On Triazoles. I. The Reaction of *N*-Cyanocarbonimidodithioic Acid Diesters With Hydrazines

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The reaction of *N*-cyanocarbonimidodithioic acid di(alkyl and aralkyl)esters with different alkyl-, aralkyl- and arylhydrazines to yield 1-substituted-3-R-thio-5-amino-1*H*-1,2,4-triazoles (**3**) and 2-substituted-3-R-thio-5-amino-2*H*-1,2,4-triazoles (**4**) was studied. Isolation of the different types of isomeric pairs of **3** and **4** helped to prove the structure of products obtained which made possible correction of some confusion in the literature. The **3** (R = H) tautomeric structure of the non-substituted derivatives was supported by comparison of their uv and cmr spectra with those of the alkylated and aralkylated derivatives **3** and **4**, respectively, again correcting confusion in the literature. An hplc determination of the ratio of products **3** and **4** formed in the above reactions with different hydrazines made it possible to prove the mechanism of the reaction.

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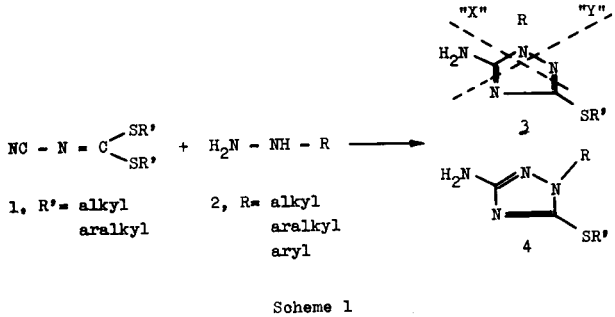
In connection with our biological research, we have studied the reaction of *N*-cyanocarbonimidodithioic acid di(alkyl and aralkyl) esters (**1**) with different alkyl-, aralkyl- and arylhydrazines (**2**) to yield 1-substituted-3-R-thio-5-amino-1*H*-1,2,4-triazole (**3**) or 2-substituted-3-R-thio-5-amino-2*H*-1,2,4-triazole (**4**) derivatives (Scheme 1, Table I).



Scheme 1

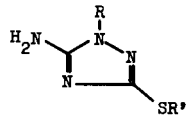
Structure **3** was proposed for all derivatives obtained in the reaction of Scheme 1 (above). In the case of **3** (R = Ph, R′ = CH_2Ph) (1) and **3** (R = Ph, R′ = CH_3) (2), no evidence is given. In the case of **3** (R = 4-Cl-Ph, R′ = CH_3) (3) the structure was proposed on the basis of the fragment ion 153 observed in the ms spectrum corresponding to the fragment ion "Y". While in the case of **3** (R = R′ = CH_3) (4,5) the structure was proposed on the basis of the pmr spectra comparing the N-CH_3 signal observed with those of the corresponding N-CH_3 signals of the known isomeric 1,3-dimethyl-5-amino-1*H*-, and 2,3-dimethyl-5-amino-2*H*-1,2,4-triazoles chosen as models. The above pmr studies (4,5) allowed us to recognize that the isomeric **4** (R = R′ = CH_3) was in the mother liquor of **3** (R = R′ = CH_3) in about 6% concentration.

We have isolated in the various types of reactions in Scheme 1 (*i.e.* R = alkyl, aralkyl and aryl, R′ = alkyl and aralkyl, respectively) both isomeric derivatives **3** and **4** (Table I) and compared their spectral data.

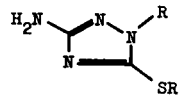
Surprisingly, the alkyl and aryl derivatives **3** and **4** (R = alkyl, aryl) can not be differentiated on the basis of the sole appearance of any of the fragment ions arising from splittings "X" or "Y" (Table II), as proposed in the literature (3). On the other hand, they could be easily separated into two distinct groups on the basis of different intensities of the fragment ions, but no decision could be made as to which one corresponded to structure **3** and which to structure **4** (6-7). The ir spectra of derivatives **3** and **4** (R = alkyl, aralkyl, aryl, R′ = alkyl, aralkyl) (Table III) again made possible their separation into two distinct groups, one characterised by two strong ν C=N bands between 1660-1500 cm^{-1} and the other one characterised by three strong ν C=N bands between 1660-1500 cm^{-1} which are accompanied in the cases of R = alkyl and aralkyl with a strong band in the 1310-1285 cm^{-1} region, while in the case of R = aryl with a strong band in the 1287-1255 cm^{-1} region (Table III). Again, no decision could be made as to which one corresponded to structure **3** and which to structure **4**.

The slight but consequent differences between the corresponding chemical shifts of the SCH_3 and NH_2 groups of derivatives **3** and **4** (R = alkyl, aralkyl, aryl; R′ = methyl), respectively in the pmr spectra (8) enabled the differentiation between the given isomeric pair [*e.g.* **3**/1 δ SCH_3 = 2.47 ppm, δ NH_2 = 6.5 ppm with **4**/1: δ SCH_3 = 2.57 ppm, δ NH_2 = 5.3 ppm; or **3**/5: δ SCH_3 = 2.46 ppm, δ NH_2 = 6.6 ppm with **4**/5: δ SCH_3 = 2.54 ppm, δ NH_2 = 5.3 ppm; or **3**/9: δ SCH_3 = 2.46 ppm, δ NH_2 = 6.5 ppm with **4**/9: CH_3 = 2.65 ppm, δ NH_2 = 5.6 ppm (all spectra taken in hexadeuteriodimethylsulfoxide)]. Again, it was not possi-

