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(54) **Novel process for producing thiolsulfonic acid derivatives.**

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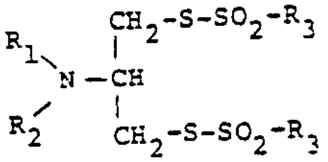
Description

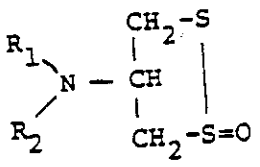
This invention relates to a process for producing a thiolsulfonic acid derivative which possesses insecticidal, acaricidal and fungicidal activities and is of value as an agricultural chemical, particularly as a pesticide.

Concretely, this invention relates to a process for producing a thiolsulfonic acid derivative of the general formula :



(I)

wherein each of R_1 and R_2 is independently a lower alkyl group or a 5- or 6-membered cycloalkyl group, or alternatively R_1 and R_2 together with the adjacent nitrogen atom form a 5- or 6-membered heterocyclic group which may further contain an oxygen, sulfur or nitrogen atom ; and R_3 is (1) an aryl group which may optionally be substituted by a lower alkyl group, a halogen, a lower alkoxy group or a lower alkylthio group, (2) a lower alkyl group which may optionally be substituted by a lower alkoxy group, (3) an aralkyl group, or (4) a cycloalkyl group, or a salt thereof, which comprises reacting a compound of the general formula :



(III)

wherein R_1 and R_2 are as defined above, or a salt thereof with a compound of the general formula :

$$R_3SO_2H \qquad \text{(II)}$$

wherein R_3 is as defined above, or a salt thereof under an acid condition.

The objective compound (I) of this invention is known in the literature, and there has been described that the compound (I) have strong insecticidal activities for example in Japanese Examined Published Patent Application Nos. 18847/1970 and 36727/1970, and British Patent No. 1264207.

The above Japanese Examined Published Patent Application Nos. 18847/1970 and 36727/1970 describe the process which comprises reacting an N,N-dialkyldihalogenopropylamine with an arenethiosulfonic acid salt or alkanethiosulfonic acid salt, but the process suffers the drawbacks that the yield of the objective compound is low, while by-products are formed in large quantities, and is unsatisfactory as an industrial production.

The present inventors continued intensive research for a process which permits the compound (I) to be produced more easily in enhanced degree of purity and in increased yield, and as a result, found that the compound (III) unexpectedly reacts with the compound (II) to give the compound (I) with high degree of purity and in high yields. The finding was furthermore followed by extensive investigation, which has culminated in the present invention.

The compound (I) can be obtained in higher yield, in higher purity and with greater ease according to the process of this invention than according to the process described in Japanese Examined Published Patent Application Nos. 18847/1970 and 36727/1970.

In the above general formulae, each of R_1 and R_2 is independently a straight-chain or branched lower alkyl group of 1 to 4 carbon atoms, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl or tert-butyl, or a 5- or 6-membered cycloalkyl group, such as cyclopentyl or cyclohexyl, or alternatively R_1 and R_2 together with the adjacent nitrogen atom form a 5- or 6-membered heterocyclic group may further contain an oxygen, sulfur or nitrogen atom, such as pyrrolidino, piperidino, piperazino, morpholino or thiazolidinyl ; R_3 is (1) an aryl group of 6 to 10 carbon atoms, such as phenyl or naphthyl, which may optionally be substituted by (a) a straight-chain or branched lower alkyl group of 1 to 4 carbon atoms, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl or tert-butyl, (b) a halogen, such as fluorine, chlorine, bromine or iodine, (c) a straight-chain or branched lower alkoxy group of 1 to 4 carbon atoms, such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy or tert-butoxy or (d) a straight-chain or branched lower alkylthio group of 1 to 4 carbon atoms, such as methylthio, ethylthio, n-propylthio, isopropylthio, n-butylthio, isobutylthio, sec-butylthio or tert-butylthio, (2) a straight-chain or branched lower alkyl group of 1 to 4 carbon atoms, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl or tert-butyl, which may optionally be substituted by a straight-chain or branched lower alkoxy group of 1 to 4 carbon atoms, such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy or tert-butoxy, (3) an aralkyl group preferably of 7 to 10 carbon atoms, such as benzyl, phenetyl or phenylpropyl, or (4) a cycloalkyl group of 4 to 7 carbon atoms, such as cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl.

