# ANOMALOUS REARRANGEMENT OF 1,2,3-THIADIAZOLES TO 1,2,3-TRIAZOLES

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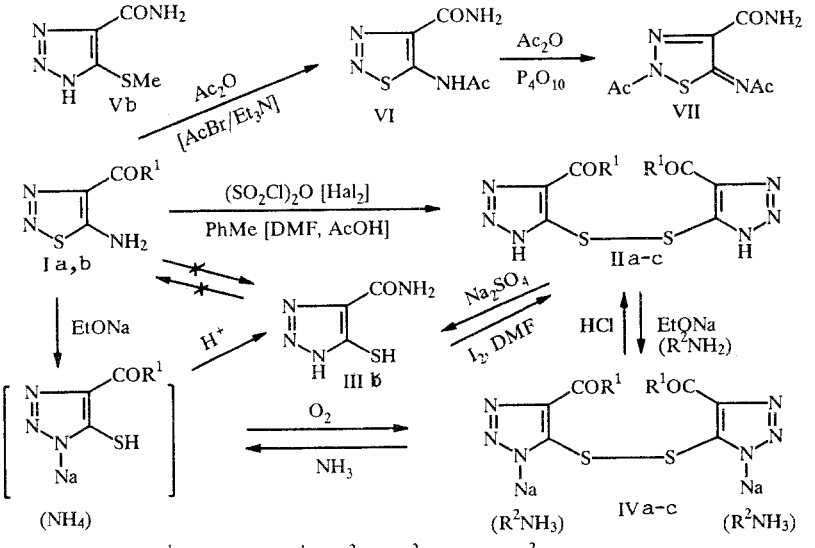
*The rearrangement of 5-amino-1,2,3-thiadiazoles under the influence of halogen-containing oxidizing to bis(triazolyl) disulfides was observed. Ammonia reduces the disulfides obtained to 5-mercapto-1,2,3-triazoles.*

The brief passage of pyrosulfuryl chloride into a refluxing solution of ethyl 5-amino-1,2,3-thiadiazole-4-carboxylate (Ia) in toluene leads to bis(4-ethoxycarbonyl-1,2,3-triazol-5-yl) disulfide (IIa). A similar result is obtained when ester Ia and 5-amino-1,2,3-thiadiazole-4-carboxylic acid amide (Ib) are treated with chlorine in toluene, bromine in hot acetic acid, and iodine in DMF. However, amine Ia does not react with hydrogen peroxide on prolonged refluxing in a buffer solution with pH 7.62. Structure of disulfide IIa was reliably confirmed by physicochemical and chemical methods and by alternative synthesis.

A signal of a molecular ion was not detected in the mass spectrum of amide IIb; this is evidently a consequence of the fact that it does not have a distinct melting point and decomposes at ~280°C. Compound IIb was also therefore obtained by amidation of ester IIa by the action of ammonium hydroxide; a side product of the process is 5-mercapto-1,2,3-triazole-4-carboxamide (IIIb). On the other hand, mercaptotriazole IIIb is the only compound formed when disulfides IIa, b are refluxed in ammonium hydroxide in the absence of oxygen.

The observed transformation might have been interpreted as oxidation of mercaptotriazoles III, which exist in equilibrium with thiadiazoles I, to give thermodynamically stable disulfides II. It is known, however, that the recyclization of 5-amino-1,2,3-thiadiazoles to 5-mercapto-1,23-triazoles occurs only in a basic medium [1]; in the presence of acidic reagents one observes the reverse process [2]. Moreover, we have that under model conditions — in the case of a suspension of 5-mercapto-1,2,3-triazole-4-carboxamide (IIIb) in toluene and in toluene with the passage into the system of hydrogen chloride — changes are not observed in the course of 10 h; even trace amounts of amine Ib are not observed. The anhydride also remains unchanged. Thus aminothiadiazoles I do not exist in equilibrium with mercaptotriazoles III either in neutral or in acidic media, and, consequently, mercaptotriazoles III are not intermediates in the reaction that we observed.




