Synthesis of some Newer 5-(5-Aryl-2*H*-tetrazol-2-ylmethyl)-4-substituted-*s*-triazole-3-thiols as Possible Antiinflammatory Agents

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Several 1-(5-aryl-2*H*-tetrazol-2-ylacetyl)-4-substituted thiosemicarbazides and 5-(5-aryl-2*H*-tetrazol-2-ylmethyl)-4-substituted-*s*-triazole-3-thiols were synthesized as possible antiinflammatory agents. These compounds were characterized by their elemental, infrared and nuclear magnetic resonance analysis.

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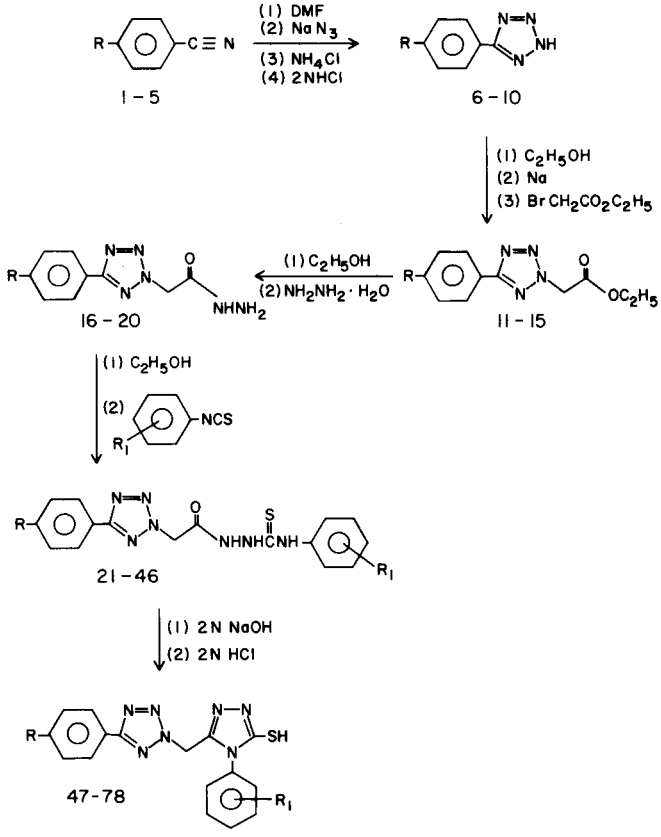
Diverse pharmacological properties have been found to be associated with triazole derivatives (1-8). These include antiinflammatory, anticholinergic, antidepressant, analgesic, sedative, antihypertensive, antiasthmatic, and tranquilizing properties. Earlier studies have reported several tetrazole derivatives to be active antiinflammatory agents (9-13). The clinical use of 5-amino-1-phenyl tetrazol in patients with rheumatoid arthritis, who had previously failed to respond to salicyclic acid, phenylbutazone, indomethacin or corticosteroids (14,15), prompted synthesis of several 1-(5-aryl-2*H*-tetrazol-2-ylacetyl)-4-substituted thiosemicarbazides and their cyclized derivatives, 5-(5-aryl-2*H*-tetrazol-2-ylmethyl)-4-substituted-*s*-triazol-3-thiols, as possible antiinflammatory agents. The synthesis of aforesaid compounds was carried out according to the steps outlined in Scheme I.



Scheme I

Various 5-aryltetrazoles (**6-10**) were obtained by the reaction of appropriate benzonitrile (**1-5**) with sodium azide in the presence of ammonium chloride where a nucleophilic attack of the azide ion (N_3^-) on the nitrile carbon is followed by cyclization of the iminoazide (16). These compounds were further treated with ethyl bromoacetate in the presence of sodium ethoxide to give ethyl 5-aryl-2*H*-tetrazol-2-ylacetate (**11-15**). The reaction of suitable acetate **11-15** with hydazine hydrate in absolute ethanol yielded 5-aryl-2*H*-tetrazol-2-ylacethydrazides (**16-20**). The acethydrazide, on refluxing with appropriate aryl isothiocyanate in absolute ethanol, gave 1-(5-aryl-2*H*-tetrazol-2-ylacetyl)-4-substituted thiosemicarbazides (**21-46**). Finally, the cyclization of **21-46** to the corresponding 5-(5-aryl-2*H*-tetrazol-2-ylmethyl)-4-substituted-*s*-triazol-3-thiols (**47-78**) was achieved by refluxing **21-46** in the presence of 2*N* sodium hydroxide solution.