The aryl group R_3 may optionally be substituted by 1 to 3 substituents (a)-(d) described above at any position of the aryl group.

The lower alkyl group R_3 may optionally be substituted by 1 to 3 lower alkoxy groups at any position of the lower alkyl group.

The examples of an aryl group which is substituted by a lower alkyl group, a halogen, a lower alkoxy group, or a lower alkylthio group, represented by R_3 include, among others, 2-, 3- or 4-methylphenyl, 2-, 3- or 4-ethylphenyl, 2-, 3- or 4-n-propylphenyl, 2-, 3- or 4-t-butylphenyl, 2-, 3- or 4-chlorophenyl, 2-, 3- or 4-bromophenyl, 2-, 3- or 4-methoxyphenyl, 2-, 3- or 4-ethoxyphenyl, 2-, 3- or 4-isopropoxyphenyl, 2-, 3- or 4-n-butoxyphenyl, 2-, 3- or 4-methylthiophenyl, 2-, 3- or 4-ethylthiophenyl, 2-, 3- or 4-n-propylthiophenyl, 2-, 3- or 4-isobutylthiophenyl, 2-methyl-4-chlorophenyl, 3-ethyl-4-bromophenyl, 2-chloro-4-methoxyphenyl, 2,4-dichlorophenyl, 2,4,6-trimethylphenyl and 2,4,6-trichlorophenyl, 1-methynaphtyl, 1-chloronaphtyl, 4-methylthionaphtyl, and so on.

The examples of a lower alkyl group which is substituted by a lower alkoxy group, represented by R_3 include, among others, methoxymethyl, methoxyethyl, 1-methoxypropyl, 2-methoxybutyl, ethoxylmethyl, ethoxylethyl, 2-ethoxypropyl, 3-ethoxypropyl, 1-ethoxy-1-methylpropyl, propoxymethyl, 2-isopropoxyethyl, t-butoxymethyl, 2-t-butoxyethyl, 3-t-butoxypropyl, 4-butoxybutyl and so on.

Among the above-mentioned ones, preferably, each of R_1 and R_2 is a straight-chain or branched lower alkyl group of 1 to 4 carbon atoms ; and R_3 is an aryl group which may optionally be substituted by (a) a straight-chain or branched lower alkyl group of 1 to 4 carbon atoms, (b) a halogen, (c) a straight-chain or branched lower alkoxy group of 1 to 4 carbon atoms, or (d) a straight-chain or branched lower alkylthio group of 1 to 4 carbon atoms. More preferably, each of R_1 and R_2 is methyl ; and R_3 is phenyl.

As the salt of the compound (I) of this invention, use is made of an agriculturally acceptable salt thereof, such as an acid addition salt with an inorganic acid, exemplified by hydrochloric acid, hydrobromic acid, sulfuric acid or phosphoric acid, or an organic acid exemplified by benzenesulfonic acid, p-toluenesulfonic acid, oxalic acid, acetic acid or maleic acid.

The compound (I) or a salt thereof is produced by reacting the compound (II) or a salt thereof with the compound (III) or a salt thereof under an acid condition, namely at pH 5 or below.

Examples of the salt of the starting compound (III) usable in the present reaction include an acid addition salt with an inorganic acid, such as hydrochloric acid, hydrobromic acid, sulfuric acid or phosphoric acid, or an organic acid, such as benzenesulfonic acid, p-toluenesulfonic acid, oxalic acid, acetic acid or maleic acid, while examples of the salt of another starting compound (II) include a salt with an alkali metal, such as sodium or potassium, an alkaline earth metal, such as calcium or magnesium, and ammonium radical.

The starting compound (III) or a salt thereof may exist in four kinds of stereoisomers due to the presence of an asymmetric carbon atom and a $>S=O$ (sulfoxide) bond in the molecule. Four kinds of these stereoisomers may be used after separating into individual optically active isomers or as a mixture of such optically active isomers.

In this reaction, the starting compound (II) or a salt thereof can be employed in about 2 moles to large excess per mole of another starting compound (III) or a salt thereof.

In order to maintain this reaction in the acid pH range of not more than 5, use is made of e. g. an inorganic acid, such as hydrochloric acid, hydrobromic acid, sulfuric acid or phosphoric acid, or an organic acid, such as benzenesulfonic acid, p-toluenesulfonic acid, oxalic acid or maleic acid. The acid is added in such an amount as to maintain the pH value of the reaction mixture at not more than 5. For example, it is desirable, in the case of the reaction in water or a mixed solvent of water and an organic solvent described below, to add the acid in such a manner as the acid concentration of the reaction mixture may be in the range of about 0.1 to 3 normal. The acid may be added at once when the reaction is initiated, or may be added little by little in such a way as to maintain the pH value of the reaction mixture in the acid range, as the reaction proceeds.

