APPLICATION FOR A PATENT

Zi' E~jLATION 9

Lt6bN1NWEALT11 OF AUSTRALIA

Patents Act 1952-1973

APPLICATION

for a Patent

for an invention entitled:

SMOKING PRODUCT CONTAINING NICOTINE N'-OXIDE

which is described in the accompanying complete specification.

This Application is a Convention Application and is based on the Application(s) numbered: P 33 44 554.0

for a Patent or similar protection made in Germany

on 9 December 1983

Our address for service is care of GRIFFITH HASSEL & FRASER, Patent Attorneys of 71 York Street, Sydney 2000, in the State of New South Wales, Commonwealth of Australia.

Dated this 7th day of December 1984

B. A. T. CIGARETEN-FABRIKEN GmbH

By their Patent Attorneys

GRIFFITH HASSEL & FRASER

TO: THE COMMISSIONER OF PATENTS

COMMONWEALTH OF AUSTRALIA
COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952 (AS AMENDED)

DECLARATION IN SUPPORT OF AN APPLICATION FOR A PATENT

(Name of applicant) in support of an Application made by B.A.T. Cigaretten-Fabriken GmbH for a patent for an invention entitled

SMOKING PRODUCT CONTAINING NICOTINE N'-OXIDE

(Title)

(Full name of signatory) 

Gunter Uhe and Ulrich Niemann

(Address of signatory) of Sonnenberg 2 and Molkeallee 27,
     2106 Bündestorf     2070 Ahrensburg
     Germany           Germany

We do solemnly and sincerely declare as follows:

1. We are authorised by the abovementioned applicant for the patent to make this Declaration on its behalf.

2. The name and address of each actual inventor of the invention is as follows:

   ...Gerald Schmezel and Dr. Gert Rudolf...

   of Schumacher Str. 72, 2200 Elmshorn and
   Simrockstr. 92, 2000 Hamburg 93, respectively

and the facts upon which the applicant is entitled to make this application are as follows:

(Invert details of assignment etc.)

The applicant is the assignee of the said invention from the said inventors

3. The basic application(s) as defined by Section 131 of the Act was (were) made as follows:

   Country: Germany on 9 December, 1983

   in the name(s): B.A.T. Cigaretten-Fabriken GmbH

   and in: on

   in the name(s): on

   and in: on

   and in: on

4. The basic application(s) referred to in the preceding paragraph of this Declaration was (were) the first application(s) made in a Convention country in respect of the invention the subject of this application.

(Place and date of signing) Declared at Hamburg this 15th day of November 1984.

Signed: B.A.T. Cigarettenfabriken GmbH

Position: director
A smoking product, in particular tobacco with or without a wrapper material, containing nicotine N'-oxide, which comprises trans-nicotine N'-oxide, which is free or substantially free of cis-nicotine N'-oxide or has a content of at most 10% by weight of the cis-isomer, in a quantity of up to 5% by weight relative to the dry weight of the smoking product.
PATENTS ACT 1952

COMPLETE SPECIFICATION

(ORIGINAL)

FOR OFFICE USE

Short Title:

Int. Cl:

Application Number: 36420/84
Lodged:

Complete Specification—Lodged:
Accepted:
Lapsed:
Published:

Priority:

Related Art:

TO BE COMPLETED BY APPLICANT

Name of Applicant: B.A.T. CIGARETTEN-FABRIKEN GmbH

Address of Applicant: Alsterufer 4, 2000 HAMBURG 36, WEST GERMANY

Actual Inventor: Gerald Schmekel and Gert Rudolf

Address for Service: GRIFFITH HASSEL & FRAZER
71 YORK STREET
SYDNEY, N.S.W. 2000, AUSTRALIA

Complete Specification for the invention entitled: SMOKING PRODUCT CONTAINING NICOTINE N'-OXIDE

The following statement is a full description of this invention, including the best method of performing it known to me:

* Note: The description is to be typed in double spacing, pica type face, in an area not exceeding 250 mm in depth and 160 mm in width, on tough white paper of good quality and it is to be inserted inside this form.
The invention relates to a smoking product, in particular tobacco with or without a wrapper material, which contains nicotine N'-oxide.

It is known from "Die Nahrung", Volume 4, 1960, No. 4, pages 310 - 332, in particular page 322, Abstract or Summary, that nicotine N'-oxide contained in smoking tobacco forms nicotine on smoking and leads to an increase in the nicotine content of the mainstream smoke and sidestream smoke.

