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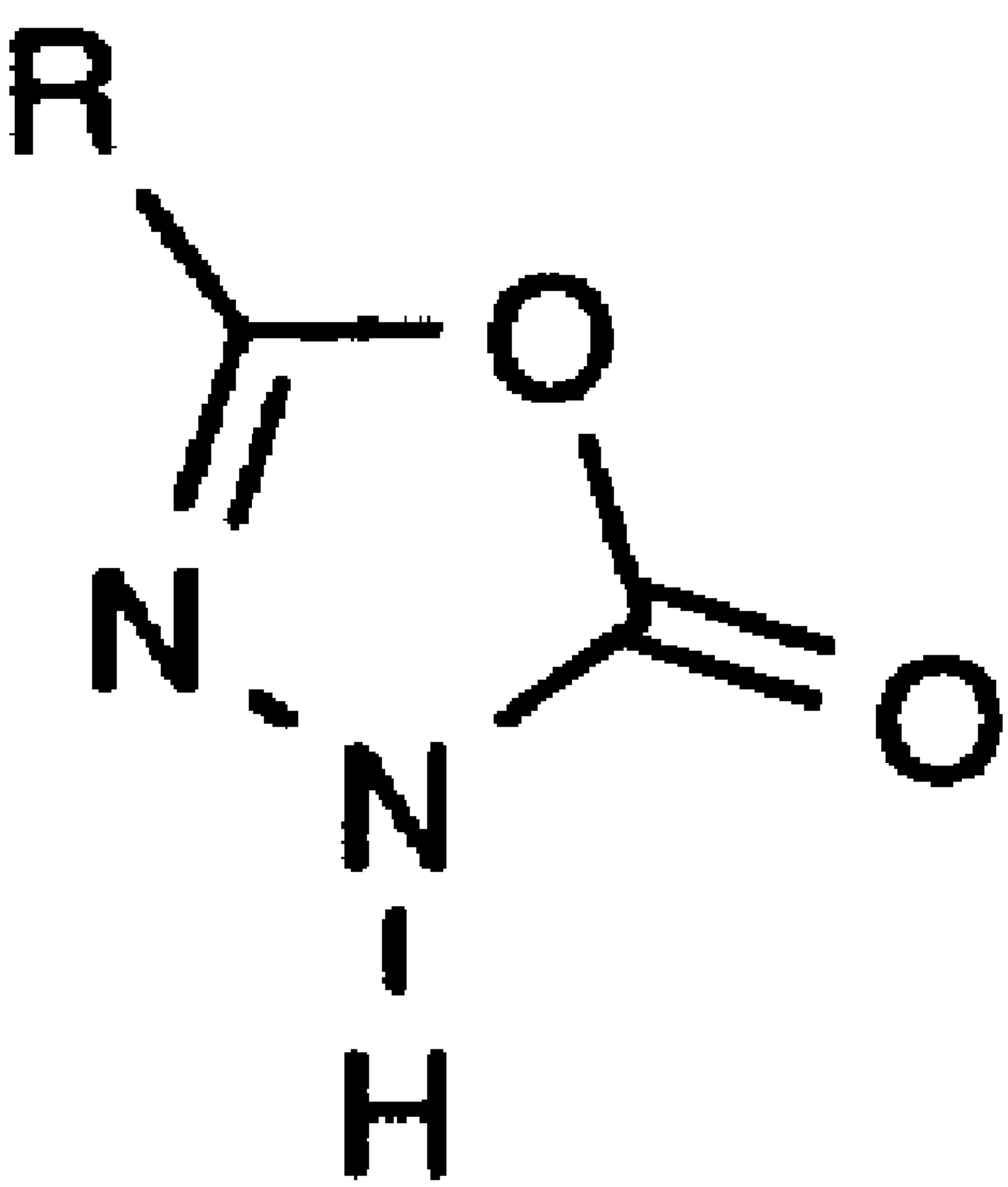
(54) Titre : PROCESSUS DE PREPARATION D'OXADIAZOLONES SUBSTITUES
(54) Title: PROCESS FOR PREPARING SUBSTITUTED OXADIAZOLONES



