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NUCLEOPHILIC SUBSTITUTION IN 1,2,3-THIADIAZOLES

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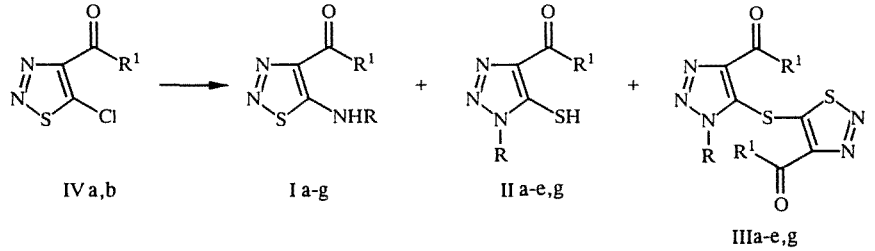
By reactions of nucleophilic substitution of the halogen atom in 5-halo-1,2,3-thiadiazoles (IV), we have obtained 5-amino- (I, V), hydrazino-(VI, VII, IX, X), and mercapto- (VIII) 1,2,3-thiadiazoles. We show that upon reaction with amines, a mixture of 5-amino-1,2,3-thiadiazoles (I) and 5-mercapto-1,2,3-triazoles (II) is formed, and also the reaction product of compounds I and IV; the selectivity of this process depends only on the type of solvent.

Reactions of nucleophilic substitution of the halogen in the 5 position of 1,2,3-thiadiazoles are a convenient method for synthesis of new compounds in this series [1-5]. However, they all include the use of such strong bases as liquid ammonia and hydrazine hydrate, which leads to the occurrence of a parallel process: the Dimroth rearrangement [6, 7] and formation of a mixture of products I-III. As was shown independently in two laboratories [4, 5], the 1,2,3-thiadiazole Ig is obtained in good yield upon treatment of chlorothiadiazole IVb with two equivalents of hydrazine hydrate, and when using a three-fold excess of hydrazine hydrate the Dimroth rearrangement occurs with formation of the product IIg. The use of an intermediate amount of nucleophile leads to the product IIIg. In this work, we have shown that, in contrast to the reaction with hydrazine hydrate, the nature of the reaction of 5-chloro-1,2,3-thiadiazoles IV with amines depends not on the ratio of the reagent, but only on the nature of the solvent used.



IV a,b I a-g II a-e,g IIIa-e,g

I—III R^1 = NHMe, a R = *i*-Pr, b Bu, c *cyclo*-C_6H_{11}, d CH_2Ph, e *t*-Bu, f Ph; g R^1 = OEt, R = NH_2; IV a R^1 = NHMe, b OEt

Analogously to the reaction with hydrazine hydrate [2], the reaction of chlorothiadiazoles IV and amines in ethanol leads to a mixture of products I-III. However, the ratio of products I-III in the reaction mixture does not depend on the amount of amine, but rather is completely determined by the nature of the solvent.

In polar solvents (see Table 1), along with nucleophilic substitution the Dimroth rearrangement occurs, and also partial reaction of the product of this rearrangement with the starting compound; as a result, a mixture of three compounds I-III is formed. The use of water (100°C) or DMF as the solvent leads to formation of exclusively the 5-mercapto-1,2,3-triazole II or the bis-heterocycle III respectively. In such aprotic solvents as chloroform and n-heptane, the Dimroth rearrangement does not occur and in this case pure 5-amino-1,2,3-thiadiazole I can be isolated. The Dimroth rearrangement also does not occur upon reaction of the chlorothiadiazole IVa with such a weak base as aniline: here only the 5-aminothiadiazole If is formed, independently of the solvent used.

