Synthesis of Some New Substituted Thiocarbamides

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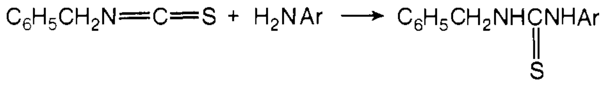
Sixteen new substituted thiocarbamides have been synthesized by reacting aryl isothiocyanates with various aromatic amines.

Buu Hoi et al. (*1*) prepared several *N,N'*-diarylthiocarbamides and found them to possess tuberculostatic activity. A number of thiocarbamide derivatives have been reported to exhibit marked antibacterial and fungicidal activity (*3, 8*). These derivatives contain the –N=C=S group, characteristic of many well-known compounds showing toxicity to fungi (*2*). Significant insecticidal (*2*) and acaricidal (*7*) activity has also been reported for these compounds. These compounds have also been proven useful in numerous chemical and biological applications (*5*). Of the many preparative methods which have been used for substituted thiocarbamides (*6*), one of the most common involves the direct reaction of isothiocyanates with amines.

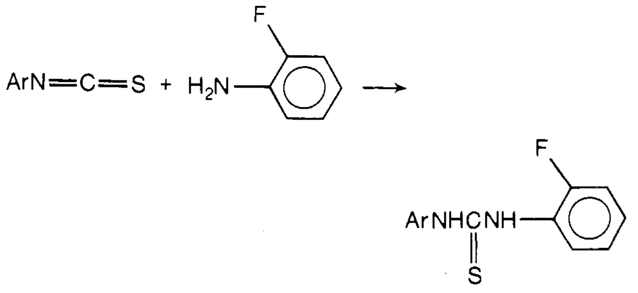
As part of a program to synthesize new compounds having potential biological activity (*4*), two series of previously unreported substituted thiocarbamides have been prepared by reacting isothiocyanates with ethanolic solutions of different aromatic and aliphatic amines. Thiocarbamides having the structures I and II were synthesized. The new compounds are recorded in Table I.

These compounds have been used to synthesize a number of 3-benzyl-2-arylimino-4-thiazolidinones and 3-aryl-2-*o*-fluorophenylimino-4-thiazolidinones.



$$C_6H_5CH_2N{=}C{=}S + H_2NAr \longrightarrow C_6H_5CH_2NH\underset{\underset{S}{\|}}{C}NHAr$$

I



II

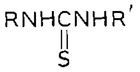
Experimental Section

All melting points were determined using the capillary method and are uncorrected.

The antitubercular effectiveness of the compounds **4, 5,** and **10** were evaluated in vitro against Mycobacterium tuberculosis strain $H_{37}Ra$ at the Division of Microbiology, Central Drug Research Institute, Lucknow, but none of them showed any activity. Compounds **4** and **10** were tested for their nematicidal, insecticidal, acaricidal, and herbicidal activities at the laboratories of Phillips-Duphar in Holland. Only 1-benzyl-3-*o*-fluorophenyl-2-thiocarbamide (compound no. **4**) showed slight herbicidal activity.

Formation of Thiocarbamides. Preparation of 1-Benzyl-3-m-anisyl-2-thiocarbamide. To a solution of benzyl isothiocyanate (2.4 g, 0.016 mol) in a minimum quantity of absolute ethanol was added a freshly distilled solution of *m*-anisidine (2 g, 0.016 mol) in a minimum of ethanol. The mixture was warmed for 10 min on a water bath and stirred with a glass rod when a precipitate was obtained. It was separated, washed with a little ether

