PREPARATION OF A NOVEL TYPE OF LIGANDS INCORPORATING TWO OR THREE 1,3,4-THIADIAZOLE UNITS

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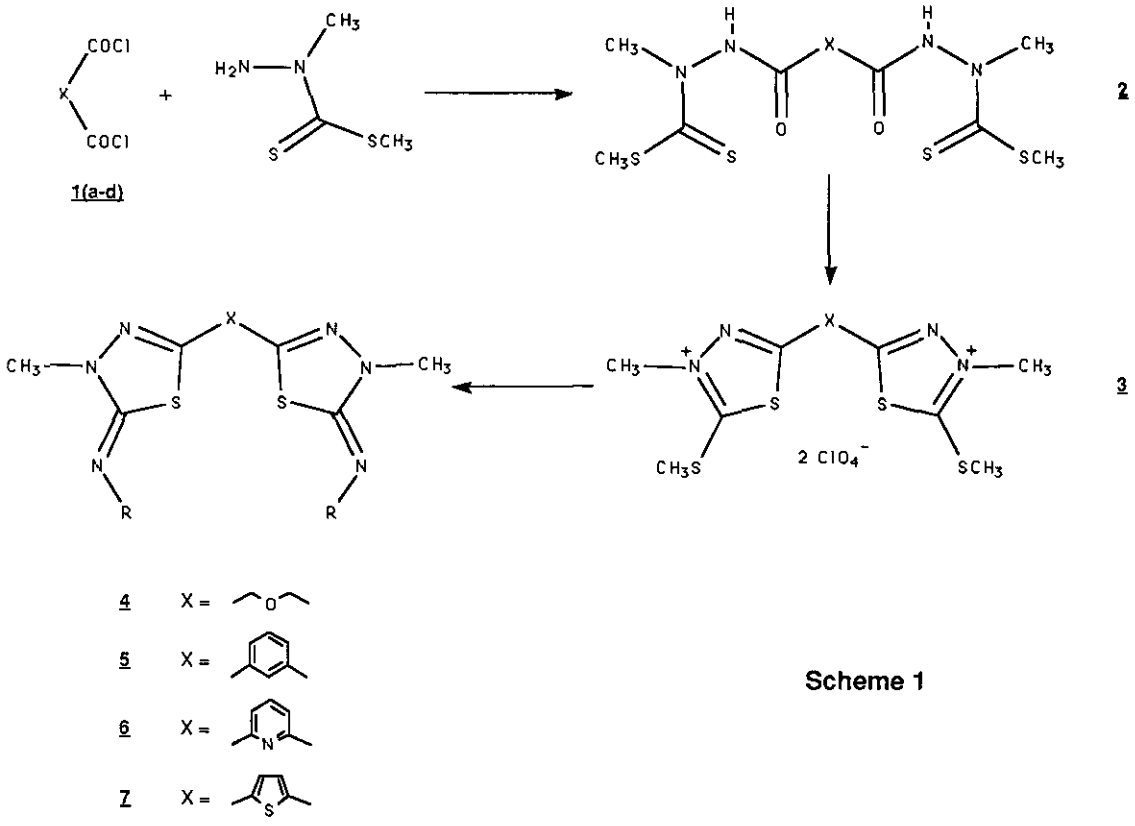
Abstract- The 1,3,4-thiadiazole annelation based on the reaction of acyl chlorides with methyl 2-methyldithiocarbazate followed by cyclization with perchloric acid and further reaction with primary amines, allows the preparation of a novel kind of ligands bearing two or three 1,3,4-thiadiazole rings connected either by an aliphatic, aromatic or heteroaromatic bridge.

Macrobicyclic ligands containing heterocyclic subunits have been shown to possess interesting functional (photochemical, electrochemical) properties conferred by aromatic heterocycles.[1] In spite of the large number of such subunits introduced in macrocyclic compounds, a few examples of 1,3,4-thiadiazole inclusion in a macrocyclic framework have been reported.[2]

We have previously reported that alkyl 2-methyldithiocarbazates, by sequential treatment with acyl chlorides and perchloric acid, lead to 2-alkylthio-1,3,4-thiadiazolium cations[3] which react with primary amines to give 2-amino-1,3,4-thiadiazole derivatives.[4]

Herein we report an efficient new method for the synthesis of previously unreported bis-(1,3,4-thiadiazole) derivatives, connected by aliphatic, aromatic or heteroaromatic bridges with suitable cavities for metal complexation, and which is based on the sequential treatment of methyl 2-methyldithiocarbazate with dicarboxylic acid chlorides and perchloric acid.

Preparation of 2,2´-bis(5-imino-1,3,4-thiadiazole) podands is outlined in Scheme 1. Methyl 2-methyldithiocarbazate undergoes acylation upon reaction with several diacyl chlorides (1) to give acyclic derivatives (2) (41-74%). These compounds undergo cyclization with perchloric acid/acetic anhydride in dry ether at room



1(a-d)

2

3

4 X =

5 X =

6 X =

7 X =

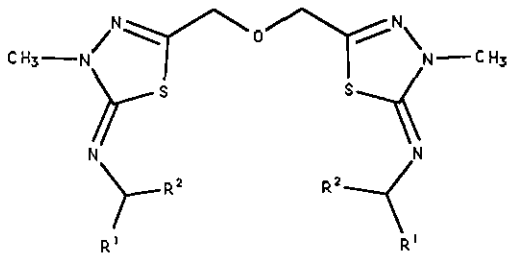
Scheme 1

temperature to give the salts (3) (73-90%), which by reaction with primary amines in the presence of equimolecular amounts of triethylamine yield the functionalized 2,2´-bis(5-imino-1,3,4-thiadiazolines) (4-7) (Scheme 1).

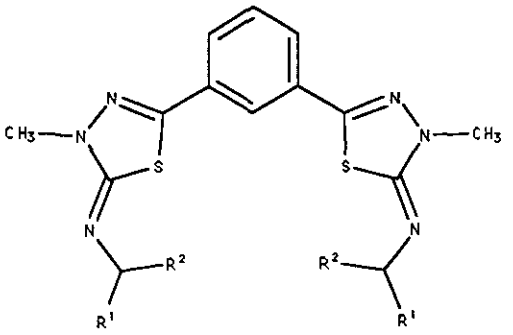
Compounds (4a) and (4b) were obtained in 20 and 68% yield from 3 (X = $-CH_2OCH_2-$), available in 73% yield, from diglycolyl dichloride[5] and using 2-aminopropanol and 2-bromoethylamine as amino components, respectively. Preparation of azide (4c) was achieved from bromide (4b) and sodium azide in dimethyl sulfoxide at 80°C in 43% yield.

Starting from isophthaloyl dichloride as acylating reagent, and ethylamine, 2-substituted ethylamines or benzylamines as amino components, the 2,2´-bis(5-imino-1,3,4-thiadiazolines) (5) (30-76%), bearing an aromatic ring as a bridge, was obtained as crystalline solid. Azide (5g) (76%) was prepared from the corresponding bromide (5f) and sodium azide in dimethyl sulfoxide at 80°C.

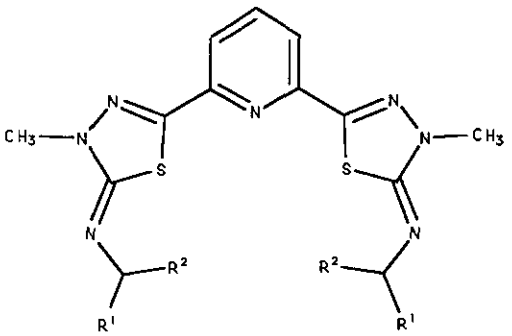
The podands (6) and (7), in which an heteroaromatic ring is placed between the two 1,3,4-thiadiazole rings, were prepared from pyridine-2,6-dicarboxilic acid dichloride and furan-2,5-dicarboxylic acid dichloride,[6] respectively.



