

PATENT SPECIFICATION

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(54) ACYCLIC DI- AND TRI-SULPHIDES

(71) We, INTERNATIONAL FLAVORS & FRAGRANCES INC., a Corporation organised and existing under the laws of the State of New York, United States of America, of 521 West 57th Street, New York, State of New York, United States of America, do hereby declare the invention for which we pray that a patent may be granted to us and the method by which it is to be performed to be particularly described in and by the following statement:—

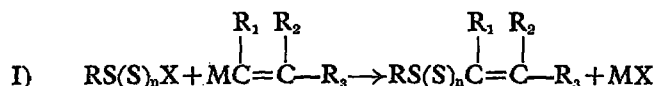
This invention relates to preparation of alkyl-1-alkenyl sulfides and trisulfides.

A wide variety of organic disulfides and trisulfides are known, typical among which are both the symmetrical and unsymmetrical saturated and unsaturated disulfides and trisulfides such as dimethyl disulfide, dimethyl trisulfide, dipropyl disulfide, methyl propyl disulfide, methyl propyl trisulfide, diallyl disulfide, allyl propyl disulfide, methyl allyl disulfide and the like. Such compounds are easily synthesized using a variety of synthetic routes. Heretofore, the art has been unsuccessful in achieving a good synthetic route to alkyl-1-alkenyl disulfides and trisul-

fides and it would be desirable indeed to provide a reliable synthetic means for producing said compounds.

The prior art techniques for producing unsaturated sulfides have generally centered around oxidative reactions using appropriately substituted mercaptans in an iodine oxidation, or by exchange between an appropriate mercaptan and allyl mercaptan. These methods have been found to be unsuitable for preparing the 1-alkenyl compounds, as indeed, have been direct attempts at isomerizing the corresponding allyl compounds.

It has now been discovered that alkyl-1-alkenyl disulfides, such as those disclosed and claimed in copending application No. 21302/69 (serial No 1252366) and also alkyl-1-alkenyl trisulfides such as those described and claimed in copending application No. 14518/71 (serial No 1252367) can be directly prepared by reacting an alkali methyl alkene or an alkaline earth metal alkenyl halide with an appropriate alkyl substituted disulfur or trisulfur halide. The reaction is depicted as follows:



where R and R₃ are alkyl and R₁ and R₂ are hydrogen or alkyl said alkyl being especially lower alkyl having from 1 to 5 carbon atoms such as methyl, ethyl, n-propyl, isopropyl, butyl, sec.-butyl or n-pentyl, X is halogen, preferably chloro or bromo and M signifies MgBr, MgCl or lithium, preferably MgBr and n is 1 or 2. Typical of the sulfide starting materials are methyl disulfur chloride, methyl trisulfur chloride, ethyl disulfur chloride, n-propyl disulfur chloride, n-propyl trisulfur chloride, n-pentyl disulfur chloride, and the corresponding bromides. Most preferred among these are methyl disulfur

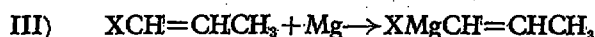
chloride and n-propyl disulfur chloride, methyl trisulfur chloride and propyl trisulfur chloride. Most preferably, R₁ and R₂ are hydrogen and R₃ is methyl.

Reaction I is highly exothermic and is preferably run in the cold and under anhydrous conditions. Temperatures below ambient temperature and more suitably between -80°C to 10°C are suitable. The reaction is preferably run in the presence of a solvent as a reaction vehicle, anhydrous solvents having low freezing points being generally employed. Typical of such solvents are ethers, such as diethyl ether, tetrahydrofuran, and diisopropyl ether,

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or hydrocarbons such as hexane, benzene or toluene. In practice it is generally found suitable to use the solvent system in which the propenyl magnesium compound was itself prepared as will be described hereinafter.

