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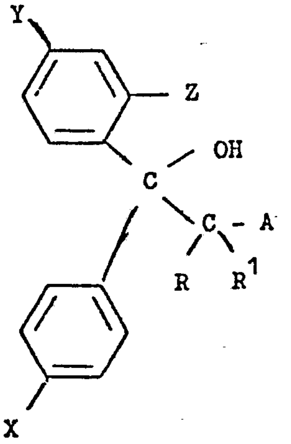
(54) Process for preparing 1,1-bis[(optionally substituted)phenyl]-2-haloalkan-1-ols

(57) 1,1-bis[(optionally substituted)-phenyl]alk-1-enes are reacted with chlorine or bromine, optionally in the presence of hydrogen peroxide, in aqueous tertiary butanol. The products which have the formula



(I)

(in which R and R^1 are each independently H or alkyl; X, Y and Z are each independently H, F or Cl; and A is Cl or Br) are useful intermediates in the synthesis of fungicides.

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The chemical formulae appearing in the printed specification were submitted after the date of filing, the formulae originally submitted being incapable of being satisfactorily reproduced.

SPECIFICATION

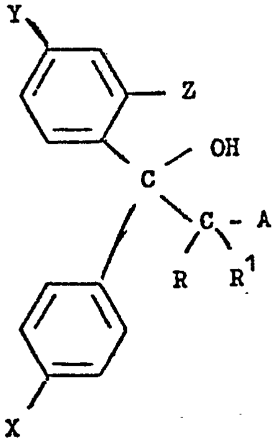
Process for preparing 1,1-bis[(optionally substituted)phenyl]-2-haloalkan-1-ols

This invention relates to a process for the preparation of certain halohydrins which are 1,1-bis[(optionally substituted)phenyl]-2-haloalkan-1-ols.

DE—AS 1172654 describes and claims a process for the preparation of chlorohydrins by reacting an olefin or polyolefin with chlorine in an aqueous medium, characterised in that an olefin or polyolefin with 5 to 40 carbon atoms in the molecule, which can also be substituted, branched chain or cyclic, is reacted with chlorine in a liquid reaction medium which contains at least 50 parts by volume of an organic solvent boiling below 200°C and which is miscible with water as well as the olefin or polyolefin used, to 100 parts by volume of water.

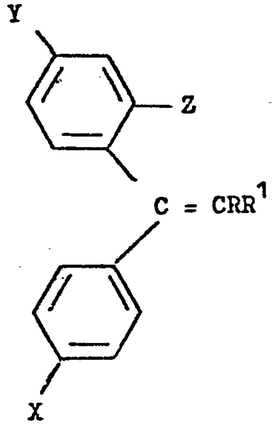
The organic solvents used in the above process preferably have a boiling point below 150°C and particularly below 100°C, and the preferred solvents contain only carbon, hydrogen and oxygen in the molecule, for example, alcohols, ethers, aldehydes, ketones, carboxylic acids and carboxylic acid esters. Acetone, acetaldehyde, methylethylketone, dioxane, propanol and tertiary butanol are exemplified. The olefins employed as starting materials are typically hexadecene-1 and mixtures of C_{13}—C_{15} alkenes.

According to the present invention there is provided a process for the preparation of halohydrins of the formula (I):



(I)

wherein R and R^1 are hydrogen or alkyl, preferably C_1—C_4 alkyl, and may be the same or different; X, Y and Z are each independently hydrogen, fluorine or chlorine and A is chlorine or bromine, which comprises reacting a substituted alkene of the formula (II):

