

## Candidate's Answer – A (Chemistry)

### Note to Examiner:

Document A discloses all the compounds disclosed by the client (both generically and specifically), apart from 5-benzyloxy-2-methyl-1,3-dioxane.

The predominantly *cis*-compounds prepared by the client are not novel compounds per se in view of document A, because:

- document A explicitly states that the compounds exist in *cis* and *trans* forms
- document A gives a method of making a mixture of *cis* and *trans* compounds, albeit predominantly *trans*.
- the *cis* and *trans* forms can be easily separated (page 2 of client's letter)
- novelty cannot be achieved by specifying a degree of diastereomeric purity (T 990/96; T 728/98), especially if the diastereomers are easily separable.

→ Product per se protection not available, due to lack of novelty, irrespective of any advantages these compounds have for a given use.

The *cis*-compounds and mixtures comprising predominantly *cis*-compounds were made available to the public in Dokument A, under the reasoning of T 990/96 and T 728/98. A person's motivation for wanting to prepare such compounds or mixtures is irrelevant to the question of novelty. Thus, T 728/98 concluded: "a document disclosing a low molecular weight chemical compound and its manufacture made this compound available to the public within the meaning of Art. 54 in all grades of purity desired by a person skilled in the art".

### NEW USE OF 1,3-DIOXANES

The present invention relates to the use of 1,3-dioxanes as herbicides or weed-killers. The present invention also relates to a method of making such 1,3-dioxanes, and herbicidal formulations which can be used in the agricultural industry. A new 1,3-dioxane compound is also provided. 1,3-dioxane and many of its derivatives are known. Document A describes a number of 1,3-dioxane derivatives which are useful as preservatives for aqueous compositions which normally spoil due to the action of bacteria and fungi. Document A describes a method of making these compounds which provides a mixture of *cis* and *trans* isomers, the *trans* isomer being present in more than 50%. These mixtures are used in tests against bacteria and fungi.

It is an object of the present invention to provide herbicides and/or weed killers. Accordingly, the present invention provides the new use of compounds of formula (2) as defined in claim 1.

*Preferred compounds of formula (2) are those where  $R^1$  is phenyl, furyl or an alkyl or haloalkyl radical having from 1 to 4 carbon atoms.*

$R^2$  is preferably phenyl, optionally substituted with a radical X in the 2-position (i.e. ortho).

$R^2$  is more preferably phenyl, 2-chlorophenyl, 2-fluorophenyl or 2-methylphenyl.

~~You will have noted that~~ The radicals  $R^1$  and  $-O-CH_2-R^2$  in formula (2) are different. As a consequence of this, the compounds of formula (2) exist in two stereoisomeric forms.

In one isomer, the radicals  $R^1$  and  $-O-CH_2-R^2$  are in cis relationship, i.e. both radicals are above, or both radicals are below, the 1,3-dioxane ring.

In the other isomer, the radicals  $R^1$  and  $-O-CH_2-R^2$  are in a trans relationship, i.e. one of the radicals is above and the other below the 1,3-dioxane ring.

In the following ~~I will refer to~~ description these stereoisomers will be referred to as the cis and trans isomers. These isomers can be easily separated and isolated since they have different physical properties, e.g. different melting and boiling points.

~~As you will recall, one of our major~~ A major fields of interest is chemicals for use in agriculture. The cis isomers of formula (2) proved to be quite effective as herbicides. Herbicides are weed killers, i.e. compounds that control undesired plant growth. Said cis isomers are effective as herbicides when applied before the emergence of the weeds (i.e. as pre-emergence herbicides) or after the emergence of the weeds (i.e. post-emergence herbicides). The trans isomers show no or only a negligible herbicidal effect. Generally mixtures of both cis and trans isomers are used in the present invention.

The compounds of formula (2) may be prepared by

(1) first reacting an aldehyde of formula (3)

$R^1-CHO$  (3)

with **glycerol** and then

(2) reacting the product of step (1) with a compound of the formula

$R^2-CH_2-Y$  (4)

where  $R^2$  has the same meaning as given above (see under formula (2)) and Y means a halogen atom.

The products of step (1) are known from GB-A-1 001 001.

As is evident, the aldehyde of formula (3) could also be reacted with a reaction product of glycerol with the compound of formula (4). However, such a process yields products of formula (2) where more than 50% is in the form of the trans isomer.

This invention provides a new class of herbicidal materials, having both pre-emergence and post-emergence activity. The materials are highly suitable for the control and elimination of grassy plants, particularly annual grasses, in the presence of broad-leaved crops, such as cotton, sugar beets, peanuts, soya beans, snap beans, lima beans or tomatoes.