The reaction is normally carried out in a solvent. The suitable solvent may be any type of solvent, unless it adversely affects the reaction. Use is made of, for example, water or an organic solvent, such as acetic acid, a lower alcohol of 1 to 3 carbon atoms, such as methyl alcohol, ethyl alcohol or isopropyl alcohol, acetone, acetonitrile, dimethylformamide or dimethylsulfoxide, solely or as a mixture of the two or more solvents. Of these, water, acetic acid and a mixed solvent of water and acetic acid are preferable.

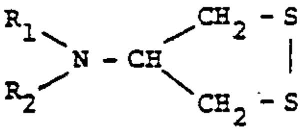
The reaction proceeds usually at about 5 °C to room temperature (about 15 °C), or the reaction may be carried out at about 60 to 100 °C. The reaction time varies with the reaction temperature, etc., and is normally in the range of 30 minutes to 4 hours.

The compound (I) or a salt thereof thus obtained is isolated and purified by means known *per se*, such as distillation, distillation under reduced pressure, solvent extraction, pH adjustment, solvent-transformation, concentration, concentration under reduced pressure, crystallization, recrystallization or/and chromatography. More concretely, after the conclusion of the reaction, the reaction mixture is adjusted, under cooling or heating, to the pH in the neighborhood of 4 to 6, if necessary with an aqueous solution of a suitable alkali (e. g. sodium hydroxide, potassium hydroxide, etc.), and by such procedure, the compound (I) can be isolated as crystals with a high degree of purity. Or, as the case may be, the reaction mixture is concentrated by distilling off the organic solvent, and the residue is neutralized with an aqueous solution of a suitable alkali (e. g., sodium hydroxide, potassium hydroxide, etc.) in the presence of an organic solvent immiscible with water, such as ether, chloroform or benzene ; then, the mixture is separated into two phases and the organic layer is separated out ; and subsequently, by following a conventional procedure known *per se*, the compound (I) may be crystallized.

In cases in which the compound (I) is difficult to be crystallized, the compound (I) can be isolated as a crystalline salt by adding an inorganic acid, such as hydrochloric acid, or an organic acid, such as oxalic acid, p-toluenesulfonic acid or picric acid to the organic layer separated from two phases as mentioned above.

The starting compound (III) or a salt thereof can be produced by a method known *per se*, such as the method as described in Agr. Biol. Chem., *34*, 935-940 (1974).

Thus, the compound (III) or a salt thereof is produced by oxidizing a compound of the general formula :



(IV)

wherein each of the symbols is as defined above, or a salt thereof, with an oxidizing agent under an acid condition. Examples of the salt of the compound (IV) include a salt with an inorganic acid, such as hydrochloric acid, sulfuric acid or hydrobromic acid, or an organic acid, such as maleic acid, oxalic acid, fumaric acid or p-toluenesulfonic acid, etc.

As the oxidizing agent in this reaction, use is made of organic and inorganic peracids. More concretely, use is made of an organic peracid, such as a percarboxylic acid e. g. performic acid, peracetic acid, trifluoroperacetic acid, permaleic acid, perbenzoic acid, m-chloroperbenzoic acid or monoperphthalic acid ; or a persulfonic acid e. g. p-toluenepersulfonic acid, and an inorganic peracid, such as hydrogen peroxide, periodic acid or persulfuric acid. These organic and inorganic peracids are employed solely or as a mixture of not less than two kinds of peracids. Among these, hydrogen peroxide is preferable. The oxidizing agent is normally used in an amount of at least equivalent preferably in about 1.1 to 1.2 moles per mole of the compound (IV). However, it is likewise possible to employ the oxidizing agent in 3 moles to large excess per mole of the compound (IV). This oxidation reaction is normally carried out in an inert solvent. Selection of the solvent varies depending particularly upon the solubility of the starting materials and type of the oxidizing agent, and for example, dichloromethane, chloroform, dimethylformamide, tetrahydrofuran, acetonitrile, water, acetic acid, ethyl acetate, etc. are used solely or as a mixed solvent consisting of these. Among the above solvents, particularly, water and acetic are preferable.

