

SEARCH REPORT

Application Number

LH 28

LT 2021528

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X,D	ZHENG JING ET AL: "Elaboration of thorough simplified vinca alkaloids as antimitotic agents based on pharmacophore similarity", EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, ELSEVIER, AMSTERDAM, NL, vol. 65, 3 May 2013 (2013-05-03), pages 158-167, XP028677359, ISSN: 0223-5234, DOI: 10.1016/J.EJMECH.2013.04.057 * page 165 - page 166; compounds 7a, 7b, 7c, 7p *	1-3	INV. C07D209/12 C07D209/14 C07B37/06
X,D	CN 102 942 515 A (UNIV JINAN) 27 February 2013 (2013-02-27) * page 6; compounds 2, 3 * * page 5, paragraph 0018 - page 6, paragraph 0027 *	1-3	
X	US 3 346 571 A (SPATZ SYDNEY M ET AL) 10 October 1967 (1967-10-10) * figure 2; compound 5 *	2,3	TECHNICAL FIELDS SEARCHED (IPC) C07D C07B
1 The present search report has been drawn up for all claims			
Munich		Date of completion of the search 26 January 2022	Examiner Miniejew, Catherine
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			

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

**LH 28
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This annex lists the patent family members relating to the patent documents cited in the above-mentioned 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.

26-01-2022

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
CN 102942515	A	27-02-2013	NONE		

US 3346571	A	10-10-1967	BE	648567 A	16-09-1964
			DE	1445447 A1	13-02-1969
			GB	1060758 A	08-03-1967
			LU	46195 A1	01-01-1972
			NL	6406262 A	07-12-1964
			US	3346571 A	10-10-1967

WRITTEN OPINION

File No. LH28	Filing date (<i>day/month/year</i>) 04.06.2021	Priority date (<i>day/month/year</i>)	Application No. LT2021528
International Patent Classification (IPC) INV. C07D209/12 C07D209/14 C07B37/06			
Applicant Kauno technologijos universitetas			

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 the opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement 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 application
- ☒ Box No. VIII Certain observations on the application

	Examiner Miniejew, Catherine
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WRITTEN OPINION

Box No. I Basis of this opinion

1. This opinion has been established on the basis of the latest set of claims filed before the start of the search.
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the application, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the application as filed.
 - ☐ filed together with the application in electronic form.
 - ☐ furnished subsequently for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto 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.
4. Additional comments:

Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1
	No: Claims	2, 3
Inventive step (IS)	Yes: Claims	
	No: Claims	1-3
Industrial applicability (IA)	Yes: Claims	1-3
	No: Claims	

2. Citations and explanations

see separate sheet

WRITTEN OPINION

Application number
LT2021528

Box No. VIII Certain observations on the application

see separate sheet

Reference is made to the following documents:

- D1 ZHENG JING ET AL: "Elaboration of thorough simplified vinca alkaloids as antimitotic agents based on pharmacophore similarity", EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, vol. 65, 2013, pages 158-167, XP028677359,
(cited in the application)
- D2 CN 102 942 515 A (UNIV JINAN) 27 February 2013 (cited in the application)
- D3 US 3 346 571 A (SPATZ SYDNEY M ET AL) 10 October 1967
(1967-10-10)

Re Item V.

V.1. Novelty

V.1.1. Claim 1 is novel on account of the used solvent (i.e. ethylene glycol) and of the T-mixer.

V.1.2. Claims 2 and 3 are not novel because they are anticipated by D1 to D3.

D1 to D3 disclose indole derivatives included in formula 6 (D1, pages 165-166 compounds 7a, 7b, 7o, 7p; D2, page 6 compounds 2, 3; D3, figure 2 compound 5).

It should be noted that a product is not rendered novel merely by the fact that it is produced by means of a novel process.

V.2. Inventive step

Since claims 2 and 3 are not novel, they cannot involve an inventive step.

D1 or D2 are regarded as being the closest prior art to the subject-matter of claim 1. They disclose the preparation of the same products by heating in alcohol a mixture of the same reactants (D1, pages 165-166 preparation of compounds 7a, 7b, 7o, 7p, respective yields 78%, 57%, 51%, 70%; D2, page 5 [0018]-[0027] compounds 2, 3, respective yields 57%, 78%). In D1 said reaction is done in ethanol. In D2 the reaction is done in a back flow reactor at 60-90°C in ethanol, propanol or butanol. The claimed process differs from those of D1 and D2 in that the reactants are dissolved in separate tanks in ethylene glycol and added afterwards in a T-mixer, wherein the tubular zone is heated for about 1h. It is written in the description that the claimed process results in higher yields and shorter reaction times (page 2 lines 7-10).

Therefore, the technical problem underlying the application is formulated as the provision of an improved process to prepare 2-styryl-3,3-trimethyl-3H-indole derivatives.

It is shown in the application that the claimed process leads to the desired products in 58-95% yield. It is also alleged on page 10 that the same reaction in a flask would be longer and would produce more by-products. However, no comparative data support these allegations. A direct comparison with the prior art is also not possible because different temperatures are used in D1 and D2 (60-90°C versus 125°C). Furthermore, D1 and D2 disclose neither a reaction time nor a reaction scale. Therefore, it is not possible to know if the above problem has been solved. Consequently, the present application does not involve an inventive step.

In the case where comparative tests are envisaged in order to support an inventive step, these must be carried out with a reaction in a flask involving the same conditions as for the claimed process (solvent, temperature, scale, work-up), such that the effect is shown to have its origins in the distinguishing feature of the claimed invention (a flow reactor with a T-mixer).

Re Item VIII.

VIII.1. It is clear from the description (page 3 - scheme 2) that the 3H-indole hydrochloride and aldehyde mentioned in claim 1 step (a) have a specific structure which are essential to the definition of the invention. Since claim 1 does not contain this feature it does not meet the requirement of clarity, that any independent claim must contain all the technical features essential to the definition of the invention.

VIII.2. Claim 2 and 3 lack clarity because it is directed to products which are defined in terms of a process for their manufacture. This formulation is in the present case however not allowable because it is possible to define the products satisfactorily by reference to their structure.