

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
10 August 2006 (10.08.2006)

PCT

(10) International Publication Number
WO 2006/084186 A3

(51) International Patent Classification:

A23L 1/226 (2006.01) C07D 401/12 (2006.01)
A23L 1/231 (2006.01) C07D 405/14 (2006.01)

(21) International Application Number:

PCT/US2006/003956

(22) International Filing Date: 6 February 2006 (06.02.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/650,029 4 February 2005 (04.02.2005) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

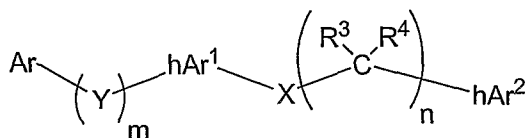
— with international search report

(88) Date of publication of the international search report:

22 February 2007

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPOUNDS COMPRISING LINKED HETERO ARYL MOIETIES AND THEIR USE AS NOVEL UMAMI FLAVOR MODIFIERS, TASTANTS AND TASTE ENHANCERS FOR COMESTIBLE COMPOSITIONS



(57) Abstract: The inventions disclosed herein relate to the discovery of the use of compounds having the formula shown below and certain subgenera or species thereof, as flavor or taste modifiers, particularly, savory ("umami") taste modifiers, savory flavoring agents and savory flavor enhancers in foods, beverages, and other comestible compositions.



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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/003956

A. CLASSIFICATION OF SUBJECT MATTER

INV. A23L1/226 A23L1/231 C07D401/12 C07D405/14

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)

A23L C07D

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, WPI Data, PAJ, FSTA, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 2005/041684 A (SENOMYX INC) 12 May 2005 (2005-05-12) cited in the application claims 1-322; examples 1-175,A-E -----	1-102, 104-111
X	EP 0 413 162 A (BASF K & F CORPORATION; GIVAUDAN-ROURE S.A) 20 February 1991 (1991-02-20) claims 1,7 -----	1-66, 100-102, 107,109, 111
X	WO 2004/026840 A (UNILEVER PLC; UNILEVER NV; HINDUSTAN LEVER LIMITED) 1 April 2004 (2004-04-01) claims 1,3,4,6,11-13,30 page 6, line 11 - page 7, line 17 ----- -/--	1-66, 100-102, 107,109, 111



Further documents are listed in the continuation of Box C.



See patent family 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
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- *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.

& document member of the same patent family

Date of the actual completion of the international search

5 October 2006

Date of mailing of the international search report

19/10/2006

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/003956

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/35768 A (J.MANHEIMER, INC) 25 May 2001 (2001-05-25) claims 1-18 -----	1-66, 100-102, 107,109, 111
A	WO 2004/080976 A (KUDOS PHARMACEUTICALS LIMITED; MAYBRIDGE LIMITED) 23 September 2004 (2004-09-23) claims 1-8; examples 1-20 -----	1-66, 100-103, 107,109, 111
A	CLARK R L ET AL: "SYNTHESIS AND ANALGESIC ACTIVITY OF 1,3-DIHYDRO-3-(SUBSTITUTED PHENYL)IMIDAZO[4,5-B]PYRIDIN-2-ONES AND 3-(SUBSTITUTED PHENYL)-1,2,3-TRIAZOLO[4,5-B]PYRIDINES" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, US, vol. 21, no. 9, 1978, pages 965-978, XP001191133 ISSN: 0022-2623 page 977, paragraph 6-12 -----	1-66, 100-102, 107,109, 111
A	BIAGI G ET AL: "N<6>-Cycloalkyl-2-phenyl-3-deaza-8-azaade nines: a new class of A1 adenosine receptor ligands. A comparison with the corresponding adenines and 8-azaadenines" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 38, no. 11-12, November 2003 (2003-11), pages 983-990, XP004475843 ISSN: 0223-5234 page 989, paragraph 2-6; figure 4 -----	1-66, 100-103, 107,109, 111
A	HUANG D ET AL: "2-{2-[3-(Pyridin-3-yloxy)phenyl]-2H-tetra zol-5-yl}pyridine: a highly potent, orally active, metabotropic glutamate subtype 5 (mGlu5) receptor antagonist" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 14, no. 22, 15 November 2004 (2004-11-15), pages 5473-5476, XP004598576 ISSN: 0960-894X page 5475, paragraph 3; table 1 -----	1-66, 100-103, 107,109, 111

