THIOUREAS

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I. Introduction

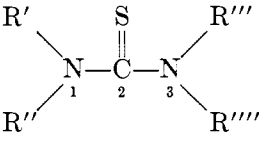
The literature concerning thiourea and its derivatives is voluminous. These compounds have found their way into almost every branch of chemistry. Commercially, they are used in dyes, photographic film, elastomers, plastics, and textiles. Certain thiourea derivatives are insecticides, preservatives, rodenticides, and pharmaceuticals. In the academic field thioureas are of great value in the characterization of organic compounds. For example, advantage is taken of the fact that amines can easily be converted into solid, sharp-melting substituted thioureas by allowing them to react with an appropriate isothiocyanate (see Section III,C). Organic acids readily yield pseudothiuronium salts which are crystalline and have sharp melting points. The ability of thiourea to form crystalline complexes with branched hydrocarbons and cycloaliphatic structures has led to their use in the separation of mixtures of organic compounds (2, 85, 86, 87, 143, 171). Thioureas are also widely used as intermediates in organic syntheses. Because of the great versatility of these compounds, it was necessary to set definite limits to the scope of this review with respect to literature sources, types of thiourea derivatives, and their uses.

A thorough investigation was made of *Chemical Abstracts* from January, 1907, through June, 1954. Some selected references from *Beilstein* were checked and, in addition, current issues of certain journals were included. Compounds classified in the tables in Section IV are those which pertain to the biological discussion or which illustrate the various methods of synthesis in Section III. Especially emphasized are the 1,3-di(substituted phenyl) compounds. Considerable attention is also paid to all substituted thioureas containing aromatic, aliphatic, alicyclic, and heterocyclic groups or any combination of the above-mentioned types. Some *N*-acyl derivatives, pseudothioureas, thiuronium salts, guanylthioureas, and *N*-cyclic thioureas where only one ureido nitrogen is involved are included. Omitted are those compounds in which both ureido nitrogens or one nitrogen and the sulfur are included in a heterocyclic ring (e.g., pyrimidines, thiazoles, etc.). Sulfanilyl- and sulfanylthioureas are not included, because they have been fully covered in a recent review article (151).

With regard to applications, only the biological properties of thioureas are considered. Some emphasis is placed on thiourea derivatives as chemotherapeutics for tuberculosis in view of recent interest in this field.

The syntheses of thioureas given in Section III are those of general application. Certain modifications are often required, owing to the peculiarities of the materials involved. These special techniques are in many cases available in the references given for specific compounds listed in Section IV.

The nomenclature used is that designated by *Chemical Abstracts*. The thiourea system is numbered as shown below:



S-Substituted thioureas are referred to as pseudothioureas rather than as isothioureas, although the latter classification is common in the literature.

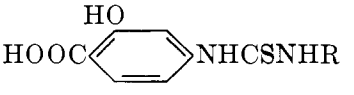
II. Biological Properties of Thioureas

A. Antituberculous Activity

In the early 1920's a remedy for tuberculosis was patented (251) which was described as the gold salt of the product obtained from the reaction of carbon disulfide and an alkali or alkaline earth hydroxide with an amino acid or an ester of an amino acid, i.e., a salt such as $(KOOCCH_2NHCS_2)_3Au$. Considerable work with gold compounds as chemotherapeutic agents for tuberculosis followed immediately. However, it was not until many years later that thioureas, which can also be prepared from carbon disulfide and an amine in the presence of alkali, were considered for the treatment of this disease.

In 1944 a patent (18) was issued for copper compounds made from thioureidobenzoic acids which were said to be active in treating tuberculosis. Since bacteria such as tubercle bacilli contain large amounts of lipoidal tissue, long-chain alkylthioureas which are lipoid-soluble were suggested by Massie (161) as therapeutic agents. Chilean workers (35, 236) have reported somewhat favorable results using thiourea itself for tuberculosis. Many thiourea derivatives have been tested for antitubercular activity. Some showed no activity at all (97, 119, 240), while others did look promising in *in vitro* studies (30, 33, 110, 219, 239). However, excluding the sulfonylthioureas, very little success was found in the treatment of tuberculosis with this class of compounds until very recently.

In 1952 a number of thiourea derivatives of *p*-aminosalicylic acid in *in vitro* tests were found to be equal to or more active than the acid itself (7, 137, 204). Maximum activity in compounds of the type



was achieved when R was aromatic. If R was aliphatic or if *o*- or *m*-aminosalicylic acid was used instead of *p*-aminosalicylic acid, the activity dropped or completely disappeared. The compound $4,3\text{-}(HOOC)(HO)C_6H_3NHCSNHC_6H_5$ was found to prolong life in animal studies but, although the disease was ar-

rested, it did not produce a complete cure. In clinical tests there was no evidence of development of resistance to this compound.

In the following year 4,4′-diethoxythiocarbanilide was found to possess high antitubercular activity in mice infected with bacillus H37Rv (121, 164); hence over three hundred thiocarbanilides were made and tested. These compounds were tested *in vitro* against *M. tuberculosis* and *in vivo* in experimentally infected mice. Almost one-third of these compounds, the majority of which were 1,3-di(4-substituted phenyl)thioureas, showed significant activity in the *in vivo* studies in mice (79). Eight of the more active thiocarbanilides were subjected to tests in guinea pigs (149), and seven of these showed suppressive effects. Two of the seven thiocarbanilides, 4-ethoxy-4′-isobutoxythiocarbanilide and 4-*n*-butoxy-4′-dimethylaminothiocarbanilide, exceeded the activities of *p*-aminosalicylic acid and streptomycin and approached that of isoniazid. Combinations with streptomycin and isoniazid gave enhanced effects.

From these data certain specific structural requirements were observed for the antituberculous activity of thiocarbanilides of the following structure:

(*a*) Shortening of the 4-substituent to CH_3O— destroys the activity.

(*b*) Lengthening of the chain in the 4-substituent increases the activity to a maximum at three to four carbon atoms. Further increase in chain length causes a decrease in activity until it completely disappears at R = $C_8H_{17}O$—.

(*c*) Replacement of the alkoxy group by an alkyl group of the same length gives similar activity.

(*d*) Branching of the alkyl at the carbon atom adjoining the ring leads to loss of activity.

(*e*) If one of the 4-alkoxy groups is replaced by a halogen or dialkylamino substituent, activity is retained.

(*f*) Replacement of both alkoxy groups by halogen or dialkylamino groups causes total loss of activity.

(*g*) That the 4-substituent is necessary in both rings is shown by the fact that replacement of one alkoxy group by hydrogen causes loss of activity. Furthermore, the 2- and 3-position isomers are inactive.

(*h*) A second substituent in the ring destroys the activity, as does an additional substituent on the ureido nitrogen.

(*i*) The thiocarbanilide moiety is necessary, since corresponding carbanilides, guanidines, guanylthiourea, dithiobiurets, and cyclohexyl-substituted thioureas are inactive.

No clear-cut correlation was found between *in vitro* and *in vivo* activities. Preliminary studies indicate that resistance to these thioureas develops slowly *in vitro*, and no resistance has been observed in animal experiments. Representative compounds showed undiminished activity against streptomycin- and isoniazid-resistant strains of *M. tuberculosis* H37Rv.

The mode of action of these thioureas is not yet known, although it has been

found that it is not based on phenoloxidase activity nor is it due to an effect on cytochrome C (164). Buu-Hoï and Xuong (36), who also prepared a number of thiocarbanilides for antituberculosis studies, believe that the metal-chelating property of thiourea and a favorable partition coefficient for the molecule between aqueous and fatty phases are instrumental in their activity.

B. ANTITHYROID ACTIVITY

One of the most widely studied aspects of thiourea and its derivatives has been their antithyroid activity. Many experimental results have been published on this subject (4, 43, 100, 126, 131, 135, 156, 159, 188, 192, 194, 195, 212, 213, 215, 229, 234, 237, 238, 246, 248). There are many discrepancies in the results of the different workers which may, in some cases, be due to differences in testing techniques. Nevertheless, certain generalities reported in several of the publications (5, 6, 165) are in agreement. Thiourea has approximately one-tenth the activity of thiouracil. Replacement of one, two, or three of its hydrogen atoms by methyl groups has no appreciable effect on the activity. However, 1,1′,3,3′-tetramethylthiourea is a considerably more potent compound. Replacement of the hydrogen atoms by higher alkyl groups usually gives less active material than unsubstituted thiourea. Exceptions to this are 1,3-diethyl-, 1,3-diisopropyl-, and 1-isopropylthiourea. Substitution of large aromatic or polar groups for one or more of the hydrogen atoms decreases the activity. Pseudothioureas are inactive, but incorporation of the thiourea moiety into a ring not involving the sulfur seems to increase the potency (247).

C. HYPNOTIC AND ANESTHETIC PROPERTIES

The relative hypnotic effects of a number of 1-aryl- and 1-alkyl-3-arylthioureas have been correlated (57). It was found that the effectiveness of these compounds improved with increasing molecular weight within a homologous series. Thioureas of the general formula $R'''C_6H_4N(R)CSNR'R''$ have been patented (34) as hypnotics suitable for use as general or local anesthetics. This patent specifies those compounds in which R = alkyl or alkenyl (less than eight carbon atoms), R′ and R″ = H, alkyl, or alkenyl (more than eight carbon atoms), and R‴ = alkyl radical of one to eight carbon atoms. High local anesthetic activity and low toxicity have been claimed (46) for a group of pseudothiuronium salts. Sulfur substituents in these salts included 2-aminoethyl, 2-butylaminoethyl, 2-(1-piperidyl), 2-(4-morpholinyl), and 3-dibutylaminopropyl groups. Another member of this class of compounds, 1,4-bis(pseudothiocarbamidomethyl)naphthalene dihydrochloride, has been reported to possess analgesic properties (8). Certain guanylthioureas of the general formula $RNHCSNH(=NH)NH_2$, where R is an aromatic radical, have shown varying degrees of analgesic action (222). Some disubstituted thioureas into which a benzothiazole moiety has been incorporated, e.g., 1-allyl-3-(ethoxybenzothiazole-2)-, 1-phenyl-3-(benzothiazole-2)-, and 1-phenyl-3-(6-chlorobenzothiazole-2)thiourea, have been reported to possess local anesthetic properties (139).

D. ANTHELMINTIC ACTIVITY

A number of patents have been granted for derivatives of thiourea which are claimed to have destructive action against trypanosomes. Certain of these compounds which are dyes as well as anthelmintics (11, 12, 13) are prepared by heating thiophosgene and amino acyl derivatives of two different aromatic amino acids, at least one of which is of the naphthalene series. A similar group of compounds for which the same properties are claimed have the formula $(ArNHX'NHX''NH)_2CS$, where Ar is phenyl or naphthyl and X′ and X″ are heterocyclic nuclei (66). Very closely related, but without the —NHX′— in the formula given above, is another group of compounds claimed to be useful in combating blood parasites (65). Thiourea derivatives of aromatic heterocyclic compounds with a quaternary nitrogen in the nucleus are said to have similar activity (209). The anthelmintic activity of eighteen monoaryl-substituted thioureas was studied with earthworms (218). Of this group, 2-carbethoxyphenylthiourea showed remarkable vermicidal activity. 1-Naphthylthiourea has been found to be efficacious against intestinal parasites in man and dogs (93). However, it is interesting to note that its 2-analog and 1,3-dinaphthylthiourea are ineffective.

E. ANTIBACTERIAL PROPERTIES

Various types of thioureas have been reported to have antibacterial activity. An aromatic or heterocyclic amine with an alkyl side chain when incorporated into a thiourea shows specific action for the bacteria which cause abortion in cattle (19). Certain guanyl compounds, such as *S*-dodecyl- and *S*-ethylguanylpseudothiourea, are claimed to have strong bactericidal properties (81). The best of a large group of arylthioureas, tested for fungicidal action in soy sauce, was $2\text{-}HOC_6H_4NHCSNH_2$ (220). Other monoarylthioureas (186) and mercury derivatives of arylthioureas (109) have shown antibacterial activity. Thiourea, allylthiourea, and butylthiourea inhibit *Cryptococcus neoformans* (207). Some 1-aryl-3-allylthioureas have been reported to be effective against bacterial infections (99). Several sources have reported activity for various pseudothiuronium salts. Especially effective against gram-negative organisms was a group of water-soluble compounds of the general formula $RC_6H_4(OA)_nSC(NHR')=NH\cdot HX$ (17), where R is an alkyl group of four to twelve carbon atoms, R′ is H, CH_3, C_2H_5, or C_4H_9, A is an alkylene group of two or three carbon atoms, n is 1, 2, or 3, and X is the anion of an acid. Numerous 2-alkylpseudothiourea hydrohalides and their 1,3-dialkyl derivatives were tested for germicidal properties and several showed marked activity (9). Maximum effect against *Staphylococcus aureus* and *Eberthella typhi* was achieved when the sulfur substituent was $C_{12}H_{25}$ or $C_{14}H_{29}$ and the nitrogen was substituted with methyl or ethyl groups. Some alkenylene-bis-pseudothiuronium compounds have been reported to be active against certain parasitic and bacterial diseases (45). It is interesting to note that some of the 1,3-di(substituted phenyl)thioureas which possessed high antituberculous activity (164) also had significant activity against several species of ac-

tinomyces and fungi. Thiocarbamido derivatives of diaryl sulfones and sulfides, both mono and bis, have shown marked antibacterial properties (128).

F. ANTIPHENOLOXIDASE ACTIVITY

The antiphenoloxidase or antityrosinase activity of thioureas is attributed to their ability to form complexes with copper, the essential metal component of the enzyme (150). Phenyl-, *p*-phenetyl-, and *p*-butoxyphenylthiourea are all potent inhibitors. In addition, 3,4-dimethylphenyl-, 2,5-dimethylphenyl-, 1-naphthyl-, benzyl-, allyl-, and ethylenethiourea have all been found to inhibit the activity of potato phenoloxidase in descending order (129). Much the same order was found in the inhibition of melanin formation. An attempt has been made to link the toxicity of certain thioureas for rats and their action on phenoloxidase, but no strict relation was observed (130).

G. INSECTICIDAL PROPERTIES

Some thioureas have been found to be useful as insecticides. Thiocarbamido-DDT is more effective than DDT against bed bugs, although its action is of shorter duration (249). Simple compounds such as phenyl-, allyl-, and tolylthiourea are useful in destroying larvae and adults of various strains of *Drosophila melanogaster* (44). 1-Allyl-3-(4-chloro-2-methylphenyl)thiourea has been claimed to be effective in controlling the Japanese beetle or the Mexican jumping bean beetle (23). Thioureas which are said to be excellent contact insecticides are those with an 1-alkyl substituent at least eight carbons in length and a 3-substituent which contains a water-soluble polar group (202). 1-Dodecyl- and 1,3-didodecylthiourea are toxic to the flesh fly larva (120). In this case, a phenyl group on the nitrogen or a substituent on the sulfur decreases the toxicity. Certain thiuronium salts of phosphorus acids are listed as insecticides (169). 2-Benzyl-1-(1-naphthyl)thiourea and its chloro derivatives were found to be effective against *Altogenus piccus* and *Tinia pellionella* (162).

H. RODENTICIDAL ACTIVITY

α-Naphthylthiourea (ANTU) is a well-known rat poison. Its success is based on the fact that it is much more toxic to rats than it is to cats, fowl, etc. (29). Numerous compounds, many of them thioureas, have been tested to see if this property can be improved. Certain specifications have been suggested for the structure of thioureas most effective as rodenticides. A study of 196 compounds showed that acute toxicity is enhanced when a single aromatic radical is attached to one nitrogen. Two or more substituents on one or both nitrogens or a substituent on the sulfur decrease the toxicity (59). Another reference makes slightly different stipulations (193). For the general formula $RR'NCSNH_2$, R must be H or an aliphatic group of not more than six carbons. R′ must be an aromatic group with a molecular weight of at least 100, so that the entire molecule has a molecular weight of at least 175. In addition to ANTU, 2-biphenylyl- and 4-biphenylylthiourea are listed as effective compounds. Phenylthiocarbamide shows high

toxicity, but its bad taste is revolting to rats. Additional compounds of mild toxicity are 1,3-bis(2,4,6-trichlorophenyl)thiourea, 1-methyl-3-phenylthiourea, and morpholinylthiourea (138).

Considerable work has been done to determine the mechanism of poisoning by ANTU and similar thioureas. It has been found that acute poisoning by γ-naphthyl-, phenyl-, and allylthiourea, as well as by thiourea itself, produces hyperglycemia in rats and guinea pigs (69, 70). ANTU and related compounds have a selective effect on capillaries of the lungs of rats and dogs and cause an increase in permeability, with large volumes of fluid collecting in the lungs and pleura (154). Thus, dogs and rats tend to die of pulmonary edema, while cats and fowl develop fatty livers (29). In studying the effects of compounds with antithyroid activity, it was found that these materials depress thyroid functional activity. The lowered basal metabolic rate and thyroid hyperplasia reflect the resulting increase in pituitary activity (159).

Certain thioureas with antithyroid activity tend to protect rats against poisoning by ANTU. Thiourea, phenylallylthiourea, *N*-ethylidenethiourea, and isopropylthiourea reduced significantly the toxic effects on rats (39, 47, 167). 1-Ethyl-1-phenylthiourea is also effective, while ethyl- and butylthiourea give some protection (203). Effective doses of these protective compounds are unrelated to their acute toxicity or to their relative antithyroid activity.

