

Synthesis and Pesticidal Activities of Sulphides and Sulphones Derived from bis[4-Aryl-1,2,4-triazoline-5-thione-3-yl]alkane and 5-Phenyl-1,3,4-oxadiazole-2-thione

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The bis[4-aryl-3-alkylthio-1,2,4-triazol-5-yl]alkanes **4** were prepared by the action of alkyl halides on bis[4-aryl-1,2,4-triazoline-5-thione-3-yl]alkanes in aqueous sodium hydroxide (5%). The prepared sulphides **4** were oxidised to give the corresponding sulphones **5** either with acidic potassium permanganate or hydrogen peroxide. Similarly, sulphides **8** were prepared from 5-phenyl-1,3,4-oxadiazole-2-thione by reaction with different alkylhalides in alkaline medium. Mannich bases **9** from 5-phenyl-1,3,4-oxadiazole-2-thione (**7**) were also prepared by stirring an equimolar solution of **6** in ethanol with formaldehyde (38%) and an amine in an ice-cold bath. All the compounds were screened for their pesticidal activities but none showed any significant activity.

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The therapeutic importance of alkyl, aryl and acylthio-1,2,4-triazoles is well documented. Several of the *s*-substituted thiotriazoles have shown biological activity against tuberculosis [2,3], as anticoccidial agents in chicken [4] and in cephalosporins as antibacterial agents [5].

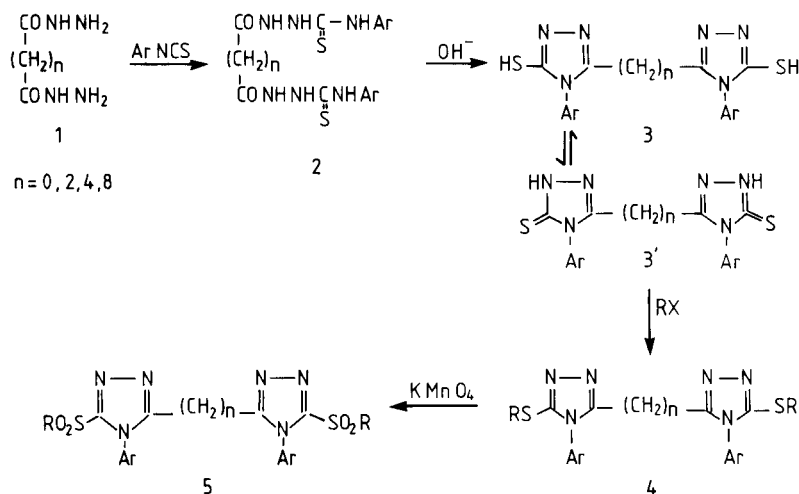
A 3-(2,4-dichlorophenoxyethyl)-5-ethylthio-1,2,4-triazole is reported by us to have good fungicidal activity against *Aspergillus niger* [6]. Recently carbamoylthiazole derivatives are reported to have significant herbicidal properties against broad-leaved weeds [7]. In order to establish a structure activity relationship we extended our previous studies [8-11] in the field of bistriazoles.

The key intermediates, bis(4-arylthiosemicarbazido)-

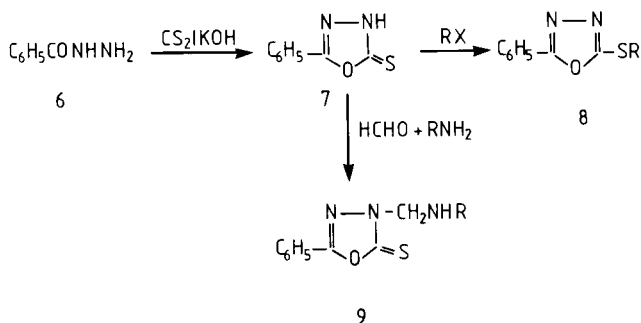
alkanes **2**, were prepared by the reaction of arylisothiocyanate with different bishydrazides **1**. The base catalysed cyclization of **2** with 5% aqueous sodium hydroxide yielded bis(4-aryl-1,2,4-triazoline-3-thione-5-yl)alkanes **3**, which were transformed into bis(4-aryl-3-alkyl/arylthio-1,2,4-triazol-5-yl)alkanes **4** by reaction with alkyl halide. Bis(4-aryl-3-alkylthio-1,2,4-triazol-5-yl)alkanes were oxidized into their corresponding sulphones either with hydrogen peroxide or acidic potassium permanganate.