The reaction temperature ranges from about —10 to 60 °C, preferably from about 0 to 40 °C. The reaction time is in the range of about 1 to 4 hours.

After the conclusion of the reaction using, for example, water or a mixture of water and organic solvent as the reaction solvent, the reaction mixture can be used in the subsequent reaction, as such and also after adding an organic solvent immiscible with water, such as benzene, chloroform or ether, neutralizing the resultant mixture with an aqueous solution of a suitable alkali (e. g., sodium hydroxide, potassium hydroxide, etc.) under cooling and concentrating the organic layer resulting after separation into the aqueous and organic phases to isolate the compound (III) as a free base form. Furthermore, the compound isolated by the above procedure may be made into a salt with an inorganic acid, such as hydrochloric acid, sulfuric acid or hydrobromic acid or an organic acid, such as maleic acid, oxalic acid, fumaric acid or p-toluenesulfonic acid, according to a *per se* conventional method, and then may be used in the subsequent reaction.

The starting compound (II) or a salt thereof has already been known in the literature, and is produced, for example, by the method as described in Organic Synthesis collective Vol. IV, page 674 or Japanese Unexamined Published Patent Application No. 7753/1981. For example, the compound (II) is produced according to the method shown below.

$$R_3{-}SO_2Cl \xrightarrow[H_2SO_3 \text{ (or } Na_2SO_3)]{\text{reduction}} R_3SO_2H \qquad \text{(II)}$$

wherein R_3 is as defined above.

The starting compound (IV) is produced by *per se* known methods, e. g. a method described in Agr. Biol. Chem., *34*, 935 (1970).

The thus obtained starting compounds are isolated and purified by means known *per se*, such as distillation, distillation under reduced pressure, solvent extraction, pH adjustment, solvent-transformation, crystallization, recrystallization or/and chromatography.

This invention is illustrated by the following non-limiting examples.

The term « % » means weight % unless otherwise specified.

In the examples, etc., the NMR spectra are measured at 60 MHz (solvent : d-trifluoroacetic acid) and expressed as τ value, whereby the symbols used herein have the following respective meanings : s, singlet ; d, doublet ; t, triplet ; qr, quartet ; ABqr, AB pattern quartet ; qn, quintet ; m, multiplet ; J, coupling constant.

Reference Example 1

Production of 4-(N,N-dimethylamino)-1,2-dithiolane-1-oxide hydrochloride.

47.8 g of 4-(N,N-dimethylamino)-1,2-dithiolane oxalate is dissolved in 200 ml of water. 75 ml of benzene is added to the solution, and the mixture is neutralized with 35 ml of a 28 % aqueous sodium hydroxide solution under stirring, while maintaining the temperature of the mixture at the neighborhood of 25 °C. The neutralized solution is filtered to separate into crystals and filtrate. The crystals are furthermore washed well with 25 ml of benzene, and the washing is combined with the filtrate as separated previously, followed by separation into the benzene and aqueous layers. The benzene layer is extracted with 58 ml of 15 % hydrochloric acid, and the aqueous extract is combined with the aqueous solution as separated previously. While maintaining the temperature of the aqueous solution at 10 °C, 22 g of a 30 % aqueous hydrogen peroxide solution is added dropwise to the solution with stirring over the period of about 1 hour. After the addition is completed, stirring is carried out at room temperature for 1 hour. High performance liquid chromatographic analysis of this solution shows that the content of the titled compound is 39.6 g (yield 98 %). The reaction solution is almost concentrated to dryness under reduced pressure, and after 150 ml of ethanol is added to the residue to bring into a slurry form, the powder obtained by filtration is dried to give 34.3 g (yield of 85 %) of the titled compound.

I.R. ν_{max}^{KBr} cm^{-1} : 1 078
UV $\lambda_{max}^{H_2O}$ nm : 241
NMR : 5.7-6.5(5H, m), 6.92(6H, s)
m.p. : 152.5-167 °C (decomp.)

By the same procedure as described above, the following compounds are produced.