The invention is based on the discovery that the cis-isomer of nicotine N'-oxide causes a considerable deterioration in the taste of the smoke. Accordingly, the invention relates above all to a smoking product, the smoke of which has an increased nicotine content due to the addition of nicotine N'-oxide, wherein the abovementioned impairment of the taste of the smoke by the cis-isomer can be avoided.

The term "smoking product", used here, is to be understood as cut tobacco, pipe tobacco, cigarettes, cigarillos or cigars of tobacco with or without added non-tobacco materials and/or reconstituted tobacco. The smoking product of the invention can have been produced with or without a wrapper material, the possible wrapper materials used being cigarette paper, cigar wrappers or cigarillo wrappers of tobacco or non-tobacco materials.

According to the invention, the smoking product of the invention contains trans-nicotine N'-oxide, which is free or substantially free of cis-nicotine N'-oxide.
or has a content of at most 10% by weight of the cis-isomer, namely in a quantity of up to 5% by weight relative to the dry weight of the smoking product.

It has been found that a content of at most 10% by weight of the cis-isomer in the trans-isomer remains without adverse effects on the taste. Higher proportions of the cis-isomers of the order of magnitude of 10 to 30% by weight can be accepted, but then require certain taste-improving additives (flavors) which can mask the disadvantageous taste of the cis-isomer, albeit not completely.

The trans-nicotine N'-oxide which is to be used according to the invention and which is free or substantially free of cis-nicotine N'-oxide or has a content of at most 10% by weight of the cis-isomer, can have been added to the tobacco or to the non-tobacco materials contained therein and/or to the wrapper materials which may be present, for example the cigarette paper or the cigar or cigarillo wrappers of tobacco and/or non-tobacco materials. Advantageously, the nicotine N'-oxide is added, for example in the form of an aqueous solution, to the finished tobacco material or, for example in an alcoholic or aqueous-alcoholic solution, to the finished wrapper material.

Furthermore, the invention relates to a process for the preparation of trans-nicotine N'-oxide, which is free or substantially free of cis-nicotine N'-oxide, in particular for use as an additive to smoking products of the invention.

Mixtures of isomers of nicotine N'-oxide were
obtained for the first time by oxidation of nicotine with aqueous hydrogen peroxide, cf. Chem. Ber. 24, 61 - 67 (1891). An improvement of this process, using a nicotine/hydrogen peroxide molar ratio of 1 : 3, is described in J. Org. Chem. 24, 275 - 277 (1970). A disadvantage of this process is in particular the long reaction period of 2 - 3 days and the large excess of oxidizing agents, which prohibits economical exploitation of this process. In addition, it was not possible to isolate the resulting mixture of isomers of nicotine N'-oxide; it was necessary to isolate and characterize the end products as the picrates.

Substantially shorter oxidation periods can be obtained in the preparation of the mixture of isomers of nicotine N'-oxide when the oxidation is carried out with organic peracids in accordance with J. Org. Chem. 35, 1721 - 1722 (1970). However, the desired reaction products require more elaborate purification work; in addition, such a process for the preparation of nicotine N'-oxides is uneconomical because of the high price of organic peracids.

The invention therefore also relates to a process for the preparation of trans-nicotine N'-oxide which is free or substantially free of cis-nicotine N'-oxide, which process requires short reaction periods and in which, in addition, only auxiliary substances are used which are acceptably safe for humans.
of non-oxidizing inorganic and/or organic acids having a pK value of less than 5. The reaction temperature during the conversion should in every case be as low as possible, since higher reaction temperatures promote the formation of decomposition products and of the cis-isomer, even though the latter is produced only to a small extent. The reaction temperature should never be above 90°C, since otherwise explosive decompositions of the hydrogen peroxide can occur. Suitable catalytically active acids having a pK\textsubscript{a} value of less than 5 are especially monocarboxylic, dicarboxylic or polycarboxylic acids and their hydroxy derivatives, keto derivatives or unsaturated derivatives. The use of natural carboxylic, dicarboxylic or polycarboxylic acids occurring in tobacco, such as are known, for example, from Chem. Rev. \textbf{68}, 169 - 171 (1968), in particular malonic, succinic and malic acid, is preferred. The use of citric acid is particularly preferred.

The reaction of nicotine with hydrogen peroxide preferably takes place in substantially equimolar amounts, hydrogen peroxide being introduced first and nicotine being added dropwise; the converse process is also possible. The oxidizing agent used advantageously is commercially available hydrogen peroxide in the form of a 35-50% aqueous solution.