(I)

(57) Abrégé/Abstract:
Substituted oxadiazolones of the formula (I), (see formula I) in which R represents optionally substituted alkyl [which are known as intermediates for the preparation of certain herbicides] are obtained in good yields and high purity when in a first step carboxylic acids of the general formula (II) R-COON (II) are reacted with hydrazine hydrate in the presence of a catalyst and, if appropriate, in the presence of an inert diluent at temperatures between 0°C and 150°C with elimination of water, and the resulting carboxylic hydrazides of the general formula R-CO-NH-NH_2 (III) are reacted in a second step in the same reaction medium - i.e. without isolation of the intermediate - with phosgene ($COCl_2$) at temperatures between 20°C and 120°C.

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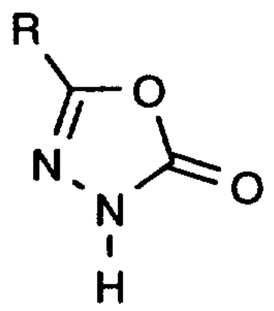
Process for preparing substituted oxadiazolones

Abstract

Substituted oxadiazolones of the formula (I),



(I)

in which

R represents optionally substituted alkyl

[which are known as intermediates for the preparation of certain herbicides] are obtained in good yields and high purity when

in a first step carboxylic acids of the general formula (II)

R-COOH (II)

are reacted with hydrazine hydrate in the presence of a catalyst and, if appropriate, in the presence of an inert diluent at temperatures between 0°C and 150°C with elimination of water, and the resulting carboxylic hydrazides of the general formula (III)

$R\text{-}CO\text{-}NH\text{-}NH_2$ (III)

are reacted in a second step in the same reaction medium - i.e. without isolation of the intermediate - with phosgene ($COCl_2$) at temperatures between 20°C and 120°C.

Process for preparing substituted oxadiazolones

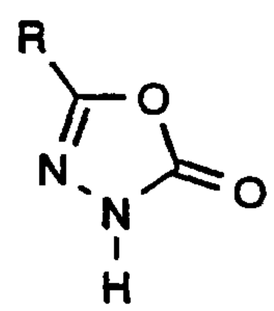
The invention relates to a novel process for preparing substituted oxadiazolones which are known as intermediates for the preparation of herbicidally active compounds.

It is known that certain substituted oxadiazolones, such as, for example, 5-methyl-1,3,4-oxadiazol-2(3H)-one, are obtained when acylated hydrazines, such as, for example, acethydrazide, are reacted with phosgene (cf. Bull. Chem. Soc. Japan 44 (1971), 870; Chem. Ber. 98 (1965), 540-545; Helv. Chim. Acta 55 (1972), 1174-1178; J. Org. Chem. 26 (1961), 1843-1846; EP 301946; EP 321833).

The acylated hydrazines required as starting materials are generally prepared in a prior reaction step from the corresponding carboxylic acids and hydrazine(hydrate) in the presence of catalysts (cf. J. Org. Chem. 30 (1965), 2486-2488; GB 1396615; EP 653419).

However, the reactions of carboxylic acids with hydrazine(hydrate) are carried out in mixtures of different solvents. This is unfavourable for industrial purposes, since these solvents cannot be readily recycled or recovered in pure form. According to the prior art, the acylated hydrazines have to be isolated and dried by a complicated procedure prior to the subsequent phosgenation. The present invention provides a preparation process for substituted oxadiazolones which is better suited to industrial purposes.

It has now been found that substituted oxadiazolones of the general formula (I)



(I)

in which

R represents optionally substituted alkyl

are obtained in good yields and in high purity when

in a first step carboxylic acids of the general formula (II)

$$R\text{-}COOH \qquad (II)$$

in which

R is as defined above

are reacted with hydrazine hydrate in the presence of a catalyst and, if appropriate, in the presence of an inert diluent at temperatures between 0°C and 150°C with elimination of water, and the resulting carboxylic hydrazides of the general formula (III)

$$R\text{-}CO\text{-}NH\text{-}NH_2 \qquad (III)$$

in which

R is as defined above

are reacted in a second step in the same reaction medium - i.e. without isolation of the intermediate - with phosgene ($COCl_2$) at temperatures between 20°C and 120°C.

