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(71) Applicant *(for all designated States except US)*:
GRINDEKS, A JOINT STOCK COMPANY [LV/LV]; 53, Krustpils street, LV-1057 Riga (LV).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **ZICANE, Daina** [LV/LV]; Azenes street 14/24, LV-1048 Riga (LV). **TURKS, Maris** [LV/LV]; Azenes street 14/24, LV-1048 Riga (LV).

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(54) Title: PROCESS FOR PREPARING 3-(2,2- DIMETHYLHYDRAZINO) METHYLPROPIONATE

(57) Abstract: The invention provides an improved, efficient method for preparing3-(2,2- dimethylhydrazino)methylpropionate.

Description

PROCESS FOR PREPARING 3- (2, 2-DIMETHYLHYDRAZINO) METHYLPROPIONATE

Technical Field

The present invention relates to an improved process for preparation of 3-(2,2-dimethylhydrazino)methylpropionate.

Background Art

A number of processes for the preparation of 3-(2,2,2-trimethylhydrazinium)propionate dihydrate is known.

The first process for preparation 3-(2,2,2-trimethylhydrazinium)propionate dihydrate is disclosed in WO 80/01068 A (INST ORGANICHESKOGO SINTEZA) 1980.05.29. . The process starts with methyl 3-(2,2-dimethylhydrazino)propionate is treated with a methyl halide or dimethylsulphate to give the appropriate trimethylhydrazinium salt, which is transferred to 3-(2,2,2-trimethylhydrazinium)propionate by Amberlite IRA-400 (OH form). After crystallization from ethanol the inner salt is obtained as a dihydrate.

This process disclosed in above patent can be considered as a common process for 3-(2,2,2-trimethylhydrazinium)propionate dihydrate preparation.

There are several processes for obtaining 3-(2,2,2-trimethylhydrazinium) propionate dihydrate, but most of them are concentrated to the avoid use of electrodialysis, which include many disadvantages: strongly basic ion exchangers are unstable and undergo decomposition and oxidation during processing; they withstand only a limited number of regeneration cycles; large quantities or solvents, acids and bases as well as deionised water are needed to regenerate the resins; low ion exchange capacity and therefore high production costs of 3-(2,2,2-trimethylhydrazinium)propionate dihydrate by this process are typical.

However at the same time, process of obtaining intermediates in high quality for producing 3-(2,2,2-trimethylhydrazinium)propionate as well is very important.

One of such intermediates is 3-(2,2-dimethylhydrazino)methylpropionate. Common process to produce this intermediate is reacting 1,1-dimethylhydrazine with methyl acrylate.

Reaction between 1,1-dimethylhydrazine with methyl acrylate which lead either to a cyclic 1,1-dimethyl-2-pyrazolinium-3-olate or to the linear product of the addition of DMH at the double bond of the ester is described in ZAPEVALOVA, N. P. , et al.

Reactions of 1,l-disubstituted hydrazines with derivatives of α,β-unsatur ated acids Communication 4. Reactions of 1,1-dimethylhydrazine with α,β-unsaturated esters. Russian Chemical Bulletin. 1966, vol.15, no.12, p.2127-2130. Another reaction of 1,1-dimethylhydrazine with acrylic acid derivatives gave a number of 1,1-dimethyl-2-(2-substituted ethyl)hydrazines which described in GILLER, S.A., et al. Derivatives of l-H-aziridine-2-carboxylic acid. Chemistry of Heterocyclic Compounds. 1975, vol.11, no.12, p.1378-1382.

Disclosure of Invention

Under standard conditions, by reaction of 1,1-dimethylhydrazine with methyl acrylate, in the absence of an antioxidant several side products IV-VII were observed. Thus, dimethylamine (IV) forms in the oxidation of 1,1-dimethylhydrazine (I). The former can react with methyl acrylate (II) and formed wanted side product methyl 3-(dimethylamino)propanoate (V). Similary, product 3-(2,2-dimethylhydrazino)methylpropionate (III) is sensitive to air and slowly oxidizes to methyl 2-(2,2-dimethylhydrazono)acetate (VI). As well that antioxidant suppresses double addition which can form unwanted dimmer dimethyl 3,3'-(2,2-dimethylhydrazine-1,1-diyl)dipropanoate (VII), see Table 1 and Table 2.

