PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference OP111065	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/CN2011/082432	International filing date *(day/month/year)* 18 November 2011 (18.11.2011)	Priority date *(day/month/year)* 19 November 2010 (19.11.2010)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant ZHEJIANG JIUZHOU PHARMA SCIENCE & TECHNOLOGY CO., LTD.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 12 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 21 May 2013 (21.05.2013)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Lingfei Bai e-mail: pt02.pct@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	01.03.2012
Applicant's or agent's file reference OP111065	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CN2011/082432	18.11.2011	19.11.2010

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

C07F9/58, B01J31/24, C07B53/00, C07C29/145, C07C33/22, C07C33/18, C07C33/46, C07C35/36, C07C35/32, C07C31/135, C07C33/28, C07C41/26, C07C43/23, C07C67/31, C07C69/732, C07C69/734, C07C69/68, C07C69/675, C07D307/83

Applicant

ZHEJIANG JIUZHOU PHARMACEUTICAL CO., LTD.

1. This opinion contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☒	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CN	Date of completion of this opinion	Authorized officer
Facsimile No.		Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CN2011/082432

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into _____ , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:

   a. (means)

      ☐ on paper

      ☐ in electronic form

   b. (time)

      ☐ in the international application as filed

      ☐ together with the international application in electronic form

      ☐ subsequently to this Authority for the purposes of search

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. II Priority

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

The priority does not mention certain groups such as R^1, R^2-R^5, and R^8-R^9 in claim 1; in particular R^1 = C_{1-8} aliphatic alkyl or saturated cyclic alkyl or cycloalkenyl (the priority mentions an alkyl group) group, and the substituent on the phenyl group is halogen; R^2-R^5 = C_{1-8} alkoxyl; R^8-R^9 = halogen, and the substituent on the phenyl group is halogen, thus meaning that the subject matter of claim 1 is not disclosed in the priority. The compound of the general formula defined by the group of claim 2 is not disclosed in the priority. Thus, the subject matter of claims 1 and 2 does not share the priority of CN 201010550836.0; the filing date of 18.11.2011 is considered as the relevant date. The PX documents listed in the search report are prior art documents influencing the novelty and inventive step of claims 1 and 2.

Where the compounds of claims 1 and 2 are involved, the process for preparing the chiral compound of claims 4-8, the chiral catalyst of claims 9-11, and the reduction method using the chiral catalyst or chiral compound of claims 12-20 all correspondingly do not share the priority of CN 201010550836.0; the filing date of 18.11.2011 is considered as the relevant date. The PX documents listed in the search report are prior art documentsinfluencing the novelty and inventive step of claims 4-20.

Box No. II **Priority**

The priority (see claim 2) discloses the subject matter of claim 3 of the present application. Therefore, claim 3 shares the priority of CN 201010550836.0. Thus, the priority date of 19.11.2010 is considered as the relevant date. The PX documents listed in the search report are not prior art documents influencing the novelty and inventive step of claim 3.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. V **Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	3	YES
	Claims	1-2, 4-20	NO
Inventive step (IS)	Claims	3	YES
	Claims	1-2, 4-20	NO
Industrial applicability (IA)	Claims	1-20	YES
	Claims		NO

2. Citations and explanations:

2.1 Reference is made to the following documents:

D1: CN 102040625 A (Nankai University) 04 May 2011 (04.05.2011), see claims 1-10 and embodiments 1 and 11;

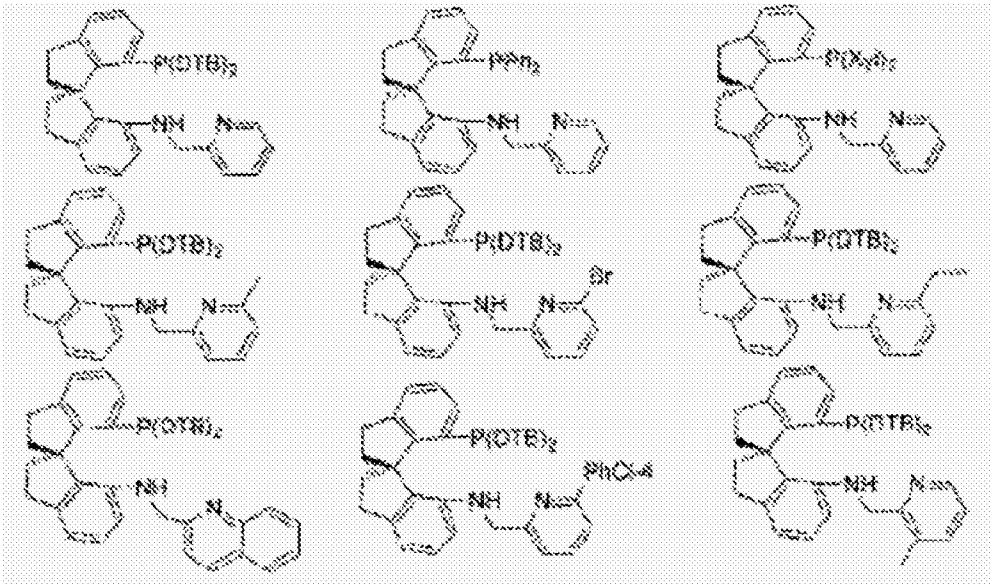
D2: CN 101671365 A (Nankai University) 17 March 2010 (17.03.2010), see the whole document, especially claims 1 and 2.