Table I



3



4

Compound No.	R	R'	Conditions of preparation: Method	r.solvent	r.temp. (°C)	r.time (min)	Yield (%)	m.p. (°C) (crystallised from)	Molecular formula or reference m.p.	Analysis Calcd. (Found): C	H	N	S	Hal
3/1	Methyl	Methyl	A	MeOH	20	60	2(a)	110-111 (b) (EtOAc)	$C_4H_8N_4S$	33.31	5.59	38.86	22.24	
							85	106-107,5(c) (EtOAc)		33.40	5.88	38.81	22.18	
4/1									(4,5)m.p.105-106°					
3/2	n-Octyl	Methyl	A	EtOH	reflux	900	26(d)	77-78 (EtOAc)	$C_{11}H_{22}N_4S$	54.51	9.15	23.12	13.23	
										54.52	9.13	23.18	13.16	
3/3	Allyl	Methyl	A	EtOH	reflux	180	16(a)	86-88 (EtOAc)	$C_6H_{10}N_4S$	42.34	5.92	32.91	18.84	
										42.27	6.17	32.60	18.95	
4/3							8(a)	120-122 (Bz)	$C_6H_{10}N_4S$	42.34	5.92	32.91	18.84	
										42.48	6.08	33.01	19.03	
3/4	2-Hydroxy-ethyl	Methyl	A	EtOH	22	300	43	125-126 (EtOH)	$C_5H_{10}N_4OS$	34.47	5.79	32.16	18.40	
										34.81	5.50	31.98	18.61	
4/4							13(a)	113-116 (EtOAc)	$C_5H_{10}N_4OS$	34.47	5.79	32.16	18.40	
										34.66	5.91	32.08	18.32	
3/5	Benzyl	Methyl	A	EtOH	reflux	15	49	140-141 (EtOAc)	$C_{10}H_{12}N_4S$	54.52	5.49	25.44	14.56	
										54.84	5.71	25.18	14.36	
4/5							7(a)	92-93 (Bz)	$C_{10}H_{12}N_4S$	54.52	5.49	25.44	14.56	
										54.88	5.71	25.39	14.73	
3/6	4-Methyl-benzyl	Methyl	A	EtOH	25	3 days	27(a)	110-112 (EtOAc:Bz=1:9)	$C_{11}H_{14}N_4S$	56.38	6.02	23.91	13.68	
										56.63	6.13	23.90	13.48	
4/6							29(a)	125-126 (EtOH)	$C_{11}H_{14}N_4S$	56.38	6.02	23.91	13.68	
										56.15	5.89	24.15	13.49	
3/7	4-Chloro-benzyl	Methyl	A	EtOH	24	60	8(a)	128-129 (Bz)	$C_{10}H_{11}ClN_4S$	47.15	4.35	22.00	12.59	13.92
										47.01	4.48	22.23	12.35	13.80
4/7							35(a)	137-138 (Bz)	$C_{10}H_{11}ClN_4S$	47.15	4.35	22.00	12.59	13.92
										46.85	4.27	19.81	12.70	13.88
3/8	2-(2,6-Dichloro-phenoxy)-ethyl	Methyl	A	Bz	35	300	4(a)	110-111 (EtOAc)	$C_{11}H_{12}Cl_2N_4OS$	41.39	3.79	17.55	10.05	22.21
										41.68	3.93	17.46	10.07	22.41
4/8							46	93-95 (EtOAc)	$C_{11}H_{12}Cl_2N_4OS$	41.39	3.79	17.55	10.05	22.21
										41.40	3.66	17.45	10.07	22.27
3/9	Phenyl	Methyl	A	EtOH	reflux	90	81	122-123 (iPrOH)	(2) m.p.105°					
4/9							0,2(e)	147-148 (iPrOH)	(30) m.p.148°					
3/10	2-Methyl-phenyl	Methyl	B	MeOH	reflux	240	50	144-146 (EtOH)	$C_{10}H_{12}N_4S$	54.52	5.49	25.44	14.56	
										54.86	5.52	25.26	14.87	
3/11	4-Methyl-phenyl	Methyl	B	MeOH	reflux	240	54	123-125 (iPrOH)	$C_{10}H_{12}N_4S$	54.52	5.49	25.44	14.56	
										54.49	5.32	25.14	14.55	
3/12	2,6-Dimethyl-phenyl	Methyl	A	EtOH	reflux	180	81	136-138 (CH_3CN)	$C_{11}H_{14}N_4S$	56.38	6.02	23.91	13.68	
										56.44	6.28	23.88	13.52	
3/13	2,6-Diethyl-phenyl	Methyl	A	EtOH	reflux	180	78	84-86 (iPrOH)	$C_{13}H_{18}N_4S$	59.51	6.92	21.36	12.22	
										59.64	6.89	21.14	12.26	
3/14	2,4,6-Trimethyl-phenyl	Methyl	C	EtOH	reflux	720	77	143-144 (EtOAc)	$C_{12}H_{16}N_4S$	58.03	6.49	22.56	12.91	
										58.12	6.60	22.49	12.85	
3/15	2-Chloro-phenyl	Methyl	B	MeOH	reflux	120	48	143-144 (iPrOH)	$C_9H_9ClN_4S$	44.90	3.77	23.28	13.32	14.73
										45.17	3.98	23.44	13.01	14.84
3/16	4-Chloro-phenyl	Methyl	A	iPrOH	reflux	240	85	155-156 (EtOH)	(3) m.p.153-155°					
3/17	2,6-Dichloro-phenyl	Methyl	B	MeOH	reflux	180	38	170-172 (EtOAc)	$C_9H_8Cl_2N_4S$	39.28	2.93	20.36	11.65	25.77
										39.37	2.54	19.97	11.89	25.98
3/18	4-Bromo-phenyl	Methyl	B	MeOH	reflux	240	27	145-147 (EtOAc)	$C_9H_9BrN_4S$	37.90	3.18	19.65	11.24	28.02
										38.08	3.40	19.37	11.31	28.15