I. MISCELLANEOUS PROPERTIES

A number of other biological properties have been observed. Thiourea, when used over a long period of time, has been reported to cause the development of thyroid tumors, some of which were malignant (185). Other investigators (51, 235) have found that in certain specific experiments thiourea inhibits cancer. 4,4′-Diaminodiphenylthiourea has also shown an inhibitory effect on experimental cancer in mice (250). Antipyretic properties have been found for some 1-alkyl-3-guanylthioureas, but these compounds are too toxic to be of any value (222). 1-Methylpseudothiourea displays appreciable anticurare activity (82, 189). In contrast to certain arylthioureas, previously mentioned under rodenticides, which cause hyperglycemia, methyl- and benzylpseudothiourea have been found to lower the blood sugar content (188). An attempt to substitute 1-allyl-3-guanylthiourea, which also possesses this characteristic, for insulin (114) was unsuccessful. A study was made of the influence of chain length in 2-alkylpseudothioureas on antiacetylcholine, antihistamine, and tonus-decreasing action on the ileum (83). Intensity of action was found to increase two- to threefold with each additional methylene group up to nine carbon atoms. At this point it dropped off, probably because of water insolubility. The search for antimalarials led to the testing of many substituted thioureas and pseudothioureas (52, 97, 163, 196). However, none of these compounds have been reported to possess antimalarial activity. No generalization can be made concerning the effect of thioureas on blood pressure, since this varies with the compound and the animal (38, 56, 188, 242). The use of thiourea for protection against lethal doses of x-ray radiation has been considered (112, 170), and in some cases has increased the

survival time of mice. Antispasmodic activity has been observed in 3-diethylaminomethyl-4-hydroxy-6-thiocarbamido-2-methylquinoline (101) and in pseudothiuronium salts prepared from various 1-(2-chloroethyl)pyrrolidines (147). 1-Carbobenzoxy-4-thiocarbamidopiperazine is claimed to be an anticonvulsant with low toxicity (103). A study of the influence of phenylthiourea and *o*- and *p*-tolylthiourea on the amyloclastic activity of amylases showed that all of these thiourea derivatives accelerated the splitting action (68). Diethylaminoethylthiourea and similar compounds have been patented as substitutes for ergot (111). In some cases multiple claims are made for particular thioureas. Thus, Théophyséme (iodoethylallylthiourea) has been said to be useful against arteriosclerosis, asthma, and scrofula (3). Recently, compounds of the type $RNHCSNHR'COCH_2CN$, where R and R′ are alkyl and aralkyl groups, have been claimed to be useful as cardiovascular, diuretic, and chemotherapeutic agents (179).

III. Preparation of Thiourea Derivatives

There are several common syntheses for derivatives of thiourea. Many variations have been applied to each of these when circumstances demanded it. As might be expected, certain advantages and disadvantages arise from the use of any one of these methods of preparation.

A. Carbon Disulfide and an Amine

$$CS_2 + 2RNH_2 \rightarrow RHNCSNHR + H_2S$$

The reaction shown in the above equation is the common way of describing the overall reaction of primary amines with carbon disulfide to give 1,3-disubstituted thioureas. It does not, however, tell the whole story. Many theories concerning the mechanism of this reaction have been published (27a, 67a, 67b, 122, 156, 158, 240a, 243a), and the conclusions are somewhat conflicting. Considering the experimental data which have been presented, the most reasonable course for the reaction seems to be:

$$(1)\quad RNH_2 + CS_2 \rightleftarrows RHN\overset{\overset{S}{\|}}{C}SH$$

$$(2)\quad RHN\overset{\overset{S}{\|}}{C}SH + RNH_2 \rightleftarrows [RHN\overset{\overset{S}{\|}}{C}S]^-[NRH_3]^+$$

$$(3)\quad [RHN\overset{\overset{S}{\|}}{C}S]^-[NRH_3]^+ \xrightarrow{\text{heat}} RNCS + RNH_2 + H_2S$$

$$(4)\quad RNCS + RNH_2 \rightarrow RHNCSNHR$$

$$2RNH_2 + CS_2 \rightarrow RHNCSNHR + H_2S$$

It is generally known that ammonia and primary and secondary aliphatic and aromatic amines form dithiocarbamic acids when treated at room temperature

with carbon disulfide (27a, 48a, 87a, 138a, 156, 158). With few exceptions (49a) these acids are unstable, but their existence has been confirmed by isolating them as salts. Dithiocarbamic acids react with a second mole of ammonia or amine to give ammonium or substituted ammonium dithiocarbamates. The salts formed with ammonia or aliphatic amines are usually stable enough for identification (3a, 24a, 27a, 48a, 170a, 243a). Those formed with aromatic amines are less stable, probably because of the lower basicity of aromatic amines (158), and usually cannot be isolated (54). It is possible, however, to prepare and identify ammonium and alkylammonium salts of aryldithiocarbamic acids (53, 54, 67a, 67b, 80a, 158). Thus, it seems reasonable to suppose that the arylammonium salts do exist for a short time, but rapidly decompose to the acid and amine or *via* step 3.

While primary amines give 1,3-disubstituted thioureas with carbon disulfide, secondary amines and carbon disulfide do not give the corresponding tetrasubstituted compounds. This fact, plus studies of the formation of certain trisubstituted thioureas when mixed salts of dithiocarbamic acids are decomposed by heat (80a, 243a), gives credence to steps 3 and 4. It has been observed that salts of monosubstituted dithiocarbamic acids when heated give thioureas, whereas salts of disubstituted dithiocarbamic acids do not.

$$[\mathrm{RHNCSS}]^-[\mathrm{NH_2R_2'}]^+ \xrightarrow{\text{heat}} \mathrm{RHNCSNR'R'} + \mathrm{H_2S}$$

$$[\mathrm{R_2NCSS}]^-[\mathrm{NH_3R'}]^+ \xrightarrow{\text{heat}} \text{no thiourea}$$

The most reasonable explanation for this is that the isothiocyanate is first formed, as shown in step 3. In order for this to occur there must be a hydrogen available in the moiety $[\mathrm{RHNCSS}]^-$. The isothiocyanate then adds the amine, either primary or secondary, which was originally involved in the formation of the ammonium salt as shown in step 4. This is borne out by the structure of the trisubstituted thiourea which is formed upon the decomposition of such a mixed dithiocarbamate and explains why tetrasubstituted thioureas cannot be prepared by this method. Further evidence of the presence of the isothiocyanate is that when the reaction of amine and carbon disulfide is carried out in alcoholic medium and the reaction time is lengthy, thiourethans are sometimes formed as well as the desired product (157).

Although the equation indicates that theoretically two moles of amine should be used per mole of carbon disulfide, it is usually wise to use an excess of the latter in view of its high volatility. Alcohol (7, 118, 178, 184, 201, 216) or benzene may be used in the reaction as solvent for the starting materials or to raise the reaction temperature. A commercial synthesis for 1,3-diarylthioureas in which the reaction is carried out in a partial vapor phase without solvent has also been patented (140). It is not necessary to isolate the intermediate dithiocarbamate, and the reaction is considered complete when the evolution of hydrogen sulfide ceases.

The most common application of this method is to synthesize 1,3-disubstituted thioureas. However, it can also be adapted to (*a*) 1-monosubstituted,

(*b*) unsymmetrical 1,3-disubstituted, and (*c*) certain 1,3,3-trisubstituted thioureas.

$$RNH_2 + CS_2 \rightarrow RHNCSSH$$

(a) $RHNCSSH + NH_3 \rightarrow [RHNCSS]^-[NH_4]^+ \xrightarrow{\text{heat}} RHNCSNH_2 + H_2S$

(b) $RHNCSSH + R'NH_2 \rightarrow [RHNCSS]^-[NR'H_3]^+ \xrightarrow{\text{heat}} RHNCSNHR' + H_2S$

(c) $RHNCSSH + R'_2NH \rightarrow [RHNCSS]^-[NR'_2H_2]^+ \xrightarrow{\text{heat}} RHNCSHR'_2 + H_2S$

If the ratio of the basicity of the two amines to be used is sufficiently great, it is possible merely to add the stronger of the two amines to the dithiocarbamate formed from the weaker amine and carbon disulfide and then apply heat.

$$[C_4H_9NHCSS]^-[NH_3C_4H_9]^+ + NH(CH_3)_2 \rightarrow$$

$$[C_4H_9NHCSS]^-[NH_2(CH_3)_2]^+ + C_4H_9NH_2$$

$$H_2S + C_4H_9NHCSN(CH_3)_2 \xleftarrow{\text{heat}}$$

If this difference in basicity is small, it is necessary to prepare the mixed dithiocarbamate *via* a different route (24a) and then to decompose by heating.

A major drawback in using this method to prepare 1,3-disubstituted thioureas is that it is often very slow. For example, it was found necessary to warm *m*-nitroaniline and carbon disulfide for 200 hr. in forming the disubstituted thiourea (174). Several means have been successfully employed to accelerate this reaction.

1. Addition of sulfur

It was reported in 1899 that the reaction rates of a number of amines with carbon disulfide could be greatly increased by adding 10 per cent of sulfur (122). In later years it was found that only a trace of sulfur was sufficient (36, 105, 123, 187). A serious disadvantage of this means of catalyzing the reaction is the removal of sulfur from the product, especially in cases where the latter possesses solubility characteristics similar to those of sulfur.

2. Addition of hydrogen peroxide

The addition of dilute aqueous hydrogen peroxide is an effective method of speeding up this reaction (25, 26, 123). Instead of hydrogen sulfide, free sulfur is formed as a by-product. Thus, the method has the same disadvantage as method A,1.

3. Addition of potassium or sodium hydroxide

The most obvious way to accelerate this reaction is to remove the hydrogen sulfide by adding a base such as sodium or potassium hydroxide. This can be done by adding either an ethanolic (153, 157, 187, 191, 221) or an aqueous (15, 90, 92, 187, 224, 225) solution of the hydroxide to the mixture of carbon disulfide and the amine. The latter is preferable, since the presence of alcohol may lead to the formation of side products, especially thiourethans (157). Optimum results are achieved by combining equimolar quantities of amine, carbon disulfide, and aqueous 40 per cent sodium (or potassium) hydroxide, with cooling

and agitation. In general, the yields are excellent. However, the method does not work with some amines, e.g., *o*- and *p*-chloroaniline and *o*-, *m*-, and *p*-nitroaniline.

4. Addition of iodine and pyridine

In 1913 an interesting variation of this general method of preparing thioureas was published (95). Pyridine was found to promote the reaction by forming an unstable addition product with hydrogen sulfide.

$$C_6H_5N + H_2S \rightleftharpoons C_6H_5N \cdot H_2S$$

Even thioureas from such amines as *o*- and *p*-chloroaniline could be prepared in this way, although yields were only moderate. More impressive results were obtained by adding the calculated amount of iodine to a solution of the amine in carbon disulfide and pyridine. The iodine eliminated the hydrogen sulfide by the reaction,

$$H_2S + I_2 \rightarrow 2HI + S$$

and the hydrogen iodide was, in turn, removed from the solution by conversion to pyridinium iodide, which is insoluble in carbon disulfide. The overall reaction is

$$2RNH_2 + CS_2 + I_2 + 2C_6H_5N \rightarrow (RNH)_2CS + 2C_6H_5N \cdot HI + S$$

Using this procedure, thioureas from such amines as aniline, *o*-, *m*-, and *p*-chloroaniline, *m*-nitroaniline, and *m*- and *p*-aminobenzoic acid were obtained in yields of 75–99 per cent (95, 187). Especially impressive was the good yield of thiourea obtained from *m*-nitroaniline in 3 hr. as compared to the 200 hr. required for a poor yield when no catalyst was added. In further studies, the relative reaction rates of halo-substituted anilines were found to be $o > m > p$ and I > Br > Cl (96).

Best results are obtained when the reactants are used in the following ratio: 2.0 moles of amine:1.0 mole of iodine:4.0 moles of pyridine:3,000 ml. of carbon disulfide. The reaction is complete when the color of iodine has disappeared and the pyridinium iodide has completely precipitated. The mixture is then steam-distilled until all traces of carbon disulfide and pyridine are gone. Pyridinium iodide is easily removed by washing with water and the product is purified by recrystallization. It is essential that the reactants be carefully weighed, since an excess of iodine may lead to the formation of the isothiocyanate:

$$RNH_2 + CS_2 + I_2 + 2C_6H_5N \rightarrow RNCS + 2C_6H_5N \cdot HI + S$$

Yields by this method are excellent if the reaction is permitted to go to completion (123), except for *o*- and *p*-nitroaniline and *o*-aminobenzoic acid.

5. Addition of ethyl potassium xanthate

Addition of a trace of ethyl potassium xanthate also catalyzes this reaction (107, 108, 191). The reaction rate is somewhat slower than when sulfur is added, but the product is purer.

Thus, the combination of carbon disulfide and primary amine is a convenient way to prepare many 1,3-disubstituted thioureas. Arylamines with strong negative substituents may fail to undergo this reaction or give only poor yields of the desired product (107, 163). Many heterocyclic amines are also reluctant to react by this method.

B. THIOPHOSGENE AND AN AMINE

Primary amines react with thiophosgene to give either an isothiocyanate (see Section III,C,1) or a 1,3-disubstituted thiourea depending upon the ratio of the reactants.

$$CSCl_2 + RNH_2 \rightarrow RNCS + 2HCl$$

$$CSCl_2 + 2RNH_2 \rightarrow RHNCSNHR + 2HCl$$

Secondary amines give only symmetrical thioureas. The mechanism of these reactions has been explained in the following manner (74):

$$RR'NH + CSCl_2 \rightarrow [RR'NHClCSCl] \rightarrow \underset{\text{I}}{RR'NCSCl} + HCl$$

(a) When R′ is not H or if R′ = H and I is stable:

$$I + RR'NH \rightarrow RR'NCSNRR' + HCl$$

(b) When R′ = H and I is unstable:

$$RHNCSCl \rightarrow RNCS + HCl$$

$$RNCS + H_2NR \rightarrow RNHCSNHR$$

Thus pri nary amines may go by either route (a) or route (b), whereas secondary amines can proceed only by way of route (a). Proof of this mechanism lies in the fact that I has been isolated and identified in certain instances even when R′ is H. When a secondary amine is used in a 1:1 ratio with thiophosgene, the reaction stops short at the thiocarbamyl chloride stage and I is often quite stable.

Preparation of thioureas by this method is best carried out by refluxing one mole of thiophosgene with two moles of the amine in an aqueous (71, 74), chloroform-aqueous (76, 78), or acetone-aqueous (172) medium. When thiophosgene no longer appears in the reflux condenser, a mole of potassium carbonate is added and the heating continued for several hours. The product is then isolated and purified in a manner appropriate to the particular compound. The laboratory procedure for the preparation of thiophosgene (72, 77) is tedious, but fortunately this substance is commercially available.

Because of the objectionable nature of thiophosgene, this method is usually reserved for those instances where other methods do not work, e.g., the conversion of aromatic amines with strong negative substituents (107) and of secondary amines to the corresponding symmetrical thioureas.

C. ORGANIC ISOTHIOCYANATE AND AN AMINE: PREPARATION OF ISOTHIOCYANATES

$$RNCS + R'R''NH \rightarrow RNHCSNR'R''$$

This is the most common method of preparing unsymmetrical thioureas. Ammonia, primary amines, or secondary amines may be used, and R, R′, and R″ may be aromatic, aliphatic, alicyclic, or heterocyclic. R may also be acyl. In this way 1-mono-, 1,1- or 1,3-disubstituted, or 1,1,3-trisubstituted thioureas have been synthesized. Because of the simplicity of the reaction and since most thioureas are solids, it is also a widely used method for characterizing amines (28, 31, 37, 94, 102, 113, 116, 177, 198, 199, 230, 232). Conversely, isothiocyanates may be characterized by conversion to a thiourea with ammonia or an amine (144).

Studies have been made to determine the effect of nuclear substituents on the reactivity of aryl isothiocyanates (32). Conclusions were based upon the ease of urethan formation when the isothiocyanate and alcohol were refluxed. It was found that halogen, nitro, *m*-methoxy, and *m*-ethoxy groups accelerate the rate of reaction, whereas alkyl or *o*- and *p*-alkoxy groups retard it. The effect of more than one substituent is additive. *m*-Substituted compounds are always more reactive than their *o*- or *p*-isomers. Acyl isothiocyanates are more reactive than alkyl or aryl; e.g., diphenylamine adds only to acyl isothiocyanates (62).

The addition of the amine to the isothiocyanate is usually carried out in the presence of a solvent such as alcohol. Frequently the reaction is exothermic, and cooling may be necessary to keep it from getting out of hand. In some cases it is necessary to heat the mixture, and then a higher alcohol (91) or preferably an inert solvent such as benzene or toluene may be used. Use of alcohol as solvent when a long reflux period is required may cause urethan formation between the alcohol and isothiocyanate to predominate over the desired thiourea synthesis. Pyridine has also been used successfully as a solvent (7, 49). The thiourea often precipitates from the cooled reaction mixture, since in most cases it is less soluble than the starting material.

In addition to urethan formation, another complication may arise. The following exchanges have been observed in a number of instances (252):

$$2RNCS + R'NH_2 \rightarrow R'NCS + (RHN)_2CS$$

$$2RNCS + (R'HN)_2CS \rightarrow 2R'NCS + (RHN)_2CS$$

Since similarly substituted thioureas melt at nearly the same temperature and isomorphism may make mixed melting points unreliable, elemental analysis or an infrared spectrum is often essential in the identification of the reaction product.

The isothiocyanates required for this synthesis may be prepared in a number of ways.

1. Thiophosgene and a primary amine

When one mole of a primary amine is permitted to react with one mole of thiophosgene an isothiocyanate is formed (see Section III,B). This synthesis

has been known for many years (89, 134, 190, 245). A number of investigators have studied its effectiveness with both aromatic (48, 71, 74, 75, 76) and aliphatic (78) amines. Certain substituents in aromatic amines were found to retard the reaction or prevent it from taking the desired course (75, 76). Cyano, bromo, iodo, and nitro groups retard isothiocyanate formation. Chloro substituents in the meta or para positions do not affect the reaction, but one *o*-chloro group hinders the reaction and two stop it entirely. The method was also found to fail with naphthyl compounds (48). In spite of the unpleasant nature of thiophosgene, this procedure is still in general use because it is an effective synthesis (7, 117) and can be used where many other methods fail.