The acids used as catalysts are preferably employed in a quantity of 10-150, in particular 20-100, mmol per mol of nicotine.

It has proved to be advantageous for separating off the trans-isomer to be prepared according to the invention with advantage be carried out using 3-propanol (pore size 9 of water can be probed above the transition temperature of the oxide nicotine; the exothermic reason is preferential to nicotine; and is therefore advantageous operatively. The nicotine reaction reaction is singled out in the invention. The mixture is cooled to 15 according to the detail below embodiments.
invention when the oxidation mixture obtained in the oxidation is dehydrated. The dehydration can here preferably be carried out by azeotropic distillation, using n-propanol as the azeotropic entrainer. Remaining traces of water can be removed by means of a molecular sieve (pore size 4 Å) from the reaction mixture thus dried. The trans-nicotine N-oxide crystallizes in a pure form out of the dry oxidation mixture. It can be added to the tobacco and/or to the wrapper material in the manner described above, it being possible to extend it, for cost reasons, with up to 10% by weight of the cis-isomer.

The remaining cis-isomer left after working-up of the oxidation mixture is advantageously reduced to nicotine; the nicotine thus obtained can be oxidized again.

The oxidation of nicotine with hydrogen peroxide is exothermic and therefore causes safety problems. On an industrial scale, the process of the invention is therefore appropriately carried out in a partially continuous operation, hydrogen peroxide being introduced first and nicotine being added azeotropically for regulating the reaction rate and hence the heat evolved. It is to be singled out as a particular advantage of the process of the invention that, surprisingly, a colourless oxidation mixture is obtained when the catalysts to be employed according to the invention are used.

The process of the invention is explained in more detail below by reference to preferred illustrative embodiments.

Example 1.
Preparation of the trans-isomer of nicotine existing in the mixture of nicotinic acid, as described previously, containing 50% of water as entrainer. The mixture is then dried by azeotropic distillation, using n-propanol as the azeotropic entrainer. Remaining traces of water can be removed by means of a molecular sieve (pore size 4 Å) from the reaction mixture, thus dried. The trans-nicotine N-oxide crystallizes in a pure form out of the dry oxidation mixture. It can be added to the tobacco and/or to the wrapper material in the manner described above, it being possible to extend it, for cost reasons, with up to 10% by weight of the cis-isomer.

Example 2.
Preparation of the trans-isomer of nicotine by azeotropic distillation of nicotine, the trans-isomer being obtained, the mixture being freed of water as described above. The trans-nicotine N-oxide crystallizes in a pure form out of the dry oxidation mixture. It can be added to the tobacco and/or to the wrapper material in the manner described above, it being possible to extend it, for cost reasons, with up to 10% by weight of the cis-isomer.

Example 3.
Preparation of the trans-isomer of nicotine on a larger scale and in an industrial process. In
Example 1.
Preparation of a cis/trans mixture of nicotine N'-oxide.

500 g of nicotine (3.08 mol) are slowly added dropwise to an equimolar 30% hydrogen peroxide solution containing 5.9 g of citric acid (30.8 mmol), the temperature being maintained below 90°C. After the addition has ended, the mixture is heated at 80°C for 5 hours.

The colorless solution which is thus obtained and is free of nicotine and hydrogen peroxide can be directly processed further.

Example 2.
Preparation of pure trans-nicotine N'-oxide.

The solution obtained in Example 1 is dehydrated by azeotropic distillation with n-propanol. The dehydrated solution is finally dried with a molecular sieve (4 Å).

On cooling, pure trans-nicotine N'-oxide which can be filtered off with suction crystallizes out of the mixture thus obtained. The residual mother liquor contains predominantly cis-nicotine N'-oxide.

The method described here for the separation of the trans-isomer from the cis-isomer is considerably simpler than the process described for only analytical quantities in Phytochemistry, 14, 2683-2690 (1975), Pergamon Press, or in Biochemical Pharmacology 19, 733-742 (1970).

Example 3.
Preparation of trans-nicotine N'-oxide on a semi-technical
hydrogen peroxide solution (68 mol) and 125 g of citric
acid (0.65 mol) are introduced first and heated to 40°C;
the preheating is important for a rapid establishment of
the operating point during the addition of nicotine and
must therefore be carried out with care. Subsequently,
10 kg of nicotine (61.8 mol) are introduced into the reac-
tor (VN = 5 l/h), the operating point of about 80°C being
established by means of the heat of reaction evolved.
After nicotine has been introduced for two hours, the
reaction is completed in batch operation at 80°C, with
supply of heat. The conversion-time curve can here be
monitored spectroscopically, titrimetrically or
electrochemically.

