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(54) **PREPARATION D'ISOTHIOCYANATES DE VINYLE**
(54) **PREPARATION OF VINYL ISOTHIOCYANATES**

(57) Divulcation d'un procédé de préparation d'isothiocyanate de vinyle, comprenant la mise en contact d'un thiocyanate d'allyle substitué par un halogène, en solution et à température élevée, avec une matière acide qui est soit un acide, soit un halogénure ou un oxyhalogénure d'un acide inorganique. Le thiocyanate d'allyle substitué par un halogène peut être préparé à partir d'un alcène dihalogéné. L'isothiocyanate de vinyle peut être subséquemment converti en thiazole.

(57) A process for preparing a vinyl isothiocyanate comprises contacting a halogen-substituted allyl thiocyanate, in solution and at an elevated temperature, with an acidic material which is either an acid or a halide or oxyhalide of an inorganic acid. The halogen-substituted allyl thiocyanate may be prepared from a dihalogenated alkene. The vinyl isothiocyanate may subsequently be converted to a thiazole.

ABSTRACT**"Preparation of vinyl isothiocyanates"**

A process for preparing a vinyl isothiocyanate comprises contacting a halogen-substituted allyl thiocyanate, in solution and at an elevated temperature, with an acidic material which is either an acid or a halide or oxyhalide of an inorganic acid. The halogen-substituted allyl thiocyanate may be prepared from a dihalogenated alkene. The vinyl isothiocyanate may subsequently be converted to a thiazole.

Preparation of vinyl isothiocyanates

The present invention relates to the preparation of vinyl isothiocyanates and is an improved process for that purpose.

Substituted vinyl isothiocyanates are useful intermediates in the preparation of substituted thiazoles. These latter compounds may in turn be important intermediates in the manufacture of agrochemical and pharmaceutical products. By way of example, we have described in Patent Specification No. GB 2305172A a process for preparing thiazoles substituted by a haloalkyl group in the 5 position, which entails reacting a halo-substituted vinyl isothiocyanate in solution with a chlorinating or brominating agent.

These halo-substituted vinyl isothiocyanates are more attractive starting materials for the preparation of the desired thiazoles than previously-proposed starting materials in that they may be more readily available. They may be prepared by a method described by K. Schulze et al in Journal fuer Praktische Chemie, 1980, Vol.322 at pages 629-637, which method entails reacting a dihalogenated alkene, for example 1,3-dichloropropene, with an alkali metal thiocyanate or ammonium thiocyanate.

The foregoing process of Schulze et al takes place in two stages, involving firstly the formation of an allyl thiocyanate

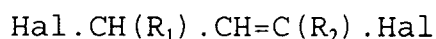
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and then, in a separate second stage, the thermal rearrangement of the allyl thiocyanate to the desired vinyl isothiocyanate. Unfortunately this process displays several disadvantages. First of all, the overall yield of vinyl isothiocyanate is low, for example as little as 35 per cent based on the quantity of the alkene starting material. Secondly, the second stage uses the toxic solvent dioxan. Attempts to replace the dioxan with less toxic hydrocarbons or chlorinated hydrocarbons as the solvent have led to product of low purity and a significant formation of undesired side products.

Against the foregoing background, it is an object of the present invention to provide an improved process for the conversion of halogen-substituted allyl thiocyanates to the corresponding vinyl isothiocyanates.

The process according to the present invention comprises contacting a halogen-substituted allyl thiocyanate, in solution and at an elevated temperature, with an acidic material which is either an acid or a halide or oxyhalide of an inorganic acid.