It is very surprising that the reaction of carboxylic acids with hydrazine hydrate can be carried out without any problems in inert solvents without using alcohols - or entirely without additional solvents - instead of the customary alcohol-benzene or

alcohol-toluene mixtures, and that the following reaction with phosgene proceeds with good results even without the isolation of the intermediate acylated hydrazines and without changing the solvent.

The process according to the invention therefore represents a useful advance in the art.

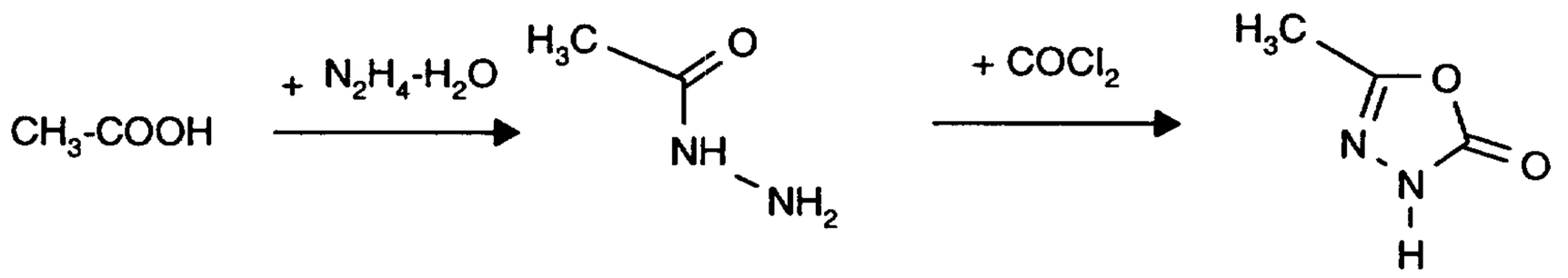
The process according to the invention preferably relates to the preparation of compounds of the formula (I) in which

R represents optionally halogen- or C_1-C_4-alkoxy-substituted straight-chain or branched alkyl having 1 to 6 carbon atoms.

The process according to the invention in particular relates to the preparation of compounds of the formula (I) in which

R represents respectively optionally fluorine-, chlorine-, methoxy- or ethoxy-substituted methyl, ethyl, n- or i-propyl, n-, i-, s- or t-butyl.

If, for example, acetic acid and hydrazine hydrate are employed as starting materials, the process according to the invention can be represented by the following scheme:



The carboxylic acids to be used as starting materials in the process according to the invention are defined in a general way by the formula (II). In the formula (II), R has preferably or in particular those meanings already listed above in connection with the

description of the compounds of the formula (I) as being preferred or particularly preferred for R.

The starting materials of formula (II) are known organic chemicals.

The process according to the invention is carried out in the presence of a catalyst. Suitable catalysts are in particular substances accelerating condensation reactions - i.e. reactions proceeding with the elimination of water - of carboxylic acids with alcohols, amines, hydrazines, etc. These are in particular (optionally activated) aluminium oxide, titanium dioxide, zirconium oxide, aluminium alkoxides, titanium alkoxides or zirconium alkoxides, or aluminium halide alkoxides, titanium halide alkoxides or zirconium halide akoxides, such as, for example, aluminium tri-i-propoxide, titanium tetramethoxide, titanium tetraethoxide, titanium tetra-n-propoxide, titanium tetra-i-propoxide, titanium tetra-n-butoxide, titanium tetra-i-butoxide or titanium tetra-s-butoxide.

Particularly preferred catalysts are aluminium oxide, titanium dioxide, titanium tetra-n-propoxide and titanium tetra-i-propoxide. Surprisingly, the metal oxides mentioned are active even when they are present as hydrates, i.e. contain water. Therefore, it is optionally possible to recover and recycle the catalyst.