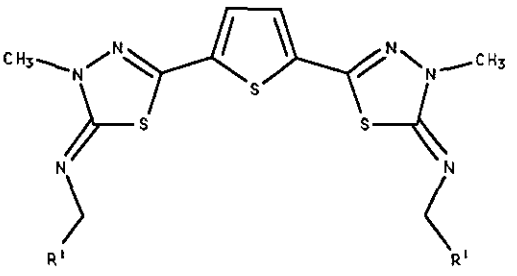
4a	$R^1 = CH_2OH$	$R^2 = CH_3$
4b	$R^1 = CH_2Br$	$R^2 = H$
4c	$R^1 = CH_2N_3$	$R^2 = H$



5a	$R^1 = C_2H_5$	$R^2 = H$
5b	$R^1 = CH_2OH$	$R^2 = CH_3$
5c	$R^1 = CH_2OCH_2CH_2OH$	$R^2 = H$
5d	$R^1 = CH_2OH$	$R^2 = H$
5e	$R^1 = CH_2SH$	$R^2 = H$
5f	$R^1 = CH_2Br$	$R^2 = H$
5g	$R^1 = CH_2N_3$	$R^2 = H$
5h	$R^1 = CH(OCH_3)_2$	$R^2 = H$
5i	$R^1 = C_6H_5$	$R^2 = H$
5j	$R^1 = C_6H_5$	$R^2 = CH_3$



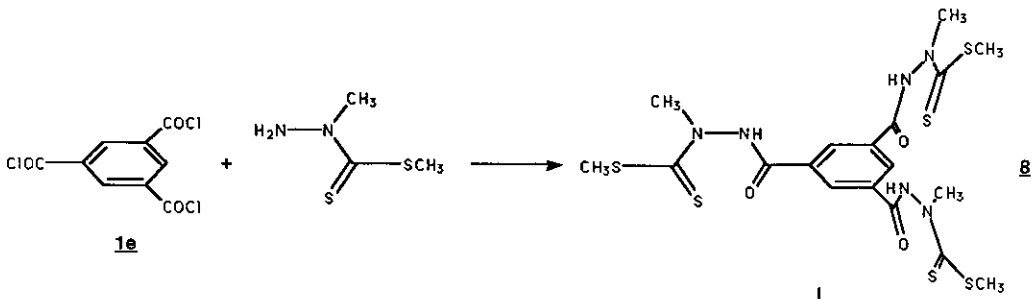
6a	$R^1 = CH_2OH$	$R^2 = CH_3$
6b	$R^1 = CH_2OCH_2CH_2OH$	$R^2 = H$
6c	$R^1 = CH_2SH$	$R^2 = H$
6d	$R^1 = CH_2Br$	$R^2 = H$
6e	$R^1 = CH_2N_3$	$R^2 = H$
6f	$R^1 = CH(OCH_3)_2$	$R^2 = H$
6g	$R^1 = C_6H_5$	$R^2 = H$
6h	$R^1 = C_6H_5$	$R^2 = CH_3$



7a	$R^1 = CH_2Br$
7b	$R^1 = CH_2N_3$

In general, this methodology shows to be useful for the preparation of compounds type (6) in moderate to good yields (44-88%). Recently it has been reported[7] the preparation and binding properties of close related ligands, bearing two identical suitably functionalized azole rings, connected by a pyridine bridge. The azide (6e) was prepared from bromide (6d) in 93% yield.

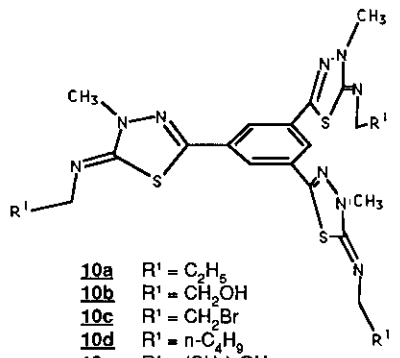
Scheme 2



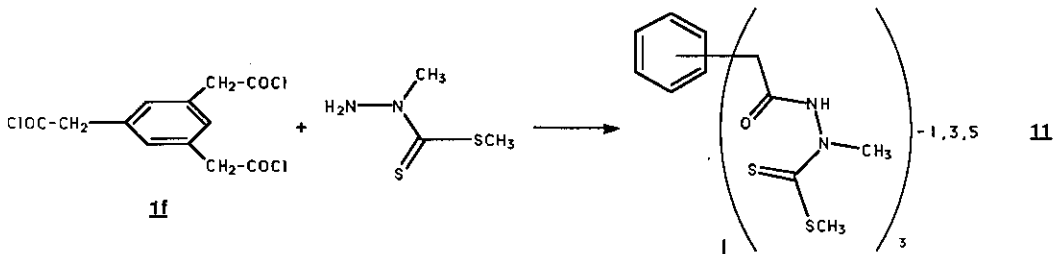
1e

8

9



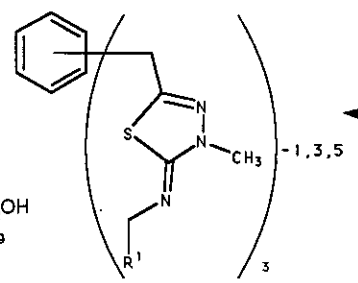
10a $R^1 = C_2H_5$
10b $R^1 = CH_2OH$
10c $R^1 = CH_2Br$
10d $R^1 = n\text{-}C_4H_9$
10e $R^1 = (CH_2)_4OH$
10f $R^1 = C_6H_5$



1f

11

12



13a $R^1 = (CH_2)_2OH$
13b $R^1 = n\text{-}C_4H_9$

Table 1: 13-C Nmr spectral data of 4,5-dihydro-5-(N-substituted) imino-4-methyl-1,3,4-thiadiazoles

Entry	N-Me	C-2	C-5	X	=N-CH	R^1	R^2
4a	35.54	143.22	157.91	67.69	64.93	67.36	16.27
4b	35.45	143.12	156.42	67.25	59.20	32.39	-
4c	35.29	142.96	158.35	67.26	57.10	51.83	-
5a	35.89	143.55	156.46	131.82 (q), 129.36, 126.48, 122.42	60.15	23.99, 12.01	-
5b	36.13	144.04	157.91	131.47 (q), 129.46, 126.76, 122.50	64.98	67.67	16.29
5c	35.93	143.69	158.68	131.36 (q), 129.46, 126.69, 122.48	57.84	72.84 (CH_2O), 71.38 (CH_2O), 61.97 (CH_2OH)	-
5d	35.47	142.61	155.68	131.33 (q), 130.10, 126.69, 121.32	60.35	61.30	-
5e	35.73	143.45	157.36	131.46 (q), 129.20, 126.41, 122.19	57.35	40.04	-
5f	35.71	143.52	157.86	131.56 (q), 129.39, 126.62, 122.44	59.49	32.24	-
5g	35.56	143.37	157.73	131.65 (q), 129.36, 126.57, 122.43	57.32	51.92	-
5h	35.66	143.36	157.98	131.65 (q), 129.29, 126.46, 122.34	60.06	104.55, 54.23	-
5i	35.79	143.45	157.42	131.70 (q), 129.33, 126.53, 122.41	61.02	139.62 (q), 128.37, 127.43, 126.84	-
5j	36.19	145.08	156.10	131.76 (q), 129.37, 126.64, 122.56	67.10	143.86 (q), 128.45, 126.96, 126.70	24.99
6a	36.05	148.67	158.76	145.84 (q), 137.12, 118.84	64.71	67.80	16.43
6b	35.93	148.45	159.84	145.69 (q), 137.09, 118.68	57.83	72.69 (CH_2O), 71.25 (CH_2O), 61.82 (CH_2OH)	-
6c	35.87	148.70	158.68	145.75 (q), 137.16, 118.84	60.30	25.91	-
6d	35.91	148.65	159.07	145.78 (q), 137.19, 118.90	58.99	32.44	-
6e	35.67	148.60	159.00	145.52 (q), 137.13, 118.77	56.87	51.87	-
6f	35.72	148.70	159.15	145.51 (q), 137.01, 118.60	59.54	104.36, 54.05	-
6g	36.52	148.53	159.78	159.30 (q), 137.98, 119.22	59.82	138.98 (q), 128.49, 127.66, 127.11	-
6h	35.96	148.95	156.73	156.65 (q), 136.92, 118.74	66.72	145.45 (q), 128.29, 126.75, 126.53	24.48
7a	35.84	138.54	157.30	134.62 (q), 126.53	59.44	32.34	-
7b	35.65	138.36	157.18	134.84 (q), 126.42	57.33	51.84	-
10a	35.75	142.40	155.78	132.34 (q), 122.54	60.40	24.05, 12.01	-
10b	38.83	169.28	150.58	130.52 (q), 127.37	60.19	54.62	-
10c	36.03	142.99	158.08	131.94 (q), 123.08	58.82	32.31	-
10d	35.68	142.31	155.58	132.45 (q), 122.45	58.59	30.48, 29.66, 22.55, 14.07	-
10e	35.48	141.51	154.35	132.11 (q), 122.07	57.69	60.87 (CH_2OH), 32.38, 30.20, 23.53	-
10f	35.83	142.46	156.96	132.21 (q), 122.71	61.08	139.51 (q), 128.38, 127.35, 126.86	-
13a	34.92	145.98	156.57	137.40 (q), 128.08, 36.51	58.74	53.80 (CH_2OH), 33.46 (CH_2)	-
13b	35.29	145.47	157.20	137.51 (q), 128.30, 37.82	58.41	30.48, 29.62, 22.54, 14.09	-

Nmr spectra were run in $CDCl_3$ solutions, except for compounds (10e) and (13a) which were run in DMSO-d_6, compound (10c) which was run in $CDCl_3$/DMSO-d_6 and compound (10b) in DMSO-d_6/TFA.

