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NOTICE OF ENTITLEMENT

(To be filed before acceptance)

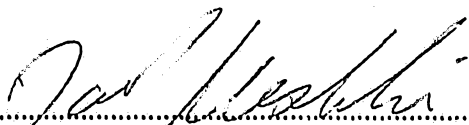
We, HOECHST AKTIENGESELLSCHAFT, of P.O. Box 80 03 20, W-6230 Frankfurt am Main 80, Federal Republic of Germany, being the applicant in respect of Application No. 83095/91 state the following:-

The Person nominated for the grant of the patent has entitlement from the actual inventor by virtue of assignment.

The person nominated for the grant of the patent is the applicant of the application listed in the declaration under Article 8 of the PCT.

The basic application listed on the request form is the first application made in a Convention country in respect of the invention.

By our Patent Attorneys,
WATERMARK PATENT & TRADEMARK ATTORNEYS


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Darryl B. Mischlewski

9 August 1994
.....

Registered Patent Attorney



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(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 653954

- (54) Title
PROCESS FOR PRODUCING AMINOMETHANEPHOSPHONIC ACID AND AMINOMETHYLPHOSPHINIC ACIDS
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WATERMARK PATENT & TRADEMARK ATTORNEYS , Locked Bag 5, HAWTHORN VIC 3122
- (56) Prior Art Documents
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- (57) Claim
1. A process for the preparation of compounds of the formula I



in which R¹ is hydroxyl, C₁-C₄-alkyl or phenyl, which comprises reacting acylaminomethanephosphonic or acylaminomethylphosphinic acids of the formula II



in which R² is hydrogen, alkyl having 1 to 6 carbon atoms, benzyl or phenyl, unsubstituted or substituted by one or more radicals from the group comprising C₁-C₄-alkyl, C₁-C₄-alkoxy and halogen, and R¹ is as defined above, with water, at 80 to 300°C.

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(81) Bestimmungsstaaten: AT (europäisches Patent), AU, BB, BE (europäisches Patent), BF (OAPI Patent), BG, BJ (OAPI Patent), BR, CA, CF (OAPI Patent), CG (OAPI Patent), CH (europäisches Patent), CI (OAPI Patent), CM (OAPI Patent), DE (europäisches Patent), DK (europäisches Patent), ES (europäisches Patent), FI, FR (europäisches Patent), GA (OAPI Patent), GB (europäisches Patent), GN (OAPI Patent), GR (europäisches Patent), HU, IT (europäisches Patent), JP, KP, KR, LK, LU (europäisches Patent), MC, MG, ML (OAPI Patent), MR (OAPI Patent), MW, NL (europäisches Patent), NO, PL, RO, SD, SE (europäisches Patent), SN (OAPI Patent), SU⁺, TD (OAPI Patent), TG (OAPI Patent), US.

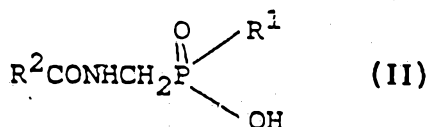
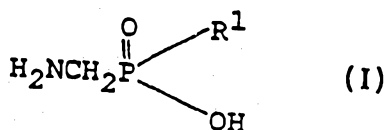
Veröffentlicht

Mit internationalem Recherchenbericht.

653954

(54) Title: PROCESS FOR PRODUCING AMINOMETHANEPHOSPHONIC ACID AND AMINOMETHYLPHOSPHINIC ACIDS

(54) Bezeichnung: VERFAHREN ZUR HERSTELLUNG VON AMINOMETHANPHOSPHONSÄURE UND AMINOMETHYL-PHOSPHINSÄUREN



(57) Abstract

Aminomethanephosphonic acid and aminomethylphosphinic acids are interesting biologically active compounds or intermediates for the production of biologically active compounds. Such compounds having the formula (I), in which R¹ is OH, C₁-C₄-alkyl or phenyl, can be produced in a technically easy manner, by reacting with water at 80 to 300 °C compounds having the formula (II), in which R² is H, C₁-C₆-alkyl, benzyl, phenyl, if necessary substituted by C₁-C₄-alkoxy and/or halogen, and R¹ has the same meaning as above.

