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सुनवाई नोटिस का लिखित तर्क प्रस्तुत

Dated: 27/05/2023

To / सेवा मे

The Controller of Patents / पेटेंट नियंत्रक

Original Jurisdiction of Patent Office/ पेटेंट कार्यालय का मूल क्षेत्राधिकार: Mumbai

Application No / आवेदन संख्या: 201821012075

Applicant / आवेदक: AMI ORGANICS PVT. LTD.

Controller / नियंत्रक: Dr. Subramaniyan S P, Deputy Controller of Patents & Designs, Patent Office, Chennai

Date of issue of Hearing Notice/ सुनवाई सूचना जारी करने की तिथि: 25/04/2023

Hearing Date & Time/: 12/05/2023 at 12:00 PM

Location: Chennai

Normal period of filing Written Submission of Hearing / सुनवाई का लिखित प्रस्तुतीकरण दाखिल करने की सामान्य अवधि (15 days): 27/05/2023

Hearing mode: Video Conferencing

Hearing Attended by/ सुनवाई में भाग लिया: Arvind Patre (IN/PA-2929)

Respected Sir,

Sub: Reply to the hearing Notice dated 25/04/2023 in respect of Patent Application No. 201821012075

We are thankful to the Ld. Controller Dr. Subramaniyan S P, for giving us an opportunity of an oral hearing in this matter and also an opportunity to provide the further response after the hearing.

In reply to the objections raised in the Hearing Notice, the hearing was held before the Controller pertaining to the subject patent application (hereinafter referred to as 'the present application') on the scheduled date.

In reply to the Hearing Notice, the following amendments, observations, and submissions are respectfully submitted in connection with the above-identified application to meet the office objection(s) for consideration of the application in order for a grant.

SUMMARY

A total number of 1-15 claims were on record at the time of receiving the hearing Notice. The limitation of claim 7 and partial limitation of original claim 13 have been incorporated in claim 1 in order to meet the raised requirements. Consequently, claim 7 has been deleted. Further, as per the directions of the Ld. Controller during the hearing the statement related to purity of 4-methylene piperidine hydrochloride is deleted from claim 1. Still further, claim 15 has been deleted as directed by the Ld. Controller during the hearing. The dependencies of original claims 4, 5, 8 and 12 (amended claims 4, 5, 7 and 11) have been corrected appropriately.

The applicant submits that through such amendments, no new matter has been added and all the amendments are based on the original specification as filed and within the scope of the invention.

Table 1: List of amended, original and cancelled claims

Serial No	**Claim Number**		**Status**
	Old	**New**	
1.	1	1	Amended

2.	2-3	2-3	Original
3.	4	4	Amended
4.	5	5	Amended
5.	6	6	Original
6.	7	-	Deleted
7.	8	7	Amended
8.	9	8	Original
9.	10	9	Original
10.	11	10	Original
11.	12	11	Amended
12.	13	12	Amended
13.	14	13	Original
14.	15	-	Deleted

Invention u/s 2(1) (ja)

1. *The Ld. Controller is of the opinion that the applicant in his argument pointed out the difference in the temperature of the alkylation step of 1-benzylpiperidine-4-one between the present application and D1. In the present application, the step of alkylation of 1-benzylpiperidine-4-one is carried out at a temperature of 60 °C to 80 °C whereas in D1 the step of alkylation of N-benzylpiperidinone is carried out at a temperature of 20-30°C. But, the said difference in temperature did not produce any special technical effect over the prior art. Further, such a difference in the reaction parameter can be seen as a minor modification that can be achieved by the skilled person through routine experimental work without exercising any inventive skill. Hence, the objection raised in the FER u/s 2(1) (j) and 2(1) (ja) of the Patents Act, 1970 is still sustained.*

The Applicant respectfully disagrees with the Ld. Controller in view of the following explanation:

The present application claims a process for preparing 4-methylene piperidine hydrochloride comprising the following steps:

a. alkylating 1-benzylpiperidine-4-one to obtain 1-benzyl-4-methylidenepiperidine;

b. debenzylating 1-benzyl-4-methylidenepiperidine to obtain N-carbethoxy-4-methylene piperidine;
c. deprotecting N-carbethoxy-4-methylene piperidine to obtain 4-methylidenepiperidine; and
d. forming a salt of 4-methylidenepiperidine in the presence of a fluid medium to obtain 4-methylene piperidine hydrochloride;

wherein the step (a) of alkylation is carried out at a temperature in the range of 60 °C to 80 °C until completion of the alkylation;

wherein the step (b) of debenzylation is carried out at a temperature in the range of 0 °C to 10 °C until completion of the debenzylation; and

wherein the step (d) of salt formation is carried out using anhydrous hydrochloride gas;

wherein the fluid medium in step (d) of salt formation is dichloromethane.

The Applicant submits that 4-Methylenepiperidine is used as an active intermediate for the preparation of Effinaconazole, which is an effective anti-fungal drug. 4-methylenepiperidine moiety is used as a reactant in the final step of the preparation of Effinaconazole. The purity of obtained salt from methylenepiperidine of the present application is upto 99%, and which is an important factor as quality of 4-methylenepiperidine will significantly impact quality of final API product and hence temperature in step (a) i.e. alkylation step is an important factor for completion of reaction to get the defined purity.

Several methods are reported for synthesis of 4-methylenepiperidine. However, these methods are associated with drawbacks such as obtaining product with low yield and/or low purity. Further, these methods involve tedious purification, thereby resulting in an expensive process.

The object of the present application is to provide a process for the preparation of 4-methylenepiperidine hydrochloride which is economical and simple.

D1 discloses a process for the preparation of 4-methylenepiperidine hydrochloride.

The alkylation step (step-a) of claim 1 of the present application is carried out at a temperature in the range of 60°C to 80°C. Whereas, in D1 the alkylation of 1-benzylpiperidine-4-one is carried out at 20°C to 30°C. The teachings of present application are reverse to the teachings of D1. **The Applicant submits that when lower temperatures are used in the alkylation reaction the rate of reaction is very slow and the reaction does not lead to completion.** Further, the debenzylation step (Step-b) of claim 1 of the present application is carried out at a temperature of 0 °C to 10 °C. Whereas, in D1 the debenzylation of 1-benzyl-4-methylidenepiperidine is carried out at a temperature of 55°C to 60°C. The teachings of the present application are reverse to the teachings of D1. D1 teaches that lower temperatures used to carry out debenzylation decreased the yield. (*Kindly refer lines 7-8 and table 2 on page 8 of D1*). Table 2 of D1 has been illustrated below for the ready reference of the Ld. Controller.

Table 2 Optimization Results of the *N*-Debenzylation Reaction

entry	$ClCO_2Et$ (equiv)	Na_2CO_3 (equiv)	temp (°C)	time (h)	conversion [b,c] (%)	15 [c,d] (area %)
1	2.5	0.1	85-90	1.5	99.7	92.5
2	1.02	0.1	85-90	8	93	83.6
3	1.1	0.1	85-90	3	99.6	95.7
4	1.1	0.1	35-40	10	82.3	81.5
5	1.1	0.1	55-60	4	99.7	97.8

[a] Conditions: **4** (10g scale), magnetic stirring. All reagents were charged followed by a nitrogen purge. [b] Conversion was calculated from the HPLC area. [c] Detected by HPLC. [d]

From entry 4 on table 2 of D1 it can be seen that as the reaction is carried out at a lower temperature (35°C-40°C) the yield of debenzylated product decreases. The debenzylation reaction carried out at higher temperature in the presence of a base as

taught by D1 would result in formation of side products/impurities and may impact the quality or purity of debenzylated product. Taking into consideration difficulties in the process, the applicant has further carried out the research and optimized the process steps in such a way that difficulties in the process will be sorted out.

It is pertinent to mention that it is an outcome of extensive research work by the inventors of the present invention as a function of several permutations and combinations and experiments conducted, which involve absolute technical knowledge, skill or input of the inventor. After an exhaustive study of each of the process steps for preparing 4-methylene piperidine hydrochloride, and considering the lacuna in the conventional prior arts; the applicant has newly devised each of the process steps, optimized the process steps, which enhanced the performance of the claimed process, and in its form is novel and inventive.