The process according to the invention is optionally carried out using an inert diluent. Suitable inert diluents in this context are essentially those organic solvents not containing easily cleavable hydrogen atoms. These are preferably aliphatic, alicyclic or aromatic, optionally halogenated hydrocarbons, such as, for example, benzine, ligroine, benzene, toluene, xylene, chlorobenzene, dichlorobenzene, hexane, heptane, octane, cyclohexane, methylcyclohexane; ethers, such as, for example, methyl tert-butyl ether, diisopropyl ether, diisobutyl ether, dioxane, tetrahydrofuran or ethylene glycol dimethyl ether or ethylene glycol diethyl ether; and nitriles, such as acetonitrile, pripionitrile or butyronitrile.

Aromatic hydrocarbons, such as, for example, toluene, xylene or chlorobenzene, are particularly preferred as diluents in the process according to the invention.

When carrying out the process according to the invention, the reaction temperatures may be varied over a relatively wide range. Generally, as mentioned above, the first step is carried out at temperatures between 0°C and 150°C, preferably between 80°C and 130°C, and the second step is carried out between 20°C and 120°C, preferably between 40°C and 90°C.

The process according to the invention is generally carried out at atmospheric pressure. However, it is also possible to carry out the process according to the invention at elevated or reduced pressure - in general between 0.1 bar and 10 bar.

To carry out the process according to the invention, in the first step generally 0.9 to 2.0 mol, preferably 1.0 to 1.2 mol, of hydrazine hydrate and 1 to 50 mmol, preferably 2 to 30 mmol, of catalyst and, in the second step, 1 to 5 mol, preferably 1.1 to 2.5 mol of phosgene are employed per mole of carboxylic acid of the formula (II).

In a preferred embodiment of the process according to the invention, the carboxylic acid of the formula (II) - if appropriate together with a diluent - is initially charged, and the hydrazine hydrate and the catalyst are metered in in any order. The reaction mixture is then heated until the reaction (first step) has ended, and the water liberated is removed using a water separator. To carry out the second step, the mixture is optionally diluted with a suitable organic solvent and phosgene is passed through until the reaction has ended. The solvent is subsequently distilled off carefully under reduced pressure and the crude product obtained as residue is optionally purified by vacuum distillation (cf. the Preparation Examples)

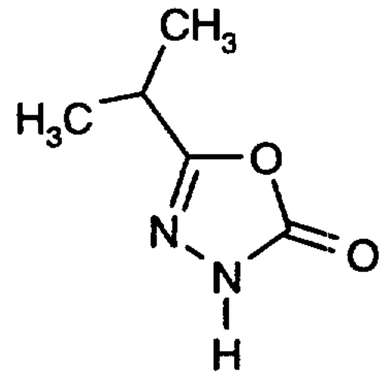
After the first step of the process according to the invention has been carried out, the carboxylic hydrazides of formula (III) can also - if desired - be isolated without

problems after hot filtration by cooling and filtration or filtration with suction, in order to remove the catalyst.

The substituted oxadiazolones of the formula (I) to be prepared by the process according to the invention are already known as starting materials for herbicidally active compounds (cf. EP 321833).

Preparation Examples:

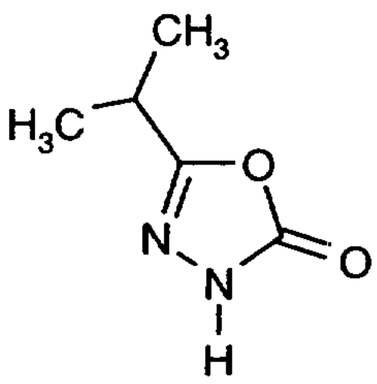
Example 1



At room temperature (about 20°C), 30 g (0.6 mol) of hydrazine hydrate are added dropwise with stirring to a solution of 44.1 g (0.5 mol) of isobutyric acid in 90 ml of toluene. At about 45°C, 1.42 g (5 mmol) of titanium tetra-i-propoxide are then added, and the reaction mixture is subsequently heated at the boil on a water separator for about 2 hours. About 23 ml of water are separated off. The titanium dioxide that has formed is separated off by filtration at boiling point (and can be recycled as catalyst). The filtrate, which is still hot, is diluted with 400 ml of toluene. At about 70°C to 80°C, 55.5 g of phosgene are then introduced over a period of about two hours. The mixture is allowed to cool slightly, and the solvent is then carefully distilled off under reduced pressure.