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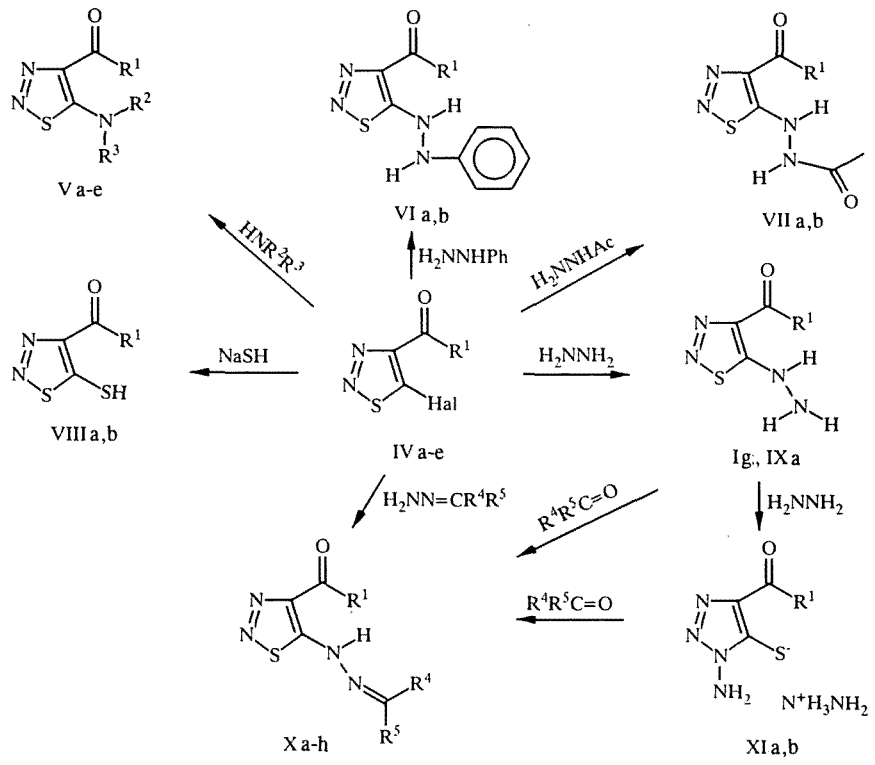
In order to determine the limits of applicability of this substitution reaction, we studied the reactions of chlorothiadiazoles IV with other nucleophiles. We showed (see Scheme 1) that this reaction is a convenient preparative method for synthesis of different 5-substituted 1,2,3-thiadiazoles.

Scheme 1



IV Hal = Cl, a R^1 = NHMe, b OEt, c NH_2; Hal = Br, d R^1 = NH_2, e NHMe; VI—IX, XI a R^1 = OEt, b NH_2; V a R^1 = OEt, R^2 = H, R^3 = CH_2CH_2OH, b R^2 = R^3 = Me; c R^1 = NH_2, R^2 = H, R^3 = CH_2CH_2OH, d R^2 = R^3 = Me; e R^1 = NHMe, R^2 = R^3 = Me; X R^1 = NH_2, R^4 = H, R^5 = C_6H_4-R^6, XIa R^6 = H, b NO_2, c OMe, d R^4 = R^5 = Me; e R^1 = OEt, R^1 = H, R^5 = $C_6H_4R^6$, R^6 = H, f NO_2, g OMe, h R^4 = R^5 = Me

The 5-chlorothiadiazoles IVa-c easily react not only with such strong nucleophiles as amines, hydrazines, and sodium hydrosulfide, but also with such weak bases as hydrazones. Compounds Xa-h also were obtained from IX and XI; we determined the conditions for selective formation of all these compounds.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were taken on the Bruker WR-80 and VXR-400 in DMSO-d_6, internal standard HMDS. The IR spectra were recorded on the IR-75 spectrometer in KBr disks. The mass spectra were obtained on the Varian MAT-311A, accelerating potential 3 kV, electron energy 70 eV. The course of the reactions and the purity of the compounds were monitored by TLC on Silufol UV-254 plates in the systems: chloroform, 15:1 chloroform-hexane, 15:1 chloroform–ethanol. The melting points were uncorrected.

The elemental analysis data for C, H, N, and S correspond to the calculated values for all the synthesized compounds.

4-N-methylcarbamoyl-5-chloro-1,2,3-thiadiazole (IVa, $C_4H_4ClN_3OS$) was obtained from 4-N-methylcarbamoyl-5-N-nitrosomaino-1,2,3-thiadiazole in 73% yield according to the technique in [3]; mp 83°C; IR spectrum: 3365, 3255, 2960, and 2870 (NH), 1620 cm^{-1} (C–O); PMR spectrum: 2.85 (3H, s, NMe), 9.0 ppm (IH, s, NH).

4-Carbamoyl-5-chloro-1,2,3-thiadiazole (IVc, $C_3H_3ClN_3OS$) was obtained analogously in 95% yield, mp 131°C; IR spectrum: 3400, 3225 and 3165 (NH), 1650 cm^{-1} (C–O).

