of a second ring, an oxadiazole ring. Simultaneously the aminothiadiazole fragment is acylated at the exocyclic nitrogen atom. By this method the derivatives of 3-(1,2,4-oxadiazole-3-yl)-1,2,4-thiadiazole (7) have been synthesized.



(7a, b)

R = Me (a), Et (b).

EXPERIMENTAL

All operations with Bu_3B were carried out in an atmosphere of dry Ar. PMR spectra were recorded on a Bruker WM-250 instrument, and ^{13}C and ^{15}N NMR spectra on a Bruker AM-300 spectrometer. Chemical shifts of the ^{13}C signals were measured relative to DMSO-d_6 solvent (δ = 39.5 ppm) and ^{15}N relative to CH_3NO_2 internal standard (δ = 0.0 ppm) without correction for diamagnetic susceptibility. The ^{15}N NMR spectra were obtained with the transfer of proton polarization by the INEPT method [6]. PMR chemical shifts were measured relative to the residual protons of the solvent (DMSO-d_6, δ = 2.5 ppm). IR spectra were recorded on a UR-20 instrument and mass spectra on a Varian MAT CH-6 spectrometer.

5-Anilino-1,2,4-thiadiazole-3-carboxamidoxime (5a). A mixture of 11.1 g (0.111 mmole) of (1) and 40.4 g (0.222 mmole) of Bu_3B was heated at 130°C until a homogeneous solution was obtained and gas evolution ceased. To the cooled mixture 40 ml of DMF and 15 g (0.111 mmole) of PITC were added and the mixture was heated at 80°C for 8 h. Then the mixture was treated with 9 ml of methanol, volatile products were distilled off under vacuum, and the residue was ground with methanol. The solid was filtered and washed with alcohol. There was obtained 15.6 g of (5a). After solvent removal from the filtrate and treatment of the residue with chloroform, there was isolated an additional 3.74 g of (5a). Total yield was 74%, mp 235-240°C (from EtOH). Found, %: C 46.07, H 3.80, N 30.30, S 13.42. $C_9H_9N_5OS$. Calculated, %: C 45.94, H 3.85, N 29.77, S 13.63. Mass spectrum, m/z: 235 (M^+). IR spectrum (in KBr, ν, cm^{-1}): 3490, 3390, 3300-2900 (OH, NH), 1660 (C=N), 1600, 1570, 940. PMR spectrum (δ, ppm): 10.95 s (OH), 10.14 s (NH), 7.65-7.00 m (Ph), 6.70 s (NH_2). ^{13}C NMR spectrum (δ, ppm): 179.9 (C^3), 163.7 t (C^3, $^3J_{NH_2-C}$ 5.7 Hz), 146.6 (C of amidoxime), 139.7, 129.2, 122.9, 117.7 (Ph).

5-Allylamino-1,2,4-thiadiazole-3-carboxamidoxime (5b) was obtained analogously to (5a). The yield was 27%, mp 202°C. Found, %: C 36.39, H 4.79, N 35.16, S 15.99. $C_6S_9N_5OS$. Calculated, %: C 36.17, H 4.55, N 35.15, S 16.09. Mass spectrum, m/z: 199 (M^+). IR spectrum (in KBr, ν, cm^{-1}): 3488, 3388, 3300-2900 (OH, NH), 1660, 1580, 940. ^{13}C NMR spectrum (δ, ppm): 182.8 (C^5), 163.2 t (C^3, $^3J_{H_2N-C}$ 4.7 Hz), 146.3, (C of amidoxime), 116.5, 133.6, 47.2 ($CH_2CH{=}CH_2$).

bis(5-Anilino-1,2,4-thiadiazol-3-yl) (6). To 2.0 g (8 mmoles) of (5a) in 70 ml of DMF 1.15 g (8 mmoles) of PITC was added and the mixture was heated for 5 h at 100-110°C. The solvent was then removed under vacuum and the residue was treated with chloroform. The product was filtered and washed with chloroform. There was obtained 1.85 g (62%) of (6). After twice precipitating with water from DMF the mp was 242-244°C (with decomposition). Found, %: C 54.33, H 3.43, N 23.79, S 18.18. $C_{16}N_{12}N_6S_2$. Calculated, %: C 54.56, H 3.43, N 23.82, S 18.18. Mass spectrum, m/z: 352 (M^+). IR spectrum (in KBr, ν, cm^{-1}): 1550, 1440, 1210. ^{13}C NMR spectrum (δ, ppm): 179.3 (C^5, $C^{5'}$), 162.7 (C^3, $C^{3'}$), 139.7, 129.3, 123.0, 117.7 (2Ph).

5-(N-Acetylanilino)-3-(5-methyl-1,2,4-oxadiazol-3-yl)-1,2,4-thiadiazole (7a). A mixture of 2.03 g (8 mmoles) of (7a) and 20 ml of acetic anhydride was boiled for 1 h, then evaporated under vacuum until dry, and the solid residue was washed with alcohol. There was obtained 1.82 g (70%) of (7a), mp 215-218°C (from alcohol). Found, %: C 51.85, H 3.93, N 23.35, S 10.39. $C_{13}H_{11}N_5O_2S$. Calculated, %: C 51.81, H 3.68, N 23.24, S 10.64. Mass spectrum, m/z: 259 [$M^+ - (CH_2{=}C{=}O)$]. IR spectrum (in KBr, ν, cm^{-1}): 3300 (NH), 1680 (C=O), 1590 (C=N).

5-(N-Propionylanilino)-3-(5-ethyl-1,2,4-oxadiazol-3-yl)-1,2,4-thiadiazole (7b) was obtained analogously to (7a). The yield was 95%, mp 174-176°C (from alcohol). Found, %: C 54.76, H 4.63, N 21.32, S 9.57. $C_{15}H_{15}N_5O_2S$. Calculated, %: C 54.69, H 4.59, N 21.26, S 9.73. IR spectrum (in $CHCl_3$, ν, cm^{-1}): 1683 (C=O), 1585 (C=N). PMR spectrum (δ, ppm): 7.67-7.60 m (Ph), 2.96 q and 2.32 q ($2CH_2$), 1.28 t and 1.05 t ($2CH_3$). ^{13}C NMR (δ, ppm): 177.6, 163.1 (C^5 and C^3 of thiadiazole), 181.7, 155.6 (C^5 and C^3 of oxadiazole), 137.9, 130.0, 129.7, 128.7 (Ph), 28.0, 19.5, 10.3, 8.2 (2Et).

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