Triazoles XXXVI [1]. The Arylation of 5-Amino-3-methylthio-1*H*-1,2,4-triazole with Activated Aryl Chlorides

Péter Trinka and József Reiter

EGIS Pharmaceuticals Ltd., H-1475 Budapest, P.O. Box 100, Hungary

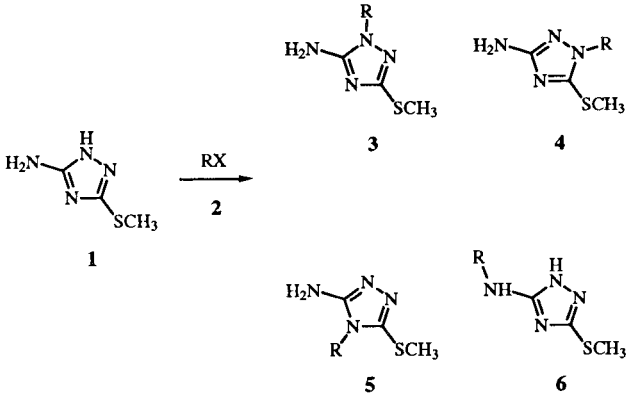
Received January 23, 1995

The possibility of the arylation of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with different chlorobenzenes activated by a nitro group was studied. The ratio of products obtained was determined by hplc using isolated products as standards. It was stated that from among the monoarylated products **8**, **9** and **10** obtained the main product is **8**. However, from the reaction mixtures diarylated derivatives **11** and **12** and different by products such as **15**, **16**, **22**, **24**, **25**, **27**, **28**, **32**, **36**, and **38** were also isolated.

J. Heterocyclic Chem., **32**, 1359 (1995).

In a previous paper of this series [2] we have reported on the alkylation of the sodium salt of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with different alkyl (**2**, R = alkyl) and aralkyl (**2**, R = aralkyl) halides to yield four isomeric alkyl derivatives **3-6** (R = alkyl and aralkyl, respectively) (Scheme 1) besides a small amount of dialkyl derivatives that were not isolated.

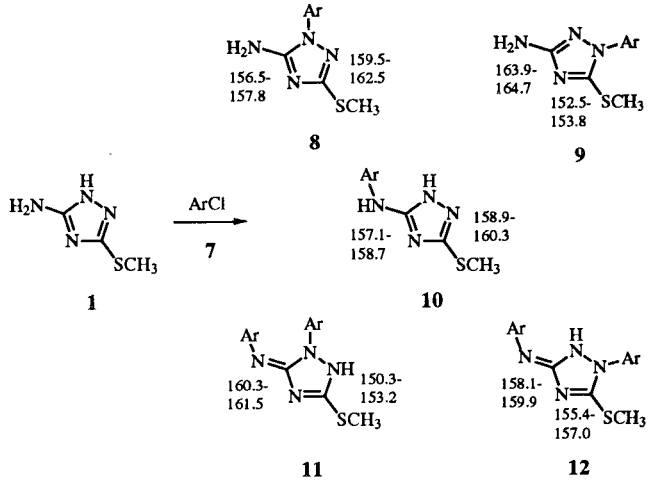
Scheme 1



In the present paper we will report on the arylation of the above triazole (**1**) or its sodium salt with chlorobenzenes (**7**) activated by a nitro group (Scheme 2).

We have studied the arylation of **1** with 2-nitrochlorobenzene (**7/1**, Ar = 2-nitrophenyl), 1,4-dichloro-2-nitrobenzene (**7/2**, Ar = 2-nitro-4-chlorophenyl), 2-nitro-4-trifluoromethylchlorobenzene (**7/3**, Ar = 2-nitro-4-trifluoromethylphenyl), 2,4-dinitrochlorobenzene (**7/4**, Ar = 2,4-dinitrophenyl), 2-nitro-4,5-dimethoxychlorobenzene (**7/5**, Ar = 2-nitro-4,5-dimethoxyphenyl), 4-nitro-1,2,3-trichlorbenzene (**7/6**, Ar = 2-nitro-5,6-dichlorophenyl), 2,3-dichloro-6-nitrobenzonitrile (**7/7**, Ar = 2-chloro-3-cyano-4-nitrophenyl), 2,6-dinitrochlorobenzene (**7/8**, Ar = 2,6-dinitrophenyl), 2,6-dinitro-4-trifluoromethylchlorobenzene (**7/9**, Ar = 2,6-dinitro-4-trifluoromethylphenyl), and 2,4,6-trinitrochlorobenzene (**7/10**, Ar = 2,4,6-trinitrophenyl), respectively, at different reaction conditions [i.e. refluxing in ethanol either in the presence (Method A_1), or absence (Method A_2) of triethylamine, reacting in dimethylformamide at different temparatures (Methods B), reacting of the sodium salt of **1** prepared with sodium hydride in dimethylformamide at different temperatures (Methods C) and heating the reactants neat at 150° (Method D)] to yield different ratios of the monoarylated derivatives **8**, **9** and **10** besides the diaryl ones **11** and **12**, respectively, (Scheme 2). The ratio of products obtained determined by hplc is summarised in Table I (data in parentheses mean isolated yields).

Scheme 2



As it can be seen from the data of Table I , except of runs 9/1-10/4 where the arylating agents were extremely reactive, from among the monoarylated derivatives the main product of the above reactions was in all cases the corresponding 1-arylated derivative **8** which is in good agreement with that of observed during our previous alkylating reactions [2]. However, depending on the reactivity of the arylating agents **7** and the reaction conditions 2- and exoarylated derivatives **9** and **10** were also formed, moreover the monoarylated derivatives **8** and **9** could be further arylated to form the diarylated derivatives **11** and

Table 1

The Ratio of Arylated Products **8-12** Obtained Determined by HPLC (Data in parentheses mean isolated yields)

Run	Method	1-subst. **8**	2-subst. **9**	Exo-subst. **10**	1,exo-subst. **11**	2,exo-subst. **12**	Unreacted **1**	Unreacted **7**	byproduct
1/1	A_1	<0.1	—		—	—	100	100	
1/2	B_1	<0.1	—		—	—	100	100	
1/3	C	7.2 (6.6)	3.8 (1.2)		3.0 (1.0)	1.1 (0.4)	30 (28)	14 (13)	**15**: 31 (12)
1/4	D	11.0			<0.1	—	71	35	
2/1	A_1	0.2	0.1		—	—	96	99	
2/2	B_1	0.3	0.1		0.1	—	97	23	
2/3	C	15 (13)	8.1 (3.3)		13 (2.2)	2.4 (0.4)	26 (13)	14 (10)	**16**: 11 (3.3)
2/4	D	30			0.2	—	63	32	
3/1	A_1	11	1.3		0.8	<0.1	85	38	
3/2	B_2	7.1	0.8		0.2	0.1	90	22	
3/3	C	29 (24)	8.0 (6.8)		19 (11)	1.3 (1.0)	23 (15)	10 (8.0)	
3/4	D	31.0			0.3	—	31	14	
4/1	A_1	21	2.8		0.9	—	68	19	**22**: 3.7
4/2	B_2	2.2	0.1		<0.1	<0.1	86	7.2	**22**: 4.6 **24**: 19
4/3	C	20 (17)	2.6 (1.9)		18 (15)	1.3 (1.2)	34 (27)	0.2	**24**: 34 (18) **23**: 2.8 (2.4)
4/4	D	0.8	0.05		2.4	—	6.8	84	
5/1	A_1	—	—		—	—	100	100	
5/2	B_2	1.0	0.3		—	—	98	98	
5/3	C	5.9 (1.2)	2.0 (0.2)		—	—	90 (70)	54 (35)	**26**: 28 (11) **27**: 15 (13)
5/4	D	1.0	—		—	—	98.0	92	**25**: 3.0
6/1	A_1	1.1	0.3		0.2	0.1	97	96	**28**: 0.2
6/2	B_2	0.2	—		—	—	99	97	**28**: 2.0
6/3	C	21 (10)	1.9 (1.6)		8.7 (4.7)	<0.5	29.4 (22)	41 (39)	**28**: 43 (8.0)
6/4	D	1.9	—		—	—	15.3	41	
7/1	A_1	0.7	0.1		<0.1	—	94.1	91	
7/2	B_2	0.8	0.1		0.4	—	91.4	89	
7/3	C	7.0 (3.1)	6.8 (4.7)		1.8 (0.3)	0.6	24.7 (20)	8.0 (7.1)	**32**: 31 (17) **36**: 7.7 (4.2)
7/4	D	5.9	2.9		<0.1	—	10.2	6.0	**32**: 5.4
8/1	A_1	2.6	—		—	—	80.7	68	
8/2	B_3	28 (7.4)	4.0 (0.6)	4.3 (2.1)	16 (13)	<0.1	28.6 (22)	33 (29)	
8/3	C	47	0.8	0.9	17	—	9.6	0.7	
8/4	D	30	3.7		7.3	0.1	10.3	2.8	
9/1	A_2	25 (11)	—	41 (32)	4.3 (2.2)	—	19 (9.3)	23 (17)	
9/2	B_4	23	0.5	31	0.2	—	24	22	
9/3	C	49 (45)	2.4 (0.6)	33 (25)	0.2	0.2 (0.1)	5.6 (2.8)	9.6 (5.1)	
9/4	D	25	—	30	0.6	—	3.1	5.9	
10/1	A_2	32	—	44	—	—	14	—	
10/2	B_4	31	—	38	—	—	3.1	—	
10/3	C	51 (45)	—	31 (25)	—	—	4.9 (2.8)	—	**38**: 10 (6.9)
10/4	D	70	—	14	—	—	5.1	—	

12, respectively. In case of severe reaction conditions or more active arylating agents different byproducts such as **15-16** (Scheme 5), **22-24** (Scheme 7), **25-27** (Scheme 8), **28** (Scheme 9), **32** (Scheme 10), **36** (Scheme 12) and **38** (Scheme 14) were also formed.

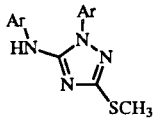
The structure proof of derivatives **8** and **9** was based on the complete analogy of their cmr chemical shifts with those of the analogues phenyl and 2,6-dimethylphenyl isomers **8** (Ar = phenyl and 2,6-dimethylphenyl) and **9** (Ar = phenyl), respectively, studied previously [3]. Compare *e.g.* the chemical shifts of the triazole carbon atoms C-3 and C-5 of the newly prepared derivatives **8** and **9** recorded in DMSO-d_6 solution (see Experimental) with those of known [3] isomers **8** and **9** (Ar = phenyl and

2,6-dimethylphenyl), respectively. Thus δ C-3 [**8/1-8/10** and **8** (Ar = phenyl and 2,6-dimethylphenyl)] = 159.5-162.5 ppm and 159.1-159.8 ppm, respectively, δ C-5 [**8/1-8/10** and **8** (Ar = phenyl and 2,6-dimethylphenyl)] = 156.5-157.8 ppm and 155.3-156.9 ppm, respectively; δ C-3 [**9/1-9/8** and **9** (Ar = phenyl)] = 152.5-153.8 ppm and 152.5 ppm, respectively, and δ C-5 [**9/1-9/8** and **9** (Ar = phenyl)] = 163.9-164.7 ppm and 165.2 ppm, respectively.

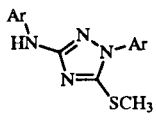
The situation was the same with the chemical shifts of the triazole carbon atoms of the exo-substituted derivatives **10** (Scheme 2) being analogues to those of derivatives **8** in agreement with that of observed previously [3].

The 1, exo-substituted **11** and 2, exo-substituted **12** structure of the isomeric diarylated derivatives was proved with the help of their pmr and cmr spectra. However, derivatives **11** and **12** may also exist in the tautomeric forms represented by structures **11a** and **12a**, respectively (Scheme 3). The tautomeric structures **11a**

Scheme 3



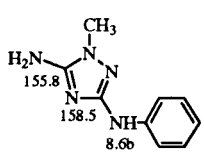
11a



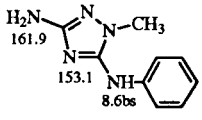
12a

and **12a** could be excluded on the basis of the chemical shifts of the NH protons in the pmr. It was known [4] that the chemical shifts of the exocyclic NH protons of the isomeric 5-amino-1-methyl-3-phenylamino-1*H*-1,2,4-triazole (**13**) and the 5-amino-2-methyl-3-(phenylamino, 2-methylphenylamino and 4-methylphenylamino)-2*H*-1,2,4-triazole derivatives **14a**, **14b** and **14c**, respectively, (Scheme 4) appeared in DMSO-d_6 solution between 7.65 and 8.6 ppm, while the triazole NH protons of even very differently substitued 5-amino-1,2,4-triazoles in positions 3 and 5 appeared at about 11 ppm [3,4]. The fact that the NH protons of all our disubstituted derivatives **11** and **12** appeared between 10.0 and 10.6 ppm proved their tautomeric structures represented by Formulas **11** and **12**. This is also in agreement with their cmr spectra where the triazole carbon atoms 3 appeared between 150.3-153.2 ppm and 155.4-157.0 ppm, respectively, and those of carbon atoms 5 which appeared between 160.3-161.5 ppm and 158.1-159.9 ppm, respec-tively, pointing out that the triazole ring should have a substituent (or a hydrogen atom) in position 2 [Compare with the corresponding chemical shifts of the known [3] 5-amino-3-methylthio-1-phenyl-1*H*-1,2,4-triazole (**8**, Ar = Phenyl)) and 5-amino-3-methylthio-2-phenyl-2*H*-1,2,4-triazole (**9**, Ar = Phenyl) discussed above].

