THE CHARACTERIZATION OF ISOTHIOCYANATES

Thesis for the Degree of M. S.

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Lowell Ernest Weller

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Lowell Arnett Weller

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Submitted to the School of Graduate Studies of Michigan State College of Agriculture and Applied Science in partial fulfillment of the requirements for the degree of

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AN ABSTRACT

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Approved _____

THE CHARACTERIZATION OF ISOTHIOCYANATES

In an investigation concerning the occurrence of isothiocyanates in plants it became necessary to identify minute quantities of isothiocyanates. Since a suitable derivative was not available, work was directed toward obtaining a solid derivative of some of the common isothiocyanates.

A number of isothiocyanates have been synthesized. Crotonic isothiocyanate was prepared from the corresponding thiocyanate by the method of Gerlich (1). Benzyl, 2-methylthioethyl and 2-methoxyethyl isothiocyanate were prepared by a method previously described (2). The following isothiocyanates were prepared according to the method as given by Delepine (3): methyl, n-propyl isopropyl, n-butyl, isobutyl, sec. butyl, amyl, isoamyl, 3-methoxypropyl, benzyl, 2-phenylethyl and 1-naphthyl. The preparation and properties of the following isothiocyanates: 2-methoxyethyl, 3-methoxypropyl (isothiocyan ethers) and 2-methylthioethyl (an isothiocyan thioether) have not been reported previously.

The melting points of the thioureas obtained by reacting the isothiocyanates listed with benzylamine are: methyl 78, ethyl 103, allyl 94.5 n-propyl 88, isopropyl 126, n-butyl 50, sec. butyl 78, isobutyl 112, crotonic 49.5, n-amyl 62, isoamyl 54, 2-methoxyethyl 71, 3-methoxypropyl 51, 2-methylthioethyl 58, phenyl 153, benzyl 148, 2-phenylethyl 118 and 1-naphthyl 173.

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PREFACE

The work to be described is only one phase of a cooperative project undertaken jointly by the Departments of Agricultural Chemistry and Horticulture. The problem was initiated in part, by the interest of Dr. G. H. Wittwer in the physiology of the expanding cauliflower head. Dr. Wittwer had observed that the crude ether extractives obtained from the "inflorescences" of cauliflower were active as a growth regulator. The preliminary work of Dr. C. T. Holmann on this ether extract indicated that an active fraction obtained from fractionation of the ether extract contained the elements of nitrogen and sulfur and gave a qualitative test for an isothiocyanate group. Also, Dr. E. H. Lucas had detected antibacterially active principle(s) in certain members of the Cruciferae family. The results of earlier experiments had suggested the presence of an isothiocyanate.

In order to attack the problem it was necessary to have available isothiocyanates of known composition for the purposes of setting up model experiments. In addition to this, it was necessary to have available a method for

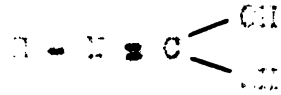
the characterization of small quantities of isohidecyanides. The work to be described in this thesis is concerned with the characterization of isohidecyanides, particularly those isohidecyanides which have been obtained from plants.

The author wishes to express his sincere thanks to Professors H. H. Hall and C. D. Hall for their friendly counsel throughout the course of this work.

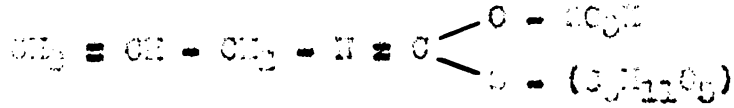
INTRODUCTION

Isothiocyanates are a class of isothiocyanic acid but are commonly known as "mustard oils". This notation has arisen since allyl isothiocyanate is the chief constituent of the oil of mustard obtained from the seed of black mustard (Brassica nigra). This class of organic compounds possesses a characteristic pungent, irritating odor. Many isothiocyanates are lachrymatory.