62.4 g (97.5% of theory) of 5-i-propyl-1,3,4-oxadiazol-2(3H)-one are obtained as a liquid with a pink tinge.

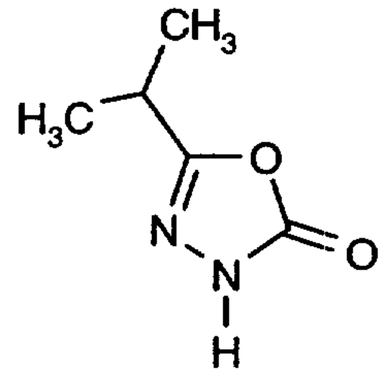
Example 2



At room temperature (about 20°C), 25 g (0.5 mol) of hydrazine hydrate are added dropwise with stirring to a mixture of 44 g (0.5 mol) of isobutyric acid and 1.4 g (5 mmol) of titanium tetra-i-propoxide. The mixture is heated at 100°C for three hours, the catalyst (re-usable) is separated off by hot filtration and the filtrate is subsequently diluted with 500 ml of toluene. At about 70°C to 80°C, 55.5 g of phosgene are then introduced over a period of about two hours. The mixture is allowed to cool slightly, the solvent is carefully distilled off under reduced pressure and the product is purified by vacuum distillation.

56.3 g (88% of theory) of 5-i-propyl-1,3,4-oxadiazol-2(3H)-one of boiling point 108°C to 110°C at 3 - 4 mbar are obtained.

Example 3



At room temperature (about 20°C), 30 g (0.6 mol) of hydrazine hydrate are added dropwise with stirring to a solution of 44.1 g (0.5 mol) of isobutyric acid in 90 ml of toluene. At about 45°C, 10 g of aluminium oxide (acidic) are then added, and the reaction mixture is subsequently heated at the boil on a water separator for about two hours. About 23 ml of water are separated off. The mixture, which is still hot, is filtered in order to remove the catalyst (re-usable), and the filtrate is diluted with 400 ml of toluene. At about 70°C to 80°C, 55.5 g of phosgene are then introduced over a period of about two hours. The mixture is allowed to cool slightly and then filtered, and the solvent is carefully distilled off from the filtrate under reduced pressure.

61.2 g (95.6% of theory) of 5-i-propyl-1,3,4-oxadiazol-2(3H)-one are obtained as a liquid with a pink tinge.

Preparation and isolation of the carboxylic hydrazides of the formula (III):

Example (III-1)

$(CH_3)_2CH\text{-}CO\text{-}NH\text{-}NH_2$

225 g (4.4 mol) of hydrazine hydrate are added to a mixture of 356 g (4.0 mol) of isobutyric acid and 1 litre of toluene. After the addition of 35.5 g (0.12 mol) of titanium tetra-i-propoxide, the mixture is heated at the boil on a water separator, via a distillation column. 164 g of an "aqueous phase" (comprising water, isopropanol and hydrazine) are separated off within a period of about 5 hours. The catalyst (re-usable) is then separated off from the hot mixture by filtration. Similarly to Examples 1 to 3, the filtrate can be reacted further in a second step. To determine the yield, the solvent is carefully distilled off under reduced pressure.

397 g of isobutyric hydrazide (content: 98.8%, yield 96% of theory) are obtained as a solid, colourless residue.