When tricarboxylic acid trichlorides were used as starting materials, this methodology allowed the preparation of three-armed open-chain podands (Scheme 2). Thus, benzene-1,3,5-tricarboxylic acid trichloride reacted with methyl 2-methyldithiocarbazate to give the acylated product (8) in 93% yield, which was cyclized by the action of perchloric acid/acetic anhydride to give the salt (9) in 91% yield. This compound reacted with several primary amines to give the ligands (10) in 55-94% yield.

Starting from 1,3,5-benzenetriacetic acid trichloride, readily available from 1,3,5-triacetylbenzene in two steps,[8] and following the same reaction pathway that the one described above, compounds (11), (12) and (13) were obtained in 78%, 50% and 46-48% yield, respectively.

For all two and three armed podands (4) - (7), (10) and (13), the characteristic ^{13}C chemical shift values belonging to the 1,3,4-thiadiazole moiety lye within the expected range and are sumarized in Table 1.

In conclusion, the 1,3,4-thiadiazole annelation methodology described in this paper represents an useful entry to a novel sort of ligands bearing two or three 1,3,4-thiadiazole units connected either by an aliphatic, aromatic or heteroaromatic bridge. Some of them show structural features that allow to anticipate the binding properties towards some metals and current studies in this topic are being developed in our laboratory.

EXPERIMENTAL

Melting points were obtained in a Kofler hot-stage apparatus and are uncorrected. Ir spectra were run using NaCl plates on a Nicolet FT-5DX spectrophotometer in Nujol emulsions. ^1H Nmr spectra were recorded using a Varian Unity (299.95 MHz) spectrometer or a Bruker AC-200 (200.13 MHz) and tetramethylsilane as internal reference. ^{13}C Nmr spectra were determined on a Varian Unity (75.43 MHz) or a Bruker AC-200 (50.13 MHz) spectrometer. The EI-mass spectra were obtained with a Hewlett-Packard 5993 C spectrometer at 70 eV. Elemental analyses were performed with a Eager 200 instrument. Compounds (2) and (3), for X = 2,6-pyridodiyl, were prepared as previously reported.[9]

General Procedure for the Preparation of Dimethyl 3,3´-Diacyl-bis- and Trimethyl 3,3´,3´´-triacyl-tris-(2-methyldithiocarbazates) (2), (8) and (11) To a vigorously stirred solution of methyl 2-methyldithiocarbazate (2.04 g, 15 mmol) in toluene (30 ml), the corresponding acyl chloride (30 or 45 mmol) was added and the resulting mixture was stirred at reflux temperature for 6 h. On cooling, the separated solid was collected by filtration, washed with ethanol (10 ml) and ether (10 ml) and then crystallized from the appropriate solvent.

Dimethyl 3,3´-diglycolyl-bis-(2-methyldithiocarbazate) (2a).- Yield: 1.14 g (41%) colorless prisms; mp 176°C (from dichloromethane). Anal. Calcd for $C_{10}H_{18}N_4O_3S_4$: C, 32.42; H, 4.90; N, 15.12. Found: C, 32.22; H, 4.78; N,

15.15. $\nu_{max.}$ (cm^{-1}) 3313, 1699, 1574, 1552, 1529, 1416, 1359, 1263, 1223, 1166, 1030, 1013, 968, 934, 900, 719; δ (^1H, 200 MHz) (DMSO-d_6) 11.05 (2H, s, NH), 4.24 (4H, s, OCH_2), 3.58 (6H, s, NCH_3), 2.45 (6H, s, SCH_3); δ (^{13}C) 201.41 (C=S), 166.75 (C=O), 69.44 (OCH_2), 43.42 (NCH_3), 19.00 (SCH_3); m/z (%) 370 (M^+, 3), 274 (36), 163 (40), 115 (33), 91 (100), 89 (6), 88 (41), 73 (18), 48 (17), 47 (33).

Dimethyl 3,3´-isophthaloyl-bis-(2-methyldithiocarbazate) (2b).- Yield: 1.81 g (60%) colorless needles; mp 217-219°C (from ethanol). Anal. Calcd for $C_{14}H_{18}N_4O_2S_4$: C, 41.77; H, 4.51; N, 13.92. Found: C, 41.65; H, 4.60; N, 13.83. $\nu_{max.}$ (cm^{-1}) 3228, 1676, 1608, 1582, 1518, 1420, 1362, 1287, 1254, 1238, 1115, 1051, 961, 928, 920, 862, 816, 731, 619; δ (^1H, 200 MHz) (DMSO-d_6) 11.83 (2H, s, NH), 8.44 (1H, s), 8.15 (1H, t, J = 7.00 Hz), 7.76 (2H, d, J = 7.00 Hz), 3.63 (6H, s, NCH_3), 2.46 (6H, s, SCH_3); δ (^{13}C) 201.61 (C=S), 163.93 (C=O), 132.02, 131.33, 129.37, 127.21, 43.53 (NCH_3), 19.01 (SCH_3); m/z (%) 402 (M^+, 6), 306 (100), 217 (39), 163 (12), 157 (29), 129 (26), 115 (7), 91 (12), 89 (4), 73 (5), 48 (97), 47 (95).

Dimethyl 3,3´-(2,5-thiophenediyldicarbonyl)-bis-(2-methyldithiocarbazate) (2c).- Yield: 2.27 g (74%) brown prisms; mp 237-239°C (from dichloromethane). Anal. Calcd for $C_{12}H_{16}N_4O_2S_5$: C, 35.28; H, 3.95; N, 13.71. Found: C, 35.42; H, 4.20; N, 13.68. $\nu_{max.}$ (cm^{-1}) 3234, 1670, 1574, 1552, 1529, 1433, 1353, 1268, 1229, 1116, 1104, 1036, 1008, 962, 934, 917, 855, 755, 743; δ (^1H, 200 MHz) (DMSO-d_6) 11.91 (2H, s, NH), 7.09 (2H, s), 3.66 (6H, s, NCH_3), 2.45 (6H, s, SCH_3); δ (^{13}C) 201.81 (C=S), 158.73 (C=O), 140.20, 130.46, 43.55 (NCH_3), 18.98 (SCH_3); m/z (%) 408 (M^+, 1), 312 (100), 252 (13), 225 (35), 183 (3), 163 (31), 135 (16), 134 (8), 91 (15), 73 (5), 72 (4), 48 (29), 47 (36).

Trimethyl 3,3´,3´´-(1,3,5-benzenetricarbonyl)-tris-(2-methyldithiocarbazate) (8).- Yield: 2.63 g (93%) colorless prisms; mp 251°C (from ethanol). Anal. Calcd for $C_{18}H_{24}N_6O_3S_6$: C, 38.28; H, 4.28; N, 14.88. Found: C, 38.30; H, 4.19; N, 14.72. $\nu_{max.}$ (cm^{-1}) 3235, 1700, 1677, 1520, 1462, 1358, 1264, 1231, 1114, 962, 924, 735; δ (^1H, 200 MHz) (DMSO-d_6) 12.07 (3H, s, NH), 8.68 (3H, s), 3.69 (9H, s, NCH_3), 2.48 (9H, s, SCH_3); δ (^{13}C) 201.75 (C=S), 163.55 (C=O), 132.86, 130.70, 43.67 (NCH_3), 19.24 (SCH_3); m/z (%) 420 (M^+-3CH_3SH, 2), 275 (5), 159 (6), 154 (7), 135 (3), 117 (13), 91 (6), 73 (6), 61 (5), 48 (83), 47 (100).

Trimethyl 3,3´,3´´-(1,3,5-benzenetriacetyl)-tris-(2-methyldithiocarbazate) (11).- Yield: 2.37 g (78%) orange prisms; mp 230°C (from methanol). Anal. Calcd for $C_{21}H_{30}N_6O_3S_6$: C, 41.56; H, 4.98; N, 13.85. Found: C, 41.70; H, 5.03; N, 13.97. $\nu_{max.}$ (cm^{-1}) 3235, 1681, 1516, 1423, 1356, 1255, 1108, 1055, 968, 722; δ (^1H, 300 MHz) (DMSO-d_6) 11.26 (3H, s, NH), 7.17 (3H, s), 3.54 (6H, s), 3.53 (9H, s, NCH_3), 2.40 (9H, s, SCH_3); δ (^{13}C) 201.40 (C=S), 168.08 (C=O), 134.50, 128.55, 43.40 (NCH_3), 39.55, 19.00 (SCH_3); m/z (%) 462 (M^+-3CH_3SH, 8), 386 (4), 310 (4), 237 (5), 234 (3), 163 (2), 135 (2), 129 (11), 121 (10), 119 (3), 117 (4), 115 (7), 105 (3), 91 (19), 76 (23), 73 (49), 60 (39), 57 (58), 48 (74), 47 (100).

General Procedure for the Preparation of 2,2´-Bis- and 2,2´,2´´-Tris-(4-methyl-5-methylthio-1,3,4-thiadiazolium) Di- and Triperchlorates, (3), (9) and (12) To a suspension of the appropriate 3,3´-diacyl-bis- (2) or 3,3´,3´´-triacyl-tris-(2-methyldithiocarbazate) (8) and (11), (5 mmol) in acetic anhydride (30 ml) at 0°C, 70% perchloric acid (1.5 ml) was added with vigorous stirring, and thereafter kept at room temperature for 48 h. The resulting solid was filtered off, washed with ether (2x15 ml), dried and crystallized from a suitable solvent.