With regard to the relative amounts of reactants employed, it is preferred for reasons of economy to use stoichiometric quantities although an excess of one or the other of the reactants may be made. As a result of the reaction, the desired alkyl-1-alkenyl disulfide or trisulfide is obtained in solution. They may be separated and recovered from the reaction



wherein X is a halogen atom preferably chloro or bromo, and most preferably bromo.

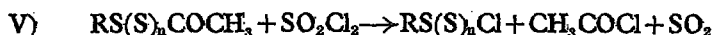
The reactions are preferably carried out under anhydrous conditions and in the presence of a solvent. The solvent is suitably one which can be used in the subsequent reaction of the alkenyl compound with the alkyl disulfur or trisulfur halide as described above in Reaction I. The reaction is exothermic and is preferably carried out under gentle reflux conditions caused autogenically by controlled addition of the halo-alkene compound to a slurry of the alkali or alkaline earth metal in the solvent.

With regard to relative amounts of reactants, it is preferred to use stoichiometric quantities although excess of either reagent



where R is alkyl as previously defined.

The starting trisulfides need not be symmetrically substituted; that is, the radicals R may be different alkyls. Symmetrical substitution is highly preferred, however, since the cleavage of a symmetrical trisulfide will result in only two sulfur halides rather than the four which are possible in the case of an unsymmetrical alkyl trisulfide starting material. The alkyl substitution is, of course,



Other halogenating agents as described above may also be used. The reaction results in the cleavage of the acetyl compound and yields the halogenated di- or tri-sulfide.

The above reactions are preferably carried out below ambient temperature and most preferably between -35°C and 40°C . It is preferred to carry out the reaction by adding the halogenating agent to the sulfide without the use of a solvent, although one may be used if desired. Solvents such as hexane, benzene, and isopentane are suitable. With regard to the amounts of reactants, it is preferred for reasons of economy to use the stoichiometric quantities.

mixture by conventional techniques, e.g. distillation. They are preferably separated therefrom by evaporation of the solvent vehicle, and submission of the resulting crude oil to chromatographic separation techniques.

Both the lithium or magnesium alkenyl compounds and the alkyl disulfur or trisulfur compounds used as starting materials in the foregoing reaction, are themselves prepared by known processes. The following equations represent the formation of the alkenyl compounds using propenyl halide for illustrative purposes:

may be used. The resulting alkene compound, e.g. propene compound is obtained in solution from which it may be separated using conventional techniques. It is preferred, however, to use the reaction mixture without further treatment in the subsequent reaction with the alkyl disulfur or trisulfur halide.

The alkyl disulfur halide is itself prepared by a process involving cleavage of an appropriate alkyl trisulfide with a strong halogenating agent. Especially preferred halogenating agents are sulfuryl chloride, chlorine and bromine.

The reaction is depicted by the following equation, shown for convenience using sulfuryl chloride as the halogenating agent:

selected on the basis of the nature of the alkyl radical desired in the final alkenyl sulfide produced in Reaction I. The preferred trisulfides are dimethyl trisulfide and di-n-propyl trisulfide, although the diethyl, dibutyl di-sec-butyl and di-n-pentyl trisulfides may be employed as well. Alternatively, alkyl di- or tri-sulfur halides are prepared by halogenation of an appropriate alkyl acetyl di- or tri-sulfide as follows:

As a result of the reactions, the di- or tri-sulfur halides are obtained in solution and are then available for reaction with the substituted alkene in Reaction I. The starting materials used in the foregoing Reactions may be all cis, all trans or any combination of the cis and trans isomeric forms.

Representative of the compounds produced by the process of the invention are:

methyl (2-methyl propenyl) trisulfide,
propyl (2-methyl propenyl) trisulfide,
ethyl (2-ethyl propenyl) trisulfide,
methyl propenyl trisulfide,
propyl propenyl trisulfide,

ethyl propenyl trisulfide,
methyl propenyl disulfide,
propyl propenyl disulfide,
methyl (2,2-dimethyl propenyl) disulfide,

5 and

propyl (2,2-dimethyl propenyl) disulfide,
in both *cis* or *trans* or mixtures of *cis* and
trans isomeric forms.