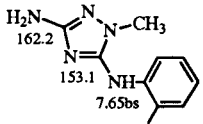
Scheme 4



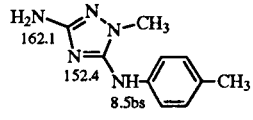
13



14a



14b



14c

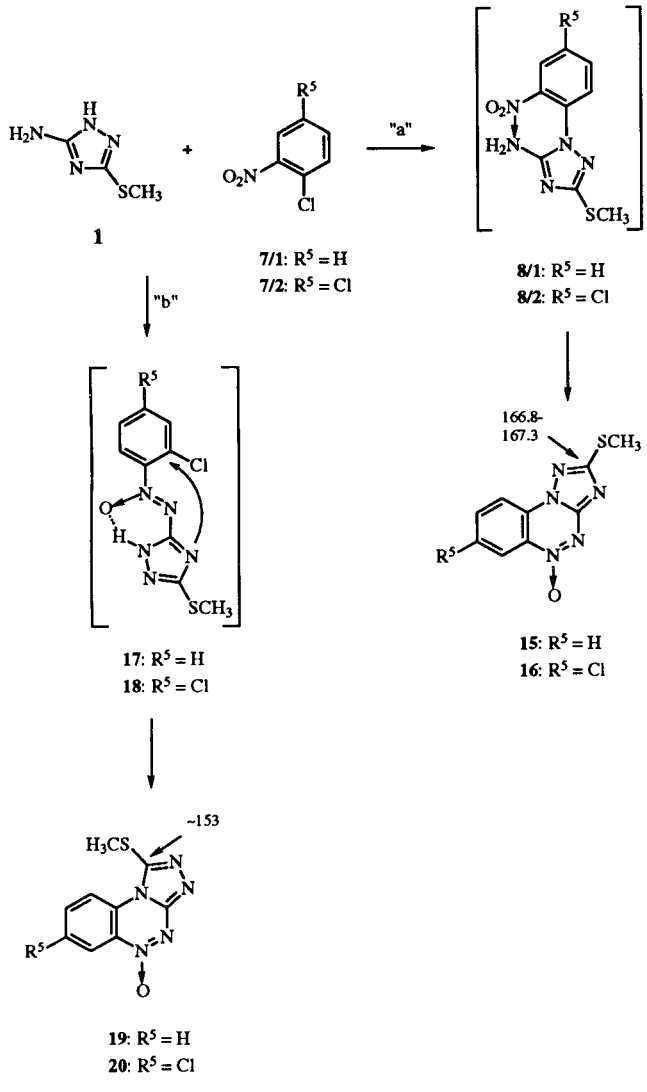
The difference in the chemical shifts of the carbon atoms 3 of derivatives **11** and **12** is caused by the electronic and sterical effect of the phenyl group on the triazole nitrogen atom 2 in derivatives **12**. This effect is also visible on the chemical shifts of the methylthio carbon atoms appearing in case of derivatives **12** shifted downfield by about 2 ppm as compared with those of derivatives **11** (see Experimental), analogously to that of observed previously [3].

The tautomeric structures **11** and **12** are also in agreement with the chemical shifts of the carbon atoms of the two benzene rings present from which those corresponding to the *ortho* and *para* carbon atoms of the phenylimino one were shifted upfield and those of the corresponding *meta* carbon atoms downfield as compared with the corresponding ones, being on the phenyl situated on the triazole ring - analogously to that of observed previously [5].

As it was just mentioned different byproducts were isolated from the reaction mixtures of the arylation reactions.

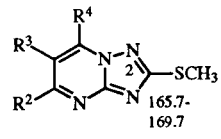
Thus from the reaction mixtures of **1** and the scarcely reactive 2-nitrochlorobenzene (**7/1**, Ar = 2-nitrophenyl) and 1,4-dichloro-2-nitrobenzene (**7/2**, Ar = 2-nitro-4-chlorophenyl) most probably due to severe reaction conditions used besides the expected **8**, **9**, **11** and **12** type derivatives the corresponding triazolobenzotriazines **15** and **16**, respectively, were isolated in good yields (Scheme 5) formed most probably by route 'a' from the corresponding monoalkylated derivatives **8/1** and **8/2**, respectively, through intramolecular cyclisation. However, the formation of triazolobenzotriazines can also be explained by route 'b' where the reaction starts with the condensation of the aromatic nitro group and the exo-amino group of the triazole ring to yield intermediates **17** and **18**, respectively (Scheme 5), stabilised by an intramolecular chelate ring in which the nitrogen atom 4 of the triazole ring becomes the most nucleophilic, thus the ring closure has to yield triazolobenzotriazines of structure **19** and **20**, respectively. Consequently, the structure of the triazolobenzotriazines obtained had to be proved. The structure proof of these derivatives was based

Scheme 5



on the chemical shifts of the triazole carbon atoms bearing the S-methyl group that was easily recognised by INEPT measurements. It was known [1] that the chemical shifts of the triazole carbon atoms 2 of the fully aromatic type **21** 2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidines having attached to the carbon atom 2 bearing the methylthio group two pyridine-like nitrogen atoms varied between 165.7-169.7 ppm (Scheme 6). On the other hand

Scheme 6

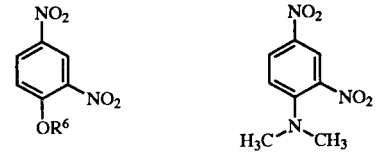


21

the carbon atom 3 of the 5-amino-3-methylthio-2-phenyl-2*H*-1,2,4-triazole (**9**, Ar = Phenyl) bearing the methylthio group having attached a pyridine-like and a pyrrol-like nitrogen atom appeared at 152.5 ppm [3]. As the corresponding carbon atoms 2 of the newly synthesised triazolobenzotriazines appeared at 166.8 and 167.3 ppm their structure should be **15** and **16**, respectively (Scheme 5).

The arylation of **1** with 2,4-dinitrochlorobenzene (**7/4**, Ar = 2,4-dinitrophenyl) yielded depending on the solvent used and the presence or absence of sodium cations the expected **8/4**, **9/4**, **11/4** and **12/4**, dinitrophenol (**22**) or its sodium salt **23** and *N,N*-dimethyl-2,4-dinitroaniline (**24**) formed by nucleophilic attack of **7/4** against the dimethylformamide used as solvent (Scheme 7).

Scheme 7

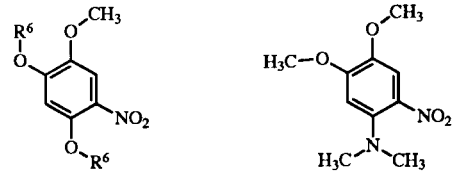


22: R^6 = H
23: R^6 = Na

24

Analogously, in the arylation reaction of **1** with 2-nitro-4,5-dimethoxychlorobenzene (**7/5**, Ar = 2-nitro-4,5-dimethoxyphenyl) the corresponding 3,4-dimethoxyphenol (**25**) or its sodium salt **26** and *N,N*-dimethyl-3,4-dimethoxyaniline (**27**) (Scheme 8) were obtained as byproducts.

Scheme 8

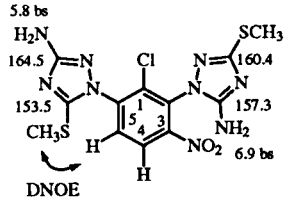


25: R^6 = H
26: R^6 = Na

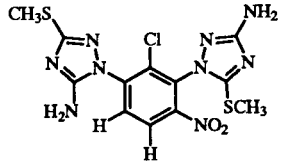
27

In case of 4-nitro-1,2,3-trichlorobenzene (**7/6**, Ar = 2-nitro-5,6-dichlorophenyl) the nitro group activated both, the *ortho* and *para* chloro substituents of the benzene ring, thus, beside the expected **8/6**, **9/6**, **11/6** and **12/6**, derivative **28** could also be isolated from the arylation reaction mixture of **1** (Scheme 9). Interestingly, in this product the two 5-amino-1,2,4-triazole rings are differently attached to the phenyl ring. Namely, one is attached through its ring nitrogen atom 1 and the other one through its ring nitrogen atom 2 as proved by the different pmr and cmr chemical shifts of the two triazole moi-

Scheme 9



28

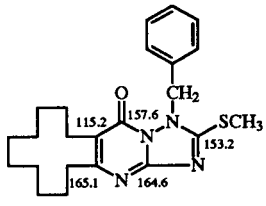


29

eties (Scheme 9) corresponding to that of derivatives **8** (Ar = Phenyl) and **9** (Ar = Phenyl), respectively, discussed above. However, the above data may also correspond to structure **29** (Scheme 9) containing the same elements in different order. The decision between structures **28** and **29** made possible a D-NOE experinemt. Thus irradiating the aromatic hydrogen atoms 4 and 5 (their selective irradiaition was not possible as they appeared within about 50 Hz) a NOE enhancement was observed on the methylthio group 3 of the triazole attached to the phenyl ring by nitrogen atom 2 indicating that this triazole moiety should be in position 6 of the benzene ring. This fact excludes structure **29** proving structure **28** unequivocally.

The arylation of **1** with 2,3-dichloro-6-nitrobenzonitrile (**7/7**, Ar = 2-chloro-3-cyano-4-nitrophenyl) led, besides the expected **8/7**, **9/7**, **11/7** and **12/7**, to a triazoloquinazolone derivative **32** (Scheme 10) formed most probably by route shown on the Scheme 10 starting with a nucleophilic attack of the triazole nitrogen atom 1 through the intermediates **30** and **31** that after work up with water hydrolised to **32**. The structure of **32** is in accordance with the chemical shift of the triazole NH proton appearing at 12.5 ppm as well as with its cmr spectra (Scheme 10) being completely analogues (if taken in account the substituent effect of the benzyl substituent and the influence of the substituted aromatic ring) with **33** (Scheme 11) described previously [6].

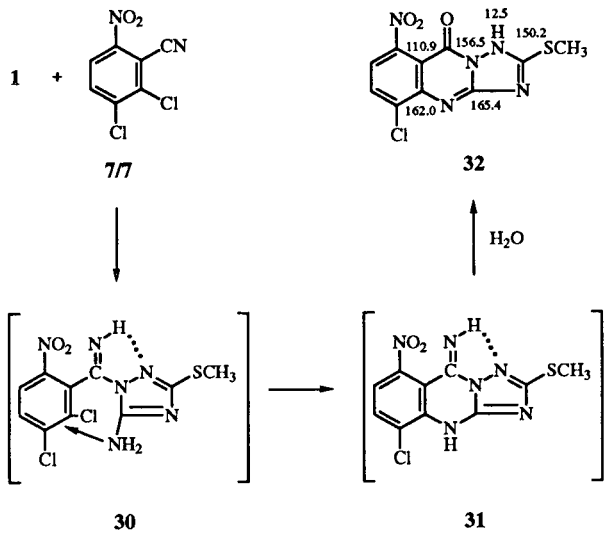
Scheme 11



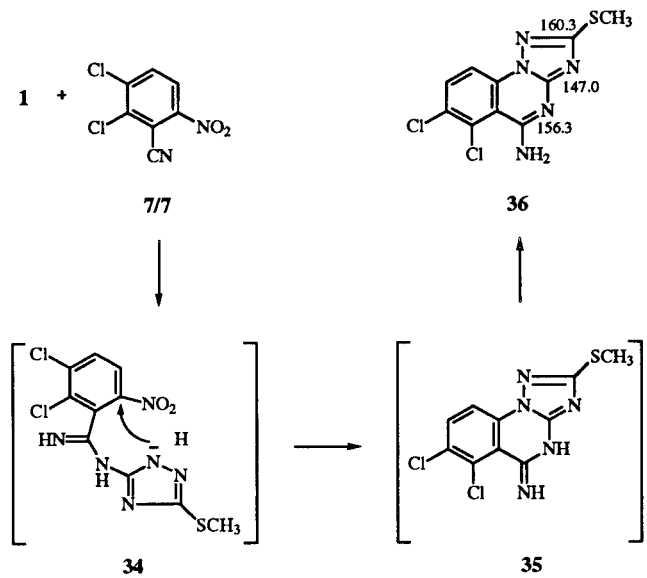
33

A further triazoloquinazoline derivative **36** (Scheme 12) was isolated from the above reaction mixture seemingly formed by route shown on Scheme 12, starting with the nucleophilic attack of the exocyclic amino nitrogen atom through intermediates **34** and **35**. The structure of **36** is in accord with the ms spectra showing the molecular peak at 299 (EI) and 300 (CI) respectively, with the presence of the amino group appearing in the ir spectra at 3496 cm^{-1} and 3292 cm^{-1} and in the pmr spectra at δ = 8.2 ppm, as well as with the cmr spectra recorded where the triazole carbon atoms 2 and 3a appeared at 160.3 and 147.0 ppm, respectively (compare with those of 2 and 3a of 7a-methyl-2-methylthio-5,6,7,7a-tetrahydro-10-trifluoromethylpyrrolo[1,2-*c*][1,2,4]triazolo[1,5-*a*][1,3,5]benzotriazepin-5(8*H*)-one (**37**) (Scheme 13) described previously [7]), while that of carbon atom 5 bearing the amino

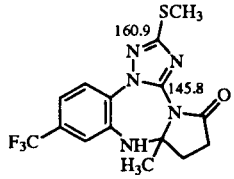
Scheme 10



Scheme 12



Scheme 13



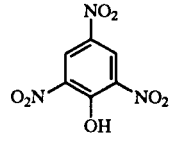
37

group appeared at 156.3 ppm.