The infrared spectra of **21-46** exhibited characteristic broad N-H stretching absorption bands in the region between 3060-3340 cm^{-1}. The C=O stretching bands were observed between 1700-1735 cm^{-1}. The regions where C=N stretching and C=C stretching of aromatic ring occur are found to overlap in these spectra and these absorption were observed between 1680-1490 cm^{-1}. The infrared spectra of **47-78** showed a characteristic C=S stretching band in the region of 1340-1310 cm^{-1}. As reported earlier, the thiol predominantly exists in its tautomeric thione form by protonating the adjacent nitrogen atom (17,18). The bands in the region of 1660-1490 cm^{-1} are assigned to C=N stretching and C=C stretching of aromatic ring.

In the nuclear magnetic resonance spectra of **21-46**, the $-CH_2-$ protons appeared as a singlet in the range of δ 5.60-5.70. The aromatic protons of these compounds exhibited multiplets in the range of δ 6.60-8.30. The signals due to -NH- protons of the thiosemicarbazide part appeared in the region of δ 9.20-11.00. The assignment of these signals to the -NH- protons is supported by the fact

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Table I

Physical Constants of 5-Aryl-2*H*-tetrazol-2-ylacethydrazides

Compound No.	R	Melting Point °C	Yield %	Recrystallization Solvent	Molecular Formula	Analysis % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
16	H	206-207.5	95	Ethanol	$C_9H_{10}N_6O$	—	—	—	—	—	—
17	OCH_3	191-192	92	Ethanol	$C_{10}H_{12}N_6O_2$	48.38	4.84	33.87	48.42	4.77	33.65
18	F	211-212	95	Ethanol	$C_9H_9FN_6O$	45.76	3.81	35.59	45.46	4.05	35.38
19	Cl	238-239	95	Ethanol--Water	$C_9H_9ClN_6O$	42.77	3.56	33.26	42.51	3.32	33.57
20	Br	237-238	98	DMF-Water	$C_9H_9BrN_6O$	36.36	3.03	28.28	36.50	2.87	28.42

(a) Compound **16** was reported earlier (23).

Table II

Physical Constants of 1-(5-Aryl-2*H*-tetrazol-2-ylacetyl)-4-substituted Thiosemicarbazides (**21-52**)