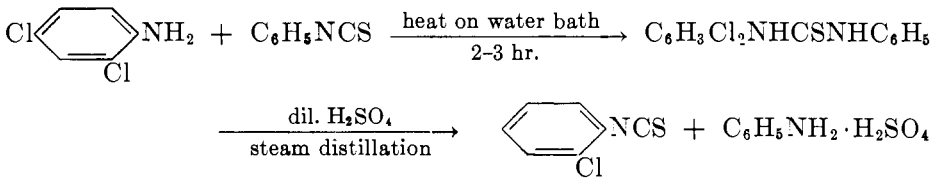
The isothiocyanate can best be prepared (73, 74) by slowly adding with agitation one mole of the amine, either pure or in aqueous solution, to one mole of thiophosgene in aqueous or chloroform solution. The mixture is heated to reflux. Upon completion of the reaction, the product is steam-distilled or extracted.

2. Decomposition of substituted thioureas

$$RHNCSNHR \rightarrow NH_2R + RNCS$$

An acid is usually used to decompose 1,3-disubstituted thioureas and tie up the liberated amine. Acetic anhydride (54, 124, 125, 198, 199), phosphoric acid (221), concentrated hydrochloric acid (155), and 30–50 per cent sulfuric acid (244) are frequently employed. The pure product is usually obtained by steam distillation.

Since certain disubstituted thioureas cannot be prepared by method III,A or III,B, the decomposition of mixed disubstituted thioureas is of interest. It has been observed (41) that the more basic moiety is isolated as the amine and the less basic portion is incorporated into the isothiocyanate. Thus, the conversion of a negatively substituted amine, such as 2,4-dichloroaniline, to the corresponding isothiocyanate can be readily achieved in this fashion:



It is not necessary to isolate the thiourea, for the decomposition can be carried out directly upon the reaction mixture. Yields are quite satisfactory, and it is possible to recover the amine from its salt and use it again.

A new synthesis for isothiocyanates has been reported (10) which fits into this general category. Monoarylthioureas when heated at 150°C. in a suitable solvent undergo fission into ammonia and the aryl isothiocyanate. The best solvent for this reaction is chlorobenzene, although others have been used. A good yield of the isothiocyanate is isolated by removal of the solvent under vacuum and extraction with light petroleum ether.

3. Decomposition of ammonium dithiocarbamates

$$RNHCSSNH_4 + MX_2 \rightarrow RNCS + NH_4X + MS + HX$$

An aromatic amine with carbon disulfide and ammonia yields the ammonium salt, $RNHCSSNH_4$. This, in turn, gives the isothiocyanate by removal of NH_4SH. Many reagents, such as ethyl chloroformate (1), cupric sulfate (158), and lead carbonate (115) have been studied as aids in the decomposition of ammonium dithiocarbamates. The cation in the salt MX_2 must be capable of forming a stable sulfide and the anion an ammonium salt. Ferrous sulfate and lead nitrate were found to be most effective (54). The success of the reaction depends upon the degree of formation of the ammonium dithiocarbamate and upon the ease and completeness of the separation of the isothiocyanate from the sulfide precipitate. A general procedure for the preparation of aryl isothiocyanates by this method using lead nitrate is given in *Organic Syntheses* (53). The method fails when applied to p-$NO_2C_6H_4NCS$ or 2-$C_{10}H_7NCS$.

This means of synthesizing isothiocyanates has also been applied to aliphatic amines. In this case ammonia is not necessary, and it is possible to decompose the amine salt of the dithiocarbamic acid with mercuric chloride (84, 118, 183). However, this involves several operations and half of the amine is lost as hydrochloride, so that certain improvements, which are effective in the aromatic series (104, 158), have been recommended (58). Upon mixing the amine, carbon disulfide, and sodium hydroxide in molar proportions, the sodium dithiocarbamate is obtained. Treatment of this with basic lead acetate gives the isothiocyanate, water, lead sulfide, and sodium acetate. Excellent yields are obtained with methyl-, propyl-, isobutyl-, and benzylamine.

A similar method has been used successfully in the preparation of aralkyl mustard oils (27). It involves treatment of the amine and carbon disulfide in alcoholic solution with iodine and sodium. The reaction proceeds in the following manner:

$$4RNH_2 + 2CS_2 \rightarrow 2RNHC(=S)S^-(NH_3R)^+ \xrightarrow{I_2} \begin{matrix} SC(=S)NHR \\ | \\ SC(=S)NHR \end{matrix} + 2RNH_3^+I^-$$

$$2S + 2NaI + 2RNCS \xleftarrow{I_2} \begin{matrix} SC(=NR)SNa \\ | \\ SC(=NR)SNa \end{matrix} \xleftarrow{2Na}$$

It was not possible to convert 4-nitrobenzylamine to the isothiocyanate by this method. (Note also that if an excess of iodine is used in method III,A,4, an isothiocyanate may be formed.)

4. Alkali thiocyanate and organic halide

Sodium, potassium, or ammonium thiocyanate reacts with an organic halide to give an organic thiocyanate which, upon heating, is converted to the isothiocyanate.

$$RCl + KSCN \rightarrow RSCN \xrightarrow{heat} RNCS$$

The reaction is usually carried out by heating the reactants in 1:1 molar ratio (a slight excess of the thiocyanate is sometimes used) in an inert solvent such as benzene (133). Anhydrous conditions are used to prevent the addition of water to the isothiocyanate. Alcohol is also avoided, since its presence may lead to urethan formation. This method is suitable for the preparation of acyl (232), alkyl (144), and aralkyl isothiocyanates.

5. Sandmeyer reaction

$$\text{Aromatic amine} + \text{HONO} \rightarrow \text{diazo compound} \xrightarrow{\text{CuSCN}} \text{thiocyanate} \xrightarrow{\text{heat}} \text{isothiocyanate}$$

This well-known adaptation of the Sandmeyer reaction has been used quite successfully in preparing aromatic isothiocyanates (60). The major restriction is that the initial amine must be able to withstand diazotization without injury to other functional groups which may be present.

6. Addition of sulfur to cyanides and cyanates

An early preparation of phenyl isothiocyanate was accomplished by heating either phenyl isocyanate or phenylurethan with phosphorus pentasulfide (P_4S_{10}) at 160°C. (168). The addition of sulfur to benzonitrile to give the isothiocyanate was reported by Weith in 1873 (243). This general approach is still used with some modifications. In a recent patent (214) organic isothiocyanates were prepared by heating an organic halide, an alkali metal cyanide, and sulfur in the presence of an oxygenated organic solvent such as an aliphatic aldehyde or ketone.

$$\text{RCl} + \text{S} + \text{NaCN} \xrightarrow{\text{heat}} \text{RNCS} + \text{NaCl}$$

Because of its simplicity and the availability of starting materials, this preparation is suited to large-scale production.

D. ALKALI THIOCYANATE AND AMINE HYDROCHLORIDE

It has long been known that heating ammonium thiocyanate at 160°C. for several hours causes it to rearrange to thiourea (127). The same rearrangement occurs when the ammonium ion is mono- or disubstituted (63), but not when it is tri- or tetrasubstituted. Use is made of this rearrangement in preparing 1-monosubstituted (57, 60, 80, 98, 153, 173, 184, 200, 211, 218) and 1,1-disubstituted (57, 148, 180, 211) thioureas.

$$\text{R'RNH} + \text{HCl} + \text{NH}_4\text{SCN} \rightarrow \text{NH}_4\text{Cl} + \text{R'RNH}_2\text{SCN}$$

$$\text{R'RNH}_2\text{SCN} \xrightarrow{\text{heat}} \text{R'RNCSNH}_2$$

The reaction can be carried out in either (*a*) an inert organic solvent (67, 211) or (*b*) aqueous medium (57, 80, 152).

(*a*) Chlorobenzene is a commonly used solvent. It is saturated with hydrogen chloride, and the amine and thiocyanate are added. The mixture is then heated

at 110–120°C., the length of time depending on the components. Organic salts are removed by filtration, and the product is isolated from the filtrate.

(*b*) One mole of the amine is dissolved in water containing 1.3 moles of hydrogen chloride. Ammonium thiocyanate is added and, after a reflux period, the solution is evaporated to dryness on a steam bath. The residue is heated for several additional hours, taken up in benzene, and washed with dilute hydrochloric acid. Evaporation of the dried benzene layer yields the product.

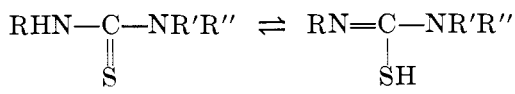
Both methods are simple to use and suitable for aromatic or aliphatic amines.

E. THIOUREAS AND ORGANIC HALIDES

Thioureas react with acyl, alkyl, aralkyl, and heterocyclic halides to give thiourea derivatives. It has been observed on many occasions (61, 62, 63, 64, 208) that when thiourea is treated with acyl halides *S*-acylation occurs first. Then, upon being heated or sometimes merely upon standing at room temperature, the acyl group transfers to an *N*-position. In other cases the transformation is so rapid that the *S*-substituted compound is never discernible. However, when an *S*-alkylpseudothiourea is heated with an acyl halide in the presence of a weak base, an *N*-acyl-*S*-alkylpseudothiourea results, indicating direct *N*-acylation (42, 210). When diacylation occurs by this method it gives a 1,1-diacylthiourea in preference to a 1,3-diacylthiourea. Thus, when the latter is desired it is necessary to use method III,C. Monoarylthioureas upon treatment with an acyl halide give first the *S*-acyl-*N*-aryl compound. Heating converts this first to the 1-aryl-1-acyl- and finally to the 1-aryl-3-acylthiourea.

Alkyl, aralkyl, and heterocyclic halides give stable *S*-substituted products with thioureas, and this is the most common method of preparing pseudothioureas. The reaction may be carried out by mixing a 1:1 molar ratio of the reactants directly in an inert solvent (9, 17, 55) or in anhydrous ethanol (24, 30, 88). Almost quantitative yields of the hydrobromide or hydroiodide salts are obtained when the halide used is the bromide or iodide. Alkyl chlorides are less reactive, and certain adjustments must be made at times in the procedure to give optimum yields of the corresponding hydrochloride. To obtain the free base of the pseudothiourea, the salt is washed with dilute alkali. Other common alkylating reagents such as dimethyl sulfate (217, 226) or esters of *p*-toluenesulfonic acid (145) can be used to prepare *S*-alkylpseudothioureas as the corresponding salts.

Pseudothioureas can be prepared from mono-, di-, and tri- but not tetrasubstituted thioureas. This is true because at least one ureido nitrogen is essential for the tautomerism which must occur with *S*-substitution:



The salts of pseudothioureas are referred to as pseudothiuronium salts. Thus, the hydrochloride of 2-methylpseudothiourea is methylpseudothiuronium

chloride, the 2-benzyl homolog is benzylpseudothiuronium chloride, etc. In the literature, several structural formulae are used for these compounds:

$$RSC(=NH)NH_2 \cdot HCl \qquad [RSC(=NH)NH_3]^+Cl^- \qquad [RSC(=NH_2)NH_2]^+Cl^-$$

Because of the simplicity of their preparation, pseudothiuronium salts of alkyl (or aralkyl) (14, 22, 31, 106, 136, 176) or heterocyclic (21, 166, 181, 182, 227) halides are often used in characterizing these compounds. Some of the more common pseudothiuronium compounds, e.g., benzyl- and 4-chlorobenzylpseudothiuronium halides, are often used in identifying carboxylic acids by conversion to the salts of the latter (50, 141, 142, 231, 233, 241). Sulfonic acids can be characterized in the same way (228).

F. SOME SPECIAL SYNTHESES OF SUBSTITUTED THIOUREAS

A great number of special syntheses for thiourea derivatives have been reported. Many of these are specific for a single compound, while others are of a general nature. Included here are those in the latter category which are less common than the methods described in Section III,A–E.

Diarylthioureas (1,3-) can be prepared by heating a primary amine with a salt of trithiocarbonic acid. Heavy metal salts have been especially recommended (67). This method appears to have little advantage over method III,A and requires more steps.

$$2CS_2 + 2C_6H_5NH_2 + 2NaOH \rightarrow SC(NHC_6H_5)_2 + Na_2CS_3 + 2H_2O$$

$$Na_2CS_3 + MCl_2 \xrightarrow{\text{aqueous medium}} MCS_3 + 2NaCl \quad (M = \text{heavy metal})$$

$$MCS_3 + 2RNH_2 \rightarrow CS(NHR)_2 + MS + H_2S$$

However, an interesting variation is

$$Na_2CS_3 + 2ArNO + H_2O \rightarrow SC(NHAr)_2 + Na_2S_2O_3$$

This has been successfully used in preparing 1,3-bis(4-hydroxyphenyl)- and 1,3-bis(4-dimethylaminophenyl)thiourea from 4-nitrosophenol and 4-nitrosodimethylaniline, respectively (146).

The addition of a sulfide to an unsaturated bond has also been used in preparing thioureas. Cyanothiourea can be prepared by heating a metal dicyanamide with hydrogen sulfide (160). Pseudothioureas are formed by heating a mercaptan and cyanamide (205, 206) in aqueous or alcoholic medium.

$$CH_3SH + (C_2H_5)_2NCN \xrightarrow[100°C.]{\text{water}} (C_2H_5)_2NC(SCH_3)=NH$$

It has also been observed that the sulfur of a 1,3-disubstituted thiourea will add to an acetylenic bond to give a pseudothiourea salt in acid medium (40).

$$RNHCSNHR' + BzC{\equiv}CH \xrightarrow[\text{solution}]{\text{acid}} RHN(R'N=)CSCH=CHBz \cdot HA$$

In some cases it has been found possible to heat thiourea and a primary amine and obtain 1-monosubstituted thioureas (175, 197). Small yields of the symmetrical disubstituted thioureas have also been observed in this reaction.

TABLE 1

Mono-N-substituted thioureas

A. Arylthioureas, $RHNCSNH_2$

R	References	
	Section II	Section III
C_6H_5—	(5, 39, 44, 57, 59, 68, 109*, 150, 165, 193, 195, 218, 219, 229)	(57, 59, 175, 218)
2-BrC_6H_4—		(76)
4-BrC_6H_4—	(218, 219, 599)	(59, 74, 218)
2-ClC_6H_4—	(59)	(59, 74, 152)
3-ClC_6H_4—	(59)	(59, 74)
4-ClC_6H_4—	(59, 119, 218, 219)	(41, 59, 74, 218)
3-FC_6H_4—		(32)
2-IC_6H_4—		(76)
3-IC_6H_4—		(76)
2-$H_2NC_6H_4$—	(218, 219)	(218)
3-$H_2NC_6H_4$—	(219)	
4-$H_2NC_6H_4$—	(218, 219)	(218)
2-HOC_6H_4—	(218, 219, 220)	(218)
3-HOC_6H_4—	(137)	(74)
4-HOC_6H_4—	(119, 218, 219)	(74, 218)
2-$CH_3C_6H_4$—	(5, 57, 59, 109*, 218, 219)	(57, 59, 74, 197, 218)
3-$CH_3C_6H_4$—	(57, 109*, 218, 219)	(57, 74, 218)
4-$CH_3C_6H_4$—	(57, 109*, 119)	(57, 74, 197, 211)
4-$C_2H_5C_6H_4$—		(32)
4-iso-$C_3H_7C_6H_4$—		(32)
2-$C_6H_5C_6H_4$—	(59, 193)	(59)
4-$C_6H_5C_6H_4$—	(59, 138, 193)	(59)
3-NCC_6H_4—		(76)
4-NCC_6H_4—		(76)
2-$CH_3OC_6H_4$—	(57, 59, 218, 219)	(57, 59, 76, 80, 218)
3-$CH_3OC_6H_4$—	(57)	(57, 76)
4-$CH_3OC_6H_4$—	(57, 59, 119, 219)	(57, 59, 60, 74, 76, 200)
2-$C_2H_5OC_6H_4$—	(57)	(57, 76)
3-$C_2H_5OC_6H_4$—	(57)	(57, 76)
4-$C_2H_5OC_6H_4$—	(57, 150)	(57, 60, 74, 76)
4-$(C_2H_5)_2NCH_2CH_2OC_6H_4$—	(19)	
4-n-$C_4H_9OC_6H_4$—	(121, 150)	
4-$C_6H_5OC_6H_4$—		(153, 211)
2-$O_2NC_6H_4$—		(74)
3-$O_2NC_6H_4$—	(218, 219)	(74, 218)
4-$O_2NC_6H_4$—	(119)	(74, 125)
4-$CH_3COC_6H_4$—		(76)
2-$HOOCC_6H_4$—	(109†, 219)	
3-$HOOCC_6H_4$—	(109)†	
4-$HOOCC_6H_4$—	(109†, 219)	
2-$CH_3OOCC_6H_4$—	(218, 219)	(217)
2-$C_2H_5OOCC_6H_4$—	(218, 219)	(74, 76, 218)
3-$C_2H_5OOCC_6H_4$—		(76)
4-$C_2H_5OOCC_6H_4$—	(218, 219)	(76, 218)
4-$(CH_3)_2NC_6H_4$—	(119)	(76)
4-[3,5-$(CH_3)_2C_6H_3O$]C_6H_4—	(186)	
1-$C_{10}H_7$—	(29, 59, 70, 93, 129, 135, 154, 193, 219)	(59, 175, 211)
2-$C_{10}H_7$—	(59, 93, 135)	(59)
1-(8-$CH_3OC_{10}H_6$)—		(211)
2,4-$Br_2C_6H_3$—		(41)
2,5-$Br_2C_6H_3$—		(76)
2,3-$Cl_2C_6H_3$—		(75)
2,4-$Cl_2C_6H_3$—		(41)
2,5-$Cl_2C_6H_3$—	(59)	(59)
2,6-$(HO)_2C_6H_3$—	(219)	

* Dimercury derivative.

† Monomercury derivative.

