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- (74) Agent: **PLOUGMANN, VINGTOFT & PARTNERS** A/S; Sankt Annae Plads 11, P.O. Box 3007, DK-1021 Copenhagen K (DK).
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- (71) Applicant (*for all designated States except US*): **BIOPARKEN AS** [NO/NO]; Sagabygget, N-1432 Ås (NO).
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- (75) Inventors/Applicants (*for US only*): **HOVDE, Henry, R.** [NO/NO]; Haugmannsvei 22, N-0586 Oslo (NO). **KLEVELAND, Karsten** [NO/NO]; Bauneveien 16, N-3960 Statthelle (NO). **NILSEN, Nils, Olav** [NO/NO]; Luftfartsveien 8, N-0770 Oslo (NO). **STENSTRØM, Yngve** [NO/NO]; Østersjøveien 146, N-0686 Oslo (NO). **SKATTEBØL, Lars** [NO/NO]; Ringstadbekkveien 82 B, N-1358 Jar (NO).
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**WO 01/06853 A3**

(54) Title: NOVEL JUVENILE HORMONE ANALOGUES AND THEIR USE AS ANTIFOULING AGENTS

(57) Abstract: The use of juvenile hormone analogues (juvenoids, juvenile hormone-like compounds, juvenile hormone mimics) compounds as antifouling agents in e.g. paint compositions for ships and immersed structures including oil drilling rigs and fish nets and novel juvenile hormone compounds. The compounds are active against barnacles including species of *Cirripedia* such as *Balanus* species and prevent crucial steps in the process of barnacle fouling on solid surfaces such as the settlement, attachment and/or metamorphosis of barnacle cyprid larvae.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 00/01003

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 A01N31/08 A01N31/14 A01N35/04 A01N37/38 A01N43/40  
 A01N43/58 A01N49/00

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)

IPC 7 A61K A01N

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, CHEM ABS Data, EMBASE, BIOSIS, MEDLINE, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 11909 A (BUCKMAN LABOR INC) 3 April 1997 (1997-04-03) abstract page 20-21; claims 1-14 ----	1
X	WO 95 17478 A (BAYER AG ;KUGLER MARTIN (DE); LONDERSHAUSEN MICHAEL (DE); SCHRAGE) 29 June 1995 (1995-06-29)  abstract page 1, line 1 -page 3, line 15 -----  -/--	1,3,4,7, 9,18-30, 32-38, 46,47

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*8\* document member of the same patent family

Date of the actual completion of the international search

12 July 2001

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27.07.01

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International Application No

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X	<p>EP 0 408 352 A (NIPPON PAINT CO LTD) 16 January 1991 (1991-01-16) abstract; claim 1</p>	1
X	<p>NAKAGAWA N ET AL: "SYNTHESIS AND BIOLOGICAL ACTIVITY OF SOME DIBROMOALKADIENYL ETHER ANALOGS OF JUVENILE HORMONE" AGRICULTURAL AND BIOLOGICAL CHEMISTRY,JP,JAPAN SOC. FOR BIOSCIENCE, BIOTECHNOLOGY AND AGROCHEM. TOKYO, vol. 45, no. 10, 1981, pages 2381-2382, XP000877226 ISSN: 0002-1369 the whole document</p>	1
X	<p>DE 23 27 736 A (HOFFMANN LA ROCHE) 3 January 1974 (1974-01-03) abstract page 10-12 page 34-37; claims 14-52; examples 1-8</p>	1
X	<p>DE 21 35 964 A (ZOECON CORP) 3 February 1972 (1972-02-03) claims 1-40; examples 1-11</p>	1
X	<p>US 4 751 225 A (NISHIDA SUMIO ET AL) 14 June 1988 (1988-06-14)  compounds 1,2 claims 1,2; table 1</p>	1-4, 7-11, 18-20, 32-35,39
X	<p>DATABASE WPI Section Ch, Week 198514 Derwent Publications Ltd., London, GB; Class C02, AN 1985-084631 XP002159870 &amp; JP 60 036403 A (SUMITOMO CHEM CO LTD), 25 February 1985 (1985-02-25) abstract</p>	1-4,7-9, 11, 18-20,39