4-(N,N-Diethylamino)-1,2-dithiolane-1-oxide hydrochloride ;
I.R. ν_{max}^{KBr} cm^{-1} : 1 080
NMR : 5.52(1H, qn), 6.48(4H, d, J = 5.5Hz), 6.56(4H, qr), 8.47(6H, t, J = 7.0Hz).
4-(N,N-Methylethylamino)-1,2-dithiolane-1-oxide hydrochloride ;
I.R. ν_{max}^{KBr} cm^{-1} : 1 085
NMR : 5.56(1H, qn), 6.44(4H, d, J = 6.0Hz), 6.65(2H, qr), 7.05(3H, s), 8.62(3H, t, J = 7.0Hz).
4-(N,N-Methylcyclohexylamino)-1,2-dithiolane-1-oxide hydrochloride ;
I.R. ν_{max}^{KBr} cm^{-1} : 1 087
NMR : 5.52(1H, m), 6.38(4H, d, J = 7.0Hz), 6.59(1H, m), 7.5-6.96(3H, d, J = 5Hz), 7.5-8.5(10H, m).
4-(N,N-Dicyclohexylamino)-1,2-dithiolane-1-oxide hydrochloride ;
I.R. ν_{max}^{KBr} cm^{-1} : 1 093
NMR : 5.55(1H, m), 6.40(4H, d, J = 6.5Hz), 6.90(2H, m), 8.0-9.2(20H, m).
4-(N,N-Piperidino)-1,2-dithiolane-1-oxide hydrochloride ;
I.R. ν_{max}^{KBr} cm^{-1} : 1 095
NMR : 5.58(1H, m), 6.46(4H, d, J = 5.5Hz), 5.9-7.1(4H, m), 7.98(6H, m).
4-Morpholino-1,2-dithiolane-1-oxide hydrochloride ;
I.R. ν_{max}^{KBr} cm^{-1} : 1 098
NMR : 5.58(1H, m), 5.70(4H, m), 6.24(4H, m), 6.43(4H, d, J = 5.0Hz).

Example 1

Production of S,S'-[2-(dimethylamino)trimethylene]bis-benzenethiosulfonate.

In 150 ml of water is dissolved 68.9 g of sodium benzenesulfinate, while stirring. To the solution is added 76.7 ml of 20 % hydrochloric acid to make a benzenesulfinic acid solution, to which 134.4 ml of a 30 w/v% aqueous solution of 4-(N,N-dimethylamino)-1,2-dithiolane-1-oxide hydrochloride is added. To the mixture is added 97 ml of 20 % hydrochloric acid is added, followed by stirring at 50 °C for 4 hours. After the completion of the reaction, the reaction mixture, while maintaining the temperature at the neighborhood of 50 °C, is gradually neutralized with a 28 % aqueous sodium hydroxide solution, whereby the pH is kept at 4. The end-point of neutralization is at the point of time when the aqueous sodium hydroxide solution is hardly consumed, and the amount of a 28 % aqueous sodium hydroxide solution consumed is about 140 ml, with 2 to 3 hours being required for the neutralization. After the conclusion of the neutralization, crystals which separate out are filtered, washed with 200 ml of water and dried to give the titled compound. Crop 84.6 g (yield of 98.0 %). m. p. : 82-83 °C.

Example 2

Production of S,S'-[2-(dimethylamino)trimethylene]bis-benzenethiosulfonate.

To 100 ml each of the below-described solvents are added 34.5 g of sodium benzenesulfinate and 38.4 ml of 20 % hydrochloric acid to make a benzenezsulfinic acid solution. 16.5 g of crystalline 4-(N,N-dimethylamino)-1,2-dithiolane-1-oxide hydrochloride is added to the solution, and 50 ml of 20 % hydrochloric acid is further added, followed by reaction at 60 °C for 1.5 hours. After the conclusion of the reaction, the solvent is distilled off under reduced pressure, and 150 ml of water is added to the residue to bring into a slurry, to which a 28 % aqueous sodium hydroxide solution is added for neutralization.

Thereafter, the same procedure as in Example 1 is conducted to give the titled compound.

The solvents employed, together with the yields, are shown in the following.

Type of solvent	Acetic acid	Ethanol	Acetonitrile	Dioxane	DMF
Crop, g	42.8	41.9	42.2	41.8	41.9
Yield, %	99.2	97.1	97.7	96.8	97.0

Example 3

Shown below are the thiosulfonic acid derivatives obtained by the same procedure as described in Example 1.