(57) Zusammenfassung

Aminomethanphosphonsäure und Aminomethyl-phosphinsäuren sind als biologisch aktive Verbindungen oder als Zwischenprodukte zur Herstellung biologisch aktiver Verbindungen interessant. Erfindungsgemäß können derartige Verbindungen der Formel (I), worin R¹ OH, C₁-C₄-Alkyl oder Phenyl bedeutet, in einer technisch einfachen Weise hergestellt werden, indem man Verbindungen der Formel (II), worin R² H, C₁-C₆-Alkyl, Benzyl, Phenyl, das gegebenenfalls durch C₁-C₄-Alkyl, -Alkoxy und/oder Halogen substituiert ist, bedeutet und R¹ wie oben definiert ist, mit Wasser bei 80 bis 300 °C umsetzt.

Description

Process for the preparation of aminomethanephosphonic acid and aminomethylphosphinic acids

Herbicidal and plant-growth-regulating actions are known of aminomethanephosphonic acid; aminomethylphosphinic acids are also industrially valuable compounds having a biological activity or can be used as intermediates for the preparation of biologically active compounds (see the article by L. Maier "Advances in the Chemistry of Amino-phosphinic Acids" in the periodical "Phosphorus and Sulfur" 1983, Vol. 14, p. 295-322, in particular 317-323 and literature cited therein). Aminomethanephosphonic acid is furthermore valuable as an intermediate for the preparation of N-phosphonomethylglycine (see EP-A-214,578).

Aminomethanephosphonic acid can be prepared from acyl-aminomethanephosphonic acids by hydrolysis with hydrochloric acid (US-A-2,304,156; US-A-2,328,358; M. Soroka, Synthesis 1989, 547). It is a disadvantage of this process that the aminomethanephosphonic acid can only be obtained in high yields during working-up when special measures are applied. For example, M. Soroka describes working-up with the aid of pyridine or propylene oxide, which cause the separation of hydrogen chloride from the aminomethanephosphonic acid. Another disadvantage is that, without complicated ultrapurification, the acyl-aminomethanephosphonic acids contain traces of formaldehyde, due to the production process. The treatment with hydrochloric acid in the hydrolysis then results in the formation of bischloromethyl ether as undesirable by-product, which has been identified clearly as a carcinogenic working substance. There is therefore a demand for hydrolysis processes which can be carried out on an industrial scale and which exclude the formation of the by-product bischloromethyl ether.



The invention relates to a process for the preparation of compounds of the formula I



5 in which R^1 is hydroxyl, $\text{C}_1\text{-C}_4$ -alkyl, preferably $\text{C}_1\text{-C}_2$ -alkyl, in particular methyl, or is phenyl, which comprises reacting acylaminomethanephosphonic or acylaminomethylphosphinic acids of the formula II



10 in which R^2 is hydrogen, alkyl having 1 to 6 carbon atoms, preferably 1 to 3 carbon atoms, or is benzyl or phenyl, unsubstituted or substituted by one or more radicals from the group comprising $\text{C}_1\text{-C}_4$ -alkyl, $\text{C}_1\text{-C}_4$ -alkoxy and halogen, and R^1 is as defined above, with water, at 80 to 300°C, preferably 150 to 250°C.

15 Some of the starting substances of the formula II are known, or some are accessible analogously to known methods. For example, the acylaminomethanephosphonic acids of the formula II can be prepared from N-(hydroxymethyl)amides and PCl_3 (see US-A-2,328,358; US-A-2,304,156
20 or M. Soroka, Synthesis 1989, 547 and literature cited therein).

25 The acylaminomethanephosphonic acids as well as the acylaminomethylphosphinic acids of the formula II can also be prepared by the process in German Patent Application P 4,026,026.7.

Examples of preferred starting substances of the



formula II are formylaminomethanephosphonic acid, acetylaminomethanephosphonic acid, benzoylaminomethanephosphonic acid, (acetylaminomethyl)(methyl)phosphinic acid and (benzoylaminomethyl)(phenyl)phosphinic acid.