Nothing in the description or teachings of **D1** discloses or suggests essential inventive feature of amended claim 1 of the present application.

Therefore, a person skilled in the art after referring to D1 would not at all be motivated to carry out the alkylation reaction at 60°C to 80°C instead of 20°C to 30°C as taught by D1. Further, a person skilled in the art would not at all be motivated to carry out the debenzylation reaction at 0°C to 10°C instead of 55°C to 60°C as taught by D1. The use of specific temperatures in alkylation and debenzylation steps results in high purity as good as 95% to 99% of the product obtained.

Further, in the present application the step (d) of salt formation is carried out using anhydrous hydrochloride gas whereas in D1 the step of salt formation is carried out using 20% HCl/EtOH.

In the present application step (d) of salt formation is carried out in a specific fluid medium dichloromethane. Whereas, in D1 the salt formation is carried out in IPA and ethanol.

In the process of the present application, the product 1-benzyl-4-methylidenepiperidine obtained in the first step (a) of alkylation is directly used in the second step (b) of debenzylation without isolating the same as clearly revealed from the experiment. Similarly, even the product of step (c) N-carbethoxy-4-methylene piperidine is used in the fourth step (d) without isolating the same as clearly revealed from the experiment. Hence, the process of the present application is simple and employs inexpensive and easily available reagents. Thus, the process of the present application is economical.

Further, the process of the present application does not involve tedious purification steps, thereby resulting in an economical process.

The cited document D1 does not disclose the specific alkylation and debenzylation temperatures as well as anhydrous hydrochloride gas and dichloromethane as fluid medium in step (d) of salt formation which results in high purity of 4-methylenepiperidine hydrochloride of the present application.

Specific parameters are required for each of the steps and have advancement due to these features. For example debenzylation carried out at much lower temperature of 0°C to 10°C without the use of base prevents the degradation of product compared to prior art where much high temperature and base are used.

Due to the use of anhydrous HCl gas, recovery of single solvent is possible as well as use of mixture of solvents is avoided.

In view of the above explanation, amended claim 1 is inventive over the cited document D1. Original claims 2-14 (amended claims 2-13) are inventive by virtue of dependency on claim 1 directly or indirectly.

In view of the above explanation, the Ld. Controller is requested to waive the objection.

Non-Patentability u/s 3

1. Further, the Ld. Controller is of the opinion that the objection raised u/s 3(d) of the Patents Act, 1970 is still sustained because the subject matter of amended claims 1-15 is related to a process for preparing 4-methylene piperidine hydrochloride which does not result in a new product or employs at least one new reactant. Therefore, the said claims are not allowable.

The Applicant respectfully disagrees with the Ld. Controller in view of the following explanation:

The present application discloses a simple and economical process for preparing 4-methylene piperidine hydrochloride.

Conventionally several methods are reported for the synthesis of 4-methylenepiperidine. However, these methods are associated with drawbacks such as obtaining product with low yield and/or low purity. Further, these methods involve tedious purification, thereby resulting in an expensive process.

As stated above in the reply to objection of inventive step the process of preparation of 4-methylene piperidine hydrochloride of the present application is entirely different than the process of preparation of 4-methylenepiperidine hydrochloride of D1. The alkylation step (step-a) of claim 1 of the present application is carried out at a temperature in the range of 60°C to 80°C. Whereas, in D1 the alkylation of 1-benzylpiperidine-4-one is carried out at 20°C to 30°C. In the present application, the purity of obtained salt from methylenepiperidine is upto 99%, and which is an important factor as quality of 4-methylenepiperidine will significantly impact quality of final API product.

The teachings of present application are reverse to the teachings of D1, for instance applicant optimized the process steps by exactly reversing temperature parameters. The Applicant submits that when lower temperatures are used in the alkylation reaction the rate of reaction is very slow and the reaction does not lead to completion.

Further, the debenzylation step (Step-b) of claim 1 of the present application is carried out at a temperature of 0 °C to 10 °C. Whereas, in D1 the debenzylation of 1-benzyl-4-methylidenepiperidine is carried out at a temperature of 55-60°C. D1 teaches that lower temperatures used to carry out debenzylation decreased the yield. (*Kindly refer lines 7-8 and table 2 on page 8 of D1*). Table 2 of D1 has been illustrated below for the ready reference of the Ld. Controller.