2,2´-Oxydimethylene-bis-(4-methyl-5-methylthio-1,3,4-thiadiazolium) diperchlorate (3a).- Yield: 1.95 g (73%) colorless needles; mp 209-210°C (from methanol). Anal. Calcd for $C_{10}H_{16}N_4O_9Cl_2S_4$: C, 22.43; H, 3.01; N, 10.46. Found: C, 22.25; H, 2.89; N, 10.16. $\nu_{max.}$ (cm^{-1}) 1467, 1376, 1280, 1268, 1206, 1098, 736, 719, 662, 623; δ (^1H, 200 MHz) (DMSO-d_6) 5.17 (4H, s, OCH_2), 4.12 (6H, s, NCH_3), 3.09 (6H, s, SCH_3); δ (^{13}C) 180.56 (C-5), 165.16 (C-2), 60.01 (OCH_2), 41.76 (NCH_3), 20.72 (SCH_3); m/z (%) 336 (M^+-2ClO_4^-, 1), 306 (100), 291 (7), 290 (57), 274 (6), 230 (4), 202 (12), 201 (30), 160 (37), 146 (11), 125 (2), 105 (6), 96 (5), 76 (11), 73 (3), 64 (23).

2,2´-m-Phenylene-bis-(4-methyl-5-methylthio-1,3,4-thiadiazolium) diperchlorate (3b).- Yield: 2.41 g (85%) colorless prisms; mp 271-272°C (from acetonitrile). Anal. Calcd for $C_{14}H_{16}N_4O_8Cl_2S_4$: C, 29.63; H, 2.84; N, 9.87. Found: C, 29.72; H, 2.68; N, 9.90. $\nu_{max.}$ (cm^{-1}) 1540, 1511, 1466, 1376, 1319, 1279, 1217, 1200, 1092, 809, 769, 724, 679, 622; δ (^1H, 200 MHz) (DMSO-d_6) 8.50 (1H, s), 8.31(2H, d, J = 8.00 Hz), 7.95 (1H, t, J = 8.00 Hz), 4.23 (6H, s, NCH_3), 3.16 (6H, s, SCH_3); δ (^{13}C) 180.15 (C-5), 163.33 (C-2), 131.93, 131.63, 127.81, 125.84, 42.06 (NCH_3), 21.07 (SCH_3); m/z (%) 368 (M^+-2ClO_4^-, 1), 338 (8), 323 (12), 322 (72), 306 (16), 262 (100), 233 (36), 183 (92), 157 (34), 146 (14), 128 (12), 105 (16), 76 (11), 73 (31), 64 (87).

2,2´-(2,5-Thiophenediyl)-bis-(4-methyl-5-methylthio-1,3,4-thiadiazolium) diperchlorate (3c).- Yield: 2.58 g (90%) colorless prisms; mp 237-239°C (from methanol). Anal. Calcd for $C_{12}H_{14}N_4O_8Cl_2S_5$: C, 25.13; H, 2.46; N, 9.77. Found: C, 24.87; H, 2.51; N, 9.60. $\nu_{max.}$ (cm^{-1}) 1563, 1540, 1302, 1280, 1217, 1200, 1093, 866, 827, 736, 725, 679; δ (^1H, 200 MHz) (DMSO-d_6) 7.53 (2H, s), 4.16 (6H, s, NCH_3), 3.15 (6H, s, SCH_3); δ (^{13}C) 179.40 (C-5), 168.00 (C-2), 139.66, 129.01, 41.95 (NCH_3), 21.00 (SCH_3); m/z (%) 374 (M^+-2ClO_4^-, 1), 344 (19), 329 (12), 328 (100), 312 (20), 268 (6), 239 (31), 163 (29), 146 (10), 135 (10), 134 (8), 105 (10), 76 (7), 73 (23), 64 (40).

2,2´,2´´-(1,3,5-Benzenetriyl)-tris-(4-methyl-5-methylthio-1,3,4-thiadiazolium) triperchlorate (9).- Yield: 3.70 g (91%) colorless prisms; mp 302°C (from acetonitrile). Anal. Calcd for $C_{18}H_{21}N_6O_{12}Cl_3S_6$: C, 26.62; H, 2.61; N, 10.35. Found: C, 26.47; H, 2.70; N, 10.26. $\nu_{max.}$ (cm^{-1}) 3025, 1709, 1431, 1397, 1296, 1140, 1100, 963, 905, 752, 679, 625; δ (^1H, 200 MHz) (DMSO-d_6) 9.76 (3H, s), 4.27 (9H, s, NCH_3), 3.18 (9H, s, SCH_3); δ (^{13}C) 180.85 (C-5), 162.06 (C-2), 129.93, 129.08, 42.12 (NCH_3), 21.13 (SCH_3); m/z (%) 468 (M^+-3ClO_4^--3CH_3, 6), 392 (4), 381 (3), 351 (16), 349 (22), 348 (11), 322 (8), 320 (11), 291 (12), 289 (6), 278 (3), 259 (13), 249 (13), 240 (16), 219 (60), 218 (33), 217 (16), 171 (16), 149 (100), 145 (16), 136 (15), 127 (14), 119 (26), 91 (43), 73 (12).

2,2´,2´´-(α,α´,α´´-Mesitylenetriyl)-tris-(4-methyl-5-methylthio-1,3,4-thiadiazolium) triperchlorate (12).- Yield: 2.14 g (50%) yellow prisms; mp 135°C (from methanol). Anal. Calcd for $C_{21}H_{27}N_6O_{12}Cl_3S_6$: C, 29.53; H,

3.19; N, 9.84. Found: C, 29.67; H, 3.08; N, 9.74. $\nu_{max.}$ (cm^{-1}) 1609, 1526, 1279, 1262, 1215, 1202, 1092, 962, 729, 679, 623; δ (^1H, 300 MHz) (DMSO-d_6) 7.37 (3H, s), 4.56 (6H, s), 4.09 (9H, s, NCH_3), 3.04 (9H, s, SCH_3); δ (^{13}C) 179.66 (C-5), 167.46 (C-2), 136.54, 129.26, 41.51 (NCH_3), 34.70, 20.54 (SCH_3); m/z (%) 555 (M^+-3ClO_4^-, 2), 552 (3), 410 (3), 277 (6), 264 (6), 185 (8), 170 (7), 160 (5), 155 (2), 146 (12), 132 (7), 105 (7), 91 (20), 76 (12), 73 (100), 72 (50), 70 (18), 69 (14).

General Procedure for the Preparation of 2,2´-Bis- and 2,2´,2´´-Tris-(5-alkylimino-4,5-dihydro-4-methyl-1,3,4-thiadiazoles), (4)-(7), (10) and (13) To a suspension of the corresponding 4-methyl-5-methylthio-1,3,4-thiadiazolium perchlorate, (3), (8) or (11) (5 mmol) in ethanol (15 ml), equimolecular amounts of the appropriate amino derivative (10 or 15 mmol) and triethylamine (10 or 15 mmol) were added. The reaction mixture was refluxed for 6 h and, on cooling, the resulting solid was filtered, washed with ether (2x10 ml), dried and crystallized from the suitable solvent.

2,2´-Oxydimethylene-bis-[4,5-dihydro-5-(1-hydroxymethylethylimino)-4-methyl-1,3,4-thiadiazole] (4a).- Yield: 0.39 g (20%) yellow prisms; mp 131-132°C (from ethanol). Anal. Calcd for $C_{14}H_{24}N_6O_3S_2$: C, 43.28; H, 6.23; N, 21.63. Found: C, 43.12; H, 6.18; N, 21.41. $\nu_{max.}$ (cm^{-1}) 3347, 1648, 1631, 1460, 1348, 1331, 1274, 1195, 1149, 1042, 946, 895, 725, 668, 645; δ (^1H, 200 MHz) ($CDCl_3$) 4.50 (2H, s, OCH_2), 3.63 (2H, d, J = 6.50 Hz, CH_2OH), 3.53 (3H, s, NCH_3), 2.95 (1H, sext, J = 6.50 Hz, CH), 2.57 (1H, s, OH), 1.11 (3H, d, J = 6.50 Hz); m/z (%) 387 (M^+-1, 1), 359 (11), 358 (22), 357 (69), 313 (19), 243 (28), 211 (85), 172 (23), 170 (58), 163 (65), 155 (48), 83 (100), 73 (22), 57 (16).