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X	<p>HAUK SOLLI ET AL.: "Pyridyl Terpenoid Ethers with High Juvenile Hormone Activity" PESTIC. SCI., vol. 7, no. 5, 1976, pages 503-511, XP000890104 abstract; table 1</p>	1-5,7, 10,11, 17-20, 32-36,39
X	<p>DATABASE WPI Section Ch, Week 198515 Derwent Publications Ltd., London, GB; Class B03, AN 1985-089601 XP002159872 &amp; JP 60 038303 A (SUMITOMO CHEM CO LTD), 27 February 1985 (1985-02-27) abstract</p>	1-4,7-9, 11, 18-20,39
X	<p>US 5 057 527 A (LONDERSHAUSEN MICHAEL ET AL) 15 October 1991 (1991-10-15)  abstract; example 6</p>	1-4,7-9, 11, 18-20,39
X	<p>EP 0 549 441 A (VIRBAC SA) 30 June 1993 (1993-06-30)  abstract; examples 1-3</p>	1-4,7-9, 11, 18-20,39
X	<p>KUWANO E ET AL: "SYNTHESIS AND PRECOCIOUS-METAMORPHOSIS-INDUCING ACTIVITY OF 3-PYRIDYL ETHERS" PESTICIDE SCIENCE,GB,ELSEVIER APPLIED SCIENCE PUBLISHER. BARKING, vol. 52, no. 3, 1998, pages 251-257, XP000877229 ISSN: 0031-613X abstract; table 4 page 252, column 1, paragraph 2 -page 257, column 1, paragraph 1</p>	1-4,7-9, 11, 18-20, 39-41
X	<p>EP 0 164 721 A (CHISSO CORP) 18 December 1985 (1985-12-18) claims 1-6</p>	1-4,7
	-/--	

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International Application No

PCT/IB 00/01003

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>ICHIKAWA Y ET AL: "SYNTHESIS OF PYRIDYL TERPENOID ETHER ANALOGS OF JUVENILE HORMONE"            AGRICULTURAL AND BIOLOGICAL CHEMISTRY, JP, JAPAN SOC. FOR BIOSCIENCE, BIOTECHNOLOGY AND AGROCHEM. TOKYO, vol. 44, no. 11, 1980, pages 2709-2715, XP000877225            ISSN: 0002-1369            page 2711, column 1, paragraph 3 -page 2714, column 2, paragraph 6; table 1</p>	1-4,7, 18-21
X	<p>KRAMER K J ET AL: "ACTIVITY OF PYRIDYL AND PHENYL ETHER ANALOGUES OF JUVENILE HORMONE AGAINST COLEOPTERA AND LEPIDOPTERA IN STORED GRAIN"            JOURNAL OF ECONOMIC ENTOMOLOGY, US, ENTOMOLOGICAL SOCIETY OF AMERICA. COLLEGE PARK, MARYLAND, vol. 71, no. 1, 1978, pages 132-134, XP000877230            ISSN: 0022-0493            abstract; figure 1; tables 1,2</p>	1-3,7, 11,18-21
A	<p>MKHIZE J N: "SYNTHETIC JUVENILE HORMONE ANALOGUES AGAINST FOUR SPECIES OF STORED PRODUCTS BEETLES"            INSECT SCIENCE AND ITS APPLICATION, KE, ICIPE SCIENCE PRESS, NAIROBI, vol. 9, no. 2, 1988, pages 275-278, XP000884660            ISSN: 0191-9040            abstract</p>	1-47
A	<p>CHAMBERLAIN W F ET AL: "APPLICATIONS OF INSECT GROWTH REGULATORS FOR CONTROL OF ANGORA GOATBITING LICE"            SOUTHWESTERN ENTOMOLOGIST, US, WESLACO, TX, vol. 1, no. 1, March 1976 (1976-03), pages 1-8, XP000884755            ISSN: 0147-1724            abstract</p>	1-47
X	<p>FAIVRE V ET AL: "SYNTHESIS OF LONG-CHAIN PICOLINIC DERIVATIVES"            BULLETIN DE LA SOCIETE CHIMIQUE DE FRANCE, FR, SOCIETE FRANCAISE DE CHIMIE. PARIS, vol. 128, 1991, pages 278-285, XP000877231            ISSN: 0037-8968            abstract; figure 1            page 279, column 2, paragraph 3 -page 285, column 2, paragraph 3</p>	1,2,4, 11,18-21