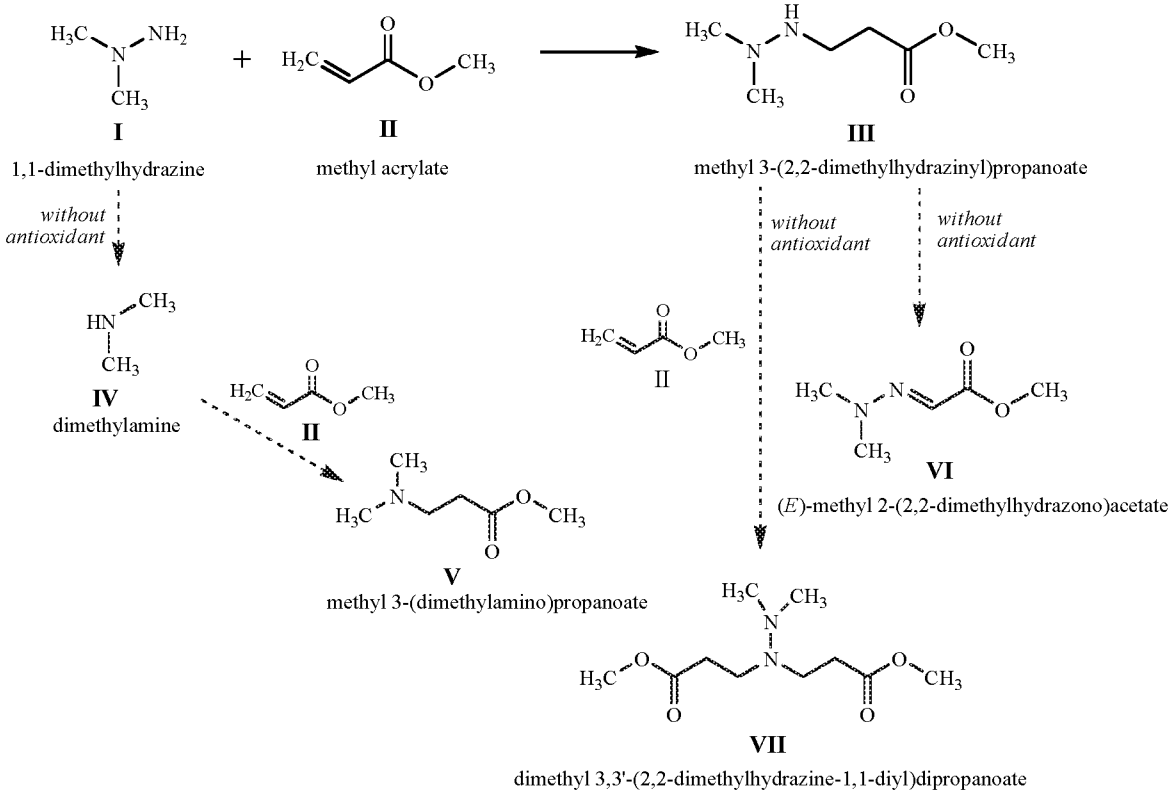


Table 1 Reaction scheme of formation of possible impurities in a process to

produce melthyl 3-(2,2-dimethylhydrazino)methylpropionate without using antioxidant

