

## SYNTHESIS AND CHARACTERIZATION OF SOME N-PHENYL-N'-[4-ARYL-5-(N-SUBSTITUTED SULPHAMIDO-AZO) THIAZOL-2-YL] THIOCARBAMIDES AS POSSIBLE ANTIBACTERIAL COMPOUNDS

R. N. GOYAL and ASHWANI MINOCHA

*Department of Chemistry, University of Roorkee, Roorkee 247 667 India.*

### SUMMARY

A variety of thiazolyl thiocarbamides properly substituted with sulphadruug moiety were prepared as possible antibacterial compounds. Their structures have been confirmed on the basis of elemental analysis, IR and mass spectral studies.

### INTRODUCTION

THIOCARBAMIDES have been the subject of growing interest from a long time. This interest is mainly due to a variety of activities associated with thiocarbamides. For example phenyl derivatives of thiocarbamides possess antituberculous activity<sup>1</sup>, N, N'-dialkoxythiocarbamides have been reported to be effective against human leprosy<sup>2</sup> and in the mice infected with influenza virus<sup>3</sup>. A large number of substituted thiocarbamides have been shown to possess antibacterial potency<sup>4</sup>. As thiazole nucleus forms a part of the structure of many compounds of biological importance possessing antibacterial and antifungal activity, attempts have also been made to synthesise thiazoles possessing diureido linkage<sup>5</sup>. In view of the great importance of thiocarbamides, N-phenyl-N'-[4-aryl-5-(N-substituted sulphamido-azo) thiazol-2-yl] thiocarbamides have been synthesised in the expectation that due to the presence of  $\text{-HN-C-NH-}$



linkage and thiazole nucleus, the biological activity of these compounds would be enhanced. Since the presence of azo-grouping promotes anticancer activity<sup>7,8</sup>, an azo group with a sulpha drug has been incorporated at 5-position of the thiazole nucleus to increase further the activity of these compounds in general. The present paper deals with the synthesis of N-phenyl-N'-[4-aryl-5-(N-substituted sulphamido azo) thiazol-2-yl] thiocarbamides by condensation of 2-amino-4-aryl-5-substituted sulphamidoazo thiazole with phenyl isothiocynate.

### EXPERIMENTAL

Melting points were determined with a Kofler hot stage apparatus and are uncorrected. IR spectra were obtained on a Beckman IR-20 infrared spectrophotometer and  $\lambda_{\text{max}}$  were determined on a uv-vis specord

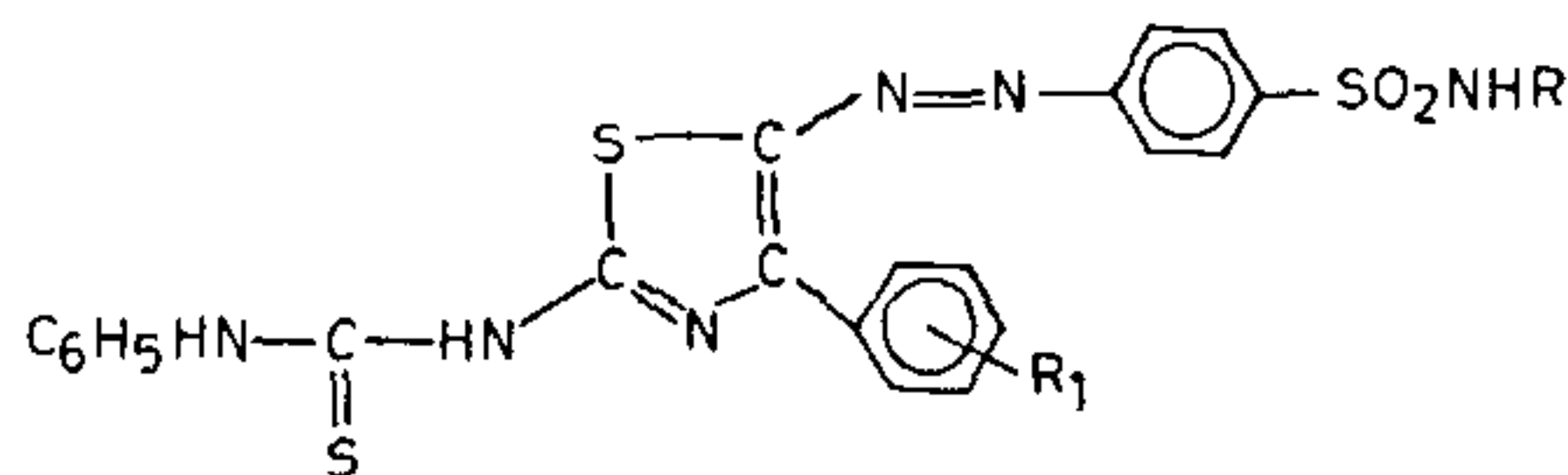
spectrophotometer (C. Zeiss, Jena). The results of elemental analysis were in good agreement with those of theoretical value. The mass spectra of some selected samples (No. 1, 8, 15, 32, 43, 55) were recorded on Hewlett Packard 5985 B instrument.