The extreme reactivity and the steric hindrance of the arylating agents containing the 2,6-dinitrophenyl moiety [i.e. the 2,6-dinitrochlorobenzene (**7/8**, Ar = 2,6-dinitrophenyl), 2,6-dinitro-4-trifluoromethylchlorobenzene (**7/9**, Ar = 2,6-dinitro-4-trifluoromethylphenyl), and 2,4,6-trinitrochlorobenzene (**7/10**, Ar = 2,4,6-trinitrophenyl)] led - again besides the expected derivatives **8**, **9**, **11**, and **12** - to the formation of exo-arylated derivatives **10**, the amount of which increased with the increasing reactivity of the arylating agents (Table 1).

From the reaction mixture of **7/10** and **1** - analogously to the arylation reactions provided with **7/4** and **7/5** (see above) - the corresponding phenol **37** was also isolated (Scheme 14).

Scheme 14



38

EXPERIMENTAL

Melting points were determined on a Koffler-Boetius micro apparatus and are not corrected. The infrared spectra were obtained as potassium bromide pellets using a Bruker IFS 113-V spectrophotometer. The pmr and the cmr measurements were performed using Bruker WM-250 and Bruker WP-80 SY instruments. All tlc determinations were carried out on Kieselgel GF_{254} (Merck) plates using different mixtures of cyclohexane and ethyl acetate as eluent. The spots were detected by uv and potassium permanganate solution. The hplc investigations were performed using KNAUER apparatus (KNAUER HPLC PUMP 64, KNAUER absorbance detector MODEL UV-1, column: KNAUER C-8; as eluents different mixtures of acetonitrile and 0.1 *M* ammonium acetate buffer, *p*H = 4.4, were used). Calibration was made by using pure samples. The dry column flash chromatographies [8] were performed using Kieselgel 60H (Merck 77-36) absorbent. As eluents different mixtures of hexane: benzene, and ethyl acetate: cyclohexane of continuously increasing polarities were used.

General Methods for the Arylation of 5-Amino-3-methylthio-1*H*-1,2,4-triazole (**1**).

Method A_1.

A mixture of 0.13 g [0.001 mole] of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9], 0.001 mole of the appropriate aryl chloride **7**, 0.10 g (0.001 mole) of triethylamine and 2 ml of ethanol was reacted with stirring at 80° for 48 hours. The solution obtained was analysed by hplc.

Method A_2.

A mixture of 0.13 g [0.001 mole] of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9], 0.001 mole of the appropriate aryl chloride **7** and 2 ml of ethanol was reacted with stirring at 80° for 48 hours. The solution obtained was analysed by hplc.

Method B_1.

A mixture of 0.13 g [0.001 mole] of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9], 0.001 mole of the appropriate aryl chloride **7** and 2 ml of dimethylformamide was reacted with stirring at 120° for 48 hours. The solution obtained was analysed by hplc.

Method B_2.

One proceeded according to Method B_1 except of that the heating was provided at 80°.

Method B_3.

See in detail at the appropriate runs described below.

Method B_4.

One proceeded according to Method B_1 except of that the heating was provided at 40°.

Method C.

See in detail at the appropriate runs described below.

Method D.

A mixture of 0.13 g [0.001 mole] of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**), and 0.001 mole of the appropriate aryl chloride **7** was heated neat at 150° for about 5 minutes. The reaction mixture obtained was analysed by hplc.

Arylation of 5-Amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with 2-Nitrochlorobenzene (**7/1**) using Sodium Hydride in Dimethylformamide (Method C, run 1/3).

To a solution of 13.2 g (0.1 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9] in 80 ml of dimethylformamide 3.2 g (0.1 mole) of sodium hydride (75% in parraffin oil, Fluka) was added in small portions with stirring below 5°. After stirring for 1 hour at 0° 15.8 g (0.1 mole) of 2-nitrochlorobenzene (**7/1**) [10] was added to the reaction mixture in small portions keeping the temperature below 15°. The mixture was stirred for 72 hours at 100° and evaporated *in vacuo* to dryness. To the residue 150 ml of ethyl acetate was added and the crystals that separated were filtered off to yield 2.68 g (12%) of 2-methylthio[1,2,4]triazolo[5,1-*c*][1,2,4]benzotriazine 5-oxide (**15**), mp 230-232° (dimethylformamide); pmr (DMSO-d_6): δ ppm 2.72 (s, 3H, SCH_3), 7.80 [dt (J = 7.8 and 1.0 Hz), 1H, H-7], 8.15 [dt (J = 8.4 and 1.2 Hz), 1H, H-8], 8.29 [dd (J = 8.4 and 1.0 Hz), 1H, H-9], 8.48 [dd (J = 7.8 and 1.2 Hz), 1H, H-6]; cmr (DMSO-d_6): δ ppm 13.6 (SCH_3), 115.6 (C-9), 122.4 (C-6), 128.3 (C-8), 130.6 (C-9a), 131.6 (C-5a), 136.9 (C-7), 152.7 (C-3a), 166.8 (C-2)

(Assignment checked by INEPT); ms (EI) M^+ = 233.

Anal. Calcd. for $C_9H_7N_5OS$ (MW 233.26): C, 46.35; H, 3.02; N, 30.02; S, 13.75. Found: C, 46.31; H, 3.08; N, 30.00; S, 13.80.

The combined mother liquors were evaporated *in vacuo* to dryness and column flash chromatographed on a silica gel column to yield in order of appearance:

First, 1.98 g (13%) of unreacted 2-nitrochlorobenzene (**7/1**) was obtained, mp 32-32.5° (cyclohexane), lit [10] mp 32°; pmr (DMSO-d_6): δ ppm 7.62 [dt (J = 8.0 and 1.8 Hz), PhH-4], 7.72 [dd (J = 8.0 and 1.8 Hz), 1H, PhH-6], 7.77 [dt (J = 8.0 and 1.4 Hz), 1H, PhH-5], 8.08 [dd (J = 8.0 and 1.4 Hz), 1H, PhH-3]. Second, 0.37 g (1.0 %) of 3-methylthio-1-(2-nitrophenyl)-5-(2-nitrophenylimino)-2*H*-1,2,4-triazole (**11/1**) was obtained, mp 181-183° (ethyl acetate); pmr (DMSO-d_6): δ ppm 2.50 (s, 3H, SCH_3), 7.22 [dt (J = 8.3 and 0.9 Hz), PhH-4"], 7.78 [dt (J = 8.4 and 0.9 Hz), 1H, PhH-4'], 7.86 [dt (J = 8.7 and 1.3 Hz), 1H, PhH-5'], 8.02 [dd (J = 8.7 and 0.9 Hz), 1H, PhH-6'], 8.02 [dd (J = 8.0 and 0.9 Hz), 1H, PhH-6"], 8.12 [dd (J = 8.4 and 1.3 Hz), 1H, PhH-3'], 8.20 [dd (J = 8.3 and 0.5 Hz), 1H, PhH-3"], 8.24 [dt (J = 8.0 and 0.5 Hz), 1H, PhH-5"], 10.0 (b, 1H, NH); cmr (DMSO-d_6): δ ppm 13.4 (SCH_3), 120.8 (PhC-6"), 122.6 (PhC-4"), 126.1 (PhC-3' and PhC-3"), 128.3 (PhC-1'), 129.3 (PhC-4'), 131.7 (PhC-6'), 135.1 (PhC-5'), 135.4 (PhC-1"), 136.1 (PhC-5"), 136.9 (PhC-2"), 145.2 (PhC-2'), 151.4 (C-3), 160.2 (C-5).

Anal. Calcd. for $C_{15}H_{12}N_6O_4S$ (MW 372.37): C, 48.39; H, 3.25; N, 22.57; S, 8.61. Found: C, 48.33; H, 3.30; N, 22.34; S, 8.63.

Third, 0.14 g (0.4%) of 3-methylthio-2-(2-nitrophenyl)-5-(2-nitrophenylimino)-1*H*-1,2,4-triazole (**12/1**) was obtained, that was contaminated with about 30% of **11/1**, mp 225-228° (2-propanol) from which the spectral data of **12/1** were deduced as: pmr (DMSO-d_6): δ ppm 2.62 (s, 3H, SCH_3), 7.23 [dt (J = 8.3 and 1.0 Hz), PhH-4"], 7.71 [dt (J = 8.3 and 1.0 Hz), 1H, PhH-4'], 7.88 [dt (J = 8.5 and 1.3 Hz), 1H, PhH-5'], 7.91 [dd (J = 8.5 and 1.0 Hz), 1H, PhH-6'], 8.01 [dd (J = 8.0 and 1.0 Hz), 1H, PhH-6"], 8.13 [dd (J = 8.3 and 1.3 Hz), 1H, PhH-3'], 8.20 [dt (J = 8.0 and 0.5 Hz), 1H, PhH-5"], 8.21 [dd (J = 8.3 and 0.5 Hz), 1H, PhH-3"], 10.0 (b, 1H, NH); ms: (EI) M^+ 372 ($C_{15}H_{12}N_6O_4S$).

Fourth, 0.31 g (1.2%) of 5-amino-3-methylthio-2-(2-nitrophenyl)-2*H*-1,2,4-triazole (**9/1**) was obtained, mp 159-160° (ethyl acetate); pmr (DMSO-d_6): δ ppm 2.60 (s, 3H, SCH_3), 5.7 (b, 2H, NH_2), 7.75 [dt (J = 8.3 and 1.1 Hz), 1H, PhH-4'], 7.85 [dt (J = 7.7 and 1.2 Hz), 1H, PhH-5'], 7.90 [dd (J = 7.7 and 1.1 Hz), 1H, PhH-6'], 8.11 [dd (J = 8.3 and 1.2 Hz), 1H, PhH-3']; cmr (DMSO-d_6): δ ppm 15.2 (SCH_3), 125.4 (PhC-3'), 128.1 (PhC-1'), 129.7 (PhC-6'), 130.2 (PhC-4'), 134.0 (PhC-5'), 145.0 (PhC-2'), 152.5 (C-3), 164.4 (C-5).

Anal. Calcd. for $C_9H_9N_5O_2S$ (MW 251.27): C, 43.02; H, 3.61; N, 27.87; S, 12.76. Found: C, 42.95; H, 3.71; N, 27.98; S, 12.70.

Fifth, 1.66 g (6.6%) of 5-amino-3-methylthio-1-(2-nitrophenyl)-1*H*-1,2,4-triazole (**8/1**) was obtained, mp 149-151° (acetonitrile), lit [11] mp 150-151°; pmr (DMSO-d_6): δ ppm 2.40 (s, 3H, SCH_3), 6.7 (b, 2H, NH_2), 7.69 [dt (J = 8.0 and 1.0 Hz), 1H, PhH-4'], 7.73 [dd (J = 7.7 and 1.0 Hz), 1H, PhH-6'], 7.86 [dt (J = 7.7 and 1.2 Hz), 1H, PhH-5'], 8.11 [dd (J = 8.0 and 1.2 Hz), 1H, PhH-3']; cmr (DMSO-d_6): δ ppm 13.3 (SCH_3), 125.6 (PhC-3'), 129.1 (PhC-1'), 129.7 (PhC-4'), 130.2 (PhC-6'), 134.6 (PhC-5'), 145.3 (PhC-2'), 156.8 (C-5), 159.7 (C-3).