Table 2 Optimization Results of the *N*-Debenzylation Reaction

entry	$ClCO_2Et$ (equiv)	Na_2CO_3 (equiv)	temp (°C)	time (h)	conversion [b,c] (%)	15 [c,d] (area %)
1	2.5	0.1	85-90	1.5	99.7	92.5
2	1.02	0.1	85-90	8	93	83.6
3	1.1	0.1	85-90	3	99.6	95.7
4	1.1	0.1	35-40	10	82.3	81.5
5	1.1	0.1	55-60	4	99.7	97.8

[a] Conditions: **4** (10g scale), magnetic stirring. All reagents were charged followed by a nitrogen purge. [b] Conversion was calculated from the HPLC area. [c] Detected by HPLC. [d]

From entry 4 on table 2 of D1 it can be seen that as the reaction is carried out at a lower temperature the yield of debenzylated product decreases. The debenzylation reaction carried out at higher temperature as taught by D1 would result in formation of side products/impurities.

Therefore, a person skilled in the art after referring to D1 would not at all be motivated to carry out the alkylation reaction at 60°C to 80°C instead of 20°C to 30°C as taught by D1. Further, a person skilled in the art would not at all be motivated to carry out the debenzylation reaction at 0°C to 10°C instead of 55°C to 60°C as taught by D1. The use of specific temperatures in alkylation and debenzylation steps results in high purity as good as 95% to 99% of the product obtained. Further, the solvents used in salt formation are also different in the present application and D1 and important one considering optimizing the process steps in the present application. In the present application anhydrous HCl is used for salt formation whereas in D1 20% HCl/EtOH is used which is also important to get the purity of 4-methylene piperidine hydrochloride upto 99%.

In the process of the present application, the product 1-benzyl-4-methylidenepiperidine obtained in the first step (a) of alkylation is directly used in the second step (b) of

debenzylation as clearly revealed from the experiment. Similarly, even the product of step (c) N-carbethoxy-4-methylene piperidine is used in the fourth step (d) without isolating the same as clearly revealed from the experiment. This is also important as intermediates obtained in steps (a) and (c) are obtained with high purity and therefore are used directly in the next step without further purification. High purity of N-carbethoxy-4-methylene piperidine (4-methylidenepiperidine-1-carboxylate (IV)) helps in obtaining high purity of final product 4-methylidene piperidine hydrochloride. The process of the present application avoids tedious purification steps.

So, the process of the present application is simple and employs inexpensive and easily available reagents. Thus, the process of the present application is economical.
Therefore, the use of specific alkylation and debenzylation temperatures, and use of reactants like anhydrous hydrochloride gas and specific fluid medium like dichloromethane in step (d) of salt formation results in the formation of 4-methylenepiperidine with a high purity as good as 95% to 99%.

Therefore, the process claimed in original claims 1-15 (amended claims 1-13) of the present application is a new one and not a mere use of known process and hence does not attract Section 3(d) of the Patent Act and rather exception to it.

Scope

1. Features of Claim 15 beyond the scope of claim 1.

Original claim 15 has been deleted as directed by the Ld. Controller during the hearing. Therefore, the objection pertaining to same is rendered moot.

Sufficiency of Disclosure u/s 10 (4)

1. The applicant fails to comply with section 10(4) (c) of the patents act 1970 because the invention in principle claim 1 is not sufficiently disclosed. Various necessary parameters of the reaction such as temperature, time, amount and type of catalyst and solvent, etc. should be clearly defined as well as brought out in the main claim for a better understanding of the scope of the present application.

Claim 1 has been amended by incorporating the limitations of original claim 7 and partial limitations of original claim 13. The necessary parameters like temperature of debenzylation, specific use of reactants like anhydrous hydrochloride gas and fluid medium such as dichloromethane in step (d) of salt formation results in the formation of 4-methylene piperidine hydrochloride with a high purity in the range of 95% to 99%.
Therefore, all the necessary parameters have been included in amended claim 1.
In view of the above explanation, the Ld. Controller is requested to waive the objection and allow the application for a grant.