Compound No.	R	R_1	Melting Point °C	Yield %	Molecular Formula	Elemental Analysis % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
21	OCH_3	H	159.5-162	98	$C_{17}H_{17}N_7O_2S$	53.26	4.43	25.58	53.15	4.33	25.79
22	OCH_3	2-CH_3	135-136.5	98	$C_{18}H_{19}N_7O_2S$	54.40	4.78	24.68	54.16	4.74	24.86
23	OCH_3	3-CH_3	145-146.5	98	$C_{18}H_{19}N_7O_2S$	54.40	4.78	24.68	54.21	4.85	24.65
24	OCH_3	4-CH_3	175-177	94	$C_{18}H_{19}N_7O_2S$	54.40	4.78	24.68	54.43	4.79	24.78
25	OCH_3	3,4-$(CH_3)_2$	155-157	91	$C_{19}H_{21}N_7O_2S$	55.47	5.10	23.84	55.79	5.14	23.68
26	OCH_3	2-OC_2H_5	200-201.5	91	$C_{19}H_{21}N_7O_3S$	53.39	4.91	22.95	53.15	4.79	23.24
27	OCH_3	4-Cl	173-176	93	$C_{17}H_{16}ClN_7O_2S$	48.86	3.83	23.47	48.61	3.74	23.60
28	F	H	215 dec.	96	$C_{16}H_{14}FN_7OS$	51.75	3.77	26.41	51.61	3.80	26.59
29	F	2-CH_3	158-159	98	$C_{17}H_{16}FN_7OS$	52.98	4.16	25.45	52.87	4.03	25.41
30	F	3-CH_3	165-166	95	$C_{17}H_{16}FN_7OS$	52.98	4.16	25.45	52.75	4.39	25.32
31	F	4-CH_3	227 dec.	98	$C_{17}H_{16}FN_7OS$	52.98	4.16	25.45	52.83	4.12	25.38
32	F	3,4-$(CH_3)_2$	166-168	94	$C_{18}H_{18}FN_7OS$	54.13	4.51	24.56	53.92	4.35	24.68
33	F	2-OC_2H_5	208.5-210	94	$C_{18}H_{18}FN_7O_2S$	52.05	4.33	23.61	52.27	4.19	23.84
34	F	4-Cl	208-210	95	$C_{16}H_{13}FClN_7OS$	47.35	3.21	24.17	47.61	3.07	24.33
35	Cl	2-CH_3	224-226	89	$C_{17}H_{16}ClN_7OS$	50.81	3.98	24.41	50.83	4.03	24.65
36	Cl	3-CH_3	224.5-226.5	93	$C_{17}H_{16}ClN_7OS$	50.81	3.98	24.41	50.72	3.92	24.26
37	Cl	4-CH_3	226-230 dec.	95	$C_{17}H_{16}ClN_7OS$	50.81	3.98	24.41	50.65	3.72	24.67
38	Cl	3,4-$(CH_3)_2$	197-198 dec.	91	$C_{18}H_{18}ClN_7OS$	51.98	4.33	23.59	51.82	4.18	23.41
39	Cl	2-OC_2H_5	227-228	96	$C_{18}H_{18}ClN_7O_2S$	50.05	4.17	22.71	49.98	4.19	22.70
40	Cl	4-Cl	208-210	98	$C_{16}H_{13}Cl_2N_7OS$	45.49	3.08	23.22	45.31	3.25	23.07
41	Br	2-CH_3	214-217 dec.	94	$C_{17}H_{16}BrN_7OS$	45.84	3.59	22.02	45.98	3.63	22.11
42	Br	3-CH_3	200-201.5	93	$C_{17}H_{16}BrN_7OS$	45.84	3.59	22.02	45.78	3.57	22.06
43	Br	4-CH_3	220-221	98	$C_{17}H_{16}BrN_7OS$	45.84	3.59	22.02	45.79	3.46	21.84
44	Br	3,4-$(CH_3)_2$	175-177	95	$C_{18}H_{18}BrN_7OS$	47.06	3.92	21.35	47.21	3.84	21.29
45	Br	2-OC_2H_5	201-202	94	$C_{18}H_{18}BrN_7O_2S$	45.47	3.78	20.63	45.24	3.64	20.51
46	Br	4-Cl	211-212	93	$C_{16}H_{13}BrClN_7OS$	41.27	2.79	21.05	41.26	2.92	21.12

that these protons are readily exchanged with deuterium. Hence, upon addition of deuterium oxide to the sample, these signals disappeared. The signal due to the protons of methylene bridge between the tetrazole and triazole rings of **47-78** appeared in the range of δ 5.90-6.06 whereas the aromatic protons appeared between δ 6.60-8.20. The nuclear magnetic resonance spectra of 5-(5-aryl-2*H*-tetrazol-2-ylmethyl)-4-(2-ethoxyphenyl)triazol-3-thiols (**51,58,65,71,77**) gave a quintet instead of quartet for the -OCH_2- protons of -OCH_2-CH_3 substituent present at position 2 of the phenyl ring attached to triazole moiety at position 4. This unusual phenomenon could be explained on the basis of steric hinderance. When a bulky ethoxy group is attached at position 2 of the phenyl ring, the rotation around N-C bond is restricted and, therefore, the phenyl ring attached at position 4 of the triazole nucleus can orient itself in a plane perpendicular to the plane of the triazole ring. In this orientation the -OCH_2- protons interact with the -CH_2- protons of methylene bridge and appear as a quintet. Also due to the same interaction, the -CH_2- protons of methylene bridge in **51, 58, 65, 71** and **77** appear as a triplet. Two separate singlets were observ-

Table III

Physical Constants of 5-(5-Aryl-2*H*-tetrazol-2-ylmethyl)-4-substituted-*s*-triazole-3-thiols (**47-78**)