5-Phenyl-1,3,4-oxadiazole-2-thione **7** was prepared from phenylhydrazide by following the procedure reported earlier [12-14] and was transformed into 2-arylthio-5-phenyl-1,3,4-oxadiazole-2-thione (**8**) by reaction with dif-

SCHEME 1



SCHEME 2



ferent alkyl halides in alkaline medium. The Mannich bases **9** were prepared by stirring an equimolar solution of **7** in ethanol, formaldehyde and amine under ice cooling.

The structures of the compounds were confirmed by spectroscopic studies and elemental analyses. The ir spec-

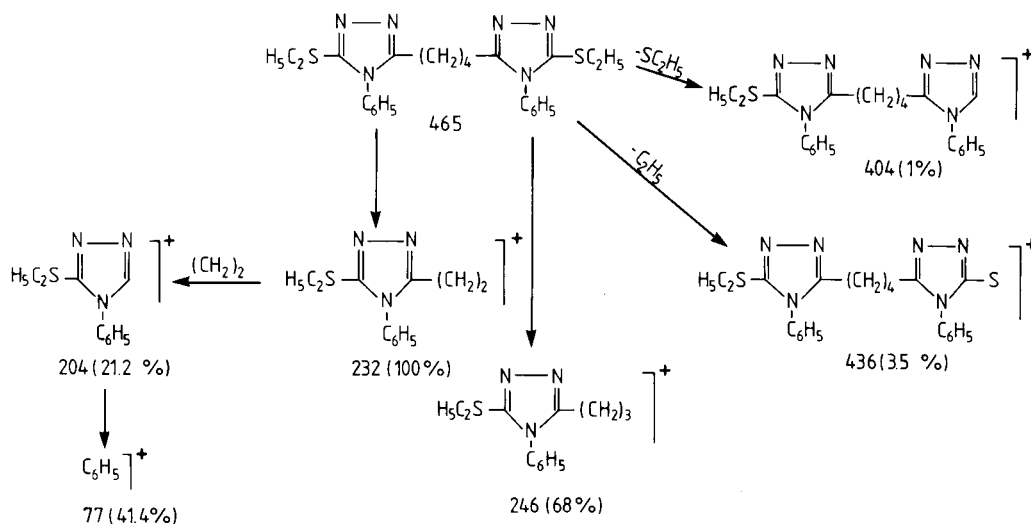
trum of **3** showed bands in the regions $1200\text{--}1130\text{ cm}^{-1}$ and $3100\text{--}3050\text{ cm}^{-1}$ due to CS and NH stretching vibrations respectively. Absence of peaks in the region $2600\text{--}2550\text{ cm}^{-1}$ established the existence of the thione form in the solid state. The sharp peaks at $1200\text{--}1100\text{ cm}^{-1}$, characteristic of a 1,2,4-triazole ring were observed in the spectrum. The ir spectrum of 1,4-bis[3-(2,4-dinitrophenylmercapto)-4-phenyl-1,2,4-triazol-5-yl]butane showed peaks at 1520 cm^{-1} and 1340 cm^{-1} , which were assigned to sym. and asym. stretching vibrations due to NO_2 groups. The mass spectrum of this compound was in agreement with the proposed structure and the fragmentation pattern was as depicted below.