10 The alkyl-1-alkenyl disulfides of the pre-
sent invention are useful in the field of food
flavouring. They possess a characteristic
cooked onion aroma and impart on onion
flavour to foods. They thus constitute a suit-
15 able artificial means for flavouring edible
materials. Such items as sauces, soups, purees,
gravies, dips, meats and meat products and
othera foods wherein an onion flavor and
aroma is desired may all be treated.

20 The compounds are typically used at levels
of from 10^{-5} to 10^{-2} percent by weight based
on the weight of the entire food item to be
treated. The particular amount selected will
depend on individual preferences in the case
25 of home consumer use or on mass appeal con-
siderations in the case of bulk food process-
ing. They may be employed alone or in com-
bination with other disulfides, such as dialkyl
disulfides illustrated by dimethyl disulfide,
dipropyl disulfide and methyl propyl disul-
30 fide; carriers such as vegetable oil, cotton-
seed oil, corn oil, starch, salt, sugar and gum
arabic may also be utilised. In composition
form they are conveniently used at between
.01 to 20 percent by weight with the re-
35 mainder being carriers or other adjuvants.
They may also be used alone, however.

40 The trisulfides find use in enhancing the
flavor, odor and aroma developed by the
alkenyl disulfides to produce a synthetic onion
flavoring composition which imparts an onion
flavor to foods virtually indistinguishable
from the natural product. They are normally
used in conjunction with the alkenyl disulfide
at levels ranging from 1 to 20 and preferably
45 3 to 6 times the weight of the alkenyl disul-
fide used. The presence of these trisulfides
gives a more fully developed character to the
flavor produced. No additional carrier or ad-
juvants are necessary but they may be em-
50 ployed as described above if desired.

Suitable compositions contain from 0.005
to 20 weight percent of the 1-alkenyl disul-
fide, from 0.005 to 95 weight percent of the
1-alkenyl trisulfide and 0.1 to 99.99 weight
55 percent of a carrier. Said compositions are
conveniently employed in foods in sufficient
amount to provide from 10^{-5} to 10^{-2} weight
percent based on the entire amount of food
to be treated. Levels outside this range, how-
60 ever, may be used depending on individual
tastes.

The invention will now be described with
reference to the following examples; examples

I to IV describe the preparation of intermedi-
ates.

65

EXAMPLE I

Preparation of Propenyl Lithium

Materials:

6.0 g.—(0.05M) 1-bromo-1-propene (dis-
tilled mixture of *cis* and *trans* isomers).

1.1 g.—(0.15 gram-atom)—Lithium wire
(low sodium content).

75 ml.—Ethyl ether (dried over sodium).

The reaction vessel consisting of a 100 ml.,
3-neck round bottom flask, addition funnel,
calcium chloride drying tube, nitrogen inlet
tube, stirrer, and reflux condenser, is
thoroughly dried *in vacuo* at 105°C, allowed
to cool, assembled and flushed with nitrogen.
A slight positive pressure of nitrogen is kept
in the reaction system throughout the sub-
sequent reaction. A slurry of finely cut lithium
wire (1.1 g.) in 75 ml. of ethyl ether is then
added to the reaction flask and vigorous stir-
ring is begun. About 20% of the 1-bromo-1-
propene is next added at once to initiate the
reaction. Initiation of reaction is indicated
by cloudiness in the reaction mixture. After
a few minutes, the reaction mixture begins
to reflux and the remainder of the bromide
is then added at rate to maintain gentle re-
flux. Total addition time is 35 minutes. The
reaction mixture is next allowed to reflux for
an additional 45 minutes, cooled and then
stored under nitrogen until ready for use.

Similar results are obtained when 1-chloro-
1-propene is used in place of 1-bromo-1-pro-
pane in the above procedure.

EXAMPLE II

Preparation of Methyl Disulphur Chloride

Materials:

5.5 g. (0.044M)—Dimethyl trisulfide (Dis-
tilled).

5.9 g. (0.044M)—Sulfuryl chloride (Dis-
tilled).