2-Amino-4-arylthiazole was prepared by the method reported in the literature<sup>9,10</sup> by reacting acetophenone, iodine and thiourea. The diazotisation of appropriate sulphadruug and then coupling with 2-Amino-4-aryl thiazoles by the method reported in the literature<sup>10</sup>, gave 2-amino-4-aryl-5-sulphadruugazo-thiazoles<sup>11</sup>.

#### *N-phenyl-N'-[4-aryl-5-(N-substituted sulphamido azo) thiazol-2-yl] Thiocarbamides*

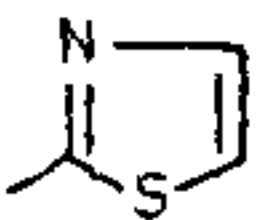
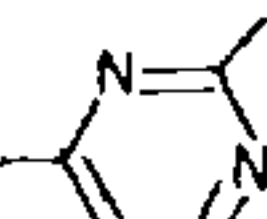
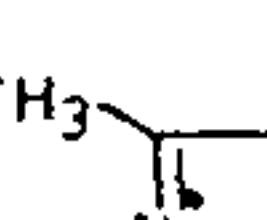
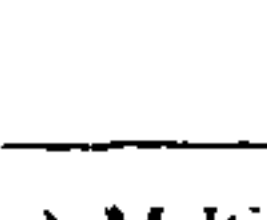
2-Amino-4-aryl-5-substituted sulphamidoazothiazole (0.01 mole) was dissolved in benzene (15 ml) and the phenylisothiocynate (0.01 mole) was added and the mixture was refluxed on a water bath for 10 to 12 hr. The benzene was removed under reduced pressure and the residue was washed with petroleum ether (3 × 25 ml). The crude thiocarbamide thus obtained was recrystallised from ethanol-DMF mixture. The characterization data of various thiocarbamides prepared by this method are summarised in table 1.

The compounds were characterised on the basis of their elemental analysis for C, H, N and S. The presence of characteristic absorption bands at  $1550\text{-}1500\text{cm}^{-1}$  and  $1610\text{-}1595\text{cm}^{-1}$  for thioureido ( $\text{-N-C=S}$ ) and azo ( $\text{-N=N-}$ ) linkage respectively<sup>12</sup> and in the region  $1380\text{-}1360\text{cm}^{-1}$  and  $1190\text{-}1170\text{cm}^{-1}$  for secondary  $\text{-SO}_2\text{-NH-}$  Grouping<sup>13</sup> further supported the proposed structure. The mass spectral studies for selected samples also provided evidence for molecular ion peak. The observed  $\lambda_{\text{max}}$  in the visible region clearly indicated that  $\pi$  chromophore system has been extended. Selected samples have been submitted to various laboratories to determine the

Table 1 Characteristics of *N*-phenyl-*N'*-[4-aryl-5-(*N*-substituted sulphamido azo)thiazol-2yl] Thiocarbamides