5-Phenyl-1,3,4-oxadiazole-2-thione (**7**) was synthesized by the procedure reported earlier [10-12]. 5-Phenyl-2-arylthio-1,3,4-oxadiazole was prepared by action of aralkyl halide on **7** in DMF using potassium carbonate as base. The ir spectrum of 2-(*p*-nitrobenzylmercapto)-5-

Table 1

Bis[4-aryl-3-alkylthio-1,2,4-triazol-5-yl]alkanes 4

Compound No.	Ar	R	MP °C	Molecular Formula	M*	Elemental Analysis (%)					
						Calcd.			Found		
						C	H	N	C	H	N
n = 0											
4a	$\text{C}_6\text{H}_5\text{-}$	$\text{CH}_2 = \text{CH-CH}_2\text{-}$	115	$\text{C}_{22}\text{H}_{20}\text{N}_6\text{S}_2$	432	61.10	4.66	19.43	61.24	4.48	19.27
4b	$\text{C}_6\text{H}_5\text{-}$	$n\text{-C}_4\text{H}_9\text{-}$	142	$\text{C}_{24}\text{H}_{28}\text{N}_6\text{S}_2$	464	62.05	6.07	18.09	62.33	6.40	18.21
4c	$\text{C}_6\text{H}_5\text{-}$	$p\text{-BrC}_6\text{H}_4\text{CH}_2\text{-}$	154	$\text{C}_{30}\text{H}_{22}\text{N}_6\text{Br}_2\text{S}_2$	690	52.19	3.21	12.17	52.31	3.27	12.36
4d	$\text{C}_6\text{H}_5\text{-}$	$o,p\text{-(NO}_2)_2\text{C}_6\text{H}_3\text{-}$	305	$\text{C}_{28}\text{H}_{16}\text{N}_{10}\text{O}_8\text{S}_2$	684	49.13	2.36	20.46	49.27	2.28	20.23
$(\text{CH}_2)_n = \text{-CH-(n-C}_4\text{H}_9)$											
4e	$\text{C}_6\text{H}_5\text{-}$	H-	270	$\text{C}_{21}\text{H}_{22}\text{N}_6\text{S}_2$	422	59.70	5.24	19.89	59.61	5.29	19.63
4f	$\text{C}_6\text{H}_5\text{-}$	$\text{C}_6\text{H}_5\text{CH}_2\text{-}$	120	$\text{C}_{35}\text{H}_{34}\text{N}_6\text{S}_2$	602	69.70	5.68	13.95	69.97	5.77	13.65
n = 2											
4g	$p\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$p\text{-BrC}_6\text{H}_4\text{CH}_2\text{-}$	180	$\text{C}_{34}\text{H}_{30}\text{N}_6\text{Br}_2\text{S}_2$	746	54.70	4.06	11.27	54.35	4.05	11.35
4h	$p\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$o,p\text{-(NO}_2)_2\text{C}_6\text{H}_3\text{-}$	> 300	$\text{C}_{32}\text{H}_{24}\text{N}_{10}\text{O}_8\text{S}_2$	740	51.89	3.26	18.93	51.66	3.38	19.21
4i	$p\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$\text{HOOC-CH}_2\text{-}$	280 dec	$\text{C}_{24}\text{H}_{24}\text{N}_6\text{O}_4\text{S}_2$	524	54.96	4.62	16.03	54.76	4.43	16.23
4j	$o\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$\text{CH}_2 = \text{CH-CH}_2\text{-}$	92	$\text{C}_{26}\text{H}_{28}\text{N}_6\text{S}_2$	488	63.93	5.78	17.21	63.67	5.77	17.34
4k	$o\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$o,p\text{-(NO}_2)_2\text{C}_6\text{H}_3\text{-}$	284	$\text{C}_{33}\text{H}_{24}\text{N}_{10}\text{O}_8\text{S}_2$	740	51.89	3.26	18.93	51.81	3.11	18.78
4l	$o\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$\text{C}_6\text{H}_5\text{CH}_2\text{-}$	170	$\text{C}_{34}\text{H}_{32}\text{N}_6\text{S}_2$	588	69.39	5.49	14.28	69.01	5.47	14.38
n = 4											
4m	$\text{C}_6\text{H}_5\text{-}$	$\text{CH}_3\text{-}$	198	$\text{C}_{22}\text{H}_{24}\text{N}_6\text{S}_2$	436	60.54	5.55	19.25	60.24	5.77	19.38
