The reaction of 2-amino-7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]-pyrimidine with carbon disulfide and alkylation of its products

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In the reaction with carbon disulfide, 2-amino-7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine (**1**) forms the alkaline salts of substituted dithiocarbamic or iminodithiocarbonic acids depending on the molar ratio between **1**, CS_2, and the alkali. The alkylation of these salts leads to the esters of *N*-(7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine-2-yl)dithiocarbamic (**2**) and diesters of (7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine-2-yl)iminodithiocarbonic acids (**3**). The synthesis of asymmetric diesters **3** may be fulfilled based on monoesters **2**.

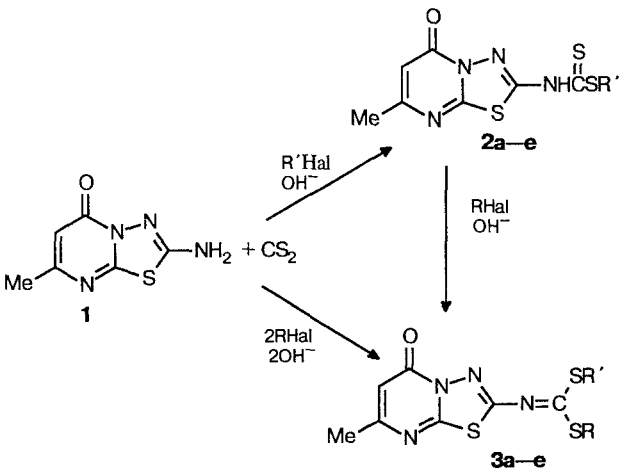
Key words: carbon disulfide, alkylation, 2-amino-7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine, esters of *N*-(7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine-2-yl)dithiocarbamic acid, diesters of (7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine-2-yl)iminodithiocarbonic acid.

Recently, the chemistry of the esters of dithiocarbamic acid and diesters of iminodithiocarbonic acid has become of considerable interest due to the high reactivity of these compounds. They have proved to be very interesting synthons, in particular, for the construction of heterocyclic systems under the conditions of nucleophilic substitution.[1—4] Although there are a number of reports[4—6] concerning the above-mentioned 2-amino-1,3,4-thiadiazol derivatives, no information about the condensed 2-amino-1,3,4-thiadiazol esters of dithiocarbamic acid and diesters of iminodithiocarbonic acid is found in literature.

In the present work, we report the results of investigating the reaction of 2-amino-7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine (**1**) with carbon disulfide. This amine, depending on the molar ratio between CS_2 and alkali, forms (at room temperature) the alkaline salts of the corresponding substituted dithiocarbamic or iminodithiocarbonic acid. Without isolation from the reaction medium, these salts may be alkylated to form the corresponding esters of *N*-(7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine-2-yl)dithiocarbamic (**2a—e**) and diesters of (7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine-2-yl)iminodithiocarbonic acids (**3a—e,d**). Compounds **2a—e** can be also converted to **2a—g** in an alkaline medium. It turned out that the asymmetric esters, *e.g.*, **3f**, may be obtained by this method. The properties of compounds **2a—e** and **3a—g** are given in Table 1.

The IR and ^1H NMR spectral data and the elemental analysis confirm the structure of the obtained esters **2a—e** and **3a—g**. The spectral characteristics of these compounds are given in Table 2.

However, it was reported[7] that propargyl esters of dithiocarbamic acids based on aliphatic primary amines are capable of intramolecular cyclization to lead to the formation of iminodithiolanes **B** through the intermediates **A**. In the case of compound **1d**, no products generated by intramolecular cyclization were determined. This fact is confirmed by the IR spectral data and the



R = Me (**2a**), $PhCH_2$ (**2b**), $CH_2{=}CHCH_2$ (**2c**), $CH{\equiv}CCH_2$ (**2d**), CH_2COOH (**2e**), R = R′ = Me (**3a**), $PhCH_2$ (**3b**), $CH_2{=}CHCH_2$ (**3c**), $CH{\equiv}CCH_2$ (**3d**), CH_2COOH (**3e**), R = Me, R′ = $PhCH_2$ (**3f**), R + R′ = $-CH_2-CH_2-$ (**3g**)

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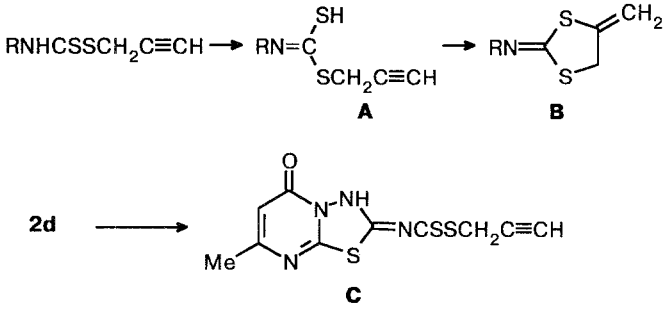

presence of signals for the protons of the NH group, the terminal acetylene group, and the CH_2 group of the propargyl radical.