Compound No.	R	R'	Conditions of preparation: Method	r.solvent	r.temp. (°C)	r.time (min)	Yield (%)	m.p. (°C) (crystallized from)	Molecular formula or reference m.p.	Analysis Calcd. (Found): C	H	N	S	Hal
3/19	2-Nitro-phenyl	Methyl	C	BuOH	reflux	270	92	150-151 (CH_3CN)	$C_9H_9N_5O_2S$	43.02 43.37	3.61 4.00	27.87 27.92	12.76 12.90	
3/20	2-Nitro-4-trifluoro-methyl-phenyl	Methyl	A	BuOH	reflux	270	65	223-224 (CH_3CN)	$C_{10}H_8F_3N_5O_2S$	37.62 37.62	2.53 2.65	21.94 22.07	10.04 10.09	17.85 17.72
3/21	4-Nitro-phenyl	Methyl	A	BuOH	reflux	300	74	195-196 (CH_3CN)	$C_9H_9N_5O_2S$	43.02 43.40	3.61 3.98	27.87 27.52	12.76 12.95	
3/22	Phenyl	n-Octyl	A	EtOH	reflux	240	40(d)	47-49 (EtOAc)	$C_{16}H_{24}N_4S$	63.12 63.36	7.95 7.99	18.40 18.32	10.53 10.60	
3/23	Methyl	Benzyl	A	EtOH	25	1 day	1(a)	102-105(f) (CH:iPrOH=3:1)	(11) m.p.104-106°					
4/23							79	87-89(g) (EtOAc)	$C_{10}H_{12}N_4S$	54.52 54.71	5.49 5.25	25.44 25.18	14.56 15.26	
3/24	Phenyl	Benzyl	A	EtOH	reflux	60	50	137-138.5 (MeOH)	(31) m.p.137°					
3/25	2,6-Dichloro-phenyl	4-Chloro-benzyl	B	MeOH	reflux	180	77	176-178 (EtOAc)	$C_{15}H_{11}Cl_3N_4S$	46.71 47.01	2.87 3.13	14.53 14.25	8.31 8.46	27.58 27.80
3/26	2,6-Dichloro-phenyl	4-Nitro-benzyl	B	MeOH	reflux	480	46	190-192 (EtOAc-Bz)	$C_{15}H_{11}Cl_2N_5O_2S$	45.46 45.78	2.80 3.05	17.68 17.41	8.09 8.32	17.89 17.91
3/27	Naphthyl	Methyl	C	EtOH	reflux	360	41	146-147 (CH_3CN)	$C_{13}H_{12}N_4S$	60.91 60.75	4.72 4.93	21.86 21.97	12.51 12.57	
3/28	H	Methyl	A	MeOH	35	240	77	136-137 (iPrOH)	(13)m.p. 135°					
3/29	H	Ethyl	A	MeOH	50	120	53	76-78 (iPrOH)	(14) (h)					
3/30	H	n-Butyl	A	EtOH	reflux	60	18	78-80 (Bz:EtOAc=5:1)	$C_6H_{12}N_4S$	41.83 42.14	7.02 7.36	32.53 32.57	18.62 18.45	
3/31	H	4-Chloro-benzyl	A	EtOH	reflux	600	78	140-143 (EtOAc)	(26) m.p.142-144°					
3/32	H	4-Nitro-benzyl	A	EtOH	reflux	600	55	191-194 (CH_3CN)	(32) (h)					

(a) Isolated by column chromatography on silica-gel. Developing solvent EtOAc. (b) Compound not isolated by (4,5). (c) Compound described with erroneous structure 3/1 previously. (d) Isolated by column chromatography on silica-gel. Developed by Bz:EtOAc=1:2 mixture. (e) Isolated by column chromatography on silica-gel. Developed by 1,2-dichloro-ethane:EtOAc=1:1 mixture. (f) Compound described with erroneous structure 4/23 previously (11). (g) Compound not isolated by (11). (h) m.p. not given

Table II

ms spectra of some isomeric derivatives 3 and 4

m/e	3/1 (R=CH_3)	4/1 (R=CH_3)	m/e	3/5 (R=CH_2Ph)	4/5 (R=CH_2Ph)	m/e	3/9 (R=Ph)	4/9 (R=Ph)
144	100 %	100 %	220	100 %	100 %	206	100 %	100 %
143	20	13	219	3	5	205	17	7.5
129	6	6	205	1	1.7	173	9.3	6
111	34	55	187	1.7	2.2	164	3.5	-
108	7	-	173	1	1	161	5.6	-
101	8	-	129	6	3.6	133	2	14
99	19	3	91	19	23	131	3	1
57(a)	9	0.7	74	1.5	2.5	119(a)	15.4	1
43(b)	8	12				118	10.6	3
						105(b)	8	9
						103	5	2
						97	8.4	20
						91	54	98
						89	6	1
						77	1.1	22
						64	3.6	8

(a) arising from fragmentation "I" (b) arising from fragmentation "K"

ble to formulate a general rule for the safe verification of the structure of those derivatives where only one isomer was isolated.