Compound No. (a)	R	R_1	Melting Point °C	Yield %	Molecular Formula	Elemental Analysis % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
47	H	2-CH_3	217-218.5	94	$C_{17}H_{15}N_7S$	58.45	4.29	28.04	58.60	4.29	28.33
48	H	3-CH_3	199-200	82	$C_{17}H_{15}N_7S$	58.45	4.29	28.04	58.31	4.28	28.06
49	H	4-CH_3	224-225 dec.	94	$C_{17}H_{15}N_7S$	58.45	4.29	28.04	58.37	4.30	27.97
50	H	3,4(CH_3)$_2$	220-221	92	$C_{18}H_{17}N_7S$	59.50	4.68	26.99	59.50	4.75	27.04
51	H	2-OC_2H_5	181-182	98	$C_{18}H_{17}N_7OS$	56.99	4.48	25.85	57.08	4.52	25.85
52	H	4-Cl	206-207	90	$C_{16}H_{12}ClN_7S$	51.96	3.24	26.52	52.02	3.25	26.52
53	OCH_3	H	217-218.5	86	$C_{17}H_{15}N_7OS$	55.89	4.10	26.84	55.87	4.19	26.90
54	OCH_3	2-CH_3	237.5-239	95	$C_{18}H_{17}N_7OS$	56.99	4.48	25.85	56.79	4.22	26.13
55	OCH_3	3-CH_3	202-203	91	$C_{18}H_{17}N_7OS$	56.99	4.48	25.85	56.99	4.33	25.85
56	OCH_3	4-CH_3	235-235.5	90	$C_{18}H_{17}N_7OS$	56.99	4.48	25.85	56.81	4.52	25.94
57	OCH_3	3,4(CH_3)$_2$	220-221.5	86	$C_{19}H_{19}N_7OS$	58.01	4.83	24.93	57.88	4.79	25.38
58	OCH_3	2-OC_2H_5	210-211	86	$C_{19}H_{19}N_7O_2S$	55.74	4.64	23.96	55.62	4.63	24.29
59	OCH_3	4-Cl	217-219	92	$C_{17}H_{14}ClN_7OS$	51.06	3.50	24.53	50.85	3.46	24.19
60	F	H	228-228.5	76	$C_{16}H_{12}FN_7S$	54.39	3.40	27.76	54.23	3.45	27.87
61	F	2-CH_3	239-240.5	82	$C_{17}H_{14}FN_7S$	55.59	3.81	26.70	55.38	3.90	26.82
62	F	3-CH_3	225-226.5	93	$C_{17}H_{14}FN_7S$	55.59	3.81	26.70	55.58	3.94	26.83
63	F	4-CH_3	237-238	92	$C_{17}H_{14}FN_7S$	55.59	3.81	26.70	55.70	3.94	26.77
64	F	3,4(CH_3)$_2$	226-227.5	94	$C_{18}H_{16}FN_7S$	56.69	4.20	25.72	56.45	4.26	25.81
65	F	2-OC_2H_5	182.5-184	88	$C_{18}H_{16}FN_7OS$	54.40	4.03	24.69	54.43	4.07	24.74
66	F	4-Cl	229-230	90	$C_{16}H_{11}FClN_7S$	49.55	2.84	25.29	49.59	2.98	25.20
67	Cl	2-CH_3	238-239	90	$C_{17}H_{14}ClN_7S$	53.19	3.65	25.55	53.15	3.83	25.71
68	Cl	3-CH_3	228-229	97	$C_{17}H_{14}ClN_7S$	53.19	3.65	25.55	53.05	3.61	25.59
69	Cl	4-CH_3	243-244	97	$C_{17}H_{14}ClN_7S$	53.19	3.65	25.55	53.10	3.60	25.67
70	Cl	3,4(CH_3)$_2$	234 dec.	98	$C_{18}H_{16}ClN_7S$	54.34	4.03	24.65	54.15	3.97	24.72
71	Cl	2-OC_2H_5	199-200.5	98	$C_{18}H_{16}ClN_7OS$	52.23	3.86	23.70	52.10	3.77	23.42
72	Cl	4-Cl	221-223	84	$C_{16}H_{11}Cl_2N_7S$	47.52	2.72	24.25	47.39	2.82	24.26
73	Br	2-CH_3	221-222.5	100	$C_{17}H_{14}BrN_7S$	47.78	3.28	22.95	47.55	3.24	22.81
74	Br	3-CH_3	228-229	95	$C_{17}H_{14}BrN_7S$	47.78	3.28	22.95	47.92	3.41	23.01
75	Br	4-CH_3	245 dec.	100	$C_{17}H_{14}BrN_7S$	47.78	3.28	22.95	47.80	3.35	23.02
76	Br	3,4(CH_3)$_2$	228 dec.	88	$C_{18}H_{16}BrN_7S$	48.98	3.63	22.22	48.85	3.48	22.39
77	Br	2-OC_2H_5	135-136	93	$C_{18}H_{16}BrN_7OS$	47.26	3.50	21.44	47.35	3.83	21.29
78	Br	4-Cl	128-130	100	$C_{16}H_{11}BrClN_7S$	42.90	2.46	21.90	43.02	2.58	21.92