Table I. 1,3-Disubstituted-2-thiocarbamides[a]



$$RNH\underset{\underset{S}{\|}}{C}NHR'$$

Compd no.	R	R'	Mp, °C	% yield	Molecular formula
1	Benzyl	*m*-Anisyl	115	76	$C_{15}H_{16}N_2OS$
2	Benzyl	*o*-Phenetyl	108	86	$C_{16}H_{18}N_2OS$
3	Benzyl	*p*-Phenetyl	104	83	$C_{16}H_{18}N_2OS$
4	Benzyl	*o*-Fluorophenyl	149	85	$C_{14}H_{13}FN_2S$
5	Benzyl	*p*-Fluorophenyl	118	97	$C_{14}H_{13}FN_2S$
6	Benzyl	2,4-Dichlorophenyl	169	79	$C_{14}H_{12}Cl_2N_2S$
7	Benzyl	2,5-Dichlorophenyl	177	77	$C_{14}H_{12}Cl_2N_2S$
8	Benzyl	4-Hydroxy-2-methylphenyl	159	72	$C_{15}H_{16}N_2OS$
9	Benzyl	5-Chloro-2-hydroxyphenyl	155	82	$C_{14}H_{13}ClN_2OS$
10	Benzyl	3-Pyrazolyl	178	88	$C_{11}H_{12}N_4S$
11	*o*-Fluorophenyl	Phenyl	141	74	$C_{13}H_{11}FN_2S$
12	*o*-Fluorophenyl	*p*-Tolyl	144	80	$C_{14}H_{13}FN_2S$
13	*o*-Fluorophenyl	*o*-Chlorophenyl	131–132	45	$C_{13}H_{10}ClFN_2S$
14	*o*-Fluorophenyl	*p*-Chlorophenyl	148	58	$C_{13}H_{10}ClFN_2S$
15	*o*-Fluorophenyl	*p*-Bromophenyl	147	60	$C_{13}H_{10}BrFN_2S$
16	*o*-Fluorophenyl	*p*-Iodophenyl	143	100	$C_{13}H_{10}FIN_2S$

[a] Analyses of all compounds for C, H, and N were performed and satisfactory results were obtained.

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and dilute alcohol, and finally recrystallized from absolute ethanol, mp 115 °C, yield 3.34 g (76%).

By adopting a similar procedure all other substituted thiocarbamides derived from benzylamine were prepared. Their characteristics are given in Table I.

Preparation of 1-o-Fluorophenyl-3-phenyl-2-thiocarbamide. A solution of phenyl isothiocyanate (1.62 g, 0.012 mol) in ethanol (10 mL) was added to a solution of *o*-fluoroaniline (1.45 g, 0.012 mol) in ethanol (5 mL). The mixture was stirred and heated gently on a water bath for 10 min and the separated solid was filtered off, washed with light petroleum, dried, and finally recrystallized from absolute ethanol, mp 141 °C, yield 2.3 g (74%).

Similarly all other thiocarbamides derived from *o*-fluoroaniline have been prepared. Their physical constants have been described in Table I.

All the aryl isothiocyanates required for the preparation of thiocarbamides described in Table I have been obtained by known literature methods.

Acknowledgment

The authors are grateful to Dr. Nitya Nand, Director, and Drs. S. K. Gupta and I. S. Mathur of the Division of Microbiology, Central Drug Research Institute, Lucknow, for the antitubercular screening tests and to authorities of Phillips-Duphar, Holland, for the herbicidal and other biological tests.

Literature Cited

(1) Buu Hoi, Ng. Ph., Xuong, Ng. D., Nom, Ng. H., *J. Chem. Soc.*, 1573 (1955).
(2) Horsfall, Rich, J. G., *Contrib. Boyce Thomson Inst.*, **16**, 313 (1951).
(3) Rao, R. P., *Indian J. Appl. Chem.*, **23**, 110 (1960).
(4) Rao, R. P., Singh, S. R., *J. Indian Chem. Soc.*, **50**, 600 and 752 (1973).
(5) Reid, E. E., "Organic Chemistry of Bivalent Sulphur", Vol. 5, Chemical Publishing Co., New York, N.Y., 1963, pp 53-61.
(6) Reid, E. E., *ibid.*, pp 40-47.
(7) Rohoff, J. S., U.S. Patent, 2 983 646; *Chem. Abstr.*, **55**, 18022 (1961).
(8) Shroeder, D. C., *Chem. Rev.*, **55**, 181 (1955).

Received for review February 24, 1977. Accepted August 12, 1977.