TABLE 1. Yields of Products of Reaction of IVa with Isopropylamine

Method		Yield of compounds, %		
solvent	T,° C	Ia	IIa	IIIa
Acetonitrile	82	12	43	44
Water	25	0	48	51
Water	100	0	99	0
Ethanol	25	2	53	42
Ethanol	78	0	47	49
DMF	25	0	3	95
Chloroform	61	99	0	0
n-Heptane	98	99	0	0

TABLE 2. ^{13}C NMR Spectra of Heterocycles I-II, δ, ppm

Compound	Thiadiazoles		Triazoles		Other signals
	C_4	C_5	C_4	C_5	
Ia	138,0	162,1			48,7 (CH), 25,9 (NMe), 22,0 (2Me), 160,2 (C=O)
IIa			142,6	130,5	51,0 (CH), 25,5 (NMe), 22,1 (2Me), 159,1 (C=O)
IIIa	148,7	159,0	142,9	128,8	51,9 (CH), 25,8 (NMe), 25,4 (NMe), 22,4 (2Me), 160,0 (C=O)

4-Carbamoyl-5-bromo-1,2,3-thiadiazole ((Vd, $C_3H_3BrN_3OS$). A solution of 7.5 g (0.1 moles) sodium nitrite in 20 ml water was added dropwise to a suspension of 4 g (2.7 millimoles) 4-carbamoyl-5-amino-1,2,3-thiadiazole in 200 ml 1N H_2SO_4 at 0°C. The reaction mass was stirred for 10 min. The residue was filtered off, washed with 40 ml water, and added in portions to 30 ml aqueous HBr with stirring at 0-5°C over the course of a day. The product was extracted with ether (3 × 100 ml). The ether extracts were dried by sodium sulfate, the ether was evaporated, and the product was recrystallized from a chloroform–hexane mixture. mp 156°C; IR spectrum: 3400, 3225 and 3165 (NH), 1650 cm^{-1} (C=O); mass spectrum, m/z (I > 10%): 209 (3), 207 (3), 181 (60), 179 (55), 153 (32), 151 (32), 138 (100), 137 (18), 136 (94), 100 (17), 84 (42), 72 (83), 68 (13).

4-Methylcarbamoyl-5-bromo-1,2,3-thiadiazole (IVe, $C_4H_5BrN_3OS$) was obtained analogously in 65% yield, mp 156°C; IR spectrum: 3410, 3215 and 3150 (NH), 1650 cm^{-1} (C–O); mass spectrum, (I > 10%): 223 (21), 221 (19), 195 (47), 193 (46), 167 (11), 166 (20), 165 (21), 164 (18), 163 (10), 138 (100), 137 (24), 136 (94), 135 (14), 114 (16), 86 (63), 85 (28), 84 (67), 71 (48), 70 (32).

1,2,3-Thiadiazoles I, V, VI, VII (general technique). The appropriate amine (0.1 moles) was added to a solution of 5-chloro-1,2,3-thiadiazole IVa-c (0.01 moles) in $CHCl_3$ (40 ml). The reaction mass was boiled for 2 h, then washed with 1 N HCl (2 × 50 ml) and water (3 × 50 ml). The solvent was evaporated at reduced pressure and the product obtained was recrystallized from methanol.

4-N-(Methylcarbamoyl-5-isopropylamino-1,2,3-thiadiazole (Ia, $C_7H_{12}N_4OS$). Yield 99%, mp 66°C; IR spectrum: 3365, 3255 and 2960 (NH), 1620 cm^{-1} (C–O); PMR spectrum: 8.3-8.7 (2H, m, 2NH), 3.0-3.5 (1H, m, CH), 2.80 (3H, d, Me), 1.27 ppm (6H, d, 2Me); ^{13}C NMR spectrum is given in Table 2.

4-N-methylcarbamoyl-5-butylamino-1,2,3-thiadiazole (Ib, $C_8H_{14}N_4OS$). Yield 98%, mp 114°C; IR spectrum: 3375, 3310 and 2950 (NH), 1620 cm^{-1} (C=O); PMR spectrum: 7.8-8.2 (2H, m, 2NH), 2.7-3.2 (1H, m, CH), 2.79 (3H, d, Me), 0.7-1.8 ppm (7H, m C_3H_7).