(a) The precursors of compounds **47** to **52** are reported earlier (23).

ed for the methyl groups present at position 3 and 4 in **50, 57, 64, 70,** and **76** while in **25, 32, 38,** and **44** both methyl groups exhibited only one singlet. These results indicated that the protons of the methyl groups are magnetically equivalent in **25, 32, 38,** and **44** and nonequivalent in **50, 57, 64, 70,** and **76.**

EXPERIMENTAL

All compounds were analyzed for their carbon, hydrogen, and nitrogen contents. The melting points of these compounds were determined using Fisher-John's melting point apparatus and are uncorrected. Infrared (ir) spectra of all the compounds were recorded in nujol as a mull using a Beckman Model-33 double beam infrared spectrophotometer. Nuclear magnetic resonance (nmr) spectra were recorded on a Varian Associates 90 MHz EM-390 instrument using deuterated dimethylsulfoxide (DMSO-d_6) as a solvent and tetramethylsilane as an internal reference.

Benzonitrile, 4-chlorobenzonitrile, and 4-methoxybenzonitrile were purchased from Aldrich Chemical Co., Milwaukee, Wisconsin, while 4-bromobenzonitrile and 4-fluorobenzonitrile were obtained from PCR, Inc., Gainesville, Florida. Ethyl bromoacetate and phenylisothiocyanate were ordered from Eastman Kodak Company, Rochester, New York, and various arylisothiocyanates were purchased from Trans World Chemicals, Inc., Washington, D.C.

5-Aryltetrazoles (**6-10**).

A mixture of the appropriate benzonitrile (0.2 mole), sodium azide (0.22 mole) and ammonium chloride (0.22 mole) in 200 ml. of dimethylformamide (DMF) was refluxed for 17 hours with stirring in an oil bath maintained at 127°. The DMF was removed by distilling under reduced pressure and the residue was suspended in cold water and acidified to *p*H 2 using 2*N* hydrochloric acid. The solid which separated out was filtered, washed with water and recrystallized from ethanol (19-21).

Ethyl 5-Aryl-2*H*-tetrazol-2-ylacetate (**11-15**).

The appropriate 5-aryltetrazole (0.1 mole) was dissolved in a solution of sodium (0.1 g. atom) in 200 ml. of absolute ethanol. The solution was refluxed in an oil bath with stirring and to this ethyl bromoacetate (0.1 mole) was added slowly. After refluxing for 16 hours, the reaction mixture was filtered while hot and the excess of the solvent was removed on a rotary vacuum evaporator. The crude ester thus obtained was

Table IV

Infrared and Nuclear Magnetic Resonance Spectral Data of 1-(5-Aryl-2*H*-tetrazol-2-ylacetyl)-4-substituted Thiosemicarbazides (**21-46**)