I, II, IVa $R^1$ = OEt; b $R^1 = R^2NH$, $R^2$ = H; c $R^2 = NH_2$

Ural Polytechnical Institute, Ekaterinburg, 620002 Russia. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 840-846, June, 1993. Original article submitted May 6, 1993.



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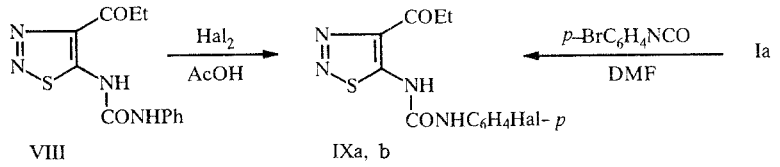
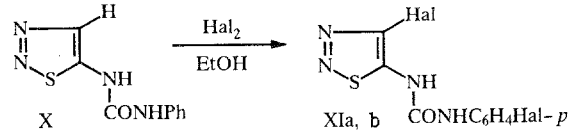
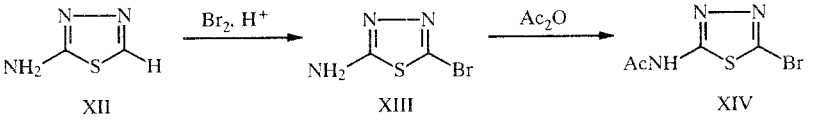


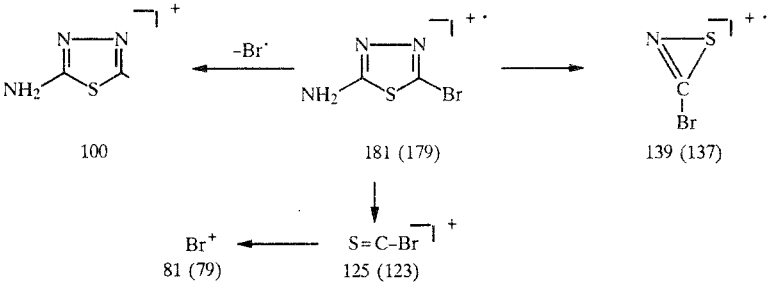

IXa Hal = Cl; IX b Hal = Br, XIa Hal = Cl; XI b Hal = Br

Moreover, neither acetamidothiadiazole VI nor diacetyl derivative VII reacts with chlorine and bromine in ethanol. Ethyl 5-(3-phenylureido)-1,2,3-thiadiazole-4-carboxylate (VIII) in acetic acid undergoes electrophilic aromatic substitution with chlorine and bromine to form the corresponding 4-halophenyl derivatives IXa, b. The structure of bromo derivative IXb was confirmed by alternative synthesis from amine Ia. When 4-unsubstituted thiadiazole X is subjected to this reaction, the 1,2,3-thiadiazole ring also is halogenated; an iodo derivative is not formed under these conditions. The isotope distributions in the molecular and $[M^+ - N_2]$ ions detected in the mass spectra of dihalo derivatives XIa, b correspond to the structures assigned to them. The halogen atoms in XIa, b are not replaced when the compounds are refluxed in concentrated ammonium hydroxide.




It is known that the isomeric aminothiadiazole, 2-amino-1,3,4-thiadiazole (XII), reacts with bromine to give 2-amino-5-bromo-1,3,4-thiadiazole (XIII); a virtually equimolar amount of bromine was used in this process [3]. After treatment of amine XII with a 1.5-fold excess of bromine, we found that, in this case, bromo-1,3,4-thiadiazole XIII is the only reaction product. 2-Amino-5-methyl-1,3,4-thiadiazole does not undergo a similar reaction.