TABLE 1—*Continued*

A. Arylthioureas, $RHNCSNH_2$—*Continued*

R	References	
	Section II	Section III
2,3-$(CH_3)_2C_6H_3$—		(76)
2,4-$(CH_3)_2C_6H_3$—		(74)
2,5-$(CH_3)_2C_6H_3$—	(129)	(74)
2,6-$(CH_3)_2C_6H_3$—		(76)
3,4-$(CH_3)_2C_6H_3$—	(129)	(74)
2,5-$(CN)_2C_6H_3$—		(76)
2,5-$(CH_3O)_2C_6H_3$—		(76)
2,6-$(CH_3O)_2C_6H_3$—		(74)
3,4-$(CH_3O)_2C_6H_3$—		(76)
5,2-(Br)$(CH_3)C_6H_3$—		(74)
3,2-(Cl)$(CH_3)C_6H_3$—	(59)	(59)
4,2-(Cl)$(CH_3)C_6H_3$—		(32)
5,2-(Cl)$(CH_3O)C_6H_3$—		(32, 80)
3,4-$(NH_2)(CH_3)C_6H_3$—	(218, 219)	(218)
2,3-$(CH_3)(NO_2)C_6H_3$—		(71)
2,4-$(CH_3)(NO_2)C_6H_3$—		(71)
2,5-$(CH_3)(NO_2)C_6H_3$—		(74)
2,5-$(CH_3O)(NO_2)C_6H_3$—		(71)
2,4-$(C_2H_5O)(NO_2)C_6H_3$—		(76)
5,2-$(NO_2)(C_3H_7O)C_6H_3$—		(184)
2,6-$(C_6H_5)(CHO)C_6H_3$—		(15)
4,3-$(CH_3OOC)(OH)C_6H_3$—	(7, 137)	(7)
5,2-$(CH_3OOC)(OH)C_6H_3$—	(218, 219)	(218)
3,4,6-$Cl_3C_6H_2$—		(75)
2,4,5-$(CH_3)_3C_6H_2$—		(74)
2,4,6-$(CH_3)_3C_6H_2$—		(74)
2,4,6,3-$(CH_3)_3(NO_2)C_6H$—		(74)

B. Alkyl- and aralkylthioureas, $RHNCSNH_2$

CH_3--	(5, 6, 59, 131, 195, 229)	(59, 78)
C_2H_5—	(59, 203)	(59, 78)
n-C_3H_7—	(165)	(78)
iso-C_3H_7—	(6, 59, 167)	(59)
n-C_4H_9—	(59, 203, 207)	(59, 78)
iso-C_4H_9—		(78)
n-C_5H_{11}—		(78)
iso-C_5H_{11}—		(78)
n-C_6H_{13}—		(78)
n-C_7H_{15}—		(78)
$C_{12}H_{25}$—	(59, 120)	(59)
CH_2=$CHCH_2$—	(39, 44, 59, 69, 100, 129, 131, 156, 167, 207)	(59)
CH_3CH=$CHCH_2$—		(144, 214)
CH_2=$CHCH(CH_3)$—		(144)
N≡C—		(160)
$C_2H_5OCH_2$—		(133)
$C_6H_5CH_2$—	(126, 128, 218, 219)	(74, 200, 218)
$C_6H_5(CH_2)_2$—		(27, 74)
$C_6H_5(CH_2)_3$—		(27)
$C_6H_5(CH_2)_4$—		(27)
4-$CH_3OC_6H_4CH_2$—		(200)
4-$CH_3OC_6H_4(CH_2)_2$—		(15)
4-$O_2NC_6H_4(CH_2)_2$—		(15)
4-$H_2NC_6H_4(CH_2)_2$—		(15)
1-$C_{10}H_7CH_2$—		(200)

TABLE 1—*Concluded*

C. Heterocyclic, alicyclic, and acyl thioureas, $RHNCSNH_2$

R	References	
	Section II	Section III
Cyclohexyl-		(221)
6-Quinolyl-	(209)	
8-Chloro-5-quinolyl-		(211)
3-Diethylaminomethyl-4-hydroxy-2-methyl-6-quinolyl-	(101)	
2-Carbazyl-		(211)
9-Ethyl-3-carbazyl-		(211)
4-Indazyl-		(211)
4-Morpholinylmethyl-	(59)	
1,2,3,4-Tetrahydro-2-naphthyl-	(59)	
C_6H_5CO—	(100)	
CH_3CO—	(5, 159, 195, 214)	(64, 173)
CH_3CH_2CO—		(173)
$CH_3(CH_2)_8CO$—		(173)
$CH_3(CH_2)_4CO$—		(173)
$CH_3(CH_2)_5CO$—		(173)
$CH_3(CH_2)_6CO$—		(173)
$CH_3(CH_2)_9CO$—		(173)
$(CH_3)_2CHCO$—		(173)
$(CH_3)_2CHCH_2CO$—		(173)
$(CH_3)_2CHCH_2CH_2CO$—		(173)
(C_2H_5)(iso-C_5H_{11})CHCO—		(173)

TABLE 2

Disubstituted thioureas

A. 1,1-Disubstituted thioureas, $RR'NCSNH_2$

R	R′	References	
		Section II	Section III
CH_3—	4-$CH_3C_6H_4$—		(125)
C_2H_5—	C_6H_5—	(203)	
C_2H_5—	1-$C_{10}H_7$—		(148)
C_2H_5—	4-$CH_3C_6H_4$—		(148)
C_2H_5—	4-$C_2H_5C_6H_4$—	(34)	
C_6H_5—	C_6H_5—		(180, 211)
C_5H_5—	2-$C_{10}H_7$—		(180)
4-$CH_3OC_6H_4$—	2-$C_{10}H_7$—		(180)
4-HOC_6H_4—	4-HOC_6H_4—		(180)
$C_6H_5CH_2$—	$C_6H_5CH_2$—	(59)	
CH_3CO—	CH_3CO—		(64)
CH_3CO—	C_6H_5—		(61)
CH_3CO—	4-BrC_6H_4—		(125)
CH_3CO—	4-ClC_6H_4—		(125)
CH_3CO—	4-$CH_3C_6H_4$—		(61)
CH_3CO—	4-$C_2H_5OC_6H_4$—		(125)
CH_3CO—	C_3H_5CO—		(64)
C_6H_5CO—	4-$CH_3C_6H_4$—		(61)

TABLE 2—*Continued*

B. 1,3-Disubstituted thioureas

(1) Diarylthioureas, $(RNH)_2CS$

R	References	
	Section II	Section III
C_6H_5—	(5, 21, 43, 59, 131, 195)	(95, 122, 140, 174, 224)
2-BrC_6H_4—		(76, 96)
3-BrC_6H_4—		(26, 96)
4-BrC_6H_4—		(26, 74, 96, 122, 198)
2-ClC_6H_4—	(59)	(26, 74, 95, 96, 174)
3-ClC_6H_4—	(59)	(26, 74, 95, 96, 225)
4-ClC_6H_4—	(59, 166)	(26, 74, 95, 96, 121)
3-FC_6H_4—		(32, 123)
4-FC_6H_4—	(59)	(32, 123)
2-IC_6H_4—		(76)
3-IC_6H_4—		(123)
4-IC_6H_4—		(26, 74, 96)
4-$H_2NC_6H_4$—	(164, 250)	
4-$C_2H_5NHC_6H_4$—		(174)
4-$CH_3CONHC_6H_4$—		(76)
3-$(CH_3)_2NC_6H_4$—		(123)
4-$(CH_3)_2NC_6H_4$—	(121, 164)	(76)
4-$(C_2H_5)_2NC_6H_4$—	(79)	(174)
3-HOC_6H_4—		(74)
4-HOC_6H_4—		(74, 174)
2-$CH_3C_6H_4$—	(5, 59)	(74, 122, 174, 177, 223, 225)
3-$CH_3C_6H_4$—	(59)	(26, 74, 174)
4-$CH_3C_6H_4$—	(5)	(26, 74, 122, 174, 223, 225)
4-*n*-$C_6H_7C_6H_4$—	(79)	
4-*n*-$C_4H_9C_6H_4$—	(79, 121, 149, 164)	
4-*tert*-$C_4H_9C_6H_4$—	(121)	
4-*n*-$C_5H_{11}C_6H_4$—	(79)	
4-iso-$C_5H_{11}C_6H_4$—	(79)	
4-*tert*-$C_5H_{11}C_6H_4$—	(165)	
4-$CH_3CH_2OCH_2CH_2C_6H_4$—	(79)	
4-$CH_3OCH_2CH_2CH_2C_6H_4$—	(79)	
2-$C_6H_5C_6H_4$—		(187)
4-$C_6H_5C_6H_4$—	(239)	(28, 31, 187)
2-(4-ClC_6H_4)C_6H_4—		(187)
4-(4-ClC_6H_4)C_6H_4—		(187)
3-$F_3CC_6H_4$—	(59)	
3-N≡CC_6H_4—		(76, 123)
4-N≡CC_6H_4—		(76, 123)
2-$CH_3OC_6H_4$—		(76, 174)
3-$CH_3OC_6H_4$—		(76, 123)
4-$CH_3OC_6H_4$—	(121)	(26, 37, 60, 74, 76, 174)
2-$C_2H_5OC_6H_4$—		(76)
3-$C_2H_5OC_6H_4$—		(76)
4-$C_2H_5OC_6H_4$—	(79, 121, 149, 164)	(26, 60, 74, 76, 122)
4-*n*-$C_3H_7OC_6H_4$—	(36, 79, 149)	(36)
4-iso-$C_3H_7OC_6H_4$—	(79)	
4-*n*-$C_4H_9OC_6H_4$—	(79, 121, 164)	
4-iso-$C_4H_9OC_6H_4$—	(36, 79)	(36)
4-*sec*-$C_4H_9OC_6H_4$—	(79)	
4-*n*-$C_5H_{11}OC_6H_4$—	(36, 79)	(36)
4-iso-$C_5H_{11}OC_6H_4$—	(36, 79)	(36)
4-*n*-$C_6H_{17}OC_6H_4$—	(121)	
4-CH_2=$CHCH_2OC_6H_4$—	(79)	
4-$CH_3CH_2OCH_2OC_6H_4$—	(79)	
4-$(C_2H_5)_2NCH_2CH_2OC_6H_4$—	(20)	
4-$C_6H_5OC_6H_4$—		(153)
2-$O_2NC_6H_4$—		(71)

TABLE 2—*Continued*

B. 1,3-Disubstituted thioureas—*Continued*

(1) Diarylthioureas, $(RNH)_2CS$—*Continued*

R	References	
	Section II	Section III
3-$O_2NC_6H_4$—		(71, 74, 95, 174, 187, 199)
4-$O_2NC_6H_4$—		(71, 74)
2-$HOOCC_6H_4$—		(76)
3-$HOOCC_6H_4$—		(95)
4-$HOOCC_6H_4$—	(7)	(7, 95)
2-$CH_3OOCC_6H_4$—		(26)
3-$C_2H_5OOCC_6H_4$—		(76)
4-$C_2H_5OOCC_6H_4$—		(26, 74, 76)
3-$CH_3COC_6H_4$—		(123)
4-$CH_3COC_6H_4$—		(76)
1-$C_{10}H_7$—	(59, 93, 135)	(108, 122, 174)
2-$C_{10}H_7$—	(59)	(122, 174)
2,5-$Br_2C_6H_3$—		(76)
3,4-$Br_2C_6H_3$—		(187)
3,5-$Br_2C_6H_3$—		(187)
2,3-$Cl_2C_6H_3$—		(75)
2,4-$Cl_2C_6H_3$—		(187)
2,5-$Cl_2C_6H_3$—		(187)
3,5-$Cl_2C_6H_3$—		(187)
2,4-$(CH_3)_2C_6H_3$—		(26, 55, 74)
2,5-$(CH_3)_2C_6H_3$—		(74, 174)
2,6-$(CH_3)_2C_6H_3$—		(76)
3,4-$(CH_3)_2C_6H_3$—		(74, 174)
2,5-$(CH_3O)_2C_6H_3$—		(76)
3,4-$(CH_3O)_2C_6H_3$—		(76)
2,4-(Br)(Cl)C_6H_3—		(187)
4,2-(Br)(Cl)C_6H_3—		(187)
3,4-(Br)$(CH_3)C_6H_3$—		(125)
5,2-(Br)$(CH_3)C_6H_3$—		(74)
5,2-(Cl)$(CH_3O)C_6H_3$—		(80)
2,5-(CH_3)(iso-C_3H_7)C_6H_3—		(155)
2,5-$(CH_3O)(CH_3)C_6H_3$—	(59)	
4,3-$(C_2H_5O)(CH_3)C_6H_3$—	(121)	
2,5-$(CH_3)(NO_2)C_6H_3$—		(71, 74)
2,5-$(CH_3O)(NO_2)C_6H_3$—		(71)
5,2-(NO_2)(*n*-$C_3H_7O)C_6H_3$—		(184)
4,3-$(COOH)(OH)C_6H_3$—	(7, 204)	(7)
4,3-$(CH_3OOC)(OH)C_6H_3$—	(7)	(7)
2,4,6-$Cl_3C_6H_2$—	(138)	
3,4,5-$Cl_3C_6H_2$—		(75)
2,4,5-$(CH_3)_3C_6H_2$—		(26, 74)
2,4,6-$(CH_3)_3C_6H_2$—		(74, 174)

(2) Dialkyl- and diaralkylthioureas, $(RNH)_2CS$

C_2H_5—	(5, 159, 165, 195, 234, 247)	
iso-C_3H_7—	(59)	
n-C_4H_9—	(5, 59, 165, 247)	
iso-C_4H_9—	(59)	
C_7H_{15}—	(6)	
$CH_3(CH_2)_{11}$—	(6, 59, 120)	
$CH_3(CH_2)_{13}$—	(161)	
$CH_3(CH_2)_{15}$—	(161)	
$CH_3(CH_2)_{17}$—	(59)	
CH_2=$CHCH_2$—	(59, 159, 247)	
CH_3CO—	(214)	
$C_6H_5CH_2$—	(126)	(74, 174)
$C_6H_5CH(CH_3)$—	(165)	

TABLE 2—*Continued*

B. 1,3-Disubstituted thioureas—*Continued*

(2) Dialkyl- and diaralkylthioureas, $(RNH)_2CS$—*Continued*

R	References	
	Section II	Section III
$C_6H_5CH_2CH_2$—		(27, 74)
$C_6H_5(CH_2)_3$—		(27)
$C_6H_5(CH_2)_4$—		(27)
$(C_6H_5)_2CH$—		(27)
$4\text{-}CH_3OC_6H_4CH_2$—	(164)	(27)
$4\text{-}CH_3OC_6H_4CH_2CH_2$—		(15)
$4\text{-}O_2NC_6H_4CH_2CH_2$—		(15)
(3) Thioureas containing heterocyclic and alicyclic groups in the 1,1-positions, $(RNH)_2CS$		
5-Quinolyl-	(209)	
6-Quinolyl-	(209)	
7-Quinolyl-	(209)	
8-Quinolyl-	(209)	
4-Amino-6-quinolyl-		(172)*
3-Quinaldenyl-	(209)	
4-Amino-6-cinnolyl-		(172)†
2-Pyridyl-	(6, 59)	
3-(6-*n*-Butoxypyridyl)-	(79)	
Cyclohexyl-	(59)	(221)
2-Methyloyclohexyl-	(59)	
1-Nitro-2-fluoryl-		(107)
2-Nitro-7-fluoryl-		(107)
(2-Hendecyl-2-imidazolin-1-yl)ethyl-	(248)	
(4a) Diarylthioureas, $C_6H_5NHCSNHR$		
$2\text{-}BrC_6H_4$—		(177)
$3\text{-}BrC_6H_4$—		(177)
$4\text{-}BrC_6H_4$—		(125, 177, 198)
$2\text{-}ClC_6H_4$—		(177)
$3\text{-}ClC_6H_4$—		(177)
$4\text{-}ClC_6H_4$—		(177)
$4\text{-}IC_6H_4$—		(177)
$4\text{-}HOC_6H_4$—		(174, 177)
$2\text{-}CH_3C_6H_4$—	(59)	(96, 177)
$3\text{-}CH_3C_6H_4$—		(96, 177)
$4\text{-}CH_3C_6H_4$—		(96, 177)
$4\text{-}C_6H_5C_6H_4$—		(28, 230)
$2\text{-}CH_3OC_6H_4$—		(177)
$4\text{-}CH_3OC_6H_4$—		(37, 177)
$4\text{-}C_2H_5OC_6H_4$—		(125)
$4\text{-}(C_2H_5)_2NCH_2CH_2OC_6H_4$—	(19, 20)	
$2\text{-}O_2NC_6H_4$—		(71)
$3\text{-}O_2NC_6H_4$—		(71, 199)
$4\text{-}O_2NC_6H_4$—		(71, 125)
$4\text{-}(4\text{-}O_2NC_6H_4S)C_6H_4$—	(128)	
$4\text{-}(4\text{-}O_2NC_6H_4SO_2)C_6H_4$—	(128)	
$1\text{-}C_{10}H_7$—	(59)	
$2,4\text{-}(CH_3)_2C_6H_3$—		(177)
$2,5\text{-}(Br)(CH_3)C_6H_3$—		(177)
$4,2\text{-}(OH)(CH_3)C_6H_3$—		(177)
$2,5\text{-}(CH_3)(NO_2)C_6H_3$—		(71)
$3,4\text{-}(CH_3)(NO_2)C_6H_3$—		(71)

* Also the dimethiodide.

† Also the dimethochloride.

