

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
22 November 2007 (22.11.2007)

PCT

(10) International Publication Number
WO 2007/132207 A3

(51) International Patent Classification:
A61K 47/48 (2006.01)

(21) International Application Number:
PCT/GB2007/001745

(22) International Filing Date: 11 May 2007 (11.05.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0609370.2 11 May 2006 (11.05.2006) GB

(71) Applicant and

(72) Inventor: **MOCK, Graham** [GB/GB]; MACRO-Conex Ltd., Diagnox Lab, Cherwell Innovation Centre, 77 Heyford Park, Upper Heyford, Oxfordshire OX25 5HD (GB).

(74) Agents: **WEBBER, Philip, Michael** et al.; Frank B. Dehn & Co., St. Bride's House, 10 Salisbury Square, London EC4Y 8JD (GB).

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BH, 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, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, 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, MT, 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
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
21 August 2008

(54) Title: PROCESS FOR CROSS-LINKING MOIETIES

(57) Abstract: The invention relates to a process for linking a first moiety with a linker and to cross-linking a first moiety such as a nucleic acid or protein with a second moiety such as an antibody or enzyme. In preferred embodiments of the invention, the linker is diisothiocyanatostilbenedisulphonic acid (DIDS) or a dimer thereof.



WO 2007/132207 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2007/001745

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K47/48

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)
A61K

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, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KAVANAUGH ET AL.: "Affinity labeling of hemoglobin with 4,4'-Diisothiocyanostilbene-2,2'-disulfonate: covalent cross-linking in the 2,3-diphosphoglycerate binding site" BIOCHEMISTRY, vol. 27, 1988, pages 1804-1808, XP007904541	1,3,4, 7-11,15, 16, 20-22, 26, 28-30, 36, 38-40, 45, 61-65,69
Y	page 1805 last paragraph; abstract.	1-11,15, 16, 19-22, 26, 28-52, 58-71

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
- *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.
- *Z* document member of the same patent family

Date of the actual completion of the international search

22 April 2008

Date of mailing of the International search report

01/07/2008

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bettio, Andrea

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2007/001745

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HUA S. ET AL.: "Lys515-Lys492 Cross-linking by DIDS Interferes with substrate Utilization by the Sarcoplasmic reticulum ATPase" BIOPHYSICAL JOURNAL, vol. 73, 1997, pages 2149-2155, XP007904540	1,4, 7-11,15, 16, 20-22, 26, 28-31, 38,39, 41,45, 47,61-64
Y	page 2149, second column, second paragraph; figure 1 page 2150	1-11,15, 16, 19-22, 26, 28-52, 58-71
X	----- EP 0 398 024 A (HOECHST AG [DE]) 22 November 1990 (1990-11-22)	1-4, 7-11,15, 20-22, 26,28, 30,31, 35-37, 39-42, 61-69
Y	page 5 lines 10-20, 53, 53, page 7 lines 21-26; claims 19-22.	1-11,15, 16, 19-22, 26, 28-52, 58-71
X	----- EP 0 584 794 A (YISSUM RES DEV CO [IL]) 2 March 1994 (1994-03-02)	1,2, 7-11,15, 16, 20-22, 26, 28-31, 33,38, 40-42, 45-47,58
Y	Example 2 page 11; Figure 10	1-11,15, 16, 19-22, 26, 28-52, 57-71
	----- -/--	

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2007/001745

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 241 863 B1 (MONBOUQUETTE HAROLD G [US]) 5 June 2001 (2001-06-05)	1,2, 6-11,15, 16, 20-22, 26, 28-31, 33,38, 42, 45-47,58
Y	column 17 line 30-50	1-11,15, 16, 19-22, 26, 28-52, 57-71
X	----- US 5 532 129 A (HELLER MICHAEL J [US]) 2 July 1996 (1996-07-02)	61-64, 66-68,71
Y	claims 1-4,9-21 -----	1-11,15, 16, 19-22, 26, 28-52, 57-71

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2007/001745

Box No. 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:

Although claims 1-11, 15, 16, 19-22, 26, 28-52, 67, 70, 71 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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:
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 No. 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 fees, this Authority did not invite payment of additional fees.
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.:
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.:

see annex

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- 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: 1-11, 15, 16, 19-22, 28-52, 58-71 in part; claims 26, 57 complete

processes for linking a moiety to a linker wherein the linker is a compound of formulae I, III, V, kits comprising said linkers and conjugates thereby obtained.

2. claims: 1-11, 15, 16, 19-22, 28-52, 58-71 in part; claims 12-14, 17, 18, 23-25, 27, 53-56 complete.

processes for linking a moiety to a linker wherein the linker is a compound of formulae II, IV, VI, VII, VIII, IX, X, kits comprising said linkers and conjugates thereby obtained.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2007/001745

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0398024	A	22-11-1990	DE 3912792 A1	25-10-1990
			DK 398024 T3	29-03-1993
			ES 2054137 T3	01-08-1994
			GR 3007136 T3	30-07-1993
			JP 2111109 C	21-11-1996
			JP 3034999 A	14-02-1991
			JP 8019156 B	28-02-1996
EP 0584794	A	02-03-1994	CA 2104711 A1	26-02-1994
			DE 69331257 D1	17-01-2002
			DE 69331257 T2	13-06-2002
			IL 102930 A	18-03-1997
			JP 2633459 B2	23-07-1997
			JP 6281613 A	07-10-1994
			US 5443701 A	22-08-1995
US 6241863	B1	05-06-2001	NONE	
US 5532129	A	02-07-1996	AT 272068 T	15-08-2004
			AT 201692 T	15-06-2001
			AU 667497 B2	28-03-1996
			AU 3136493 A	07-06-1993
			CA 2123133 A1	13-05-1993
			DE 69231853 D1	05-07-2001
			DE 69231853 T2	13-09-2001
			DE 69233391 D1	02-09-2004
			DK 620822 T3	27-08-2001
			EP 0620822 A1	26-10-1994
			ES 2159282 T3	01-10-2001
			GR 3036456 T3	30-11-2001
			JP 3509859 B2	22-03-2004
			JP 7502992 T	30-03-1995
			WO 9309128 A1	13-05-1993
			US 5565322 A	15-10-1996