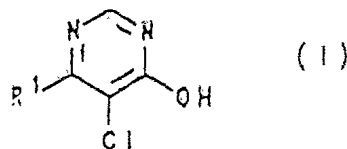




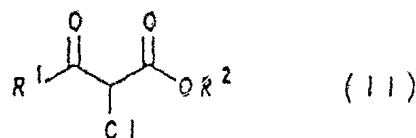
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- (54) Title
METHOD OF PREPARING 5-CHLORO-4-HYDROXYPYRIMIDINES, 2-CHLORENAMINES AS INTERMEDIATES IN THE METHOD, AND USE OF THE COMPOUNDS THUS PREPARED
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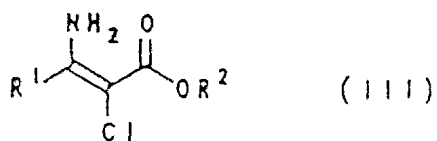
1. A process for preparing a compound of the formula I



in which R¹ is alkyl, cycloalkyl, aryl or benzyl, all of which are optionally substituted, which includes reacting a compound of the formula II

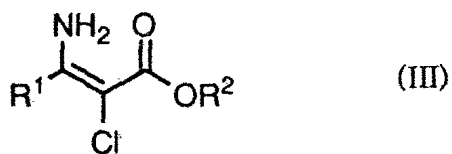


in which R¹ is as defined above, and R² is alkyl, benzyl or another carboxyl protective group, with ammonia or an ammonium salt to give a compound of the formula III



which is subsequently condensed in a polar protic solvent in the presence of a base with formamide to give a compound of the formula I.

9. A compound of the formula III



in which R¹ and R² are as defined in one of the preceding claims, excepting 3-amino-2-chloro-but-2-enoic acid (C₁-C₄)-alkylester.



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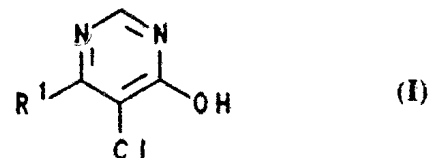
*Mit internationalem Recherchenbericht.
Vor Ablauf der für Änderungen der Ansprüche zugelassenen
Frist. Veröffentlichung wird wiederholt falls Änderungen
eintreffen.*

(54) **Title:** METHOD OF PREPARING 5-CHLORO-4-HYDROXYPYRIMIDINES, 2-CHLORENAMINES AS INTERMEDIATES IN THE METHOD, AND USE OF THE COMPOUNDS THUS PREPARED

(54) **Bezeichnung:** VERFAHREN ZUR HERSTELLUNG VON 5-CHLOR-4-HYDROXYPYRIMIDINEN, 2-CHLORENAMINE ALS ZWISCHENPRODUKTE DIESES VERFAHRENS UND DEREN VERWENDUNG

(57) **Abstract**

The invention concerns a method of preparing compounds of formula (I), in which R¹ is optionally substituted alkyl, cycloalkyl, aryl or benzyl, by converting a chloroacetic ester with ammonia or an ammonium salt into the corresponding chlorenamine and condensing the chlorenamine with formamide in the presence of a base. The invention also concerns 2-chlorenamines as intermediates in the method.



(57) **Zusammenfassung**

Die Erfindung betrifft ein Verfahren zur Herstellung von Verbindungen der Formel (I), in welcher R¹ ggf. substituiertes Alkyl, Cycloalkyl, Aryl oder Benzyl bedeutet, bei welchem man einen Chloracetessigester mit Ammoniak oder einem Ammoniumsalz in das entsprechende Chlorenamin überführt und letzteres in Gegenwart einer Base mit Formamid kondensiert. Die Erfindung betrifft weiterhin 2-Chlorenamine als Zwischenprodukte des Verfahrens.

Description

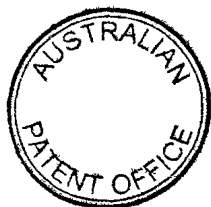
A process for preparing 5-chloro-4-hydroxypyrimidines, 2-chloro enamines as intermediates in this process and their use

- 5 5-Chloro-4-hydroxypyrimidines are important intermediates for preparing crop protection agents and pharmaceuticals as proposed, for example, in PCT/EP 93/00536.