4-N-Methylcarbamoyl-5-cyclohexylamino-1,2,3-thiadiazole (Ic, $C_{10}H_{16}N_4OS$). Yield 99%, mp 130°C; IR spectrum: 3355, 3280 and 2920 (NH), 1625 cm^{-1} (C=O); PMR spectrum: 8.4-8.6 (2H, m, 2NH), 2.7-3.2 (1H, m, CH), 2.79 (3H, d, Me), 0.9-1.9 ppm (10H, m, C_5H_{10}).

4-N-Methylcarbamoyl-5-benzylamino-1,2,3-thiadiazole (Id, $C_{11}H_{12}N_{14}OS$). Yield 98%, mp 139°C; IR spectrum: 3360 and 3330 (NH), 1620 cm^{-1} (C=O); PMR spectrum: 9.08 (1H, t, NH), 8.51 (1H, q, NH), 7.33 (5H, s, Ph), 4.48 (2H, d, CH_2), 2.81 ppm (3H, d, Me).

4-N-Methylcarbamoyl-5-tert-butylamino-1,2,3-thiadiazole (Ie, $C_8H_{14}N_4OS$). Yield 94%, mp 80°C; IR spectrum: 3380, 3300 and 2950 (NH), 1630 cm^{-1} (C=O); PMR spectrum: 9.07 (1H, s, NH), 8.64 (1H, q, NH), 2.80 (3H, d, Me), 1.31 ppm (9H, s, 3Me).

4-N-Methylcarbamoyl-5-anilino-1,2,3-thiadiazole (If, $C_{10}H_{10}N_4OS$). Yield 88%, mp 163°C; IR spectrum: 3370, 3295 and 2920 (NH), 1625 cm^{-1} (C=O); PMR spectrum: 8.9 (2H, m, 2NH). 7.2-7.5 (5H, m, Ph), 2.87 ppm (3H, d, Me).

4-Ethoxycarbonyl-5-(2-hydroxyethyl)amino-1,2,3-thiadiazole (Va, $C_7H_{11}N_3OS$). Yield 47%, mp 48°C. IR spectrum: 3330, 3250 and 2970 (NH), 1680 cm^{-1} (C=O).

4-Ethoxycarbonyl-5-dimethylamino-1,2,3-thiadiazole (Vb, $C_7H_{11}N_3O_2S$). Yield 87%, mp 77°C; IR spectrum: 2980, 2940, 1700 cm^{-1} (C=O).

4-Carbamoyl-5-(2-hydroxyethyl)amino-1,2,3-thiadiazole (Vc, $C_5H_8N_4O_2S$). Yield 80%, mp 238°C; IR spectrum: 3330, 3250 and 3150 (NH), 1670 cm^{-1} (C−O).

4-Carbamoyl-5-dimethylamino-1,2,3-thiadiazole (Vd, $C_5H_8N_4OS$). Yield 99%, mp 158°C; IR spectrum: 2990, 2930, 2870, 1680 cm^{-1} (C=O).

4-N-Methylcarbamoyl-5-dimethylamino-1,2,3-thiadiazole (Ve, $C_6H_{10}N_4OS$). Yield 99%, mp 112°C; IR spectrum: 3360, 2930, 2860 and 2790 (NH, CH), 1630 cm^{-1} (C=O).

4-Ethoxycarbonyl-5-(2-phenyl)hydrazino-1,2,3-thiadiazole (VIa, $C_{11}H_{12}N_4O_2S$). Yield 62%, mp 222°C; IR spectrum: 3450, 3330 and 3180 (NH), 1670 cm^{-1} (C−O).

4-Carbamoyl-5-(2-phenyl)hydrazino-1,2,3-thiadiazole (VIb, $C_9H_9N_5OS$). Yield 62%. mp 199°C; IR spectrum: 3400, 3300, 3000 and 2980 (NH), 1680 cm^{-1} (C=O).

4-Ethoxycarbonyl-5-(2-acetyl)hydrazino-1,2,3-thiadiazole (VIIa, $C_7H_{10}N_4O_3S$). Yield 42%, mp 175°C; IR spectrum:: 3320 and 2980 (NH), 1690 and 1660 cm^{-1} (C−O).

4-Carbamoyl-5-(2-acetyl)hydrazino-1,2,3-thiadiazole (VIIb, $C_5H_7N_5O_2S$). Yield 92%, mp 245°C; IR spectrum: 3250 and 3150 (NH), 1680 and 1630 cm^{-1} (C=O).