TABLE 2—*Continued*

(4a) Diarylthioureas, $C_6H_5NHCSNHR$—*Continued*

R	References	
	Section II	Section III
4,2-$(CH_3)(NO_2)C_6H_3$—		(71)
4,3-$(CH_3)(NO_2)C_6H_3$—		(71)
2,5-$(CH_3O)(NO_2)C_6H_3$—		(71)
4,3-$(HOOC)(OH)C_6H_3$—	(7, 204)	(7)
4,3-$(CH_3OOC)(OH)C_6H_3$—	(7)	(7)

(4b) Diarylthioureas, $4\text{-}C_2H_5OC_6H_4NHCSNHR$

4-BrC_6H_4—		(125)
4-FC_6H_4—	(79)	
4-IC_6H_4—	(79)	
4-$C_6H_5NHC_6H_4$—	(79)	
4-$(CH_3)_2NC_6H_4$—	(79)	
4-$(C_2H_5)_2NC_6H_4$—	(79)	
4-$(n\text{-}C_4H_9)_2NC_6H_4$—	(79)	
4-HOC_6H_4—	(79)	
4-$CH_3C_6H_4$—		(125)
4-iso-$C_3H_7C_6H_4$—	(36, 79)	(36)
4-$n\text{-}C_4H_9C_6H_4$—	(79)	
4-*tert*-$C_4H_9C_6H_4$—	(79)	
4-$n\text{-}C_5H_{11}C_6H_4$—	(79)	
4-$n\text{-}C_6H_{13}C_6H_4$—	(79)	
4-$C_6H_5C_6H_4$—		(28)
4-$CH_3CH_2OCH_2C_6H_4$—	(79)	
4-$CH_3OCH_2CH_2C_6H_4$—	(79)	
4-$CH_3OCH_2CH_2CH_2C_6H_4$—	(79)	
4-$CH_3OC_6H_4$—	(79)	
2-$C_2H_5OC_6H_4$—	(121)	
3-$C_2H_5OC_6H_4$—	(121)	
4-$n\text{-}C_3H_7OC_6H_4$—	(36, 79)	(36)
4-iso-$C_3H_7OC_6H_4$—	(79)	
4-$n\text{-}C_4H_9OC_6H_4$—	(36, 79, 164)	(36)
4-iso-$C_4H_9OC_6H_4$—	(36, 79, 149, 164)	(36)
4-*sec*-$C_4H_9OC_6H_4$—	(79)	
4-$n\text{-}C_5H_{11}OC_6H_4$—	(36, 79)	(36)
4-iso-$C_5H_{11}OC_6H_4$—	(36, 79)	(36)
4-$n\text{-}C_6H_{13}OC_6H_4$—	(79, 121)	
4-$n\text{-}C_7H_{15}OC_6H_4$—	(79)	
4-$C_6H_5OC_6H_4$—	(79)	
4-$C_5H_9OC_6H_4$—	(79)	
4-$HOCH_2CH_2OC_6H_4$—	(79)	
4-$C_2H_5OCH_2CH_2OC_6H_4$—	(79)	
4-$(CH_3)_2NCH_2CH_2OC_6H_4$—	(59, 79)	
4-$(C_2H_5)_2NCH_2CH_2OC_6H_4$—	(79)	
4-$C_2H_5SC_6H_4$—	(79)	
4-$n\text{-}C_3H_7SC_6H_4$—	(79)	
4-$C_2H_5OCH_2CH_2SC_6H_4$—	(79)	
4-$CH_3CH_2COC_6H_4$—	(79)	
2,3-$(Cl)(C_2H_5O)C_6H_3$—	(79)	
3,4-$(CH_3CONH)(C_2H_5O)C_6H_3$—	(79)	

TABLE 2—*Continued*

(4c) Diarylthioureas, RHNCSNHR′

R	R′	References	
		Section II	Section III
2-BrC_6H_4—	2-$CH_3C_6H_4$—		(177)
3-BrC_6H_4—	2-$CH_3C_6H_4$—		(177)
4-BrC_6H_4—	4-ClC_6H_4—		(125, 198)
4-BrC_6H_4—	2-HOC_6H_4—		(198)
4-BrC_6H_4—	2-$CH_3C_6H_4$—		(177)
4-BrC_6H_4—	4-$CH_3C_6H_4$—		(41, 125, 198)
4-BrC_6H_4—	4-$C_6H_5C_6H_4$—		(28)
4-BrC_6H_4—	4-(4-$O_2NC_6H_4SO_2$)C_6H_4—	(128)	
4-BrC_6H_4—	4-$CH_3OC_6H_4$—		(37)
4-BrC_6H_4—	4-*n*-$C_4H_9OC_6H_4$—	(79)	
4-BrC_6H_4—	4-iso-$C_5H_{11}OC_6H_4$—	(36)	(36)
4-BrC_6H_4—	2-$O_2NC_6H_4$—		(71, 198)
4-BrC_6H_4—	3-$O_2NC_6H_4$—		(71, 198, 199)
4-BrC_6H_4—	4-$O_2NC_6H_4$—		(71, 125)
4-BrC_6H_4—	1-$C_{10}H_7$—		(198)
4-BrC_6H_4—	2-$C_{10}H_7$—		(198)
4-BrC_6H_4—	3,4-(Br)(CH_3)C_6H_3—		(198)
4-BrC_6H_4—	2,5-(CH_3)(NO_2)C_6H_3—		(71)
4-BrC_6H_4—	3,4-(CH_3)(NO_2)C_6H_3—		(71)
4-BrC_6H_4—	4,2-(CH_3)(NO_2)C_6H_3—		(71)
4-BrC_6H_4—	4,3-(CH_3)(NO_2)C_6H_3—		(71)
4-BrC_6H_4—	6,2-(CH_3O)(NO_2)C_6H_3—		(71)
4-BrC_6H_4—	2,5-(CH_3O)(NO_2)C_6H_3—		(71)
2-ClC_6H_4—	2-$CH_3C_6H_4$—		(177)
2-ClC_6H_4—	4-$C_6H_5C_6H_4$—		(28)
2-ClC_6H_4—	4-$CH_3OC_6H_4$—		(37)
2-ClC_6H_4—	4,3-(HOOC)(HO)C_6H_3—	(7)	(7)
3-ClC_6H_4—	2-$CH_3C_6H_4$—		(177)
3-ClC_6H_4—	4,3-(HOOC)(HO)C_6H_3—	(7)	(7)
4-ClC_6H_4—	2-$CH_3C_6H_4$—		(41, 177)
4-ClC_6H_4—	4-$CH_3C_6H_4$—		(41)
4-ClC_6H_4—	4-*n*-$C_4H_9C_6H_4$—	(79)	
4-ClC_6H_4—	4-$C_6H_5C_6H_4$—		(28)
4-ClC_6H_4—	4-*n*-$C_3H_7OC_6H_4$	(79)	
4-ClC_6H_4—	4-iso-$C_6H_7OC_6H_4$—	(79)	
4-ClC_6H_4—	4-*n*-$C_4H_9OC_6H_4$—	(79, 121)	
4-ClC_6H_4—	4-*n*-$C_5H_{11}OC_6H_4$—	(79)	
4-ClC_6H_4—	4-*n*-$C_7H_{15}OC_6H_4$—	(79)	
4-ClC_6H_4—	4-CH_2=$CHCH_2OC_6H_4$—	(79)	
4-ClC_6H_4—	4-$C_5H_9OC_6H_4$—	(79)	
4-ClC_6H_4—	3-$O_2NC_6H_4$—		(199)
4-ClC_6H_4—	4-$O_2NC_6H_4$—		(71)
4-ClC_6H_4—	2,3-(Cl)(NO_2)C_6H_3—		(71)
4-ClC_6H_4—	4,3-(HOOC)(HO)C_6H_3—	(7)	(7)
4-FC_6H_4—	4-*n*-$C_4H_9OC_6H_4$—	(79)	
4-FC_6H_4—	3,4-(CH_3)(NO_2)C_6H_3—		(71)
4-IC_6H_4—	2-$CH_3C_6H_4$—		(177)
4-IC_6H_4—	4-*n*-$C_4H_9OC_6H_4$—	(79)	
4-IC_6H_4—	4-(4-$O_2NC_6H_4S$)C_6H_4—	(128)	
4-IC_6H_4—	4-(4-$O_2NC_6H_4SO_2$)C_6H_4—	(128)	
4-$(CH_3)_2NC_6H_4$—	4-*n*-$C_4H_9C_6H_4$—	(79, 149)	
4-$(CH_3)_2NC_6H_4$—	4-*n*-$C_6H_7OC_6H_4$—	(79)	
4-$(CH_3)_2NC_6H_4$—	4-*n*-$C_4H_9OC_6H_4$—	(79, 121, 164)	
4-$(CH_3)_2NC_6H_4$—	4-iso-$C_4H_9OC_6H_4$—	(79)	
4-$(CH_3)_2NC_6H_4$—	4-iso-$C_5H_{11}OC_6H_4$—	(36, 79)	(36)
4-$(CH_3)_2NC_6H_4$—	4,3-(HOOC)(HO)C_6H_3—	(7)	(7)
4-$(C_2H_5)_2NC_6H_4$—	4-*n*-$C_4H_9OC_6H_4$—	(79)	
4-$(C_2H_5)_2NC_6H_4$—	4-*n*-$C_5H_{11}OC_6H_4$—	(79)	
2-HOC_6H_4—	4-$O_2NC_6H_4$—		(199)

TABLE 2—*Continued*

(4c) Diarylthioureas, RHNCSNHR′—*Continued*

R	R′	References	
		Section II	Section III
4-HOC_6H_4—	2-$CH_3C_6H_4$—		(177)
4-HOC_6H_4—	4-$(C_2H_5)_2NCH_2CH_2OC_6H_4$—	(20)	
4-HOC_6H_4—	3-$O_2NC_6H_4$—		(199)
2-$CH_3C_6H_4$—	3-$CH_3C_6H_4$—		(177)
2-$CH_3C_6H_4$—	4-$CH_3C_6H_4$—		(177)
2-$CH_3C_6H_4$—	4-$C_6H_5C_6H_4$—		(28)
2-$CH_3C_6H_4$—	4-$CH_3OC_6H_4$—		(37)
2-$CH_3C_6H_4$—	2-$O_2NC_6H_4$—		(71)
2-$CH_3C_6H_4$—	3-$O_2NC_6H_4$—		(71, 199)
2-$CH_3C_6H_4$—	4-$O_2NC_6H_4$—		(71)
2-$CH_3C_6H_4$—	2,5-(Br)$(CH_3)C_6H_3$—		(177)
2-$CH_3C_6H_4$—	4,2-(OH)$(CH_3)C_6H_3$—		(177)
2-$CH_3C_6H_4$—	2,4-$(CH_3)_2C_6H_3$—		(177)
2-$CH_3C_6H_4$—	5,2-(iso-C_6H_7)$(CH_3)C_6H_3$—		(155)
2-$CH_3C_6H_4$—	2,4-$(CH_3)(NO_2)C_6H_3$—		(71)
2-$CH_3C_6H_4$—	2,5-$(CH_3)(NO_2)C_6H_3$—		(71)
2-$CH_3C_6H_4$—	4,2-$(CH_3)(NO_2)C_6H_3$—		(71)
2-$CH_3C_6H_4$—	4,3-$(CH_3)(NO_2)C_6H_3$—		(71)
2-$CH_3C_6H_4$—	2,5-$(CH_3O)(NO_2)C_6H_3$—		(71)
2-$CH_3C_6H_4$—	4,3-(HOOC)(HO)C_6H_3—	(7)	(7)
3-$CH_3C_6H_4$—	4-$CH_3OC_6H_4$—		(37)
3-$CH_3C_6H_4$—	2-$O_2NC_6H_4$—		(71)
3-$CH_3C_6H_4$—	3-$O_2NC_6H_4$—		(71, 199)
3-$CH_3C_6H_4$—	4-$O_2NC_6H_4$—		(71)
3-$CH_3C_6H_4$—	5,2-(iso-C_3H_7)$(CH_3)C_6H_3$—		(155)
3-$CH_3C_6H_4$—	2,4-$(CH_3)(NO_2)C_6H_3$—		(71)
3-$CH_3C_6H_4$—	2,5-$(CH_3)(NO_2)C_6H_3$—		(71)
3-$CH_3C_6H_4$—	4,2-$(CH_3)(NO_2)C_6H_3$—		(71)
3-$CH_3C_6H_4$—	4,3-$(CH_3)(NO_2)C_6H_3$—		(71)
3-$CH_3C_6H_4$—	2,5-$(CH_3O)(NO_2)C_6H_3$—		(71)
4-$CH_3C_6H_4$—	4-$C_6H_5C_6H_4$—		(28)
4-$CH_3C_6H_4$—	4-$CH_3OC_6H_4$—		(37)
4-$CH_3C_6H_4$—	4-n-$C_4H_9OC_6H_4$—	(79)	
4-$CH_3C_6H_4$—	2-$O_2NC_6H_4$—		(71)
4-$CH_3C_6H_4$—	3-$O_2NC_6H_4$—		(71, 199)
4-$CH_3C_6H_4$—	4-$O_2NC_6H_4$—		(71, 125)
4-$CH_3C_6H_4$—	2,4-$(Cl)_2C_6H_3$—		(41)
4-$CH_3C_6H_4$—	3,2-(Cl)$(CH_3)C_6H_3$—		(32)
4-$CH_3C_6H_4$—	3,4-(Cl)$(CH_3)C_6H_3$—		(32)
4-$CH_3C_6H_4$—	5,3-(Cl)$(CH_3)C_6H_3$—		(32)
4-$CH_3C_6H_4$—	5,3-(Cl)$(CH_3O)C_6H_3$—		(32)
4-$CH_3C_6H_4$—	5,2-(iso-C_3H_7)$(CH_3)C_6H_3$—		(155)
4-$CH_3C_6H_4$—	2,4-$(CH_3)(NO_2)C_6H_3$—		(71)
4-$CH_3C_6H_4$—	2,5-$(CH_3)(NO_2)C_6H_3$—		(71)
4-$CH_3C_6H_4$—	3,4-$(CH_3)(NO_2)C_6H_3$—		(71)
4-$CH_3C_6H_4$—	4,2-$(CH_3)(NO_2)C_6H_3$—		(71)
4-$CH_3C_6H_4$—	4,3-$(CH_3)(NO_2)C_6H_3$—		(71)
4-$CH_3C_6H_4$—	6,2-$(CH_3)(NO_2)C_6H_3$—		(71)
4-$CH_3C_6H_4$—	3,5-$(CH_3O)_2C_6H_3$—		(32)
4-$CH_3C_6H_4$—	2,5-$(CH_3O)(NO_2)C_6H_3$—		(71)
4-$CH_3C_6H_4$—	4,3-(HOOC)(HO)C_6H_3—	(7)	(7)
4-n-$C_4H_9C_6H_4$—	4-n-$C_4H_9OC_6H_4$—	(79)	
4-$C_6H_5C_6H_4$—	4-$(C_2H_5)_2NCH_2CH_2OC_6H_4$—	(20, 79, 164)	
4-$C_6H_5C_6H_4$—	2-$CH_3OC_6H_4$—		(28)
4-$C_6H_5C_6H_4$—	4-$CH_3OC_6H_4$—		(37)
2-$CH_3OC_6H_4$—	4,3-(HOOC)(HO)C_6H_3—	(7)	(7)
3-$CH_3OC_6H_4$—	4,3-(HOOC)(HO)C_6H_3—	(7)	(7)
4-$CH_3OC_6H_4$—	4-$O_2NC_6H_4$—		(71)
4-$CH_3OC_6H_4$—	1-$C_{10}H_7$—		(37)

TABLE 2—*Continued*

(4c) Diarylthioureas, RHNCSNHR′—*Continued*

R	R′	References	
		Section II	Section III
4-$CH_3OC_6H_4$—	2-$C_{10}H_7$—		(37)
4-$CH_3OC_6H_4$—	4,3-(HOOC)(HO)C_6H_3—	(7)	(7)
4-*n*-$C_3H_7OC_6H_4$—	4-*n*-$C_5H_9OC_6H_4$—	(36)	(36)
4-*n*-$C_3H_7OC_6H_4$—	4-iso-$C_5H_{11}OC_6H_4$—	(36)	(36)
4-*n*-$C_4H_9OC_6H_4$—	4-iso-$C_4H_9OC_6H_4$—	(36)	(36)
4-*n*-$C_4H_9OC_6H_4$—	4-*n*-$C_5H_{11}OC_6H_4$—	(36, 79)	(36)
4-*n*-$C_4H_9OC_6H_4$—	4-iso-$C_5H_{11}OC_6H_4$—	(36)	(36)
4-*n*-$C_4H_9OC_6H_4$—	4-$(C_2H_5)_2NCH_2CH_2OC_6H_4$—	(79, 149)	
4-iso-$C_4H_9OC_6H_4$—	4-$CH_3OCH_2CH_2CH_2C_6H_4$—	(79)	
4-iso-$C_4H_9OC_6H_4$—	4-iso-$C_5H_{11}OC_6H_4$—	(36)	(36)
4-*n*-$C_5H_{11}OC_6H_4$—	4-iso-$C_5H_{11}OC_6H_4$—	(36)	(36)
2-$O_2NC_6H_4$—	3-$O_2NC_6H_4$—	(71)	(199)
2-$O_2NC_6H_4$—	1-$C_{10}H_7$—		(71)
2-$O_2NC_6H_4$—	2-$C_{10}H_7$—		(71)
2-$O_2NC_6H_4$—	2,5-$(CH_3)(NO_2)C_6H_3$—		(71)
3-$O_2NC_6H_4$—	4-$O_2NC_6H_4$—		(71, 199)
3-$O_2NC_6H_4$—	1-$C_{10}H_7$—		(71, 199)
3-$O_2NC_6H_4$—	2-$C_{10}H_7$—		(71, 199)
3-$O_2NC_6H_4$—	3,4-$(Br)(CH_3)C_6H_3$—		(199)
3-$O_2NC_6H_4$—	2,4-$(CH_3)(NO_2)C_6H_3$—		(71)
3-$O_2NC_6H_4$—	2,5-$(CH_3)(NO_2)C_6H_3$—		(71)
3-$O_2NC_6H_4$—	4,2-$(CH_3)(NO_2)C_6H_3$—		(71)
3-$O_2NC_6H_4$—	4,3-$(CH_3)(NO_2)C_6H_3$—		(71)
3-$O_2NC_6H_4$—	2,5-$(CH_3O)(NO_2)C_6H_3$—		(71)
4-$O_2NC_6H_4$—	1-$C_{10}H_7$—		(71)
4-$O_2NC_6H_4$—	2-$C_{10}H_7$—		(71)
4-$O_2NC_6H_4$—	2,4-$(CH_3)(NO_2)C_6H_3$—		(71)
4-$O_2NC_6H_4$—	2,5-$(CH_3)(NO_2)C_6H_3$—		(71)
4-$O_2NC_6H_4$—	4,2-$(CH_3)(NO_2)C_6H_3$—		(71)
4-$O_2NC_6H_4$—	4,3-$(CH_3)(NO_2)C_6H_3$—		(71)
4-$O_2NC_6H_4$—	2,5-$(CH_3)(NO_2)C_6H_3$—		(71)
4-$O_2NC_6H_4$—	4,3-$(CH_3OOC)(HO)C_6H_3$—	(7)	(7)
4,3-$(CH_3OOC)(HO)C_6H_3$—	2,4,5-$(CH_3)(HO)$(iso-$C_3H_7)C_6H_2$—	(7)	(7)
1-$C_{10}H_7$—	3,4-$(Cl)(CH_3O)C_6H_3$—		(32)
1-$C_{10}H_7$—	4,3-$(Cl)(CH_3O)C_6H_3$—		(32)
1-$C_{10}H_7$—	2,3-$(CH_3)(NO_2)C_6H_3$—		(71)
1-$C_{10}H_7$—	2,4-$(CH_3)(NO_2)C_6H_3$—		(71)
1-$C_{10}H_7$—	2,5-$(CH_3)(NO_2)C_6H_3$—		(71)
1-$C_{10}H_7$—	4,2-$(CH_3)(NO_2)C_6H_5$—		(71)
1-$C_{10}H_7$—	4,3-$(CH_3)(NO_2)C_6H_3$—		(71)
1-$C_{10}H_7$—	5,2-$(CH_3)(NO_2)C_6H_3$—		(71)
1-$C_{10}H_7$—	2,5-$(CH_3O)(NO_2)C_6H_3$—		(71)
2-$C_{10}H_7$—	2,3-$(Cl)(CH_3)C_6H_3$—		(32)
2-$C_{10}H_7$—	2,4-$(Cl)(CH_3)C_6H_3$—		(32)
2-$C_{10}H_7$—	2,5-$(Cl)(CH_3)C_6H_6$—		(32)
2-$C_{10}H_7$—	2,6-$(Cl)(CH_3)C_6H_3$—		(32)
2-$C_{10}H_7$—	4,3-$(Cl)(CH_6)C_6H_3$—		(32)
2-$C_{10}H_7$—	5,2-$(Cl)(CH_3)C_6H_3$—		(32)
2-$C_{10}H_7$—	2,4-$(CH_3)(NO_2)C_6H_3$—		(71)
2-$C_{10}H_7$—	2,5-$(CH_3)(NO_2)C_6H_3$—		(71)
2-$C_{15}H_7$—	4,2-$(CH_3)(NO_2)C_6H_3$—		(71)
2-$C_{10}H_7$—	4,3-$(CH_3)(NO_2)C_6H_3$—		(71)
2-$C_{10}H_7$—	5,2-$(CH_3)(NO_2)C_6H_3$—		(71)
2-$C_{10}H_7$—	2,5-$(CH_3O)(NO_2)C_6H_3$—		(71)
2-$C_{10}H_7$—	2,4,6-$(CH_3)_3C_6H_2$—		(32)
2-$C_{10}H_7$—	6,3,5-$(Cl)(CH_6)_2C_6H_2$—		(32)
2-$C_{10}H_7$—	6,2,4,5-$(Cl)(CH_3)_3C_6H$—		(32)