The fragmentation of the molecular ion from bromo-1,3,4-thiadiazole XIII is in agreement with the structure assigned to it. However, its melting point [178-180°C (dec.)] proved to be 20°C lower than that determined by Pathgeb [3]. We also obtained XIII by the method described in [3], and it had the same melting point. Nevertheless, XIII was additionally characterized in the form of 2-acetamido derivative XIV.




Thus 2-amino-1,3,4-thiadiazoles and N-carbonyl-substituted 5-amino-1,2,3-thiadiazoles doe not undergo the transformation that we noted in the case of 5-amino-1,2,3-thiadiazoles. This correlates with the hindered (or unrealized) Dimroth rearrangement of the former compounds [4]. In addition to this, we obtained evidence in favor of the fact that our observed conversion of 5-amino-1,2,3-thiadiazoles to bis(1,2,3-triazol-5-yl) disulfides by the action of chlorine(bromine)-

TABLE 1. NMR Spectra of the Synthesized Compounds

| Compound | | Chemical, δ, ppm |
|---|---|---|
| IIa | $^1H$ | 1,31 (6H, t, $J$ = 7,055, $CH_3$); 4,328 (2H, j, $J$ = 7,073, $CH_2$) |
| | $^{13}C$ | 13,995 ($CH_3$); 61,189 ($CH_2$); 135,465 ($C_{(4)}$); 142,534 ($C_{(5)}$); 159,759 (C=O) |
| IIc | $^1H$ | 2,79 (2H, d $J$ = 4,5, NHN$\underline{H}_2$); 8,3...8,7 (1H, m N$\underline{H}$N$H_2$) |
| VI | $^1H$ | 2,39 (3H, s $CH_3$); 7,97 (1H, s 4-CON$\underline{H}$); 8,27 (1H, s., 4-CON$\underline{H}$); 11,50 (1H, s, 5-N$\underline{H}$Ac) |
| VII | $^1H$ | 2,40 (3H, s $CH_3$); 2,45 (3H, s, $CH_3$); 10,92 (1H, br.s , CON$\underline{H}$); 11,68 (1H, br.s CON$\underline{H}$) ( $D_2O$ + NaOD: 1,96 (3H, s $CH_3$); 2,52 (3H, s $CH_3$)) |
| IXa | $^1H$ | 1,41 (3H, t, $J$ = 7,2, $CH_3$); 4,49 (2H, q, $J$ = 7,1, $CH_2$); 7,34; 7,43; 7,49; 7,58 (4H, AB, $C_6H_4$); 10,70 (1H, s, NH); 10,80 (1H, s, NH) |
| IXb | $^1H$ | 1,42 (3H, t, $J$ = 6,9, $CH_3$); 4,50 (2H, j, $J$ = 7,2, $CH_2$); 7,50 (4H, s, $C_6H_4$); 10,67 (1H, br.s, NH); 10,78 (1H, br.s, NH) |
| XIa | $^1H$ | 7,31 (5H, br.s, $C_6H_5$); 9,25 (1H, d, $J$ = 6,0, NH); 10,30 (1H, s, NH) |
| XIb | $^1H$ | 7,48 (5H, br.s, $C_6H_5$); 9,55 (1H, d, $J$ = 6,0, NH); 10,23 (1H, s, NH) |
| XIII | $^1H$ | 7,47 (2H, br.s, $NH_2$) |
| XIV | $^1H$ | 2,22 (3H, s, $CH_3$); 12,7 (1H, br.s, N$\underline{H}$) |

containing oxidizing agents in neutral and acidic media is not a variation of the Dimroth reaction. A study of the mechanism of this reaction and its extension to other subjects will constitute the subject of subsequent studies.