Allyl isothiocyanate was one of the first isothiocyanates obtained from a plant source. According to Gadamer (1) allyl isothiocyanate does not occur as such in plants but in the form of a glucoside. This glucoside is reducible to a hypothetical allyl thiohydroximic acid of the general formula:



Thus sinigrin (the glucoside of allyl isothiocyanate) exists as:



In the presence of water and an enzyme (viz. myrosinase) sinigrin is hydrolyzed to allyl isothiocyanate, D-glucose and potassium hydrogen sulfate.

Isothiocyanates, in general have been obtained principally from the seeds of many Cruciferae. However, they are also distributed in other parts of the plant. They appear to be linked to glycosidic complexes (viz. sinigrin). It has been demonstrated that many of the plants which yield isothiocyanates also contain an enzyme capable of freeing the isothiocyanate from its glycosidic complex (3).

Following hydrolysis of the glycoside a number of other products may be obtained in addition to the isothiocyanate. These include carbon disulfide and the cyanide of the corresponding isothiocyanate present. At low temperatures Schmidt (3) even found traces of the isomeric thiocyanate present.

Isothiocyanates have been obtained usually from members of the Cruciferae family. However, some have been obtained from certain parts of other plant families. Table I contains a summary of the principle sources which have yielded isothiocyanates along with the names which have been proposed for the glycosidic complexes.

TABLE I

THE OCCURRENCE OF ISOTHIOCYANATES IN NATURE

Isothiocyanate	Glycoside	Botanical Name
Allyl	Sinigrin	Brassica nigra Brassica juncea Alliaria officinalis Cardamine amara Sisymbrium alliaria
sec. Butyl	Glucocochlearin	Cochlearia officinalis Cochlearia danica Cardamine amara Cardamine pratensis
Butenyl	Gluconapin	Brassica juncea Brassica napus Brassica campestris
2-phenylethyl	Gluconasturtiin	Nasturtium officinale Barbarea praecox Brassica rapa Cochlearia armoracia
p-hydroxybenzyl	Sinalbin	Sinapis alba Brassica alba
$CH_3-SO_2-(CH_2)_2-CH_2-$	Glucocheirolin	Cheiranthus cheiri Erysimum [illegible]
$CH_3-SO_2-(CH_2)_3-CH_2-$		Erysimum perofskianum
Benzyl	Glucotropaeolin	Lepidium sativum
$CH_3-S-CH=CH-CH_2-CH_2-$		Raphanus sativus

The biological significance of the presence of isothiocyanates poses a very interesting problem, one which has received some attention. Miller and co-workers (1,2,3) in a series of experiments with isothiocyanates attempted to correlate antifungal activity of the isothiocyanate to present with the disease resistance of certain plants and concluded that the compounds do exist in potentially effective concentrations but probably not in a free state. However, antibacterial concentration of isothiocyanates were also noted to exert a stimulatory action toward fungi. Allyl isothiocyanate vapors were observed to be inhibitory to a number of fungi (4). However, sinigrin, the glucosidic precursor of allyl isothiocyanate, is non-toxic to fungi. The fungicidal activity of a number of synthetic isothiocyanates is given as allyl > phenyl > methyl > ethyl isothiocyanate. Chairolin ($CH_2=CO_2-(CH_2)_8-NCS$) inhibited almost all fungi tested (7).

Peter and Collet reported that horseradish vapors possessed bacterial inhibitory properties and that these properties resulted from the allyl isothiocyanate present (8). Working with synthetic isothiocyanates, Foter reported that methyl, ethyl and allyl isothiocyanate were bactericidal (9).

methyl isothiocyanate was more effective and ethyl less effective than the allyl analogue. Money stated that sinigrin, present in common cauliflower, is responsible for the antibacterial activity observed (10).

One of the most recent studies concerning isothiocyanates was reported by Walsh and Kaye (11,12). They obtained a substance named sulforaphen (CH_3-SO-CH=CH-CH_2-CH_2-NCS) from the seeds of Lepidium sativum. They state that sulforaphen is antibiotic in a one percent solution against various microorganisms. It also possessed decided bactericidal properties in dilutions of 1:1000. However, synthetic butyl, phenyl and allyl isothiocyanate were ineffective at dilutions of 1:1000.