5-Chloro-4-hydroxypyrimidines are also called 5-chloro-4-pyrimidones or 5-chloro-4-pyrimidinols. They are
10 generally prepared by chlorination of 4-hydroxypyrimidines in position 5. Chlorinating agents used for this purpose are, for example, N-chlorosuccinimide, sodium hypochlorite, thionyl chloride [D. J. Brown, The Chemistry of Heterocyclic Compounds, The Pyrimidines (1962);
15 ibid.; The Pyrimidines Supplement I (1970); ibid., The Pyrimidines Supplement II (1985); all published by John Wiley & Sons Inc., New York] or chlorine gas [JP 8222070]. In these cases the yields are frequently poor, which is unfavorable for an industrial process. It
20 is also a disadvantage that the 4-hydroxypyrimidines required as starting materials can be obtained only with difficulty.

The previously disclosed processes leading to 4-hydroxypyrimidines are to be dealt with in detail hereinafter.

- 25 In the first case, a β -keto acid ester is condensed with thiourea to give the corresponding 2-thiouracil, and subsequently sulfur is removed with Raney nickel [H. M. Foster, H. R. Snyder, Org. Synth., Coll. Vol. IV, 638]. However, this sulfur removal is impractical for an
30 industrial process.



Another process described for preparing 4-hydroxypyrimidines is the condensation reaction of a β -keto acid ester with formamidine acetate [M. Butters, J. Heterocycl. Chem., 29, 1369 (1992)]. However, the yield of this reaction is very low, and the amount of salt produced is relatively high; in addition, formamidine acetate is a relatively costly condensing agent so that this process does not represent an industrial alternative.

10 Another possible preparation of 4-hydroxypyrimidines is the reaction of an enamine prepared from a β -keto ester with formamide [EP-A-0326389]. This synthesis is suitable per se for an industrial process but has the disadvantage that 4-hydroxypyrimidines unsubstituted in position 5, in particular those with short-chain alkyl radicals in the 6 positions are considerably more difficult to work up, because of their high solubility in water, than the corresponding representatives substituted with chlorine in position 5. Because of these losses on workup, and owing to the previously mentioned losses in the subsequent 5-chlorination, this is a disadvantageous route for the purposes of an industrial synthesis.

By contrast, it is significantly more favorable to carry out a condensation reaction in which there is direct formation of a 5-chloro-4-hydroxypyrimidine.

A process of this type, in which 2-chloro- β -keto acid esters are reacted with formamidine salts to give 5-chloro-4-hydroxypyrimidines directly has already been described [EP-A-0370391]. However, this process has the disadvantage that it depends on the use of a relatively costly condensing agent in formamidine acetate. In addition, the waste situation is not without problems; the unfavorable stoichiometry unavoidably leads to polymerization of the part of the formamidine acetate which is used in excess, and it cannot therefore be recovered. Furthermore, a large base excess is necessary

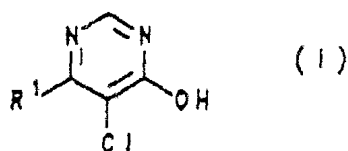


to liberate formamidine from its salt, which is associated with a heavy salt load.

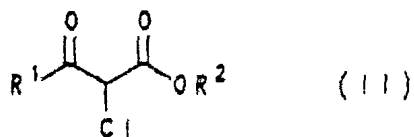
The object of the invention was therefore to find a process for preparing 5-chloro-4-hydroxypyrimidines which can be carried out on an industrial scale using a low-cost condensing agent and displays a favorable environmental balance (= small amount of salt produced).

The object according to the invention is surprisingly achieved by converting a 2-chloro- β -keto ester with ammonia or an ammonium salt into the corresponding enamine, which is subsequently condensed with formamide to give 5-chloro-4-hydroxypyrimidine. Of the enamines used as intermediates for this, ethyl 3-amino-2-chloro-crotonate has already been disclosed in Ann. Chim. (Paris) 24 [1891] p. 64.