(1) S,S'-[2-(Dimethylamino)trimethylene]bis-ethylthiosulfonate.
yield 95 %, m. p. 78.5-80 °C (decomp.).
Elemental analysis, for $C_{11}H_{27}NO_4S_4$
Calcd. : C, 28.62 ; H, 5.89 ; N, 3.03 (%)
Found : C, 28.62 ; H, 5.90 ; N, 3.03 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 315, 1 130
NMR : 5.85(1H, m), 6.24(4H, d, J = 6.0Hz), 6.79(6H, d, J = 5.0Hz), 6.39(4H, qr.), 8.43(6H, t, J = 7.0Hz).

(2) S,S'-[2-(Dimethylamino)trimethylene]bis-β-ethoxyethylthiosulfonate.
Elemental analysis, for $C_{13}H_{29}NO_6S_4$
Calcd. : C, 36.86 ; H, 6.90 ; N, 3.30 (%)
Found : C, 36.42 ; H, 7.05 ; N, 3.70 (%)
IR $\nu_{max}^{liquid\ film}$ cm^{-1} : 1 320, 1 120
NMR : 6.68(5H, s), 7.65(6H, s).

(3) S,S'-[2-(Dimethylamino(trimethylene]bis-benzylthiosulfonate oxalate. Yield 90 %, m. p. 151 °C (decomp.).
Elemental analysis, for $C_{21}H_{27}NO_8S_4$
Calcd. : C, 45.88 ; H, 4.95 ; N, 2.55 (%)
Found : C, 45.58 ; H, 4.90 ; N, 2.51 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 320, 1 130
NMR : 2.43(10H, s), 5.23(4H, m), 6.60(1H, m), 7.15(4H, d, J = 6.0Hz), 7.19(6H, d, J = 5.0Hz).

(4) S,S'-[2-(Dimethylamino)trimethylene]bis-p-toluenethiosulfonate. Yield 92 %, m. p. 114-115 °C.
Elemental analysis, for $C_{19}H_{25}NO_4S_4$
Calcd. : C, 49.64 ; H, 5.48 ; N, 3.05 (%)
Found : C, 49.74 ; H, 5.69 ; N, 3.03 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 320, 1 134
NMR : 2.21, 2.66(8H, ABqr, J = 8Hz), 6.99(5H, s), 7.55(6H, s), 7.83(6H, s).

(5) S,S'-[2-(Dimethylamino)trimethylene]bis-p-chlorobenzenethiosulfonate. Yield 95 %, m. p. 143-144 °C.
Elemental analysis, for $C_{17}H_{19}Cl_2NO_4S_4$
Calcd. : C, 40.79 ; H, 3.83 ; N, 2.80 (%)
Found : C, 41.04 ; H, 3.79 ; N, 2.53 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 324, 1 143
NMR : 2.13, 2.42(8H, ABqr, J = 9.0Hz), 6.92(5H, s), 7.78(6H, s).

(6) S,S'-[2-(Dimethylamino)trimethylene]bis-p-methoxybenzenethiosulfonate. Yield 90 %, m. p. 115.5-117 °C.
Elemental analysis, for $C_{19}H_{25}NO_6S_4$
Calcd. : C, 48.53 ; H, 5.62 ; N, 2.69 (%)

Found : C, 48.33 ; H, 5.59 ; N, 2.58 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 326, 1 137
NMR : 2.14, 2.94(8H, ABqr, J = 9.0Hz), 6.08(6H, s), 6.79(5H, s), 7.80(6H, s).

(7) S,S'-[2-(Dimethylamino)trimethylene]bis-p-methylbenzenethiosulfonate. Yield 91 %, m. p. 102-104°C.
Elemental analysis, for $C_{19}H_{25}NO_4S_6$
Calcd. : C, 43.57 ; H, 4.81 ; N, 2.67 (%)
Found : C, 43.34 ; H, 4.76 ; N, 2.54 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 320, 1 142
NMR : 2.22, 2.68(8H, ABqr, J = 8.5Hz), 6.97(5H, s), 7.46(6H, s), 7.82(6H, s).

(8) S.S'-[2-(Dimethylamino)trimethylene]bis-β-naphthylthiosulfonate. Yield. 90 %, m. p. 110-115 °C.
Elemental analysis, for $C_{25}H_{25}NO_4S_4$
Calcd. : C, 56.47 ; H, 4.74 ; N, 2.63 (%)
Found : C, 56.07 ; H, 4.68 ; N, 2.60 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 313, 1 122
NMR : 1.85-2.4(14H, m), 6.93(5H, s), 7.87(6H, s).