4-Ethoxycarbonyl-5-mercapto-1,2,3-thiadiazole (VIIIa, $C_5H_6N_2O_2S_2$). Sodium hydrosulfide (5.6 g, 0.1 moles) was added to a solution of 5-chloro-1,2,3-thiadiazole IVb (1.8, g, 0.01 moles) in ethanol (40 ml) and stirred at room temperature for 2 h. The solvent was evaporated at reduced pressure. 1 N HCl (50 ml) was added to the residue. After filtration, the product was recrystallized from methanol. Yield 1.6 g (91%), mp 65°C; IR spectrum: 2990 (NH), 2525 (SH), 1685 cm^{-1} (C=O).

The following compounds were obtained analogously.

4-Carbamoyl-5-mercapto-1,2,3-thiadiazole (VIIIb, $C_3H_3N_3OS_2$). Yield 87%, mp 214°C; IR spectrum: 3440, 3290 and 3165 (NH), 2535 (SH), 1660 cm^{-1} (C=O).

4-Carbamoyl-5-hydrazino-1,2,3-thiadiazole (IXb, $C_5H_8N_4O_2S$, HCl) in 87% yield (from IVc according to the technique in [2]), mp 213°C; IR spectrum: 3250, 3170, 3130, 2960 and 2880 (NH), 1650 cm^{-1} (C−O).

4-Carbamoyl-5-benzylidenehydrazino-1,2,3-thiadiazole (Xa, $C_{10}H_9N_5OS$). Benzylidene hydrazine (1.2 g, 0.1 moles) was added to a solution of 5-chloro-1,2,3-thiadiazole IVa (1.7 g, 0.01 moles) in ethanol (40 ml) and boiled for 2 h. The solvent was evaporated at reduced pressure and the residue was recrystallized from methanol. Yield 80%, mp 230°C, IR spectrum: 3370, 3255 (NH), 1630 cm^{-1} (C=O); PMR spectrum: 11.8 (1H, s, NH), 8.65 (1H, s, CH), 8.0 (2H, s, NH_2), 7.3-7.8 ppm (5H, m, Ph): PMR spectrum; ^{13}C NMR spectrum: 165.5 (C_5), 163.3 (C−O), 148.7 (=CH), 133.4 (C_i), 132.9 (C_4), 130.2 (C_p), 128.8 (C_m), 126.9 ppm (C_o).

This compound also was obtained in 60-70% yield upon reaction of equimolar ratios of IXb or XIb and benzaldehyde in ethanol.

The following compounds were obtained analogously.

4-Carbamoyl-5-(4-nitrobenzylidene)hydrazino-1,2,3-thiadiazole (Xb, $C_{10}H_8N_6O_3S$) in 86% yield (from IVc, 73% yield (from IXb), 68% yield (from XIb), mp 244°C, IR spectrum: 3320, 3250 and 3100 (NH), 1660 cm^{-1} (C−O); PMR spectrum: 11.9 (1H, s, NH), 8.7 (1H, s, CH), 7.8-8.4 ppm (7H, m, Ph and NH_2); PMR spectrum ^{13}C: 165.4 (C_5), 163.1 (C−O), 147.8 (C_p), 146.1 (CH), 139.5 (C_i), 133.5 (C_4), 127.7 (C_m), 124.1 ppm (C_o).

4-Carbamoyl-5-(4-methoxybenzylidene)hydrazino-1,2,3-thiadiazole (Xc, $C_{11}H_{11}N_5O_2S$) in 87% yield (from IVc), 65% yield (from IXb), 88% yield (from XIb), mp 247°C, IR spectrum: 3345, 3200 and 3150 (NH), 1635 cm^{-1} (C=O).

4-Carbamoyl-5-isopropylidenehydrazino-1,2,3-thiadiazole (Xd, $C_6H_9N_5OS$) in 92% yield (from IVc), 75% yield (from IXb), 60% yield (from XIb), mp 246°C, IR spectrum: 3170, 2880 and 2760 (NH), 1640 cm^{-1} (C=O).

4-Ethoxycarbonyl-5-benzylidenehydrazino-1,2,3-thiadiazole (Xe, $C_{12}H_{12}N_4O_2S$) in 78% yield (from IVc), 65% yield (from IXb), 70% yield (from XIb), mp 208°C, IR spectrum: 3340, 3060 and 2950 (CH), 1685 cm^{-1}; PMR spectrum ^{13}C: 167.7 (C_5), 161.3 (C=O), 149.7 (CH), 133.0 (C_i), 130.6 (C_p), 129.8 (C_4), 128.9 (C_m), 127.0 (C_0), 60.7 (OCH_2), 14.2 ppm (CH_3).