R	R <sub>1</sub>	Molecular Formula	Colour	Percent yield	M.P. °C	λ <sub>max</sub> nm
1	2	3	4	5	6	7
-H	-H	C <sub>22</sub> H <sub>18</sub> N <sub>6</sub> S <sub>3</sub> O <sub>2</sub>	DBr	63	249-51	273
	4-OCH <sub>3</sub>	C <sub>23</sub> H <sub>20</sub> N <sub>6</sub> S <sub>3</sub> O <sub>3</sub>	Br	68	269-73	269
	4-OC <sub>2</sub> H <sub>5</sub>	C <sub>24</sub> H <sub>22</sub> N <sub>6</sub> S <sub>3</sub> O <sub>3</sub>	R	70	260-2	275
	4-Br	C <sub>22</sub> H <sub>17</sub> N <sub>6</sub> S <sub>3</sub> O <sub>2</sub> Br	Br	71	315-7	280
	4-Cl	C <sub>22</sub> H <sub>17</sub> N <sub>6</sub> S <sub>3</sub> O <sub>2</sub> Cl	R	62	302-3	276
	3-NH <sub>2</sub>	C <sub>22</sub> H <sub>19</sub> N <sub>7</sub> S <sub>3</sub> O <sub>2</sub>	R	63	325-7	278
	-H	C <sub>23</sub> H <sub>20</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub>	DBr	68	254-6	273
	4-OCH <sub>3</sub>	C <sub>24</sub> H <sub>22</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	R	67	258-60	270
	4-OC <sub>2</sub> H <sub>5</sub>	C <sub>25</sub> H <sub>24</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	R	63	265-7	275
	4-Br	C <sub>23</sub> H <sub>19</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub> Br	R	67	292-3	279
	4-Cl	C <sub>23</sub> H <sub>19</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub> Cl	DBr	68	265-7	280
	3-NH <sub>2</sub>	C <sub>23</sub> H <sub>21</sub> N <sub>9</sub> S <sub>3</sub> O <sub>2</sub>	Br	65	289-9	268
	-H	C <sub>26</sub> H <sub>20</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub>	R	73	272-4	275
	4-OCH <sub>3</sub>	C <sub>27</sub> H <sub>22</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	DBr	76	326-7	270
	4-OC <sub>2</sub> H <sub>5</sub>	C <sub>28</sub> H <sub>24</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	R	70	260-1	278
	4-Br	C <sub>26</sub> H <sub>19</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub> Br	DBr	62	293-5	276
	4-Cl	C <sub>26</sub> H <sub>19</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub> Cl	DBr	69	249-1	275
	3-NH <sub>2</sub>	C <sub>26</sub> H <sub>21</sub> N <sub>9</sub> S <sub>3</sub> O <sub>2</sub>	DBr	75	304-6	274
	-H	C <sub>27</sub> H <sub>22</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub>	R	65	329-31	273
	4-OCH <sub>3</sub>	C <sub>28</sub> H <sub>24</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	R	69	300-1	274
	4-OC <sub>2</sub> H <sub>5</sub>	C <sub>29</sub> H <sub>26</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	Br	70	299-	276
	4-Br	C <sub>27</sub> H <sub>21</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub> Br	DBr	71	269-71	280
	4-Cl	C <sub>27</sub> H <sub>21</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub> Cl	R	63	273-5	277
	3-NH <sub>2</sub>	C <sub>27</sub> H <sub>23</sub> N <sub>9</sub> S <sub>3</sub> O <sub>2</sub>	R	70	295-7	281
	-H	C <sub>31</sub> H <sub>24</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub>	DBr	72	222-4	279
	4-OCH <sub>3</sub>	C <sub>32</sub> H <sub>26</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	Br	63	281-3	272
	4-OC <sub>2</sub> H <sub>5</sub>	C <sub>33</sub> H <sub>28</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	DBr	72	265-7	276
	4-Br	C <sub>31</sub> H <sub>23</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub> Br	R	64	155-7	274
	4-Cl	C <sub>31</sub> H <sub>23</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub> Cl	Br	68	167-9	282
	3-NH <sub>2</sub>	C <sub>31</sub> H <sub>25</sub> N <sub>9</sub> S <sub>3</sub> O <sub>2</sub>	Br	67	215-7	272
	-H	C <sub>27</sub> H <sub>22</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	DBr	69	260-2	275
	4-OCH <sub>3</sub>	C <sub>28</sub> H <sub>24</sub> N <sub>8</sub> S <sub>3</sub> O <sub>4</sub>	R	70	335-7	276
	4-OC <sub>2</sub> H <sub>5</sub>	C <sub>29</sub> H <sub>26</sub> N <sub>8</sub> S <sub>3</sub> O <sub>4</sub>	Br	71	225-7	278
	4-Br	C <sub>27</sub> H <sub>21</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub> Br	Br	74	327-9	276
	4-Cl	C <sub>27</sub> H <sub>21</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub> Cl	R	73	285-7	274
	3-NH <sub>2</sub>	C <sub>27</sub> H <sub>22</sub> N <sub>9</sub> S <sub>3</sub> O <sub>3</sub>	O	74	285-7	279
	-H	C <sub>28</sub> H <sub>24</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub>	C	62	260-3	282

Table 1 Characteristics of *N*-phenyl-*N'*-[4-aryl-5-(*N*-substituted sulphamido azo)thiazol-2-yl]Thiocarbamides