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>FR 2 413 877 A (LILLY CO ELI) 3 August 1979 (1979-08-03)</p> <p>page 1, line 1 -page 5, line 10 page 10, line 26 -page 22, line 28; claims 1-7; examples 2-4; tables 1-4</p>	<p>1-4, 10, 21, 22, 26-30, 32-38, 46, 47</p>
X	<p>US 4 678 504 A (SCHULZ GUENTER ET AL) 7 July 1987 (1987-07-07) abstract examples 1, 2</p>	<p>1-4, 7, 10, 18-20</p>
X	<p>EP 0 244 509 A (BASF AG) 11 November 1987 (1987-11-11)</p> <p>abstract page 2, line 1 -page 3, line 1 page 5 -page 9 page 10, line 21-25; claims 1-4; example 1</p>	<p>1-4, 7, 10, 18-22, 26-37, 46, 47</p>
X	<p>US 4 061 757 A (HOLST PREBEN LINDHOLM ET AL) 6 December 1977 (1977-12-06)</p> <p>abstract column 1, line 26 -column 2, line 31 column 6, line 27 -column 10, line 51; claims 1-29</p>	<p>1-5, 7, 10, 11, 17-20, 32-36, 39</p>
X	<p>FR 2 124 279 A (ZOECON CORP) 22 September 1972 (1972-09-22) page 1, line 1 -page 2, line 36 claims 1-48; examples 1-63</p>	<p>1, 18-20, 32-36</p>
X	<p>NAKAYAMA, A. ET AL.: "Quantitative structure-activity relationship of insect juvenile hormone mimetic compounds" J. MED. CHEM., vol. 27, no. 11, 1984, pages 1493-1502, XP000993269 the whole document</p>	<p>1, 18-20, 32-36</p>
X	<p>HENRICK, C. ET AL.: "Insect juvenile hormone activity of alkyl (2E, 4E)-3,7,11-trimethyl-2,4-dodecadienoat es. Variations in the ester function and in the carbon chain" J. AGRIC. FOOD CHEM., vol. 24, no. 2, 1976, pages 207-218, XP000993265 abstract; table 1</p>	<p>1, 18-20, 32-36</p>

INTERNATIONAL SEARCH REPORT

International Application No  
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	VIG, O. P. ET AL: "Insect juvenile hormone analogs: part I. Synthesis of terpenoids bearing a cyclopropane ring" INDIAN J. CHEM., SECT. B (1978), 16B(6), 452-4 , 1978, XP001010303 the whole document ----	1-8, 20-22, 32-35,39
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E	WO 01 07047 A (JENSEN LONE ;FORSKNINGSPARKEN I AAS AS (NO); SYVERTSEN CHRISTIAN () 1 February 2001 (2001-02-01) the whole document -----	1-20

# INTERNATIONAL SEARCH REPORT

I. International application No.  
PCT/IB 00/01003

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: -  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
1-8, 10, 11, 16, 18-44, 46, 47 (partially)
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.



## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-8,10,11,18-44,46,47 (partially) 9

Compounds of formula I, wherein Y is nitrogen and Z is nitrogen, methine or nitrogen oxide, and use of these compounds as anti-fouling agents and compounds of formula I per se.

2. Claims: 1-8,10,11,18-44,46,47 (partially)

Compounds of formula I, wherein Y is methine and Z is nitrogen or nitrogen oxide, and use of these compounds as anti-fouling agents and compounds of formula I per se.

3. Claims: 1-8,18-30, 32-41,43,44 (partially), 2-10

Compounds of formula I, wherein Y is methine and Z is methine, and use of these compounds as anti-fouling agents and compounds of formula I per se.

4. Claims: 1,12,14,15,18-30,32-47 (partially)

Method of preparing a compound of formula II wherein R3 and R4 do not form a methylenedioxy group, use of these compounds as anti-fouling agents and compounds of formula II wherein R3 and R4 do not form a methylenedioxy group per se.

5. Claims: 1,12,14,15,18-30,32-40,42,44,46,47 (partially) 13

Method of preparing a compound of formula II wherein R3 and R4 form a methylenedioxy group, use of these compounds as anti-fouling agents and compounds of formula II wherein R3 and R4 form a methylenedioxy group per se.

6. Claims: 1,18-30,32-40,42-44,46,47 (partially), 16

Method of preparing a compound of formula III, use of these compounds as anti-fouling agents and compounds of formula III per se.

7. Claims: 1,17-30,32-42,44,46,47 (partially)

Method of preparing a compound of formula IV, use of these compounds as anti-fouling agents and compounds of formula IV per se as far as not comprised in any of inventions 1-4.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

8. Claims: 1,17-30,32-44, 46,47 (partially)

Method of preparing a compound selected from the group consisting of octylmorpholine, 1-octylpiperidine, 1,4-dioctylpiperazine, use of these compounds as anti-fouling agents and compounds per se.

9. Claims: 1,17-30,32-40,42,44,46,47 (partially)

Method of preparing a compound selected from the group consisting of 3,3-dimethylocta-2,6-dienoic acid dimethylamide and 3,3-dimethyl-3-oxaundecanoic acid dimethylamide, use of these compounds as anti-fouling agents and compounds per se.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-8,10,11,16,18-44,46,47 relate to an extremely large number of possible compounds/uses. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds/uses claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Present claims 1-8,10,11,16,18-44,46,47 relate to a compounds/uses defined by reference to a desirable characteristic or property, namely

- a juvenile hormone analogue
- a compound defined by the EC-50 as given in claims 18,19.

The claims cover all compounds/uses having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds/uses. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds/uses by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds specifically mentioned in the claims per se and their use as far as comprised within the first, second and sixth invention.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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