2,2´-Oxydimethylene-bis-[5-(2-bromoethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (4b).- Yield: 1.65 g (68%) yellow needles; mp 95-97°C (from ethanol). Anal. Calcd for $C_{12}H_{18}N_6OBr_2S_2$: C, 29.64; H, 3.73; N, 17.28. Found: C, 29.42; H, 3.60; N, 17.12. $\nu_{max.}$ (cm^{-1}) 1631, 1618, 1562, 1417, 1368, 1268, 1194, 1051, 940, 902, 729, 625; δ (^1H, 200 MHz) ($CDCl_3$) 4.50 (2H, s, OCH_2), 3.58 (2H, t, J = 6.30 Hz, CH_2OH), 3.55 (3H, s, NCH_3), 3.53 (2H, t, J = 6.30 Hz, CH_2N); m/z (%) 488 (M^++4, 1), 486 (M^++2, 2), 484 (M^+, 1), 407 (68), 405 (61), 393 (20), 391 (20), 197 (52), 170 (10), 156 (43), 149 (63), 107 (13), 86 (12), 72 (16), 70 (19), 69 (100).

2,2´-m-Phenylene-bis-(4,5-dihydro-4-methyl-5-propilimino-1,3,4-thiadiazole) (5a).- Yield: 1.48 g (76%) colorless prisms; mp 114-115°C (from methanol). Anal. Calcd for $C_{18}H_{24}N_6S_2$: C, 55.64; H, 6.23; N, 21.63. Found: C, 55.77; H, 6.12; N, 21.50. $\nu_{max.}$ (cm^{-1}) 1631, 1535, 1467, 1348, 1285, 1274, 1263, 1223, 1098, 1070, 1013, 957, 900, 889, 787, 747, 725, 679, 623; δ (^1H, 200 MHz) ($CDCl_3$) 7.87 (1H,s), 7.63 (2H, dd, ^3J = 8.00 Hz, ^4J = 1.50 Hz), 7.43 (1H, t, J = 8.00 Hz), 3.66 (6H, s, NCH_3), 3.14 (4H, t, J = 7.00 Hz), 1.73 (4H, sext, J = 7.00 Hz), 1.00 (6H, t, J = 7.00 Hz); m/z (%) 388 (M^+, 24), 361 (10), 360 (20), 359 (100), 258 (6), 230 (6), 229 (37), 203 (30), 165 (82), 157 (17), 156 (15), 146 (39), 129 (59), 102 (22), 81 (14), 73 (25).

2,2´-m-Phenylene-bis-[4,5-dihydro-5-(1-hydroxymethylethylimino)-4-methyl-1,3,4-thiadiazole] (5b).- Yield: 0.63 g (30%) yellow prisms; mp 143-145°C (from acetonitrile). Anal. Calcd for $C_{18}H_{24}N_6O_2S_2$: C, 51.41; H, 5.75; N, 19.98. Found: C, 51.35; H, 5.70; N, 19.78. $\nu_{max.}$ (cm^{-1}) 3370, 1631, 1540, 1342, 1291, 1257, 1223, 1098, 1041, 1007, 956, 781, 718, 679; δ (^1H, 200 MHz) ($CDCl_3$) 7.87 (1H, s), 7.63 (2H, dd, ^3J = 7.69 Hz, ^4J = 1.50 Hz), 7.45 (1H, t, J = 7.69 Hz), 3.69 (10H, m, CH_2OH + NCH_3), 3.09 (2H, sext, J = 6.50 Hz), 2.60 (2H, s, OH), 1.18 (6H, d, J = 6.50 Hz, CH_3); m/z (%) 421 (M^+, 8), 391 (13), 390 (22), 389 (100), 243 (49), 217 (35), 179 (77), 146 (40), 129 (33), 114 (12), 102 (19), 86 (59), 76 (4), 73 (24).

2,2´-m-Phenylene-bis-{4,5-dihydro-5-[2-(2´-hydroxyethoxy)ethylimino]-4-methyl-1,3,4-thiadiazole} (5c).- Yield: 1.06 g (44%) yellow prisms; mp 146-147°C (from methanol). Anal. Calcd for $C_{20}H_{28}N_6O_4S_2$: C, 49.98; H, 5.87; N, 17.49. Found: C, 49.80; H, 5.76; N, 17.62. $\nu_{max.}$ (cm^{-1}) 3364, 1631, 1614, 1460, 1348, 1314, 1285, 1262, 1229, 1127, 1076, 1013, 991, 957, 900, 781, 742, 719, 679; δ (^1H, 200 MHz) ($CDCl_3$) 7.87 (1H, s), 7.62 (2H, dd, ^3J = 7.00 Hz, ^4J = 1.00 Hz), 7.45 (1H, t, J = 7.00 Hz), 3.86 (4H, t, J = 5.20 Hz), 3.71 (10H, m), 3.66 (6H, s. NCH_3), 3.30 (4H, t, J= 5.20 Hz); m/z (%) 480 (M^+, 4), 406 (25), 405 (100), 318 (6), 247 (3), 229 (51), 203 (18), 165 (47), 146 (31), 129 (36), 117 (18), 116 (67), 115 (15), 73 (15), 69 (30).

2,2´-m-Phenylene-bis-[4,5-dihydro-5-(2-hydroxyethylimino)-4-methyl-1,3,4-thiadiazole] (5d).- Yield: 0.86 g (44%) yellow needles; mp 214-215°C (from ethanol). Anal. Calcd for $C_{16}H_{20}N_6O_2S_2$: C, 48.96; H, 5.14; N, 21.41. Found: C, 48.72; H, 5.01; N, 21.30. $\nu_{max.}$ (cm^{-1}) 3320, 1614, 1534, 1421, 1364, 1268, 1092, 1053, 962, 900, 781, 719, 679; δ (^1H, 200 MHz) ($CDCl_3$) 7.88 (1H, s), 7.64 (2H, d, J = 8.4 Hz), 7.45 (1H, t, J = 8.4 Hz), 3.63 (4H, t, J = 6.10 Hz, CH_2OH), 3.56 (6H, s, NCH_3), 3.21 (4H, t, J = 6.10 Hz, NCH_2); m/z (%) 392 (M^+, 10), 362 (13), 361 (100), 318 (6), 229 (48), 203 (23), 165 (44), 146 (33), 129 (49), 102 (23), 73 (23), 72 (26), 69 (35).

2,2´-m-Phenylene-bis-[4,5-dihydro-5-(2-mercaptoethylimino)-4-methyl-1,3,4-thiadiazole] (5e).- Yield: 0.83 g (39%) yellow plates; mp 176-178°C (from acetonitrile). Anal. Calcd for $C_{16}H_{20}N_6S_4$: C, 45.26; H, 4.75; N, 19.79. Found: C, 45.34; H, 4.70; N, 19.65. $\nu_{max.}$ (cm^{-1}) 1622, 1537, 1464, 1376, 1360, 1273, 1221, 1097, 1040, 905, 787, 718, 681; δ (^1H, 200 MHz) ($CDCl_3$) 7.89 (1H, s), 7.63 (2H, d, J = 8.4 Hz), 7.44 (1H, t, J = 8.4 Hz), 3.62 (6H, s, NCH_3), 3.47 (4H, t, J = 6.50 Hz, NCH_2), 3.06 (4H, t, J = 6.50 Hz); m/z (%) 424 (M^+, 4), 391 (4), 377 (4), 229 (100), 216 (34), 203 (10), 157 (52), 156 (30), 129 (74), 102 (34), 72 (21), 69 (22).

2,2´-m-Phenylene-bis-[5-(2-bromoethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (5f).- Yield: 1.66 g (64%) yellow plates; mp 153-154°C (from ethanol). Anal. Calcd for $C_{16}H_{18}N_6Br_2S_2$: C, 37.08; H, 3.50; N, 16.21. Found: C, 36.84; H, 3.32; N, 16.18. $\nu_{max.}$ (cm^{-1}) 1622, 1535, 1441, 1360, 1270, 1209, 1087, 1049, 900, 780, 720, 686, 622; δ (^1H, 200 MHz) ($CDCl_3$) 7.88 (1H, s), 7.64 (2H, dd, ^3J = 8.4 Hz, ^4J = 1.20 Hz), 7.45 (1H, t, J = 8.4 Hz), 3.61 (6H, s, NCH_3), 3.56 (4H, t, J = 6.42 Hz), 3.55 (4H, t, J = 6.42 Hz); m/z (%) 520 (M^++ 4, 2), 518 (M^++ 2, 4), 516 (M^+, 2), 439 (6), 437 (6), 425 (19), 423 (17), 229 (97), 203 (33), 165 (74), 129 (100), 102 (45), 86 (13), 72 (25), 69 (42).