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/003956

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 02/064631 A (SENOYX, INC; ADLER, JON, ELLIOTT; LI, XIAODONG; STASZEWSKI, LENA; O'C) 22 August 2002 (2002-08-22) cited in the application page 94, paragraph 235 page 8, paragraph 35 -----	1-111
A	US 4 535 084 A (LOMBARDINO ET AL) 13 August 1985 (1985-08-13) examples 15-21,25 -----	103
A	US 4 810 715 A (SCHICKANEDER ET AL) 7 March 1989 (1989-03-07) claim 1 -----	103
A	US 3 625 949 A (GUSTAV SCHORRE ET AL) 7 December 1971 (1971-12-07) claim 1; examples 1-31 -----	103
A	PERNAK J ET AL: "ACTIVITY OF NEW QUATERNARY AMMONIUM COMPOUNDS ON STRAINS OF BACTERIA AND FUNGI. PART 5: SYNTHESIS OF 3-METHYL-N-ALKYLTHIOMETHYLPYRIDINE-, 1-METHYL-3-N-ALKYLTHIOMETHYLIMIDAZOLE- AND 1-ETHYL-3-N-ALKYLTHIOLIMID AZOLINE CHLORIDES / WIRKUNG NEUER QUARTARER AMMONIUMVERBINDUNGEN AUF BAKTERIEN UND PILZE. T" PHARMAZIE, DIE, GOVI VERLAG, ESCHBORN, DE, vol. 38, no. 11, 1983, pages 752-754, XP008069005 ISSN: 0031-7144 page 752, paragraphs 2,3 -----	103
A	EVANGELISTA S ET AL: "SINTESI ED ATTIVITA' ANTIULCERA DI ALCUNI NUOVI COMPOSTI A STRUTTURA ARILTIOMETIL-PIRIDINICA/SYNTHESIS AND ANTI-ULCER ACTIVITY OF SOME NEW COMPOUNDS WITH ARYLTHIOMETHYL-PYRIDINE STRUCTURE" FARMACO, EDIZIONE SCIENTIFICA, SOCIETA CHIMICA ITALIANA, PAVIA, IT, vol. 43, no. 11, November 1988 (1988-11), pages 901-908, XP008068997 ISSN: 0430-0920 page 905 -----	103
A	WO 2004/081018 A (NESTEC SA [CH]; BLANK IMRE [CH]; GRIGOROV MARTIN [CH]; HOFMANN THOMAS) 23 September 2004 (2004-09-23) claims 1,4; example 3 -----	1-111

INTERNATIONAL SEARCH REPORT

International application No.
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Box II Observations where certain claims were found unsearchable (Continuation of item 2 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.: 1-102, 104-111 (partially)
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 III Observations where unity of invention is lacking (Continuation of item 3 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.:
1-102, 103 partially, 104-111
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

Continuation of Box II.2

Claims Nos.: 1-102,104-111 (partially)

The present claims 1-102,104-111 relate to an extremely large number of possible compounds. There are huge amount of options for different subgroups (claims 1,67,101,104,106,108,110) making the total amount of different combinations extremely high. It appears impossible to a skilled person to distinguish which all compounds fall into the scope of the claims.

Taking into account the extremely broad definitions of claims 1-102, 104-111 (especially 1,67,101,104,106,108,110) it is inherently quite unlikely that each of the claimed compounds are capable of solving the technical problem. There are no instructions in the description to prepare all such derivatives falling under the claims. If all optional compounds claimed in claims 1,67,101,104,106,108,110 solve the problem, there are a lot of other compounds solving the problem as well and there is no suprising effect.

Moreover, support and disclosure in the sense of Article 6 and 5 PCT is to be found however for only a very small proportion of the compounds see [examples, tables A,B,C on pages 83-88]. The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of claims 1-102, 104-111 (PCT Guidelines 9.19 and 9.23).

The search of claim 1-102, 104-111 was restricted to those claimed compounds which appear to be supported, namely the compounds in examples, tables A,B,C on pages 83-88.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-102,103 (partially),104-111

A taste modified comestible composition and a method for modulating the savory taste comprising:

- a) at least one comestible product, or one or more precursors thereof, and
- b) at least a savory flavor modulating amount of at least one compound having the formula $\text{Ar-hAr1-x-CR3R4-har2}$ or $\text{Ar-Y-hAr1-x-CR3R4-har2}$. 2-((5-(2-methoxy-4-methylphenyl)-1H-1,2,4-triazol-3-ylthio)methyl)pyridine (example 1) and 2-((5-(2-methoxy-4-methylphenyl)-1H-1,2,4-triazol-3-ylthio)methyl)-5-pyridine (example 2)

2. claim: 103 (partially)

2-((5-(2,4-dimethylphenyl)-1H-1,2,4-triazol-3-ylthio)methyl)pyridine (example 3)

