

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
18 August 2005 (18.08.2005)

PCT

(10) International Publication Number  
**WO 2005/074598 A3**

- (51) International Patent Classification<sup>7</sup>: **C07D 245/00**, 209/04, 207/33, 209/48
- (21) International Application Number: PCT/US2005/003183
- (22) International Filing Date: 28 January 2005 (28.01.2005)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/540,688 30 January 2004 (30.01.2004) US  
60/632,456 2 December 2004 (02.12.2004) US
- (71) Applicant (for all designated States except US): **JOHNS HOPKINS UNIVERSITY** [US/US]; 100 N. Charles Street, 5th Floor, Baltimore, MD 21201 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **TOSCANO, John, P., III** [US/US]; 709 Regester Avenue, Baltimore, MD 21212 (US). **PAVLOS, Christopher, M.** [US/US]; 14018 Chetnue Court, Laurel, MD 20707 (US). **BOPPANA, Preeya, Kapur** [US/US]; 8577 Indian Spring Rd., Frederick, MD 21702 (US).
- (74) Agent: **CORLESS, Peter, F.**; Edwards & Angell LLP, P.O. Box 55874, Boston, MA 02205 (US).
- (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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, 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, 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  
— 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: 15 December 2005
- 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.*



WO 2005/074598 A3

(54) Title: NITROXYL PROGENITOR COMPOUNDS AND METHODS OF USE

(57) Abstract: Described herein are nitroxyl progenitor compounds, and compositions including, and methods of generating, the compounds thereof, and methods of treating or preventing disease and disease symptoms using the compounds and compositions.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US05/03183

<p><b>A. CLASSIFICATION OF SUBJECT MATTER</b>                  IPC(7) : C07D 245/00, C07D 209/04, C07D 207/33, C07D 209/48                  US CL : 564/300, 548/483, 548/557, 548/475                  According to International Patent Classification (IPC) or to both national classification and IPC</p>																						
<p><b>B. FIELDS SEARCHED</b></p> <p>Minimum documentation searched (classification system followed by classification symbols)                  U.S. : 564/300, 548/483, 548/557, 548/475</p> <p>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched</p> <p>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)                  STN Online (CAPLUS)</p>																						
<p><b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b></p> <table border="1"> <thead> <tr> <th>Category *</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X</td> <td>BIVALACQUA, T. Analysis of vasodilator Responses to Novel Nitric Oxide Donors in the Hindquarters Vascular Bed of the Cat, J. of Cardiovascular Pharm. (2001) 38(1), pp. 120-129, especially fig. 1.</td> <td>46</td> </tr> <tr> <td>Y</td> <td>XIAOPING T. Synthesis of Peptide-diazeniumdiolate conjugates: towards enzyme activated antitumor agents, Tetrahedron Letters (2001) vol. 42, pp. 2625-2629, especially p. 2625.</td> <td>46</td> </tr> <tr> <td>X</td> <td>ALOKA S. Chemistry of the Diazeniumdiolates, J. Am. Chem. Soc. 2001, 123, pp. 5465-5472, especially p. 5469 (Scheme 4, compound No. 6).</td> <td>46</td> </tr> </tbody> </table>			Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	BIVALACQUA, T. Analysis of vasodilator Responses to Novel Nitric Oxide Donors in the Hindquarters Vascular Bed of the Cat, J. of Cardiovascular Pharm. (2001) 38(1), pp. 120-129, especially fig. 1.	46	Y	XIAOPING T. Synthesis of Peptide-diazeniumdiolate conjugates: towards enzyme activated antitumor agents, Tetrahedron Letters (2001) vol. 42, pp. 2625-2629, especially p. 2625.	46	X	ALOKA S. Chemistry of the Diazeniumdiolates, J. Am. Chem. Soc. 2001, 123, pp. 5465-5472, especially p. 5469 (Scheme 4, compound No. 6).	46								
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.																				
X	BIVALACQUA, T. Analysis of vasodilator Responses to Novel Nitric Oxide Donors in the Hindquarters Vascular Bed of the Cat, J. of Cardiovascular Pharm. (2001) 38(1), pp. 120-129, especially fig. 1.	46																				
Y	XIAOPING T. Synthesis of Peptide-diazeniumdiolate conjugates: towards enzyme activated antitumor agents, Tetrahedron Letters (2001) vol. 42, pp. 2625-2629, especially p. 2625.	46																				
X	ALOKA S. Chemistry of the Diazeniumdiolates, J. Am. Chem. Soc. 2001, 123, pp. 5465-5472, especially p. 5469 (Scheme 4, compound No. 6).	46																				
<p><input type="checkbox"/> Further documents are listed in the continuation of Box C.      <input type="checkbox"/> See patent family annex.</p>																						
<p>* Special categories of cited documents:</p> <table border="0"> <tr> <td>"A"</td> <td>document defining the general state of the art which is not considered to be of particular relevance</td> <td>"T"</td> <td>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</td> </tr> <tr> <td>"E"</td> <td>earlier application or patent published on or after the international filing date</td> <td>"X"</td> <td>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</td> </tr> <tr> <td>"L"</td> <td>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)</td> <td>"Y"</td> <td>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</td> </tr> <tr> <td>"O"</td> <td>document referring to an oral disclosure, use, exhibition or other means</td> <td>"&amp;"</td> <td>document member of the same patent family</td> </tr> <tr> <td>"P"</td> <td>document published prior to the international filing date but later than the priority date claimed</td> <td></td> <td></td> </tr> </table>			"A"	document defining the general state of the art which is not considered to be of particular relevance	"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	"E"	earlier application or patent published on or after the international filing date	"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	"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)	"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	"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family	"P"	document published prior to the international filing date but later than the priority date claimed		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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																			
"E"	earlier application or patent published on or after the international filing date	"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																			
"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)	"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																			
"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family																			
"P"	document published prior to the international filing date but later than the priority date claimed																					
<p>Date of the actual completion of the international search                  22 June 2005 (22.06.2005)</p>		<p>Date of mailing of the international search report                  01 NOV 2005  <i>Valere Bell-Hano</i>  <b>KAMAL A. SAEED, PH.D.</b>  <b>PRIMARY EXAMINER</b> for</p>																				
<p>Name and mailing address of the ISA/US                  Mail Stop PCT, Attn: ISA/US                  Commissioner for Patents                  P.O. Box 1450                  Alexandria, Virginia 22313-1450                  Facsimile No. (571) 272-8781</p>		<p>Authorized officer                  Nyeemah Grazier                  Telephone No. (571) 272-1600</p>																				

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International application No.  
PCT/US05/03183

The numerous variables, such as R1, R2, m and n for instance, and their voluminous and complex meanings and their virtual incomprehensible permutations and combinations make it impossible to determine the full scope and complete meaning of the claimed subject matter. As presented, the claimed subject matter cannot be regarded as being a clear and concise description for which protection is sought and as such the abovementioned claims (1-45 and 47-52) do not comply with the requirements of PCT Article 6. Thus, it is impossible to carry out a meaningful search report on same. A search was carried out on the first discernable invention, which is Claim 46, based on the compounds in Table 1 of the specification.

