Derivatives of 1,1-Dimethyl-3-Oxobutylthiocyanate. I. 1,4-Dihydro-1-(2-Mercaptobenzothiazol-6-Yl)-2-Thioxo-4,4,6-Trimethylpyrimidine.

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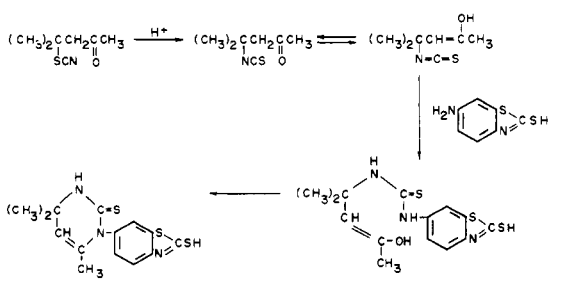
The reaction of 1,1-dimethyl-3-oxobutylthiocyanate with 6-amino-2-mercaptobenzothiazole under acidic conditions gave 1,4-dihydro-1-(2-mercaptobenzothiazol-6-yl)-2-thioxo-4,4,6-trimethylpyrimidine, I. Oxidation of I gave 2,2'-dithiobis-[6-(1,4-dihydro-2-thioxo-4,4,6-trimethylpyrimidin-1-yl)-benzothiazole]. Forty-nine derivatives of I were prepared. The infrared spectrum of I was obtained.

ALTHOUGH 2-MERCAPTOBENZOTHIAZOLE was prepared by Hofmann (*6*) in 1887 it was not until 1921 that both Bedford (*1*) and Bruni (*2*) discovered that it possessed accelerating activity for the vulcanization of rubber with sulfur. This great discovery has stimulated many workers to prepare and extensively evaluate its derivatives. Most of the commercial accelerators, in particular *N*-cyclohexyl-2-benzothiazolesulfenamide (commercially available as SANTOCURE) (*5*), *N-tert*-butyl-2-benzothiaxolesulfenamide (commercially available as SANTOCURE NS) (*3*), and 2-(2,6-dimethylmorpholinothio)benzothiazole (commercially available as SANTOCURE 26) (*4*) are still derived from 2-mercaptobenzothiazole. The 2-mercaptobenzothiazole and its derivatives containing substituents, other than the ethoxy, hydroxyl and amino radicals, in the 6-position have been prepared only in a limited number of examples. Since 2-thioxo-4,4,6-trimethyl-1,2,3,4-tetrahydropyrimidine (*7, 8*) and its derivatives possess moderate accelerating activity, a compound containing both benzothiazolylthio and 2-thioxo-4,4,6-trimethyl-1,2,3,4-tetrahydropyrimidinyl radicals would exhibit a synergistic effect and produce a chemical with greater activity than 2-mercaptobenzothiazole and its derivatives. The new heterocyclic compound was prepared by the reaction of 6-amino--mercaptobenzothiazole with 1,1-dimethyl-3-oxobutylthiocyanate under acidic conditions producing 1,4-dihydro-1-(2-mercaptobenzothiazol-6-yl)-2-thioxo-4, 4, 6-trimethylpyrimidine, I. The product, a tan colored solid, m.p. 207–209° C. after recrystallization from ethyl alcohol, was obtained in 97.5% yield. The reaction may be represented as:



I

The infrared spectra of I were obtained as Nujol and halocarbon mulls using a Perkin-Elmer Model 21 Infrared Spectrophotometer. The infrared spectra were consistent with the proposed structure. The C = C stretching vibration assigned to 2-thioxo-4,4,6-trimethyl-1,2,3,4-tetrahydropyrimidine (*9*) was observed at 1700 cm.$^{-1}$. Other band assignments in (cm.$^{-1}$) were as follows:

3247(M)	Hydrogen-bonded N—H stretching
3030(M)	C—H aromatic and alkene stretching
2985(M)2924(W)	Aliphatic C—H stretching
1600(M)	C = C skeletal in-plant-vibrations
1531(S)	Thioureide (—N(H)—C = S)
1486(S)broad	C—H deformation and C = C skeletal in-plane vibrations
1399(M)	—CH_3 sym. deformation
1344(S)	Unassigned
1339(S)	C—N stretching as in 2-mercaptobenzothiazole

The strong 4-adjacent hydrogen out-of-plane band of 2-mercaptobenzothiazole normally found at 756 cm.$^{-1}$ was absent and a 817 cm.$^{-1}$ (M) band was observed in the region of 2-adjacent hydrogen which is in agreement with the proposed structure.