PRAYER

It is therefore submitted that:

(a) in view of the detailed observations submitted herein, the office objections may be dropped, withdrawn or waived, as the case may be;

(b) since all office requirement(s) have been met by the Applicant the application may be favorably considered for early grant without a hearing;

(c) alternatively a hearing opportunity may be given to the Applicant under Section 14, in the interest of natural justice in case of any outstanding issue/objections;

(d) In case, the applicant is unable to attend a hearing either because of non-receipt of the hearing notice or mail failure of hearing notice due to technical snag at the Patent Office server or due to any other reason, the applicant's authorized attorney may be reached over phone on the scheduled hearing date to ascertain the status/intention of the applicant.

Even if the applicant has not appeared for a hearing for whatsoever reason, the Controller is requested to proceed with the application as per the provisions of Rule 28(5) to be read along with Section 15 and 80

Rule 28(5) *After hearing the applicant, or* ***without a hearing*** *if the applicant has not attended or has notified that he does not desire to be heard, the Controller may specify or permit such amendment of the specification as he thinks fit to be made.*

(e) if any further requirement or clarification is required by the Controller, the Applicant is ready to consider the amendments proposed by the Controller to his satisfaction under the provisions of **Section 15, Rule 28(5)** prior to the Controller passing an order in this matter.

(f) in case, the Controller, prima facie, after going through the written submission has an adverse opinion to the applicant's interest, a further hearing opportunity may be given under Section 80.

DATED 27 May 2023

ARVIND TARACHAND PATRE (IN/PA-2929)
of R.K.DEWAN & COMPANY
AGENT FOR THE APPLICANT

TO
THE CONTROLLER OF PATENTS
THE PATENT OFFICE, AT MUMBAI

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Enclosures:
1. Amended claims (marked and clean copy).

WE CLAIM:

1. A process for preparing 4-methylene piperidine hydrochloride comprising the following steps:

    a. alkylating 1-benzylpiperidine-4-one to obtain 1-benzyl-4-methylidenepiperidine;

    b. debenzylating 1-benzyl-4-methylidenepiperidine to obtain N-carbethoxy-4-methylene piperidine;

    c. deprotecting N-carbethoxy-4-methylene piperidine to obtain 4-methylidenepiperidine; and

    d. forming a salt of 4-methylidenepiperidine in the presence of a fluid medium to obtain 4-methylene piperidine hydrochloride ~~having purity in the range of 95% to 99%~~;

    wherein the step (a) of alkylation is carried out at a temperature in the range of 60 °C to 80 °C until completion of the alkylation;~~.~~

    wherein the step (b) of debenzylation is carried out at a temperature in the range of 0 °C to 10 °C until completion of the debenzylation; and

    wherein the step (d) of salt formation is carried out using anhydrous hydrochloride gas;

    wherein the fluid medium in step (d) of salt formation is dichloromethane.

2. The process as claimed in claim 1, wherein the step (a) of alkylation is carried out using methyl triphenylphosphonium bromide as an alkylating agent; in the presence of an alkali selected from the group consisting of sodium methoxide, sodium ethoxide and sodium t-butoxide; and a first fluid medium selected from the group consisting of toluene, tetrahydrofuran and ether.

3. The process as claimed in claim 1, wherein the step (a) of alkylation comprises the step of adding 1-benzylpiperidine-4-one and the alkylating agent in parts of equal volume to a mixture comprising the alkali and the first fluid medium over a period of time in the range of 20 to 40 minutes.

4. The process as claimed in claim ~~-~~2 ~~1~~, wherein the molar ratio of 1-benzylpiperidine-4-one and the alkali is in the range of 1: 20 to 1: 25.

5. The process as claimed in claim ~~-~~2 ~~1~~, wherein the molar ratio of 1-benzylpiperidine-4-one and the alkylating agent is in the range of 1: 1 to 1: 3.

6. The process as claimed in claim 1, wherein the step (b) of debenzylation is carried out using ethyl chloroformate in the presence of a second fluid medium selected from the group consisting of toluene, tetrahydrofuran and ether.