The situation was just the same in the case of the uv spectra of alkyl, aralkyl and aryloxylalkyl derivatives **3** and **4**, the spectra of which could again be well separated into two distinct groups (compare the spectra of **3**/1-**3**/8 and **4**/1-**4**/8, respectively, Table III). Again, no decision could be made as to which one corresponded to structure **3** and which to structure **4** (9). Moreover the spectra strongly depended on the nature of the R and R' groups, (compare *e.g.* **3**/1, **3**/9, **3**/16 and **3**/21, or **3**/1 and **3**/23, respectively, Table III) and in the case of R = *ortho*-substituted phenyl, they were influenced by the steric effects. This is excluding the coplanarity of the phenyl and 1,2,4-triazole rings (compare *e.g.* **3**/9 with **3**/10, **3**/12, **3**/13, **3**/15 or **3**/17, Table III).

In the hope of excluding the above uncertainties, derivatives **3** and **4** were transformed into their Schiff bases **5** and **6** (Scheme 2, Table IV), where as a consequence of the prolonged linear conjugation in derivatives **5**, a batho-

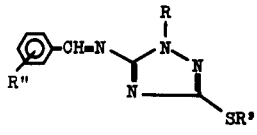
Table III

Compound No.	ir (cm^{-1}) νNH_2	ir (cm^{-1}) $\nu C \equiv N$	ir (cm^{-1}) Other charact. bands	uv λ_{max} ($.10^{-3}$) 96 % EtOH	uv λ_{max} ($.10^{-3}$) 10 % EtOH + 90 % 0.1 NaOH	uv λ_{max} ($.10^{-3}$) 10 % EtOH + 90 % 0.1 N HCl
3/1	3420 3310 3110	1652 1581 1514	1310 1302	238sh (2.3)	238sh (2.7)	213 (8.9) 237sh (4.3)
4/1	3400 3310 3210	1612 1535		228sh (4.1) 247 (3.6)	228sh (3.8) 245 (4.1)	253 (4.9)
3/2	3340 3140 3105	1650 1568 1510	1292	242sh (3.5)	240sh (2.6)	236sh (6.0)
3/3	3360 3320 3130	1648 1572 1515	1290	218sh (6.5) 239sh (2.8)	237sh (4.0)	213 (9.8) 238sh (4.6)
4/3	3340 3220	1642 1546		231 (4.0) 247 (4.0)	244 (4.3)	255 (5.4)
3/4	3420 3320 3200	1660 1580 1520	1298	216sh (7.0) 239sh (2.4)	238sh (2.9)	213 (9.4) 238sh (4.2)
4/4	3410 3320 3210 3180	1645 1545		227 (4.1) 247 (4.2)	229sh (4.0) 244 (4.5)	256 (5.6)
3/5	3310 3180	1654 1560 1505	1298	240sh (3.8)	240sh (4.1)	206 (16.2) 240sh (5.0)
4/5	3410 3320 3220	1629 1550		230sh (5.3) 248sh (4.5)	247 (5.5)	256 (5.6)
3/6	3300 3160	1656 1563 1512	1302	216sh (15.0) 240sh (4.0)	239sh (4.5)	215 (17.9) 238sh (5.3)
4/6	3400 3320 3220	1628 1546		249sh (4.5)	245 (4.9)	218sh (11.2) 256 (5.8)
3/7	3360 3320 3120	1655 1572 1513	1298	218 (16.3) 241 (4.0)	239 (4.7)	220 (19.7) 238 (6.0)
4/7	3400 3320 3220	1630 1545		219 (14.4) 250 (4.6)	246 (5.0)	219 (14.0) 256 (5.6)
3/8	3320 3160	1645 1570 1508	1310 1300	218sh (16.1) 241sh (2.7)	240sh (3.2)	216sh (17.9) 240sh (4.3)
4/8	3360 3220	1645 1545		220sh (13.3) 249 (4.7)	245 (4.8)	220sh (11.6) 256 (5.7)
3/9	3400 3380 3300 3150	1640 1600 1550 1500	1287	260 (8.9)	257 (8.6)	247 (8.7)