Quartz equipment is heated for 1 hour at
105°C *in vacuo*. After cooling, the joints are
all sealed with phosphoric acid (85%) and
the entire system then flushed with dry hydro-
gen chloride gas.

The dimethyl trisulfide is then cooled to
-20°C and the sulfuryl chloride is then
added. The reaction mixture changes in color
almost immediately to reddish-orange. The
mixture is allowed to warm to 0°C and the
sulfur dioxide formed in the reaction is then
removed under slight vacuum. The reaction
mixture is then distilled and methane sul-
furyl chloride is collected at 25°C/50 mm
Hg. in a dry-ice isopropanol trap. The methyl
disulfur chloride is collected at 29°-30°C/
12 mm Hg. in a quartz receiver.

EXAMPLE III

Preparation of Ethyl Disulphur Chloride
Materials:

- 5 6.8 g.—(0.044M)—Diethyl trisulfide (Dis-
tilled).
5.9 g.—(0.044M)—Sulfuryl chloride (Dis-
tilled).

10 The procedure for this preparation is identical to that of Example II except that the reaction is run at -30°C . The first fraction is collected up to $30^{\circ}\text{C}/13\text{mm}$. Hg. The ethyl disulfur chloride is collected at $30-32^{\circ}\text{C}/13\text{mm}$ Hg.

EXAMPLE IV

Preparation of n-Propyl Disulphur Chloride
Materials:

- 15 8.0 g. (0.044M)—Di-n-propyl trisulfide (Distilled).
20 5.9 g. (0.044M)—Sulfuryl chloride (Dis-
tilled).

The procedure of Example II is followed using the above materials. The first fraction is collected up to $33^{\circ}\text{C}/12\text{mm}$. Hg. and the n-propyl disulfur chloride is collected at $34-36^{\circ}\text{C}/12\text{mm}$. Hg. In each of Examples II—IV, bromine or chlorine can be substituted in equivalent amounts for the sulfuryl chloride to obtain the corresponding disulfur halide. Similarly, di-n-butyl or di-n-pentyl trisulfides may be used in place of the dimethyl, diethyl or dipropyl trisulfides, to give the corresponding n-butyl or n-pentyl disulfur halide.

EXAMPLE V

Preparation of Methyl Propenyl Disulfide

- 35 To 0.93 g. (0.008M) of methyl disulfur chloride (CH_3SSCl) cooled to -30°C is added 25 ml. of an ethereal propenyl lithium solution at a rapid dropwise rate. The reaction mixture is then poured into 25 ml. of cold (10°C) 0.1 N hydrochloric acid. After layer separation the aqueous phase is extracted with three, 10 ml. portions of ethyl ether. The combined ether extracts are washed with 25 ml. of 0.1 N hydrochloric acid and dried over anhydrous sodium sulfate. Solvent removal gives a dark brown oil which is fractionated by vapor/liquid chromatography. Repeated injections on a $10 \times 1/4$ " Carbowax (20%M) on Chromosorb, column, temperature programmed from 75 to 225°C at $2^{\circ}/\text{min}$. gives separation of the isomers yielding a total 0.043 g. of cis and trans methyl propenyl disulfide. (Chromosorb and Carbowax are Trade Marks). Analysis by a vapor/liquid chromatography—rapid scan mass spectrometry combination and NMR and IR data confirm the structure.

EXAMPLE VI

Preparation of n-Propyl Propenyl Disulfide

60 The procedure of Example V is followed, except that 2.06 g. (0.0144M) of n-propyl disulfur chloride and 35 ml. of ethereal propenyl lithium solution were used. Isolation

as in Example V gives 0.04 g. of cis and trans n-propyl propenyl disulfides. The isomers are separated as described above and analyzed individually.

Analysis by vapor/liquid chromatography—rapid scan mass spectrometry combination, NMR and IR spectra confirm the structure.