4n	$\text{C}_6\text{H}_5\text{-}$	$\text{C}_2\text{H}_5\text{-}$	172	$\text{C}_{24}\text{H}_{26}\text{N}_6\text{S}_2$	464	62.06	6.08	18.09	62.09	6.24	18.34
4o	$\text{C}_6\text{H}_5\text{-}$	$\text{C}_6\text{H}_5\text{CH}_2\text{-}$	193	$\text{C}_{34}\text{H}_{32}\text{N}_6\text{S}_2$	588	69.35	5.49	14.28	69.73	5.77	14.39
4p	$\text{C}_6\text{H}_5\text{-}$	$p\text{-ClC}_6\text{H}_4\text{CH}_2\text{-}$	190	$\text{C}_{34}\text{H}_{30}\text{N}_6\text{Cl}_2\text{S}_2$	657	62.10	4.60	12.78	62.44	4.64	12.93
4q	$\text{C}_6\text{H}_5\text{-}$	$o\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{-}$	154	$\text{C}_{34}\text{H}_{30}\text{N}_6\text{O}_2\text{S}_2$	678	60.16	4.45	16.51	60.14	4.57	16.39
4r	$\text{C}_6\text{H}_5\text{-}$	$p\text{-NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{-}$	286	$\text{C}_{34}\text{H}_{30}\text{N}_6\text{O}_2\text{S}_2$	678	60.16	4.45	16.51	60.12	4.37	16.21
4s	$\text{C}_6\text{H}_5\text{-}$	$o,p\text{-(NO}_2)_2\text{C}_6\text{H}_2\text{-}$	299	$\text{C}_{32}\text{H}_{22}\text{N}_{12}\text{O}_{12}\text{S}_2$	830	46.27	2.67	20.26	46.38	2.64	20.48
4t	$o\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$\text{CH}_3\text{-}$	182	$\text{C}_{26}\text{H}_{28}\text{N}_6\text{S}_2$	464	62.06	6.08	18.09	62.33	6.01	18.33
4u	$o\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$\text{C}_2\text{H}_5\text{-}$	137	$\text{C}_{26}\text{H}_{32}\text{N}_6\text{S}_2$	492	63.40	6.55	17.07	63.67	6.89	17.31
4v	$o\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$\text{CH}_2 = \text{CH-CH}_2\text{-}$	105	$\text{C}_{28}\text{H}_{32}\text{N}_6\text{S}_2$	516	65.10	6.25	16.28	65.01	6.04	16.39
4w	$o\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$\text{C}_6\text{H}_5\text{CH}_2\text{-}$	106	$\text{C}_{36}\text{H}_{36}\text{N}_6\text{S}_2$	616	70.11	5.89	13.63	70.32	5.87	13.82
4x	$p\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$p\text{-Br-C}_6\text{H}_4\text{CH}_2\text{-}$	120	$\text{C}_{36}\text{H}_{34}\text{N}_6\text{Br}_2\text{S}_2$	774	55.82	4.43	10.86	55.91	4.09	11.03
4y	$p\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$\text{CH}_2 = \text{CH-CH}_2\text{-}$	100	$\text{C}_{28}\text{H}_{32}\text{N}_6\text{S}_2$	516	65.10	6.25	16.28	65.32	6.21	16.21
n = 8											
4z	$\text{C}_6\text{H}_5\text{-}$	$\text{C}_6\text{H}_5\text{CH}_2\text{-}$	130	$\text{C}_{38}\text{H}_{40}\text{N}_6\text{S}_2$	644	70.75	6.26	13.04	70.61	6.09	13.11
4α	$\text{C}_6\text{H}_5\text{-}$	$o,p\text{-(NO}_2)_2\text{C}_6\text{H}_3\text{-}$	255	$\text{C}_{36}\text{H}_{32}\text{N}_{10}\text{O}_8\text{S}_2$	796	54.27	4.06	17.60	54.31	4.38	17.82
4β	$p\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$\text{C}_6\text{H}_5\text{CH}_2\text{-}$	135	$\text{C}_{40}\text{H}_{44}\text{N}_6\text{S}_2$	672	71.41	6.60	12.50	71.28	6.42	12.48
4γ	$p\text{-CH}_3\text{C}_6\text{H}_4\text{-}$	$o,p\text{-(NO}_2)_2\text{C}_6\text{H}_3\text{-}$	190	$\text{C}_{38}\text{H}_{36}\text{N}_{10}\text{O}_8\text{S}_2$	824	55.33	4.41	17.00	55.12	4.39	17.31