~~7. The process as claimed in claim 1, wherein the step (b) of debenzylation is carried out at a temperature in the range of 0 °C to 10 °C until completion of the debenzylation.~~

~~8.~~7.The process as claimed in claim ~~–~~6 ~~1~~, wherein the molar ratio of 1-benzyl-4-methylidenepiperidine and ethyl chloroformate is in the range of 1: 10 to 1: 15.

~~9.~~8.The process as claimed in claim 1, wherein the step (b) of debenzylation further comprises treating N-carbethoxy-4-methylene piperidine with diethyl ether to obtain N-carbethoxy-4-methylene piperidine having purity in the range of 95% to 99%.

~~10.~~9. The process as claimed in claim 1, wherein the step of (c) of de-protection is carried out using a base selected from sodium hydroxide and potassium hydroxide and in the presence of a third fluid medium selected from ethylene glycol and di-ethylene glycol.

~~11.~~10. The process as claimed in claim 1, wherein the step of (c) of de-protection is carried out at a temperature in the range of 100 °C to 130 °C until completion of the deprotection.

~~12.~~11. The process as claimed in claim ~~–~~9 ~~1~~, wherein the molar ratio of N-carbethoxy-4-methylene piperidine and the base is in the range of 1: 5 to 1: 10.

~~13.~~12. The process as claimed in claim 1, wherein the step (d) of salt formation is carried out ~~using anhydrous hydrochloride gas and in the presence of a fourth fluid medium selected from the group consisting of dichloromethane, dichloroethane, and acetonitrile and~~ at a temperature 0°C to 10 °C.

~~14.~~13. The process as claimed in claim 1, wherein the step (d) of salt formation further comprises treating 4-methylene piperidine hydrochloride with acetone at a temperature 0 °C to 5 °C to obtain 4-methylene piperidine hydrochloride having purity in the range of 95% to 99%.

15. The process as claimed in claim 1 comprising:

i. charging a first reactor with sodium methoxide and toluene under stirring, followed by heating at 70°C to obtain a first mixture; adding methyl triphenylphosphonium bromide and N-benzyl piperidone to said first mixture over a period of 20 minutes in 10 parts of equal volumes; and continuing heating at 70°C until complete consumption of N-benzyl piperidone to obtain a first product mixture comprising 1-benzyl-4-methylidenepiperidine;

ii. washing said first product mixture with water to obtain a first organic layer comprising 1-benzyl-4-methylidenepiperidine;

iii. cooling first organic layer comprising 1-benzyl-4-methylidenepiperidine to 5 °C in a second reactor; followed by addition of ethyl chloroformate in drop-wise manner and continuing stirring at 5 °C until complete consumption of 1-benzyl-4-methylidenepiperidine to obtain a second product mixture comparing N-carbethoxy-4-methylene piperidine;

iv. washing said second product mixture with water to obtain a second organic layer comprising N-carbethoxy-4-methylene piperidine; removing the volatiles present in said second organic layer under reduced pressure to obtain first residue comprising N-carbethoxy-4-methylene piperidine; treating said first residue with diethyl ether to obtain N-carbethoxy-4-methylene piperidine having purity in the range of 95% to 99%;

v. charging a third reactor with N-carbethoxy-4-methylene piperidine and mono-ethylene glycol to obtain a third mixture; adding aqueous solution of potassium hydroxide in drop-wise manner to said third mixture; followed by heating at 110 °C until complete consumption of N-carbethoxy-4-methylene piperidine to obtain a third product mixture comprising 4-methylidenepiperidine; and

vi. cooling said third product mixture comprising 4-methylidenepiperidine to 10 °C; and diluting said cooled third product mixture with methylene dichloride to obtain a fourth mixture; cooling said fourth mixture to 5 °C and purging anhydrous hydrochloride gas through said cooled fourth mixture till pH of the resultant mixture is 1 to obtain a fourth product mixture comprising 4-methylene piperidine hydrochloride;

vii. removing the volatiles present in said fourth product mixture under reduced pressure to obtain a second residue comprising 4-methylene piperidine hydrochloride; treating said second residue with acetone to obtain 4-methylene piperidine hydrochloride having purity in the range of 95% to 99%.