TABLE 2—*Continued*

(5) Aryl-heterocyclic and aryl-alicyclic thioureas, RHNCSNHR′

R	R′	References	
		Section II	Section III
C_6H_5—	2-Pyridyl-	(196)	
C_6H_5—	5-Phenyl-2-oxazolyl-		(94)
C_6H_5—	5-Benzylmercaptomethyl-2-oxazolinyl-		(94)
C_6H_5—	2-Thiazolinyl-		(94)
C_6H_5—	5-Methyl-2-thiazolyl-		(94)
C_6H_5—	5-Phenyl-2-thiazolyl-		(94)
C_6H_5—	2-Benzothiazolyl-	(139)	
C_6H_5—	6-Chloro-2-benzothiazolyl-	(139)	
C_6H_5—	5-Chloro-2-thenyl-		(113)
C_6H_5—	5-Methyl-2-thenyl		(113)
C_6H_5—	5-*tert*-Butyl-2-thenyl-		(113)
C_6H_5—	5-Anilino-3-(1,2,4-triazolyl)-		(94)
C_6H_5—	5-Anilino-1-phenyl-3-(1,2,4-triazolyl)-		(94)
C_6H_5—	5-Benzylthio-3-(1,2,4-triazolyl)-		(94)
C_6H_5—	3-Benzylthio-1-phenyl-5-(1,2,4-triazolyl)-		(94)
C_6H_5—	5-Benzylthio-1-phenyl-3-(1,2,4-triazolyl)-		(94)
C_6H_5—	5-Methylthio-1-phenyl-3-(1,2,4-triazolyl)-		(94)
C_6H_5—	1-Phenyl-5-thio-3-(1,2,4-triazolyl)-		(94)
C_6H_5—	1-Butyl-2-(2-thienyl)ethyl-		(102)
C_6H_5—	1-Ethyl-2-(5-chloro-2-thienyl)ethyl-		(102)
C_6H_5—	1-Ethyl-2-(5-ethyl-2-thienyl)ethyl-		(102)
C_6H_5—	1-Ethyl-2-(5-methyl-2-thienyl)ethyl-		(102)
C_6H_5—	1-Ethyl-2-(5-propyl-2-thienyl)ethyl-		(102)
C_6H_5—	Cyclohexyl-		(221)
4-ClC_6H_4—	2-Pyridyl-	(196)	
4-HOC_6H_4—	2-Pyridyl-	(19)	
3-$CH_3C_6H_4$—	2-Pyridyl-	(196)	
4-$CH_3C_6H_4$—	2-Pyridyl-	(196)	
4-$C_6H_5C_6H_4$—	Cyclohexyl-		(31)
4-$C_6H_5C_6H_4$—	Bornyl-		(31)
4-$C_6H_5C_6H_4$—	Camphyl-		(31)
4-$CH_3OC_6H_4$—	Cyclohexyl-		(37)
4-$C_2H_5OC_6H_4$—	3-Quinolyl-	(79)	
4-$C_2H_5OC_6H_4$—	4-Piperidyl-	(79)	
4-$C_2H_5OC_6H_4$—	4-Ethoxycyclohexyl-	(121)	
4-$(C_2H_5)_2NCH_2CH_2OC_6H_4$—	2-Pyridyl-	(19)	
1-$C_{10}H_7$—	Cyclohexyl-		(230)
2-$C_{10}H_7$—	Cyclohexyl-		(31)
2-$C_{10}H_7$—	Camphyl-		(31)
4,3-(HOOC)(HO)C_6H_3—	Cyclohexyl-	(7)	(7)
4,3-(CH_3OOC)(HO)C_6H_3—	2-Thiazolyl-	(7)	(7)
4,3-(CH_3OOC)(HO)C_6H_3—	2-Piperidyl-	(7)	(7)
4,3-(CH_3OOC)(HO)C_6H_3—	2-Piperidinoethyl-	(7)	(7)
4,3-(CH_3OOC)(HO)C_6H_3—	4-Amino-2-methyl-6-quinolyl-	(7)*	(7)*
4,3-(CH_3OOC)(HO)C_6H_3—	2,3-Dimethyl-1-phenyl-5-pyrazolin-4-yl-	(7)	(7)
4,3-(CH_3OOC)(HO)C_6H_3—	Cyclohexyl-	(7)	(7)

(6) Aryl-aralkyl and aryl-acyl thioureas, RNHCSNHR′

C_6H_5—	$C_6H_5(CH_2)_2$—		(27)
4-$C_6H_5C_6H_4$—	$C_6H_5CH_2$—		(31)
4-$CH_3OC_6H_4$—	$C_6H_5CH_2$—		(37)
4-$CH_3OC_6H_4$—	$C_6H_5CH(CH_3)$—		(37)
1-$C_{10}H_7$—	$C_6H_5CH_2$—		(230)
2-$C_{10}H_7$—	$C_6H_5CH_2$—		(31)
4,3-(HOOC)(HO)C_6H_3—	$C_6H_5CH_2$—	(7)	(7)
4,3-(CH_3OOC)(HO)C_6H_3—	4,3-(C_2H_5OOC)(HO)$C_6H_3CH_2$—	(7)	(7)

* Hydrochloride.

TABLE 2—*Continued*

(6) Aryl-aralkyl and aryl-acyl thioureas, RNHCSNHR′—*Continued*

R	R′	References	
		Section II	Section III
3,4,6-$(CH_3)(NO_2)_2C_6H_2$—	$C_6H_5CH_2$—		(31)
C_6H_5—	3-$O_2NC_6H_4CO$—		(232)
4-BrC_6H_4—	3-$O_2NC_6H_4CO$—		(232)
4-ClC_6H_4—	3-$O_2NC_6H_4CO$—		(232)
2-$CH_3C_6H_4$—	3-$O_2NC_6H_4CO$—		(232)
3-$CH_3C_6H_4$—	3-$O_2NC_6H_4CO$—		(232)
4-$CH_3C_6H_4$—	3-$O_2NC_6H_4CO$—		(232)
2-$O_2NC_6H_4$—	3-$O_2NC_6H_4CO$—		(232)
3-$O_2NC_6H_4$—	3-$O_2NC_6H_4CO$—		(232)
4-$O_2NC_6H_4$—	3-$O_2NC_6H_4CO$—		(232)
2-$HOOCC_6H_4$—	3-$O_2NC_6H_4CO$—		(232)
4-$HOOCC_6H_4$—	3-$O_2NC_6H_4CO$—		(232)
1-$C_{10}H_7$—	3-$O_2NC_6H_4CO$—		(232)
2-$C_{10}H_7$—	2-$O_2NC_6H_4CO$—		(232)
3,4-(Br)$(CH_3)C_6H_3$—	3-$O_2NC_6H_4CO$—		(232)
4,3-$(CH_3)(NO_2)C_6H_3$—	3-$O_2NC_6H_4CO$—		(232)

(7) Aryl-alkyl and aralkyl-alkyl thioureas, RHNCSNHR′

C_6H_5—	CH_3—	(57, 138)	(57)
C_6H_5—	n-C_3H_7—	(57)	(57)
C_6H_5—	n-C_4H_9—	(57, 59)	(57)
C_6H_5—	n-C_5H_{11}—	(57)	(57)
C_6H_5—	$C_{12}H_{25}$—	(6, 59)	
C_6H_5—	$C_{14}H_{29}$—	(161)	
C_6H_5—	$C_{16}H_{33}$—	(161)	
C_6H_5—	CH_2=$CHCH_2$—	(59)	
C_6H_5—	CH_2=$C(CH_3)CH_2$—		(144)
C_6H_5—	CH_2=$CHCH(CH_3)$—		(144)
C_6H_5—	CH_3CH=$CHCH_2$—		(144)
C_6H_5—	CH_2=$CHCH_2CH_2$—		(144)
C_6H_5—	CH_3OCH_2—		(132)
C_6H_5—	$C_2H_5OCH_2$—		(132, 133)
C_6H_5—	(iso-$C_5H_{11}O$)CH_2—		(133)
4-ClC_6H_4—	CH_3—		(125)
4-ClC_6H_4—	iso-C_3H_7—		(84)
4-ClC_6H_4—	N≡C—		(84)
4-$H_2NC_6H_4$—	CH_2=$CHCH_2$—	(99)	
3-$CH_3CONHC_6H_4$—	CH_2=$CHCH_2$—	(99)	
4-$CH_3CONHC_6H_4$—	CH_2=$CHCH_2$—	(99)	
2-$CH_3C_6H_4$—	CH_3—	(57)	(57)
2-$CH_3C_6H_4$—	n-C_3H_7—	(57)	(57)
2-$CH_3C_6H_4$—	n-C_4H_9—	(57)	(57)
2-$CH_3C_6H_4$—	n-C_5H_{11}—	(57)	(57)
3-$CH_3C_6H_4$—	CH_3—	(57)	(57)
3-$CH_3C_6H_4$—	n-C_3H_7—	(57)	(57)
3-$CH_3C_6H_4$—	n-C_4H_9—	(57)	(57)
3-$CH_3C_6H_4$—	n-C_5H_{11}—	(57)	(57)
4-$CH_3C_6H_4$—	CH_3—	(57)	(57)
4-$CH_3C_6H_4$—	n-C_3H_7—	(57)	(57)
4-$CH_3C_6H_4$—	n-C_4H_9—	(57)	(57)
4-$CH_3C_6H_4$—	n-C_5H_{11}—	(57)	(57)
4-$CH_3C_6H_4$—	CH_2=$CHCH_2$—	(59)	
4-$CH_3C_6H_4$—	CH_2=$CHCH(CH_3)$—		(144)
4-$CH_3C_6H_4$—	CH_2=$C(CH_3)CH_2$—		(144)
4-$CH_3C_6H_4$—	CH_3CH=$CHCH_2$—		(144)
4-$CH_3C_6H_4$—	CH_2=$CHCH_2CH_2$—		(144)
4-$CH_3C_6H_4$—	CH_3OCH_2—		(132)

TABLE 2—*Continued*

(7) Aryl-alkyl and aralkyl-alkyl thioureas, RHNCSNHR′—*Continued*

R	R′	References	
		Section II	Section III
4-$CH_3C_6H_4$—	$C_2H_5OCH_2$—		(132, 133)
4-$CH_3C_6H_4$—	iso-$C_5H_{11}OCH_2$—		(132, 133)
4-$C_6H_5C_6H_4$—	CH_3—		(31)
4-$C_6H_5C_6H_4$—	C_2H_5—		(31)
4-$C_6H_5C_6H_4$—	n-C_3H_7—		(31)
4-$C_6H_5C_6H_4$—	n-C_4H_9—		(31)
4-$C_6H_5C_6H_4$—	n-C_5H_{11}—		(31)
4-$C_6H_5C_6H_4$—	n-C_7H_{15}—		(31)
3-HOOCCH=CHC_6H_4—	CH_2=$CHCH_2$—	(99)	
2-$CH_3OC_6H_4$—	CH_3—	(57)	(57)
2-$CH_3OC_6H_4$—	n-C_3H_7—	(57)	(57)
2-$CH_3OC_6H_4$—	n-C_4H_9—	(57)	(57)
2-$CH_3OC_6H_4$—	n-C_5H_{11}—	(57)	(57)
3-$CH_3OC_6H_4$—	CH_3—	(57)	(57)
3-$CH_3OC_6H_4$—	n-C_3H_7—	(57)	(57)
3-$CH_3OC_6H_4$—	n-C_4H_9—	(57)	(57)
3-$CH_3OC_6H_4$—	n-C_5H_{11}—	(57)	(57)
4-$CH_3OC_6H_4$—	CH_3—	(57)	(57)
4-$CH_3OC_6H_4$—	n-C_3H_7—	(57)	(57)
4-$CH_3OC_6H_4$—	n-C_4H_9—	(57)	(37, 57)
4-$CH_3OC_6H_4$—	iso-C_4H_9—		(37)
4-$CH_3OC_6H_4$—	n-C_5H_{11}—	(57)	(37, 57)
4-$CH_3OC_6H_4$—	n-C_7H_{15}—		(37)
2-$C_2H_5OC_6H_4$—	CH_3—	(57)	(57)
2-$C_2H_5OC_6H_4$—	n-C_3H_7—	(57)	(57)
2-$C_2H_5OC_6H_4$—	n-C_4H_9—	(57)	(57)
2-$C_2H_5OC_6H_4$—	n-C_5H_{11}—	(57)	(57)
3-$C_2H_5OC_6H_4$—	CH_3—	(57)	(57)
3-$C_2H_5OC_6H_4$—	n-C_3H_7—	(57)	(57, 125)
3-$C_2H_5OC_6H_4$—	n-C_4H_9—	(57)	(57)
3-$C_2H_5OC_6H_4$—	n-C_5H_{11}—	(57)	(57)
4-$C_2H_5OC_6H_4$—	CH_3—	(57)	(57)
4-$C_2H_5OC_6H_4$—	n-C_3H_7—	(57)	(57)
4-$C_2H_5OC_6H_4$—	n-C_4H_9—	(57)	(57)
4-$C_2H_5OC_6H_4$—	n-C_5H_{11}—	(57)	(57)
4-$C_2H_5OC_6H_4$—	$HOCH_2CH_2$—	(59)	
4-$(C_2H_5)_2NCH_2CH_2OC_6H_4$—	CH_2=CH—CH_2—	(19, 20)	
4-(4-$O_2NC_6H_4S$)C_6H_4—	CH_2=$CHCH_2$—	(128)	
4-(4-$O_2NC_6H_4SO_2$)C_6H_4—	CH_2=$CHCH_2$—	(128)	
3-$O_2NC_6H_4$—	n-C_3H_7—		(71)
4-$O_2NC_6H_4$—	n-C_3H_7—		(71)
4-$O_2NC_6H_4$—	CH_2=$CHCH_2$—	(59)	
3-HOOCC_6H_4—	CH_2=$CHCH_2$—	(18, 126, 131)	
3-$CH_3OOCC_6H_4$—	CH_2=$CHCH_2$—	(18)	
1-$C_{10}H_7$—	CH_3—		(78, 230)
1-$C_{10}H_7$—	C_2H_5—		(78, 230)
1-$C_{10}H_7$—	n-C_3H_7—		(230)
1-$C_{10}H_7$—	iso-C_3H_7—		(230)
1-$C_{10}H_7$—	n-C_4H_9—		(230)
1-$C_{10}H_7$—	2-C_4H_9—		(230)
1-$C_{10}H_7$—	n-C_5H_{11}—		(230)
1-$C_{10}H_7$—	iso-C_5H_{11}—		(230)
1-$C_{10}H_7$—	$(CH_3)_2CHCH(CH_3)$—		(230)
1-$C_{10}H_7$—	n-C_6H_{13}—		(230)
1-$C_{10}H_7$—	iso-C_6H_{13}—		(230)
1-$C_{10}H_7$—	n-C_7H_{15}—		(230)
1-$C_{10}H_7$—	2-C_7H_{15}—		(230)
1-$C_{10}H_7$—	n-C_8H_{17}—		(230)
1-$C_{10}H_7$—	2-C_8H_{17}—		(230)