## EXPERIMENTAL

The PMR spectra of solutions of the compounds in $d_6$-DMSO were recorded with Perkin–Elmer R12B (60 MHz), Bruker WP-80 (80.13 MHz), and Tesla 567A (100 MHz) spectrometers with hexamethyldisiloxane (HMDS) as the internal standard. The $^{13}C$ NMR spectrum of IIa was obtained with a Bruker WP-80 spectrometer (80.13 MHz) under the same conditions. The IR spectra of KBr pellets were recorded with an IR-75 spectrometer. The mass spectra were obtained with a Varian MAT 311A spectrometer; the accelerating voltage was 3 kV, and the electron-ionization energy was 70 eV. The progress of the reactions and the purity of the compounds were monitored by TLC on Silufol UV-254 plates in chloroform, chloroform–ethanol (9:1), chloroform–ethanol–ammonium hydroxide (25%) (15:8:1) systems. The mercapto compounds were additionally identified from the rapidly developing blue coloration of the chromatographic spot or a sample of the solution with a solution of $FeCl_3$ in dilute hydrochloric acid. The melting points were not corrected.

The results of elementary analysis for C, N, and H for all of the synthesized compounds were in agreement with the calculated values.

The spectral characteristics of the substances are presented in Tables 1-3.

**Bis(4-ethoxycarbonyl-1,2,3-triazol-5-yl) Disulfide (IIa). A.** Pyrosulfuryl chloride or chlorine was passed into a refluxing solution of 2.305 g (13.3 mmole) of amine Ia in 16 ml of toluene. The precipitate that began to form after 10 min subsequently increased the volume of the reaction mixture by a factor of ~1/3. After 30 min, the reaction mixture was cooled, washed with cold toluene and hexane, and dried to give 1.85 g (83%) of IIa. Crystallization from ethanol–water using charcoal gave 1.750 g (76%) of colorless, finely crystalline disulfide with mp 171-174°C (dec.).

**B.** A 1.549-g (8.953 mmole) sample of amine Ia was added to a solution of 206 mg (8.953 mmole) of sodium in 10 ml of absolute ethanol, and air was then bubbled into the resulting solution for 10 h. The reaction mixture was then evaporated in vacuo to dryness, and the residue was reprecipitated from solution in ethanol by adding ether to give 1.140 g (62%) of bis(4-ethoxycarbonyl-1,2,3-triazol-5-yl) disulfide disodium salt (IVa) with mp ~180°°C (dec.). Salt IVa was dissolved in the minimum amount of water, and the solution was acidified to pH 2 with sulfuric acid. The precipitate was removed by filtration, washed with water, and dried to give 522 mg (34%) of disulfide IIa. With respect to the results of TLC, the melting point, and the IR spectrum, the compound obtained matched up with disulfide IIa synthesized by method A.

**Bis(4-ethoxycarbonyl-1,2,3-triazol-5-yl) Disulfide (IVa). B.** A solution of 36 mg (1.581 mmole) of sodium in 2 ml of ethanol was added to a solution of 272 mg (0.791 mmole) of disulfide IIa in 6 ml of ethanol, and the resulting solution had pH ~7. Dry ether was added to the solution, and the mixture was allowed to stand overnight. The solvents were then removed by decantation, the precipitate was washed with ether, the mixture was again decanted, and the residue was dried to