The postulated synergistic effect was not observed since the accelerator activity of I and its derivatives was either equal or slightly inferior to 2-mercaptobenzothiazole and its corresponding derivatives. The detailed evaluation data of I and its derivatives will be reported in forthcoming publications.

The oxidation of I with either ammonium persulfate or sodium hypoiodite furnished 2,2'-dithiobis-[6-(1,4-dihydro-2-thioxo-4, 4, 6-trimethylpyrimidin-1-yl)benzothiazole] in yields of 99.5 and 90%, respectively. The product, a tan colored solid, melted at 266–268° C. with decomposition after recrystallization from dimethylformamide.

The condensation of I and formaldehyde with hexamethylenimine or aniline gave 1,4-dihydro-1-(3-hexamethyleniminomethylthiobenzothiazol-6-yl)-2-thioxo-4, 4,-6-trimethylpyrimidine, II, and 1-[3-(anilinomethylthio) benzothiazol-6-yl]-1, 4-dihydro-2-thioxo-4, 4, 6-trimethylpyrimidine, III, in yields of 60 and 80% respectively. Products II and III melted at 208–210° C. with decomposition and 181–183° C. after recrystallization from ethyl alcohol, respectively.

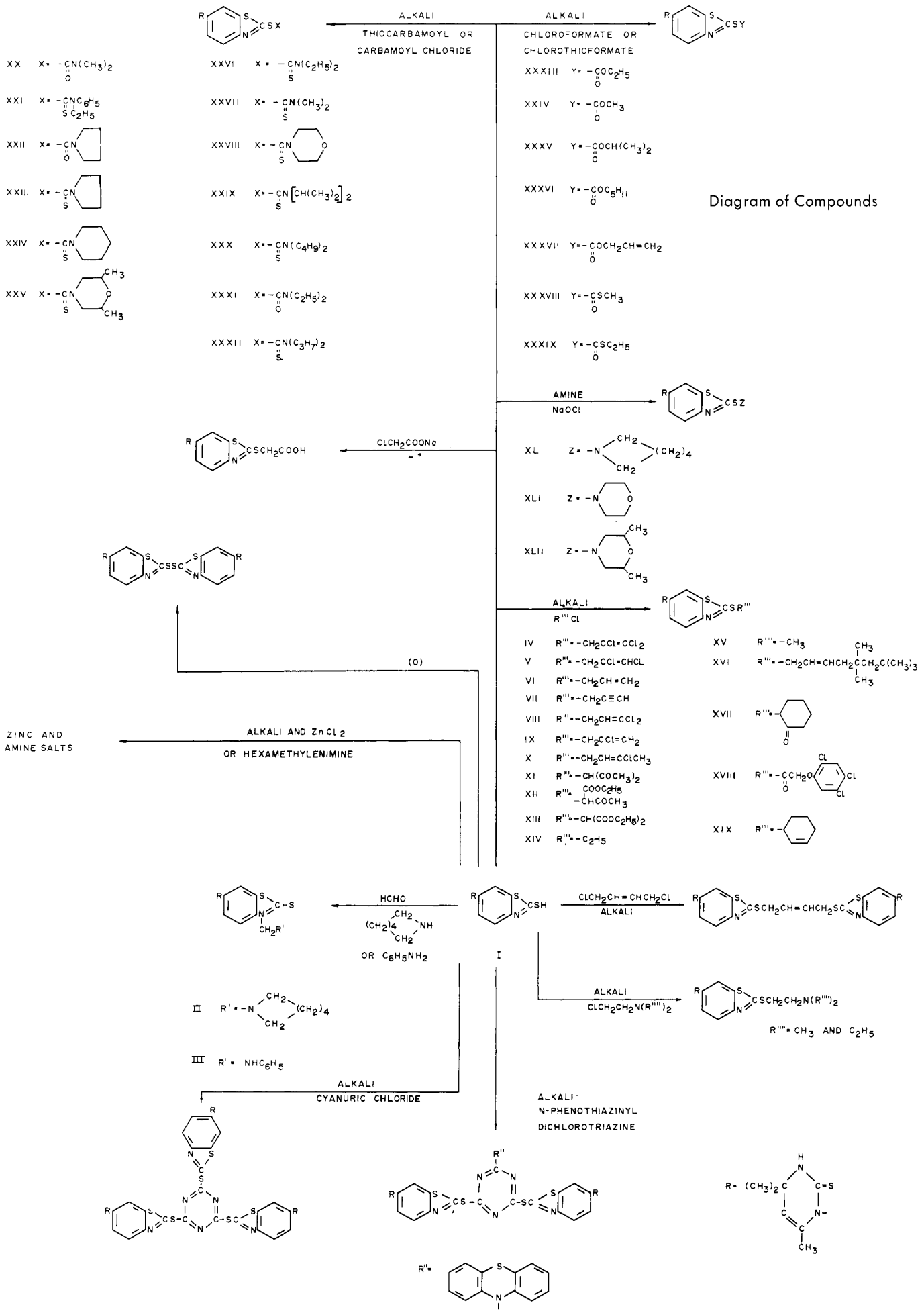
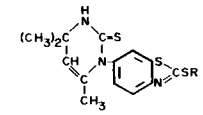