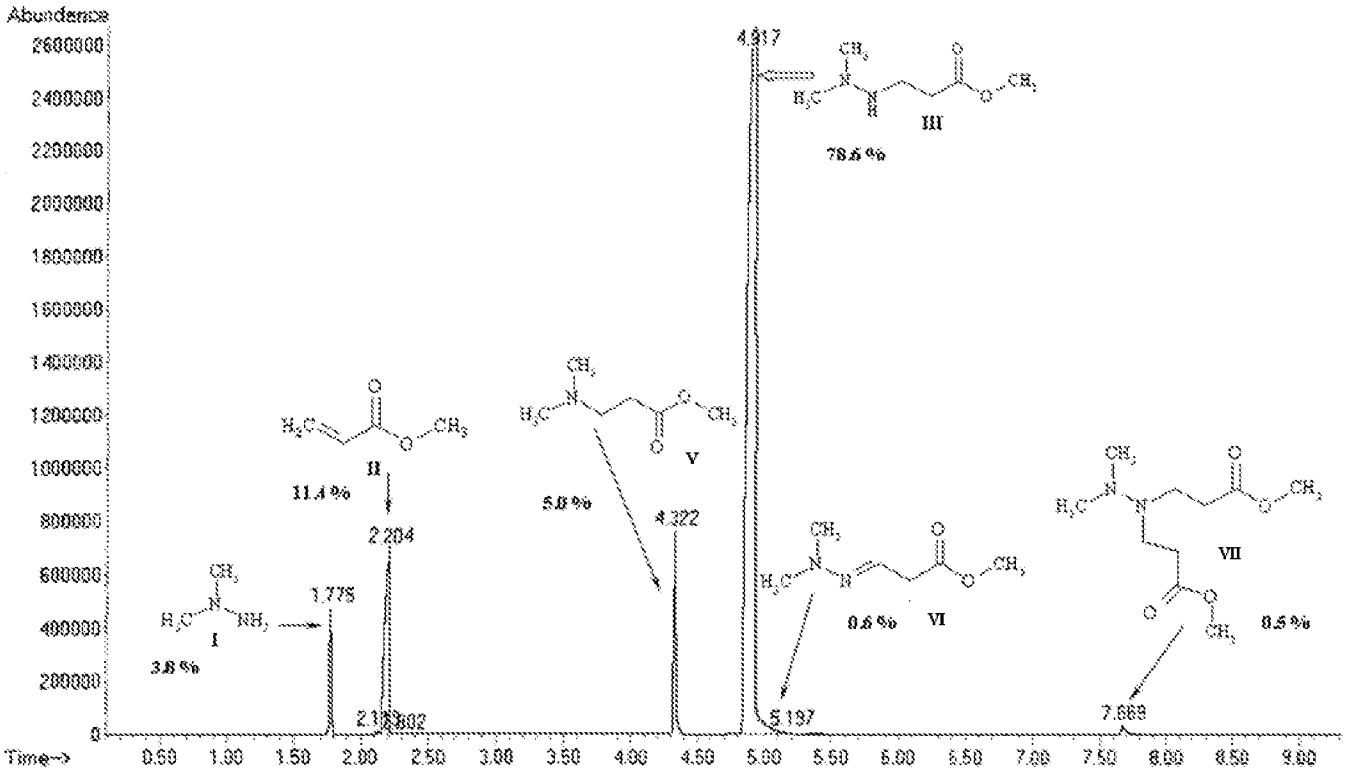


Table 2 GH/MS chromatogram of 3-(2,2-dimethylhydrazino)methylpropionate purity without using antioxidant

Surprisingly, we found out what the above objective is achieved according to present invention by reaction of 1,1-dimethylhydrazine (I) with methyl acrylate (II) by using antioxidant, thus preparation of 3-(2,2-dimethylhydrazino)methylpropionate (III).

In GB950622 A (CELANESE CORP) 1964.02.26 is disclosed what antioxidant, such as hydroquinone, can be used in order to stabilize methyl acrylate and to prevent its polymerization.

However, the present invention deals with stabilization of 1,1-dimethylhydrazine and 3-(2,2-dimethylhydrazino)methylpropionate, besides yield and purity of 3-(2,2-dimethylhydrazino)methylpropionate was increased significantly by using antioxidant.

As antioxidants can be used phenol derivatives, such as 2-tert-butylhydroquinone, acts as weak protic acid, nevertheless carboxylic acid derivatives, such as citric

acid as well can be used as antioxidant and catalyzed first step process and reducing formation of impurities, such us IV-VII, which form by oxidation of 3-(2,2-dimethylhydrazino)methylpropionate as well remains of starting products 1,1-dimethylhydrazine and methyl acrylate, see Table 3 and Table 4.