EXAMPLE VII

Preparation of Ethyl Propenyl Disulfide
Materials:

- 3.58 g. (0.278M)—Ethyl disulfur chloride 75
40 ml.—Propenyl lithium in ether from Example 1.

This compound is prepared in the manner set forth in Example V.

G.L.C.—Mass Spec. detects two compounds of molecular weight 134, which are cis and trans ethyl propenyl disulfides which are collected and combined as described in Example VI.

EXAMPLE VIII

Preparation of Methyl Propenyl Disulfide

Into a 250 ml. round bottom flask equipped with stirrer, condenser, nitrogen purge, calcium chloride drying tube and dropping funnel, are added 20 ml. tetrahydrofuran and 1.4 gms. magnesium turnings. A crystal of iodine and a few drops of methyl iodide with approximately 0.5 ml. of 1-bromo-1-propene are added to initiate the reaction which is indicated by the disappearance of the iodine color and the formation of a pale brown color. The remaining 1-bromo-1-propene is added in 20 ml. of tetrahydrofuran at a rate to maintain the reaction mass temperature between $40-45^{\circ}\text{C}$. The total amount of 1-bromo-1-propene added is 7.1 gms. The addition time is $1/2$ hour. The reaction mass is then heated for one hour at $70-80^{\circ}\text{C}$. with continued stirring.

The reaction mixture is then allowed to cool to 40°C with stirring. The propenyl magnesium bromide solution is then added dropwise to a solution of methyl disulfur chloride (8.5 g.) in tetrahydrofuran chilled in a dry ice/isopropanol bath to -70°C to -75°C . The addition is stopped when the reaction mixture turns dark brown. Isopentane (100 ml.) is added and the resulting mixture transferred to a separating funnel containing 100 ml. water. The water layer is separated and the organic layer washed with water (4×100 ml.), dried over Na_2SO_4 and the solvent removed to give 7.5 g. of dark colored oil. High vacuum distillation ($0.02-0.05$ mm. Hg.) at room temperature gives 3.5 g. of material collected at -80°C . A 75 lambda sample (0.0839 g.) is subjected to vapor/liquid chromatography and gives 0.025 g. of a mixture of cis and trans methyl propenyl disulfide. The structures are determined by NMR, IR and Mass Spectra.

When the foregoing procedure is repeated

using an equivalent amount of 1-chloro-1-propene in place of 1-bromo-1-propene similar results are obtained. Repeat of the above procedure using 12.0 g. of ethyl disulfur chloride gives after high vacuum distillation 4.2 g. Vapor/liquid chromatography of 0.75 lambda (0.077 g.) of the mixture gives 0.032 g. of cis and trans ethyl propenyl disulfide. The structures are determined by NMR, IR and Mass Spectra.

Repeat of the above procedure using 13.6 g. of n-propyl disulfur chloride gives after high vacuum distillation 6.2 g. Vapor/liquid chromatography of 75 lambda (0.077 g.) of this mixture gives 0.028 g. of cis and trans propyl propenyl disulfide. The structure of these compounds is determined by NMR, IR and Mass Spectra.

EXAMPLE IX

Preparation of Trisulfides

a) Methyl trisulfur chloride

Materials:

3.5 gm. (0.044 moles) of HSSCH₃ (Methyl hydrosulfide)

4.8 gm. of (0.044) of $\text{CH}_3-\text{C} \begin{array}{l} \text{O} \\ \parallel \\ \text{S}-\text{Cl} \end{array}$ (acetyl chlorosulfide)

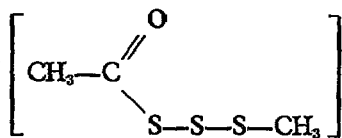
Quartz equipment including a 10 ml. flask is heated for 1 hour at 105°C *in vacuo*. After cooling, the joints are sealed with phosphoric acid (85%) and the entire system flushed with dry hydrogen chloride gas.

The methyl hydrodisulfide is added to the 10 ml. flask and cooled to -20°C and the acetyl chlorosulfide is added with stirring. The mixture is allowed to warm to 0°C and the reaction mass subjected to a slight vacuum. The reaction mixture is distilled and

funnel are added the following ingredients:

20 ml tetrahydrofuran;
1.4 gms magnesium turnings.