Example (III-2)

$(CH_3)_2CH\text{-}CO\text{-}NH\text{-}NH_2$

225 g (4.4 mol) of hydrazine hydrate are added to a mixture of 356 g (4.0 mol) of isobutyric acid and 1 litre of toluene. After the addition of 21.1 g (0.12 mol) of titanium catalyst (prepared separately earlier on by reaction of titanium tetra-n-propoxide with water), the mixture is heated at the boil on a water separator, via a distillation column. After about one hour, the catalyst (re-usable) is separated off by

filtration at boiling point (20.4 g, 97% recovery) and washed with hot toluene. Similarly to Examples 1 to 3, the filtrate can be reacted further in a second step. To determine the yield, the filtrate is cooled to about 10°C and the crystalline product is isolated by filtration with suction.

408 g of isobutyric hydrazide (content: 98.4%, yield: 98% of theory) are obtained.

Example (III-3)

$$(CH_3)_2CH\text{-}CO\text{-}NH\text{-}NH_2$$

214.5 g (4.2 mol) of hydrazine hydrate are added to a mixture of 356 g (4.0 mol) of isobutyric acid and 1 litre of toluene. After the addition of 12.8 g (0.16 mol) of titanium dioxide, the mixture is heated at the boil on a water separator, via a distillation column. After about 90 minutes (separation of 116 g of "aqueous phase"), the catalyst (re-usable) is separated off from the hot solution by filtration (12.4 g, 97% recovery) and washed with hot toluene. Similarly to Examples 1 to 3, the filtrate can be reacted further in a second step. To determine the yield, the solvent is carefully distilled off under reduced pressure.

410 g of isobutyric hydrazide (content: 97.9%, yield: 98% of theory) are obtained.

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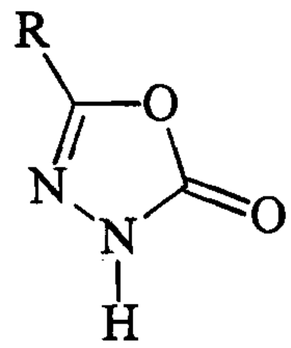
CLAIMS:

1. A process for preparing a substituted oxadiazolone of the general formula (I):



(I)

wherein:

R represents optionally substituted alkyl, which process comprises, reacting:

in a first step, in the absence of an alcohol a carboxylic acid of the general formula (II):

$$R\text{-}COOH \qquad (II)$$

wherein R is as defined above, with hydrazine hydrate in the presence of a catalyst at a temperature between 0°C and 150°C with elimination of water, and reacting a carboxylic hydrazide of the general formula (III) so formed:

$$R\text{-}CO\text{-}NH\text{-}NH_2 \qquad (III)$$

wherein R is as defined above, in a second step in the same reaction medium, without isolation of the intermediate, with phosgene ($COCl_2$) at a temperature between 20°C and 120°C.

2. A process according to Claim 1, wherein

R represents optionally halogen- or C_1-C_4-alkoxy-substituted straight-chain or branched alkyl having 1 to 6 carbon atoms.

3. A process according to Claim 1, wherein

R represents respectively optionally fluorine-, chlorine-, methoxy- or ethoxy-substituted methyl, ethyl, n- or i-propyl, n-, i-, s- or t-butyl.

4. A process according to Claim 1, 2 or 3, wherein the first process step is carried out at a temperature between 80°C and 130°C.

5. A process according to any one of Claims 1 to 4, wherein the second process step is carried out at a temperature between 40°C and 90°C.

6. A process according to any one of Claims 1 to 5, wherein the catalyst used in the first process step is aluminium oxide, titanium dioxide, zirconium oxide, an aluminium, titanium or zirconium alkoxide or an aluminium, titanium or zirconium halide alkoxide.

7. A process according to Claim 6, wherein the catalyst used is aluminium tri-i-propoxide, titanium tetramethoxide, titanium tetraethoxide, titanium tetra-n-propoxide, titanium tetra-i-propoxide, titanium tetra-n-butoxide, titanium tetra-

i-butoxide or titanium tetra-s-butoxide.

8. A process according to Claim 6, wherein the catalyst used is aluminium oxide, titanium dioxide, titanium tetra-n-propoxide or titanium tetra-i-propoxide.