These observations might lead to speculation in regard to the biological significance of isothiocyanates. An obvious explanation might be that they provide a mechanism for the protection of the plant against microbial attack. Sinalbin (precursor of allyl isothiocyanate) is non-toxic toward fungi, but the allyl isothiocyanate which may be liberated by enzymatic action is inhibitory toward a number of fungi. The hydrolysis of sinalbin may be brought about initially by damage to the plant tissue which permits contact of the sample with the precursor which exists in

different cells in the plant. The biosynthetic effects of many lectinocytosis (11,13) associated with the occurrence of lectinocytosis in the seeds of many Graminaceae would suggest that these compounds may be associated with the enzyme system regulating the germination of seeds.

In our investigation concerning the occurrence and biological properties of lectinocytosis from plant sources it became necessary to identify small quantities of lectinocytosis. In order to facilitate this work, it seemed desirable to have available a suitable derivative for the purposes of identification. Since the literature yielded no information on a simple reagent used to prepare solid derivatives of lectinocytosis, work was directed towards that end.

Methods for the Preparation of Lectinocytosis

There are available a number of methods which can be utilized for the synthesis of lectinocytosis. These methods are readily available in the existing literature so only a brief discussion of the more common methods of preparation will be included here.

Thiocyanate. (11,13,18) Lectinocytosis may be prepared by the thermal rearrangement of the normal

thiocyanate.

$$R - S - C \equiv N \rightleftharpoons R - N = C = S$$

This reaction is interesting from the point of the organic chemistry involved but it is of limited importance as a preparative method. The heat catalyzed rearrangement is accompanied by some decomposition. Decomposition is rather limited for the low molecular weight isothiocyanates but becomes excessive upon prolonged heating of the higher molecular weight isothiocyanates. This method would be a more practical one if a catalyst were known which would permit the rearrangement to take place at lower temperatures or at a faster rate. In addition, the separation of the corresponding thiocyanate and isothiocyanate is effected with some difficulty.

Isocyanide. The addition of sulfur to the isocyanide leads to the formation of isothiocyanate.

$$R - NC + S \longrightarrow R - NCS$$

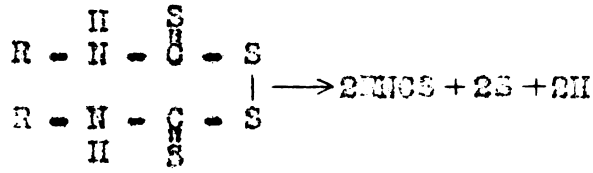
This method has had very limited use.

Thiophosgene. (17) The reaction of thiophosgene with primary amines leads to the formation of isothiocyanates.

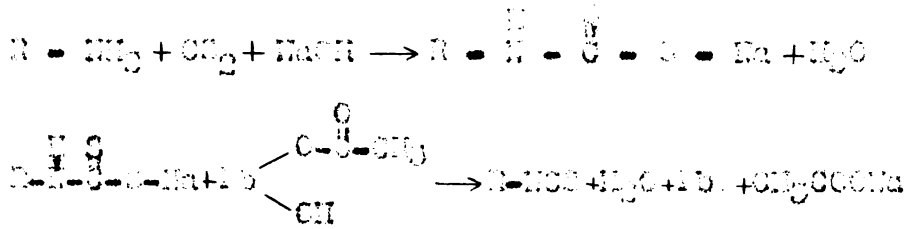
$$RNH_2 + CSCl_2 \longrightarrow R - NCS + 2HCl$$

This method, although not widely used, has been successfully utilized for the preparation of alkyl and halogen substituted aromatic isothiocyanates.

Thiourandisulfide. (18,19) Isothiocyanates have been prepared from sym. N, N' dialkyl thiourandisulfide by the action of iodine or by heating with water or alcohol.