TABLE 2. IR Spectra of the Synthesized Compounds

| Compound | ν, $cm^{-1}$ |
|---|---|
| IIa | 780, 1080, 1220, 1270, 1470, 1495, 1700, 1720 (C=O), 2870, 2930, 2980, 3120 |
| IIb | 880, 980, 1090, 1110, 1215, 1320, 1370, 1480, 1520, 1600, 1670 (C=O), 2630, 2750, 2810, 2970, 3180, 3215, 3275, 3320, 3380, 3410, 3510 |
| IIc | 570, 690, 770, 980, 1080, 1240, 1290, 1570, 1620, 1700 (C=O), 3440 |
| IVa | 780, 830, 995, 1090, 1250, 1290, 1320, 1380, 1450, 1470, 1655, 1685 (C=O), 2925, 3080, 3645 |
| VI | 655, 735, 785, 1030, 1075, 1210, 1260, 1315, 1400, 1460, 1520, 1650 (C=O), 3220, 3425 |
| VII | 730, 770, 860, 1015, 1035, 1160, 1220, 1260, 1290, 1360, 1410, 1520, 1680 (C=O), 1730 (C=O), 3260 |
| IXa | 690, 775, 810, 830, 1020, 1090, 1170, 1210, 1300, 1430, 1485, 1520, 1590, 1680 (C=O), 2970, 3170, 3330 |
| IXb | 770, 820, 845, 1030, 1170, 1220, 1305, 1405, 1435, 1525, 1585, 1670 (C=O), 2960, 3160, 3330 |
| XIa | 1200, 1245, 1305, 1435, 1485, 1540, 1560, 1610, 1690 (C=O), 3130, 3275 |
| XIb | 690, 750, 820, 860, 930, 1030, 1070, 1300, 1310, 1350, 1400, 1490, 1540, 1620, 1700 (C=O), 2970, 3130, 3270 |
| XIII | 540, 600, 670, 101, 1115, 1310, 1360, 1420, 1500, 1590, 1630, 3090, 3215, 3330 |
| XIV | 660, 780, 960, 1020, 1230, 1310, 1370, 1410, 1560, 1690 (C=O), 2770, 2880, 3010, 3130 |

give 294 mg (90%) of disodium salt IVa. According to the IR spectrum, the sample obtained was identical to salt IVa, synthesized by method A, and can be used for the preparation of disulfide IIa, just as in method B.

**Bis(4-carbamoyl-1,2,3-triazol-5-yl) Disulfide (IIb). A.** Chlorine was passed into a refluxing suspension of 2.126 g (14.8 mmole) of aminothiadiazole Ib in 50 ml of toluene; a new precipitate began to form immediately. After bubbling in the chlorine for 15 min, the precipitate was removed by filtration, washed on the filter with petroleum ether, and dried. It was then washed on the filter with boiling water (2 × 25 ml) and reprecipitated from aqueous NaOH (pH ~8) by the addition of hydrochloric acid (pH ~3) to give 832 mg (39%) of light-gray, powdered disulfide IIb, which decomposed at ~280°C.

**B.** A 3.6-ml (70 mmole) sample of bromine was added to a suspension of 2.02 (14.0 mmole) amine Ib in 25 ml of acetic acid, and the reaction mixture warmed up spontaneously. After 20 min, the excess bromine and solvent were evaporated at atmospheric pressure to the point of almost dryness. The residue was cooled, removed by filtration, and reprecipitated from ammonium hydroxide (pH ~9) by the addition of hydrochloric acid to give 1.69 g (84%) of disulfide IIb.

**C.** Iodine was added in small portions with stirring to a solution of 638 mg (4.43 mmole) of mercaptotriazole IIIb in 10 ml of DMF until a positive test for the mercapto group [11] was no longer obtained. At the end of the reaction, the solution had a light-brown color and pH ~1-2. Precipitation was effect by the addition of 40 ml of water, the suspension was cooled, and the precipitate was removed by filtration, washed on the filter with water (2 × 20 ml), and dried to give 600 mg (95%) of disulfide IIb. Reprecipitation from aqueous alkali by the addition of hydrochloric acid gave 530 mg (84%) of an analytically pure sample of disulfide IIb.

**D.** A 2.24-g (17.24 mmole) sample of iodine was added to a solution of 1.271 mg (8.83 mmole) of amine Ib in 3.5 ml of DMF, and the solution was allowed to stand for 24 h until the starting compound vanished (TLC monitoring). Water (100 ml) was then added, and the suspension was refluxed until it was colorless and cooled. The precipitate was removed by filtration and washed on the filter with boiling water (2 × 20 ml) and dried to give 537 mg (43%) of disulfide IIb, which was then reprecipitated. The yield of an analytically pure sample was 496 mg (40%).