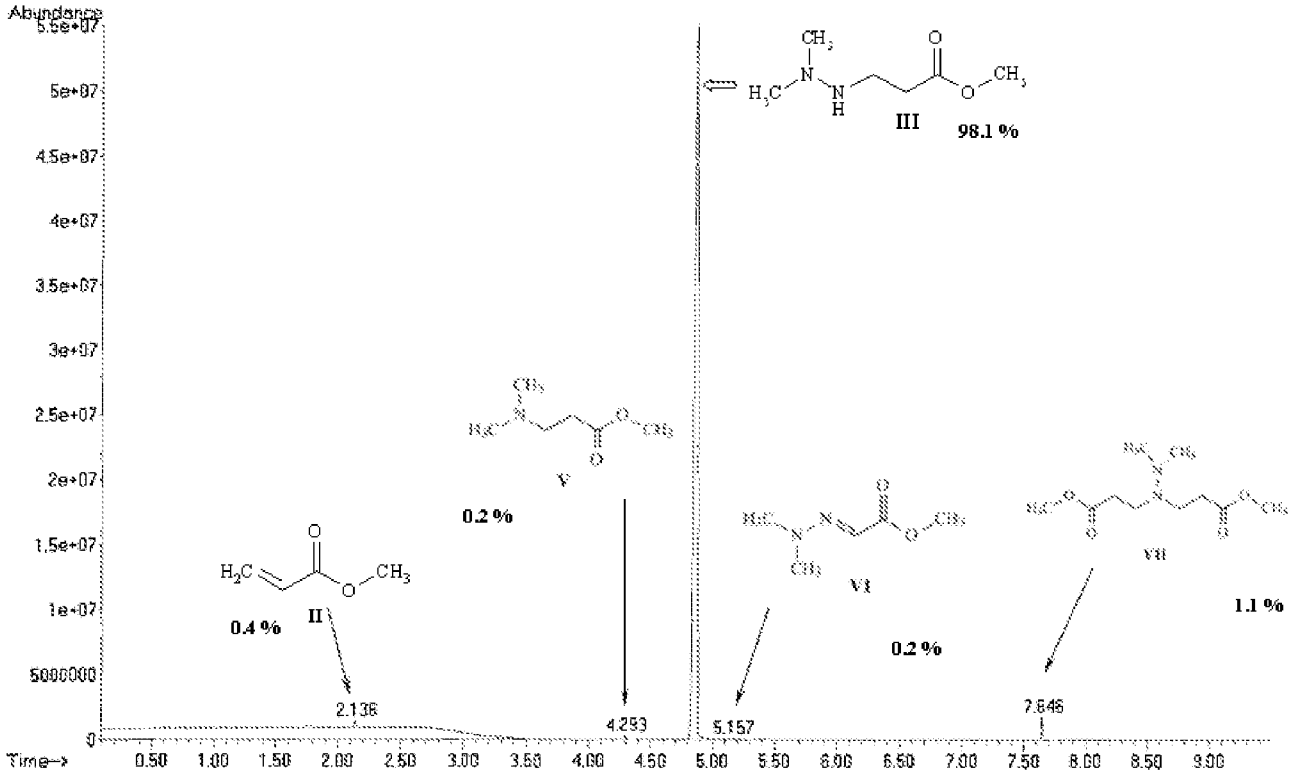


Table 3 GH/MS chromatogram of 3-(2,2-dimethylhydrazino)methylpropionate purity with using antioxidant (2,6-di-tert-butyl-4-metoxyphenol)