Carbon Disulfide. (20) Probably the most important method for the preparation of isothiocyanates is the reaction of an amine with carbon disulfide to form the alkylammonium salt of the alkyldithiocarbamic acid. The elimination of hydrogen sulfide from these salts by a number of reagents produces the isothiocyanate. The reaction is most economically carried out by treating the amine with equivalent amounts of carbon disulfide and alkali, thus forming the metallic salt in place of the alkyl ammonium salt, a condition which increases the amount of amine which otherwise would be tied up as the salt becomes available for the preparative reaction.



There are a number of modifications of the above reaction. Potassium hydroxide and ammonium hydroxide have been used in place of sodium hydroxide and a number of reagents have been used in place of the basic lead acetate (Lead nitrate (31), ferrous sulfate (31), copper sulfate (31,32) and ethyl chloroformate (33)).

EXPERIMENTAL

Methods Used for the Synthesis of Isothiocyanates

All of the isothiocyanates herein reported (with the exception of the commercial preparations) were prepared either by the thiocyanate method or by some modification of the amine dithiolic procedure. The preparations of most of these compounds have been previously reported. Since the prime purpose here was to obtain isothiocyanates of known composition, the synthesis will be described as briefly as possible. In order to do this, a typical preparation will be described in detail for each of the methods of synthesis used. Table I contains a summation of the preparation and properties of all the isothiocyanates prepared.

Method 1. Preparation of Benzoic Isothiocyanate. Fifty-five grams (0.60 mole) of potassium thiocyanate was added to a solution of fifty grams (0.37 mole) of 1-bromobenzene-3 in 100 ml. of anhydrous ethanol. The resulting solution was heated for twenty hours on a water bath at such a rate so as to maintain gentle refluxing. The alcohol was distilled off under reduced pressure and the residue fractionated under reduced pressure. Distillation

was continued until the distillate gave no isothiocyanate reaction. This yielded a fraction boiling over a rather large range. The distillate was redistilled yielding nine grams of crotonic isothiocyanate having a boiling range of 86-88° C./.7-.8 mm.

Ethyl C. Preparation of n-butyl isothiocyanate. Twenty-seven grams (0.35 mole) of carbon disulfide and forty-five ml. of ammonium hydroxide (sp. g. 0.9) were placed in a 500 ml. round-bottom, three neck flask which had previously been fitted with a stirrer, thermometer and a dropping funnel and cooled to 0° C. in an ice-salt bath. Twenty-five grams (0.34 mole) of n-butylamine was added dropwise with constant stirring. After the addition of the amine was completed the cooling bath was removed and stirring continued for thirty minutes. The reaction mixture was then permitted to stand for an additional thirty minutes.

The heavy yellow precipitate obtained was dissolved in 400 ml. of water and the solution transferred to a five liter flask. To the solution was added with vigorous stirring, a solution of 114 grams of trihydrate of lead acetate (0.30 mole) in 800 ml. of water. The mixture was then steam distilled into a receiver containing ten ml.

of sulfuric acid. Distillation was continued until only small amounts of oil came over. The bulk of the oil was distilled over after 500 ml. of distillate had been collected. The product was separated from the aqueous phase and weighed 30.0 grams. The oil was dried over calcium chloride and distilled under reduced pressure. The fraction which distilled at 38-40° C./1-2 m. weighed 27.0 grams. This fraction when redistilled under reduced pressure yielded twenty-six grams (74 percent of the theoretical amount) of normal butyl isothiocyanate boiling at 37-38° C./4-5 m.

Method C. Preparation of β-phenylethyl isothiocyanate. A solution of ten grams (0.30 mole) potassium hydroxide in 100 ml. of water and twenty-three grams (0.30 mole) of carbon disulfide was cooled to 0° in a 500 ml. three neck flask which had previously been fitted with a stirrer, thermometer and dropping funnel. Forty grams (0.33 mole) of β-phenylethyl amine was added dropwise to the mixture with constant stirring. The cooling bath was removed and stirring continued for thirty minutes and then permitted to stand an additional thirty minutes. Thirty-two grams (0.33 mole) of ethyl chloroformate was then added dropwise with stirring. During the addition of the ethyl chloroformate

the temperature rose gradually some 11-13° C. The flask and contents were cooled and the organic layer separated from the aqueous layer. The organic phase was dried over calcium chloride and distilled. The main fraction (37.6 grms) distilled at 111-120° C./0-4 mm. This fraction was redistilled yielding 33.9 grms of 2-phenylethyl isothiocyanate b.p. 97-100° C./.3-.4 mm.