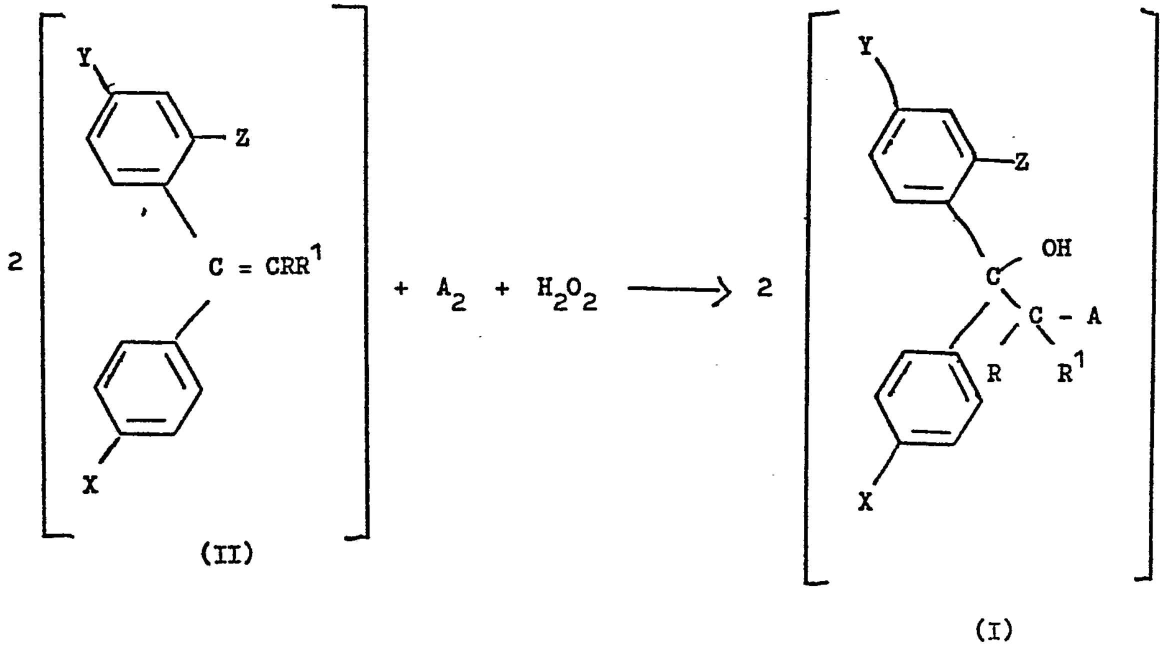


(II)

wherein R, R^1, X, Y and Z have the meanings hereinbefore defined, with chlorine or bromine in aqueous tertiary butanol.

In a preferred aspect of the process, the substituted alkene is reacted with chlorine or bromine in the presence of hydrogen peroxide which promotes more efficient use of the halogen reactant.

When hydrogen peroxide is used the overall reaction can be represented by the following scheme:—



from which it can be seen that 2 mols of alkene (II) require 1 mole of chlorine or bromine and 1 mol of hydrogen peroxide to give 2 mols of the halohydrin (I). This optimum theoretical stoichiometry may not be achievable in practice, but the above process does ensure that a substantial part of the halogen employed is utilised in halohydrin formation.

The amount of chlorine or bromine which is used is preferably in slight excess over 1 mol per 2 mols of the alkene of formula (II), and is conveniently from 1.05 to 1.5 mols per 2 mols of the alkene.

Hydrogen peroxide may be used in any amount preferably up to 1.5 mols per 2 mols of the alkene. An amount of about 1 mol per 2 mols of the alkene has been found effective. The hydrogen peroxide is conveniently employed in the form of the commercially available 30% (100 volume) aqueous solution, although other strengths may be used if desired.

A reaction temperature from normal room temperature up to about 80°C may be used.

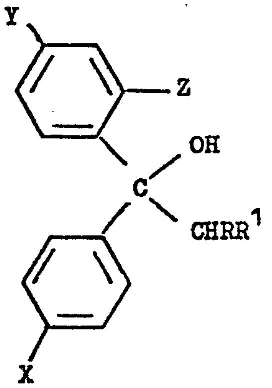
The reaction may be carried out by stirring a dispersion of alkene of formula (II) in a mixture of water and tertiary butanol and then adding chlorine or bromine and, if desired, hydrogen peroxide whilst maintaining the desired reaction temperature. A useful working concentration of alkene in the total reaction mixture is about 20% w/w although concentrations up to about 30% w/w or even higher may be used.

The reaction may conveniently be conducted by forming a suspension of the alkene in the aqueous tertiary butanol and then adding the chlorine or bromine slowly, followed by the hydrogen peroxide if used. Alternatively, the chlorine or bromine, and the hydrogen peroxide, may be added simultaneously or alternately in portions to the alkene and aqueous tertiary butanol or the alkene, chlorine or bromine and hydrogen peroxide may be added simultaneously or alternately in portions to the aqueous tertiary butanol. Further all or part of the chlorine or bromine may be added in the form of hypochlorous or hypobromous acid or a salt thereof. If, after all of the halogen has been added, a test of the reaction mixture shows that some alkene remains unreacted, further additions of chlorine or bromine and hydrogen peroxide may be made until all of the alkene has been used up. The product may be isolated by diluting the reaction mixture to, for instance, about twice its volume with water, removing and recovering the tertiary butanol by distillation and collecting the product as an oil which may crystallise after a period of stirring at room temperature. The crude product is washed with water and dried.