2,2´-m-Phenylene-bis-[5-(2,2´-dimethoxyethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (5h).- Yield: 1.03 g (43%) colorless needles; mp 126-128°C (from ethanol). Anal. Calcd for $C_{20}H_{28}N_6O_4S_2$: C, 49.98; H, 5.87; N, 17.49. Found: C, 49.79; H, 5.80; N, 17.22. $\nu_{max.}$ (cm^{-1}) 1625, 1540, 1348, 1263, 1200, 1138, 1081, 1053, 968, 906, 849, 787, 719, 682; δ (^1H, 200 MHz) ($CDCl_3$) 7.89 (1H, s), 7.63 (2H, dd, ^3J = 8.40 Hz, ^4J = 1.30 Hz), 7.44 (1H, t, J = 8.40 Hz), 4.63 (2H, t, J = 5.25 Hz), 3.65 (6H, s, NCH_3), 3.45 (12H, s, OCH_3), 3.32 (4H, d, J = 5.25 Hz, CH_2N); m/z (%) 480 (M^+, 1), 406 (1), 405 (2), 230 (1), 229 (5), 203 (2), 156 (2), 146 (4), 129 (5), 114 (1), 102 (2), 76 (3), 75 (100), 74 (2), 73 (3), 72 (3), 69 (5), 47 (15).

2,2´-m-Phenylene-bis-(5-benzylimino-4,5-dihydro-4-methyl-1,3,4-thiadiazole) (5i).- Yield: 1.14 g (47%) brown needles; mp 134-136°C (from ethanol). Anal. Calcd for $C_{26}H_{24}N_6S_2$: C, 64.44; H, 4.99; N, 17.34. Found: C, 64.23; H, 4.78; N, 17.28. $\nu_{max.}$ (cm^{-1}) 1622, 1611, 1584, 1529, 1452, 1404, 1361, 1281, 1262, 1227, 1215, 1092, 1057, 1045, 966, 918, 883, 833, 797, 770, 741, 729, 702, 681; δ (^1H, 200 MHz) ($CDCl_3$) 7.87 (1H, s), 7.61 (2H, d, J = 7.65 Hz), 7.24-7.45 (12H, m), 4.40 (4H, s, CH_2N), 3.70 (6H, s, NCH_3); m/z (%) 484 (M^+, 42), 407 (7), 306 (14), 305 (14), 229 (9), 203 (7), 186 (16), 157 (69), 156 (26), 146 (29), 129 (47), 121 (13), 120 (11), 106 (26), 105 (34), 91 (100), 73 (26).

2,2´-m-Phenylene-bis-(4,5-dihydro-4-methyl-5-α-methylbenzylimino-1,3,4-thiadiazole) (5j).- Yield: 1.31 g (51%) yellow needles; mp 180-183°C (from ethanol). Anal. Calcd for $C_{28}H_{28}N_6S_2$: C, 65.60; H, 5.50; N, 16.39. Found: C, 65.33; H, 5.35; N, 16.18. $\nu_{max.}$ (cm^{-1}) 1630, 1618, 1582, 1368, 1298, 1281, 1101, 1090, 1049, 795, 756, 737, 725, 702, 681, 608; δ (^1H, 200 MHz) ($CDCl_3$) 7.23-7.83 (14H, m), 4.03 (2H, q, J = 6.50 Hz), 3.73 (6H, s, NCH_3), 1.59 (6H, d, J = 6.50 Hz); m/z (%) 514 (M^+, 3), 512 (23), 498 (34), 497 (100), 305 (13), 279 (7), 241 (26), 148 (31), 146 (25), 121 (29), 105 (96), 103 (28), 79 (24), 77 (46), 73 (17).

2,2´-(2,6-Pyridodiyl)-bis-[4,5-dihydro-5-(1-hydroxymethylethylimino)-4-methyl-1,3,4-thiadiazole] (6a).- Yield: 1.20 g (57%) yellow prisms; mp 197-198°C (from acetonitrile). Anal. Calcd for $C_{17}H_{23}N_7O_2S_2$: C, 48.44; H, 5.50; N, 23.26. Found: C, 48.60; H, 5.41; N, 23.12. $\nu_{max.}$ (cm^{-1}) 3228, 1608, 1563, 1540, 1460, 1342, 1308, 1274, 1149, 1036, 923, 810, 776, 730, 640; δ (^1H, 200 MHz) ($CDCl_3$) 7.84 (3H, m), 3.69 (10H, m, CH_2OH + NCH_3), 3.15 (2H, sext, J = 6.20 Hz), 2.58 (2H, s, OH), 1.20 (6H, d, J = 6.20 Hz, CH_3); m/z (%) 421 (M^+, 5), 391 (21), 390 (85), 275 (2), 244 (36), 219 (13), 218 (86), 179 (100), 167 (13), 149 (43), 130 (31), 103 (41), 86 (65), 83 (58), 77 (12), 73 (27).

2,2´-(2,6-Pyridodiyl)-bis-{4,5-dihydro-5-[2-(2´-hydroxyethoxy)ethylimino]-4-methyl-1,3,4-thiadiazole} (6b).- Yield: 1.06 g (44%) yellow prisms; mp 153-155°C (from methanol). Anal. Calcd for $C_{19}H_{27}N_7O_4S_2$: C, 47.39; H, 5.65; N, 20.36. Found: C, 47.36; H, 5.78; N, 20.17. $\nu_{max.}$ (cm^{-1}) 3364, 3234, 1608, 1563, 1540, 1460, 1353, 1314, 1274, 1132, 1087, 1059, 968, 929, 912, 815, 776, 736, 640; δ (^1H, 200 MHz) ($CDCl_3$) 7.84-7.69 (3H, m), 3.86 (4H, t, J = 5.21 Hz), 3.76-3.69 (10H, m), 3.66 (3H, s, NCH_3), 3.32 (4H, t, J = 5.21 Hz); m/z (%) 481 (M^+, 2), 407 (23), 406 (100), 318 (5), 248 (2), 230 (20), 204 (10), 165 (13), 147 (3), 130 (4), 116 (3), 73 (2).

2,2´-(2,6-Pyridodiyl)-bis-[4,5-dihydro-5-(2-mercaptoethylimino)-4-methyl-1,3,4-thiadiazole] (6c).- Yield: 1.87 g (88%) yellow flakes; mp 160-162°C (from ethanol). Anal. Calcd for $C_{15}H_{19}N_7S_4$: C, 42.33; H, 4.50; N, 23.04. Found: C, 42.50; H, 4.43; N, 23.15. $\nu_{max.}$ (cm^{-1}) 1631, 1568, 1534, 1438, 1359, 1308, 1279, 1087, 1036, 920, 809, 775, 730, 673; δ (^1H, 200 MHz) ($CDCl_3$) 7.97-7.80 (2H, m), 7.29 (1H, dd, J = 8.79 Hz, J = 6.59 Hz), 3.67 (6H, s, NCH_3), 3.41 (4H, t, J = 6.70 Hz), 2.86 (4H, q, J = 6.70 Hz), 1.73 (2H, t, J = 6.70 Hz, SH); m/z (%) 425 (M^+, 4), 392 (7), 378 (32), 230 (100), 217 (3), 204 (24), 158 (6), 157 (8), 130 (46), 103 (38), 72 (29), 69 (27).

2,2´-(2,6-Pyridodiyl)-bis-[5-(2-bromoethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (6d).- Yield: 2.03 g (78%) yellow flakes; mp 208-209°C (from ethanol). Anal. Calcd for $C_{15}H_{17}N_7Br_2S_2$: C, 34.70; H, 3.30; N, 18.88. Found: C, 34.74; H, 3.21; N, 19.02. $\nu_{max.}$ (cm^{-1}) 1642, 1614, 1562, 1531, 1445, 1360, 1277, 1206, 1088, 1034, 916, 810, 774, 642, 623; δ (^1H, 200 MHz) ($CDCl_3$) 7.88 (3H, m), 3.66 (6H, s, NCH_3), 3.62 (8H, s); m/z (%) 521 (M^++4, 13), 519 (M^++2, 26), 517 (M^+, 12), 440 (2), 438 (2), 426 (100), 424 (80), 230 (88), 204 (64), 166 (96), 130 (68), 103 (66), 86 (15), 72 (29), 69 (43).

2,2´-(2,6-Pyridodiyl)-bis-[5-(2,2´-dimethoxyethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (6f).- Yield: 1.54 g (64%) colorless prisms; mp 129-131°C (from ethanol). Anal. Calcd for $C_{19}H_{27}N_7O_4S_2$: C, 47.39; H, 5.65; N, 20.36. Found: C, 47.30; H, 6.73; N, 20.51. $\nu_{max.}$ (cm^{-1}) 1631, 1563, 1342, 1274, 1132, 1081, 1053, 962, 923, 809, 775, 741, 645; δ (^1H, 200 MHz) ($CDCl_3$) 7.88 (2H, m), 7.79 (1H, dd, J = 8.79 Hz, J = 6.59 Hz), 4.66 (2H, t, J = 5.28 Hz), 3.66 (6H, s, NCH_3), 3.46 (12H, s), 3.36 (4H, d, J = 5.28 Hz); m/z (%) 481 (M^+, 2), 230 (9), 204 (5), 157 (3), 147 (4), 130 (9), 103 (7), 76 (4), 75 (100), 69 (9).