Synthesis of New Isothiocyanates

2-Methoxyethyl Isothiocyanate. 2-Methoxyethyl isothiocyanate is a member of the class of isothiocyanates known as isothiocyan ethers. The first members of this class of isothiocyanates were prepared by Johnson and Grant (19) by the thermal rearrangement of the corresponding thiocyanate. 2-Methoxyethyl isothiocyanate was prepared by reacting the corresponding amine and carbon disulfide. A solution of twenty grms (0.5 mole) sodium hydroxide in fifty ml. water and forty grms (0.53 mole) carbon disulfide was added to a three neck flask fitted with a stirrer, thermometer, reflux condenser and a dropping funnel. The flask was cooled to 0° C. and fifty grms (0.5 mole) of a 65-70 percent aqueous solution of 2-methoxyethylamine was added dropwise to the flask with constant stirring. After the addition of the amine was

completed, stirring was continued for one hour during which time the mixture was gently refluxed. The flask was cooled to 50° C. and fifty-four grams (0.5 mole) of chloroethyl carbonate added dropwise with stirring. The temperature gradually increased during the addition of the chloroethyl carbonate. Stirring was continued until the temperature of the mixture fell to 30° C. The mixture was then cooled, the organic layer separated, dried over calcium chloride and distilled. The fraction distilling at 80-85° C./11-13 mm. was collected as β-methoxyethyl isothiocyanate. This fraction was redistilled yielding thirty-four grams of isothiocyanate distilling at 57-60° C./.1-.3 mm.

β- chloroethyl Isothiocyanate. A mixture of fifty-four grams (0.71 mole) of carbon disulfide and ninety-five ml. of concentrated ammonium hydroxide was cooled to 0° C. in a three neck flask fitted with a stirrer, thermometer and dropping funnel. Fifty-four grams (0.6 mole) of β- aminopropyl sulfate was added dropwise with stirring. After the reaction was complete, 600 ml. of water was added and the solution transferred to a five liter flask. A solution of 500 grams of the trihydrate of lead acetate in 600 ml. water was added with vigorous stirring. The oil which was steam distilled from the mixture was dried over calcium chloride and twice redistilled. The fraction

distilling at 44-47° 3./4-.5 mm. was collected as 3-methoxypropyl isothiocyanate. The yield was 17.3 gms.

Preparation of a New Class of Isothiocyanates

Following the system of classification of Johnson and Hou (10) this class of isothiocyanates could be called isothiocyan thiocarbams. The preparation of 3-methylthiobutyl isothiocyanates represents the first reported synthesis of any member of this class. Since the preparation of the corresponding amine (3-methylthiobutyl amine) has not previously been reported, its synthesis will also be described briefly.

3-Bromobutylamine hydrobromide. 3-bromobutylamine hydrobromide (3') was prepared by dropping 68 gms. of 3-butenol-1 into cold 48 percent aqueous hydrobromic acid, refluxing for several hours and distilling off the excess acid.

3-Methylthiobutyl bromide. This amine was prepared by the general procedure of Levi-Ben Nun et al. (11) for the preparation of butyl-3-thiobutylamine. An ethanolic solution of 3-bromobutylamine hydrobromide was treated with an ethanolic solution of the sodium salt of methyl mercaptan. This yielded the hydrobromide of 3-methylthiobutyl amine. The solution was subsequently made alkaline, the alcohol distilled off under reduced pressure and the amine extracted

from the residue with ether. This procedure yielded 12.0 grams of a basic compound which distilled at 60-65° C./ 1-3 mm.