4/9	3380 3320 3220 3190	1640 1590 1550 1500		217sh (12.0) 274 (7.6)	265 (6.4)	217sh (11.4) 267 (6.8)
3/10	3390 3250 3080	1620 1540 1495	1270	210sh (21.7) 242sh (5.0) 266 (2.4)	240sh (4.8) 266sh (1.1)	240sh (7.4) 266sh (1.3)
3/11	3420 3250 3060	1620 1535 1500	1265	212sh (21.9) 256 (10.5)	250 (8.6)	238sh (10.8)
3/12	3420 3250 3090	1615 1540 1495	1280	212sh (22.8) 241sh (4.8) 270sh (1.6)	240sh (4.5) 270 (1.0)	206 (24.3) 240sh (7.3) 270 (1.5)
3/13	3460 3280 3200 3120	1632 1555 1510	1275	215sh (19.8) 243sh (4.3) 272 (1.3)	242sh (4.3) 262sh (1.3) 271 (0.8)	210 (19.8) 241sh (6.2) 264sh (1.8) 271 (1.5)
3/14	3470 3280 3200 3090	1638 1555 1510	1275	216sh (18.6) 244sh (5.8) 274sh (1.1)	241sh (5.6)	215sh (18.9) 240sh (7.5) 272sh (1.0)
3/15	3280 3110	1620 1540 1495	1265	212sh (36.0) 240sh (6.3)	240sh (5.3) 270sh (1.9)	206sh (36.3) 236sh (10.8) 270sh (1.7)
3/16	3450 3280 3120	1650 1560 1505	1275	218sh (16.6) 267 (10.9)	259 (9.5)	216 (16.4) 249 (10.2)
3/17	3380 3340 3300 3120	1650 1625 1560 1500	1260	212 (26.4) 240sh (4.6) 270sh (2.6) 278sh (2.3)	240sh (3.9) 270sh (1.3) 278sh (1.7)	212 (25.3) 240sh (4.4) 270sh (2.1) 278sh (1.8)
3/18	3400 3250 3100	1630 1540 1485	1260	216sh (14.8) 266 (10.1)	260 (8.1)	216sh (14.4) 250 (9.3)
3/19	3420 3310 3160	1650 1605 1587 1567	1280	248 (8.9) 330sh (1.3)	248 (8.4)	240 (10.4)
3/20	3430 3310 3110	1650 1625 1585 1560	1270	270sh (5.1) 332sh (1.5)	240sh (10.0) 262sh (7.5)	240sh (12.0)
3/21	3390 3260 3190	1640 1540 1490	1270	238 (11.2) 336 (9.4)	238 (10.0) 330 (7.3)	212sh (18.1) 238sh (11.9) 302 (7.4)
3/22	3340 3300 3120	1640 1600 1555 1505	1270	258 (10.1)	252 (6.8)	246 (9.6)
3/23	3360 3130	1650 1580 1505	1310 1300	215sh (16.3) 249sh (2.6)	246 (3.0)	214sh (13.6) 252sh (3.3)
4/23	3330 3200	1650 1540		216sh (11.9) 258 (4.1)	256 (3.9)	217sh (8.0) 263 (5.1)
3/24	3410 3280 3080	1630 1550 1505	1270	215sh (25.5) 258 (10.1)	252 (7.6)	244sh (8.4)
3/25	3440 3280 3080	1635 1550 1500	1265	218sh (35.7) 248sh (5.2) 280sh (2.3)	248sh (4.0) 278sh (1.7)	214sh (29.1) 248sh (5.5) 278sh (1.9)
3/26	3420 3320 3180	1650 1560 1510	1255	216sh (30.0) 268 (12.0)	272 (9.7) 278 (9.7)	216sh (26.0) 270 (10.4) 278 (10.4)
3/27	3440 3280 3090	1640 1552 1508	1270	222 (26.3) 258 (7.5) 285 (4.1) 296sh (3.3)	256 (7.6) 284sh (3.8)	221 (25.4) 249 (8.5) 279sh (3.0)
3/28	3430 3300 3160 3140	1647 1598 1552 1503	1292 1285	240sh (2.1)	241sh (2.7)	209 (8.8) 236sh (3.7)
3/29	3460 3330 3190 3080	1640 1500	1298	209 (8.9) 238sh (2.1)	222 (9.2) 240sh (3.2)	214 (8.5) 240sh (3.6)
3/30	3420 3330 3240 3210	1622 1550 1520	1270	240sh (2.8)	240sh (3.3)	238sh (4.1)
3/31	3430 3330 3220 3110	1620 1550	1280	221 (18,0) 249sh (3.1) (a)	223 (16.6) 247sh (4.2) 263sh (3.1)	223 (18.9) 248sh (4.0)
3/32	3440 3300 3240 3180	1630 1505	1280	214sh (13.8) 273 (9.9) (a)	275 (10.0)	214sh (15.6) 273 (10.1)