**E.** A mixture of 1.028 g (3.0 mmole) of disulfide IIa and 20 ml of 25% ammonium hydroxide was heated in a sealed ampul (with a volume of ~150 ml) on a boiling-water bath for 24 h, after which the reaction solution was evaporated to 1/3 of its original volume, and the concentrate was acidified to pH 1 with hydrochloric acid. The precipitate was removed by filtration and washed successively on the filter with 25 ml of water and boiling ethanol (5 × 20 ml). The alcohol extract was concentrated to a volume of 10 ml, and 50 ml of ether was added to precipitate 90 mg (11%) of 5-mercapto-1,2,3-triazole-4-carboxamide, the melting point and IR spectrum of which were identical to those of a genuine sample [1]. Reprecipitation from ammonium hydroxide by the addition of dilute (1:2) sulfuric acid gave 459 mg (57%) of amide IIb.

The samples obtained by methods A-E had the same TLC values, melting points, and IR spectra.

**5-Mercapto-1,2,3-triazole-4-carboxamide (IIIb). A.** A suspension of 375 mg (1.31 mmole) of disulfide IIb in a solution of 597 mg (2.51 mmole) of sodium dithionate in 7 ml of water was refluxed with stirring for 3 min. The resulting solution was acidified to pH 2 with dilute hydrochloric acid, during which a precipitate formed. The suspension was evaporated

TABLE 3. Mass Spectra of the Synthesized Compounds

| Compound | m/z ($I_{rel}$, %) |
|---|---|
| IIa | 344 ($M^+$, 29,6); 205 (42,5); 173 (28,5); 159 (30,2); 145 (29,5); 144 (26,3); 129 (18,3); 128 (26,0); 127 (100,0) |
| IIb | 178 (4,2); 145 (5,5); 144 (89,4); 129 (4,6); 128 (10,5); 127 (100,0); 99 (6,3); 89 (8,2) |
| IIc | 162 (12); 160 (12); 159 (12); 158 ($M^{2+}$ + $M_{1/2}^{2+}$, 98); 157 (18); 140 (15); 128 (36); 127 (32); 113 (22); 73 (29); 72 (18); 70 (18); 68 (16); 64 (21); 59 (18); 58 (100); 57 (46); 56 (15) |
| VI | 186 ($M^+$, 16,7); 158 ($M^+$—$N_2$, 100); 141 (17,5); 117 (78,0); 116 (76,2); 110 (13,2); 100 (15,1); 99 (24,5); 91 (15,0); 89 (43,0); 88 (12,9); 85 (34,1) |
| VII | 228 ($M^+$, 41,0); 200 ($M^+$—CO, 13,9); 159 (17,0); 158 (100,0); 142 (14,8); 131 (86,9); 117 (91,5); 116 (37,0); 103 (26,0); 100 (24,2); 99 (35,3); 88 (17,1) |
| XIa | 288 : 290 : 292 ($M^+$, 19,8 : 11,5 ; 2,7); 260 : 262 : 264 ($M^+$ - 28, 10,4 : 6,4 ; 1,5); 154 (33,9); 153 (45,7); 128 (22,9); 126 (65,3); 111 (37,1); 109 (30,5); 107 (100,0); 99 (27,3) |
| XIb | 376 : 378 : 380 ($M^+$, 5,0 : 10,3 : 4,8); 348 : 350 : 352 ($M^+$—$N_2$, 3,2 : 5,5 : 2,8); 300 (16,0); 298 (16,8); 272 (12,4); 270 (13,4); 200 (12,1); 199 (21,0); 198 (11,7); 197 (18,8); 191 (10,2); 190 (11,2); 181 (8,6); 179 (8,5); 173 (7,0); 172 (22,3); 171 (9,4); 170 (23,9); 157 (13,1); 155 (16,0); 153 (100), 151 (86,6); 147 (6,2); 137 (7,2); 135 (6,9); 125 (11,0); 123 (11,1); 121 (9,4); 120 (88,2); 119 (49,3); 104 (6,0); 93 (20,5); 92 (95,6); 91 (48,2); 90 (25,2); 82 (10,4); 81 (6,2); 80 (11,0); 79 (6,8) |
| XIII | 179 : 181 ($M^+$, 96,0 : 90,8); 139 (8,7); 137 (7,6); 125 (17,6); 123 (17,7); 100 ($M^+$—Br, 100); 92 (7,6); 81 (11,9); 79 (11,9) |
| XIV | 225 : 223 : 221 ($M^+$, 2,6 : 26,6 : 25,6); 195 (3,0); 193 (2,9); 183 : 181 : 179 (6,7 : 100 : 98,6); 125 (10,7); 123 (10,4); 100 (14,7); 74 (18,4) |