ALKALI
THIOCARBAMOYL OR
CARBAMOYL CHLORIDE
ALKALI
CHLOROFORMATE OR
CHLOROTHIOFORMATE
Diagram of Compounds
AMINE
NaOCl
ClCH2COONa
H+
ALKALI
R'''Cl
(O)
ZINC AND
AMINE SALTS
ALKALI AND ZnCl2
OR HEXAMETHYLENIMINE
HCHO
OR C6H5NH2
ClCH2CH=CHCH2Cl
ALKALI
ClCH2CH2N(R'''')2
R''''= CH3 AND C2H5
ALKALI
CYANURIC CHLORIDE
ALKALI
N-PHENOTHIAZINYL
DICHLOROTRIAZINE

Table I. 1-(2-Substituted-Thiobenzothiazol-6-yl)-1,4-Dihydro-2-Thioxo-4,4,6-Trimethylpyrimidine



No.	R	Halogen Compound	Reaction Conditions: Temp., °C.	Reaction Conditions: Time, hr.	Yield Crude %	M.P., °C.	Empirical Formula	N, % Calcd.	N, % Found	S, % Calcd.	S, % Found	Cl, % Calcd.	Cl, % Found
IV	$-CH_2CCl=CCl_2$	1,1,2,3-Tetrachloro-1-propene	50–60	4	51.5	200–202	$C_{17}H_{16}Cl_3N_3S_3$	9.04	8.84	20.69	20.61	22.88	22.95
V	$-CH_2CCl=CHCl$	*cis*- and *trans*-1,2,3-trichloropropene	50–60	4	23.2	182–186	$C_{17}H_{17}Cl_2N_3S_3$	9.76	9.58	22.35	22.61	16.47	16.79
VI	$-CH_2CH=CH_2$	Allyl Chloride	50–60	3	99.5	202–203[a]	$C_{17}H_{19}N_3S_3$	11.62	12.02	26.61	26.05	...	...
VII	$-CH_2C\equiv CH$	3-Bromo-1-propyne	25–30	6	97.5	204–206[b]	$C_{17}H_{17}N_3S_3$	11.69	11.23	...	...	...	...
VIII	$-CH_2CH=CCl_2$	1,1,3-Trichloro-1-propene	50–60	4	81.4	187–188[a]	$C_{17}H_{17}Cl_2N_3S_3$	9.76	9.74	...	...	...	...
IX	$-CH_2CCl=CH_2$	2,3-Dichloro-1-propene	50–60	4	93.5	202–203[c]	$C_{17}H_{18}ClN_3S_3$	10.61	10.32	...	...	...	...
X	$-CH_2CH=CClCH_3$	1,3-Dichloro-2-butene	50–60	4	92.5	159–161[a]	$C_{18}H_{20}ClN_3S_3$	10.25	10.33	...	...	8.64	8.69
XI	$-CH(COCH_3)_2$	3-Chloro-2,4-pentanedione	50–56	5	88.5	194–196[d]	$C_{19}H_{21}N_3O_2S_3$	10.02	9.66	...	...	...	...
XII	$-CHCOCH_3$ $\vert$ $COOC_2H_5$	Ethyl α-chloroacetoacetate	50–56	5	51.3	172–173[e]	$C_{20}H_{23}N_3O_3S_3$	9.35	9.55	21.40	21.04	...	...
XIII	$-CH(COOC_2H_5)_2$	Diethylchloromalonate	50–56	8	83.6	168–170[b]	$C_{21}H_{25}N_3O_4S_3$	8.76	8.91	20.05	20.59	...	...
XIV	$-C_2H_5$	Ethyl bromide	50–56	5	74.0	202–204[f]	$C_{16}H_{19}N_3S_3$	12.02	11.93	...	...	...	...
XV	$-CH_3$	Methyl iodide	50–56	5	83.4	216–218[f]	$C_{15}H_{17}N_3S_3$	12.53	12.10	28.67	28.14	...	...
XVI	$-CH_2CH=CHCH_2\overset{\displaystyle CH_3}{\overset{\vert}{C}}-CH_2C(CH_3)_3$ $\vert$ CH_3	5,5,7,7-Tetramethyl-2-octenyl chloride	50–56	5	86.5	168–170[f]	$C_{26}H_{37}N_3S_3$	8.62	8.43	19.72	19.13	...	...