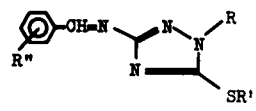
(a) UV taken in 50 % EtOH

chromic shift of the highest maxima is expected as compared with those of derivatives **6** (9). The observed uv maxima of derivatives **5** and **6** (R'' = H) (Table V) fully supported the above idea (λ max **5** = 328-341 nm, λ max **6**

Table IV



5



6

Compound No.	R	R'	R''	Conditions of preparation: r.solvent	r.temp. (°C)	r.time (min)	Yield (%)	m.p. (°C) (crystallised from)	Molecular formula or reference m.p.	Analysis Calcd. (Found) C	H	N	S	Hal
3/1	Methyl	Methyl	H	EtOH	reflux	180	37	85-86 (iPrOH)	$C_{11}H_{12}N_4S$	56.87 57.04	5.21 5.10	24.12 23.86	13.80 14.01	
4/1	Methyl	Methyl	H	EtOH	reflux	900	58	86-87 (iPrOH)	$C_{11}H_{12}N_4S$	56.87 56.99	5.21 5.31	24.12 23.97	13.80 13.87	
4/2	Methyl	Methyl	4-Chloro	iPrOH	reflux	360	95	140-141.5 (iPrOH)	$C_{11}H_{11}ClN_4S$	49.53 49.68	4.16 4.32	21.01 20.87	12.02 11.83	13.29 13.28
3/3	2-Hydroxy-ethyl	Methyl	H	EtOH	reflux	40	34	104-105 (EtOH)	$C_{12}H_{14}N_4OS$	54.94 55.32	5.38 5.58	21.36 21.04	12.22 12.48	
4/3	2-Hydroxy-ethyl	Methyl	H	EtOH	reflux	60	38	162-163 (iPrOH)	$C_{12}H_{14}N_4OS$	54.94 54.68	5.38 5.42	21.36 21.04	12.22 12.22	
3/4	Benzyl	Methyl	H	EtOH	reflux	180	42	102-103 (iPrOH)	$C_{17}H_{16}N_4S$	66.20 66.10	5.23 5.55	18.17 18.12	10.40 10.73	
4/4	Benzyl	Methyl	H	EtOH	reflux	360	49	115-116 (EtOAc)	$C_{17}H_{16}N_4S$	66.20 66.12	5.23 5.00	18.17 18.10	10.40 10.58	
3/5	4-Methyl-benzyl	Methyl	H	EtOH	reflux	30	59	133-135 (CH_3CN)	$C_{18}H_{18}N_4S$	67.05 67.18	5.63 5.92	17.38 17.71	9.95 9.64	
4/5	4-Methyl-benzyl	Methyl	H	EtOH	reflux	30	71	133-134 (CH_3CN)	$C_{18}H_{18}N_4S$	67.05 67.42	5.63 5.85	17.38 17.67	9.95 10.06	
3/6	4-Chloro-benzyl	Methyl	H	EtOH	reflux	90	45	111-113 (iPrOH)	$C_{17}H_{15}ClN_4S$	59.55 59.84	4.41 4.55	16.34 16.12	9.35 9.37	10.34 10.48
4/6	4-Chloro-benzyl	Methyl	H	EtOH	reflux	40	25	114-115 (iPrOH)	$C_{17}H_{15}ClN_4S$	59.55 59.88	4.41 4.57	16.34 16.41	9.35 9.01	10.34 10.56
3/7	2-(2,6-Dichloro-phenoxy)-ethyl	Methyl	H	EtOH	reflux	420	59(a)	86-88 (iPrOH)	$C_{18}H_{16}Cl_2N_4OS$	53.07 53.23	3.96 4.13	13.76 13.75	7.87 7.92	17.41 17.28
3/8	2-(2,6-Dichloro-phenoxy)-ethyl	Methyl	4-Chloro	iPrOH	reflux	600	98	102-104 (CH_3CN)	$C_{18}H_{15}Cl_3N_4OS$	48.94 48.79	3.22 3.50	12.68 12.68	7.26 7.22	24.08 24.19
3/9	Phenyl	Methyl	H	EtOH	reflux	540	65	71-72 (iPrOH)	$C_{16}H_{14}N_4S$	65.28 65.39	4.79 5.09	19.03 18.94	10.89 10.93	
4/9	Phenyl	Methyl	H	EtOH	reflux	360	24	133-134 (EtOAc)	$C_{16}H_{14}N_4S$	65.28 64.98	4.79 5.03	19.03 18.75	10.89 11.01	
3/10	Phenyl	Methyl	4-Chloro	iPrOH	reflux	360	79	126-127.5 (iPrOH)	$C_{16}H_{13}ClN_4S$	58.44 58.67	3.99 4.20	17.04 16.95	9.75 9.98	10.78 11.01
3/11	Phenyl	Methyl	3,4,5-tri-methoxy	EtOH	reflux	240	38	104.5-105 (EtOH)	$C_{19}H_{20}N_4O_3S$	59.35 59.49	5.24 5.35	14.57 14.29	8.34 8.61	
3/12	2,6-Dimethyl-phenyl	Methyl	H	EtOH	reflux	540	20	109-111 (EtOAc)	$C_{18}H_{18}N_4S$	67.05 66.77	5.63 5.79	17.38 17.43	9.95 10.13	
3/13	Naphthyl	Methyl	4-Chloro	iPrOH	reflux	900	48	158-160 (DMF)	$C_{20}H_{15}ClN_4S$	63.40 63.31	3.99 3.98	14.79 14.81	8.46 8.51	9.36 9.33
3/14	Naphthyl	Methyl	3,4-Methylene-dioxy	iPrOH	reflux	840	44	165-168 (DMF)	$C_{21}H_{16}N_4O_2S$	64.93 64.96	4.15 4.19	14.43 14.32	8.26 8.21	
3/15	Methyl	Benzyl	H	EtOH	reflux	30	21	86.5-89.5 (EtOH)	$C_{17}H_{16}N_4S$	66.20 66.07	5.23 5.45	18.17 18.02	10.40 10.61	
4/15	Methyl	Benzyl	H	EtOH	reflux	120	94	77-78 (iPrOH)	$C_{17}H_{16}N_4S$	66.20 65.93	5.23 5.35	18.17 17.91	10.40 10.23	
3/16	Phenyl	Benzyl	H	EtOH	reflux	60	42	98-100 (CH_3CN)	$C_{22}H_{18}N_4S$	71.32 71.32	4.90 5.06	15.12 14.98	8.66 8.71	

(a) Isolated by column chromatography on silica-gel. Eluent Bz:EtOAc=1:2 .

= 297-304 nm) enabling the safe verification of the structure of all the derivatives of **3** and **4** containing different R and R' groups even if only one isomer was isolated. This method was of general validity but in each case required the synthesis of the corresponding Schiff bases.

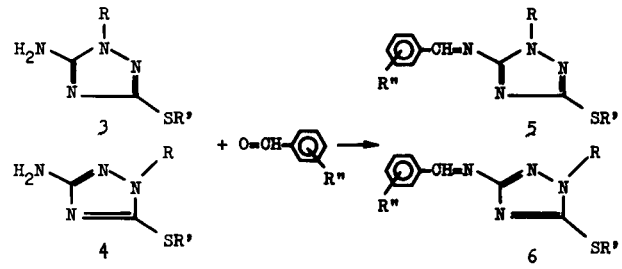
The chemical shifts of the two triazole carbon atoms of derivatives **3** and **4** differed either by 0.3-3.0 ppm, or by 12-13 ppm and were not influenced significantly by the quality of the R and R' groups, again enabling the separation of the derivatives into two distinct groups (8). The un-