Dated this 27th day of March, 2019

MOHAN RAJKUMAR DEWAN (IN/PA-25)
of R.K. DEWAN & COMPANY
APPLICANT'S PATENT ATTORNEY

TO,
THE CONTROLLER OF PATENTS,
THE PATENT OFFICE, AT MUMBAI

WE CLAIM:

1. A process for preparing 4-methylene piperidine hydrochloride comprising the following steps:

    a. alkylating 1-benzylpiperidine-4-one to obtain 1-benzyl-4-methylidenepiperidine;

    b. debenzylating 1-benzyl-4-methylidenepiperidine to obtain N-carbethoxy-4-methylene piperidine;

    c. deprotecting N-carbethoxy-4-methylene piperidine to obtain 4-methylidenepiperidine; and

    d. forming a salt of 4-methylidenepiperidine in the presence of a fluid medium to obtain 4-methylene piperidine hydrochloride;

    wherein the step (a) of alkylation is carried out at a temperature in the range of 60 °C to 80 °C until completion of the alkylation;

    wherein the step (b) of debenzylation is carried out at a temperature in the range of 0 °C to 10 °C until completion of the debenzylation; and

    wherein the step (d) of salt formation is carried out using anhydrous hydrochloride gas;

    wherein the fluid medium in step (d) of salt formation is dichloromethane.

2. The process as claimed in claim 1, wherein the step (a) of alkylation is carried out using methyl triphenylphosphonium bromide as an alkylating agent; in the presence of an alkali selected from the group consisting of sodium methoxide, sodium ethoxide and sodium t-butoxide; and a first fluid medium selected from the group consisting of toluene, tetrahydrofuran and ether.

3. The process as claimed in claim 1, wherein the step (a) of alkylation comprises the step of adding 1-benzylpiperidine-4-one and the alkylating agent in parts of equal volume to a mixture comprising the alkali and the first fluid medium over a period of time in the range of 20 to 40 minutes.

4. The process as claimed in claim 2 , wherein the molar ratio of 1-benzylpiperidine-4-one and the alkali is in the range of 1: 20 to 1: 25.

5. The process as claimed in claim 2 , wherein the molar ratio of 1-benzylpiperidine-4-one and the alkylating agent is in the range of 1: 1 to 1: 3.

6. The process as claimed in claim 1, wherein the step (b) of debenzylation is carried out using ethyl chloroformate in the presence of a second fluid medium selected from the group consisting of toluene, tetrahydrofuran and ether.

7. The process as claimed in claim 6, wherein the molar ratio of 1-benzyl-4-methylidenepiperidine and ethyl chloroformate is in the range of 1: 10 to 1: 15.

8. The process as claimed in claim 1, wherein the step (b) of debenzylation further comprises treating N-carbethoxy-4-methylene piperidine with diethyl ether to obtain N-carbethoxy-4-methylene piperidine having purity in the range of 95% to 99%.

9. The process as claimed in claim 1, wherein the step of (c) of de-protection is carried out using a base selected from sodium hydroxide and potassium hydroxide and in the presence of a third fluid medium selected from ethylene glycol and di-ethylene glycol.

10. The process as claimed in claim 1, wherein the step of (c) of de-protection is carried out at a temperature in the range of 100 °C to 130 °C until completion of the deprotection.

11. The process as claimed in claim 9, wherein the molar ratio of N-carbethoxy-4-methylene piperidine and the base is in the range of 1: 5 to 1: 10.

12. The process as claimed in claim 1, wherein the step (d) of salt formation is carried out at a temperature 0°C to 10 °C.

13. The process as claimed in claim 1, wherein the step (d) of salt formation further comprises treating 4-methylene piperidine hydrochloride with acetone at a temperature 0 °C to 5 °C to obtain 4-methylene piperidine hydrochloride having purity in the range of 95% to 99%.

Dated this 27th day of March, 2019

MOHAN RAJKUMAR DEWAN (IN/PA-25)
of R.K. DEWAN & COMPANY
APPLICANT'S PATENT ATTORNEY

TO,
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