The proportion of tertiary butanol and water is not critical. Thus, from 4 to 0.25 parts by volume. and typically from 3 to 1 parts by volume, of tertiary butanol to 1 part by volume of water may be used.

The process may be operated either batchwise or continuously.

The alkenes of formula (II) which are used as starting materials in the present process may be obtained by dehydration of a tertiary alcohol of formula (III):



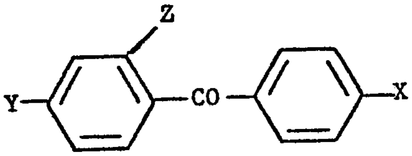
(III)

wherein R, R^1, X, Y and Z have the previously defined meanings, using methods known from the literature for such dehydrations, for example, by heating the alcohol of formula (III) in the presence of a catalytic amount of a strong acid such as *p*-toluene sulphonic acid.

The alcohols of formula (III) may themselves be obtained by a Grignard reaction between an alkyl magnesium halide of formula (IV):

$RR^1HCMgHal$ (IV)

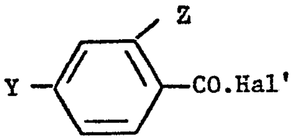
and a benzophenone of formula (V):



(V)

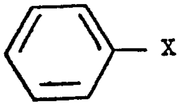
wherein R, R^1, X, Y and Z have the previously defined meanings and Hal is chlorine, bromine or iodine; under conditions known from the literature for the conduct of such reactions.

The benzophenones of formula (V) may be prepared in known manner by Friedel-Crafts reaction between a benzoyl halide of formula (VI):



(VI)

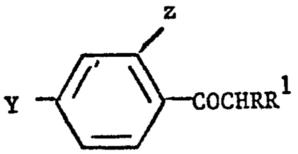
and a benzene derivative of formula (VII):



(VII)

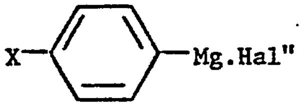
wherein X, Y and Z have the previously defined meanings and Hal′ represents bromine or preferably chlorine, in the presence of a Lewis acid such as aluminium chloride.

Alternatively, the alcohols of formula (III) may be obtained by reaction in known manner of a compound of formula (VIII):



(VIII)

wherein R, R^1, Y and Z have the previously defined meanings with a Grignard compound of formula (IX):

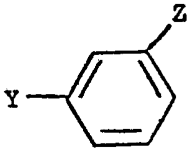

(IX)

wherein X has the previously defined meaning and Hal" is bromine or iodine.

The compounds of formula (VIII) may be obtained by methods known from the art, for example, by Friedel-Crafts reaction of an acid halide of formula (X):

$$RR^1CH \cdot COA \qquad (X)$$

wherein A, R and R^1 have the previously defined meanings, with a benzene derivative of formula (XI):


(XI)

in which Y and Z have the previously defined meanings.

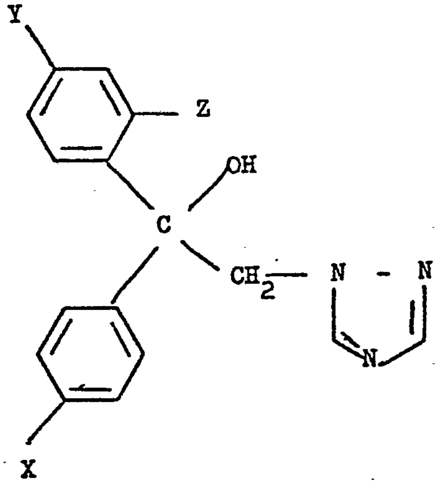
Yet again, the tertiary alcohols of formula (III) in which X and Y are the same and Z is hydrogen may be prepared by reaction in known manner between 2 mol proportions of a Grignard compound of formula (IX) and 1 mol proportion of an ester of formula (XII):

$$RR^1 \cdot CH \cdot COOR^2 \qquad (XII)$$

wherein R and R^1 have the previously defined meanings and R^2 is a hydrocarbon radical, preferably an alkyl radical and particularly a (C_1—C_4) alkyl radical. An example of an ester of formula (XII) which may be used is ethyl acetate.