The invention therefore relates to a process for preparing 5-chloro-4-hydroxypyrimidines of the formula I

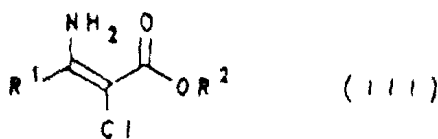


which comprises reacting a 2-chloro- β -keto ester of the formula II



with ammonia or the ammonium salt of, preferably, an organic acid to give a 2-chloro enamine of the formula III

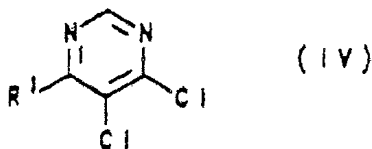




(the reaction can be carried out in polar protic or aprotic solvents or without solvents) and which is subsequently condensed in a polar protic solvent in the presence of a base with formamide to give the compound of the formula I.

The process according to the invention is preferably carried out without isolation of the 2-chloro enamine of the formula III (as "one-pot reaction").

There is then, for example, the possibility of reacting the resulting product of the formula I with POCl₃ in a manner known per se to give a 4,5-dichloropyrimidine of the formula IV



In the formulae I-IV,

R¹ is optionally substituted alkyl, cycloalkyl, aryl or benzyl,

R² is alkyl, benzyl or another carboxyl protective group.

R¹ is preferably (C₁-C₄)-alkyl, (C₁-C₄)-haloalkyl, (C₁-C₄)-alkoxy-(C₁-C₄)-alkyl or (C₁-C₄)-alkylthio-(C₁-C₄)-alkyl, in particular (C₁-C₄)-alkyl, such as methyl or ethyl, or methoxymethyl; ethyl is very particularly preferred.

R² is preferably (C₁-C₄)-alkyl, benzyl or another



carboxyl protective group, in particular (C₁-C₄) alkyl, such as methyl, ethyl or tert butyl, benzyl or modified benzyl; methyl is very particularly preferred.

5 Unless otherwise defined in the specific case, alkyl is straight-chain or branched and is preferably (C₁-C₆)-alkyl, such as methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, pentyl or hexyl. A corresponding
10 statement applies to radicals derived therefrom, such as alkoxy, alkylthio and haloalkyl.

Cycloalkyl preferably has 3 to 8 carbon atoms and represents radicals such as cyclobutyl, cyclopentyl and cyclohexyl.

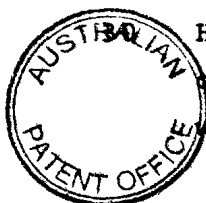
15 Aryl preferably has 6 to 12 carbon atoms and is, for example, phenyl, naphthyl or biphenyl; phenyl is preferred.

Substituted alkyl, cycloalkyl, aryl or benzyl is preferably substituted by 1 to 3 identical or different radicals which are inert under the conditions of the process
20 according to the invention and are selected from halogen, (C₁-C₄)-alkoxy, (C₁-C₄)-alkylthio and, in the case of the cyclic radicals, (C₁-C₄)-alkyl.

Halogen means fluorine, chlorine, bromine or iodine, preferably fluorine or chlorine.

25 Haloalkyl is an alkyl radical which is as defined above and in which one, a plurality of or all the hydrogen atoms are replaced by identical or different halogen atoms.

Carboxyl protective groups are described, for example, in Hubbuch, Kontakte Merck 3/79, pages 14 and 19 ff. Frequently used are methyl, ethyl, benzyl and tert-butyl, as well as modified benzyl radicals such as p-chlorobenzyl,



p-nitrobenzyl and p methoxybenzyl.

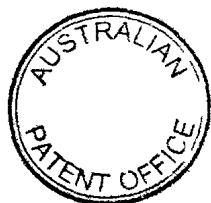
The invention also relates to 2-chloro enamines of the formula II in which R¹ and R² are as defined above, excepting ethyl 3-amino-2-chlorocrotonate.

5 The 2-chloro- β -keto esters depicted in formula II can be prepared in a known manner by chlorination of the corresponding β -keto esters with sulfuryl chloride either using an aprotic solvent or without solvents [W. R. Böhme, Org. Synth. Coll. Vol. IV, 590 (1963)] and with
10 chlorine gas as chlorinating agent.

The 2-chloro enamine of the formula III can be prepared by using the crude product from stage 1 after removal of the solvent and the gases. The reaction can be carried out with NH₃ gas without solvent, in polar protic solvents
15 such as alcohols or formamide or in polar aprotic solvents, for example dioxane, dimethylformamide or acetonitrile. It is also possible to use ammonium salts as ammonia donors in place of NH₃. Alcohols used are lower alcohols such as methanol, ethanol, isopropanol or
20 butanol. When ammonium salts are used, addition of polyethylene glycol effects an increase in the yield.