- 5 The starting substances of the formula II are treated with water, if appropriate with an excess of water, and the mixture is brought to reaction temperature, and it may be necessary to carry out this process under pressure, as a function of the temperature.
- 10 The extent of the excess of water is not particularly critical for the reaction; for example, for reasons of better handling, it may be advantageous to use a 2 to 30 molar, preferably 10 to 25 molar, excess of water. The reaction temperatures are 80 to 300°C, preferably 150 to 250°C. The reaction times depend on the substrate,
- 15 reaction temperature and pressure and are generally in the range from 5 to 40 hours, preferably 10 to 35 hours.

- When the reaction is complete, working-up can be carried out in a simple manner, for example by removing the carboxylic acid as a solid (for example benzoic acid) or by distillation (for example acetic acid). The resulting aminomethanephosphonic acid, or aminomethylphosphinic acids, generally already have high purity. If appropriate, they can be obtained in ultrapure form by customary
- 20 methods, preferably by crystallization.
- 25

Example 1

- 20 g (0.093 mol) of benzoylaminomethanephosphonic acid and 20 g of water were placed in a sealed tube and maintained at 200°C for 20 hours. After cooling, the reaction material was digested with 100 ml of water. The benzoic acid was subsequently filtered off with suction.
- 30 The filtrate was concentrated in vacuo by distillation until it had reached an internal temperature of 75°C. There remained 10.3 g (100 % of theory) of aminomethane-



phosphonic acid which, according to ^{31}P -NMR spectrum analysis, had a purity of 95 %.

Example 2

5 20 g (0.093 mol) of benzoylaminomethanephosphonic acid and 20 g of water were placed in a sealed tube and maintained at 150°C for 20 hours. After cooling, the reaction material was then digested with methanol and filtered off with suction. 8.2 g (80 % of theory) of
10 aminomethanephosphonic acid of a decomposition point of 310°C were obtained.

Example 3

15 20 g (0.093 mol) of benzoylaminomethanephosphonic acid and 20 g of water were refluxed for 30 hours. After cooling, the reaction material was digested with 100 ml of methanol and filtered off with suction. 5.3 g (52 % of theory) of aminomethylphosphonic acid of a decomposition point of 275°C were obtained. Unreacted benzoylamino-methanephosphonic acid could be isolated from the filtrate.

20 Example 4

25 21.3 g (0.1 mol) of benzoylaminomethylmethylphosphinic acid and 42 g of water were placed in a sealed tube and maintained at 200°C for 20 hours. After cooling, the mixture was digested with water, and benzoic acid was removed by filtration with suction. The filtrate was evaporated to dryness in vacuo. The crystalline residue was digested with methanol and filtered off with suction. 8 g (73 % of theory) of aminomethylmethylphosphinic acid of a melting point of 255-261°C were obtained.

30 Example 5

20 g (0.073 mol) of benzoylaminomethylphenylphosphinic



acid and 40 ml of water were placed in a sealed tube and maintained at 225°C for 23 hours. The benzoic acid was then removed by filtration with suction, followed by rinsing with water. The filtrate was concentrated to dryness in vacuo. There remained 12.5 g (100 % of theory) of crude aminomethylphenylphosphinic acid. After digestion with methanol, the substance obtained had a melting point of 276-278°C.

Example 6

10 14.4 g (0.094 mol) of acetylaminomethanephosphonic acid and 28 g of water were fed into a sealed tube and maintained at 200°C for 20 hours. The mixture was then cooled, and the resulting reaction solution was freed in vacuo from water and acetic acid. The residue was digested with a mixture of 30 ml of methanol and 1 ml of water. 15 9.6 g (92 % of theory) of aminomethanephosphonic acid of a decomposition point of 270-278°C were obtained.



Patent claims:

1. A process for the preparation of compounds of the formula I



5 in which R¹ is hydroxyl, C₁-C₄-alkyl or phenyl, which comprises reacting acylaminomethanephosphonic or acylaminomethylphosphonic acids of the formula II



10 in which R² is hydrogen, alkyl having 1 to 6 carbon atoms, benzyl or phenyl, unsubstituted or substituted by one or more radicals from the group comprising C₁-C₄-alkyl, C₁-C₄-alkoxy and halogen, and R¹ is as defined above, with water, at 80 to 300°C.