(9) S,S'-[2-(Methylethylamino)trimethylene]bis-p-toluenethiosulfonate. Yield 89 %, m. p. 97-98 °C.
Elemental analysis, for $C_{20}H_{27}NO_4S_4$
Calcd. : C, 50.71 ; H, 5.74 ; N, 2.96 (%)
Found : C, 50.45 ; H, 5.58 ; N, 2.79 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 320, 1 135
NMR : 2.16, 2.61(4H, ABqr, J = 8.5Hz), 6.92(5H, s), 7.58(2H, qr), 7.62(6H, s), 7.86(3H, s), 9.09(3H, t, J = 7.0Hz).

(10) S,S'-[2-(Methylcyclohexylamino)trimethylene]bis-p-toluenethiosulfonate. Yield 91 %, m. p. 120-121 °C.
Elemental analysis, for $C_{23}H_{35}NO_4S_4$
Calcd. : C, 50.55 ; H, 5.71 ; N, 2.27 (%)
Found : C, 50.32 ; H, 5.73 ; N, 2.31 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 330, 1 140.
NMR : 2.07, 2.47(4H, ABqr, J = 8.5Hz), 5.49(1H, m), 6.38(4H, d, J = 7.0Hz), 6.59(1H, m), 6.96(3H, d, J = 5.0Hz), 7.36(6H, s), 7.5-8.7(10H, m).

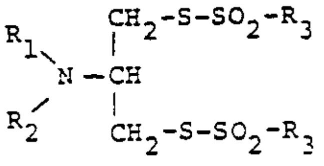
(11) S,S'-[2-(Dicyclohexylamino)trimethylene]bis-p-toluenethiosulfonate. Yield 92 %, m. p. 104-106 °C.
Elemental analysis, for $C_{29}H_{41}NO_4S_4$
Calcd. : C, 58.45 ; H, 6.93 ; N, 2.35 (%)
Found : C, 58.39 ; H, 6.91 ; N, 2.33 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 325, 1 140
NMR : 2.14, 2.60(4H, ABqr, J = 8.5Hz), 6.90(5H, s), 6.90(2H, m), 7.52(6H, s), 8.0-9.2(20H, m).

(12) S,S'-[2-(Piperidino-trimethylene]-bis-p-toluenethiosulfonate. Yield 95 %, m. p. 122-123 °C.
Elemental analysis, for $C_{22}H_{29}NO_4S_4$
Calcd. : C, 52.87 ; H, 5.85 ; N, 2.80 (%)
Found : C, 52.76 ; H, 5.72 ; N, 2.82 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 315, 1 140
NMR : 2.22, 2.65(4H, ABqr, J = 8.5Hz), 6.96(5H, s), 7.68(4H, m), 8.60(6H, m).

(13) S,S'-[2-(Morpholino-trimethylene)-bis-p-toluenethiosulfonate. Yield 95 %, m. p. 124-125 °C.
Elemental analysis, for $C_{23}H_{31}NO_4S_4$
Calcd. : C, 53.77 ; H, 6.08 ; N, 2.73 (%)
Found : C, 53.55 ; H, 6.33 ; N, 2.67 (%)
IR ν_{max}^{KBr} cm^{-1} : 1 320, 1 135
NMR : 2.21, 2.63(4H, ABqr, J = 8.0Hz), 6.42(4H, m), 6.93(5H, s), 6.93(4H, m), 7.54(6H, s).

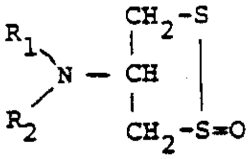
Claims

1. A process for producing a thiolsulfonic acid derivative of the general formula :



$$\begin{matrix} R_1 & & CH_2-S-SO_2-R_3 \\ & N-CH & \\ R_2 & & CH_2-S-SO_2-R_3 \end{matrix}$$

wherein each of R_1 and R_2 is independently a lower alkyl group or a 5- or 6-membered cycloalkyl group, or alternatively R_1 and R_2 together with the adjacent nitrogen atom form a 5- or 6-membered heterocyclic group wich may further contain an oxygen, sulfur or nitrogen atom ; and R_3 is (1) an aryl group which may optionally be substituted by a lower alkyl group, a halogen, a lower alkoxy group or a lower alkylthio group, (2) a lower alkyl group which may optionally be substituted by a lower alkoxy group, (3) an aralkyl group or (4) a cycloalkyl group, or a salt thereof, which comprises reacting a compound of the general formula :



wherein R_1 and R_2 are as defined above, or a salt thereof with a compound of the general formula :

$$R_3SO_2H$$

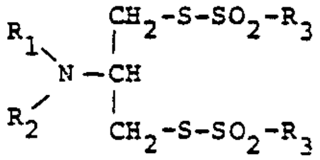
wherein R_3 is as defined above, or a salt thereof under an acid condition.