Table V

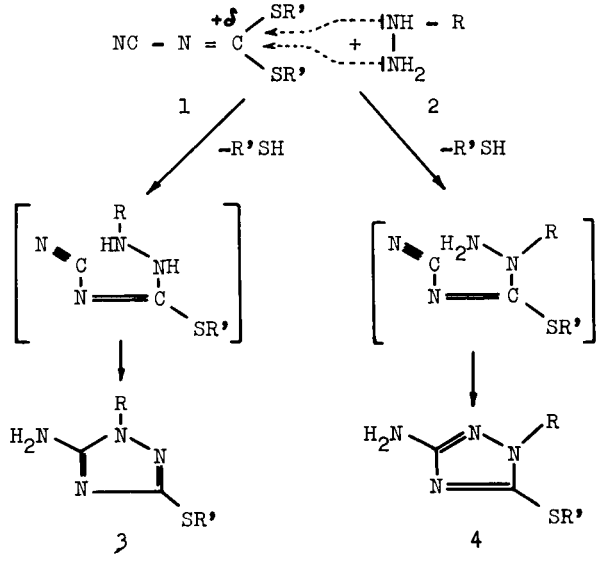
Compound No.	ir (cm^{-1}) νOH	νC = N	Other charact. bands	uv λ_{max} ($.10^{-3}$) 96 % EtOH
5/1		1620 1580 1518	1295	217sh (14.4) 273 (15.5) 328 (12.6)
6/1		1615 1580 1500		215 (15.0) 262 (13.0) 301 (13.3)
6/2		1620 1595 1570 1500		218 (14.8) 272 (14.8) 312 (15.0)
5/3	3310	1610 1600 1578 1510	1295	217sh (15.5) 274 (15.5) 330 (12.3)
6/3	3320	1615 1575		215sh (15.9) 263 (13.2) 301 (12.9)
5/4		1610 1575 1505	1290	276 (15.7) 333 (12.6)
6/4		1618 1578 1500		263 (14.3) 304 (14.3)
5/5		1612 1580 1515 1503	1290	215sh (22.0) 274 (15.0) 331 (12.0)
6/5		1618 1580 1510		215sh (23.0) 262 (13.9) 302 (13.8)
5/6		1615 1580 1505	1285	219 (25.4) 275 (15.4) 331 (12.2)
6/6		1620 1580 1505		218 (25.9) 263 (14.8) 302 (14.6)
5/7		1615 1600 1580 1570	1290	216sh (25.0) 274 (15.6) 330 (12.0)
5/8		1612 1595 1568 1502	1291	216sh (24.3) 281 (17.3) 333 (13.8)
5/9		1610 1600 1580 1500	1300	254 (19.8) 276 (18.0) 341 (10.7)
6/9		1620 1600 1580 1506		214sh (21.8) 261 (20.0) 306 (15.3)
5/10		1605 1595 1568 1495	1297	233sh (13.8) 252 (16.0) 285 (17.6) 347 (10.6)
5/11		1610 1600 1580 1500	1300	221 (22.0) 239 (23.4) 347 (19.2) (a)
5/12		1610 1580 1490	1300	213sh (26.6) 275 (17.0) 330 (12.3)
5/13		1630 1603 1590 1562 1510	1297	223 (57.7) 254 (31.9) 280 (25.9) 340 (11.6)
5/14		1612 1591 1512 1500	1280 1275	219 (55.0) 246 (31.0) 285sh (13.6) 358 (19.1)
5/15		1615 1600 1575 1517	1302 1298	214sh (23.0) 274 (15.6) 328 (12.7)
6/15		1615 1575		214sh (23.3) 265 (14.2) 297 (13.4)
5/16		1600 1572 1492	1306	257 (19.3) 276sh (17.9) 340 (9.4)

(a) in 50 % EtOH

equivocal adaptation of these groups to structures **3** and **4** made possible the $^3J_{C,H}$ couplings between the triazole carbon atoms and the R groups. Consequently, the splitting scheme of the two triazole carbon atoms of the two isomers must be different (*e.g.* the carbon atoms 3 of the *N*-benzyl derivatives **3**/5 and **4**/5 had to appear as a quartet and a multiplet, respectively, while the corresponding carbon atoms 5 of the above derivatives had to appear as a triplet and singulet, respectively (Figure 1)). The



Scheme 2



Scheme 3

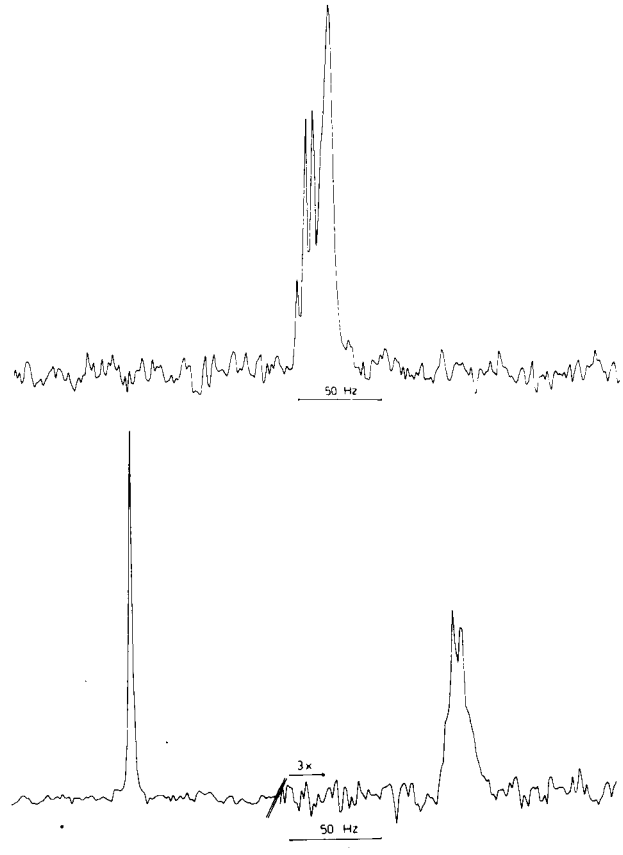


Figure 1

above results were in full agreement with the X-ray studies of derivatives **3**/1, **4**/6 and **4**/9 (10) which were chosen as models.