Anal. Calcd. for $C_9H_9N_5O_2S$ (MW 251.27): C, 43.02; H, 3.61; N, 27.87; S, 12.76. Found: C, 43.05; H, 3.65; N, 27.95; S, 12.78.

Sixth, 3.55 g (28 %) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) was obtained, mp 135-136° (ethanol), lit [9] mp 136-137°.

Arylation of 5-Amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with 1,4-Dichloro-2-nitrobenzene (**7/2**) using Sodium Hydride in Dimethylformamide (Method C, run 2/3).

To a solution of 13.2 g (0.1 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9] in 80 ml of dimethylformamide 3.2 g (0.1 mole) of sodium hydride (75% in paraffin oil, Fluka) was added in small portions with stirring below 5°. After stirring for 1 hour at 0° 22.6 g (0.1 mole) of 1,4-dichloro-2-nitrobenzene (**7/2**) [12] was added to the reaction mixture in small portions keeping the temperature below 15°. The mixture was then stirred for a futher 6 hours at 60° and evaporated *in vacuo* to dryness. The residue was dry-column flash chromatographed to yield in order of appearence:

First, 2.00 g (10%) of unreacted 1,4-dichloro-2-nitrobenzene (**7/2**), mp 55-56°, lit [12] mp 54-56°. Second, 0.95 g (3.3%) of 7-chloro-2-methylthio[1,2,4]triazolo[5,1-*c*][1,2,4]benzotriazine-5-oxide (**16**) was obtained, mp 200-202° (acetonitrile); pmr (DMSO-d_6): δ ppm 2.72 (s, 3H, SCH_3), 8.20 [dd (J = 8.9 and 2.1 Hz), 1H, PhH-8], 8.32 [d (J = 8.9 Hz), 1H, PhH-9], 8.52 [d (J = 2.1 Hz), 1H, PhH-6; cmr (DMSO-d_6): δ ppm 13.7 (SCH_3), 117.8 (PhC-9), 121.8 (PhC-6), 129.7 (PhC-9a), 132.1 (PhC-5a), 132.5 (PhC-8), 137.0 (PhC-7), 152.7 (C-3a), 167.3 (PhC-2).

Anal. Calcd. for $C_9H_6N_5ClOS$ (MW 267.70): C, 40.38; H, 2.26; N, 26.16; Cl, 13.24; S, 11.98. Found: C, 40.40; H, 2.23; N, 26.28; Cl, 13.29; S, 11.92.

Third, 0.95 g (3.3%) of 5-amino-3-methylthio-2-(2-nitro-4-chlorophenyl)-2*H*-1,2,4-triazole (**9/2**) was obtained, mp 154-156° (acetonitrile); pmr (DMSO-d_6): δ ppm 2.60 (s, 3H, SCH_3), 5.75 (bs, 2H, NH_2), 7.80 [d (J = 8.5 Hz), 1H, PhH-6'], 7.96 [dd (J = 8.5 and 2.3 Hz), 1H, PhH-5'], 8.26 [d (J = 2.3 Hz), 1H, PhH-3']; cmr (DMSO-d_6): δ ppm 15.6 (SCH_3), 123.3 (PhC-3'), 129.2 (PhC-1'), 129.7 (PhC-6'), 132.5 (PhC-5'), 133.8 (PhC-4'), 144.5 (PhC-2'), 152.7 (C-3), 164.0 (C-5).

Anal. Calcd. for $C_9H_8N_5ClO_2S$ (MW 285.72): C, 37.84; H, 2.82; N, 24.51; Cl, 12.41; S, 11.22. Found: C, 37.85; H, 2.80; N, 24.58; Cl, 12.45; S, 11.28.

Fourth, 0.95 g (2.2%) of 3-methylthio-1-(2-nitro-4-chlorophenyl)-5-(2-nitro-4-chlorophenylimino)-2*H*-1,2,4-triazole (**11/2**), mp 186-187° (methanol); pmr (DMSO-d_6): δ ppm 2.48 (s, 3H, SCH_3), 7.84 [dd (J = 8.6 and 2.5 Hz), 1H, PhH-5'], 8.01 [d (J = 8.5 Hz), 1H, PhH-6"], 8.05 [d (J = 8.6 Hz), 1H, PhH-6'], 8.12 [dd (J = 8.5 and 2.5 Hz), 1H, PhH-5"], 8.15 [d (J = 2.5 Hz), 1H, PhH-3'], 8.42 [d (J = 2.5 Hz), 1H, PhH-3"], 10.0 (b, 1H, NH); cmr (DMSO-d_6): δ ppm 13.2 (SCH_3), 123.1 (PhC-6"), 125.4 (PhC-3'), 126.1* (PhC-3"), 126.2* (Ph-C-4"), 127.2 (PhC-1'), 130.7 (PhC-6'), 134.1 (PhC-4'), 134.9 (PhC-5'), 135.4* (PhC-1"), 135.5* (PhC-5"), 138.0 (PhC-2"), 145.6 (PhC-2'), 151.4 (C-3), 160.5 (C-5).

Anal. Calcd. for $C_{15}H_{10}N_6Cl_2O_4S$ (MW 441.26): C, 40.83; H, 2.28; N, 19.05; Cl, 16.07; S, 7.27. Found: C, 40.82; H, 2.32; Cl, 16.27; N, 19.00; S, 7.32.

Fifth, 0.16 g of a 1:2 mixture of **12/2** and **11/2** was obtained, that after many recrystallisations from methanol afforded pure 3-methylthio-2-(2-nitro-4-chlorophenyl)-5-(2-nitro-4-chlorophenylimino)-1*H*-1,2,4-triazole (**12/2**), mp 168-170°; pmr (DMSO-d_6): δ ppm 2.65 (s, 3H, SCH_3), 7.85 [dd (J = 8.5 and

2.3 Hz), 1H, PhH-5'], 8.03 [d (J = 8.5 Hz), 1H, PhH-6'], 8.07 [d (J = 8.6 Hz), 1H, PhH-6"], 8.14 [d (J = 2.3 Hz), 1H, PhH-3'], 8.16 [dd (J = 8.6 and 2.4 Hz), 1H, PhH-5"], 8.45 [d (J = 2.4 Hz), 1H, PhH-3"], 9.95 (bs, 1H, NH); cmr (DMSO-d_6): δ ppm 15.5 (SCH_3), 124.2 (PhC-6"), 124.8 (PhC-3'), 125.1 (PhC-4"), 126.4 (PhC-3"), 128.3 (PhC-1'), 130.1 (PhC-6'), 133.1 (PhC-5'), 134.2 (PhC-4'), 135.1 (PhC-1"), 135.5 (PhC-2"), 137.8 (PhC-5"), 145.0 (PhC-2'), 155.4 (C-3), 159.8 (C-5).

Anal. Calcd. for $C_{15}H_{10}N_6Cl_2O_4S$ (MW 441.26): C, 40.83; H, 2.28; N, 19.05; Cl, 16.07; S, 7.27. Found: C, 40.89; H, 2.27; Cl, 16.13; N, 19.09; S, 7.31.

Sixth, 3.60 g (13%) 5-amino-3-methylthio-1-(2-nitro-4-chlorophenyl)-1*H*-1,2,4 -triazole (**8/2**) was obtained, mp 197-198°; pmr (DMSO-d_6): δ ppm 2.41 (s, 3H, SCH_3), 6.8 (b, 2H, NH_2), 7.74 [d (J = 8.6 Hz), 1H, PhH-6'], 7.95 [dd (J = 8.6 and 2.4 Hz), 1H, PhH-5'], 8.28 [d, (J = 2.4 Hz), 1H, PhH-3']; cmr (DMSO-d_6): δ ppm 13.4 (SCH_3), 125.4 (PhC-3'), 128.4 (PhC-1'), 130.5 (PhC-6'), 133.7 (PhC-4'), 134.0 (PhC-5'), 145.5 (PhC-2'), 156.6 (C-5), 159.6 (C-3).

Anal. Calcd. for $C_9H_8N_5ClO_2S$ (MW 285.72): C, 37.84; H, 2.82; N, 24.51; Cl, 12.41; S, 11.22. Found: C, 37.80; H, 2.82; N, 24.55; Cl, 12.44; S, 11.33.

Seventh, 1.70 g (13%) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**), mp 136-137° (ethanol), lit [9] 136-137°.

Arylation of 5-Amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with 2-Nitro-4-trifluoromethylchlorobenzene (**7/3**) using Sodium Hydride in Dimethylformamide (Method C, run 3/3).

To a solution of 13.2 g (0.1 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9] in 80 ml of dimethylformamide 3.2 g (0.1 mole) of sodium hydride (75% in paraffin oil, Fluka) was added in small portions with stirring below 5°. After stirring for 1 hour at 0° 22.6 g (0.1 mole) of 2-nitro-4-trifluorochlorobenzene (**7/3**) [13] was added to the reaction mixture in small portions keeping the temperature below 15°. It was stirred at 70° for a futher 3 hours and then the reaction mixture was evaporated *in vacuo* to dryness. To the black oily residue 300 ml of water was added and the mixture stirred for 3 hours. The organic layer was separated, 20 ml of benzene was added to it, and after 2 hours the crystals which precipitated were filtered off to yield 11.0 g of crystals that were recrystallised from 150 ml of ethanol. This way 6.17 g (19%) of 5-amino-3-methylthio-1-(2-nitro-4-trifluoromethylphenyl)-1*H*-1,2,4-triazole (**8/3**) was obtained, mp 224-224.5°, lit [11] mp 223-224°; pmr (DMSO-d_6): δ ppm 2.43 (s, 3H, SCH_3), 6.9 (b, 2H, NH_2), 8.00 [d (J = 8.4 Hz), 1H, PhH-6'], 8.27 [dd (J = 8.4 and 1.7 Hz), 1H, PhH-5'], 8.52 [d (J = 1.7 Hz), 1H, PhH-3']; cmr (DMSO-d_6): δ ppm 13.4 (SCH_3), 122.8 [qa (J = 273 Hz, CF_3'], 123.0 [qa (J = 4.2 Hz), PhC-3'], 129.5 [qa, (J = 33.9 Hz), PhC-4'], 129.6 (PhC-1'), 131.0 [qa, (J = 4.2 Hz), PhC-5'], 132.8 (PhC-6'), 144.9 (PhC-2'), 156.7 (C-5), 160.4 (C-3), (Assignment checked by INEPT).

Anal. Calcd. for $C_{10}H_8N_5F_3O_2S$ (MW 319.27): C, 37.62; H, 2.53; N, 21.94; F, 17.85; S, 10.04. Found: C, 37.60; H, 2.58; N, 21.91; F, 17.86; S, 10.05.

The mother liquor was evaporated *in vacuo* to dryness and the residue was dry-column flash chromatographed to yield in order of appearence:

First, 1.81 g (8.0%) of unreacted 2-nitro-4-trifluormethylchlorobenzene (**7/3**) was obtained, oily product identified with hplc. Second, 5.35 g (11%) of 3-methylthio-1-(2-nitro-4-trifluormethylphenyl)-5-(2-nitro-4-trifluormethylphenylimino)-2*H*-1,2,4-triazole (**11/3**) was obtained, mp 123.5-124.5° (2-propanol); pmr (DMSO-d_6): δ ppm, 2.51 (s, 3H, SCH_3), 8.26 [dd (J = 9.0 and 2.0 Hz), 1H, PhH-5'], 8.34 [d (J = 9.0 Hz), 1H, PhH-6'], 8.40 [d (J = 8.4 Hz), 1H, Ph-6"], 8.53 [d (J = 2.0 Hz), 1H, Ph-3'], 8.56 [dd (J = 8.4 and 1.6 Hz), 1H, PhH-5"], 8.79 [d (J = 1.6 Hz), 1H, Ph-3"], 10.5 (b, 1H, NH); cmr (DMSO-d_6): δ ppm 13.5 (SCH_3), 121.7 [qa, (J = 3.4 Hz), PhC-3'], 122.3 [qa, (J = 34.0 Hz), PhC-4"], 122.3 [qa, (J = 273 Hz), CF_3'], 123.3 [qa (J = 273 Hz), CF_3"], 123.5 [qa (J = 3.5 Hz), PhC-3"], 123.6 (PhC-6"), 129.8 (PhC-1'), 130.9 [qa, (J = 34.0 Hz), PhC-4'], 131.6 (PhC-6'), 131.9 [qa, (J = 3.5 Hz), PhC-5'), 136.5 (PhC-1"), 136.5 [qa, (J = 3.5 Hz), PhC-5"], 138.3 (PhC-2"), 144.3 (PhC-2'), 150.6 (C-3), 161.1 (C-5).

Anal. Calcd. for $C_{17}H_{10}N_6F_6O_4S$ (MW 508.37): C, 40.17; H, 1.98; N, 16.53; F, 22.42; S, 6.31. Found: C, 40.19; H, 2.03; N, 16.50; F, 22.43; S, 6.34.