The reaction can be carried out in a temperature range from -40 to 80°C, preferably from 20 to 78°C. Ammonium salts which are preferably used are ammonium salts of the
25 carboxylic acids such as formic acid, acetic acid, oxalic acid or of carbonic acid. Working up is preferably carried out under anhydrous conditions by removing the solvent in vacuo and then dissolving the substance in an aprotic solvent such as diisopropyl ether or methyl
30 isobutyl ketone, and removing excess ammonium salt by filtration. The recovered ammonium salt can be reused.

Polar protic solvents such as water, methanol, ethanol, i-propanol or butanol are preferably used for the condensation reaction. It is preferable to use the alcohol



which corresponds to the relevant ester, i.e. methanol or ethanol. In an azeotropic procedure it is advantageous to add the required amount of an entrainer, for example toluene.

5 Alkali metal alcoholates, hydroxides, carbons or bicarbonates are used as bases. The preferred procedure uses an alkali metal alcoholate in the corresponding alcohol. In this case it is possible where appropriate to add a desiccant, for example magnesium sulfate or 30 nm
10 molecular sieves, to bind the water being liberated in the reaction. The reaction temperature is between 20 and 80°C. It is preferable to use an excess of 1.5-3.5 mol of the theoretically required formamide. Part of the excess formamide is not used during the reaction and can be
15 reused after distillation. 1-2.2 mol of base are needed for 1 mol of 2-chloro enamine of the formula III used. After the reaction is complete, the prepared 5-chloro-4-hydroxypyrimidine of the formula I can, after dissolving in water, be extracted by extraction with a
20 polar solvent at a pH of 3-7. With some derivatives, the 5-chloropyrimidine crystallizes out of water at the stated pH so that it can subsequently be filtered off with suction.

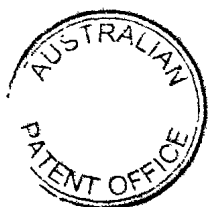
However, it is also possible that crude product to react,
25 after acidification to pH 3-7 and removal of the solvent in vacuo, without further purification with POCl₃, to give the corresponding 4,5-dichloropyrimidine.

The following examples illustrate the invention without intending to restrict it to them.

30 Example 1

Methyl 3-amino-2-chloro-2-pentenoate

Dry NH₃ gas is passed through 48.9 g (0.30 mol) of methyl 2-chloro-3-oxovalerate at 70°C for a period of 2 h. After



removal of volatile constituents in vacuo, the crude product is dissolved in diisopropyl ether and washed with a little ice water. After drying over $MgSO_4$, the solvent is removed in vacuo.

5 Yield: 80.0% [GC]

Example 2

Methyl 3-amino-2-chloro-2-pentenoate

A solution of 576.1 g (3.5 mol) of methyl 2-chloro-3-oxovalerate and 674.5 g (8.75 mol) of ammonium acetate
10 in 1.2 l of methanol is heated at 65°C with stirring for a period of 4 h. After cooling, the solvent is removed in vacuo, the residue is taken up in 2.5 l of diisopropyl ether, and the solid is removed. The solid is dissolved in a little water and subsequently extracted with ethyl
15 acetate. The organic fractions are combined, dried over $MgSO_4$, and evaporated in vacuo.

Yield: 94.7% [GC]

Example 3

Methyl 3-amino-2-chloro-2-pentenoate

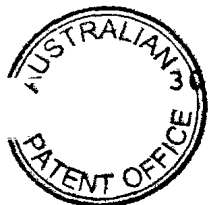
20 A solution of 47.5 g (0.75 mol) of ammonium formate and 49.0 g (0.3 mol) of methyl 2-chloro-3-oxovalerate in 800 ml of ethanol are reacted and worked up in analogy to Example 2.

Yield: 72.0% [GC]

25 Example 4

Methyl 3-amino-2-chloro-2-pentenoate

Dry NH_3 gas is passed through a solution of 376.3 g (2.064 mol) of methyl 2-chloro-3-oxovalerate in 100 ml of methanol while stirring at 65°C for 3 h. The solvent is removed in vacuo, the residue is taken up in diisopropyl



ether, the solution is filtered through sea sand, and the solvent is evaporated.