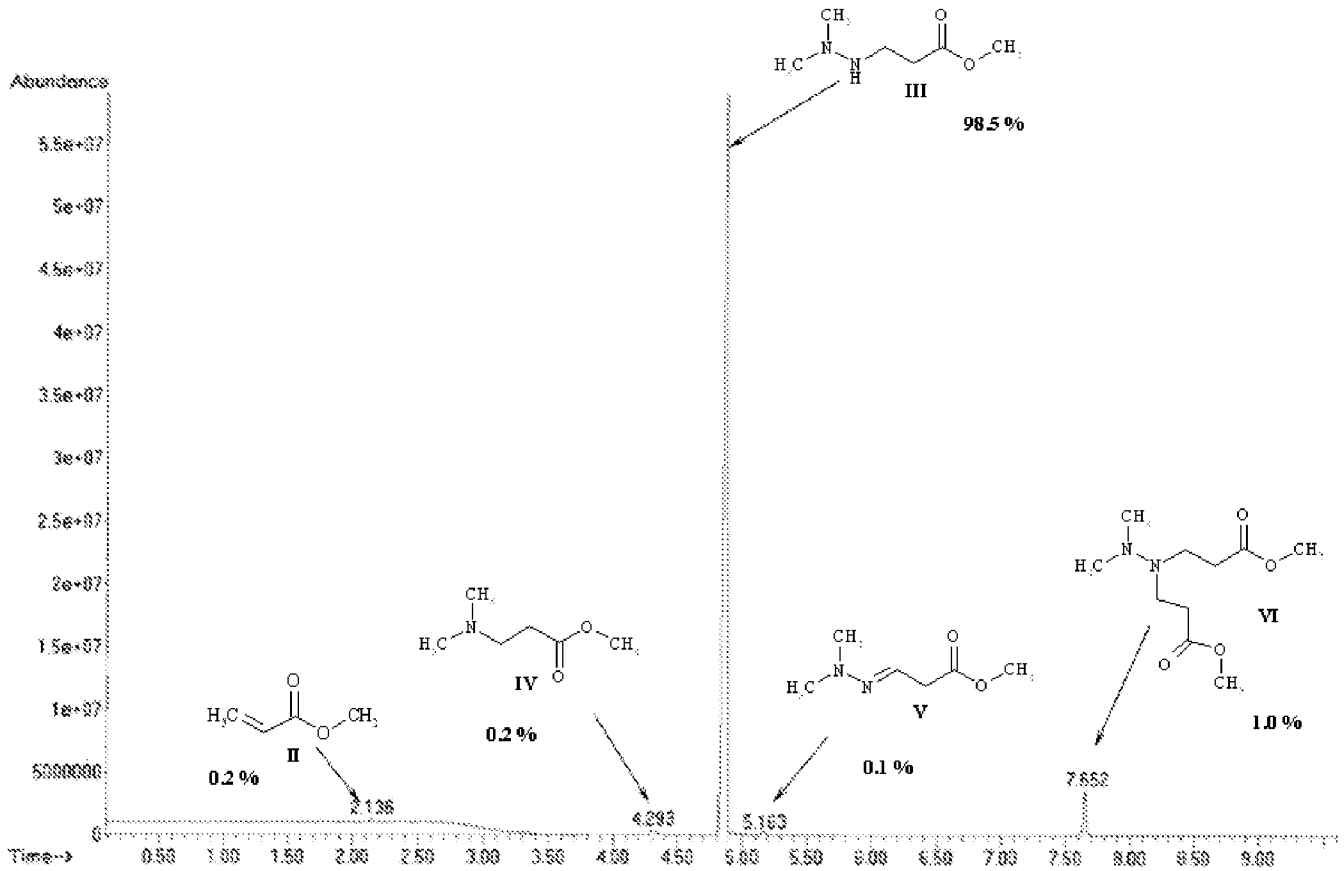


Table 4 GH/MS chromatogram of 3-(2,2-dimethylhydrazino)methylpropionate purity with using antioxidant citric acid

Thus, the subject matter of the present invention is a process for preparing a compound 3-(2,2-dimethylhydrazino)methylpropionate having formula III, by reaction of compound I with methyl acrylate of formula II to yield 3-(2,2-dimethylhydrazino)methylpropionate of formula III by using antioxidant, which acts as catalizator, such as 2-tert-butylhydroquinone, and citric acid.

Best Mode for Carrying Out the Invention

The present invention will be described in more detail by referring to the following non-limiting examples.