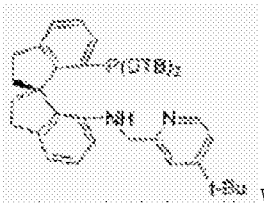
2.2 Assessment of Novelty

Claims 1-2 relate to a chiral spiro pyridinylamino phosphine compound of general formula I; claim 3 relates to particular compounds corresponding to the general formula; claims 4-8 relate to a process for preparing the chiral compound; claims 9-11 relate to a chiral catalyst containing the compound; and claims 12-20 relate to a process for synthesizing an alcohol using the chiral catalyst.

D1 is considered to be the prior art document closest to claims 1-2, and 4-20. D1 discloses a chiral spiro pyridinylamino phosphine compound of general formula I (see claim 1); the particular compounds disclosed in claim 3 of D1 (see the following figures)

fall into the scopes of claims 1 and 2 of the present application; therefore, with respect to D1, claims 1 and 2 are not novel and do not meet the requirements of PCT Article 33(2).





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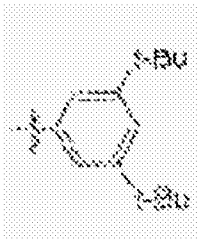
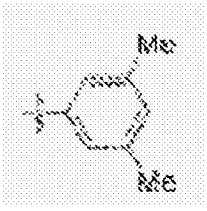
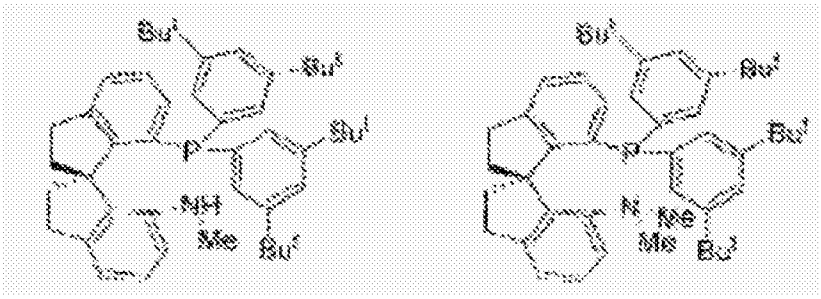


xyl is:

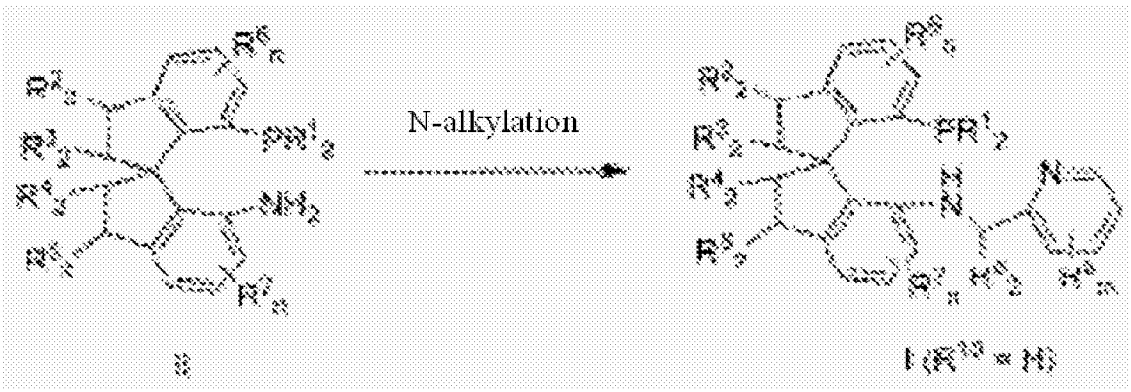


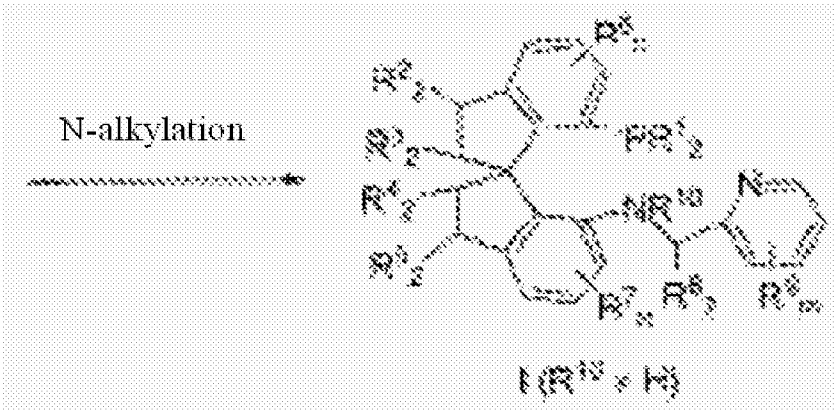
D2 is the prior art document closest to claim 3. The following compounds disclosed in claim 2 of D2 are closest to the compound of claim 3 in the present application, and are different in the substituent on the amino group; in claim 3 of the present application, the group is a substituted or unsubstituted pyridinylmethyl group, whereas in D2 it is a methyl group or hydrogen.