to dryness and evaporated once again with ethanol. Extraction of the residue with boiling ethanol (3 × 20 ml) gave mercaptotriazole IIIb, which proved to be identical, by repeated TLC, to a sample obtained by an independent method [1]; the extract also gave a positive test for a mercapto group. From a solution of IIIb we obtained, by the method described in [11], 243 mg (59%) of 5-methylmercapto-1,2,3-triazole-4-carboxamide (Vb), which was a completely authentic sample with a genuinely known sample [1].

**B.** Nitrogen or ammonia was passed into an ampul containing a solution of 4.36 mmole of disulfide IIa or IIb in 30 ml of 25% ammonium hydroxide for 5 min, after which the ampul was sealed and heated for 20 h at 120°C. The solution was then evaporated to a volume of 10 ml and filtered. The filtrate was acidified with dilute (1:1) sulfuric acid to pH 1. The suspension was cooled to 0-5°C, the precipitate was removed by filtration, washed on the filter with 10 ml of ice water, and dried. With respect to its melting point and the TLC data, the mercaptotriazole IIIb was identical to a sample with a genuinely known structure [1] and had a mass of 712 mg (57%).

**Bis(4-hydrazinocarbonyl-1,2,3-triazol-5-yl) Disulfide (IIc).** A solution of 800 mg (2.33 mmole) of ester IIa in a mixture of 4.8 ml of 25% (23 mmole) of aqueous hydrazine hydrate and 5 ml of water was heated in a sealed ampul for 16 h at 120°C, after which the hot solution was acidified to pH 1 with dilute (1:2) sulfuric acid and cooled. The precipitate was removed by filtration, washed on the filter with water (2 × ml), and dried to give 363 mg (50%) of hydrazide IIa. Reprecipitation from ammonium hydroxide (pH 8-9) by the addition of dilute (1:2) sulfuric acid gave 302 mg (41%) of colorless crystals of the analytically pure disulfide IIc with mp 241-242°C (dec.).

**5-Acetamido-1,2,3-thiadiazole-4-carboxamide (VI). A.** A suspension of 3.129 g (21.73 mmole) of aminothiadiazole Ib in 20 ml of acetic anhydride was heated with stirring for 10 min at 80-100°C, after which the mixture was cooled to 0°C. The precipitate was removed by filtration, washed on the filter with ether (2 × 5 ml), and dried to give 2.323 g (58%) of acetamido derivative VI. Crystallization from DMF—water (the larger part of which was water) or from ethanol gave 2.09 g (52%) of pure VI in the form of colorless needles with mp 232-234°C (sublimation).

**B.** A 3.52-ml (24.13 mmole) sample of triethylamine was added to a suspension of 3.159 g (21.94 mmole) of amine Ib in 50 ml of acetone, after which 1.78 ml (24.13 mmole) of acetyl bromide was added to the mixture with stirring. The precipitate was removed by filtration, washed with water (2 × 15 ml), and dried to give 1.868 g (46%) of acetamido derivative VI. Crystallization from 300 ml of water gave 1.531 g (38%) of light-yellow needles of VI, which, according to the TLC and IR-spectral data, were in agreement with the data for the sample obtained by method A.