XVII	2-Oxocyclohexyl	2-Chlorocyclohexanone	50–56	4	83.7	194–195[c]	$C_{20}H_{23}N_3OS_3$	10.06	10.03	...	...	...	...
XVIII	2,4,5-Trichlorophenoxyacetyl	2,4,5-Trichlorophenoxyacetyl chloride	50–56	6	98.6	178–180	$C_{22}H_{18}Cl_3N_3O_2S_2$	7.98	7.66	...	...	20.19	19.50
XIX	3-Cyclohexenyl	3-Bromocyclohexene	50–56	4	89.5	217–219	$C_{20}H_{23}N_4S_4$	10.46	10.16	...	...	...	...

[a] Recrystallization from ethyl acetate and chloroform. [b] Recrystallization from chloroform. [c] Recrystallization from benzene and chloroform. [d] Recrystallization from benzene. [e] Recrystallization from ethyl acetate. [f] Recrystallization from acetone.

The reaction of the potassium salt of I with cyanuric chloride or *N*-phenothiazinyl dichlorotriazine in an acetone medium gave 2,4, 6-tris-[6-(1,4-dihydro-2-thioxo-4, 4, 6-trimethylpyrimidin-1-yl) benzothiazol-2-ylthio]-*S*-triazine and 10-[2, 6-bis[6-(1,4-dihydro-2-thioxo-4, 4, 6-trimethylpyrimidin-1-yl) benzothiazol-2-ylthio]-*S*-triazin-4-yl]phenothiazine in yields of 98 and 94.5%, respectively. The melting points of both products was greater than 300° C.

The reaction of an aqueous solution of the sodium salt of I with zinc chloride furnished the zinc salt of I in 99% yield. The hexamethylenimine salt of I, m.p. 185–187° C. was prepared in 79.2% yield by stirring an ether slurry of I with hexamethylenimine.

The 1-(2-substituted-thiobenzothiazol-6-yl)-1, 4-dihydro-2-thioxo-4, 4, 6-trimethylpyrimidines (IV-XIX) were prepared by the reaction of the sodium or potassium salt of I in either an aqueous or acetone medium with the appropriate halogen compounds which are listed in Table I. The use of 1,4-dichloro-2-butene in this reaction furnished 2,2′-(2-butenylenedithio) bis [6-(1, 4-dihydro-2-thioxo-4, 4, 6-trimethylpyrimidin-1-yl)benzothiazole], m.p. 158–160° C., in 98% yield.

The sodium salt of I in an aqueous solution reacted with β-diethyl or dimethylaminoethyl chloride hydrochloride to form 1, 4-dihydro-1-[2-(diethylaminoethylthio) benzothiazol-6-yl]-2-thioxo-4, 4, 6-trimethylpyrimidine and the corresponding dimethyl derivative. The former compound, m.p. 160–162° C. after recrystallization from ethyl alcohol and the latter compound, m.p. 185–187° C. after recrystallization from ethyl alcohol, were obtained in yields of 97.5 and 94.5%, respectively.