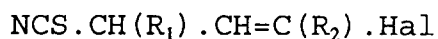
The process is of particular advantage in carrying out the two-stage conversion of a dihalogenated alkene to a vinyl isothiocyanate. Thus the invention includes a two-stage process of this type which comprises reacting a dihalogenated alkene of the general formula



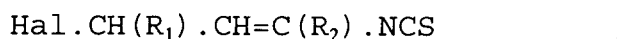
wherein the symbols Hal each represents a chlorine or bromine atom, which may be the same or different, and the symbols R_1 and R_2 each represents a hydrogen atom or an alkyl group containing from 1 to 3 carbon atoms, with an alkali metal thiocyanate or with ammonium thiocyanate, and contacting the halogen-substituted allyl thiocyanate so obtained, in solution and at an elevated temperature, with an acidic material which is either an acid or a halide or oxyhalide of an inorganic acid. The allyl thiocyanate which is the

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intermediate in this two-stage reaction has the general formula



and, by thermal rearrangement in the presence of the specified acidic material, this compound is converted to the desired vinyl isothiocyanate of the general formula



in both of which general formulae the symbols Hal, R_1 and R_2 have the meanings given above.

Thus, in its simplest form, as applied to the two-stage production of a vinyl isothiocyanate, the process comprises reacting 1,3-dichloropropene with an alkali metal thiocyanate, for example sodium thiocyanate, and contacting the 1-chloro allyl thiocyanate so produced, in solution and at an elevated temperature, with the acidic material, whereby to obtain 3-chloro-prop-1-enyl isothiocyanate.

The acidic material in the presence of which the thermal rearrangement of the halogen-substituted allyl thiocyanate is effected in the process according to the present invention may be a mineral acid, for example hydrochloric, sulphuric or nitric acid, or an organic acid, for example an aliphatic acid of general formula $\text{R}_3 \cdot \text{COOH}$ in which the symbol R_3 represents an alkyl group containing 1 to 3 carbon atoms. In a particularly preferred form of the invention, the acid is an organic sulphonic acid, for example methanesulphonic acid or p-toluenesulphonic acid. The acidic material may alternatively be a halide or oxyhalide of an inorganic acid. Among such materials, thionyl chloride and phosphorus oxychloride have proved to be particularly effective.

The acidic material preferably is added in an amount equal to between 1 and 25 mole per cent of the allyl thiocyanate, more preferably between 1 and 10 mole per cent.

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The thermal rearrangement of the allyl thiocyanate is carried out in solution. A wide range of solvents are suitable for this purpose. Such solvents include aliphatic, cycloaliphatic and aromatic hydrocarbons, for example heptane, cyclohexane or toluene, and chlorinated hydrocarbons, for example 1,2-dichlorethane, 1,1,2-trichloroethane or chlorobenzene. The chlorinated hydrocarbons are particularly preferred solvents if the vinyl isothiocyanate prepared by the process of the present invention is to be further reacted to form a thiazole as discussed above, in that the solvent may also be the solvent for this further reaction, thus enabling the isothiocyanate to be reacted without first being isolated from the solvent.

The process according to the present invention for rearrangement of the allyl thiocyanate is conducted at an elevated temperature. For example temperatures within the range from 50° to 150° C may be used. The selected temperature should take account of the solvent in which the reaction is carried out but reaction temperatures within the range from 80° to 130° C are preferred.

The halogen-substituted vinyl isothiocyanate prepared by the method according to the present invention may be isolated from the reaction mixture and purified if desired. The isolation and such purification may be carried out by conventional methods, for example by distillation. However, the yields of isothiocyanate achievable by means of the present process are such that, if the solvent chosen is compatible with the requirements of any subsequent reaction, the isothiocyanate may be further reacted as described above without first requiring to be isolated from the reaction mixture.

A further important advantage of the present invention is that, surprisingly, the ratio of the trans-isomer to the cis-isomer of the vinyl isothiocyanate obtained by the process is significantly higher than would otherwise be expected and significantly favours the trans-isomer. Thus the ratio of

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trans-isomer to cis-isomer in the product may exceed 2:1 or 3:1. When the vinyl isothiocyanate is subsequently to be converted to a thiazole by reacting with a chlorinating or brominating agent, the trans-isomer reacts more readily, so the present process has the advantage of producing a particularly advantageous starting material for that subsequent conversion.

The invention will now be further described with reference to the following Examples, which illustrate, by way of example only, the preparation of 3-chloro-prop-1-enyl isothiocyanate by the process according to the present invention.