4-Ethoxycarbonyl-5-(4-nitrobenzylidene)hydrazino-1,2,3-thiadiazole (Xf, $C_{12}H_{11}N_5O_4S$) in 85% yield (from IVc), 62% yield (from IXb), 78% yield (from XIb), mp 240°C, IR spectrum: 3140, 3110 and 2975 (CH), 1685 cm^{-1} (C=O); PMR spectrum: 8.64 (1H, s, CH), 7.4-7.7 (4H, m, Ph), 4.42 (2H, q, CH_2), 1.38 ppm (3H, t, CH_3).

4-Ethoxycarbonyl-5-(4-methoxybenzylidene)hydrazino-1,2,3-thiadiazole (Xg, $C_{13}H_{14}N_4O_3S$) in 82% yield (from IVc), 69% yield (from IXb), 60% yield (from XIb), mp 237°C, IR spectrum: 3160, 3080 and 3060 (CH), 1670 cm^{-1} (C−O).

4-Ethoxycarbonyl-5-isopropylidenehydrazino-1,2,3-thiadiazole (Xh, $C_8H_{12}N_4O_2S$) in 98% yield (from IVc), 92% (from IXb), 88% yield (from XIb), mp 152°C, IR spectrum: 3160, 3080 and 3060 (CH), 1670 cm^{-1} (C−O); PMR spectrum: 10.0 (1H, s, NH), 4.5 (2H, q, CH_2), 2.05 (6H, s, $2CH_3$), 1.4 ppm (3H, s, CH_3); ^{13}C NMR spectrum: 167.5 (C_5), 161.6 (C−O), 157.7 (CMe_2), 129.9 (C_4), 60.5 (OCH_2), 24.2 (Me), 16.7 (Me), 13.8 ppm (Me).

1-Amino-4-carbamoyl-5-mercapto-1,2,3-triazole (XIb, $C_3H_5N_5OS \cdot N_2H_4$) (according to the technique in [4, 5] from IVc in 99% yield, mp 164°C.

5-Mercapto-1,2,3-triazoles IIa-e (general technique). The appropriate amine (0.1 moles) was added to a solution of 5-chloro-1,2,3-thiadiazole IVa-c (0.01 moles) in water (40 ml). The reaction mass was boiled for 1 h. After cooling, 10 ml 1 N HCl was added. After filtration, the product was recrystallized from methanol.

1-Isopropyl-4-N-methylcarbamoyl-5-mercapto-1,2,3-triazole (IIa, $C_7H_{12}N_4OS$). Yield 99%, mp 181°C; IR spectrum: 3220, 3090 and 2940 (NH), 1640 cm^{-1} (C−O); PMR spectrum: 8.43 (1H, s, NH), 4.84 (1H, center, CH), 2.71 (3H, d, Me), 1.46 ppm (6H, d, 2Me); ^{13}C NMR spectrum is given in Table 2.

1-Butyl-4-N-methylcarbamoyl-5-mercapto-1,2,3-triazole (IIb, $C_8H_{14}N_4OS$). Yield 97%, mp 122°C; IR spectrum: 3200, 3050 and 2950 (NH), 1650 cm^{-1} (C=O); PMR spectrum: 8.9 (1H, s, NH), 4.30 (2H, t, CH_2), 2.76 (3H, d, Me), 0.7-1.9 ppm (7H, m, C_3H_7).

1-Cyclohexyl-4-N-methylcarbamoyl-5-mercapto-1,2,3-triazole (IIc, $C_{10}H_{16}N_4OS$). Yield 95%, mp 190°C; IR spectrum: 3190, 3080 and 2960 (NH), 1645 cm^{-1} (C=O); PMR spectrum: 9.0-9.5 (1H, m, NH), 4.4-4.9 (1H, m, CH), 2.84 (3H, d, Me), 0.9-2.1 ppm (10H, m, C_5H_{10}).