Thus, D1 does not explicitly or implicitly disclose the subject matter of claim 3. Hence, according to D1, claim 3 is novel, and meets the requirements of PCT Article 33(2).



Claim 3 in D1 discloses the following reaction process, and where it refers to claim 2 falls into the protective scope of claim 4 of the present application; therefore according to D1, claim 4 is not novel, and does not meet the requirements of PCT Article 33(2).





The reaction process of claim 4 in D1 is identical

to that of claim 5 in the present application; where the reaction process is defined as the process for preparing a particular compound of claim 2, this technical solution falls into the scope of claim 5 of the present application. Hence, with respect to D1, claim 5 lacks novelty, and does not meet the requirements of PCT Article 33(2). Claim 4 in D1 discloses the additional technical features of claims 6-8 of the present application; where the claim to which claims 6-8 refer is not novel, claims 6-8 also lack novelty, and do not meet the requirements of PCT Article 33(2). Where the compound of claim 2 in D1 is used as a raw material, the chiral catalyst of claim 8 in D1 falls in the scope of claims 9-11 of the present application; therefore, with respect to D1, claims 9-11 lack novelty, and do not meet the requirements of PCT Article 33(2).

Embodiment 11 of D1 discloses a process for first synthesizing a chiral catalyst and then reducing the substrate, wherein in the section of reduction, D1 discloses that the substrate is a carbonyl compound, the pressure is 8-10 atm, the reduction time is 10 minutes to 24 hours, the base added is potassium tert-butanoxide and the solvent is ethanol. Hence, the process in the embodiment falls into the scope of claims 12-15 of the present application, and claims 12-15 lack novelty, and do not meet the requirements of PCT Article 33(2). D1 discloses in embodiment 11 in the section of synthesizing a chiral catalyst that ethanol is the solvent, stirring is carried out for 1 hour at room temperature, and then a hydrogen atmosphere of 1 atm is maintained for 1 hour; and the reduction section is disclosed as above. Hence, the technical solution in the embodiments falls into the

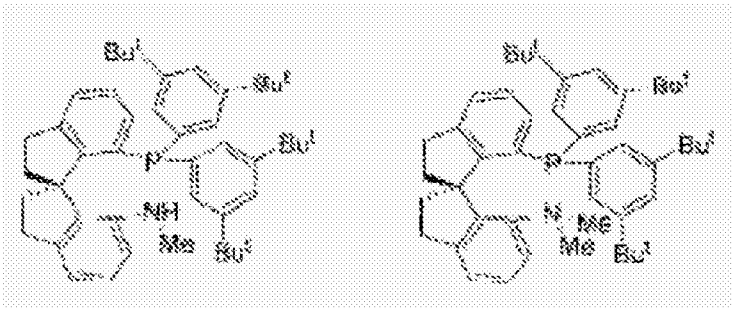
scope of claims 16-20 of the present application, and claims 16-20 lack novelty, and do not meet the requirements of PCT Article 33(2).

2.3 Assessment of Inventive Step

D1 is the prior art document closest to claims 1 and 2 and 4-20. With respect to D1, claims 1 and 2, and 4-20 lack novelty. Therefore, the subject matter of these claims would be obvious to a person skilled in the art. That is to say, with respect to D1, claims 1 and 2 and 4-20 do not involve an inventive step, and do not meet the requirements of PCT Article 33(3).

D2 is the prior art document closest to claim 3. The following compounds disclosed in claim 2 of D2 are closest to the compound of claim 3 in the present application, and the compounds are different in the substituent on the amino group; in claim 3 of the present application, the group is a substituted or unsubstituted pyridinylmethyl group, whereas in D2 it is a methyl group or hydrogen. Therefore, the technical problem to be solved in claim 3 of the present application is to provide a new chiral spiro pyridinylamino phosphine compound able to be used as a catalytic reductant. In the art, the volumes and properties of the substituents determine the catalytic performance of the resulting compounds. When a hydrogen in a methyl group on the amino group is substituted by a (substituted) pyridinyl group in the following compounds disclosed in D2, the structure of the substance varies greatly. Based on D2 or by combining D2 with common knowledge, a person skilled in the art could not foresee that the resulting compound after such a relatively large change would still have a

similar catalytic performance. That is to say such a change needs inventive effort. Hence, with respect to D2, the compound of claim 3 involves an inventive step, and meets the requirements of PCT Article 33(3).



2.4 Assessment of Industrial Applicability:

Claims 1-20 can be used in the field of catalytic chemistry, thus these claims are industrially applicable and meet the requirements of PCT Article 33(4).

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CN2011/082432

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1. In the definitions of the groups in claim 1, heteroaryl group and furanyl and thienyl groups appear many times in juxtaposition, but both the furanyl and thienyl groups belong to the heteroaryl group; thus such a definition renders the protective scope of claim 1 unclear, and does not meet the requirements of PCT Article 6.