Third, 0.50 g (1.0%) of 3-methylthio-2-(2-nitro-4-trifluoromethylphenyl)-5-(2-nitro-4-trifluoromethylphenylimino)-1*H*-1,2,4-triazole (**12/3**) mp 143-145° (acetonitrile); pmr (DMSO-d_6): δ ppm 2.77 (s, 3H, SCH_3), 7.78 [dd (J = 8.3 and 1.9 Hz), 1H, PhH-5'], 7.86 [d (J = 8.3 Hz), 1H, PhH-6'], 8.04 [d (J = 8.5 Hz), 1H, PhH-6"], 8.32 [d (J = 1.9 Hz), 1H, PhH-3'], 8.52 [dd (J = 8.5 and 1.7 Hz, 1H, PhH-5"], 8.55 [d (J = 1.7 Hz), 1H, PhH-3"], 10.5 (b, 1H, NH); cmr (DMSO-d_6): δ ppm 15.6 (SCH_3), 119.8 [qa (J = 3.5 Hz), PhC-3'], 122.9 [qa (J = 273 Hz), CF_3'], 123.1 [qa (J = 3.4 Hz), PhC-3"], 123.5 [qa (J = 273 Hz), CF_3"], 123.8 [qa (J = 34.0 Hz), PhC-4"], 123.8 (PhC-6"), 130.0 (PhC-1'), 131.6 (PhC-6'), 131.8 [qa (J = 35.0 Hz), PhC-4'], 132.1 [qa (J = 3.5 Hz), PhC-5'], 134.7 (PhC-5"), 136.0 (PhC-1"), 139.2 (PhC-2"), 144.9 (PhC-2'), 155.7 (C-3), 158.6 (C-5).

Anal. Calcd. for $C_{17}H_{10}N_6F_6O_4S$ (MW 508.37): C, 40.17; H, 1.98; N, 16.53; F, 22.42; S, 6.31. Found: C, 40.20; H, 2.00; N, 16.63; F, 22.50; S, 6.42.

Fourth, 2.16 g (6.8%) of 5-amino-3-methylthio-2-(2-nitro-4-trifluoromethylphenyl)-2*H*-1,2,4-triazole (**9/3**) was obtained, mp 126-127° (acetonitrile); pmr (DMSO-d_6): δ ppm 2.65 (s, 3H, SCH_3), 5.9 (bs, 2H, NH_2), 8.03 [d (J = 8.5 Hz), 1H, PhH-6'], 8.28 [dd (J = 8.5 and 1.6 Hz), 1H, PhH-5'], 8.52 [d (J = 1.6 Hz), 1H, PhH-3']; cmr (DMSO-d_6): δ ppm 15.6 (SCH_3), 123.0 [qa (J = 3.8 Hz), PhC-3'], 123.4 [qa (J = 273 Hz), CF_3], 129.3 [qa (J = 3.8 Hz), PhC-5'], 129.9 [qa (J = 34.0 Hz), PhC-4'], 132.8 (PhC-1' and 6'), 144.7 (PhC-2'), 154.7 (C-3), 164.7 (C-5), (Assignment checked by INEPT).

Anal. Calcd. for $C_{10}H_8N_5F_3O_2S$ (MW 319.27): C, 37.62; H, 2.53; N, 21.94; F, 17.85; S, 10.04. Found: C, 37.64; H, 2.55; N, 21.90; F, 17.89; S, 9.97.

Fifth, 1.58 g (5.0%) of 5-amino-3-methylthio-1-(2-nitro-4-trifluoromethylphenyl)-1*H*-1,2,4-triazole (**8/3**) was obtained, mp 224-225° (acetonitrile). The product is identical (ir, mixed mp) with that of **8/3** obtained above. Sixth, 1.93 g (15%) of unreacted 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) was obtained, mp 134-136° (ethanol), lit [9] mp 136-137°.

Arylation of 5-Amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with 2,4-Dinitrochlorobenzene (**7/4**) using Sodium Hydride in Dimethylformamide (Method C, run 4/3).

To a solution of 13.2 g (0.1 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9] in 70 ml of dimethylformamide 3.2 g (0.1 mole) of sodium hydride (75% in parraffin oil, Fluka, washed with cyclohexane) was added in small portions with stirring below 5°. After stirring for an hour at 0° 20.2 g (0.1 mole) of 2,4-dinitrochlorobenzene (**7/4**) [14] was added to the reaction mixture in small portions keeping the temperature below 15°.

The mixture was stirred for a futher 2 hours at 60° and evaporated *in vacuo* to dryness. The remaining black oil was dry-column flash chromatographed to yield in order of appearence:

First, 6.95 g (15%) of 3-methylthio-1-(2,4-dinitrophenyl)-5-(2,4-dinitrophenylimino)-2*H*-1,2,4-triazole (**11/4**) was obtained, mp 238.5-240° (dioxane); pmr (DMSO-d_6): δ ppm 2.46 (s, 3H, SCH_3), 8.11 [d (J = 9.3 Hz), 1H, PhH-6"], 8.23 [d (J = 8.8 Hz), 1H, PhH-6'], 8.49 [dd (J = 9.3 and 2.8 Hz), 1H, PhH-5"], 8.71 [dd (J = 8.8 and 2.5 Hz), 1H, PhH-5'], 8.76 [d (J = 2.8 Hz), 1H, PhH-3"], 8.88 [d (J = 2.5 Hz), 1H, PhH-3'], 10.6 (b, 1H, NH); cmr (DMSO-d_6): δ ppm 13.6 (SCH_3), 121.0 (PhC-3'), 121.7 (PhC-3"), 122.4 (PhC-6"), 129.1 (PhC-5'), 129.5 (PhC-6'), 129.8 (PhC-5"), 132.8 (PhC-1'), 135.8 (PhC-1"), 140.4* (PhC-2"), 140.5* (PhC-4"), 144.0 (PhC-2'), 147.3 (PhC-4'), 150.3 (C-3), 161.5 (C-5).

Anal. Calcd. for $C_{15}H_{10}N_8O_8S$ (MW 462.36): C, 38.97; H, 2.18; N, 24.23; S, 6.93. Found: C, 39.04; H, 2.20; N, 24.29; S, 6.90.

Second, 3.9 g (18%) of *N,N*-dimethyl-2,4-dinitroaniline (**24**) was obtained, mp 85-86° (2-propanol); lit [15] mp 87°; pmr (DMSO-d_6): δ ppm 3.05 (s, 6H, N-CH_3), 7.05 [d (J = 10.0 Hz), PhH-6], 8.25 [dd (J = 10.0 and 2.5 Hz), PhH-5], 8.62 [d (J = 2.5 Hz), PhH-3]; cmr (DMSO-d_6): δ ppm 42.5 (CH_3), 116.6 (PhC-3), 124.2 (PhC-5), 127.8 (PhC-6), 135.4 (PhC-1), 136.7 (PhC-4), 149.2 (PhC-2).

Third, 0.5 g (2.4%) of sodium 2,4-dinitrophenolate (**23**) was obtained, mp 320-330° (2-propanol); pmr (DMSO-d_6): δ ppm 6.38 [d (J = 9.8 Hz), 1H, PhH-6], 7.82 [dd (J = 9.8 and 3.1 Hz), 1H, PhH-5], 8.64 (d (J = 3.1 Hz), PhH-3); cmr (DMSO-d_6): δ ppm 125.2 (PhC-3), 127.0 (PhC-5), 127.8 (PhC-6), 135.8 (PhC-4), 138.2 (PhC-2), 170.8 (PhC-1).

Fourth, 0.53 g (1.2%) of 3-methylthio-2-(2,4-dinitrophenyl)-5-(2,4-dinitrophenylimino)-1*H*-1,2,4-triazole (**12/4**) was obtained, mp 178-180° (methanol); pmr (DMSO-d_6): δ ppm 2.77 (s, 3H, SCH_3), 8.19 [d (J = 8.8 Hz), 1H, PhH-6'], 8.23 [d (J = 9.3 Hz), 1H, PhH-6"], 8.44 [dd (J = 9.3 and 2.3 Hz), 1H, PhH-5"], 8.72 [dd (J = 8.8 and 2.5 Hz), 1H, PhH-5'], 8.80 [d (J = 2.3 Hz), 1H, PhH-3"], 8.90 [d (J = 2.5 Hz), 1H, PhH-3'], 10.6 (bs, 1H, NH); cmr (DMSO-d_6): δ ppm 15.7 (SCH_3), 119.2 (PhC-3'), 121.8 (PhC-3"), 122.6 (PhC-6"), 128.4 (PhC-5'), 129.0 (PhC-6'), 129.9 (PhC-5"), 130.1 (PhC-1'), 134.0 (PhC-1"), 139.0 (PhC-2"), 141.0 (PhC-4"), 144.4 (PhC-2'), 147.8 (PhC-4'), 156.2 (C-3), 158.1 (C-5).

Anal. Calcd. for $C_{15}H_{10}N_8O_8S$ (MW 462.36): C, 38.97; H, 2.18; N, 24.23; S, 6.93. Found: C, 38.81; H, 2.23; N, 24.32; S, 6.90.

Fifth, 0.54 g (1.9%) of 5-amino-2-(2,4-dinitrophenyl)-3-methylthio-2*H*-1,2,4-triazole (**9/4**), mp 152-154° (2-propanol); pmr (DMSO-d_6): δ ppm 2.66 (s, 3H, SCH_3), 5.9 (s, 2H, NH_2), 8.07 [d (J = 8.8 Hz), 1H, PhH-6'], 8.65 [dd (J = 8.8 Hz and 2.5 Hz), 1H, PhH-5'], 8.84 [d (J = 2.5 Hz), 1H, PhH-3']; cmr (DMSO-d_6): δ ppm 15.7 (SCH_3), 121.5 (PhC-3'), 128.5 (PhC-5' and 6'), 133.9 (PhC-1'), 143.9 (PhC-4'), 146.4 (PhC-2'), 153.8 (C-3), 164.7 (C-5).

Anal. Calcd. for $C_9H_8N_6O_4S$ (MW 296.27): C, 36.49; H, 2.72; N, 28.37; S, 10.82. Found: C, 36.55; H, 2.75; N, 28.43; S, 10.75.

Sixth, 4.80 g (17%) of 5-amino-1-(2,4-dinitrophenyl)-3-methylthio-1*H*-1,2,4-triazole (**8/4**) was obtained, mp 196-198° (2-propanol); pmr (DMSO-d_6): δ ppm 2.41 (s, 3H, SCH_3), 7.0 (bs, 2H, NH_2), 8.02 [d (J = 8.8 Hz), 1H, PhH-6'], 8.62 [dd (J = 8.8 Hz and 2.5 Hz), 1H, PhH-5']; 8.85 [d (J = 2.5 Hz), 1H, Ph-3']; cmr (DMSO-d_6): δ ppm 13.2 (SCH_3), 121.0 (PhC-3'), 128.4 (PhC-5'), 129.0 (PhC-6'), 134.2 (PhC-1'), 144.0 (PhC-4'), 146.2 (PhC-2'), 156.5 (C-5), 160.8 (C-3); (Assignment checked by INEPT).

Anal. Calcd. for $C_9H_8N_6O_4S$ (MW 296.27): C, 36.49; H, 2.72; N, 28.37; S, 10.82. Found: C, 36.47; H, 2.76; N, 28.32; S, 10.80.

Seventh, 3.54 g (27%) of unreacted 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) was obtained, mp 133-135° (ethanol), lit [9] mp 136-137°.

Arylation of 5-Amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with 3,4-Dimethoxy-6-nitrchlorobenzene (**7/5**) using Sodium Hydride in Dimethylformamide (Method C, run 5/3).

To a solution of 6.60 g (0.05 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9] in 35 ml of dimethylformamide 1.6 g (0.05 mole) of sodium hydride (75% in parraffin oil, Fluka, washed with cyclohexane) was added in small portions with stirring bellow 5°. After stirring for an hour at 0° 10.9 g (0.05 mole) of 3,4-dimethoxy-6-nitrochlorobenzene (**7/5**) [16] were added to the reaction mixture in small portions keeping the temperature below 5°. The reaction mixture was stirred at 70° for 48 hours. After cooling 200 ml of water was added to it, and the crystals that precipitated were filtered off to yield 3.70 g (34%) of unreacted 3,4-dimethoxy-6-nitrochlorobenzene (**7/5**), mp 116-118° (ethanol) lit [16] mp 119°.

The mother liquor was concentrated *in vacuo* to obtain 21 g of a dark solution that after cooling crystallized again. The crystals that precipitated were filtered off to obtain 3.04 g (11%) of disodium (4-methoxy-6-nitro)resorcinate (**26**), mp 340° (ethanol-water); pmr (DMSO-d_6): δ ppm 3.68 (s, 3H, OCH_3), 6.14 (s, 1H, PhH-2), 7.43 (s, 1H, PhH-5); cmr (DMSO-d_6): δ ppm 55.4 (OCH_3), 107.7 (PhC-5), 119.5 (PhC-2), 124.5 (PhC-1), 126.0 (PhC-3), 149.0 (PhC-4), 170.1 (PhC-6).