Yield: 87.6% [GC]

Example 5

5 Methyl 3-amino-2-chloro-2-butenolate

50 g (0.33 mol) of methyl 2-chloroacetoacetate are reacted with 64 g (0.83 mol) of ammonium acetate in 100 ml of methanol and worked up in analogy to Example 2. Yield: 63.9% [GC]

10 Example 6

Ethyl 3-amino-2-chloro-2-hexenoate

61.5 g (0.32 mol) of ethyl 2-chloro-3 oxohexanoate are reacted with 61.5 g (0.80 mol) of ammonium acetate in 120 ml of methanol and worked up in analogy to Example 2. Yield: 95.5% [GC]

Example 7

Ethyl 3-amino-2-chloro-4-methyl-2-pentenoate

59.5 g (0.31 mol) of ethyl 2-chloro-4-methyl-3-oxopentanoate are reacted with 59.8 g (0.78 mol) of ammonium acetate in 120 ml of methanol and worked up in analogy to Example 2. Yield: 88.0% [GC]

Example 8

Ethyl 3-amino-2-chloro-3-phenylpropenoate

25 58.25 g (0.26 mol) of ethyl 2-chloro-3-oxo-3-phenylpropionate are reacted with 49.52 g (0.64 mol) of ammonium acetate in 100 ml of methanol and worked up in analogy to Example 2.



Yield: 91.6% [GC]

Example 9

5-Chloro-6-ethyl-4-hydroxypyrimidine

A mixture of 163.6 g (1.0 mol) of methyl 3-amino-
5 2-chloro-2-pentenoate, 90.8 g (2.0 mol) of formamide and
150 ml of methanol is added dropwise with stirring to
485.8 ml of a 30% strength NaOMe solution in methanol at
room temperature. The mixture is subsequently slowly
heated to the reflux temperature over the course of 3 h,
10 and is left to stir at this temperature for a further
12 h. Evaporation of the reaction mixture is followed by
dissolving in a little H₂O, adjustment to a pH of 3.8
with HCl and extraction with ethyl acetate. Drying over
MgSO₄ and evaporation provide 177.5 g of crude product
15 which is subsequently recrystallized from water.
Yield: 130.4 g (82%)

Example 10

5-Chloro-6-ethyl-4-hydroxypyrimidine

Two dropping funnels are used for simultaneous dropwise
20 addition of a solution of 35.5 g (0.2 mol) of methyl
3-amino-2-chloro-2-pentenoate and 31.5 g (0.7 mol) of
formamide in 150 ml of methanol with stirring to 90.3 ml
of a 30% strength sodium methoxide solution in methanol
at room temperature. The mixture is heated slowly to the
25 reflux temperature and left at this for 10 h. After the
mixture has cooled, dry HCl gas is passed through the
solution until the pH is 3. Evaporation of the solvent is
followed by extraction with butanone, drying and evapora-
tion in a rotary evaporator.
30 Yield: 87% [HPLC]



Example 11

5-Chloro-4-hydroxy-6-methylpyrimidine

25.9 g (0.17 mol) of methyl 3-amino-2-chloro-2-butenate
are reacted with 11.7 g (0.26 mol) of formamide and 51 ml
5 of sodium methoxide solution in 20 ml of methanol and
worked up in analogy to Example 9 (reaction time 20 h).
Yield: 16.6 g (67.5%)

Example 12

5-Chloro-4-hydroxy-6-propylpyrimidine

10 58.1 g (0.30 mol) of ethyl 3-amino-2-chloro-2-hexenoate
are reacted with 47.7 g (1.1 mol) of formamide and 140 ml
of sodium methoxide solution in 175 ml of methanol and
worked up in analogy to Example 9 (reaction time 6 h).
Yield: 42.2 g (81.5%)