R	R <sub>1</sub>	Molecular Formula	Colour	Percent yield	M.P. °C	λ <sub>max</sub> nm
2	3	4	5	6	7	8
	4-OCH <sub>3</sub>	C <sub>29</sub> H <sub>26</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	R	68	298-1	280
	4-OC <sub>2</sub> H <sub>5</sub>	C <sub>30</sub> H <sub>28</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	DBr	67	305-7	276
	4-Br	C <sub>28</sub> H <sub>23</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub> Br	R	60	325-7	278
	4-Cl	C <sub>28</sub> H <sub>23</sub> N <sub>8</sub> S <sub>3</sub> O <sub>2</sub> Cl	Br	73	315-7	276
	3-NH <sub>2</sub>	C <sub>28</sub> H <sub>25</sub> N <sub>9</sub> S <sub>3</sub> O <sub>2</sub>	O	72	275-7	277
	-H	C <sub>25</sub> H <sub>19</sub> N <sub>7</sub> S <sub>4</sub> O <sub>2</sub>	Br	65	301-2	279
	4-OCH <sub>3</sub>	C <sub>26</sub> H <sub>21</sub> N <sub>7</sub> S <sub>4</sub> O <sub>3</sub>	DBr	70	225-7	278
	4-OC <sub>2</sub> H <sub>5</sub>	C <sub>27</sub> H <sub>23</sub> N <sub>7</sub> S <sub>4</sub> O <sub>3</sub>	Br	63	215-2	276
	4-Br	C <sub>25</sub> H <sub>18</sub> N <sub>7</sub> S <sub>4</sub> O <sub>2</sub> Br	R	70	275-7	271
	4-Cl	C <sub>25</sub> H <sub>18</sub> N <sub>7</sub> S <sub>4</sub> O <sub>2</sub> Cl	Br	70	255-7	278
	3-NH <sub>2</sub>	C <sub>23</sub> H <sub>20</sub> N <sub>8</sub> S <sub>4</sub> O <sub>2</sub>	R	63	315-7	276
	-H	C <sub>28</sub> H <sub>24</sub> N <sub>8</sub> S <sub>3</sub> O <sub>4</sub>	R	72	305-9	277
	4-OCH <sub>3</sub>	C <sub>29</sub> H <sub>26</sub> N <sub>8</sub> S <sub>3</sub> O <sub>5</sub>	DBr	73	315-7	279
	4-OC <sub>2</sub> H <sub>5</sub>	C <sub>30</sub> H <sub>28</sub> N <sub>8</sub> S <sub>3</sub> O <sub>5</sub>	R	68	335-7	283
	4-Br	C <sub>28</sub> H <sub>23</sub> N <sub>8</sub> S <sub>3</sub> O <sub>4</sub> Br	DBr	65	340-2	281
	4-Cl	C <sub>28</sub> H <sub>23</sub> N <sub>8</sub> S <sub>3</sub> O <sub>4</sub> Cl	DBr	64	352-4	282
	3-NH <sub>2</sub>	C <sub>28</sub> H <sub>25</sub> N <sub>9</sub> S <sub>3</sub> O <sub>4</sub>	O	67	315-5	275
	H	C <sub>27</sub> H <sub>23</sub> N <sub>7</sub> S <sub>3</sub> O <sub>3</sub>	Br	69	325-7	279
	4-OCH <sub>3</sub>	C <sub>28</sub> H <sub>25</sub> N <sub>7</sub> S <sub>3</sub> O <sub>4</sub>	Br	72	254-6	277
	4-OC <sub>2</sub> H <sub>5</sub>	C <sub>29</sub> H <sub>27</sub> N <sub>7</sub> S <sub>3</sub> O <sub>4</sub>	R	63	325-7	275
	4-Br	C <sub>27</sub> H <sub>22</sub> N <sub>7</sub> S <sub>3</sub> O <sub>3</sub> Br	DBr	65	335-7	273
	4-Cl	C <sub>27</sub> H <sub>22</sub> N <sub>7</sub> S <sub>3</sub> O <sub>3</sub> Cl	R	67	365-6	272
	3HN <sub>2</sub>	C <sub>25</sub> H <sub>24</sub> N <sub>8</sub> S <sub>3</sub> O <sub>3</sub>	R	70	325-6	271

a) Melting points were determined by Kofler hot stage apparatus and are uncorrected.

b) Br = Brown; DBr = Dark brown; G = Grey; Y = Yellow; C = Colourless and O = Orange.

activity of these compounds and their results will be reported later.