2-((5-(4-Ethylphenyl)-1H-1,2,4-triazol-3-ylthio)methyl)pyridine (example 4)

4. claim: 103 (partially)

2-((5-(4,5-dimethylfuran-2-yl)-1H-1,2,4-triazol-3-ylthio)methyl)pyridine (example 5)

5. claim: 103 (partially)

2-((5-(4-Ethyl-2-methylphenyl)-1H-1,2,4-triazol-3-ylthio)methyl)pyridine (example 10)

6. claim: 103 (partially)

2-((5-(4-ethyl-2-methoxyphenyl)-1H-1,2,4-triazol-3-ylthio)methyl)pyridine (example 18a)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/003956

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2005041684	A	12-05-2005	AU 2004263871 A1	17-02-2005
			AU 2004285410 A1	12-05-2005
			CA 2535036 A1	12-05-2005
			CA 2535045 A1	17-02-2005
			EP 1660859 A2	31-05-2006
			EP 1659881 A2	31-05-2006
			WO 2005015158 A2	17-02-2005
EP 0413162	A	20-02-1991	CA 2012826 A1	18-02-1991
			DE 69030470 D1	22-05-1997
			DE 69030470 T2	06-11-1997
			JP 3080973 B2	28-08-2000
			JP 3218390 A	25-09-1991
			KR 164848 B1	15-01-1999
			SG 48363 A1	17-04-1998
			US 5147463 A	15-09-1992
WO 2004026840	A	01-04-2004	AU 2003266321 A1	08-04-2004
			BR 0314447 A	19-07-2005
			CN 1694872 A	09-11-2005
			EP 1546114 A1	29-06-2005
			JP 2006512294 T	13-04-2006
			US 2006106217 A1	18-05-2006
			US 2004067970 A1	08-04-2004
WO 0135768	A	25-05-2001	AU 1607701 A	30-05-2001
WO 2004080976	A	23-09-2004	AU 2004220321 A1	23-09-2004
			BR PI0408284 A	07-03-2006
			CA 2517629 A1	23-09-2004
			EP 1633724 A1	15-03-2006
			GB 2415430 A	28-12-2005
			HR 20050895 A2	31-12-2005
			JP 2006519827 T	31-08-2006
			MA 27758 A1	01-02-2006
			MX PA05009661 A	08-03-2006
WO 02064631	A	22-08-2002	CA 2433514 A1	22-08-2002
			CN 1525981 A	01-09-2004
			EP 1430083 A2	23-06-2004
			JP 2005500817 T	13-01-2005
			MX PA03005989 A	04-05-2004
			NO 20033030 A	14-08-2003
US 4535084	A	13-08-1985	NONE	
US 4810715	A	07-03-1989	AU 565518 B2	17-09-1987
			AU 1264883 A	10-11-1983
			CA 1213279 A1	28-10-1986
			DD 208801 A5	11-04-1984
			DE 3216843 A1	17-11-1983
			DK 188183 A	06-11-1983
			EP 0093252 A2	09-11-1983
			ES 8401755 A1	16-03-1984
			GR 78961 A1	02-10-1984
			HU 189272 B	30-06-1986
			IE 55263 B1	18-07-1990
			IL 68228 A	20-12-1987

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/003956

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4810715	A		JP 58203965 A	28-11-1983
			KR 8601578 B1	10-10-1986
			MX 7122 E	29-06-1987
			PT 76614 A	01-05-1983
			US 4866066 A	12-09-1989
			YU 91483 A1	28-02-1986
			ZA 8302203 A	28-12-1983
US 3625949	A	07-12-1971	AT 278792 B	10-02-1970
			AT 278793 B	10-02-1970
			CH 555827 A	15-11-1974
			CH 560191 A5	27-03-1975
			CH 565765 A5	29-08-1975
			CH 554863 A	15-10-1974
			CH 560192 A5	27-03-1975
			CH 551972 A	31-07-1974
			CH 551973 A	31-07-1974
			CH 565764 A5	29-08-1975
			CH 552590 A	15-08-1974
			DE 1770222 A1	11-11-1971
			DE 1695428 A1	15-04-1971
			ES 354787 A1	01-11-1969
			FR 7678 M	16-02-1970
			GB 1156769 A	02-07-1969
			JP 52050793 B	27-12-1977
			NL 6808029 A	09-12-1968
			SE 346995 B	24-07-1972
			US 3755336 A	28-08-1973
WO 2004081018	A	23-09-2004	AU 2003229557 A1	30-09-2004
			CA 2513504 A1	23-09-2004
			EP 1603928 A1	14-12-2005
			JP 2006514089 T	27-04-2006
			US 2006204629 A1	14-09-2006