The mother liquor was evaporated *in vacuo* to dryness and the remaining black oil (17.0 g) was dry-column flash chromatographed to yield in order of appearence:

First, 0.84 g (1.9%) of 3,4-dimethoxy-6-nitrochlorobenzene (**7/5**) was obtained, mp 116-117° (ethanol), lit [16] mp 119°.

Second, 1.43 g (13%) of *N,N*-dimethyl-3,4-dimethoxy-6-nitroaniline (**27**) was obtained, mp 125-127° (2-propanol), lit [17] 130-131°; pmr (DMSO-d_6): δ ppm 2.82 (s, 6H, N-CH_3), 3.76 (s, 3H, 4-OCH_3), 3.90 (s, 3H, 3-OCH_3), 6.64 (s, 1H, PhH-5), 7.44 (s, 1H, PhH-2); cmr (DMSO-d_6): δ ppm 42.7 (N-CH_3), 55.9* (3-OCH_3), 56.0* (4-OCH_3), 101.7 (PhC-2), 109.2 (PhC-5), 130.7 (PhC-6), 141.5 (PhC-4), 143.6 (PhC-1), 154.1 (PhC-3).

Third, 1.91 g (1.2%), of 5-amino-3-methylthio-1-(3,4-dimethoxy-6-nitrophenyl)-1*H*-1,2,4-triazole (**8/5**) was obtained, mp 164-165° (ethanol); pmr (DMSO-d_6): δ ppm 2.40 (s, 3H, SCH_3), 3.79 (s, 3H, 4-OCH_3), 3.93 (s, 3H, 3-OCH_3), 6.9 (b, 2H, NH_2), 7.05 (s, 1H, PhH-5'), 8.38 (s, 1H, PhH-2'); cmr (DMSO-d_6): δ ppm 13.4 (SCH_3), 57.1* (4-OCH_3), 57.4* (3-OCH_3), 109.3 (PhC-2'), 114.7 (PhC-5'), 132.1 (PhC-1'), 144.0 (PhC-6'), 151.2 (PhC-4'), 156.3 (PhC-3'), 156.5 (C-5), 160.1 (C-3).

Anal. Calcd. for $C_{11}H_{13}N_5O_4S$ (MW 311.33): C, 42.44; H, 4.21; N, 22.50; S, 10.30. Found: C, 42.41; H, 4.25; N, 22.63; S, 10.24.

Fourth, 0.05 g (0.3%), of a 3:1 mixture (pmr) of **8/5** and 3-methylthio-2-(3,4-dimethoxy-6-nitrophenyl)-2*H*-1,2,4-tr iazole (**9/5**) was obtained, from which the spectral data of **9/5** could be deduced as: pmr (DMSO-d_6): δ ppm 2.63 (s, 3H, SCH_3), 3.80 (s,

3H, 4-OCH_3), 3.95 (s, 3H, 3-OCH_3), 5.7 (bs, 2H, NH_2), 7.10 (s, 1H, PhH-5'), 8.35 (s, 1H, PhH-2'); cmr (DMSO-d_6): δ ppm 15.6 (SCH_3), 56.7* (4-OCH_3), 56.8* (3-OCH_3), 110.2 (PhC-2'), 115.8 (PhC-5'), 131.7 (PhC-1'), 145.1 (PhC-6'), 145.4 (PhC-4'): 155.9 (PhC-3'), 153.2 (C-3), 163.9 (C-5).

Anal. Calcd. for $C_{11}H_{13}N_5O_4S$ (MW 311.33): C, 42.44; H, 4.21; N, 22.50; S, 10.30. Found: C, 42.48; H, 4.20; N, 22.59; S, 10.35.

Fifth, 9.1 g (70%) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) was obtained, mp 133-135° (ethanol), lit [9] mp 136-137°.

Arylation of 5-Amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with 4-Nitro-1,2,3-trichlorobenzene (**7/6**) using Sodium Hydride in Dimethylformamide (Method C, run 6/3).

To a solution of 13.2 g (0.1 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9] in 70 ml of dimethylformamide 3.2 g (0.1 mole) of sodium hydride (75% in parraffin oil, Fluka, washed with cyclohexane) was added in small portions with stirring below 5°. After stirring for an hour at 0° 27.2 g (0.1 mole) of 4-nitro-1,2,3-trichlorobenzene (**7/6**) [18] were added to the reaction mixture in small portions keeping the temperature below 5°. The reaction mixture was stirred for further 4 hours at 60° and evaporated *in vacuo* to dryness. The remaining black oil (38.3 g) was dry-column flash chromatographed to yield in order of appearence:

First, 8.83 g (39%) of unreacted 4-nitro-1,2,3-trichlorobenzene (**7/6**) was obtained, mp 54-56°, lit [18] mp 55-56°.

Second, 2.41 g (4.7%) of 3-methylthio-1-(2,3-dichloro-6-nitrophenyl)-5-(2,3-dichloro-6-nitrophenylimino)-2*H*-1,2,4-triazole (**11/6**) was obtained, mp 227-229° (acetonitrile); pmr (DMSO-d_6): δ ppm 2.52 (s, 3H, SCH_3), 7.85 [d (J = 9.3 Hz), 1H, PhH-4"], 8.13 [d (J = 9.1 Hz), 1H, PhH-4'], 8.26 [d (J = 9.3 Hz, PhH-5"], 8.30 [d (J = 9.1 Hz, PhH-5'], 9.9 (s, 1H, NH); cmr (DMSO-d_6): δ ppm 13.4 (SCH_3), 121.8 (PhC-2"), 124.0 (Ph-C-5'), 124.5 (PhC-5"), 125.8 (PhC-4"), 128.5 (PhC-2'), 132.8 (PhC-4'), 133.2 (PhC-1'), 136.1 (PhC-1"), 137.0 (PhC-3'), 138.0 (PhC-3"), 142.1 (PhC-6"), 146.7 (PhC-6'), 151.2 (C-3), 160.8 (C-5).

Anal. Calcd. for $C_{15}H_8N_6Cl_4O_4S$ (MW 510.16): C, 35.32; H, 1.58; N, 16.47; Cl, 27.80; S, 6.29. Found: C, 35.39; H, 1.60; N, 16.57; Cl, 27.95; S, 6.27.

Third, 2.90 g (10.1%) of 3-methylthio-1-(2,3-dichloro-6-nitrophenyl)-1*H*-1,2,4-tri azole (**8/6**) was obtained, mp 201-202° (ethanol); pmr (DMSO-d_6): δ ppm 2.40 (s, 3H, SCH_3), 6.8 (b, 2H, NH_2), 8.10 [d (J = 9.0 Hz), 1H, PhH-4'], 8.17 [d (J = 9.0 Hz, PhH-5']; cmr (DMSO-d_6): δ ppm 13.3 (SCH_3), 124.4 (PhC-5'), 129.1 (PhC-2'), 132.0 (PhC-4'), 133.8 (PhC-1'), 137.9 (PhC-3'), 146.4 (PhC-6'), 157.1 (C-3), 160.4 (C-5).

Anal. Calcd. for $C_9H_7N_5Cl_2O_2S$ (MW 320.16): C, 33.77; H, 2.20; N, 21.87; Cl, 22.15; S, 10.01. Found: C, 33.87; H, 2.22; N, 21.99; Cl, 22.10; S, 10.13.

Fourth, 0.65 g (2.1%) of a 1:3 mixture (hplc) of **8/6** and 3-methylthio-2-(2,3-dichloro-6-nitrophenyl)-2*H*-1,2,4-triazole (**9/6**) was obtained, from which the spectral data of **9/6** could be deduced as: pmr (DMSO-d_6): δ ppm 2.63 (s, 3H, SCH_3), 5.7 (b, 2H, NH_2), 8.20 [d (J = 9.0 Hz), 1H, PhH-4'], 8.27 [d (J = 9.0 Hz, PhH-5']; cmr (DMSO-d_6): δ ppm 15.1 (SCH_3), 125.7 (PhC-5'), 129.0 (PhC-2'), 132.3 (PhC-4'), 133.5 (PhC-1'), 138.3 (PhC-3'), 146.2 (PhC-6'), 153.6 (C-3), 164.2 (C-5).

Anal. Calcd. for $C_9H_7N_5Cl_2O_2S$ (MW 320.16): C, 33.77; H, 2.20; N, 21.87; Cl, 22.15; S, 10.01. Found: C, 33.77; H, 2.23; N, 21.82; Cl, 22.20; S, 9.90.

Fifth, 3.31 g (8.0%), of 2-(5-amino-3-methylthio-1*H*-1,2,4-triazol-1-yl)-6-(5-amino-3-methylthio-2*H*-1,2,4-triazol-2-yl)-3-nitrochlorobenzene (**28**), mp 212-214° (ethanol); pmr (DMSO-d_6): δ ppm, 2.41 (s, 3H, SCH_3-2'), 2.61 (s, 3H, SCH_3-6'), 5.8 (bs, 2H, NH_2-6'), 6.9 (bs, 2H, NH_2-2'), 8.02 [d (J = 8.8 Hz), 1H, PhH-4], 8.29 [d (J = 8.8 Hz, PhH-5]; irradiated at 8.02 and 8.29 ppm NOE at 2.61 ppm; cmr (DMSO-d_6): δ ppm 13.4 (SCH_3-2'), 15.6 (SCH_3-6'), 124.6 (PhC-4), 129.3 (PhC-5), 131.5 (PhC-6), 133.6 (PhC-2), 139.4 (PhC-1), 147.8 (PhC-3), 153.5 [PhC-3(6')], 157.3 [PhC-5(2')], 160.4 [PhC-3(2')], 164.5 [PhC-5(6')].

Anal. Calcd. for $C_{12}H_{12}N_9ClO_2S_2$ (MW 413.87): C, 34.83; H, 2.92; N, 30.46; Cl, 8.57; S, 15.49. Found: C, 34.93; H, 2.94; N, 30.59; Cl, 8.73; S, 15.53.

Sixth, 2.89 g (22%) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) was obtained, mp 133-135° (ethanol), lit [9] mp 136-137°.

Arylation of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with 2,3-Dichloro-6-nitrobenzonitrile (**7/7**) using Sodium Hydride in Dimethylformamide (Method C, run 7/3).

To a solution of 13.2 g (0.1 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9] in 70 ml of dimethylformamide 3.2 g (0.1 mole) of sodium hydride (75% in parraffin oil, Fluka, washed with cyclohexane) was added in small portions with stirring below 5°. After stirring for an hour at 0° 21.7 g (0.1 mole) of 2.3-dichloro-6-nitrobenzonitrile (**7/7**) [19] were added to the reaction mixture in small portions keeping the temperature below 5°. The mixture was stirred for 4 hours at 60°. After cooling 300 ml of water was added to the reaction mixture and the crystals that precipitated were filtered off to yield 5.17 g (17%) of 9-chloro-2-methylthio-6-nitro[1,2,4]triazolo[5,1-*b*]quinazolin-5(3*H*)-one (**32**), mp >315° (dimethylformamide); ir: ν C=O = 1711 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.62 (s, 3H, SCH_3), 7.81 [d (J = 8.7 Hz), 1H, PhH-8], 8.18 [d (J = 8.7 Hz), 1H, PhH-7] 12.5 (bs, 1H, NH); cmr (DMSO-d_6): δ ppm 13.6 (SCH_3), 110.9 (C-5a), 122.7 (C-7), 133.9 (C-8), 138.6 (C-9), 148.7 (C-6), 150.2 (C-2), 156.5 (C-5), 162.0 (C-9a), 165.4 (C-10a); ms: (CI) $(M+1)^+$ = 312.

Anal. Calcd. for $C_{10}H_6N_5ClO_3S$ (MW 311.71): C, 38.53; H, 1.94; N, 22.47; Cl, 11.37; S, 10.29. Found: C, 38.57; H, 1.98; N, 22.53; Cl, 11.30; S, 10.23.

The mother liquor was evaporated *in vacuo* to dryness and the remaining black oil was dry-column flash chromatographed to yield in order of appearence:

First, 1.53 g (7.1%) of unreacted 2,3-dichloro-6-nitrobenzonitrile (**7/7**)was obtained, mp 89-90°, lit [19] mp 90-93°.