#### ACKNOWLEDGEMENT

The authors thank the Director, I.I.P., Dehradun for permitting to carry out the elemental analysis and to Mr. S. K. Tyagi, University of Oklahoma, Norman USA for the mass spectral results. The help of S.G. Pharmaceuticals, Baroda, Roche product Limited, Bombay, Parke-Davis Bombay and May and Baker India Limited, Bombay for the gift samples of sulphadiazole is duly acknowledged. One of the authors (AM) is grateful to the UGC, New Delhi for a fellowship.

18 July 1984; Revised 3 September 1984

1. Mayer, R. L., *Rev. Medicale France*, Nov, 1941, 3.
2. BuuHoi, N. P., *Int. J. Leprosy*, 1954, 22, 16.
3. BuuHoi, N. P., Gley, P., Xuong, N. D. and Bouffenis, A., *C.R. Acad. Sci., Paris*, 1954, 238, 2582.
4. Beaver, D. I., Roman, D. P. and Stoffel, P. J., *J. Med. Chem.*, 1963, 6, 501.
5. Agarwal, R. K., Agarwal, R. C., Saxena, V. K., Singh, A. R. and Mehra, S. C., *J. Indian Chem. Soc.*, 1981, 58, 787.
6. Upadhyaya, J. S. and Srivastava, P. K., *J. Indian Chem. Soc.*, 1982, 59, 683.
7. Harmon, R. E., Dutton, F. E. and Warren, H. D., *J. Med. Chem.*, 1968, 11, 627.
8. Modest, E. J., Schlein, H. N. and Foley, G. K., *J. Pharma. Pharmacol.*, 1957, 9, 68.

9. Dodson, R. M. and King, L. C., *J. Am. Chem. Soc.*, 1945, **67**, 2242.
10. King, L. C. and Hlavacek, R. J., *J. Am. Chem. Soc.*, 1950, **72**, 3722.
11. Goyal, R. N. and Minocha, A., *J. Fuer Prakt. Chemie*, (Communicated).
12. Silverstein, R. M., Bassler, C. G. and Morrill, T. C., *Spectrometric identification of organic compounds*, Wiley International, 1974, p. 73.
13. Rao, C. N. R., *Chemical applications of infrared spectroscopy*, Academic Press, New York, 1963.

---

## NEWS

---

### PUMPED STORAGE NEAR MOSCOW

No river in the Moscow region is big enough to make possible the construction of a 1.2 million KW hydro-power station, but even the tiny Kunia river in the Zagorsk district has a sufficiently high hydro potential to ensure the reliable operation of a pumped storage of the same capacity to be built here.

The need to build this station has been prompted by the requirements for electricity of Moscow, one of the biggest electricity consumer. Demand for electricity varies with the time of the day. It is at its peak during

the morning and the evening hours, and drops to the minimum at night. To regulate intragrid loads, Moscow needs a pumped storage. At night the pumped storage will use excessive electricity, generated by other power plants, to pump water from the bottom to the upper basin. At the time of greater demand for electricity that water will activate generating units of the pumped storage. (*Soviet Features*, Vol. XXIV, No. 4, January 8, 1985).

---

### COMPACT POWER STATION INSTEAD CAR BATTERY

A RAF minibus with the chemical formula of hydrogen painted on its sides that has appeared in the streets of Moscow recently is hardly different from the ordinary vehicles of this type. Yet there is one special thing about it—it has been fitted out with a unique generator supplying electricity to the electric engine.

An ecologically harmless battery-driven car is a great asset for urban transport, but its major shortcoming is in its storage battery. Heavy, costly and short-lived, it so far does not suit designers of electrically driven means of transportation.

According to some experts, electro-chemical generators can be used instead of the bulky storage batteries. An electro-chemical device code-named Istok and developed by Moscow's scientists differs from the previous models in the efficiency of energy conversion

and simple maintenance. The device is actually a compact electric power station.

The device consists of six fuel cells arranged in three blocs. Electricity is generated in a special reactor during interaction between hydrogen and oxygen. Steam that forms during the process is quickly discharged from the fuel cell. The processes of energy generation in the unit are controlled automatically. Commands to the unit are shot from the instrument panel in the driver's cabin.

Tests of the Istok generator have shown it quite effective when installed at an electrically driven vehicle which can be driven for up to 150 kilometres without hydrogen refuelling. (*Soviet Features*, Vol. XXIV, No. 4, January 8, 1985).

---