TABLE 2—*Concluded*

(7) Aryl-alkyl and aralkyl-alkyl thioureas, RHNCSNHR′—*Concluded*

R	R′	References	
		Section II	Section III
2-$C_{10}H_7$—	CH_3—		(31)
2-$C_{10}H_7$—	C_2H_5—		(31)
2-$C_{10}H_7$—	*n*-C_3H_7—		(31)
2-$C_{10}H_7$—	*n*-C_4H_9—		(31)
2-$C_{10}H_7$—	*n*-C_5H_{11}—		(31)
2-$C_{10}H_7$—	*n*-C_7H_{15}—		(31)
3,4-(Br)$(CH_3)C_6H_3$—	CH_3—		(125)
4,2-(Cl)$(CH_3)C_6H_3$—	CH_2=$CHCH_2$—	(23)	
2,4-$(CH_3)(NO_2)C_6H_3$—	*n*-C_3H_7—		(71)
2,5-$(CH_3)(NO_2)C_6H_3$—	*n*-C_3H_7—		(71)
4,2-$(CH_3)(NO_2)C_6H_3$—	*n*-C_3H_7—		(71)
4,3-$(CH_3)(NO_2)C_6H_3$—	*n*-C_3H_7—		(71)
2,5-$(CH_3O)(NO_2)C_6H_3$—	*n*-C_3H_7—		(71)
4,3-(HOOC)(HO)C_6H_3—	CH_3—	(7)	(7)
4,3-(HOOC)(HO)C_6H_3—	C_2H_5—	(7)	(7)
4,3-(HOOC)(HO)C_6H_3—	*n*-C_3H_7—	(7)	(7)
4,3-(HOOC)(HO)C_6H_3—	*n*-C_4H_9—	(7)	(7)
4,3-(HOOC)(HO)C_6H_3—	CH_2=$CHCH_2$—	(7, 33)	(7)
4,3-$(CH_3OOC)(HO)C_6H_3$—	$(C_2H_5)_2NCH_2CH_2$—	(7)	(7)
3,4,6-$(CH_3)(NO_2)_2C_6H_2$—	CH_3—		(31)
3,4,6-$(CH_3)(NO_2)_2C_6H_2$—	C_2H_5—		(31)
3,4,6-$(CH_3)(NO_2)_2C_6H_2$—	*n*-C_3H_7—		(31)
3,4,6-$(CH_3)(NO_2)_2C_6H_2$—	*n*-C_4H_9—		(31)
3,4,6-$(CH_3)(NO_2)_2C_6H_2$—	iso-C_4H_9—		(31)
3,4,6-$(CH_3)(NO_2)_2C_6H_2$—	*n*-C_5H_{11}—		(31)
3,4,6-$(CH_3)(NO_2)_2C_6H_2$—	iso-C_5H_{11}—		(31)
$(C_6H_5)_2CH$—	iso-C_5H_{11}—		(27)

(8) Other 1,3-disubstituted thioureas, RHNCSNHR′

C_3H_7—	$(C_6H_5)_2CHCO$—	(165)	
4-$C_2H_5OC_6H_4$—	4-$CH_3OC_6H_4CH_2$—	(79)	
CH_3—	iso-C_3H_7—	(179)	
CH_3=$CHCH_2$—	$CH_3(CH_2)_{11}$—	(59)	
$HO_3SCH_2CH_2$—	$CH_3(CH_2)_{11}$—	(202)	
CH_3—	1-Methyl-5-carbethoxy-4-imidazolyl-		(49)
CH_3—	2-Benzyl-5-carbethoxy-1-methyl-4-imidazolyl-		(49)
CH_3—	5-Carbethoxy-1-methyl-2-phenyl-4-imidazolyl-		(49)
iso-C_3H_7—	2-Pyridyl-	(196)	
iso-C_3H_7—	6-Methoxy-8-quinolyl-	(163)	(163)
CH_3=$CHCH_2$—	2-Pyridyl-	(196)	
CH_2=$CHCH_2$—	2-Thiazolinyl-		(94)
CH_2=$CHCH_2$—	5-Methyl-2-thiazolyl-		(94)
CH_2=$CHCH_2$—	6-Ethoxy-2-benzothiazolyl-		(94)
CH_2=$CHCH_2$—	6-Ethoxy-8-quinolyl-		(94)
CH_2=$CHCH_2$—	5-Benzylthiomethyl-2-oxazolinyl-		(94)
CH_2=$CHCH_2$—	5-Anilino-3-(1,2,4-triazolyl)-		(94)
CH_2=$CHCH_2$—	5-Benzothio-3-(1,2,4-triazolyl)-		(94)
CH_2=$CHCH_2$—	3-Benzylthio-1-phenyl-5-(1,2,4-triazolyl)-		(94)
CH_2=$CHCH_2$—	5-Benzylthiomethyl-1-phenyl-3-(1,2,4-triazolyl)-		(94)
CH_2=$CHCH_2$—	5-Methylthio-1-phenyl-3-(1,2,4-triazolyl)-		(94)
CH_2=$CHCH_2$—	1-Phenyl-5-thio-3-(1,2,4-triazolyl)-		(94)
CH_3CO—	5-Carbethoxy-2-phenyl-4-imidazolyl-		(49)
CH_3CO—	5-Carbethoxy-1-methyl-2-phenyl-4-imidazolyl-		(49)

TABLE 3

1,1,3-Trisubstituted thioureas, RR'NCSNHR''

R	R'	R''	References	
			Section II	Section III
CH_3—	CH_3—	CH_3—	(131)	
CH_3—	CH_3—	4-$C_6H_5C_6H_4$—		(31)
CH_3—	CH_3—	2-$C_{10}H_7$—		(31)
C_2H_5—	C_2H_5—	C_6H_5—	(59)	
C_2H_5—	C_2H_5—	4-$C_6H_5C_6H_4$—		(31)
C_2H_5—	C_2H_5—	4-$CH_3OC_6H_4$—		(37)
C_2H_5—	C_2H_5—	1-$C_{10}H_7$—		(230)
C_2H_5—	C_2H_5—	2-$C_{10}H_7$—		(31)
C_2H_5—	C_2H_5—	Cyclohexyl-	(59)	
n-C_3H_7—	*n*-C_3H_7—	4-$C_6H_5C_6H_4$—		(31)
n-C_3H_7—	*n*-C_3H_7—	1-$C_{10}H_7$—		(230)
n-C_3H_7—	*n*-C_3H_7—	2-$C_{10}H_7$—		(31)
n-C_3H_7—	*n*-C_3H_7—	3,4,6-$(CH_3)(NO_2)_2C_6H_2$—		(31)
n-C_4H_9—	*n*-C_4H_9—	4-$C_6H_5C_6H_4$—		(31)
n-C_4H_9—	*n*-C_4H_9—	4-$CH_3OC_6H_4$—		(37)
n-C_4H_9—	*n*-C_4H_9—	1-$C_{10}H_7$—		(230)
iso-C_4H_9—	iso-C_4H_9—	2-$C_{10}H_7$—		(31)
n-C_5H_{11}—	*n*-C_5H_{11}—	4-$C_6H_5C_6H_4$—		(31)
n-C_5H_{11}—	*n*-C_5H_{11}—	2-$C_{10}H_7$—		(31)
n-C_5H_{11}—	*n*-C_5H_{11}—	3,4,6-$(CH_3)(NO_2)_2C_6H_2$—		(31)
iso-C_5H_{11}—	iso-C_5H_{11}—	1-$C_{15}H_7$—		(230)
C_6H_5—	C_6H_5—	CH_3CO—		(62)
C_6H_5—	C_6H_5—	C_6H_5CO—		(62)
C_6H_5—	C_6H_5—	3-$O_2NC_6H_4CO$—		(232)
C_6H_5—	C_6H_5—	CH_3OOC—		(62)
C_6H_5—	C_6H_5—	C_2H_5OOC—		(62)
$C_6H_5CH_2$—	$C_6H_5CH_2$—	1-$C_{10}H_7$—		(230)
$C_6H_5CH_2$—	$C_6H_5CH_2$—	4-$CH_3OC_6H_4$—		(37)
Cyclohexyl-	Cyclohexyl-	4-$CH_3OC_6H_4$—		(37)
$C_6H_5CH_2CH_2$—	CH_3—	CH_3—		(27)
4-(HOOC)C_6H_4—	CH_3—	CH_3—	(7)	(7)
4,3-(HOOC)(HO)C_6H_3—	CH_3—	CH_3—	(7)	(7)
N≡CCH_2CO—	*n*-C_3H_7—	*n*-C_3H_7—	(179)	
N≡CCH_2CO—	iso-C_4H_9—	iso-C_4H_9—	(179)	
CH_3OOC—	C_6H_5—	C_6H_5—		(62)
CH_3—	4-$C_2H_5OC_6H_4$—	4-$C_2H_5OC_6H_4$—	(121)	
CH_3CO—	4-$C_2H_5OC_6H_4$—	4-$C_2H_5OC_6H_4$—	(79)	
CH_3—	C_6H_5—	iso-$C_5H_{11}OCH_2$—		(133)
CH_3—	C_6H_5—	4-BrC_6H_4—		(125)
CH_3—	C_6H_5—	4-$CH_3OC_6H_4$—		(37)
CH_3—	C_6H_5—	4,3-$(CH_3OOC)(HO)C_6H_3$—	(7)	(7)
CH_3—	C_6H_5—	3-$O_2NC_6H_4CO$—		(232)
CH_3—	C_6H_5—	5-Hydroxymethyl-2-thenyl		(113)
CH_3—	N≡CCH_2CO—	iso-C_5H_7—	(179)	
CH_3—	1-*Ethyl*-5-tetrazolyl-	C_6H_5—		(116)
CH_3—	1-Isobutyl-5-tetrazolyl-	C_6H_5—		(116)
CH_3—	1-*n*-Heptyl-5-tetrazolyl-	C_6H_5—		(116)
CH_3—	1-Cyclohexyl-5-tetrazolyl-	C_6H_5—		(116)
CH_3—	1-Phenyl-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	C_6H_5—	4-$CH_3OC_6H_4$—		(37)
C_2H_5—	C_6H_5—	4,3-$(C_2H_5OOC)(HO)C_6H_3$—	(7)	(7)
C_2H_5—	N≡CCH_2CO—	*n*-C_3H_7—	(179)	
C_2H_5—	N≡CCH_2CO—	$C_6H_5CH_2$—	(179)	
C_2H_5—	1-Methyl-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	1-Ethyl-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	1-*n*-Propyl-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	1-Isopropyl-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	1-*n*-Butyl-5-tetrazolyl-	C_6H_5—		(116)

TABLE 3—*Concluded*

1,1,3-Trisubstituted thioureas, RR'NCSNHR''—*Concluded*

R	R'	R''	References	
			Section II	Section III
C_2H_5—	1-Isobutyl-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	1-*n*-Amyl-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	1-Isoamyl-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	1-(3-Amyl)-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	1-Cyclohexyl-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	1-Phenyl-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	1-Benzyl-5-tetrazolyl-	C_6H_5—		(116)
C_2H_5—	1-Phenethyl-5-tetrazolyl-	C_6H_5—		(116)
iso-C_4H_9—	1-Ethyl-5-tetrazolyl-	C_6H_5—		(116)
$C_6H_5CH_2$—	1-Methyl-5-tetrazolyl-	C_6H_5—		(116)
$C_6H_5CH_2$—	1-Ethyl-5-tetrazolyl-	C_6H_5—		(116)
$C_6H_5CH_2$—	1-Cyclohexyl-5-tetrazolyl-	C_6H_5—		(116)
$C_6H_5CH_2CH_2$—	1-Ethyl-5-tetrazolyl-	C_6H_5—		(116)
$C_6H_5CH_2CH_2$—	1-Cyclohexyl-5-tetrazolyl-	C_6H_5—		(116)

TABLE 4

Pseudothioureas

A. *S*-Substituted thioureas and thiuronium salts, HN=C(SR)NH_2

R	References	
	Section II	Section III
CH_3—	(5, 82, 188, 189, 195)	(31, 145[a], 230)
C_2H_5—	(6, 30)	(24[b], 31, 145[a], 205)
n-C_3H_7—		(31)
iso-C_3H_7—		(31)
n-C_4H_9—	(30)	(31, 145[a])
iso-C_4H_9—		(31, 145[a])
sec-C_4H_9—		(31)
n-C_5H_{11}—	(56)	(31)
iso-C_5H_{11}—		(31)
sec-C_5H_{11}—		(31)
n-C_6H_{13}—		(31, 145[a])
n-C_8H_{17}—	(30)	(136)[e]
$CH_3(CH_2)_5CH(CH_3)$—		(136)[e]
$CH_3(CH_2)_3CH(C_2H_5)CH_2$—		(136)[e]
n-C_9H_{19}—		(136)[e]
n-$C_{10}H_{21}$—	(9)[b][c][d]	(9[b][c][d], 136[e])
n-$C_{11}H_{23}$—		(136)[e]
n-$C_{12}H_{25}$—	(9[b][c][d], 81[b])	(9[b][c][d], 136[e], 145[a])
$C_{14}H_{29}$—	(9)[b][c][d]	(9)[b][c][d]
$C_{16}H_{33}$—	(9)[b][c][d]	(9)[b][c][d]
n-$C_{18}H_{37}$—	(240)	(145)[a]
CH_2=$CHCH_2$—		(31)
$HOCH_2CH_2$—		(136)[e]
$HOCH_2C(CH_3)$=CH_2—		(176)[e]
$C_4H_9OCH_2$—		(31)
iso-$C_5H_{11}OCH_2$—		(31)
$C_{12}H_{25}OCH_2$—	(81)[b]	
$CH_3OCH_2C(CH_3)$=CH_2—		(176)[e]
$C_2H_5OCH_2C(CH_3)$=CH_2—		(176)[e]
n-$C_3H_7OCH_2C(CH_3)$=CH_2—		(176)[e]
iso-$C_5H_7OCH_2C(CH_3)$=CH_2—		(176)[e]
$C_4H_9OCH_2C(CH_3)$=CH_2—		(176)[e]
$HOOCCH_2$—	(165)	
$HOOCH_2CH_2$—		(14)[c]

TABLE 4—*Continued*

A. *S*-Substituted thioureas and thiuronium salts, $HN{=}C(SR)NH_2$—*Continued*

R	References	
	Section II	Section III
$HOOCCH_2CH(CH_3)$—		(14)[c]
$CH_3COOCH_2C(CH_3){=}CH_2$—		(176)[e]
$C_2H_5COOCH_2C(CH_3){=}CH_2$—		(176)[e]
n-$C_3H_7COOCH_2C(CH_3){=}CH_2$—		(176)[e]
iso-$C_3H_7COOCH_2C(CH_3){=}CH_2$—		(176)[e]
$HOOCCHBrCH_2$—		(14)[c]
$HOOCCHClCH_2$—		(14)[c]
$HOOCCHClCH(CH_3)$—		(14)[c]
$CH_3OOCCHClCH_2$—		(14)[c]
$OHCCHClCH_2$—		(14)[c]
C_6H_5—		(55)
1-$C_{10}H_7$—	(165)	
$C_6H_5CH_2$—	(59, 188)	(31, 136[c], 145[a])
$(C_6H_5)_2CH$—	(6)	(22)[b]
1-$C_{10}H_7CH_2CH_2$—	(56)	
4-$(CH_3)_3CCH_2C(CH_3)_2C_6H_4OCH_2CH_2$—	(17)[b]	
4-$(CH_3)_3CCH_2C(CH_3)_2C_6H_4(OC_2H_4)_3$—	(17)[b]	
4-$CH_3C_6H_4SO_3CH_2CH_2$—	(17)[c]	
$C_6H_5COCH_2CH_2$—		(40)[c]
$C_6H_5COCH{=}CH$—		(40)[c]
Cyclohexyl-		(145)[a]
Phthalimidomethyl-		(106)[b]
3-Phthalimidopropyl-		(106)[b]
4-Phthalimidobutyl-		(106)[b]
5-Phthalimidoamyl-		(106)[b]
Tetraacetyl-β-D-glucopyranosyl-		(21)[b]
Tetraacetyl-β-D-galactopyranosyl-		(21)[b]
Triacetyl-β-D-xylopyranosyl-		(21)[c]
Heptaacetyl-β-D-cellobiosyl-		(21)[b]
Tetraacetyl-β-D-glucopyranosyl-		(21)[f]
2-Pyridyl-		(166)[b]
2-Amino-4-thiazolylmethyl-		(227)[g]
2-Methyl-4-thiazolylmethyl-		(227)[g]
2-Phenyl-4-thiazolylmethyl-		(227)[g]
2,4-Dimethyl-6-pyrimidyl-		(182[c], 181[c])
4,6-Dimethyl-2-pyrimidyl-		(166)[c]
2-Methylmercapto-4-methyl-6-pyrimidyl-		(181[c], 182[c])
2-Ethylmercapto-4-methyl-6-pyrimidyl-		(181)[c]
4-Amino-5-nitro-6-methyl-2-pyrimidyl-		(182)[c]
4-Methyl-5-nitro-6-amino-2-pyrimidyl-		(181)[c]
2-(1-Pyrrolidyl)ethyl-	(147)[g]	
2-(2-Methyl-1-pyrrolidyl)ethyl-	(147)[g]	
1-Methyl-2-(1-pyrrolidyl)ethyl-	(147)[g]	
1-Methyl-3-(1-pyrrolidyl)propyl-	(147)[g]	
4-(1-Pyrrolidyl)butyl-	(147)[g]	

[a] *p*-Toluenesulfonate.
[b] Hydrobromide.
[c] Hydrochloride.
[d] Hydroiodide.
[e] Picrate.
[f] Acetate.
[g] Dihydrochloride.