For use as a herbicide it is most economical to use materials of high cis content made by a process which reduces, or avoids, the formation of the trans isomer. The higher the cis content the greater is the herbicidal effect of the given mixture of cis and trans isomers. In the most preferred forms of the invention, the cis compound is present in an amount at

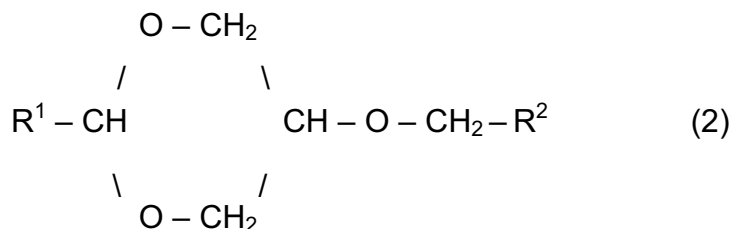
least equal to that of the corresponding *trans* compound, preferably the *cis:trans* ratio is more than 1.5:1, more preferably over 2:1 and still more preferably at least 3:1.

The products of formula (2) may be combined with other herbicides. ~~The research department informed me yesterday that combinations~~ Combinations of the *cis* isomers of formula (2) with the known herbicides bromoxynil show a synergetic effect against weeds whilst having a good crop tolerance. ~~I will send you a summary of these experiments as soon as possible.~~

For herbicidal applications, the active 1,3-dioxanes of formula (2) are formulated by admixture, with the adjuvants and carriers, normally employed for agricultural applications. Thus, these active herbicidal compounds may be formulated as granules, as powders, as emulsifiable concentrates, as solutions, or as any of several other known types of formulations, depending on the desired mode of application. Preferred formulations for both pre- and post-emergence herbicidal application are powders, emulsifiable concentrates, and granules. These formulations may contain as little as 0.5% to as much as 95% by weight of active ingredient.

The invention, in particular the preparation, properties and herbicidal activities of compounds of formula (2), is now illustrated further in the following Examples.

1. Use of a compound of formula (2)



where R<sup>1</sup> is alkyl, haloalkyl, alkoxyalkyl, aryl, heteroaryl or substituted aryl;

R<sup>2</sup> is a phenyl radical which is optionally substituted with up to three radicals X selected from halogen, -CN, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>4</sub> alkyl and C<sub>1</sub>-C<sub>4</sub> alkoxy, provided that the compound of formula (2) is not all *trans*-isomer; as a herbicide or weed killer.

2. Use according to claim 1 wherein the *cis*-isomer is present in an amount at least equal to that of the corresponding *trans*-isomer in the compound of formula (2).
3. Use according to claim 1 wherein the *cis:trans* ratio is at least 3:1 in the compound of formula (2).
4. Use according to claims 1 to 3 wherein R<sup>2</sup> is phenyl, optionally substituted with a radical X in the 2-position.
5. Use according to claim 4 wherein R<sub>2</sub> is phenyl, 2-chlorophenyl, 2-fluorophenyl or 2-methylphenyl.

6. Use according to claims 1 to 5 wherein R<sup>1</sup> is phenyl, furyl or an alkyl or haloalkyl radical having from 1 to 4 carbon atoms.
7. Use according to claims 1 to 6 wherein the compound of formula (2) is used as a pre-emergence or post-emergence herbicide.
8. Use according to claim 1 to 7 wherein the compound of formula (2) is used for control and/or elimination of grassy plants in the presence of broad-leaved crops.
9. A method of controlling and/or eliminating grassy plants in the presence of broad-leaved crops comprising spraying a compound of formula (2) onto soil for a pre-emergence herbicidal treatment or spraying onto plants for a post-emergence herbicidal treatment.
10. A method of preparing a compound of formula (2) comprising the steps of:

(1) first reacting on aldehyde of formula (3)



with glycerol and then

(2) reacting the product of step (1) with a compound of the formula (4)



where R<sup>1</sup> and R<sup>2</sup> are as defined in claim 1, and Y is a halogen atom.

11. A combination of a compound of formula (2) with a herbicide, for use as a herbicide or weed-killer.
12. A combination of the *cis*-isomer of formula (2) with bromoxynil and/or ioxynil, for use as a herbicide or weed-killer.
13. A herbicidal formulation comprising a compound of formula (2) as defined in claims 1 to 6, or the combination of claims 11 or 12, and adjuvants and carriers normally employed for agricultural applications.
14. The herbicidal formulation according to claim 13 suitable for pre- and post-emergence herbicidal application, wherein the herbicidal compound is a powder, emulsifiable concentrate or granules.
15. The herbicidal formulation according to claim 14 wherein the weight of active ingredient in the formulation is from 0.5% to 95%.
16. A compound which is 5-benzyloxy-2-methyl-1,3-dioxane.
17. The compound of claim 16 wherein the *cis*-isomer is present in an amount at least equal to the *trans*-isomer.
18. The compound of claim 16 wherein the *cis:trans* ratio is at least 3:1.