The presence of the decoupling constant $J_{CH\equiv CCH_2}$ = 2.5 Hz also confirms the presence of the propargyl group. The chemical shifts of these proton signals are given in Table 2.

Apparently, the stability of ester **2d** is related to the ease of its transformation to the imine form **C** by way of a hydride shift of the exocyclic hydrogen atom of the amino group to the endocyclic nitrogen atom. The esters of dithiocarbamic acid **2** have higher melting points than those of the corresponding diesters of iminodithiocarbonic acid **3**. In the **1a—e** series, compound **1d** has an abnormally low melting point that is comparable with those of compounds **3a—g**. This can probably be explained by the realization of the **C** form due to the

Table 1. Properties of synthesized esters **2a—e** and **3a—g**

Compound	Yield (%)	M.p./°C	Found / Calculated (%) C	H	Molecular formula
2a	95	302	35.33 / 35.14	3.85 / 3.31	$C_8H_8N_4OS$
2b	96	315—317	48.29 / 48.25	3.96 / 3.47	$C_{14}H_{12}N_4OS_3$
2c	82	301—304	40.76 / 40.24	3.10 / 3.37	$C_{10}H_{10}N_4OS_3$
2d	94	128	39.93 / 40.52	2.95 / 2.71	$C_{10}H_8N_4OS_3$
2e	95	275 (decomp.)	34.05 / 34.16	2.89 / 2.50	$C_9H_8N_4O_3S_3$
3a	90	205	37.76 / 37.74	3.63 / 3.51	$C_9H_{10}N_4OS_3$
3b	82	185—187	57.61 / 57.50	3.95 / 4.13	$C_{21}H_{18}N_4OS_3$
3c	96	72—74	46.21 / 46.12	4.48 / 4.16	$C_{13}H_{14}N_4OS_3$
3d	92	123—126	46.56 / 46.68	3.36 / 3.01	$C_{13}H_{10}N_4OS_3$
3e	90	210—215 (subl.)	31.53 / 32.02	3.08 / 2.95	$C_{11}H_{10}N_4O_5S_3$
3f	63	150—152	49.39 / 49.70	4.04 / 3.89	$C_{15}H_{14}N_4OS_3$
3g	74	215—217	38.31 / 38.01	3.01 / 2.83	$C_9H_8N_4OS_3$

Table 2. Spectral characteristics of **2a—e** and **3a—g**

Compound	IR spectrum (ν/cm^{-1}) C=O	C=N	C=S	NH	Others	^{1}H NMR spectrum, δ, ppm
2a	1625	1510	1225	3355		6.12 (s, H, CH), 2.52 (s, 3 H, CH_3), 2.2 (s, 3 H, CH_3)
2b	1685	1515	1230	3350		7.25 (m, 5 H, Ph), 6.12 (s, H, CH), 4.25 (s, 2 H, CH_2), 2.2 (s, 3 H, CH_3)
2c	1690	1510	1225	3350		6.17 (s, H, CH), 5.77 (m, H, CH), 5.2 (s, 2 H, CH_2), 3.65 (s, 2 H, CH_2), 2.25 (s, 3 H, CH_3)
2d	1700	1500	1200	3400		6.17 (s, H, CH), 5.17 (s, H, NH), 4.00 (d, 2 H, CH_2), 3.08 (t, H, CH), 2.25 (s, 3 H, CH_3)
2e	1620	1500	3345		1740, 2750 (COOH)	6.12 (s, H, CH), 5.4 (s, H, COOH), 4.08 (s, 2 H, CH_2), 2.3 (s, 3 H, CH_3)
3a	1725	1520, 1540				6.15 (s, H, CH), 3.75 (s, 2 H, CH_2), 2.58 (s, 3 H, CH_3), 2.17 (s, 3 H, CH_3)
3b	1700	1485				7.25 (s, 5 H, Ph), 6.17 (s, H, CH), 4.37 (s, 2 H, CH_2), 2.25 (s, 3 H, CH_3)
3c	1710	1500, 1580				6.22 (s, H, CH), 5.82 (m, H, CH), 5.22 (m, 2 H, CH_2), 3.87 (m, 2 H, CH_2), 2.28 (s, 3 H, CH_3)
3d	1720	1515	1200			6.12 (s, H, CH), 4.12 (d, 2 H, CH_2), 3.3 (t, H, CH), 2.22 (s, 3 H, CH_3)
3e	1650	1510, 1570			1745, 2760 (COOH)	6.15 (s, H, CH), 4.83 (m, H, COOH), 4.00 (s, 2 H, CH_2), 2.22 (s, 3 H, CH_3)
3f	1625	1525, 1575	1160		3085 (Ph)	7.3 (m, 5 H, Ph), 6.15 (s, H, CH), 4.47 (s, 2 H, CH_2), 3.3 (s, 3 H, CH_3), 2.17 (s, 3 H, CH_3)
3g	1720	1515	1405			6.17 (s, H, CH), 3.75 (s, 2 H, CH_2), 2.17 (s, 3 H, CH_3)

amino-imine tautomerism which is known for 2-amino-1,3,4-thiadiazols.