15 Example 13

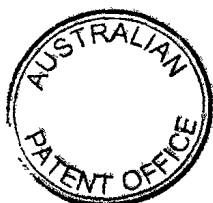
5-Chloro-4-hydroxy-6-phenylpyrimidine

45.73 g (0.20 mol) of ethyl 3-amino-2-chloro-3-phenyl-
propenoate are reacted with 31.9 g (0.71 mol) of forma-
mide and 93 ml of sodium methoxide solution in 120 ml of
20 methanol and worked up in analogy to Example 9 (reaction
time 16 h).
Yield: 32.9 g (79.7%)

Example 14

5-Chloro-4-hydroxy-6-isopropylpyrimidine

25 45.1 g (0.24 mol) of ethyl 3-amino-2-chloro-4-methyl-
2-pentenoate are reacted with 36.8 g (0.59 mol) of
formamide and 109 ml of sodium methoxide solution in
130 ml of methanol and worked up in analogy to Example 9.



Yield: 34.5 g (83.3%)

Example 15

4,5-di-Chloro-6-ethylpyrimidine (one pot process)

134.0 g (0.82 mol) of methyl 3-amino-2-chloro-
5 2-pentenoate and 125.3 g of formamide, dissolved in
150 ml of methanol, are simultaneously added dropwise
with stirring to 357.8 ml of a 30% strength sodium
methoxide solution in methanol at room temperature. The
mixture is heated to the reflux temperature over the
10 course of 5 h and is then left at this for 10 h. After
cooling, dry HCl gas is passed through until the pH
reaches 3. The solvent and the excess formamide are
removed by distillation and subsequently 100 ml of
toluene are added and removed by distillation twice.
15 145.3 ml of POCl₃ are added to the mixture, which is
heated at 70-80°C with stirring for 5 h. The excess POCl₃,
is then removed by distillation, the mixture is added to
ice water and neutralized with K₂CO₃. The residue after
extraction with ethyl acetate and evaporation of the
20 solvent is distilled at 110-112°C under 25 mbar.

Yield: 114.0 g (78.5%)

Example 16

5-Chloro-6-ethyl-4-hydroxypyrimidine

NH₃ gas is passed with cooling (max. 50°C) through a
25 solution of 99.7 g (0.6 mol) of methyl 2-chloro-3-oxo-
valerate in 130 ml of formamide until the mixture takes
up no more NH₃ (about 1 h). The ammonia residues are
removed by blowing out with nitrogen and applying a
vacuum. The reaction solution is subsequently added
30 dropwise to 450 ml of a 30% NaOMe solution in methanol at
50°C. Addition of a further 50 ml of formamide is fol-
lowed by heating at 50°C for 3 h. The volatile constitu-
ents are evaporated in vacuo, and subsequently the



mixture is added to water and the pH is adjusted to 6 with HCl. Extraction with ethyl acetate and evaporation provide 91.2 g of crude product, which is recrystallized from cold acetone.

5 Yield: 66.3 g (70%)

Example 17

5-Chloro-6-ethyl-4-hydroxypyrimidine

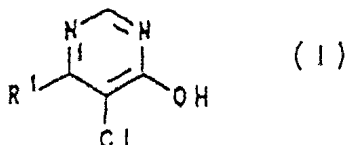
Dry NH_3 gas is passed with cooling (reaction temperature max. 50°C) through a solution of 150 g (0.88 mol) of methyl 2-chloro-3-oxovalerate in 100 ml of methanol until the mixture takes up no more NH_3 (2.5 h). The ammonia residues are removed by blowing out with N_2 and briefly applying a vacuum. Subsequently, 140 ml of formamide are added, and the solution is added dropwise to 472 ml of a 30% NaOMe solution in methanol at 50°C . Heating at 50°C for 4 h is followed by working up in analogy to Example 16.

15 Yield: 114.4 g (82%)

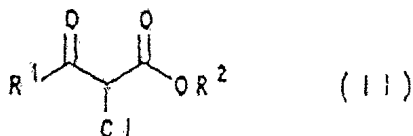


Patent claims:

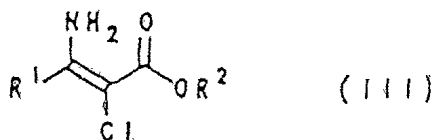
1. A process for preparing a compound of the formula I



- 5 in which R¹ is alkyl, cycloalkyl, aryl or benzyl, all of which are optionally substituted, which includes reacting a compound of the formula II



- in which R¹ is as defined above, and R² is alkyl, benzyl or another carboxyl protective group, with ammonia or an ammonium salt to give a compound of the formula III



- 10 which is subsequently condensed in a polar protic solvent in the presence of a base with formamide to give a compound of the formula I.