**2-Acetyl-5-acetylimino-$\Delta^3$-1,2,3-thiadiazoline-4-carboxamide (VII).** The suspension obtained in the synthesis of acetamido derivative VI by method A was diluted with heating with acetic anhydride until it dissolved, ~2 g of $P_4O_{10}$ was added, and the mixture was refluxed for 6-10 min, after which acetic anhydride was added with refluxing until the solid phase dissolved. Activated charcoal was added, and the mixture was filtered. The filtrate was cooled, and the precipitate was

removed by filtration and washed with cold ethanol and ether and dried to give 1.174 g (48%) of light-brown plates. Crystallization from acetonitrile, washing with cold ethanol and ether, and drying gave 840 mg (35%) of light-yellow platelet crystals of diacetyl derivative VII with mp 216-217°C.

**Ethyl [3-(4-Halophenyl)ureido]-1,2,3-thiadiazole-4-carboxylates IXa, b. A.** Chlorine was passed into a refluxing solution of 1.311 g (4.49 mmole) of phenylureidothiazole VIII in 60 ml of acetic acid for 30 min, or 0.690 ml (13.5 mmole) of bromine was added. The solution was cooled to −20°C and filtered, and the solid material was washed with ether and dried on the filter. It was then washed with boiling water (2 × 30 ml) and dried to give 711 mg (52%) of colorless fluffy crystals of chloro derivative IXa or 1067 mg (41%) of IXa and 833 mg (50%) of IXb, respectively, with mp 275-276°C (dec., IXa) and 283°C (dec., IXb).

**B.** A 2.8-ml (2.0) sample of triethylamine was added to a solution of 5.84 g (20.0 mmole) amine Ia in 30 ml of DMF, and the mixture was cooled to 0°C, and 20 mmole of 4-bromophenyl isocyanate was added dropwise with stirring at this temperature. The suspension was then stirred at this temperature for 2 h, and the precipitate was removed by filtration, washed on the filter with boiling water (2 × 50 ml), and crystallized from DMF to give 7.20 g (97%) of a compound, which, with respect to its IR spectrum and melting point, was identical to ureido derivative IXb obtained by method A.

**5-[3-(4-Halophenyl)ureido]-4-halo-1,2,3-thiadiazoles XIa, b.** Chlorine was passed for 10 min into a suspension of 2.549 g (11.59 mmole) of 5-(3-phenylureido)-1,2,3-thiadiazole (X) in 70 ml of refluxing ethanol, or else 3.5 ml (67.9 mmole) of bromine was added. A copious precipitate began to form immediately. After bubbling in chlorine for 10 min (or refluxing after the addition of bromine), the suspension was cooled to 0°C, the precipitate was removed by filtration, washed on the filter with cold ethanol (2 × 30 ml) and ether, and dried to give 2.218 g (66%) of colorless dichloro derivative XIa or 2.315 g (48%) of fine, light-pink, fluffy crystals of dibromothiadiazole XIIb. The latter compound was crystallized from a large amount of ethanol in the form of colorless fluffy crystals. Crystallization from DMF−water gave 822 mg (25%) of an analytically pure sample of XIa or 2.206 g (46%) of XIb [mp 271-274°C (dec., XIa) and mp 253-254°C (dec., XIb).

**2-Acetamido-5-bromo-1,3,4-thiadiazole (XIV).** A 410-mg (2.28 mmole) sample of amine XIII was added to 3 ml of acetic anhydride, and the mixture was heated gently on a hot-water bath, during which we observed the formation of a precipitate. The suspension was cooled, and the precipitate was removed by filtration, washed on the filter (2 × 10 ml), and dried to give 488 mg (89%) of colorless needles of acetamido derivative XII. Crystallization from acetonitrile and washing with a small amount of ether gave 390 mg (77%) of pure XIV in the form of fine, colorless crystals with mp 228-229°C (dec.).

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