

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 denned herein.