Second, 2.42 g (4.7%) of 5-amino-2-(2-chloro-3-cyano-4-nitrophenyl)-3-methylthio-2*H*-1,2,4-triazole (**9/7**) was obtained, mp 206-207° (ethyl acetate); pmr (DMSO-d_6): δ ppm 2.66 (s, 3H, SCH_3), 5.6 (bs, 2H, NH_2), 7.89 [d (J = 8.3 Hz), 1H, PhH-6'], 8.25 [d (J = 8.3 Hz), 1H, PhH-5']; cmr (DMSO-d_6): δ ppm 15.3 (SCH_3), 109.3 (PhC-3'), 112.2 (CN), 125.1 (PhC-5'), 136.0 (PhC-6'), 137.9 (PhC-2'), 138.7 (PhC-1'), 150.4 (PhC-4'), 152.7 (C-3), 164.2 (C-5).

Anal. Calcd. for $C_{10}H_7N_6ClO_2S$ (MW 310.73): C, 38.66; H, 2.27; N, 27.05; Cl, 11.41; S, 10.32. Found: C, 38.63; H, 2.30; N, 27.14; Cl, 11.42; S, 10.39.

Third, 0.96 g (3.1%) of 3-methylthio-1-(2-chloro-3-cyano-4-nitrophenyl)-5-amino-1*H*-1,2,4-triazole (**8/7**), mp 238-240° (ethyl acetate); pmr (DMSO-d_6): δ ppm 2.45 (s, 3H, SCH_3), 6.8 (b, 2H, NH_2), 8.16 [d (J = 8.8 Hz), 1H, PhH-6'], 8.46 [d (J = 8.8 Hz), 1H, PhH-5'], irradiated at 6.8 ppm NOE enhancement at

8.16 ppm; cmr (DMSO-d_6): δ ppm 13.3 (SCH_3), 110.1 (PhC-3'), 112.6 (CN), 125.6 (PhC-5'), 135.2 (PhC-6'), 137.6 (PhC-2'), 140.0 (PhC-1'), 149.7 (PhC-4'), 156.9 (C-5), 160.5 (C-3).

Anal. Calcd. for $C_{10}H_7N_6ClO_2S$ (MW 310.73): C, 38.66; H, 2.27; N, 27.05; Cl, 11.41; S, 10.32. Found: C, 38.68; H, 2.31; N, 27.13; Cl, 11.46; S, 10.35.

Fourth, 0.15 g (0.3%) of 3-methylthio-1-(2-chloro-3-cyano-4-nitrophenyl)-5-(2-chloro-3-cyano-4-nitrophenylimino)-2*H*-1,2,4-triazole (**11/7**) was obtained, mp 173-175° (2-propanol); ir: ν CN = 2246 and 2252 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.57 (s, 3H, SCH_3), 8.27 [d (J = 8.8 Hz), 1H, PhH-6'], 8.34 [d (J = 7.9 Hz), 1H, PhH-6"], 8.38 [d (J = 7.9 Hz), 1H, PhH-5"], 8.54 [d (J = 8.8 Hz), 1H, PhH-5'], 9.8 (b, 1H, NH); cmr (DMSO-d_6): δ ppm 13.5 (SCH_3), 109.5 (PhC-3'), 110.2 (PhC-3"), 112.5 (CN-3'), 113.2 (CN-3"), 125.5 (PhC-5'), 126.0 (PhC-5"), 134.6 (PhC-2"), 135.4 (PhC-6'), 137.0 (PhC-6"), 137.5 (PhC-2'), 139.4 (PhC-1'), 139.5 (PhC-4"), 143.4 (PhC-1"), 149.9 (PhC-4'), 151.6 (C-3), 161.0 (C-5).

Anal. Calcd. for $C_{17}H_8N_8Cl_2O_4S$ (MW 491.28): C, 41.56; H, 1.64; N, 22.81; Cl, 14.43; S, 6.53. Found: C, 41.51; H, 1.68; N, 22.98; Cl, 14.45; S, 6.54.

Fifth, 1.27 g (4.2%) 5-amino-6,7-dichloro-2-methylthio-[1,2,4]triazolo[1,5-*a*]quinazoline (**36**), mp 300-303° (dimethylformamide); ir: ν NH_2 = 3494 and 3291 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.62 (s, 3H, SCH_3), 8.07 [d (J = 9.0 Hz), 1H, H-9], 8.1 (b, 2H, NH_2), 8.14 [d (J = 9.0 Hz), 1H, H-8]; cmr (deuteriochloroform + a few drops of trifluoroacetic acid): δ ppm 13.1 (SCH_3), 110.1 (C-5a), 116.0 (C-9a), 131.0 (C-8), 135.1 (C-9), 135.6 (C-7), 138.0 (C-6), 147.0 (C-3a), 160.0 (C-2), 161.6 (C-5); ms (CI): $(M+1)^+$ = 300; ms: (EI) M^+ = 299.

Anal. Calcd. for $C_{10}H_7N_5Cl_2S$ (MW 300.17491.28): C, 40.02; H, 2.35; N, 23.33; Cl, 23.62; S, 10.68. Found: C, 40.11; H, 2.38; N, 23.40; Cl, 23.55; S, 10.64.

Sixth, 2.60 g (20%) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**), mp 133-135° (ethanol), lit [9] mp 136-137°.

Arylation of 5-Amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with 2,6-Dinitro-chlorobenzene (**7/8**) using Triethylamine in Dimethylformamide (Method B_3, run 8/2).

A solution of 6.65 g (0.05 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9], 13.6 g (0.05 mole) of 2,6-dinitrochlorobenzene (**7/8**) [20] and 7.0 g (0.07 mole) of triethylamine in 40 ml of dimethylformamide was stirred at 80° for 24 hours. After cooling 30 ml of water was added to the reaction mixture, and the crystals that precipitated were filtered off to yield 2.74 g (12%) of 3-methylthio-1-(2,6-dinitrophenyl)-5-(2,6-dinitrophenylimino)-2*H*-1,2,4-triazole (**11/8**), mp 250-251° (acetonitrile); pmr (DMSO-d_6): δ ppm 2.37 (s, 3H, SCH_3), 7.67 [t (J = 8.1 Hz), 1H, PhH-4'], 8.15 [t (J = 8.3 Hz), 1H, PhH-4"], 8.28 [d (J = 8.1 Hz), 2H, PhH-3' and 5'], 8.64 [d (J = 8.3 Hz), 2H, PhH-3" and 5"], 10.0 (b, 1H, NH); cmr (DMSO-d_6): δ ppm 13.3 (SCH_3), 122.5 (PhC-4"), 125.7 (PhC-4'), 127.5 (PhC-1'), 129.9 (PhC-3' and PhC-5'), 130.5 (PhC-3" and 5"), 133.7 (PhC-1"), 146.1 (PhC-2" and 6"), 147.3 (PhC-2' and 6'), 153.2 (C-3), 160.8 (C-5).

Anal. Calcd. for $C_{15}H_{10}N_8O_8S$ (MW 462.36): C, 38.97; H, 2.18; N, 24.23; S, 6.93. Found: C, 39.03; H, 2.21; N, 24.02; S, 6.88.

The mother liquor was kept at 0° for 24 hours and the crystals that precipitated again were filtered off to yield 0.84 g (5.7%) of 5-amino-1-(2,6-dinitrophenyl)-3-methylthio-1*H*-1,2,4-triazole (**8/8**), mp 199-200 ° (acetonitrile); pmr (DMSO-d_6): δ ppm 2.41 (s, 3H, SCH_3), 6.8 (b, 2H, NH_2), 7.38 [t (J = 8.0 Hz), 1H, PhH-4'], 8.29 [d (J = 8.0 Hz), 2H, PhH-3' and PhH-5']; cmr (DMSO-d_6): δ ppm 13.6 (SCH_3), 122.2 (PhC-4'), 130.1 (PhC-1'), 130.9 (PhC-3' and 5'), 142.9 (PhC-2' and 6'), 157.9 (C-5), 162.7 (C-3).

Anal. Calcd. for $C_9H_8N_6O_4S$ (MW 296.27): C, 36.49; H, 2.72; N, 28.37; S, 10.82. Found: C, 36.45; H, 2.75; N, 28.47; S, 10.80.

The mother liquor was evaporated *in vacuo* to dryness, 30 ml of benzene was added to it and the crystals that precipated were filtered off to yield 1.90 g (19%) of unreacted 2,6-dinitrochlorobenzene (**7/8**), mp 80-82°, lit [20] mp 81-83°.

The mother liquor was evaporated *in vacuo* to dryness, 30 ml of 2-propanol was added to it and the crystals that precipitated were filtered off to yield 1.09 g (17%) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**), mp 136-137°, lit [9] 136-137°.

The mother liquor was again evaporated *in vacuo* to dryness and the remaining black oil was dry-column flash chromatographed to yield in order of appearence:

First, 0.14 g (0.6%) of 3-methylthio-1-(2,6-dinitrophenyl)-5-(2,6-dinitrophenylimino)-2*H*-1,2,4-triazole (**11/8**) was obtained, mp 250-251° (acetonitrile), that was identical (ir, mixed mp) with that of **11/8** obtained above.

Second, 0.98 g (9.7%) of 2,6-dinitrochlorobenzene (**7/8**)was obtained, mp 81-82°, lit [20] mp 81-83°.

Third, 0.31 g (2.1%) of 5-(2,6-dinitrophenylamino)-3-methylthio-1*H*-1,2,4-triazole (**10/8**) was obtained, mp 241-243° (2-propanol); pmr (DMSO-d_6): δ ppm 2.48 (s, 3H, SCH_3), 7.38 [t (J = 8.1 Hz), 1H, PhH-4'], 8.28 [d (J = 8.1 Hz), 2H, PhH-3' and 5'], 9.7 (b, 1H, exo-NH), 14.5 (bs, 1H, 1-NH); cmr (DMSO-d_6): δ ppm 13.4 (SCH_3), 130.0 (PhC-4'), 130.7 (PhC-1'), 130.9 (PhC-3' and 5'), 143.5 (PhC-2' and 6'), 157.1 (C-5), 159.0 (C-3).

Anal. Calcd. for $C_9H_8N_6O_4S$ (MW 296.27): C, 36.49; H, 2.72; N, 28.37; S, 10.82. Found: C, 36.45; H, 2.71; N, 28.43; S, 10.92.

Fourth, 0.18 g (0.6%) of a 3:1 mixture of **8/8** and **9/8** was obtained, that after many recrystallisations from 2-propanol afforded pure 5-amino-2-(2,6-dinitrophenyl)-3-methylthio-2*H*-1,2,4-triazole (**9/8**), mp 171-173 ° (2-propanol); pmr (DMSO-d_6): δ ppm 2.62 (s, 3H, SCH_3), 6.0 (b, 2H, NH_2), 7.63 [t (J = 8.1 Hz), 1H, PhH-4'], 8.31 [d (J = 8.1 Hz), 2H, PhH-3' and 5'].

Fifth, 0.25 g (1.7%) of 5-amino-1-(2,6-dinitrophenyl)-3-methylthio-1*H*-1,2,4-triazole (**8/8**), mp 198-199° (acetonitrile), that was identical (ir, mixed mp) with that of **8/8** obtained above.

Sixth, 0.35 g (5.4%) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) was obtained, mp 134-135° (ethanol), lit [9] mp 136-137°.

Arylation of 5-Amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with 2,6-Dinitro-4-trifluoromethylchlorobenzene (**7/9**) using Sodium Hydride in Dimethylformamide (Method C, run 9/3).

To a solution of 13.2 g (0.1 mole) of 5-amino-3-methyl-thio-1*H*-1,2,4-triazole (**1**) [9] in 70 ml of dimethylformamide 3.2 g (0.1 mole) of sodium hydride (75% in parraffin oil, Fluka, washed with cyclohexane) was added in small portions with stirring below 5°. After stirring for an hour at 0° 27.2 g (0.1 mole) of 2,6-dinitro-4-trifluoromethylchlorobenzene (**7/9**) [21] was added to the reaction mixture in small portions keeping the temperature below 5°. The mixture was stirred for futher 10 minutes and was evaporated *in vacuo* to dryness. The remaining black oil (51.0 g) was dry-column flash chromatographed to yield in order

of appearence:

First, 0.064 g (0.1%) of 3-methylthio-2-(2,6-dinitro-4-trifluoromethylphenyl)-5-(2,6-dinitro-4-trifluoromethylphenylimino)-1*H*-1,2,4-triazole (**12/9**) was obtained, mp 196-197° (acetonitrile); pmr (DMSO-d_6): δ ppm 2.61 (s, 3H, SCH_3), 8.67 (s, 2H, PhH-3' and 5'), 9.07 (s, 2H, PhH-3" and 5"], 10.6 (b, 1H, NH); cmr (DMSO-d_6): δ ppm 15.5 (SCH_3), 122.5 [q (J = 274 Hz), CF_3'], 124.5 [qa (J = 35.5 Hz), PhC-4"], 122.8 [qa (J = 273.5 Hz), CF3"], 127.6 [qa (J = 3.4 Hz), PhC-3" and 5"], 128.2 [qa (J = 3.5 Hz), PhC-3' and 5'], 131.6 (PhC-1'), 132.5 (Ph-C-1"), 134.5 [qa (J = 35.7 Hz), PhC-4'], 142.2 (PhC-2" and 6"), 147.1 (PhC-2' and 6'), 157.0 (C-3), 159.9 (C-5).