2-Diethylaminoethyl Isothiocyanate. The crude 2-diethylaminoethyl amine, 10.0 grams (0.2 mole) was added dropwise to a stirred solution of eight grams (0.2 mole) of sodium hydroxide in twenty ml. water and 10.0 grams (0.2 mole) of carbon disulfide. After the addition of the amine the resulting solution was refluxed on a steam bath for twenty minutes. The solution was cooled to 25° C. and twenty-two grams (0.2 mole) of ethyl chloroformate was added dropwise with stirring. Subsequently the organic layer was separated, dried over calcium chloride and distilled. The fraction distilling at 60-65° C./ 1-3 mm. was collected as 2-diethylaminoethyl isothiocyanate. The yield was ten grams.

TABLE II

[illegible]

Dithiocarbamate	B.p. °C. Observed	B.p. °C. Lit.	Yield %	Method of synthesis
methyl	m.p. 55	119.	11	B
n-propyl	[illegible]-60/.7-.8 mm.	102.7	60	B
isopropyl	[illegible]-24/1-2 mm.	107.-107.5	40	B
n-butyl	57-[illegible]/.4-.5 mm.	137.	74	B
isobutyl	51-52/.6-.7 mm.	10[illegible].	21	B
sec. butyl	50-51/.7-.8 mm.	100.-105.	74	B
crotonic	56 -[illegible]/.7-.8 mm.	1[illegible].-1[illegible].	21	A
n-amyl	55-63/3-4 mm.	103.4	41	B
isoamyl	42-48/1-2 mm.	102.	55	B
2-methoxyethyl[a]	57-[illegible]/.1-.2 mm.		57	C
3-methoxypropyl[a]	44-47/.4-.5 mm.		35	B
2-methylthioethyl[a]	55-60/1-2 mm.		37	C
benzyl	75-80/.4-.5 mm.	2[illegible].	22	C
2-phenylethyl	90-102/.3-.4 mm.	250.	44	C
1-naphthyl	m.p. 58	m.p. 58	10	B

[a]Preparation and properties not reported in the literature.

Derivatives of Isothiocyanates

The reaction of isothiocyanates with amines has been utilised by a number of investigators using isothiocyanates as reagents for the characterization of amines. A number of aryl isothiocyanates have been suggested for this purpose. Phenyl isothiocyanate is frequently used but generally fails to form derivatives with meta and para-nitro and di-ortho substituted anilines (33), and with many aliphatic amines low melting solids are formed which are both difficult to isolate and crystallise (33). The latter difficulty can be minimised by increasing the molecular weight of the reagent. Thus, 1-naphthyl isothiocyanate (37), 2-naphthyl isothiocyanate (38) and 4-biphenyl isothiocyanate have been reported as satisfactory reagents. The thioureas are usually easily obtained and possess convenient, sharp melting points. Isothiocyanates less frequently used include o-tolyl (31), p-chlorophenyl, p-bromophenyl (31), m-nitrobenzyl (31) and p-methoxybenzyl (33).

The reaction of an isothiocyanate with an amine may also be used for the characterization of isothiocyanates utilising an amine as the reagent instead of the isothiocyanate. However, the low molecular weight amines do not yield solid derivatives with many isothiocyanates.

this difficulty can be minimized by the proper choice of amine. The reaction of benzylamine with the isothiocyanates herein reported yields substituted benzylthioureas which are crystalline compounds possessing convenient melting points. This reaction yields the thioureas as addition products which can be isolated in nearly quantitative yields. Since there are no by-products in such a reaction the thioureas formed can be purified relatively easily. Also, since many of the isothiocyanates encountered are liquids, the reaction involving two liquids to give a solid derivative is an ideal situation for identification work.

Additionally, the melting points of some of the substituted benzylthioureas of the isothiocyanates listed in Table III are too close to differentiate the isothiocyanates on the basis of the melting point of t is derivative. In such cases a mixed melting point with an authentic specimen may be necessary for more definite identification.