Compound No.	Ir Absorption Bands (a), (cm^{-1})				Nmr Chemical Shifts (b) (δ)			
	N-H Stretch	C=O Stretch	C=N Stretch/ C=C Stretch	$-CH_2-$	Aromatic	NH	R	R_1
21	3360 (m br) 3260 (m br) 3140 (m br)	1770 (s)	1620 (m), 1610 (m) 1565 (m sh) 1510 (s sh)	5.6 (s)	7.0-8.1 (m)	9.8-11.0 (br)	3.8 (s)	
22	3230 (s br)	1700 (s)	1620 (m)	5.6 (s)	6.9-8.3 (m)	9.6-11.0 (br)	3.8 (s)	2.16 (s)
23	3280 (m br)	1730 (m)	1630 (m), 1555 (m sh)	5.53 (s)	6.8-8.0 (m)	9.6-11.0 (br)	3.77 (s)	2.23 (s)
24	3260 (m br) 3160 (m br)	1720 (s)	1620 (w), 1520 (m sh)	5.57 (s)	7.0-8.1 (m)	9.66 (s) 9.7-11.0 (br)	3.8 (s)	2.27 (s)
25	3280-3270 (m br)	1710 (m)	1620 (m), 1550 (m br)	5.6 (s)	7.0-8.1 (m)	9.6 (s) 9.6-11.0 (br)	3.8 (s)	2.2 (s)
26	3340 (m) 3260 (m br) 3160 (m br)	1710 (s)	1620 (s), 1560 (s)	5.6 (s)	6.7-8.1 (m)	9.16 (s) 9.8 (s) 10.63 (br)	3.8 (s)	4.03 (q) 1.33 (t)
27	3240 (m br)	1710 (m)	1620 (m), 1550 (m br)	5.6 (s)	6.9-8.2 (m)	9.8 (s) 9.8-11.0 (br)	3.8 (s)	
28	3300 (m br)	1710 (m)	1610 (w br) 1555 (m br) 1505 (w)	5.7 (s)	7.0-8.3 (m)	9.83 (s) 10.66 (br)		
29	3340 (w sh) 3220 (m) 3120 (m)	1725 (m) 1700 (s)	1615 (w), 1595 (vw) 1535 (m)	5.63 (s)	7.0-8.3 (m)	9.6 (s) 10.0 (s) 10.66 (s)		2.16 (s)
30	3280 (m br)	1700 (s)	1615 (m), 1540 (s)	5.66 (s)	6.8-8.2 (m)	9.8 (s) 10.66 (br)		2.26 (s)
31	3320 (w) 3250 (w br)	1735 (m)	1610 (m), 1565 (m) 1520 (m)	5.66 (s)	7.0-8.2 (m)	9.73 (s) 10.66 (br)		2.27 (s)
32	3240 (m br)	1725 (m) 1705 (m)	1600 (w), 1535 (w)	5.66 (s)	6.9-8.2 (m)	9.66 (br s)		2.17 (s)
33	3320 (m) 3240 (m br)	1710 (m)	1610 (w), 1540 (w)	5.66 (s)	6.7-8.2 (m)	9.2 (s) 9.9 (br) 10.73 (s)		4.03 (q) 1.33 (t)
34	3260 (m) 3200 (w sh)	1705 (m)	1605 (w), 1535 (w)	5.63 (s)	7.2-8.2 (m)	9.8 (s) 10.6 (br)		
35	3320 (m) 3260 (w sh)	1710 (s)	1605 (m), 1540 (s)	5.63 (s)	7.0-8.2 (m)	9.53 (s) 9.66 (s) 10.63 (s)		2.16 (s)
36	3280 (m br) 3180 (m br)	1705 (s)	1610 (w), 1540 (s) 1490 (m)	5.66 (s)	6.8-8.2 (m)	9.66 (s) 10.6 (br)		2.26 (s)
37	3320 (m) 3250 (m br)	1730 (s)	1670 (m), 1610 (m) 1560 (s), 1520 (w)	5.66(s)	7.0-8.2 (m)	9.7 (s) 10.6 (br)		2.3 (s)
38	3220 (s)	1710 (s)	1600 (w), 1540 (m)	5.66 (s)	6.9-8.1 (m)	9.8 (s) 10.66 (br)		2.2 (s)
39	3280 (s)	1715 (s)	1610 (m), 1550 (s)	5.66 (s)	6.6-8.3 (m)	9.16 (s) 9.86 (s) 10.7 (s)		4.06 (q) 1.33 (t)
40	3200 (m br)	1700 (m sh)	1680 (s), 1610 (w) 1560 (m br)	5.7 (s)	7.0-8.2 (m)	9.8 (s) 9.8-11.0 (br)		
41	3200 (s br)	1700 (s)	1610 (m), 1530 (s br)	5.66 (s)	7.1-8.2 (m)	9.57 (s) 9.75 (s) 10.7 (s)		2.2 (s)
42	3270 (s) 3170 (s br)	1700 (s)	1670 (m), 1610 (m) 1540 (s), 1490 (s)	5.66 (s)	6.8-8.1 (m)	9.7 (s) 10.8 (br)		2.3 (s)
43	3210 (m br)	1715 (m)	1690 (m), 1610 (w) 1580 (w), 1550 (w)	5.66 (s)	7.0-8.2 (m)	9.7 (s) 10.8 (br)		2.3 (s)
44	3220 (m br) 3180 (m br)	1710 (s)	1620 (w), 1545 (w)	5.6 (s)	7.0-8.2 (m)	9.8 (s) 10.60 (br)		2.16 (s)
45	3270 (s br)	1710 (s)	1610 (m), 1550 (s)	5.66 (s)	6.7-8.2 (m)	9.16 (s) 9.83 (br s) 10.8 (s)		4.03 (q) 1.33 (t)