Experimental

The ^{1}H NMR spectra were recorded on a Tesla BS-5873C spectrometer with 80 MHz frequency in DMSO, with HMDS as the internal standard, δ-scale, ppm. The IR spectra were obtained on a UR-20 spectrometer in KBr tablets (ν/cm^{-1}). The melting points were determined on a Boetius micro heating table.

Synthesis of 2-amino-7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine (1). 2.46 g (0.01 mol) of 2-bromo-7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine[8] was dissolved in 40 mL of a dioxane—water mixture (1:2). 5 mL of 25 % NH_4OH solution was added, and the reaction mixture was boiled for 2 h. After cooling to ~20 °C, the mixture was filtered, diluted with water, and dried in the air. The yield was 1.6 g (87 %), m.p. was 359 °C (from aqueous DMF; cf. with literature data: m.p. of **1** is 340—345 °C[9] and >300 °C[10]).

General procedure for the synthesis of the esters of *N*-(7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine-2-yl)dithiocarbamic (2a—e) and diesters of (7-methyl-5-oxo-5*H*-1,3,4-thiadiazolo[3,2-*a*]pyrimidine-2-yl)iminodithiocarbonic (3a—e,g) acids. 1.82 g (0.01 mol) of compound **1** was suspended in 20 mL of DMF. 0.76 g (0.01 mol) of carbon disulfide was added, and the mixture was cooled to 0 °C. After addition of 0.4 g (0.01 mol) of NaOH (in the cases of **3a—e,g** 0.02 mol), the mixture was stirred until complete dissolution. 0.01 mol of the corresponding alkyl halide (in the cases of **3a—e,g**, 0.02 mol) was added, and the mixture was stirred for a period of time from 0.5 to 2 h at ~20 °C until the reaction was neutral to a universal indicator. When the reaction was finished, the mixture was poured into water. The precipitate that formed was filtered off, dried, and crystallized from a dioxane—water mixture (1:2).

Synthesis of compound 3f. 2.73 g (0.01 mol) of ester **2a** and 0.4 g (0.01 mol) of NaOH were mixed until complete dissolution in 20 mL of DMF at 0 °C. After addition of 1.26 g (0.01 mol) of benzyl chloride, the mixture was stirred for 2 h at ~20 °C until the reaction was neutral to a universal indicator. When the reaction was finished, the mixture was diluted with water (100 mL). The precipitate was filtered off, dried, and crystallized from a dioxane—water mixture (1:2).

References

1. J. Garín, E. Meléndez, F. L. Merchan, P. Merino, J. Orduna, and T. Tejero, *J. Heterocycl. Chem.*, 1990, **27**, 1341.
2. J. Garín, E. Meléndez, F. L. Merchan, P. Merino, J. Orduna, and T. Tejero, *J. Heterocycl. Chem.*, 1990, **27**, 1345.
3. E. Melendez, F. L. Merchan, P. Merino, J. Orduna, and R. Urchegni, *J. Heterocycl. Chem.*, 1991, **28**, 653.
4. R. Strivastava and S. Sharma, *Indian J. Chem.*, 1990, **29 B**, 142.
5. Sh. A. Shams El-Dine and O. Glauder, *Acta Chim.* (Budapest), 1973, **76**, 295.
6. V. K. Pandey and A. K. Agarwal, *Indian Chem. J.*, 1979, **13**, 24 (R. Zh. Khim., 1980, 14zh339).
7. S. V. Amosova, N. I. Ivanova, G. A. Kalabin, S. V. Zinchenko, and M. V. Sigalov, *Tez. dokl. 18 Konf. po khimii i tekhnologii organicheskikh soyedinenii sery* [*Reports at the 18th Conference on the Chemistry and Technology of Organic Sulfur Compounds*], part 2, Kazan, 1992, 139 (in Russian).
8. USSR Pat. 1648068 *Bul. Izobret.*, 1991, 270 (in Russian).
9. H. Paul and A. Sitte, *Monatsh Chem.*, 1971, **102**, 550.
10. T. Tsuji and Y. Otsuka, *Chem. Pharm. Bull. Japan*, 1978, **26**, 2765.

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