A crystal of iodine and a few drops of methyl iodide with approximately 0.5 ml. of 1-bromo-1-propene are added to initiate the reaction which is indicated by the disappearance of the iodine color and the formation of a pale brown color. The remaining 1-bromo-1-propene is added in 20 ml. of tetrahydrofuran at a rate to maintain the reaction mass temperature between 40-45°C. The total amount of 1-bromo-1-propene is 7.1 gms. The addition time is 1/2 hour. The reaction mass is then heated for one hour at 70-80°C with continued stirring and the reaction mixture cooled with stirring to 0°C via an ice bath. The stirring is continued to keep the reagent in suspension. The trisulfur chloride obtained in step a) is then added fairly rapidly from the dropping funnel. As more is added, the reaction mixture becomes more liquid and dark brown in color. The reaction mixture is then washed twice with water and then filtered through sodium bicarbonate in order to dry it. The mass is concentrated in vacuum to a dark brown oil, containing methyl cis propenyl trisulfide and methyl trans propenyl trisulfide. These may be separated and isolated using vapor/liquid chromatographic techniques as previously described.



(acetyl methyl trisulfide) is collected under vacuum. The acetyl methyl trisulfide is placed into a 10 ml. quartz flask and cooled to -35°C. Sulfuryl chloride (0.044 moles) is added while maintaining the reaction mass at -35°C during the period of addition (30 minutes. Immediately subsequent to the addition, the reaction mass is allowed to warm to room temperature and SO₂ and acetyl chloride are removed.

The material remaining in the flask, methyl trisulfur chloride (CH₃SSSCL), is used in step b).

When the above procedure is repeated using in place of the methyl hydrodisulfide equivalent amounts of other alkyl hydrodisulfides, the corresponding alkyl trisulfur chloride is obtained.

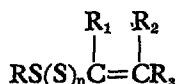
b) Methyl propenyl trisulfide

Into a 250 ml. round bottom flask equipped with stirrer, condenser, nitrogen purge, calcium chloride drying tube and dropping

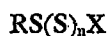
The corresponding trisulfides are obtained when equivalent amounts of other 1-bromo-1-alkenes are used in place of the 1-bromo-1-propene in the above procedure as well as when other alkyl trisulfur halides are used in place of the methyl trisulfur chloride. Thus, the use of propyl trisulfur chloride results in propyl propenyl trisulfide and 1-bromo-1-methyl-1-propene results in the appropriate alkyl (1-methyl propenyl) trisulfide.

WHAT WE CLAIM IS:—

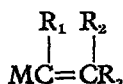
1. The method for preparing an alkyl-1-alkenyl sulfide of the formula:



- 5 wherein R and R₃ are alkyl, R₁ and R₂ are hydrogen or alkyl, and n is 1 or 2 which comprises contacting an alkyl sulfur halide of the formula:



- 10 wherein X is halogen with an alkane of the formula:



wherein M is lithium, —MgBr, or —MgCl.

2. The method according to claim 1 wherein R is methyl, ethyl or propyl.
 15 3. The method according to claim 1 wherein R₁ and R₂ are hydrogen and R₃ is methyl.
 4. The method according to claim 2 where-

in R₁ and R₂ are hydrogen and R₃ is methyl.

5. The method according to claim 4 wherein n is 1.

6. The method according to claim 4 wherein n is 2.

7. The method according to claim 4 wherein X is chloro or bromo.

8. The method according to claim 4 wherein M is —MgBr.

9. The method according to claim 4 wherein said contacting is carried out at below ambient temperature.

10. A method of preparing an alkyl-1-alkenyl sulfide as defined in claim 1 substantially as hereinbefore described in Examples V—IX.

11. An alkyl-1-alkenyl sulfide as defined in claim 1 whenever prepared by the method of any one of Claims 1 to 10.

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