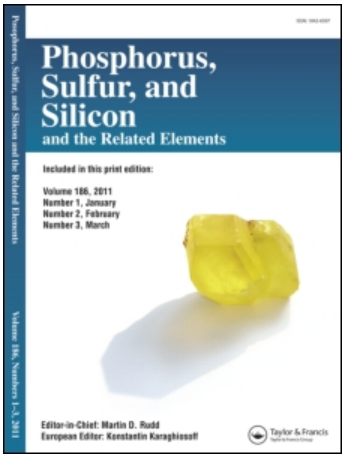

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

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Anita Gupta[a]; Shalini Shukla[a]; L. Prakash[a]
[a] Department of Chemistry, University of Rajasthan, Jaipur, India

To cite this Article Gupta, Anita , Shukla, Shalini and Prakash, L.(1993) 'SYNTHESIS OF THIOUREA DERIVATIVES OF s-TRIAZINE AND THEIR ANTIMICROBIAL ACTIVITY', Phosphorus, Sulfur, and Silicon and the Related Elements, 79: 1, 1 — 5
To link to this Article: DOI: 10.1080/10426509308034391
URL: http://dx.doi.org/10.1080/10426509308034391

Phosphorus, Sulfur, and Silicon, 1993, Vol. 79, pp. 1–5
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SYNTHESIS OF THIOUREA DERIVATIVES OF s-TRIAZINE AND THEIR ANTIMICROBIAL ACTIVITY

ANITA GUPTA, SHALINI SHUKLA and L. PRAKASH*
Department of Chemistry, University of Rajasthan, Jaipur-302004, India

(Received August 25, 1992; in final form February 17, 1993)

Synthesis of trisubstituted derivatives of s-triazine containing thiourea group by the replacement reaction. The elemental analysis, IR, ^{13}C, ^{19}F and ^{1}H NMR spectral data confirm the structure of the compounds. The synthesized compounds have been tested for antimicrobial activity.

Key words: Thiourea containing s-triazine; ^{1}H, ^{13}C and ^{19}F NMR and IR.

INTRODUCTION

A survey of the literature reveals that s-triazine possess diverse biological activity such as antiinflammatory,[1] fungicidal,[2–3] antibacterial,[4–5] insecticidal[6] and anticancer.[7–8] Keeping in mind the therapeutic importance of s-triazine derivatives, new types of thiourea derivatives of s-triazine have been synthesized in the hope of finding better antimicrobial activity. The structure of the compounds (**IIIa–IIIh**) were established by IR, NMR (^{1}H, ^{13}C and ^{19}F) spectral studies. Elemental and physical data are given in Table I.

RESULTS AND DISCUSSION

2-(Arylanilino) substituted-4-(methylamino)-6-(thioureido)-1,3,5-triazine (**III**) were synthesized by the condensation of 2-chloro substituted-4-(methylamino)-6-(thioureido)-1,3,5-triazine with different aromatic amines in dioxane maintaining the temperature at 85–90°C. 2-Chloro substituted-4-(methylamino)-6-(thioureido)-1,3,5-triazine (**II**) were prepared by the reaction of methyl amine with 2,4-dichloro-6-(thioureido)-1,3,5-triazine (**I**) in acetone maintaining the temperature at 30–35°C.

2,4-Dichloro-6-(thioureido)-1,3,5-triazine (**I**) was synthesized by the reaction of 1,3,5-triazine with thiourea in acetone at 0–5°C (Scheme I).

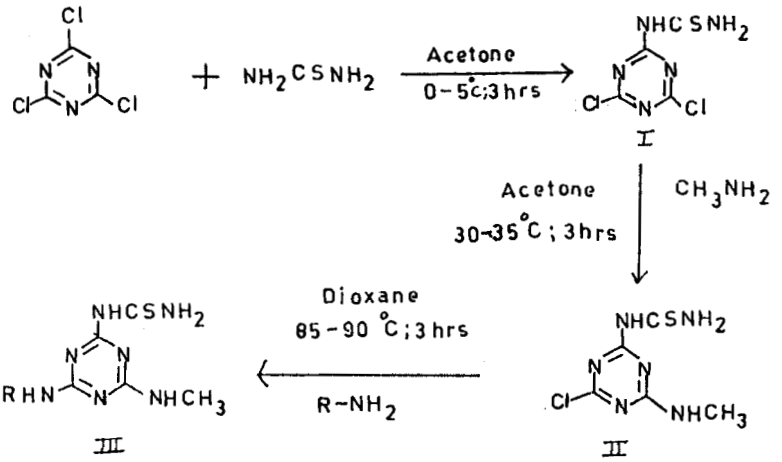
All the synthesized s-triazine derivatives were tested for antimicrobial activity and were found to be active against the *S. aureus*, *E. coli* and the fungi, e.g., *Aspergillus flavus*, *Aspergillus niger*, *Fusarium moniliformae* and *Curvularia lunata*. All the newly synthesized compounds were obtained as white solids and soluble in DMSO and DMF.