2. A process as claimed in Claim 1, wherein each of R_1 and R_2 is independently methyl, and R_3 is phenyl.

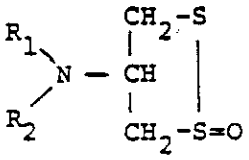
3. A process as claimed in Claim 1, wherein the acid condition means pH 5 or below.

Patentansprüche

1. Verfahren zur Herstellung eines Thiolsulfonsäure-Derivats der allgemeinen Formel



in der R_1 und R_2 jeweils unabhängig voneinander eine niedere Alkyl-Gruppe oder eine 5- oder 6-gliedrige Cycloalkyl-Gruppe sind oder alternativ R_1 und R_2 zusammen mit dem benachbarten Stickstoff-Atom eine 5- oder 6-gliedrige heterocyclische Gruppe bilden, die weiterhin ein Sauerstoff-, Schwefel- oder Stickstoff-Atom enthalten kann, und R_3 (1) eine Aryl-Gruppe, die gegebenenfalls durch eine niedere Alkyl-Gruppe, ein Halogen, eine niedere Alkoxy-Gruppe oder eine niedere Alkylthio-Gruppe substituiert sein kann, (2) eine niedere Alkyl-Gruppe, die gegebenenfalls durch eine niedere Alkoxy-Gruppe substituiert sein kann, (3) eine Aralkyl-Gruppe oder (4) eine Cycloalkyl-Gruppe ist, oder eines Salzes desselben, das die Reaktion einer Verbindung der allgemeinen Formel



in der R_1 und R_2 die im Vorstehenden angegebenen Bedeutungen haben, oder eines Salzes derselben mit einer Verbindung der allgemeinen Formel

$$R_3SO_2H$$

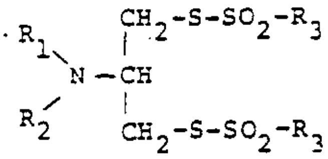
in der R_3 die im Vorstehenden angegebenen Bedeutungen hat, oder einem Salz derselben unter sauren Bedingungen umfaßt.

2. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß R_1 und R_2 jeweils unabhängig voneinander Methyl sind und R_3 Phenyl ist.

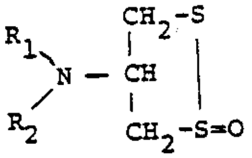
3. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß als saure Bedingungen ein pH-Wert von 5 oder weniger verstanden wird.

Revendications

1. Procédé de production d'un dérivé d'acide thiolsulfonique de formule générale :



dans laquelle chacun des groupes R_1 et R_2 est, indépendamment, un groupe alkyle inférieur ou un groupe cycloalkyle à 5 ou 6 chaînons, ou bien R_1 et R_2 forment ensemble, avec l'atome d'azote adjacent, un groupe hétérocyclique à 5 ou 6 chaînons qui peut encore contenir un atome d'oxygène, de soufre, ou d'azote ; et R_3 est (1) un groupe aryle, qui peut être éventuellement substitué par un groupe alkyle inférieur, un atome d'halogène, un groupe alcoxy inférieur ou un groupe alkylthio inférieur, (2) un groupe alkyle inférieur qui peut être éventuellement substitué par un groupe alcoxy inférieur, (3) un groupe aralkyle ou (4) un groupe cycloalkyle, ou d'un sel de ce dérivé, qui comprend la réaction d'un composé de formule générale :



dans laquelle R_1 et R_2 sont tels que définis ci-dessus, ou d'un sel de ce composé, avec un composé de formule générale :

$$R_3SO_2H$$

dans laquelle R_3 est tel que défini ci-dessus, ou avec un sel de ce composé, dans des conditions acides.

2. Procédé conforme à la revendication 1, dans lequel chacun des R_1 et R_2 est indépendamment un groupe méthyle, et R_3 est un groupe phényle.

3. Procédé conforme à la revendication 1, dans lequel les conditions acides signifient un pH égal ou inférieur à 5.

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