phenyl-1,3,4-oxadiazole showed peaks at 1520 and 1340 cm^{-1} due to sym. and asym. stretching vibrations of the NO_2 group. Peaks at 1600 cm^{-1} were assigned to CH bending vibrations.

Mannich bases **9** were prepared by stirring an equimolar mixture of 5-phenyl-1,3,4-oxadiazole-2-thione, primary amine and formaldehyde (38%) at 0-5°. The isolated Mannich bases were characterized by spectral studies and elemental analyses.

The prepared compounds were screened for fungicidal, bactericidal, virucidal and insecticidal activities but none showed any significant activity.

EXPERIMENTAL

Melting points were determined on a Thomas-Hoover apparatus (capillary method) and are uncorrected. The ir and mass spectra of the compounds were recorded on a Perkin Elmer Spectrophotometer and a MS 312 Finnigan respectively.

Bis(4-aryl-3-thio-1,2,4-triazol-5-yl)alkanes (**3**).

These compounds were prepared by base cyclisation of bis(4-arylthiosemicarbazido)alkanes as described earlier [9-11].

Bis(4-aryl-3-alkylthio-1,2,4-triazol-5-yl)alkanes **4**.

A solution of bis(4-aryl-3-thio-1,2,4-triazol-5-yl)alkane in 8% aqueous sodium hydroxide was treated with an equimolar amount of alkylhalide and stirred for 2-3 hours at room temperature. During this period, the

Table 2

Bis[4-aryl-3-alkylsulphonyl-1,2,4-triazol-5-yl]alkanes **5**

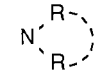

Compound No.	Ar	R	n	MP °C	Molecular Formula	M*	Elemental Analysis (%)					
							Calcd.			Found		
							C	H	N	C	H	N
5a	C_6H_5-	$n-\text{C}_4\text{H}_9-$	0	140	$\text{C}_{24}\text{H}_{28}\text{N}_6\text{O}_4\text{S}_2$	528	54.54	5.35	15.91	54.78	5.44	16.07
5b	$p-\text{CH}_3\text{C}_6\text{H}_4-$	C_2H_5-	0	165	$\text{C}_{22}\text{H}_{24}\text{N}_6\text{O}_4\text{S}_2$	500	52.80	4.84	16.79	52.64	4.87	16.91
5c	$o-\text{CH}_3\text{C}_6\text{H}_4-$	CH_3-	2	210	$\text{C}_{22}\text{H}_{24}\text{N}_6\text{O}_4\text{S}_2$	500	52.80	4.84	16.79	52.64	4.89	16.97
5d	$p-\text{CH}_3\text{C}_6\text{H}_4-$	$\text{C}_6\text{H}_5\text{CH}_2-$	4	167	$\text{C}_{36}\text{H}_{36}\text{N}_6\text{O}_4\text{S}_2$	680	63.55	5.34	12.35	63.29	5.45	12.47
5e	C_6H_5-	$\text{C}_6\text{H}_5\text{CH}_2-$	8	135	$\text{C}_{38}\text{H}_{40}\text{N}_6\text{O}_4\text{S}_2$	708	64.40	5.70	11.86	64.12	5.29	11.81