1-Benzyl-4-N-methylcarbamoyl-5-mercapto-1,2,3-triazole (IId, $C_{11}H_{12}N_4OS$). Yield 99%, mp 199°C; IR spectrum: 3200, 3070 and 2950 (NH), 1650 cm^{-1} (C=O); PMR spectrum: 9.1 (1H, s, NH), 7.2 (5H, s, Ph), 5.78 (2H, s, CH_2), 2.86 ppm (3H, d, Me).

1-tert-Butyl-4-N-methylcarbamoyl-5-mercapto-1,2,3-triazole (IIe, $C_8H_{14}N_4OS$). Yield 90%, mp 185°C; IR spectrum: 3380, 3190 and 3080 (NH), 1640 cm^{-1} (C=O); PMR spectrum: 9.15 (1H, q, NH), 2.87 (3H, d, Me), 1.74 ppm (9H, s, 3Me).

Bis-heterocycles IIIa-e (general technique). The appropriate amine (0.1 moles) was added to a solution of 5-chloro-1,2,3-thiadiazole IVa (0.01 moles) in DMF (10 ml). This was stirred at room temperature for 1 h and then 10 ml water was added. After filtration, the product was recrystallized from methanol.

4-N-Methylcarbamoyl-5-(4′-methylcarbamoyl-1′-isopropyl-1′,2′,3′-triazolyl-5′)mercapto-1,2,3-thiadiazole (IIIa, $C_{11}H_{14}N_7O_2S_2$). Yield 98%, mp 210°C; IR spectrum: 3370, 2975 and 2930 (NH), 1660 cm^{-1} (C=O); PMR spectrum: 8.12 (1H, q, NH), 8.71 (1H, q, NH), 5.02 (1H, center, CH), 2.88 (3H, d, Me), 1.51 ppm (6H, d, 2Me); ^{13}C NMR spectrum is given in Table 2.

4-N-Methylcarbamoyl-5-(4′-methylcarbamoyl-1′-butyl-1′, 2′, 3′-triazolyl-5′)mercapto-1, 2, 3-thiadiazole (IIIb, $C_{12}H_{17}N_7O_2S_2$). Yield 89%, mp 112°C; IR spectrum: 3190, 3040 and 2960 (NH), 1615 and 1610 cm^{-1} (C−O); PMR spectrum: 8.9-9.1 (1H, m, NH), 8.54 (1H, q, NH), 3.3 (2H, q, CH), 2.80 (3H, d, Me), 2.74 (3H, d, Me), 0.7-1.9 ppm (7H, m, C_3H_7).

4-N-Methylcarbamoyl-5-(4′-methylcarbamoyl-1′-cyclohexyl-1′,2′,3′-triazolyl-5′) mercapto-1, 2, 3-thiadiazole (IIIc, $C_{14}H_{19}N_7O_2S_2$). Yield 92%, mp 180°C; IR spectrum: 3420, 3370 and 3340 (NH), 1660 and 1655 cm^{-1} (C=O); PMR spectrum: 8.9-9.1 (1H, q, NH), 8.54 (1H, q, NH), 4.4-4.9 (1H, m, CH), 2.88 (3H, d, Me), 2.73 (3H, d, Me), 0.7-2.1 ppm (10H, m, C_5H_{10}).

4-N-Methylcarbamoyl-5-(4′-methylcarbamoyl-1′-benzyl-1′, 2′, 3′-triazolyl-5′)mercapto-1, 2, 3-thiadiazole (IIId, $C_{15}H_{15}N_7O_2S_2$). Yield 92%, mp 155°C; IR spectrum: 3365 and 3330 (NH), 1660 and 1650 cm^{-1} (C=O); PMR spectrum: 9.05 (1H, q, NH), 8.75 (1H, q, NH), 7.18 (5H, s, Ph), 5.78 (2H, s, CH_2), 2.86 (3H, d, Me), 2.72 ppm (3H, d, Me).

4-N-Methylcarbamoyl-5-(4′-methylcarbamoyl-1′-tert-butyl-1′,2′,3′-triazolyl-5′)mercapto-1,2,3-thiadiazole(IIIe, $C_{12}H_{17}N_7O_2S_2$). Yield 87%, mp 180°C; IR spectrum: 3190, 3040 and 2960 (NH), 1650 and 1640 cm^{-1} (C=O); PMR spectrum: 9.15 (1H, q, NH), 8.67 (1H, q, NH), 2.88 (3H, d, Me), 2.72 (3H, d, Me), 1.72 ppm (9H, s, 3Me).

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