Anal. Calcd. for $C_{17}H_8N_8F_6O_8S$ (MW 598.36): C, 34.13; H, 1.35; N, 18.73; F, 19.05; S, 5.36. Found: C, 34.10; H, 1.39; N, 18.90; F, 19.01; S, 5.39.

Second, 1.38 g (5.1%), of unreacted 2,6-dinitro-4-trifluormethylchlorobenzene (**7/9**) was obtained, as an oily product identified by hplc.

Third, 9.21 g (25%) of 5-(2,6-dinitro-4-trifluoromethylphenylamino)-3-methylthio-1*H*-1,2,4-triazole (**10/9**) was obtained, mp 256-258° (ethanol); pmr (DMSO-d_6): δ ppm, 2.52 (s, 3H, SCH_3), 8.61 (s, 2H, PhH-3' and 5'], 10.2 (s, 1H, exo-NH), 13.6 (s, 1H, 1-NH); cmr (DMSO-d_6): δ ppm 14.0 (SCH_3), 122.7 [q (J = 273 Hz), CF_3], 128.1 (qa (J = 3.2 Hz), PhC-3' and 5'], 128.3 (PhC-1'), 133.5 [q (J = 35.0 Hz), PhC-4'], 141.9 (PhC-2' and 6'), 157.1 (C-5), 158.9 (C-3); ms (EI): $M^+ = 364$.

Anal. Calcd. for $C_{10}H_7N_6F_3O_4S$ (MW 364.27): C, 32.97; H, 1.94; N, 23.07; F, 15.65; S, 8.80. Found: C, 33.01; H, 2.00; N, 23.03; F, 15.70; S, 8.74.

Fourth, 16.5 g (45%) of 5-amino-1-(2,6-dinitro-4-trifluoromethylphenyl)-3-methylthio-1*H*-1,2,4-triazole (**8/9**) was obtained, mp 159-160° (benzene); pmr (DMSO-d_6): δ ppm 2.39 (s, 3H, SCH_3), 7.0 (s, 2H, NH_2), 8.95 (s, 2H, PhH-3' and 5']; cmr (DMSO-d_6): δ ppm 13.2 (SCH_3), 122.8 [qa (J = 274 Hz), CF_3], 126.8 (PhC-1'), 127.2 [qa (J = 3.5 Hz), PhC-3' and 5'], 131.1 [q (J = 35.3 Hz), PhC-4'], 147.2 (PhC-2' and 6'), 157.8 (C-5), 162.1 (C-3).

Anal. Calcd. for $C_{10}H_7N_6F_3O_4S$ (MW 364.27): C, 32.97; H, 1.94; N, 23.07; F, 15.65; S, 8.80. Found: C, 32.95; H, 1.98; N, 23.16; F, 15.70; S, 8.83.

Fifth, 0.36 g (1.0%) of a 2:3 mixture of **8/9** and **9/9** was obtained, that after many recrystallisations from benzene afforded pure of 5-amino-2-(2,6-dinitro-4-trifluoromethylphenyl)-3-methylthio-2*H*-1,2,4-triazole (**9/9**), mp 135-136° (benzene); pmr (DMSO-d_6): δ ppm 2.62 (s, 3H, SCH_3), 6.0 (b, 2H, NH_2), 8.63 (s, 2H, PhH-3' and 5']; ms: (CI) $(M+1)^+ = 365$.

Sixth, 0.36 g (2.8%) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) was obtained, mp 136-137°, lit [9] 136-137°.

Arylation of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with 2,6-Dinitro-4-trifluoromethylchlorobenzene (**7/9**) in Ethanol (Method A_2, run 9/1).

A suspension of 13.2 g (0.1 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9] and 27.2 g (0.1 mole) of 2,6-dinitro-4-trifluoromethylchlorobenzene (**7/9**) [21] in 120 ml of ethanol was refluxed for 12 hours. After cooling the crystals that precipitated were filtered off to yield 11.51 g (32%) of 5-(2,6-dinitro-4-trifluoromethylphenylimino)-3-methylthio-1*H*-1,2,4-triazole (**10/9**), mp 256-258° (benzene). The product is identical (ir, mixed mp) with that of **10/9** obtained by Method C.

The mother liquor was evaporated *in vacuo* to dryness and the remaining black oil (49.0 g) was dry-column flash chromatographed to yield in order of appearence:

First, 1.32 g (2.2%) of 3-methylthio-1-(2,6-dinitro-4-trifluoromethylphenyl)-5-(2,6-dinitro-4-trifluoromethylphenylimino)-2*H*-1,2,4-triazole (**11/9**) was obtained, mp 218-219° (acetonitrile); pmr (DMSO-d_6): δ ppm 2.38 (s, 3H, SCH_3), 8.81 (s, 2H, Ph-3' and Ph-5'), 8.21 (s, 2H, Ph-3" and Ph-5"], 10.3 (b, 1H, NH); cmr (DMSO-d_6): δ ppm 13.3 (SCH_3), 122.5 [q (J = 274 Hz), CF_3'], 122.8 [qa (J = 273 Hz), CF_3"], 123.3 [qa (J = 35.0 Hz), PhC-4"], 126.9 (PhC-1'), 127.0 [qa (J = 3.5 Hz), PhC-3' and 5'], 128.4 [qa (J = 3.4 Hz), PhC-3" and 5"], 131.1 [qa (J = 35.3 Hz), PhC-4'), 131.8 (PhC-1"), 144.2 (PhC-2" and 6"), 150.6 (PhC-2' and 6'), 151.6 (C-3), 160.6 (C-5).

Anal. Calcd. for $C_{17}H_8N_8F_6O_8S$ (MW 598.36): C, 34.13; H, 1.35; N, 18.73; F, 19.05; S, 5.36. Found: C, 34.20; H, 1.33; N, 18.78; F, 19.10; S, 5.37.

Second, 4.7 g (17%) of unreacted 2,6-dinitro-4-trifluoromethylchlorobenzene (**7/9**) was obtained as an oily product which was identical (ir, hplc) with **7/9**.

Third, 3.9 g (11%) of 5-amino-1-(2,6-dinitro-4-trifluoromethylphenyl)-3-methylthio-1*H*-1,2,4-triazole (**8/9**) was obtained, mp 159-160° (benzene). The product is identical (ir, mixed mp) with that of **8/9** obtained by Method C.

Fourth, 1.2 g (9.3%) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) was obtained, mp 135-136° (ethanol), lit [9] mp 136-137°.

Arylation of 5-Amino-3-methylthio-1*H*-1,2,4-triazole (**1**) with 2,4,6-Trinitrochlorobenzene (**7/10**) using Sodium Hydride in Dimethylformamide (Method C, run 10/3).

To a solution of 2.6 g (0.02 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) [9] in 20 ml of dimethylformamide 0.6 g (0.02 mole) of sodium hydride (75% in parraffin oil, Fluka, washed with cyclohexane) was added in small portions with stirring below 5°. After stirring for an hour at 0° 5.0 g (0.02 mole) of 2,4,6-trinitrochlorobenzene (**7/10** prepared by the known method [22]) was added to the reaction mixture in small portions keeping the temperature below 5°. The mixture was stirred for futher 10 minutes and evaporated *in vacuo* to dryness. The remaining black oil (9.0 g) was dry-column flash chromatographed to yield in order of appearence:

First, 0.32 g (6.9%) of 2,4,6-trinitrophenole (**38**) was obtained, mp 121-123° (2-propanol), lit [23] mp 122-122.5°.

Second, 1.7 g (25%) of 3-methylthio-5-(2,4,6-trinitrophenylamino)-1*H*-1,2,4-triazole (**10/10**) was obtained, mp 257-258° (benzene); pmr (DMSO-d_6): δ ppm 2.45 (s, 3H, SCH_3), 8.5 (b, 1H, exo-NH), 9.14 (s, 2H, PhH-3' and 5'], 12.1 (b, 1H, NH); cmr (DMSO-d_6): δ ppm, 13.2 (SCH_3), 124.4 (PhC-3' and 5'), 127.1 (PhC-1'), 144.8 (PhC-2' and 6'), 145.8 (PhC-4'), 158.7 (C-5), 160.3 (C-3).

Anal. Calcd. for $C_9H_7N_7O_6S$ (MW 341.27): C, 31.68; H, 2.07; N, 28.73; S, 9.40. Found: C, 31.71; H, 2.13; N, 28.75; S, 9.44.

Third, 3.05 g (45%) of 5-amino-3-methylthio-1-(2,4,6-trinitrophenyl)-1*H*-1,2,4-triazole (**8/10**) was obtained, mp 189-191° (benzene); pmr (DMSO-d_6): δ ppm 2.40 (s, 3H, SCH_3), 7.2 (b, 2H, NH_2), 9.24 (s, 2H, PhH-3' and 5']; cmr (DMSO-d_6): δ ppm, 13.2 (SCH_3), 128.1 (PhC-1'), 128.6 (PhC-3' and 5'), 146.7 (PhC-2' and 6'), 147.0 (PhC-4'), 157.7 (C-5), 162.5 (C-3).

Anal. Calcd. for $C_9H_7N_7O_6S$ (MW 341.27): C, 31.68; H, 2.07; N, 28.73; S, 9.40. Found: C, 31.62; H, 2.02; N, 28.70; S,

9.33.

Fourth, 0.07 g (2.8%) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**) was obtained, mp 134-135° (2-propanol), lit [9] mp 136-137°.

Acknowledgement.

The authors wish to express their thanks to Mrs. Sándorné Sólyom for recording the ir spectra, to Mr. Attila Fürjes for recording the nmr spectra, to Dr. István Kövesdi for helpful nmr discussions, to Dr. Éva Szabó and Dr. Péter Slégel for recording the ms spectra, to Mrs. Hirkóné Magdolna Csík for performing the elementar analyses and to Miss Mónika Páljános, Mr. Ádám Sárosi and Mr. Tibor Merczel for technical assistance.

REFERENCES AND NOTES

[1] For part XXXV see: J. Reiter, L. Pongó, I. Kövesdi and I. Pallagi, *J. Heterocyclic Chem.*, (in press).

[2] J. Reiter, T. Somorai, P. Dvortsák and Gy. Bujtás, *J. Heterocyclic Chem.*, **22**, 385 (1985).

[3] P. Dvortsák, J. Reiter, T. Somorai and P. Sohár, *Magn. Res. Chem.*, **23**, 194 (1985).

[4] J. Reiter, L. Pongó, T. Somorai and P. Dvortsák, *J. Heterocyclic Chem.*, **23**, 401 (1986).

[5] P. Sohár, G. Fehér and L. Toldy, *Org. Magn Reson.*, **11**, 9 (1978).

[6] J. Reiter and G. Berecz, *J. Heterocyclic Chem.*, **28**, 721 (1991).

[7] J. Reiter, P. Vágó, K. Esses-Reiter, L. Pongó, and H. Molnár, *J. Heterocyclic Chem.*, **25**, 1751 (1988).

[8] L. M. Harwood, *Aldrichimica Acta*, **18**, 25 (1985).

[9] F. Arndt and C. Milde, *Ber.*, **54**, 2089 (1921).

[10] F. K. Beilstein, P. Kurbalow, *Liebigs Ann. Chem.*, **182**, 107 (1876).

[11] J. Reiter, T. Somorai, Gy. Jerkovich and P. Dvortsák, *J. Heterocyclic Chem.*, **19**, 1157 (1982).

[12] H. Körner, *Gazz Chim. Ital.*, **4**, 373 (1874).

[13] R. H. Cox, *J. Mol. Spectrosc.*, **31**, 172-175 (1970).

[14] F. Ullmann, G. Nadai, *Ber.*, **41**, 1873 (1908).

[15] J. van Romburgh, *Rec. Trav. Chim. Pays-Bas*, **2**, 40 (1883).

[16] J. Slooff, *Rec. Trav. Chim. Pays-Bas*, **54**, 995-1005 (1935).

[17] A. H. Parijs, *Thesis, Lieden*, 194, (1928).

[18] F. K. Beilstein, P. Kurbalow, *Liebigs Ann. Chem.*, **192**, 235 (1878).

[19] GB Patent No. 951.770; *Chem. Abstr.*, **63**, P 6923g (1965).

[20] W. Borsche, A. Rantscheff, *Liebigs Ann. Chem.*, **379**, 158 (1910).

[21] US Patent No. 3,111,403; *Chem. Abstr.*, **60**; P 13184d (1964).

[22] L. Bodewing, *Jahresbreicht Forschritte Chem.*, 394 (1879).

[23] H. Körner, *Jahresbreicht Forschritte Chem.*, 616 (1876).