After a total reaction period of 5 hours, a nicot-
ine conversion of 98% is obtained; the residual hydrogen
peroxide content is 1.5%. The resulting oily solution
of the oxidation products has a yellowish color and
exhibits no odor of nicotine.

The mixture obtained has a cis/trans ratio of the
nicotine N'-oxides of 1 : 1.67.

25 kg of n-propanol are added to the crude product
thus obtained and the mixture is distilled. n-Propanol/
water in a ratio of 75 : 25 then distills off as the azo-
trape. The reaction residue thus dehydrated is then fin-
ally dried with 5 kg of molecular sieve (4 Å) in 5 kg of
methylene chloride.

Pure trans-nicotine N'-oxide (4 kg; melting point
171-172°C) crystallizes out of the dry reaction mixture.
It is filtered off with suction, with addition of 5 kg
of acetone, and

Yield:
58.7% relative

Example 4.

In a re
(61.8 mol) at
40°C. Subse-
which 125 g of
are fed very s
10 kg pump. The
reaction tempe
volumetric tic
more rapid hav
on that the 4
75 After the hyd
2 hours), the
being supplied
hours, a nico-
dual hydrogen
20 due obtained
nicotine. Th
nicotine N'-

The de
25 added, and a
n-propanol/2
vacuum.

The water conten
of acetone, and is dried in a drying cabinet at 60°C.

Yield: 36.4% relative to nicotine employed, and
58.7% relative to trans-nicotine N'-oxide formed.

Example 4.

In a reactor with agitator, 10 kg of nicotine (61.8 moles) are introduced first and preheated to about
40°C. Subsequently, 4.62 kg (68 moles) of 50% H₂O₂, to
which 128 g of citric acid (0.65 mole) have been added,
are fed very slowly to the reactor with the aid of a meter-
ing pump. The rate of addition is adjusted such that a
reaction temperature of about 80°C is obtained. The
volumetric flow fed in depends on the reaction control,
more rapid heat removal being ensured by built-in cooling,
so that the feed volume per unit time can be increased.

After the hydrogen peroxide has been introduced (about
2 hours), the reaction is completed at 80°C with heat
being supplied. With a total reaction period of about 3
hours, a nicotine conversion of 98% is obtained; the resid-
ual hydrogen peroxide content is 1.5% by mass. The resi-
due obtained is a yellow, at first smoky and exhibits no odor of
nicotine. The cis/trans ratio of the two isomers of nicotine N'-oxides is 1:1.67.

The reaction mixture is subjected to acetic acid
dehydration. For this purpose, 10.6 kg of n-propanol are
added, and a water-containing distillate (75% by mass of
n-propanol/25% of water) is separated off under a slight
vacuum.

The residue is low in water and has a residual
water content of 7.7% by mass.

Example 5.

Nicotinization

The nicotine N'-oxide of Example 3 of a treated cigarette
is washed with water free of acetone.

The washed nicotine N'-oxide is dried, obtaining
10 kg of n-octatized nicotine N'-oxide in the form
of a yellowish powder.

Example 6.

Cigarette rod

A total of 15.66% is raised by means of a
smoke tube. The citrate is obtained by means of a
mixture of citrate, sucrose, and water.

Example 7.

Nicotinization

Antiseptic

200 ml

25 ml of a 20% n-propanol solution is added before the
back by a stream of air obtained from a color and me
Example 5.

Nicotinization of a cigarette rod.

The nicotine content of tobacco is raised by 1.13% to 2.62% by means of a 10% alcoholic solution of trans-
5 nicotine N'-oxide; the addition is effected by spraying
onto the tobacco material.

The cigarettes produced from the tobacco material,
thus obtained have, in a smoking test under DIN conditions,
a smoke nicotine yield which is increased by 0.3 mg. The
10 condensate content remains unchanged as compared with
untreated cigarettes.

Example 6.

Cigarette rod nicotinization.

A tobacco mixture having a nicotine content of
15 1.66% is raised to 6.1% nicotine content in the cut leaf
by means of a 20% aqueous trans-nicotine N'-oxide solu-
tion. The cigarettes subsequently produced from this
10 tobacco material give, in a smoking test under DIN condi-
tions, a smoke nicotine yield which is increased by 0.3 mg.
20 The condensate content did not change compared with un-
treated cigarettes.

Example 7.

Nicotinization of cigarette paper.