Example 1

Preparation of 3-(2,2-dimethylhydrazino)methylpropionate by antioxidant

1,1-Dimethylhydrazine was added to stirred antioxidant in 3-neck round bottom flask fitted with mechanical stirrer, a dropping funnel and a reflux condenser. The reaction mixture was stirred and heated to 50±5°C, at which point methyl acrylate was added. Thereafter the reaction mixture was heated at 80±85°C until formation 3-(2,2-dimethylhydrazino)methylpropionate (controlled by GM-MS).

Great list of antioxidants were used, but surprisingly just two of them are the most suitable for used as an antioxidant, by obtaining 3-(2,2-dimethylhydrazino)methylpropionate in high yields, see Table 5.

Antioxidant	**Time, h**	**Yield of** 3-(2,2-dimethylhydrazino) methylpropionate **(%)**
Hydroquinone	1	87
	2	90
2,5-di-*tert*-butylhydroquinone	1	86,2
	2	**95**
2,6-di-*tert*-butyl-4-methylphenol	1	85,4
	2	87
6-*O*-palmitoyl ascorbic acid	1	87,1
	2	89
propyl gallate	1	83,3
	2	88
butylated hydroxyanisole	1	91,7
	2	91
n-dodecyl gallate	1	85,5
	2	90
L(+)-ascorbic acid	1	85
	2	88,5
L-ascorbic acid sodium salt	1	87
	2	89
D-isoascorbic acid	1	86,5
	2	88,5
Citric acid	1	89,5
	2	**97.3**

Example 2

Preparation of 3-(2,2-dimethylhydrazino)methylpropionate by using 2-tert-butylhydroquinone as antioxidant

1,1-Dimethylhydrazine (35.0g, 0.63 mol) was added to stirred 2-tert-butylhydroquinone (0.18 g, 1.1 mmol) in 3-neck round bottom flask fitted with mechanical stirrer, a dropping funnel and a reflux condenser.

The reaction mixture was stirred and heated to 50±5°C, at which point methyl acrylate (51.6g, 0.6mol) was added. Thereafter the reaction mixture was heated at 80±85°C for 2.5 hours until formation 3-(2,2-dimethylhydrazino)methylpropionate (controlled by GM-MS). Yield 95%.

Example 3

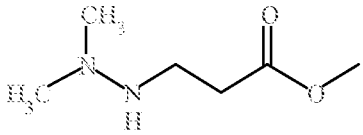
Preparation of 3-(2,2-dimethylhydrazino)methylpropionate by using citric acid as antioxidant

1,1-Dimethylhydrazine (37.9g, 0.63 mol) was added to stirred citric acid (0.19 g, 1.1 mmol) in 3-neck round bottom flask fitted with mechanical stirrer, a dropping funnel and a reflux condenser.

The reaction mixture was stirred and heated to 50±5°C, at which point methyl acrylate (47.9g, 0.6 mol) was added. Thereafter the reaction mixture was heated at 80±85°C until formation 3-(2,2-dimethylhydrazino)methylpropionate (controlled by GM-MS). Yield 97.3%.

Claims

1. A process for preparing 3-(2,2-dimethylhydrazino)methylpropionate of formula III



III

by reaction of 1,1-dimethylhydrazine with methyl acrylate in presence of antioxidant .

2. A process according to claim 1 wherein antioxidant is derivative of phenol, such as 2-tert-butylhydroquinone, 2,6-di-tert-butyl-4-methylphenol and 2,6-di-tert-butyl-4-metoxyphenol.
3. A process according to claim 1 wherein antioxidant is derivative of carboxylic acid, such as citric acid.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2009/056370

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07C241/02 C07C243/14

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)
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)
EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 1965, XP002540342 retrieved from STN Database accession no. 64:3589	1-2
A	abstract & KOST, A. N. ET AL: "Solvent effect and steric factors in the Michael reaction" ZHURNAL ORGANICHESKOI KHIMII , 1(8), 1341-8 CODEN: ZORKAE; ISSN: 0514-7492, 1965, -----	3

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search	Date of mailing of the international search report
6 August 2009	20/08/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Österle, Carmen