



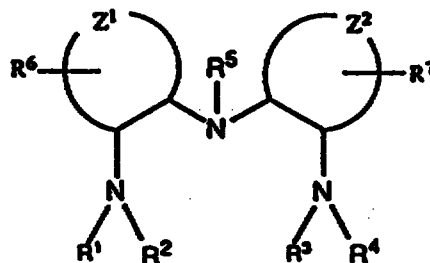
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(21) International Application Number: PCT/GB95/00832 (22) International Filing Date: 12 April 1995 (12.04.95) (30) Priority Data: 08/227,161 13 April 1994 (13.04.94) US (71) Applicant: NYCOMED IMAGING AS [NO/NO]; Nycoveien 2, N-0401 Oslo (NO). (71) Applicant (for GB only): COCKBAIN, Julian [GB/GB]; 27 Ladbroke Road, London W11 3PD (GB). (72) Inventors: ILLIG, Carl, Root; 25 Jonathon Drive, Phoenixville, PA 19460 (US). CAULFIELD, Thomas, Joseph; 2951 Appledale Road, Audubon, PA 19403 (US). TONER, John, Luke; 109 Brookhollow Drive, Downingtown, PA 19355 (US). GUO, Peng; Apartment LO7, 800 Kimberton Road, Phoenixville, PA 19460 (US). LADD, David, Lee; 1375 Thomas Road, Wayne, PA 19087 (US). (74) Agents: COCKBAIN, Julian et al.; Frank B. Dehn & Co., Imperial House, 15-19 Kingsway, London WC2B 6UZ (GB).	(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, <u>SG</u>, SI, SK, TJ, TM, TT, UA, UG, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, 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), ARIPO patent (KE, MW, SD, SZ, UG). Published With international search report. 9611518-3	

(54) Title: CYCLIC TRIAMINE CHELATING AGENTS

(57) Abstract

The present invention provides compounds of formula (I) wherein Z¹ and Z² each represent the atoms necessary to complete a monocyclic or polycyclic carbocyclic or heterocyclic ring system, said Z¹ and Z² independently optionally substituted with R⁶ and R⁷, respectively; R¹, R², R³ and R⁴ are independently carboxyalkyl (C₁-C₂), -(CH₂)_n-C(=O)-NH-R⁸, or -(CH₂)_n-C(=O)-O-R⁸, R⁵ is carboxyalkyl (C₁-C₂); R⁶ and R⁷ are independently, hydrogen, benzyl, or benzyloxy, said benzyl or benzyloxy optionally substituted with one, two or three substituents selected from the group consisting of amino, isocyanato (-N=C=O),



(I)

isothiocyanato (-N=C=S), -NH-C(=O)-X or -NH-C(=S)-X; R⁸ is alkyl (C₁-C₂₀), -(CH₂)_m-Ar, or polyhydroxyalkyl (C₁-C₂₀); n is 1 or 2; m is 1 to 15; X is a targeting moiety; and Ar is phenyl optionally substituted with one, two or three substituents selected from the group consisting of amino, acylamino, hydroxy, alkyl (C₁-C₅) and halogen. The compounds of the invention can be chelated with a metal ion and used as contrast agents for magnetic resonance imaging and for other applications. The present invention also provides pharmaceutical compositions comprising a compound of the invention and a pharmaceutically acceptable carrier or diluent. The invention further provides a method of providing an image of an internal region of a patient comprising administering to a patient a compound of the invention and scanning the patient using magnetic resonance imaging to obtain visible images of the region.