Example 1

Crude 3-chloroallyl thiocyanate was prepared by reaction of 100g of 1,3-dichloropropene and 110g of sodium thiocyanate in 200 ml. of water. The product was separated by extraction into 300 ml. of 1,2-dichloroethane, giving a solution of the thiocyanate of about 24 per cent concentration.

To the solution of the thiocyanate, 5.0g (3 mole per cent) of p-toluenesulphonic acid was added and the solution was subjected to azeotropic distillation until all residual water had been removed. The solution was placed in an autoclave and the thermal rearrangement was carried out by heating the solution to 110° C for 12 hours.

The resulting isothiocyanate solution was filtered through a bed of charcoal and yielded 460g of a clear yellow solution of 3-chloro-prop-1-enyl isothiocyanate. GC analysis showed that the product comprised 87 per cent of this compound in the form of a mixture of trans- and cis-isomers in the ratio 2.2:1, together with just 4 per cent of unconverted dichloropropene and 7 per cent of 1,3-bis (isothiocyanato) propenes.

Comparative Example

The solution of 3-chloroallyl thiocyanate in 1,2-dichloroethane was prepared as above and the compound was subjected to thermal rearrangement by heating to 110° C for 12 hours but in the absence of acid. A large amount of tarry solid was formed. This solid was removed by filtration through charcoal and yielded 400g of a clear yellow solution. GC analysis showed that the product comprised only 56 per cent of 3-chloro-prop-1-enyl isothiocyanate as a mixture of trans- and cis-isomers in the ratio 1.5:1, together with 12 per cent of unconverted dichloropropene, 21 per cent of 1,3-bis (isothiocyanate) propenes and numerous minor impurities.

Example 2

A solution of 3-chlorallyl thiocyanate in 1,2-dichlorethane, of concentration 24 per cent by weight, prepared by the process described in Example 1, was heated with 5 mole per cent of methanesulphonic acid at 115°C for 10 hours. The resulting solution comprised a mixture of trans- and cis-isomers of 3-chloro-prop-1-enyl isothiocyanate, in a yield of 91 per cent based on the 3-chlorallyl thiocyanate. The overall yield of the product based on the 1,3-dichloropropene was determined by GC analysis to be 78 per cent by weight.

Example 3

A solution of 3-chlorallyl thiocyanate in 1,2-dichloroethane, of concentration 24 per cent by weight, prepared by the process described in Example 1, was placed in an autoclave with 1 mole per cent of p-toluenesulphonic acid. The mixture was heated to 105 -110°C for 13 hours and yielded a solution of 3-chloro-prop-1-enyl isothiocyanate as a mixture of trans- and cis-isomers in the ratio of 2.1:1, which mixed isomers comprised 83 per cent of the total product.

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The isothiocyanate solution was directly chlorinated with 1.2 mole equivalent of sulphuryl chloride, at -20° to 0°C , as described in our UK Patent Specification No 2305172A. The 2-chloro-5-chloromethyl thiazole hydrochloride formed was removed from the reaction mixture by filtration and amounted to an overall yield of 53 per cent based on the 1,3-dichloropropene starting material.

Examples 4 to 10

3-chloroallyl thiocyanate, prepared by reaction of 1,3-dichloropropene and sodium thiocyanate in water, was extracted into 1,1,2-trichloroethane to give a 20 per cent by weight solution of the thiocyanate. The solution was heated at 110°C for 5 to 10 hours until the conversion was completed. In Examples 5 to 10, the heating was carried out in the presence of the respective acidic material specified in the following table; in Example 4, the acidic material was omitted for comparison purposes. The yield of 3-chloro-prop-1-enyl isothiocyanate in each case is given below, together with the ratio of trans- to cis-isomer in the product.