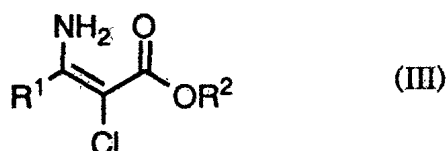
2. A process as claimed in claim 1, wherein the intermediate of the formula III is not isolated.
- 15 3. A process as claimed in claim 1 or 2, wherein compounds of the formula I in which R¹ is (C₁-C₄)-alkyl, (C₁-C₄)-haloalkyl, (C₁-C₄)-alkoxy-(C₁-C₄)-alkyl or (C₁-C₄)-alkylthio-(C₁-C₄)-alkyl are prepared.

4. A process as claimed in any of claims 1 to 3, where-



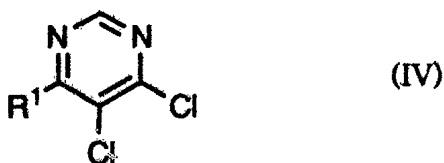
in compounds of the formula I in which R¹ is (C₁-C₄)-alkyl, preferably methyl or ethyl, or methoxymethyl are prepared.

5. A process as claimed in any of claims 1 to 4, wherein compounds of the formula I in which R¹ is ethyl are prepared.
6. A process as claimed in any of claims 1 to 5, which starts from compounds of the formula II in which R² is (C₁-C₄)-alkyl, benzyl or another carboxyl protective group.
7. A process as claimed in any of claims 1 to 6, which starts from compounds of the formula II in which R² is (C₁-C₄)-alkyl, preferably methyl, ethyl or tertbutyl, benzyl or modified benzyl.
8. A process as claimed in any of claims 1 to 7, which starts from compounds of the formula II in which R² is methyl.
9. A compound of the formula III



in which R¹ and R² are as defined in one of the preceding claims, excepting 3-amino-2-chloro-but-2-enoic acid (C₁-C₄)-alkylester.

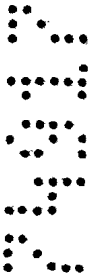
10. A process as claimed in claim 1, wherein the compound of the formula I thus obtained is reacted with POCl₃ to give a 4,5-dichloropyrimidine of the formula IV



in which R¹ is defined as in claim 1.

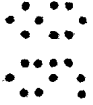
DATED this 10th day of September, 1998

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Abstract of the disclosure

A process for preparing 5-chloro-4-hydroxypyrimidines, 2-chloro enamines as intermediates in this process and their use

The invention relates to a process for preparing compounds of the formula



in which R¹ is optionally substituted alkyl, cycloalkyl, aryl or benzyl, in which a chloroacetic ester is converted with ammonia or an ammonium salt into the corresponding chloro enamine and the latter is condensed in the presence of a base with formamide. The invention furthermore relates to 2-chloro enamines as intermediates in the process.



INTERNATIONAL SEARCH REPORT

 Internat. Application No
 PCT/EP 94/02244

 A. CLASSIFICATION OF SUBJECT MATTER
 IPC 6 C07D239/36 C07C229/30

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 Minimum documentation searched (classification system followed by classification symbols)
 IPC 6 C07D C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP,A,0 568 041 (SUMITOMO CHEMICAL CY.) 3 November 1993 see page 4; claims; example V ----	9
A	EP,A,0 370 391 (LONZA) 30 May 1990 cited in the application see page 1 - page 5 ----	1-10
A	EP,A,0 326 389 (UBE INDUSTRIES) 2 August 1989 cited in the application see the whole document -----	1-10

 Further documents are listed in the continuation of box C.

 Patent family members are listed in annex.

* Special categories of cited documents:

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- "O" document referring to an oral disclosure, use, exhibition or other means
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Date of the actual completion of the international search

10 November 1994

Date of mailing of the international search report

17. 11. 94

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Internat. Application No
PCT/EP 94/02244

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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EP-A-0370391	30-05-90	CA-A- 2002671 JP-A- 2180873 US-A- 4977264	21-05-90 13-07-90 11-12-90
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