TABLE I

Physical and analytical data of the compounds (**IIIa–IIIh**)

Compound No.	R	Yield (%)	Molecular formula	Elemental Analysis (%) Found (Calcd.)			
				C	H	N	S
IIIa	p-$NO_2C_6H_4$	64.5	$C_{11}H_{12}N_8O_2S$	41.27 (41.25)	3.78 (3.75)	34.88 (35.00)	10.20 (10.00)
IIIb	p-FC_6H_4	72.0	$C_{11}H_{12}N_7FS$	45.22 (45.20)	4.12 (4.10)	33.54 (33.56)	10.93 (10.95)
IIIc	p-BrC_6H_4	68.0	$C_{11}H_{12}N_7BrS$	37.30 (37.29)	3.41 (3.39)	27.68 (27.69)	9.02 (9.04)
IIId	p-ClC_6H_4	62.6	$C_{11}H_{12}N_7ClS$	42.66 (42.64)	3.86 (3.88)	31.65 (31.67)	10.31 (10.33)
IIIe	p-$CH_3C_6H_4$	74.0	$C_{12}H_{15}N_7S$	49.80 (49.82)	5.20 (5.19)	33.8 (33.9)	11.09 (11.07)
IIIf	C_6H_5	64.2	$C_{11}H_{13}N_7S$	48.20 (48.00)	4.70 (4.73)	35.64 (35.63)	11.61 (11.63)
IIIg	m-$CH_3C_6H_4$	60.0	$C_{12}H_{15}N_7S$	49.80 (49.82)	5.20 (5.19)	33.8 (33.9)	11.06 (11.07)
IIIh	m-ClC_6H_4	66.0	$C_{11}H_{12}N_7ClS$	42.63 (42.60)	3.90 (3.88)	31.64 (31.67)	10.32 (10.33)

Melting point of all the synthesized compounds is >300°C.



SCHEME I

SPECTRAL STUDIES

The spectroscopic information of the synthesized compounds are consistent with the formation of proposed structures and some important features may be summarized as follows.

IR Spectra

All the synthesized s-triazine exhibited bands in the region 3450–3100 cm^{-1} which are due to the —NH linkage. Bands are observed in the region 1570–1420 cm^{-1} due to the —NH—C═S group. Absorption around 825–800 cm^{-1} is due to the presence of C_3N_3 group.

^1H, ^{19}F and ^{13}C NMR Spectra

In the ^1H NMR spectra of the synthesized s-triazines, the singlet of CH_3 protons was observed in the region at δ 2.2–2.64 ppm. The multiplet in the region δ 6.65–8.98 ppm is due to phenyl protons. The NH protons occur as a broad peak in the region δ 8.5–11.38 ppm.

^{19}F NMR spectra of the compound **IIIb**, the fluorine atom carried on the phenyl ring indicated its presence by a characteristic signal at −108.258 ppm.

In the ^{13}C NMR spectra the signal at 174 ppm is due to the —C═S group.[9] The signals in the region 162–165 ppm are due to the —C═N— group.[10]

ANTIMICROBIAL ACTIVITY

Compounds **IIIa–IIIh** of the series were tested for their antimicrobial activity, following the method of Gould *et al.*,[11] using streptomycin in antibacterial and mycostatin in antifungal activity as reference compounds.

TABLE II

Antimicrobial activity of the synthesized compounds (**IIIa–IIIh**)

Test organism	Inhibition zone (mm)							
	IIIa	**IIIb**	**IIIc**	**IIId**	**IIIe**	**IIIf**	**IIIg**	**IIIh**
Gram positive bacterium								
S. aureus	12.8	10.6	12.8	8.5	12.0	9.4	8.2	9.6
	(1.12)	(0.92)	(1.12)	(0.74)	(1.05)	(0.82)	(0.77)	(0.90)
Gram negative bacterium								
E. coli	10.6	10.9	11.2	12.5	11.0	12.8	10.5	9.5
	(1.00)	(1.03)	(1.07)	(1.19)	(1.04)	(1.22)	(0.97)	(0.88)
Fungi								
Aspergillus flavus	9.2	8.8	7.6	8.5	8.0	11.5	9.2	8.9
	(1.15)	(1.1)	(0.95)	(1.06)	(1.00)	(1.32)	(1.06)	(1.02)
Aspergillus niger	9.8	7.6	9.2	10.0	6.9	8.6	8.0	8.6
	(1.18)	(0.91)	(1.1)	(1.20)	(0.83)	(1.03)	(1.07)	(1.14)
Fusarium moniliformae	10.8	11.5	7.9	9.2	8.9	8.2	10.5	8.8
	(1.24)	(1.32)	(0.91)	(1.06)	(1.02)	(0.94)	(1.28)	(1.07)
Curvularia lunata	9.5	9.6	9.0	8.5	8.0	9.8	7.6	9.2
	(1.16)	(1.17)	(1.1)	(0.04)	(0.98)	(1.18)	(0.91)	(1.11)

Values in parentheses represent activity index: Activity index = inhibition area of the sample/inhibition area of the standard.