Table 3

2-Alkylthio-5-phenyl-1,3,4-oxadiazole-2-thiones **8**

Compound No.	R	MP °C	Molecular Formula	M*	C	Elemental Analysis (%)				
						Calcd.	H	N	C	Found H
8a	$o-\text{NO}_2\text{C}_6\text{H}_4\text{CH}_2-$	115	$\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}_3\text{S}$	313	57.51	3.54	13.41	57.22	3.19	13.27
8b	$p-\text{NO}_2\text{C}_6\text{H}_4\text{CH}_2-$	145	$\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}_3\text{S}$	313	57.51	3.54	13.41	57.33	3.32	13.07
8c	$o,p-(\text{NO}_2)_2\text{C}_6\text{H}_3-$	186	$\text{C}_{14}\text{H}_8\text{N}_4\text{O}_2\text{S}$	344	48.84	2.35	16.27	48.57	2.30	16.43
8d	$p-\text{ClC}_6\text{H}_4\text{CH}_2-$	113	$\text{C}_{15}\text{H}_{11}\text{N}_2\text{ClOS}$	302	59.51	3.68	9.27	59.28	3.71	9.15

Table 4.
3-aryl/arylaminomethyl-1,3,4-oxadiazole-2-thiones **9**

Compound No.		MP °C	Molecular Formula	M ⁺	Elemental Analysis (%)					
					Calcd.	Found				
					C	H	N	C	H	N
9a	-NH-CH-(C ₆ H ₅) ₂	143	C ₂₂ H ₁₉ N ₃ OS	373	70.75	5.13	11.26	70.47	5.12	11.33
9b	-N-(CH ₂ C ₆ H ₅) ₂	150	C ₂₃ H ₂₁ N ₃ OS	387	71.29	7.02	10.85	71.43	7.18	10.93
9c	-NH-C ₆ H ₃ -(2,3)(CH ₃) ₂	131	C ₁₇ H ₁₇ N ₃ OS	311	65.57	5.50	13.49	65.34	5.18	13.48
9d	-NH-CH ₂ - 	145	C ₁₄ H ₁₃ N ₃ O ₂ S	287	58.52	4.57	14.63	58.41	4.38	14.39
9e	-NH-C ₆ H ₃ -(2,5)(CH ₃) ₂	95	C ₁₇ H ₁₇ N ₃ OS	311	65.57	5.50	13.49	65.44	5.41	13.38

precipitate thus obtained was filtered, washed with water and crystallized from a suitable solvent.

Compounds thus prepared are listed in Table 1 with their relevant data.

Bis(4-aryl-3-alkylsulphonyl-1,2,4-triazol-5-yl)alkanes **5**.

A solution of bis(4-aryl-3-alkylthio-1,2,4-triazol-5-yl)alkanes in glacial acetic acid was dropwise treated with 3% aqueous potassium permanganate until the violet colour persisted. The precipitate thus obtained was filtered, washed with water and finally crystallized from dilute acetic acid.

The compounds thus prepared are listed in Table 2.

2-(p-Nitrobenzylmercapto)-5-phenyl-1,3,4-oxadiazole (**8**).

An equimolar mixture of **7**, p-nitrobenzyl bromide, and potassium carbonate in DMF was stirred for 2-3 hours at room temperature. The precipitate obtained after dilution of the reaction mixture was filtered off, washed with water and crystallized from DMF:water yielding 65% of **8b**; ms: m/z = 313 (M⁺), 177 (M⁺ -CH₂C₆H₄NO₂), 145 (M⁺ -SCH₂C₆H₄NO₂).

Other compounds were prepared similarly and are presented in Table 3 with their relevant data.

3-Aralkyl/arylaminomethyl-5-phenyl-1,3,4-oxadiazole-2-thione (**9**).

An alcoholic solution of 5-phenyl-1,3,4-oxadiazole-2-thione was treated with an equimolar amount of amine and formaldehyde (38%) at 0-5°. After 2-3 hours a white precipitate separated out, which was filtered, washed with ethanol and finally crystallized from a suitable solvent.

The title compounds thus prepared are listed in Table 4 along with their physical data.

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