2,2´-(2,6-Pyridodiyl)-bis-(5-benzylimino-4,5-dihydro-4-methyl-1,3,4-thiadiazole) (6g).- Yield: 1.65 g (68%) orange prisms; mp 163-164°C (from ethanol). Anal. Calcd for $C_{25}H_{23}N_7S_2$: C, 61.83; H, 4.77; N, 20.19. Found: C, 61.91; H, 4.83; N, 20.02. $\nu_{max.}$ (cm^{-1}) 1636, 1620, 1564, 1533, 1456, 1342, 1281, 1026, 918, 814, 770, 729, 704, 697, 640; δ (^1H, 200 MHz) ($CDCl_3$) 7.86-7.74 (3H, m), 7.40-7.19 (10H, m), 4.42 (4H, s), 3.74 (6H, s, NCH_3); m/z (%) 485 (M^+, 100), 484 (30), 408 (12), 307 (9), 306 (12), 230 (9), 204 (11), 158 (26), 157 (9), 130 (21), 121 (13), 105 (13), 103 (16), 91 (74), 73 (20).

2,2´-(2,6-Pyridodiyl)-bis-[4,5-dihydro-4-methyl-5-(α-methyl)benzylimino-1,3,4-thiadiazole] (6h).- Yield: 1.44 g (56%) yellow needles; mp 188-190°C (from ethanol). Anal. Calcd for $C_{27}H_{27}N_7S_2$: C, 63.13; H, 5.30; N, 19.09. Found: C, 63.01; H, 5.48; N, 18.92. $\nu_{max.}$ (cm^{-1}) 1631, 1568, 1540, 1365, 1342, 1280, 1155, 1064, 1030, 923, 810, 787, 770, 758, 735, 702, 644, 610; δ (^1H, 300 MHz) ($CDCl_3$) 7.84-7.77 (2H, m), 7.70 (1H, dd, J = 8.26 Hz, J = 7.21 Hz), 7.44 (4H, d, J = 7.87 Hz), 7.31 (4H, td, J = 7.08 Hz, J = 1.31 Hz), 7.25-7.17 (2H, m), 4.12 (2H, q, J = 6.30 Hz), 3.75 (6H, s, NCH_3), 1.59 (6H, d, J = 6.30 Hz); m/z (%) 515 (M^+, 2), 513 (16), 499 (29), 498 (100), 306 (12), 280 (10), 241 (35), 148 (23), 145 (16), 121 (17), 105 (60), 103 (26), 79 (14), 77 (25), 73 (8).

2,2´-(2,5-Thiophenediyl)-bis-[5-(2-bromoethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (7a).- Yield: 0.66 g (25%) yellow flakes; mp 164-166°C (from ethanol). Anal. Calcd for $C_{14}H_{16}N_6Br_2S_3$: C, 32.07; H, 3.08; N,

16.03. Found: C, 31.95; H, 3.13; N, 16.20. $\nu_{max.}$ (cm^{-1}) 1634, 1614, 1443, 1354, 1290, 1209, 1047, 877, 785, 654, 633; δ (^1H, 200 MHz) ($CDCl_3$) 7.07 (2H, s), 3.61 (6H, s, NCH_3), 3.58 (4H, t, J = 5.60 Hz), 3.57 (4H, t, J = 5.60 Hz); m/z (%) 526 (M^++4, 1), 524 (M^++2, 2), 522 (M^+, 1), 235 (20), 209 (6), 170 (11), 135 (48), 108 (21), 86 (21), 72 (47), 69 (100).

2,2´,2´´-(1,3,5-Benzenetriyl)-tris-(4,5-dihydro-4-methyl-5-propylimino-1,3,4-thiadiazole) (10a).- Yield: 1.85 g (68%) yellow prisms; mp 213°C (from ethanol). Anal. Calcd for $C_{24}H_{33}N_9S_3$: C, 53.01; H, 6.12; N, 23.18. Found: C, 52.94; H, 6.09; N, 23.30. $\nu_{max.}$ (cm^{-1}) 1639, 1597, 1464, 1315, 1279, 1082, 895, 854, 762, 752, 725, 673; δ (^1H, 300 MHz) ($CDCl_3$) 7.74 (3H, s), 3.65 (9H, s, NCH_3), 3.13 (6H, t, J = 6.96 Hz), 1.73 (6H, qt, J = 7.32 Hz, J = 6.96 Hz), 1.01 (9H, t, J = 7.32 Hz); m/z (%) 543 (M^+, 5), 542 (18), 514 (31), 513 (98), 384 (6), 383 (24), 357 (20), 271 (15), 253 (19), 242 (100), 227 (21), 186 (27), 177 (24), 164 (38), 156 (2), 153 (7), 136 (4), 127 (4), 73 (4).

2,2´,2´´-(1,3,5-Benzenetriyl)-tris-[4,5-dihydro-5-(2-hydroxyethylimino)-4-methyl-1,3,4-thiadiazole] (10b).- Yield: 1.76 g (64%) yellow needles; mp 266°C (from acetonitrile). Anal. Calcd for $C_{21}H_{27}N_9O_3S_3$: C, 45.89; H, 4.95; N, 22.93. Found: C, 46.01; H, 5.02; N, 22.81. $\nu_{max.}$ (cm^{-1}) 3325, 1614, 1535, 1404, 1359, 1336, 1225, 1217, 1087, 1053, 968, 872, 761, 745, 725, 675; δ (^1H, 300 MHz) (DMSO-d_6/TFA) 8.34 (3H, s) 4.08 (9H, s, NCH_3), 3.92 (6H, br s), 3.66 (6H, br s); m/z (%) 549 (M^+, 1), 515 (17), 514 (29), 513 (100), 384 (5), 383 (21), 357 (18), 285 (4), 282 (4), 253 (16), 242 (76), 227 (18), 207 (2), 191 (5), 186 (20), 177 (18), 164 (29), 154 (6).

2,2´,2´´-(1,3,5-Benzenetriyl)-tris-[5-(2-bromoethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (10c).- Yield: 2.66 g (72%) yellow prisms; mp 214°C (from acetonitrile). Anal. Calcd for $C_{21}H_{24}N_9Br_3S_3$: C, 34.16; H, 3.28; N, 17.07. Found: C, 34.30; H, 3.20; N, 17.15. $\nu_{max.}$ (cm^{-1}) 1625, 1535, 1364, 1285, 1207, 1086, 762, 731, 675, 621; δ (^1H, 300 MHz) ($CDCl_3$/DMSO-d_6) 7.87 (3H, s), 3.72 (9H, s, NCH_3), 3.65 (6H, t, J = 5.84 Hz), 3.63 (6H, t, J = 5.84 Hz); m/z (%) 498 (M^+-3Br, 2), 495 (3), 342 (20), 228 (8), 207 (11), 186 (7), 177 (8), 168 (3), 166 (3), 164 (8), 153 (5), 137 (3), 133 (3), 127 (3), 110 (12), 108 (12), 96 (93), 95 (17), 94 (100), 93 (20), 81 (27), 79 (27).

2,2´,2´´-(1,3,5-Benzenetriyl)-tris-(4,5-dihydro-4-methyl-5-pentylimino-1,3,4-thiadiazole) (10d).- Yield: 2.32 g (74%) yellow prisms; mp 182°C (from 1,4-dioxane). Anal. Calcd for $C_{30}H_{45}N_9S_3$: C, 57.38; H, 7.22; N, 20.08. Found: C, 57.40; H, 7.33; N, 19.97. $\nu_{max.}$ (cm^{-1}) 1626, 1597, 1406, 1335, 1285, 1263, 1082, 1030, 858, 758, 673; δ (^1H, 300 MHz) ($CDCl_3$) 7.73 (3H, s), 3.64 (9H, s, NCH_3), 3.15 (6H, t, J = 7.08 Hz), 1.71 (6H, pseudo-quint, J = 7.08 Hz), 1.43-1.36 (12H, m), 0.94 (9H, t, J = 6.84 Hz); m/z (%) 597 (M^+-2CH_3, 3), 596 (2), 572 (6), 414 (2), 228 (7), 208 (2), 187 (15), 178 (19), 165 (31), 158 (12), 154 (7), 136 (6), 127 (5), 125 (100), 116 (27), 101 (4), 73 (8), 72 (11), 69 (28).

2,2´,2´´-(1,3,5-Benzenetriyl)-tris-[4,5-dihydro-5-(5-hydroxypentylimino)-4-methyl-1,3,4-thiadiazole] (10e).- Yield: 1.86 g (55%) yellow prisms; mp 194-195°C (from acetonitrile). Anal. Calcd for $C_{30}H_{45}N_9O_3S_3$: C, 53.31; H, 6.71; N, 18.65. Found: C, 53.38; H, 6.63; N, 18.50. $\nu_{max.}$ (cm^{-1}) 3234, 1637, 1597, 1336, 1285, 1075, 1028, 753, 723, 674; δ (^1H, 300 MHz) (DMSO-d_6) 7.63 (3H, s), 3.55 (9H, s, NCH_3), 3.43 (6H, t, J = 6.22 Hz), 3.10 (6H, t, J

= 6.83 Hz), 1.64 (6H, pseudo-quint, J = 6.96 Hz), 1.52-1.39 (12H, m); m/z (%) 488 (2), 484 (4), 432 (5), 428 (5), 343 (10), 286 (17), 271 (5), 244 (15), 216 (8), 182 (9), 171 (31), 170 (37), 169 (34), 154 (19), 144 (22), 127 (21), 102 (16), 87 (12), 86 (28), 85 (52), 84 (100), 55 (35), 54 (21).