15 2. The process as claimed in claim 1, in which R¹ is hydroxyl.

3. The process as claimed in claim 1, in which R¹ is methyl, ethyl or phenyl.

4. The process as claimed in claim 1, 2 or 3, in which R² is H, C₁-C₃-alkyl, benzyl or phenyl.

20 5. The process as claimed in claim 1, 2 or 3, in which R² is phenyl.

6. The process as claimed in one or more of claims 1 to 5, in which the reaction temperature is 150 to 250°C.

7. The process as claimed in one or more of claims 1 to 6, in which a 2 to 30 molar excess of water, based on 1 mol of compound of the formula II, is employed.

5 8. The process as claimed in one or more of claims 1 to 7, in which the reaction time is in the range from 5 to 40 hours.

HOE 90/F 249

Abstract of the disclosure:

Process for the preparation of aminomethanephosphonic acid and aminomethylphosphinic acids

Aminomethanephosphonic acid and aminomethylphosphinic acids are interesting as biologically active compounds or as intermediates for the preparation of biologically active compounds. According to the invention, such compounds of the formula I



in which R^1 is OH, $\text{C}_1\text{-C}_4$ -alkyl or phenyl, can be prepared in a technically simple manner by reacting compounds of the formula II



in which R^2 is H, $\text{C}_1\text{-C}_6$ -alkyl, benzyl, phenyl, optionally substituted by $\text{C}_1\text{-C}_4$ -alkyl, -alkoxy and/or halogen, and R^1 is as defined above, with water, at 80 to 300°C.



INTERNATIONAL SEARCH REPORT

International Application No PCT/EP 91/01494

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC		
Int.Cl. ⁵ C 07 F 9/30; C 07 F 9/38		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
Int.Cl. ⁵	C 07 F	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹		
Category ¹⁰	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
Y	DE, A, 3824961 (BASF AG) 25 January 1990 see the whole document ---	1-8
Y	EP, A, 0370992 (MONSANTO COMPANY) 30 May 1990 see the whole document ---	1-8
Y	CHEMICAL ABSTRACTS, vol. 107, No. 5, 3 August 1987 Columbus, Ohio, US; abstract No. 39933, PULWER M.J. : "a convenient synthesis of aminomethylphosphonic acid" see abstract ---	1-8
Y	SYNTHESIS, No. 7 1989, STUTTGART DE pages 547- 548; SOROKA M. : "comments on the synthesis of aminomethylphosphonic " see the whole document -----	1-8
¹⁰ Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
28 October 1991 (28.10.91)	25 November 1991 (25.11.91)	
International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE		

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.**

EP 9101494
SA 50041

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information. 28/10/91

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE-A-3824961	25-01-90	None	
EP-A-0370992	30-05-90	AU-A- 4552389	31-05-90
		CA-A- 2003852	25-05-90
		US-A- 5041627	20-08-91