The undoubted proof of the structure of derivatives **3** and **4** by the cmr technique pointed out the error of Heitke and McCarty (4,5) and Blank and Coworkers (11) made in describing derivatives **3**/1, **4**/1 and **3**/23 with just the opposite structure.

The full analogy of the uv and cmr spectra (8) of the non-substituted derivatives **3**/28-**3**/32 (R = H) with those of the alkylated and aralkylated derivatives **3**/1-**3**/8 strongly supports the idea that these derivatives exist at least in solution in the tautomeric form **3** (R = H) (*i.e.* in the 1*H* form). X-Ray studies (12) established the 1*H* tautomeric form of the analogues 3-amino-1,2,4-triazole exists in the solid state as well.

These results again made it possible to correct the error in the literature describing the above derivatives as imino-(13), 2*H*- (14-24), or (4*H*)- (25-29) tautomeric forms.

Proving the correct structure of the derivatives **3** and **4**, as well as determination of their ratio, made it possible to establish the mechanism of the reaction in which they were formed. Thus the reaction starts with a nucleophilic attack on one of the hydrazino nitrogen atoms against the central - and probably the most nucleophilic - carbon atom of the *N*-cyanocarbonimidodithioic acid dialkyl ester, which is followed by the formation of an isothiosemicarbazide intermediate and its intramolecular cyclisation to form **3** or **4** (Scheme 3).

If this mechanism is correct, then in the case of electron withdrawing R-substituents the nucleophilic attack of the hydrazine NH_2 group is expected, leading to the formation of type **3** products, while in the case of electron attracting R groups the nucleophilic attack of the NH group would predominate giving rise to the formation of type **4** derivatives.

The ratio of products formed in the reaction of Scheme 1 determined by high pressure liquid chromatography (hplc) (**3**/1:**4**/1 = 3:97; **3**/5:**4**/5 = 73:27; **3**/6:**4**/6 = 69.31; **3**/7:**4**/7 = 67:33; **3**/9:**4**/9 = 99:1) gave unequivocal proof of the correctness of the above mechanism.

EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are uncorrected. The infrared spectra were obtained as potassium bromide pellets using a Perkin-Elmer 577 spectrophotometer. The electron impact mass spectra were determined with a Varian MAS SM-1 spectrometer. The ultraviolet spectra were obtained by a Varian Cary 118 and a Pye Unicam SP 8-150 instrument. The hplc determinations were performed using a Varian 8500 pump, Variscan spectrophotometer, Varian Stop-Flow sampler and a Varian A-25 recorder.

General Method for the Preparation of Derivatives **3** and **4**.

Method A.

To a stirred solution of 0.1 mole of the appropriate *N*-cyanocarbonimidodithioic acid di(alkyl or aralkyl) ester in 100 ml of the appropriate solvent (Table I) 0.12 mole of the appropriate alkyl-, aralkyl- or arylhydrazine was added and the solution stirred under conditions given in Table I. During the reaction the appropriate alkyl- or aralkylthiol was liberated. After the reaction had ceased the solution was evaporated to dryness and the residue crystallised from an appropriate solvent (Table I). The corresponding isomers were obtained from the mother liquors by column chromatography on silica gel (Table I).

Method B.

To a stirred mixture of 0.1 mole of the appropriate *N*-cyanocarbonimidodithioic acid di(alkyl or aralkyl) ester, 0.1 mole of the corresponding alkyl-, aralkyl- or arylhydrazine hydrochloride and 100 ml of an appropriate solvent (Table I) a solution of 4.0 g (0.1 mole) of sodium hydroxide in 50 ml of methanol was added and the mixture stirred under conditions given in Table I. During the reaction the appropriate alkyl- or aralkylthiol was liberated. After the reaction had ceased the mixture was evaporated to dryness, the residue was partitioned between water and chloroform, the organic layer was dried, evaporated to dryness and the residue recrystallised from an appropriate solvent (Table I).

Method C.

To a stirred mixture of 0.1 mole of the appropriate *N*-cyanocarbonimidodithioic acid di(alkyl or aralkyl) ester, 0.1 mole of the corresponding alkyl-, aralkyl- or arylhydrazine hydrochloride and 100 ml of an appropriate solvent (Table I) 13.7 ml (10.1 g = 0.1 mole) of triethylamine was added and the mixture was stirred under conditions given in Table I. During the reaction the appropriate alkyl-, or aralkylthiol was liberated. After the reaction had ceased the mixture was evaporated to dryness, the residue was partitioned between water and chloroform, the organic layer was dried, evaporated to dryness and the residue recrystallised from an appropriate solvent (Table I).

General Method for the Preparation of Schiff Bases **5** and **6**.

A solution of 0.1 mole of the appropriate 1- or 2-(alkyl-, aralkyl-, aryloxyalkyl- or aryl)-3-(alkyl- or aralkylthio)-5-amino-1,2,4-triazole (**3** or **4**, respectively) in 100 ml of an appropriate solvent (Table IV), 0.3 mole of the corresponding aldehyde and 1 ml of piperidine was added and the reaction mixture was stirred under conditions given in Table IV. After the reaction had ceased the reaction mixture was evaporated to dryness and the residue was recrystallised from an appropriate solvent (Table IV).

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