TABLE 4—*Continued*

B. Pseudothiuronium salts of carboxylic acids, $H_2NC(=NH)SR \cdot A$

R	A	References Section III
$C_6H_5CH_2$—	*trans*-4-Octene-1-carboxylic acid	(50)
$C_6H_5CH_2$—	*trans*-1,*trans*-7-Undecadien-1-carboxylic acid	(50)
$C_6H_5CH_2$—	*cis*-1,*trans*-7-Undecadien-1-carboxylic acid	(50)
$C_6H_5CH_2$—	2,4-$(C_2H_5O)(CH_3O)C_6H_3COOH$	(142)
$C_6H_5CH_2$—	2,4-$(CH_3O)_2C_6H_3COOH$	(142)
4-$BrC_6H_4CH_2$—	$CH_3CH_2COCH_2COCOOH$	(141)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_4CH(CH_3)CH(CH_3)COOH$	(233)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_5CH{=}CHCOOH$	(141)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_4CO(CH_2)_2COOH$	(141)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_7CHOHCOOH$	(141)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_6CH(CH_3)CH(CH_3)COOH$	(233)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_5COCH_2CHOHCOOH$	(141)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_7CH{=}CHCOOH$	(141)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_6CH(CH_3)COOH$	(233)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_6CH(CH_3)CH_2COOH$	(233)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_6CH(CH_3)CH(CH_3)COOH$	(233)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_5CH{=}CHCOOH$	(141)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_6COCH_2CHOHCOOH$	(141)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_{10}CH(CH_3)CH_2COOH$	(233)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_{10}CH(CH_3)CH(CH_3)COOH$	(233)
4-$BrC_6H_4CH_2$—	$CH_3(CH_2)_{11}CH{=}CHCOOH$	(141)
4-$ClC_6H_4CH_2$—	$C_6H_5CH(SO_3H)COOH$	(231)
4-$ClC_6H_4CH_2$—	$C_6H_5CH_2CH(SO_3H)COOH$	(231)
4-$ClC_6H_4CH_2$—	$C_6H_5(CH_2)_2CH(SO_3H)COOH$	(231)
4-$ClC_6H_4CH_2$—	$C_6H_5(CH_2)_4CH(SO_3H)COOH$	(231)
4-$ClC_6H_4CH_2$—	$(C_3H_5)(C_2H_5)C(SO_3H)COOH$	(231)

C. Di(*S*-substituted) thiuronium salts, $[H_2NC(=NH \cdot HX)S]_2R$

R	X	References	
		Section II	Section III
$-CH_2-$	Picrate		(136)
$-CH_2CH_2-$	*p*-Toluenesulfonate		(145)
$-(CH_2)_3-$	Bromide		(106)
$-(CH_2)_4-$	Bromide		(106)
$-(CH_2)_5-$	Picrate		(136)
$-(CH_2)_5-$	Bromide		(106)
$-(CH_2)_6-$	*p*-Toluenesulfonate		(145)
$-(CH_2)_7-$	Picrate		(136)
$-(CH_2)_8-$	Picrate		(136)
$-(CH_2)_9-$	Picrate		(136)
$-(CH_2)_{10}-$	Bromide		(106)
$-CH_2C{\equiv}CCH_2-$	Chloride	(45)	
$-CH_2C(=CH_2)CH_2-$	Chloride	(45)	
$-CH_2CH(CH=CH_2)-$	Chloride	(45)	
$-CH_2CH=CClCH_2-$	Bromide	(45)	
$-CH_2CH=CHCH(CH_3)-$	Bromide	(45)	
$-CH_2CH_2CH=CHCH_2CH_2-$	Bromide	(45)	
$-CH_2C{\equiv}C-C{\equiv}CCH_2-$	Bromide	(45)	
$-CH_2CH=CHCH=CHCH_2-$	Bromide	(45)	
$-CH_2CH_2C{\equiv}CCH_2CH_2-$	Bromide	(45)	
2-Amino-4,6-pyrimidylene-	Chloride		(182)
6-Methyl-2,4-pyrimidylene-	Chloride		(182)
4-Methyl-5-nitro-2,6-pyrimidylene-	Chloride		(181)
6-Methyl-5-nitro-4,6-pyrimidylene-	Chloride		(181)

TABLE 4—*Concluded*

D. *S*- and *N*-substituted thioureas, RSC(=NR′)NR″R‴

R	R′	R″	R‴	References	
				Section II	Section III
CH_3—	H—	*n*-C_6H_{13}—	H—		(88)*
CH_3—	H—	CH_2=$CHCH_2$—	H—		(88)*
CH_3—	H—	C_6H_5—	H—		(88)*
CH_3—	H—	4-ClC_6H_4—	H—	(97)	(84, 226)
CH_3—	H—	4-$CH_3OC_6H_4$—	H—		(88)*
CH_3—	H—	2-$C_{10}H_7$—	H—		(226)
C_2H_5—	H—	iso-C_3H_7—	H—	(52)	
C_2H_5—	H—	C_6H_5—	H—	(30)	(30)
C_2H_5—	H—	4-$C_4H_9OC_6H_4$—	H—	(30)	(30)
C_2H_5—	H—	1-$C_{10}H_7$—	H—	(242)	
n-C_4H_9—	H—	C_6H_5—	H—	(30)	(30)
n-C_6H_{17}—	H—	C_6H_5—	H—	(30)	(30)
$HOOCCHClCH_2$—	H—	C_2H_5—	H—		(14)†
C_6H_5COCH=CH_2—	H—	$C_6H_5CH_2$—	H—		(40)†
CH_3CO—	H—	2-$CH_3C_6H_4$—	H—		(61)
CH_3CO—	H—	4-$CH_3C_6H_4$—	H—		(61)
CH_3—	CH_3—	C_6H_5—	H—		(88)*
CH_3—	CH_3—	$C_6H_5CH_2$—	H—		(88)*
CH_3—	C_2H_5—	C_2H_5—	H—		(88)*
CH_3—	iso-C_3H_7—	6-Methoxy-8-quinolyl-	H—	(163)	(163)
CH_3—	C_6H_5—	4-BrC_6H_4—	H—	(55)	(55)
CH_3—	C_6H_5—	Cyclohexyl-	H—		(88)*
CH_3—	$C_6H_5CH_2$—	Cyclohexyl-	H—		(88)*
CH_3—	CH_3CO—	CH_3CO—	H—		(210)
CH_3—	C_6H_5CO—	C_6H_5CO—	H—		(210)
CH_3—	4-$O_2NC_6H_4CO$—	4-$O_2NC_6H_4CO$—	H—		(210)
C_2H_5—	C_6H_5—	C_6H_5—	H—	(30)	
C_2H_5—	CH_3CO—	CH_3CO—	H—		(42, 210)
C_2H_5—	C_6H_5CO—	C_6H_5CO—	H—		(42, 210)
C_2H_5—	4-$O_2NC_6H_4CO$—	4-$O_2NC_6H_4CO$—	H—		(42, 210)
n-C_3H_7—	C_6H_5—	C_6H_5—	H—		(55)*
n-C_3H_7—	C_6H_5—	4-BrC_6H_4—	H—		(55)
n-C_3H_7—	4-$CH_3C_6H_4$—	4-$CH_3C_6H_4$—	H—		(55)*
n-C_4H_9—	C_6H_5—	C_6H_5—	H—		(55)
n-C_4H_9—	C_6H_5—	4-BrC_6H_4—	H—		(55)
$C_{10}H_{21}$—	CH_3—	CH_3—	H—	(9)*†‡	(9)*†‡
$C_{10}H_{21}$—	C_2H_5—	C_2H_5—	H—	(9)*†‡	(9)*†‡
$C_{10}H_{21}$—	iso-C_3H_7—	iso-C_3H_7—	H—	(9)*†‡	(9)*†‡
$C_{10}H_{21}$—	*n*-C_4H_9—	*n*-C_4H_9—	H—	(9)*†‡	(9)*†‡
$C_{12}H_{25}$—	CH_3—	CH_3—	H—	(9)*†‡	(9)*†‡
$C_{12}H_{25}$—	C_2H_5—	C_2H_5—	H—	(9)*†‡	(9)*†‡
$C_{12}H_{25}$—	iso-C_3H_7—	iso-C_3H_7—	H—	(9)*†‡	(9)*†‡
$C_{12}H_{25}$—	*n*-C_4H_9—	*n*-C_4H_9—	H—	(9)*†‡	(9)*†‡
$C_{14}H_{29}$—	CH_3—	CH_3—	H—	(9)*†‡	(9)*†‡
$C_{14}H_{29}$—	C_2H_5—	C_2H_5—	H—	(9)*†‡	(9)*†‡
$C_{14}H_{29}$—	iso-C_3H_7—	iso-C_3H_7—	H—	(9)*†‡	(9)*†‡
$C_{14}H_{29}$—	*n*-C_4H_9—	*n*-C_4H_9—	H—	(9)*†‡	(9)*†‡
$C_{16}H_{33}$—	CH_3—	CH_3—	H—	(9)*†‡	(9)*†‡
$C_{16}H_{33}$—	C_2H_5—	C_2H_5—	H—	(9)*†‡	(9)*†‡
$C_{16}H_{33}$—	iso-C_3H_7—	iso-C_3H_7—	H—	(9)*†‡	(9)*†‡
C_6H_5COCH=CH_2—	$C_6H_5CH_2$—	$C_6H_5CH_2$—	H—		(40)†
CH_3CO—	C_6H_5—	C_6H_5—	H—		(61)
CH_3CO—	2-$CH_3C_6H_4$—	2-$CH_3C_6H_4$—	H—		(61)
CH_3—	H—	CH_3—	CH_3—		(205, 206)
CH_3—	H—	CH_3—	$C_6H_5CH_2$—		(88)*
CH_3—	H—	C_2H_5—	C_2H_5—		(205)
2-Benzothiazolylmethyl-	H—	C_2H_5—	C_2H_5—	(59)	
CH_3—	C_6H_5—	CH_3—	CH_3—		(88)*

* Hydroiodide. †Hydrochloride. ‡Hydrobromide.

TABLE 5

Guanylthioureas

R	References	
	Section II	Section III
$H_2NC(=NH)NHCSNH_2$	(5, 195)	
$H_2NC(=NH)NHCSNHCH_3$	(222)	(222)
$H_2NC(=NH)NHCSNHC_2H_5$	(222)	(222)
$H_2NC(=NH)NHCSNHC_6H_7$	(222)	(222)
$H_2NC(=NH)NHCSNH$-iso-C_4H_9	(222)	(222)
$H_2NC(=NH)NHCSNHC_3H_5$	(114)	
$H_2NC(=NH)NHCSNH[4$-$(CH_3)_2NC_6H_4]$	(222)	(222)
$H_2NC(=NH)NHCSNH(3$-$HOC_6H_4)$	(222)	(222)
$H_2NC(=NH)NHCSNH(4$-$HOC_6H_4)$	(222)	(222)
$H_2NC(=NH)NHCSNH(4$-$CH_3OC_6H_4)$	(222)	(222)
$H_2NC(=NH)NHCSNH(4$-$C_2H_5OC_6H_4)$	(222)	(222)
$H_2NC(=NH)NHCSNH(4$-$C_2H_5OOCC_6H_4)$	(222)	(222)
$H_2NC(=NH)NHCSNH(4$-$CH_3COOC_6H_4)$	(222)	(222)
$H_2NC(=NH)NHCSNH[3,4$-$(Br)(C_2H_5O)C_6H_3]$	(222)	(222)
4-$ClC_6H_4NHC(=NH)CSNH_2$	(119)	
4-$(CH_3)_2NC_6H_4NHC(=NH)CSNH_2$	(119)	
4-$HOC_6H_4NHC(=NH)CSNH_2$	(119)	
4-$CH_3C_6H_4NHC(=NH)CSNH_2$	(119)	
4-$CH_3OC_6H_4NHC(=NH)CSNH_2$	(119)	
4-$O_2NC_6H_4NHC(=NH)CSNH_2$	(119)	
4-$H_2NSO_2C_6H_4NHC(=NH)CSNH_2$	(119)	
$(C_6H_5NHCSNH)_2C=NH$	(222)	(222)
$(iso$-$C_5H_{11}NHCSNH)_2C=NH$	(222)	(222)
$(C_6H_5NHCSNH)_2C=NH$	(222)	(222)
$(4$-$C_2H_5OC_6H_4NHCSNH)_2C=NH$	(222)	(222)
$C_6H_5NHC(=NC_6H_5)NHCSNHCH_3$		(91)
2-$CH_3C_6H_4NHC[=N(2$-$CH_3C_6H_4)]NHCSNHC_6H_5$		(91)
$1,4$-$[NHCSNHC(=NH)NH_2]_2C_6H_4$	(222)	(222)
$H_2NC(=NH)NHC(=NH)SC_2H_5$	(81)	
$H_2NC(=NH)NHC(=NH)SC_{12}H_{25}$	(81)	

TABLE 6

N-Cyclic thioureas, RCSR′

R	R′	References	
		Section II	Section III
1-Piperidyl-	4-$CH_3OC_6H_4NH$—		(37)
1-Piperidyl-	$C_6H_5(CH_2)_4NH$—		(27)
1-Piperazyl-	4-$CH_3OC_6H_4NH$—		(37)
1-Piperazyl-	$4,3$-$(C_2H_5OOC)(HO)C_6H_3NH$—	(7)	(7)
4-Carbobenzoxy-1-piperazyl-	NH_2—	(103)	
4-Morpholinyl-	NH_2—	(138)	
2-Imino-3-thiazolinyl-	C_6H_5NH—		(94)
2-Imino-3-thiazolinyl-	C_6H_5NH—		(94)
2-Imino-5-methyl-3-oxazolinyl-	C_6H_5NH—		(94)
2-Imino-5-benzylthiomethyl-3-oxazolinyl-	C_6H_5NH—		(94)
2-Imino-5-benzylthiomethyl-3-oxazolinyl-	C_6H_5NH—		(94)

TABLE 7

Miscellaneous thioureas

R	References	
	Section II	Section III
$(CH_3)_2NCSN(CH_3)_2$	(131, 195, 247)	
$(C_2H_5)(C_6H_5)NCSN(C_2H_5)(C_6H_5)$	(6)	
$H_2NCSNHCSNH_2$	(5, 59)	
$C_5H_5NHCSNHCSNH_2$	(59)	
$4\text{-}ClC_6H_4NHCSNHCSNH_2$	(119)	
$4\text{-}(CH_3)_2NC_6H_4NHCSNHCSNH_2$	(119)	
$4\text{-}H_2NSO_2C_6H_4NHCSNHCSNH_2$	(119)	
$4\text{-}HOC_6H_4NHCSNHCSNH_2$	(119)	
$4\text{-}CH_3C_6H_4NHCSNHCSNH_2$	(119)	
$4\text{-}CH_3OC_6H_4NHCSNHCSNH_2$	(119)	
$4\text{-}BrC_6H_4NHCSNHC(SC_2H_5)=NC_6H_7(i)$	(52)	
$3\text{-}ClC_6H_4NHCSNHC(SC_2H_5)=NC_6H_7(i)$	(52)	
$4\text{-}ClC_6H_4NHCSNHCSNHC_6H_7(i)$	(97)	
$4\text{-}ClC_6H_4NHCSNHCSNH(4\text{-}ClC_6H_4)$	(97)	
$4\text{-}ClC_6H_4NHCSNHC(SCH_3)=N(4\text{-}ClC_6H_4)$	(97)	
$4\text{-}ClC_6H_4NHCSNHC(SC_2H_5)=NCH_3$	(52)	
$4\text{-}ClC_6H_4NHCSNHC(SC_2H_5)=NC_2H_5$	(52)	
$4\text{-}ClC_6H_4NHCSNHC(SC_2H_5)=NC_6H_7(i)$	(52)	
$4\text{-}ClC_6H_4NHCSNHC(SC_2H_5)=NC_4H_9$	(52)	
$4\text{-}IC_6H_4NHCSNHC(SC_2H_5)=NC_6H_7(i)$	(52)	
$3,4\text{-}Cl_2C_6H_4NHCSNHC(SC_2H_5)=NC_6H_7(i)$	(52)	
$[H_2NC(=NH)SCH_2]_2$		(31)
$(4\text{-}CH_3OC_6H_4NHCSNHCH_2)_2$		(37)
$1,3\text{-}(C_6H_5NHCSNH)_2C_6H_4$	(202)	
$1,4\text{-}(C_6H_5NHCSNH)_2C_6H_4$	(202)	
$[4\text{-}(H_2NCSNHC_6H_4)]_2$	(59)	
$[4\text{-}(4\text{-}CH_3OC_6H_4NHCSNH)C_6H_4]_2$		(37)
$4\text{-}ClC_6H_4NHCSNHCONHCH_3$	(97)	
$4\text{-}ClC_6H_4NHCSNHCONHC_6H_5$	(97)	
$4\text{-}ClC_6H_4N=C(SCH_3)NHCONHCH_3$	(97)	
1,4-Bis(pseudothiocarbamidomethyl)naphthalene	(8)	
$(4\text{-}C_6H_5NHCSNHC_6H_4)_2SO_2$	(128)	
$(4\text{-}C_5H_5NHCSNHC_6H_4)_2SO_2$	(128)	
$[4\text{-}(4\text{-}BrC_6H_4NHCSNHC_6H_4)]_2SO_2$	(128)	
$[4\text{-}(4\text{-}ClC_6H_4NHCSNHC_6H_4)]_2SO_2$	(128)	
$[4\text{-}(4\text{-}IC_6H_4NHCSNHC_6H_4)]_2SO_2$	(128)	
$[4\text{-}(2\text{-}CH_3C_5H_4NHCSNHC_6H_4)]_2SO_2$	(128)	
$[4\text{-}(3\text{-}CH_3C_6H_4NHCSNHC_5H_4)]_2SO_2$	(128)	
$[4\text{-}(4\text{-}CH_3C_5H_4NHCSNHC_6H_4)]_2SO_2$	(128)	

Another novel approach to the preparation of substituted thioureas is to heat a thiourethan, a primary amine, and phosphorus pentoxide in xylene at 140–150°C. In some cases a good yield of disubstituted thiourea is obtained (197).

Ethereal thioureas undergo a transfer with alcohols (132).

$$RNHCSNHCH_2OR + R'OH \rightleftharpoons RNHCSNHCH_2OR' + ROH$$

This is a reversible reaction, and it is not influenced by the boiling point of the alcohol or the size of the alkyl group in the ether moiety.

Guanylthioureas are usually prepared by method III,C, using guanidine and an isothiocyanate (222). Syntheses for thioureas labeled with C^{14} and S^{35} have been reported (16) which are useful in metabolic studies of thiourea derivatives.

IV. Classified Tables of Thioureas

In tables 1 to 7 thioureas are classified according to the nature and the number of the substituents. The references for each compound are segregated to show whether they pertain to the biological discussion in Section II or to the methods of synthesis in Section III.

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