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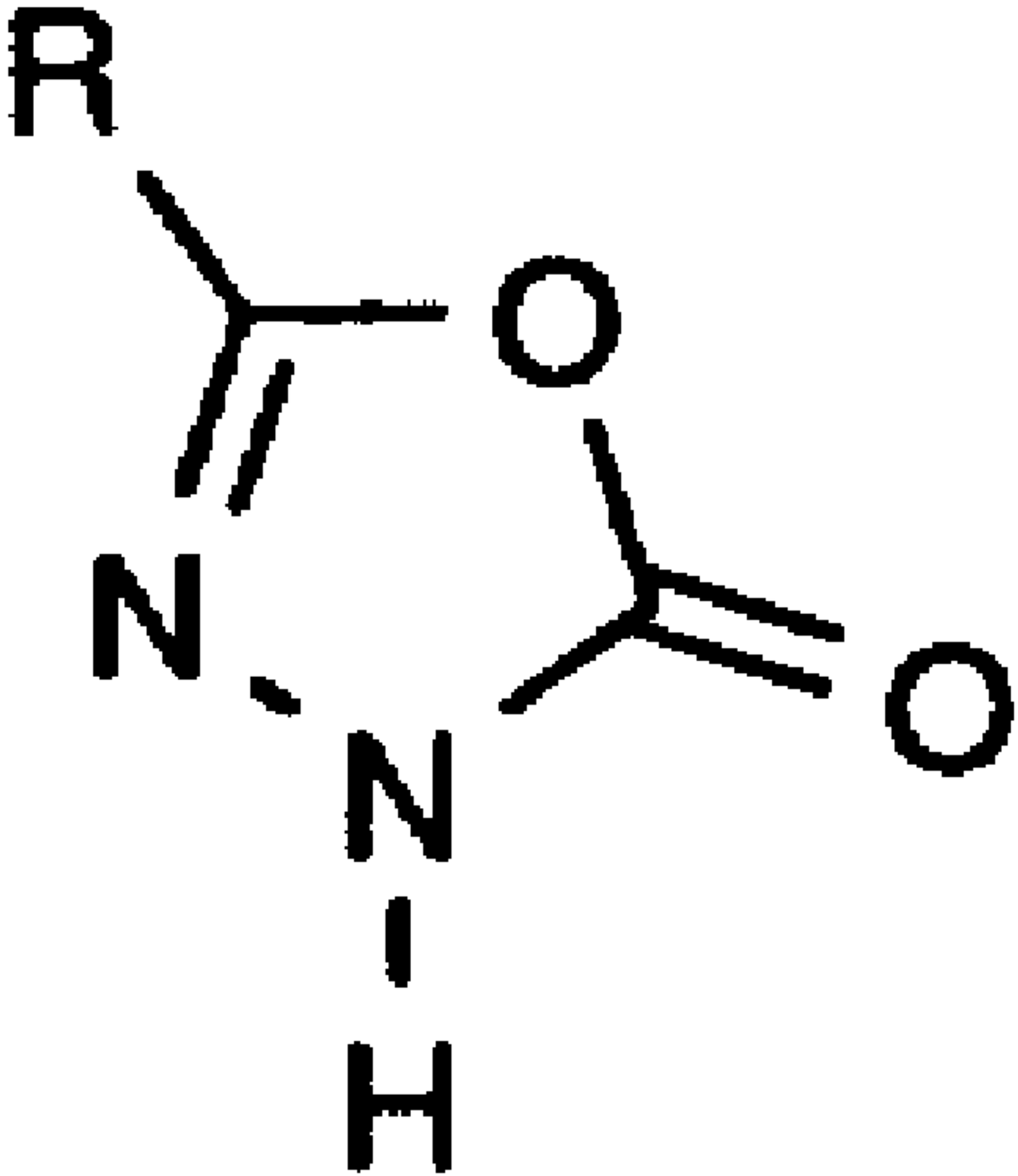

(I)