46	3240 (s br)	1725 (s)	1690 (m), 1620 (w) 1560 (s), 1510 (s)	5.63 (s)	7.2-8.1 (m)	9.8 (s)

(a) The intensities of the infrared absorption bands are denoted by: s = strong, m = medium w = weak, br = broad, sh = shoulder. (b) Signal multiplicity in nmr: s = singlet, b = broad, m = multiplet, t = triplet and q = quartet, qu = quintet.

Table V

Infrared and Nuclear Magnetic Resonance Spectral Data of 5-(5-Aryl-2*H*-tetrazol-2-ylmethyl)-4-substituted-*s*-triazole-3-thiols (**47-78**)

Compound No.	Ir Absorption Bands (a) (cm^{-1}) C=N Stretch/C=C Stretch	C=S Stretch	Nmr (Chemical Shifts (b) δ) -CH_2-	Aromatic	R	R_1
47	1585 (w), 1540 (w) 1500 (m), 1495 (s)	1340 (m)	5.97 (s)	7.0-8.0 (m)		1.87 (s)
48	1640 (s), 1590 (w) 1525 (m), 1500 (w)	1330 (m)	6.0 (s)	6.8-8.0 (m)		2.2 (s)
49	1590 (w), 1540 (m) 1490 (s)	1325 (m)	6.0 (s)	7.0-8.0 (m)		2.3 (s)
50	1600 (w), 1590 (m) 1540 (m), 1510 (m)	1325 (m)	5.96 (s)	6.6-8.0 (m)		2.03 (s) 2.1 (s)
51	1610 (w), 1600 (w sh) 1540 (w), 1510 (m)	1325 (m)	5.9 (t)	6.8-8.2 (m)		3.86 (qu) 1.06 (t)
52	1575 (w), 1500 (m) 1495 (m)	1335 (m)	6.06 (s)	7.2-8.1 (m)		
53	1600 (w), 1585 (w) 1535 (s), 1505 (m)	1310 (m)	5.97 (s)	6.9-7.9 (m)	3.77 (s)	
54	1630 (w), 1590 (m) 1540 (m), 1500 (m)	1330 (s)	5.77 (s)	6.9-8.0 (m)	3.8 (s)	1.87 (s)
55	1620 (w), 1580 (w) 1530 (m), 1500 (m)	1310 (w)	6.0 (s)	6.8-8.0 (m)	3.8 (s)	2.2 (s)
56	1620 (w), 1585 (w)	1310 (m)	5.96 (s)	6.8-8.0 (m)	3.8 (s)	2.3 (s)
57	1620 (w), 1585 (w)	1330 (s) 1310 (m)	5.97 (s)	6.8-8.0 (m)	3.8 (s)	2.06 (s) 2.16 (s)
58	1620 (m), 1585 (w) 1510 (s)	1320 (s)	5.87 (t)	6.8-8.0 (m)	3.8 (s)	3.8 (qu) 1.06 (t)
59	1620 (w), 1490 (sh)	1330 (s) 1310 (s)	6.0 (s)	6.8-8.0 (m)	3.8 (s)	
60	1620 (m), 1590 (m) 1510 (s), 1490 (s)	1330 (s)	6.0 (s)	7.2-8.2 (m)		
61	1615 (m), 1580 (m) 1505 (m), 1490 (s)	1325 (s)	5.97 (s)	7.1-8.2 (m)		1.87 (s)
62	1620 (m), 1575 (m) 1540 (w), 1490 (s)	1325 (m)	6.03 (s)	6.8-8.2 (m)		2.2 (s)
63	1620 (w), 1590 (w) 1535 (m), 1500 (s)	1330 (m)	6.0 (s)	7.1-8.2 (m)		2.3 (s)
64	1620 (m), 1580 (m) 1540 (w), 1495 (w)	1335 (m)	6.0 (s)	6.7-8.1 (m)		2.1 (s) 2.16 (s)
65	1600 (w), 1585 (m) 1540 (m), 1500 (s)	1305 (s)	5.90 (t)	6.8-8.3 (m)		3.9 (qu) 1.06 (t)
66	1620 (w), 1590 (m) 1535 (w), 1490 (w)	1310 (m)	6.06 (s)	7.2-8.2 (m)		
67	1600 (w), 1590 (m) 1540 (m), 1490 (m)	1310 (m)	5.97 (s)	7.1-8.0 (m)		1.87 (s)
68	1615 (m), 1580 (s) 1490 (s)	1330 (m)	6.0 (s)	6.8-8.1 (m)		2.2 (s)
69	1620 (vw), 1590 (vw) 1530 (w), 1550 (w)	1335 (m)	6.0 (s)	7.0-8.0 (m)		2.26 (s)
70	1610 (w), 1590 (m) 1535 (w), 1495 (w)	1315 (m)	5.97 (s)	7.1-8.0 (m)		2.06 (s) 2.16 (s)
71	1660 (s), 1610 (m) 1570 (s)	1330 (m) 1305 (m)	5.93 (t)	6.8-8.2 (m)		3.87 (qu) 1.1 (t)