2,2′,2′′-(1,3,5-Benzenetriyl)-tris-(5-benzylimino-4,5-dihydro-4-methyl-1,3,4-thiadiazole) (10f).- Yield: 3.23 g (94%) red prisms; mp 203°C (from ethanol). Anal. Calcd for $C_{36}H_{33}N_9S_3$: C, 62.86; H, 4.84; N, 18.32. Found: C, 62.81; H, 4.74; N, 18.20. $\nu_{max.}$ (cm^{-1}) 1636, 1598, 1419, 1363, 1282, 1054, 1027, 855, 756, 725, 695, 673; δ (^1H, 300 MHz) ($CDCl_3$) 7.77 (3H, s), 7.43-7.24 (15H, m), 4.39 (6H, s), 3.70 (9H, s, NCH_3); m/z (%) 506 (3), 456 (12), 430 (5), 416 (6), 255 (5), 212 (4), 185 (6), 177 (4), 164 (4), 135 (6), 132 (4), 128 (14), 121 (12), 116 (17), 106 (14), 105 (27), 101 (7), 92 (26), 91 (100), 77 (29), 73 (40).

2,2′,2′′-(α,α′,α′′-Mesitylenetriyl)-tris-[4,5-dihydro-5-(3-hydroxypropylimino)-4-methyl-1,3,4-thiadiazole] (13a).- Yield: 1.46 g (46%) colorless prisms; mp 117°C (from n-hexane). Anal. Calcd for $C_{27}H_{39}N_9O_3S_3$: C, 51.16; H, 6.20; N, 19.89. Found: C, 51.20; H, 6.12; N, 19.97. $\nu_{max.}$ (cm^{-1}) 3370, 1641, 1611, 1366, 1338, 1268, 1159, 1045, 737, 657; δ (^1H, 200 MHz) (DMSO-d_6) 7.13 (3H, s),4.01 (6H, s), 3.46 (9H, s, NCH_3), 3.45 (6H, t, J = 6.30 Hz), 2.98 (6H, t, J = 6.64 Hz), 1.68 (6H, tt, J = 6.64 Hz, J = 6.30 Hz); m/z (%) 502 (1), 488 (4), 474 (3), 373 (3), 278 (33), 277 (79), 221 (6), 201 (32), 199 (38), 185 (18), 183 (39), 171 (9), 154 (13), 149 (20), 143 (6), 129 (17), 115 (11), 97 (22), 95 (26), 85 (16), 83 (23), 73 (27), 71 (26), 69 (100), 60 (31), 57 (62), 55 (65).

2,2′,2′′-(α,α′,α′′-Mesitylenetriyl)-tris-(4,5-dihydro-4-methyl-5-pentylimino-1,3,4-thiadiazole] (13b).- Yield: 1.61 g (48%) colorless prisms; mp 92-93°C (from acetone). Anal. Calcd for $C_{33}H_{51}N_9S_3$: C, 59.16; H, 7.67; N, 18.81. Found: C, 59.04; H, 7.70; N, 18.91. $\nu_{max.}$ (cm^{-1}) 1651, 1604, 1364, 1336, 1261, 1114, 1090, 1026, 803, 738, 730, 653; δ (^1H, 300 MHz) ($CDCl_3$) 7.06 (3H, s), 3.93 (6H, s), 3.52 (9H, s, NCH_3), 3.00 (6H, t, J = 7.05 Hz), 1.61 (6H, pseudo-quint, J = 7.15 Hz), 1.37-1.28 (12H, m), 0.89 (9H, t, J = 6.75 Hz); m/z (%) 669 (M^+, 3), 612 (2), 513 (33), 512 (100), 511 (5), 510 (7), 496 (4), 459 (16), 443 (20), 385 (6), 355 (14), 354 (62), 298 (10), 296 (16), 284 (14), 270 (12), 256 (14), 228 (21), 198 (25), 184 (8), 169 (35), 129 (11), 73 (12), 57 (11), 55 (16).

General Procedure for the Preparation of 2,2′-Bis-[5-(2-azidoethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole].- To a 80°C heated solution of the corresponding 2,2′-bis[5-(2-bromoethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (5 mmol) in DMSO (40 ml), sodium azide (0.65 g, 10 mmol) was added. The reaction mixture was allowed to stand at this temperature for 6 h and immediately afterwards dropped into ice/water (100 ml). The resulting solid was filtered, dried and crystallized from n-hexane.

2,2′-Oxydimethylene-bis-[5-(2-azidoethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (4c).- Yield: 0.88 g (43%) yellow plates; mp 66-68°C. Anal. Calcd for $C_{12}H_{18}N_{12}OS_2$: C, 35.11; H, 4.42; N, 40.95. Found: C, 34.89; H, 4.50; N, 40.80. $\nu_{max.}$ (cm^{-1}) 2098, 1618, 1339, 1273, 1200, 1080, 1053, 941, 831, 733, 655; δ (^1H, 200 MHz) ($CDCl_3$) 4.44 (2H, s, OCH_2), 3.48 (3H, s, NCH_3), 3.43 (2H, t, J = 5.50 Hz, CH_2N_3), 3.24 (2H, t, J = 5.50 Hz, CH_2N);

m/z (%) 410 (M^+, 1), 354 (2), 197 (21), 170 (2), 156 (13), 149 (9), 107 (2), 77 (22), 70 (15), 69 (100).

2,2´-m-Phenylene-bis-[5-(2-azidoethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (5g).- Yield: 1.68 g (76%) yellow plates; mp 85-87°C. Anal. Calcd for $C_{16}H_{18}N_{12}S_2$: C, 43.43; H, 4.10; N, 37.98. Found: C, 43.70; H, 4.22; N, 37.70. $\nu_{max.}$ (cm^{-1}) 2100, 1625, 1540, 1348, 1263, 1104, 1053, 951, 900, 781, 719, 679; δ (^1H, 200 MHz) ($CDCl_3$) 7.89 (1H, s), 7.63 (2H, d, J = 8.00 Hz), 7.44 (1H, t, J = 8.00 Hz), 3.65 (6H, s, NCH_3), 3.52 (4H, t, J = 5.50 Hz, CH_2N_3), 3.37 (4H, t, J = 5.50 Hz, CH_2N); m/z (%) 442 (M^+, 4), 386 (31), 230 (15), 229 (100), 203 (38), 165 (56), 146 (66), 129 (98), 102 (50), 72 (64), 69 (67).

2,2´-(2,6-Pyridodiyl)-bis-[5-(2-azidoethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (6e).- Yield: 2.06 g (93%) colorless flakes; mp 153-155°C. Anal. Calcd for $C_{15}H_{17}N_{13}S_2$: C, 40.62; H, 3.86; N, 41.06. Found: C, 40.47; H, 3.91; N, 40.96. $\nu_{max.}$ (cm^{-1}) 2101, 1641, 1566, 1360, 1281, 1115, 1082, 1036, 918, 808, 769, 731, 640; δ (^1H, 300 MHz) ($CDCl_3$) 8.20-7.50 (2H, m), 7.79 (1H, dd, J = 8.79 Hz, J = 6.59 Hz), 3.67 (6H, s, NCH_3), 3.54 (4H, t, J = 5.50 Hz), 3.42 (4H, t, J = 5.50 Hz); m/z (%) 443 (M^+, 2), 387 (18), 230 (53), 204 (40), 166 (40), 157 (10), 130 (62), 103 (68), 73 (59), 72 (100), 69 (88).

2,2´-(2,5-Thiophenediyl)-bis-[5-(2-azidoethylimino)-4,5-dihydro-4-methyl-1,3,4-thiadiazole] (7b).- Yield: 1.82 g (81%) colorless flakes; mp 121-123°C. Anal. Calcd for $C_{14}H_{16}N_{12}S_3$: C, 37.49; H, 3.60; N, 37.47. Found: C, 37.55; H, 3.81; N, 37.28. $\nu_{max.}$ (cm^{-1}) 2105, 1651, 1456, 1360, 1283, 1087, 1035, 880, 856, 794, 734; δ (^1H, 200 MHz) ($CDCl_3$) 7.07 (2H, s), 3.60 (6H, s, NCH_3), 3.51 (4H, t, J = 5.60 Hz), 3.34 (4H, t, J = 5.60 Hz); m/z (%) 448 (M^+, 2), 392 (5), 235 (92), 209 (5), 162 (34), 152 (45), 135 (100), 134 (31), 108 (12), 73 (50), 72 (76), 70 (42), 69 (91).

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