All the compounds were active against gram positive bacterium *S. aureus* and gram negative bacterium *E. coli*.

All the compounds showed activity against all the fungi tested, e.g. *Aspergillus flavus*, *Aspergillus niger*, *Fusarium moniliformae* and *Curvularia lunata*.

The results are recorded in Table II.

EXPERIMENTAL

Melting points were determined in sealed evacuated capillary tubes and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer 577 grating spectrophotometer (ν_{max} cm^{-1}), NMR (^1H and ^{19}F) spectra in DMSO-d_6 on Jeol FX 90 Q (90 MHz) using TMS as internal standard.

Synthesis of 2,4-dichloro-6-(thioureido)-1,3,5-triazine. 2,4,6-Trichloro-1,3,5-triazine (0.03 mole) was dissolved in acetone (30 ml) the solution of thiourea (0.03 mole) in acetone (10 ml) was added slowly with stirring at 0–5°C followed by the addition of NaOH solution (0.03 mole in 10 ml of water). The reaction mixture was stirred further for 3 hours at 0–5°C. The whole content was poured into ice cold water and acidified with HCl. The product was filtered, washed and dried. It was recrystallized from ethanol.

Synthesis of 2-chloro substituted-4-(methylamine)-6-(thioureido)-1,3,5-triazine. 2,4-Dichloro-6-(thioureido)-1,3,5-triazine (**I**) (0.012 mole) was dissolved in acetone (40 ml). The solution of methylamine (0.012 mole) in acetone (10 ml) was added with continuous stirring followed by the addition of NaOH solution (0.012 mole in 10 ml of water). The mixture was stirred for 3 hours at 30–35°C after cooling the reaction mixture, it poured into ice cold water and acidified with HCl. It was filtered, washed, dried and recrystallized from ethanol and DMF (1:1).

Synthesis of 2-(arylanilino) substituted-4-(methylamino)-6-(thioureido)-1,3,5-triazine. 2-Chloro substituted-4-(methylamino)-6-(thioureido)-1,3,5-triazine (**II**) (0.003 mole) was dissolved in 1,4-dioxane (6 ml). The solution of different types of aromatic amines (0.003 mole) in dioxane (6 ml) was added slowly in the above solution, followed by the addition of NaOH solution (0.003 mole in 5 ml of water). The whole content heated for 3 hours, at 85–90°C. After cooling it was poured into ice cold water. The product was filtered, washed, dried and recrystallized from DMF.

ACKNOWLEDGEMENT

Financial support from the University Grants Commission, New Delhi is gratefully acknowledged.

REFERENCES

1. Yu. A. Azev, V. L. Rusinov, I. P. Loginova, A. B. Koshokov, E. C. Pidemskui, A. F. Goleneva and G. A. Aleksandrova, (Ural. Politekh, Inst., Sverdlovska USSR) *Khim-Farm Zh.*, **25,** 10 (1991).
2. K. S. Pandya and K. A. Thaker, *J. Inst. Chemists,* 52 (1980).
3. Y. J. Fernandes and Hansa Parekh, *J. Inst. Chem.*, **62,** 208–210 (1990).
4. B. R. Parekh, J. N. Patel and K. A. Thaker, *J. Inst. Chem.*, **59,** 237 (1987); *Chem. Abstr.*, **109,** 149480 (1988).
5. A. J. Cowper, G. S. Trivedi, R. R. Astik and K. A. Thaker, *J. Inst. Chem.*, **53,** 85 (1981).
6. B. R. Parekh, N. C. Desai and K. A. Thaker, *J. Inst. Chem.*, **57,** 233 (1985).
7. K. R. Desai, M. M. Pathak and S. K. Kapadia, *Natl. Acad. Sci.*, 56th Annual Session, Jaipur, Oct. 25–27, 1986; *Sect. Physical Sciences*, p. 18.
8. E. Cioranesh, *Rev. Chim. (Bucharest),* **5,** 425 (1954).
9. G. Assef, J. Kister and J. Metzger, *Tetrahedron Lett.*, **37,** 3313–3316 (1976).
10. ^{13}C NMR-Spektrosckopie Hans-ott Kalinowski Stefan Berger Siegmar Braun 142 Abbildungen, 200 Tabellen page 352 (1984).
11. J. C. Gould and J. H. Bowie, *Edinb Med. J.*, **59,** 178 (1950).