72	1620 (w)	1325 (m)	6.1 (s)	7.1-8.0 (m)	
73	1640 (w), 1615 (w) 1590 (w), 1490 (m)	1330 (w)	6.0 (s)	7.1-8.2 (m)	1.87 (s)
74	1610 (w), 1580 (w) 1490 (s)	1340 (w) 1330 (m)	6.0 (s)	6.8-8.0 (m)	2.16 (s)
75	1610 (w), 1590 (w) 1520 (m), 1490 (s)	1325 (m)	6.0 (s)	6.9-8.0 (m)	2.26 (s)
76	1610 (m), 1590 (m) 1510 (m), 1490 (s)	1330 (m) 1305 (w)	6.0 (s)	6.8-8.0 (m)	2.06 (s) 2.16 (s)
77	1650 (s), 1600 (m) 1570 (s), 1490 (s)	1330 (m)	5.9 (t)	6.8-8.0 (m)	3.87 (qu) 1.06 (t)
78	1650 (m br), 1600 (m) 1575 (w), 1500 (s)	1310 (s)	6.03 (s)	7.2-8.0 (m)	

(a,b) See footnotes in Table IV.

recrystallized from aqueous ethanol (20-22).

5-Aryl-2*H*-tetrazol-2-ylacethydrazides (**16-20**).

A mixture of 0.1 mole of suitable ester **11-15** and 0.15 mole of hydrazine hydrate (99%) in 150 ml. of absolute ethanol was refluxed on an oil bath for 8 hours. The reaction mixture was then concentrated by removing excess ethanol under reduced pressure. The solid which separated out on cooling was filtered and recrystallized from aqueous ethanol. The physical constants of various 5-aryl-2*H*-tetrazol-2-ylacethydrazides are recorded in Table I.

1-(5-Aryl-2*H*-tetrazol-2-ylacetyl)-4-substituted Thiosemicarbazides (**21-46**).

Equimolar quantities of the appropriate hydrazide **16-20** (0.01 mole) and suitable aryl isothiocyanate (0.01 mole) were refluxed in 50 ml. of absolute ethanol for 1 hour. The excess of ethanol was removed under reduced pressure using a rotary vacuum evaporator. The solid residue which separated out on cooling was filtered and recrystallized from aqueous dimethylformamide. Physical data for the various 1-(5-aryl-2*H*-tetrazol-2-yl)-4-substituted thiosemicarbazides are listed in Tables II and IV.

5-(5-Aryl-2*H*-tetrazol-2-ylmethyl)-4-substituted-*s*-triazol-3-thiols (**47-78**).

To the suitable 1-(5-aryl-2*H*-tetrazol-2-ylacetyl)-4-substituted thiosemicarbazide (0.005 mole) was added 50 ml. of 2*N* sodium hydroxide and the mixture was refluxed for 2-3 hours. The reaction mixture was cooled, filtered and the filtrate was acidified to *p*H 2 using 2*N* hydrochloric acid. In some cases where the solid separated upon cooling, the reaction mixture was filtered and acidified while hot. The precipitate thus obtained was filtered, washed with ice-cold water and dried. The crude product was recrystallized from dimethylformamide. The various triazoles were characterized by their sharp melting points, elemental analyses and ir and nmr spectral data (Tables III and V).

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