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen

PCT/EP 91/01494

I. KLASSIFIKATION DES ANMELDUNGSGEGENSTANDS (bei mehreren Klassifikationssymbolen sind alle anzugeben) ⁶		
Nach der Internationalen Patentklassifikation (IPC) oder nach der nationalen Klassifikation und der IPC		
Int.Kl. 5 C07F9/30 ; C07F9/38		
II. RECHERCHIERTE SACHGEBIETE		
Recherchierter Mindestprüfstoff ⁷		
Klassifikationssystem	Klassifikationssymbole	
Int.Kl. 5	C07F	
Recherchierte nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Sachgebiete fallen ⁸		
III. EINSCHLAGIGE VERÖFFENTLICHUNGEN ⁹		
Art. ⁹	Kennzeichnung der Veröffentlichung ¹¹ , soweit erforderlich unter Angabe der maßgeblichen Teile ¹²	Betr. Anspruch Nr. ¹³
Y	DE,A,3 824 961 (BASF AG) 25. Januar 1990 siehe das ganze Dokument ---	1-8
Y	EP,A,0 370 992 (MONSANTO COMPANY) 30. Mai 1990 siehe das ganze Dokument ---	1-8
Y	CHEMICAL ABSTRACTS, vol. 107, no. 5, 3. August 1987, Columbus, Ohio, US; abstract no. 39933, PULWER M.J.: 'a convenient synthesis of aminomethylphosphonic acid' siehe Zusammenfassung --- -/-	1-8
¹⁰ Besondere Kategorien von angegebenen Veröffentlichungen : "A" Veröffentlichung, die den allgemeinen Stand der Technik definiert, aber nicht als besonders bedeutsam anzusehen ist "E" älteres Dokument, das jedoch erst am oder nach dem internationalen Anmeldedatum veröffentlicht worden ist "L" Veröffentlichung, die geeignet ist, einen Prioritätsanspruch zweifelhaft erscheinen zu lassen, oder durch die das Veröffentlichungsdatum einer anderen im Recherchenbericht genannten Veröffentlichung belegt werden soll oder die aus einem anderen besonderen Grund angegeben ist (wie ausgeführt) "O" Veröffentlichung, die sich auf eine mündliche Offenbarung, eine Benutzung, eine Ausstellung oder andere Maßnahmen bezieht "P" Veröffentlichung, die vor dem internationalen Anmeldedatum, aber nach dem beanspruchten Prioritätsdatum veröffentlicht worden ist "T" Spätere Veröffentlichung, die nach dem internationalen Anmeldedatum oder dem Prioritätsdatum veröffentlicht worden ist und mit der Anmeldung nicht kollidiert, sondern nur zum Verständnis des der Erfindung zugrundeliegenden Prinzips oder der ihr zugrundeliegenden Theorie angegeben ist "X" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann nicht als neu oder auf erfinderischer Tätigkeit beruhend betrachtet werden "Y" Veröffentlichung von besonderer Bedeutung; die beanspruchte Erfindung kann nicht als auf erfinderischer Tätigkeit beruhend betrachtet werden, wenn die Veröffentlichung mit einer oder mehreren anderen Veröffentlichungen dieser Kategorie in Verbindung gebracht wird und diese Verbindung für einen Fachmann naheliegend ist "Z" Veröffentlichung, die Mitglied derselben Patentfamilie ist		
IV. BESCHREIBUNG		
Datum des Abschlusses der internationalen Recherche	Abschendedatum des internationalen Recherchenberichts	
28. OKTOBER 1991	25. 11. 91	
Internationale Recherchenbehörde	Unterschrift des bevollmächtigten Bediensteten	
EUROPAISCHES PATENTAMT	BESLIER L.M. 	

III. EINSCHLAGIGE VERÖFFENTLICHUNGEN (Fortsetzung von Blatt 2)		
Art °	Kennzeichnung der Veröffentlichung, soweit erforderlich unter Angabe der maßgeblichen Teile	Betr. Anspruch Nr.
Y	SYNTHESIS. Nr. 7, 1989, STUTTGART DE Seiten 547 - 548; SOROKA M.: 'comments on the synthesis of aminomethylphosphonic' siehe das ganze Dokument ---	1-8

**ANHANG ZUM INTERNATIONALEN RECHERCHENBERICHT
ÜBER DIE INTERNATIONALE PATENTANMELDUNG NR.**

EP 9101494
SA 50041

In diesem Anhang sind die Mitglieder der Patentfamilien der im obengenannten internationalen Recherchenbericht angeführten Patentedokumente angegeben.

Die Angaben über die Familienmitglieder entsprechen dem Stand der Datei des Europäischen Patentamts am
Diese Angaben dienen nur zur Unterrichtung und erfolgen ohne Gewähr.

28/10/91

Im Recherchenbericht angeführtes Patentedokument	Datum der Veröffentlichung	Mitglied(er) der Patentfamilie	Datum der Veröffentlichung
DE-A-3824961	25-01-90	Keine	
EP-A-0370992	30-05-90	AU-A- 4552389	31-05-90
		CA-A- 2003852	25-05-90
		US-A- 5041627	20-08-91