The 6-(1, 4-dihydro-2-thioxo-4, 4, 6-trimethylpyrimidin-1-yl)benzothiazol-2-yl ester of *N,N*-dialkylthiol (or dithio) carbamic acids (XX-XXXII) were prepared by the reaction of the potassium salt of I with the appropriate *N,N*-disubstituted thiocarbamoyl or carbamoyl chloride which are listed in Table II.

The substitution of alkyl chloroformate or alkyl chlorothioformate for the *N,N*-disubstituted thiocarbamoyl or carbamoyl chlorides in the above reaction furnished the *S*-[6-(1, 4-dihydro-2-thioxo-4, 4, 6-trimethylpyrimidin-1-yl) benzothiazol-2-yl] *O* (or *S′*)-alkyl thiol (or dithiol)carbonates (XXXIII-XXXIX) which are listed in Table III.

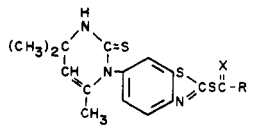
The oxidative condensation of I with hexamethylenimine, morpholine or *cis*- and *trans*-2,6-dimethylmorpholine furnished the thiazolesulfenamides in yields of 77 to 98% (Table IV).

The reaction of the alkali salt of I with the sodium salt of chloroacetic acid followed by neutralization of the reaction mixture with concentrated hydrochloric acid gave 6-(1, 2, 3, 4-tetrahydro-2-thioxo-4, 4, 6-trimethylpyrimidin-1-yl)benzothiazol-2-yl thioacetic acid, m.p. 196–198° C. with decomposition, in 79% yield.

ACKNOWLEDGMENT

The writers wish to acknowledge their indebtedness to M. Steele, E.E. Null, and C. Raynes for analyses performed.

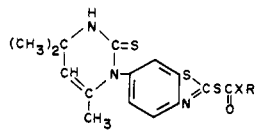
Table II. 6-(1,4-Dihydro-2-Thioxo-4,4,6-Trimethylpyrimidin-1-yl) Benzothiazol-2-yl Ester of *N,N*-Dialkylthiol (or Dithio) Carbamic Acids



No.	X	R	Disubstituted Carbamoyl or Thiocarbamoyl Chloride	Yield Crude, %	M.P., °C.	Empirical Formula	N, % Calcd.	N, % Found	S, % Calcd.	S, % Found
XX	*O*	$(CH_3)_2N$—	$(CH_3)_2NCOCl$	61.4	196–198[a]	$C_{17}H_{20}N_4OS_3$	14.27	13.70	24.51	24.99
XXI	*S*	$C_6H_5N(C_2H_5)$—	$C_6H_5NCSCl(C_2H_5)$	97.5	173–175[b]	$C_{23}H_{24}N_4S_4$	11.56	11.82	...	...
XXII	*O*	Pyrrolidyl	1-Pyrrolidinecarbonyl chloride	52.5	181–183[b]	$C_{19}H_{22}N_4OS_3$	13.39	12.96	...	...
XXIII	*S*	Pyrrolidyl	1-Pyrrolidinethiocarbonyl chloride	11.5	218–220	$C_{19}H_{22}N_4S_4$	12.89	12.16	...	...
XXIV	*S*	Piperidyl	1-Piperidinethiocarbonyl chloride	89.4	151–153[c]	$C_{20}H_{24}N_4S_4$	12.49	11.93	28.59	28.44
XXV	*S*	2,6-Dimethylmorpholinyl	4-(2,6-Dimethylmorpholinethiocarbonyl)-chloride	41.9	173–174[b]	$C_{21}H_{26}N_4OS_4$	11.70	11.89	26.79	26.25
XXVI	*S*	$(C_2H_5)_2N$—	$(C_2H_5)_2NCSCl$	96.5	227[d]	$C_{19}H_{24}N_4S_4$	12.83	12.30	...	...
XXVII	*S*	$(CH_3)_2N$-	$(CH_3)_2NCSCl$	61.3	213–215[e]	$C_{17}H_{20}N_4S_4$	13.71	13.98	...	...
XXVIII	*S*	Morpholinyl	4-Morpholinethiocarbonyl chloride	97.5	199–201[e]	$C_{19}H_{22}N_4OS_4$	12.43	12.25	...	...
XXIX	*S*	$[(CH_3)_2CH]_2N$-	$[(CH_3)_2CH]_2NCSCl$	88.2	197–199[e]	$C_{21}H_{28}N_4S_4$	12.06	12.27	27.60	27.36
XXX	*S*	$(C_4H_9)_2N$-	$(C_4H_9)_2NCSCl$	99.5	180–182[e]	$C_{23}H_{32}N_4S_4$	...	...	26.03	25.82
XXXI	*O*	$(C_2H_5)_2N$-	$(C_2H_5)_2NCOCl$	76.0	144–146	$C_{19}H_{24}N_4OS_3$	13.32	13.39	22.87	23.08
XXXII	*S*	$(C_3H_7)_2N$-	$(C_3H_7)_2NCSCl$	54.0	185–187[e]	$C_{21}H_{28}N_4S_4$	12.06	12.12	27.60	26.95