200 m of a cigarette paper web are moistened on
25 the back by means of rollers with a 10% trans-nicotine
N'-oxide solution in water/ethanol (1:1) and dried in
a stream of hot air. After drying, the cigarette paper
obtained resembles the untreated sample with respect to
color and mechanical strength, and contributes to a
nicotine increase in the smoke. The quantity of trans-
nicotine N'-oxide applied according to the process is 5% 
relative to the weight of the cigarette paper.

Example 8.

5 Nicotine compensation by addition of trans-nicotine N'-
oxide before an expansion process.

50 kg of a filler grade having a nicotine content of 1.6% by weight and a moisture content of 11% by weight are brought to an expansion moisture content of about 18% by weight by means of a trans-nicotine N'-oxide solution consisting of 4.3 l of water and 203 g of trans-nicotine 
N'-oxide.

The quantity of trans-nicotine N'-oxide applied compensates the 255 nicotine loss, which is always to be 
expected in tobacco expansion processes, so that the 
expanded tobacco can contribute with its original nicotine 
content to the preparation of the mixture.

This example clearly shows the advantage obtain-
able with an addition of trans-nicotine N'-oxide in tobacco 
material, the volume of which is to be increased in a 
conventional expansion step; this expansion is always con-
nected with a loss of nicotine.
CLAIMS
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A smoking product, in particular tobacco with or without a wrapper material, containing nicotine N'-oxide, which comprises trans-nicotine N'-oxide, which is free or substantially free of cis-nicotine N'-oxide or has a content of at most 10% by weight of the cis-isomer, in a quantity of up to 5% by weight relative to the dry weight of the smoking product.

2. A smoking product as claimed in claim 1, wherein the trans-nicotine N'-oxide, which is free or substantially free of cis-nicotine N'-oxide or has a content of at most 10% by weight of the cis-isomer, has been added to the tobacco and/or to the wrapper material.

3. A process for the preparation of trans-nicotine N'-oxide, which is free or substantially free of cis-nicotine N'-oxide, for use in a smoking product as claimed in claim 1 or 2, by oxidation of nicotine with aqueous HNO₃ solutions, wherein the oxidation is carried out in the presence of catalytic amounts of non-oxidizing inorganic and/or organic acids having a pH value of less than 5.

4. A process as claimed in claim 3, wherein CO₂ and
nicotine are added in substantially equimolar quantities.

5. A process as claimed in claim 3 or 4, wherein the 
   \( \text{H}_2\text{O}_2 \) is introduced first and the nicotine is added 
   dropwise.

6. A process as claimed in claim 4, wherein the nicotine 
   is introduced first and the \( \text{H}_2\text{O}_2 \) is added dropwise.

7. A process as claimed in any of claims 3 to 6, 
   wherein the \( \text{H}_2\text{O}_2 \) is used in the form of a 30-50% 
   aqueous solution.

8. A process as claimed in any of claims 3 to 7, 
   wherein the catalyst is added in a quantity of 10-150 mmol 
   per mol of nicotine.

9. A process as claimed in any of claims 3 to 8, 
   wherein natural carboxylic, dicarboxylic or polycarboxylic 
   acids occurring in tobacco are used as the catalyst.

10. A process as claimed in any of claims 3 to 9, 
    wherein citric acid is used as the catalyst.

11. A process as claimed in any of claims 3 to 10, 
    wherein the oxidation mixture obtained in the oxidation 
    is dehydrated.

12. A process as claimed in any of claims 3 to 11, 
    wherein the reaction mixture obtained in the oxidation is 
    dehydrated by azeotropic distillation.

13. A process as claimed in any of claims 3 to 12, 
    wherein \( n \)-propanol is used as the azeotropic entrainer.

14. A process as claimed in any of claims 3 to 13, 
    wherein traces of water are removed from the dried reaction 
    mixture by means of a molecular sieve.

15. A process as claimed in any of claims 3 to 14,
14. Wherein the trans-nicotine N'-oxide crystallizing out of the dry oxidation mixture is separated off.

16. A process for the preparation of trans-nicotine N'-oxide, which is free or substantially free of cis-nicotine N'-oxide, substantially as herein described with reference to the Examples.

17. A smoking product as defined in claim 1 or claim 2 substantially as herein described with reference to the Examples.

Dated this 7th day of December 1984

B.A.T. CIGARETTEN-TABRIKEN GmbH
By their Patent Attorney
GRiffith HASSel & FraZER
According to the invention, the smoking product of the invention contains trans-nicotine N'-oxide, which is free or substantially free of cis-nicotine N'-oxide.