Example	Acidic material (mole per cent based on thiocyanate)	Yield of thiocyanate	Ratio of trans- to cis-isomers
4	None	37.2%	1.3:1
5	36% Hydrochloric acid (5%)	62.8%	2.1:1
6	98% Sulphuric acid (5%)	59.4%	2.4:1
7	Thionyl chloride (5%)	58.7%	1.8:1

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8	Phosphorus oxychloride (5%)	66.1%	2.8:1
9	p-Toluenesulphonic acid (5%)	73.1%	3.1:1
10	Methanesulphonic acid (5%)	75.8%	4.0:1

Examples 11 to 17

3-chloroallyl thiocyanate, prepared by reaction of 1,3-dichloropropene and sodium thiocyanate in water, was extracted into toluene to give a 30 per cent by weight solution of the thiocyanate. The solution was heated under reflux for 6 to 12 hours until the conversion was completed. In Examples 12 to 17, the heating was carried out in the presence of the respective acidic material specified in the following table; in Example 11, acidic material was omitted for comparison purposes. The yield of 3-chloro-prop-1-enyl isothiocyanate in each case is given below, together with the ratio of trans- to cis-isomer in the product.

Example	Acidic material (mole per cent based on thiocyanate)	Yield of thiocyanate	Ratio of trans - to cis-isomers
11	None	44.7%	1.6:1
12	36% Hydrochloric acid (5%)	74.0%	2.2:1
13	98% Sulphuric acid (5%)	60.5%	2.6:1

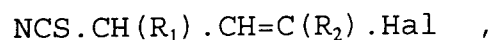
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14	Thionyl chloride (5%)	59.1%	1.8:1
15	Phosphorus oxychloride (5%)	80.3%	4.1:1
16	p-Toluenesulphonic acid (5%)	66.0%	4.2:1
17	Methanesulphonic acid (5%)	78.9%	4.7:1

CLAIMS

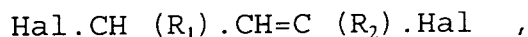
1. A process for the preparation of a vinyl isothiocyanate, which process comprises contacting a halogen-substituted allyl thiocyanate, in solution and at an elevated temperature, with an acidic material which is either an acid or a halide or oxyhalide of an inorganic acid.

2. A process as claimed in Claim 1, wherein the halogen-substituted allyl thiocyanate is of general formula



wherein the symbols R_1 and R_2 each represents a hydrogen atom or an alkyl group containing from 1 to 3 carbon atoms and the symbol Hal represents a chlorine or bromine atom.

3. A process as claimed in Claim 2, wherein the halogen - substituted allyl thiocyanate is produced by reacting a dihalogenated alkene of the general formula



wherein the atoms represented by the symbols Hal may be the same or different, with an alkali metal thiocyanate or with ammonium thiocyanate.

4. A process as claimed in Claim 3, wherein the dihalogenated alkene is 1,3-dichloropropene and the vinyl isothiocyanate is 3-chloro-prop-1-enyl isothiocyanate.

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5. A process as claimed in any of Claims 1 to 4, wherein the acidic material is hydrochloric, sulphuric or nitric acid, an aliphatic acid of general formula $R_3\text{COOH}$, in which the symbol R_3 represents an alkyl group containing 1 to 3 carbon atoms, or an organic sulphonic acid.

6. A process as claimed in Claim 5, wherein the organic sulphonic acid is methanesulphonic acid or p-toluenesulphonic acid.

7. A process as claimed in any of Claims 1 to 4, wherein the acidic material is thionyl chloride or phosphorus oxychloride.

8. A process as claimed in any of Claims 1 to 7, wherein the amount of the acidic material is between 1 and 25 mole per cent of the allyl thiocyanate.

9. A process as claimed in Claim 8, wherein the amount of the acidic material is between 1 and 10 mole per cent of the allyl thiocyanate.

10. A process as claimed in any of Claims 1 to 9, wherein the contacting of the halogen-substituted allyl thiocyanate with an acidic material is carried out in solution in an aliphatic, cycloaliphatic or aromatic hydrocarbon or a chlorinated hydrocarbon.

11. A process as claimed in Claim 10, wherein the solvent for said solution is heptane, cyclohexane, toluene, 1,2-dichloroethane or 1,1,2-trichloroethane.

12. A process as claimed in any of Claims 1 to 11, wherein the contacting of the halogen-substituted allyl thiocyanate with an acidic material is carried out at a temperature within the range from 50° to 150°C.

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13. A process as claimed in Claim 12, wherein said temperature lies within the range from 80° to 130°C.

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