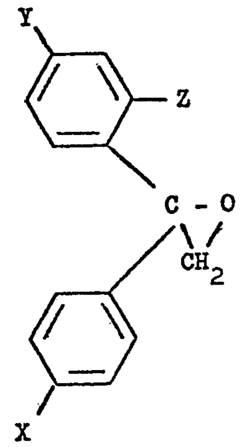
The substituted alkenes of formula (II) may also be obtained directly from the Grignard reaction between an alkyl magnesium halide of formula (IV) and a benzophenone of formula (V) as already indicated above, without isolation of the intermediate alcohol of formula (III). The Grignard reaction mixture, after completion of the reaction, is poured into dilute aqueous acid, and the organic layer collected. This organic layer contains the alcohol of formula (III) in the organic solvent or mixture of organic solvents, for example, a mixture of tetrahydrofuran and toluene, which was used in carrying out the preparation of the Grignard compound and its subsequent reaction with the benzophenone. A dehydrating agent is added to the organic layer and the whole heated to effect dehydration of the intermediate alcohol.

The halohydrins of formula (I) are useful intermediates for fungicides. Those in which R and R^1 are both hydrogen are intermediates for the preparation of fungicidal compounds of formula (XIII):


(XIII)

wherein X, Y and Z have the previously defined meanings.

Compounds of formula (XIII) and methods for their preparation including that from a halohydrin of formula (I), are disclosed in European Patent Publication No. 0015756. Normally they will be obtained via the epoxide of formula (XIV):



(XIV)

which is readily formed from the halohydrin under the normally basic conditions of the triazole addition.

Particularly useful halohydrins of formula (I) for the synthesis of fungicidal compounds of formula (XIII) are those in which R and R^1 are hydrogen and at least one of X, Y and Z is chlorine or fluorine, and especially those in which R and R^1 are hydrogen and X, Y and Z are selected from the following substitution patterns:

X	*Y*	*Z*
F	F	H
F	H	F
F	H	Cl
Cl	H	Cl
Cl	F	H
F	Cl	Cl

The invention is illustrated by the following Example in which parts and percentages are by weight.

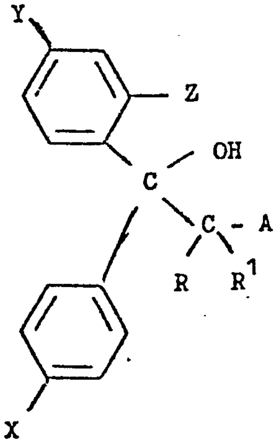
Example

A suspension of 1-(2-fluorophenyl)-1-(4-fluorophenyl)-ethene (64.8 parts) in t-butanol (60 parts) and water (40 parts) was stirred at 30°C. Bromine (28.3 parts) and 30% hydrogen peroxide solution (18 parts) were added alternately in aliquots (0.2 parts and 1.0 parts respectively) over 50 minutes. After stirring overnight, the reaction mixture showed no residual alkene. Water (100 parts) was added and the t-butanol removed under vacuum. This yielded 98.1 parts of crude product as a viscous oil, containing 69.7 parts of 1-(2-fluorophenyl)-1-(4-fluorophenyl)-2-bromoethanol [74.2% conversion based on 1-(2-fluorophenyl)-1-(4-fluorophenyl-ethene; analysis by H.P.L.C.].

By way of comparison, replacement of the tertiary butanol in the above example by acetone, methanol or propanol is found to give a less satisfactory process as considerable quantities of unwanted products are formed by reaction of halogen or reaction intermediates with the replacement solvent.

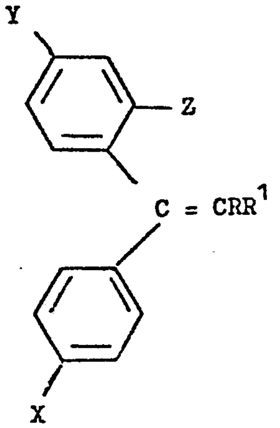
Claims

1. A process for the preparation of halohydrins of the formula (I):



(I)

wherein R and R^1 are hydrogen or alkyl and may be the same or different; X, Y and Z are each independently hydrogen, fluorine or chlorine and A is chlorine or bromine, which comprises reacting a substituted alkene of the formula (II):



(II)

wherein R, R^1, X, Y and Z have the meanings hereinbefore defined, with chlorine or bromine in aqueous tertiary butanol.

2. A process according to claim 1 in which the alkene is reacted with chlorine or bromine in the presence of hydrogen peroxide.

3. A process according to claim 1 or 2 in which the amount of chlorine or bromine used is from 1.05 to 1.5 mols per 2 mols of the alkene.

4. A process according to claim 2 in which the amount of hydrogen peroxide used is about 1 mol per 2 mols of the alkene.

5. A process according to any one of the preceding claims in which the proportion of tertiary butanol and water is from 4 to 0.25 parts by volume of tertiary butanol to 1 part by volume of water.

6. A process substantially as hereinbefore described with reference to the Example.

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