Preparation of Substituted Benzylthioureas. A mixture of 0.01 mole of the isothiocyanate in five ml. of 95 percent ethanol and an equimolar amount of benzylamine dissolved in five ml. of the same solvent (five ml.) was boiled gently for five minutes. Water was added until the hot solution appeared cloudy, then enough ethanol was added to clear the hot

solution. If upon cooling an oil separates out it can usually be caused to crystallize readily by scratching the sides of the vessel. However, a better procedure at this point was to redissolve the oil in the hot solvent and then increase the ethanol content of the solution. Upon slow cooling the product will usually crystallize out. Ethyl 3 was used for the first recrystallization of n-butyl, aromatic and isoamyl benzylthiourea since these did not crystallize readily from their aqueous ethanolic solutions. If benzylamine was added to the bromoacetate in the absence of a solvent the reaction proceeded spontaneously with the evolution of heat. Aqueous ethanol (60-70 percent) was then used for recrystallizing the product. Usually two recrystallizations were sufficient for purification. The yields of the recrystallized products were approximately 60-70 percent. The nitrogen values reported in Table III are the averages of two Kjeldahl determinations (30).

TABLE III

[illegible]

[illegible] OF [illegible]

Isothiocyanate	Formula	M.P., °C.	Nitrogen Content, Calcd.	Nitrogen Content, Found
methyl	C_9H_{10}[illegible]	73	15.6	15.5
ethyl	$C_{10}H_{12}$[illegible]	106	14.2	14.4
allyl	$C_{11}H_{12}$[illegible]	94.5	13.6	13.6
n-propyl	$C_{11}H_{14}$[illegible]	88	13.3	13.4
isopropyl	$C_{11}H_{14}$[illegible]	1[illegible]6	13.4	13.4
n-butyl	$C_{12}H_{16}$[illegible]	50	12.8	12.6
sec. butyl	$C_{12}H_{16}$[illegible]	70	12.4	12.6
isobutyl	$C_{12}H_{16}$[illegible]	113	12.7	12.6
crotonic	$C_{12}H_{14}$[illegible]	48.5	12.7	12.7
n-amyl	$C_{13}H_{18}$[illegible]	62	12.0	11.8
isoamyl	$C_{13}H_{18}$[illegible]	54	11.8	11.8
2-methoxyethyl[a]	$C_{11}H_{14}$[illegible]O	71	12.5	12.5
3-methoxypropyl[a]	$C_{12}H_{16}$[illegible]O	51	11.7	11.8
2-methylthioethyl[a]	$C_{11}H_{14}$[illegible]	58	11.7	11.7
phenyl	$C_{14}H_{14}$[illegible]	153	11.4	11.6
benzyl	$C_{15}H_{16}$[illegible]	140	11.0	10.9
2-phenylethyl	$C_{16}H_{18}$[illegible]	113	10.5	10.4
1-naphthyl	$C_{18}H_{16}$[illegible]	172[b]	9.7	9.6

[a] Preparation and properties not reported in the literature.

[b] Previously reported as 171-172°, ([illegible]).

Abstract

A number of isothiocyanates have been synthesized. Crotonic isothiocyanate was prepared by the thermal rearrangement of crotonic thiocyanate. The following isothiocyanates were prepared by various modifications of the reaction of the corresponding amines with carbon disulfide: methyl, n-propyl, isopropyl, n-butyl, isobutyl, sec. butyl, allyl, isoamyl, β-methoxyethyl, β-methoxypropyl, β-methylthioethyl, benzyl, β-phenylethyl and 1-naphthyl.

The preparation and properties of the new isothiocyanates, β-methoxypropyl and β-chloropropyl are given.

The preparation of a new amine β-thioethyl amine and β-thioethyl isothiocyanate is described. This isothiocyanate is the first reported member of a class of isothiocyanates which have been called isothiocyan thioethers.

The substituted benzyl isomers of a number of aliphatic and aromatic isothiocyanates have been prepared by reacting the isothiocyanates with benzylamine. There are no by-products of this reaction so purification of the derivative is relatively easy. These derivatives

are crystalline compounds with convenient melting points and are suitable for the purposes of identification.

An abstract of the material presented here has been accepted for publication by the Journal of the American Chemical Society.

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