[a] Recrystallization from ethyl alcohol and acetone. [b] Recrystallization from acetone. [c] Recrystallization from ethyl alcohol and chloroform. [d] Recrystallization from chloroform and ethyl acetate. [e] Recrystallization from chloroform and ethyl ether.

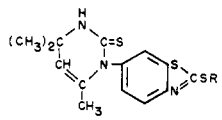
Table III. S-[6-(1,4-Dihydro-2-Thioxo-4,4,6-Trimethylpyrimidin-1-yl) Benzothiazol-2-yl] O (or S')-Alkyl Thiol (or Dithiol) Carbonates



No.	X	R	Chloroformate or Chlorothioformate	Yield Crude, %	M.P., °C.	Empirical Formula	N, % Calcd.	N, % Found	S, % Calcd.	S, % Found
XXXIII	O	C_2H_5-	$ClC(O)OC_2H_5$	86.2	127–129[a]	$C_{17}H_{19}N_3O_2S_3$	10.68	10.02	24.44	24.49
XXXIV	O	CH_3-	$ClC(O)OCH_3$	79.2	120–122[a]	$C_{16}H_{17}N_3O_2S_3$	11.07	11.26	25.35	25.00
XXXV	O	$(CH_3)_2CH$-	$ClC(O)OCH(CH_3)_2$	83.8	156–158[a]	$C_{18}H_{21}N_3O_2S_3$	10.31	9.78	...	...
XXXVI	O	C_5H_{11}-	$ClC(O)OC_5H_{11}$	45.9	142–144[a]	$C_{20}H_{25}N_3O_2S_3$	9.65	9.95	22.08	21.79
XXXVII	O	$CH_2=CHCH_2$-	$ClC(O)OCH_2CH=CH_2$	14.9	133	$C_{18}H_{19}N_3O_2S_3$	10.36	10.58	...	...
XXXVIII	S	CH_3-	$ClC(O)SCH_3$	93.0	146–148	$C_{16}H_{17}N_3OS_4$	10.62	10.67	...	...
XXXIX	S	C_2H_5-	$ClC(O)SC_2H_5$	90.5	135–137[a]	$C_{17}H_{19}N_3OS_4$	10.26	10.63	31.31	30.75

[a] Recrystallization from ethyl alcohol.

Table IV. Sulfenamides



No.	R	Amine	Mole Ratio Amine to J	Yield Crude, %	M.P., °C.	Empirical Formula	N, % Calcd.	N, % Found	S, % Calcd.	S, % Found
XL	Hexamethylen-imino	Hexamethylen-imine	1.5:1	93.5	170–173[a]	$C_{20}H_{26}N_4S_3$	13.38	13.56	22.98	22.66
XLI	Morpholinyl	Morpholine	3:1	77.0	168–170[a]	$C_{18}H_{22}N_4OS_3$	13.78	13.70	23.60	23.75
XLII	2,6-Dimethyl-morpholinyl	*cis*- and *trans*-2,6-Dimethyl-morpholine	3:1	98.0	123–125[a]	$C_{20}H_{26}N_4OS_3$	12.89	12.59	...	...

[a] Melting point with decomposition. Recrystallization from ethyl alcohol.

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