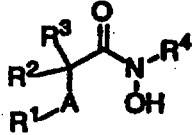




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(21) International Application Number: PCT/US98/02987 (22) International Filing Date: 17 February 1998 (17.02.98) (30) Priority Data: 08/806,728 27 February 1997 (27.02.97) US (71) Applicant: AMERICAN CYANAMID COMPANY [US/US]; Five Giralda Farms, Madison, NJ 07940-0874 (US). (72) Inventors: VENKATESAN, Aranapakam, Mudumbai; 97-07 63rd Road #9K, Rego Park, NY 11374 (US). GROSU, George, Theodore; 117 Prospect Place, Pearl River, NY 10965 (US). DAVIS, Jamie, Marie; 20 High Avenue, Nyack, NY 10960 (US). BAKER, Jannie, Lea; 127 Rockinchair Road, White Plains, NY 10607 (US). (74) Agents: ALICE, Ronald, W.; American Home Products Cor- poration, One Campus Drive, Parsippany, NJ 07054 (US) et al.		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: N-HYDROXY-2-(ALKYL, ARYL OR HETEROARYL SULFANYL, SULFINYL OR SULFONYL)-3-SUBSTITUTED ALKYL, ARYL OR HETEROARYLAMIDES AS MATRIX METALLOPROTEINASE INHIBITORS (57) Abstract Matrix metalloproteinases (MMPs) are a group of enzymes that have been implicated in the pathological destruction of connective tissue and basement membranes. These zinc containing endopeptidases consist of several subsets of enzymes including collagenases, stromelysins and gelatinases. TNF-α converting enzyme (TACE), a pro-inflammatory cytokine, catalyzes the formation of TNF-α from membrane bound TNF-α precursor protein. It is expected that small molecule inhibitors of MMPs and TACE therefore have the potential for treating a variety of disease states. The present invention provides low molecular weight, non-peptide inhibitors of matrix metalloproteinases (MMPs) and TNF-α converting enzyme (TACE) for the treatment of arthritis, tumor metastasis, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, diabetes (insulin resistance) and HIV infection having formula (I) wherein R² and R³ form a heterocyclic ring and A is S, S(O), or S(O)₂, and R¹ and R⁴ are defined herein.  (I)		