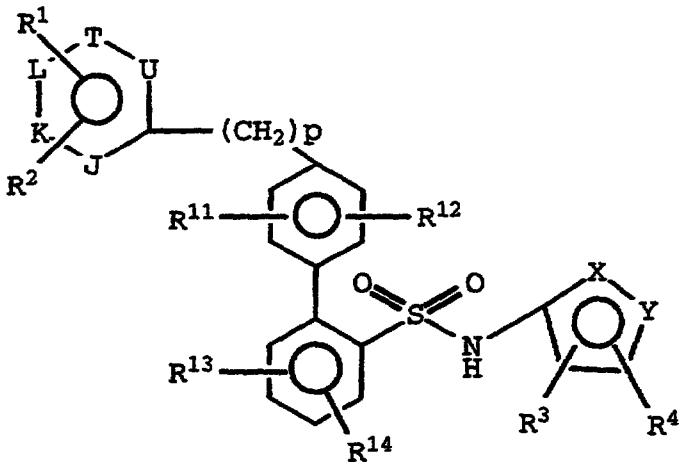
Abstract

SUBSTITUTED BIPHENYL SULFONAMIDE ENDOTHELIN ANTAGONISTS

Compounds of the formula



inhibit the activity of endothelin. The symbols are defined as follows:

R^1 and R^2 are each directly bonded to a ring carbon and are each independently

(a) hydrogen;

(b) alkyl or alkoxy;

(c) hydroxyl;

(d) halo; or

(e) amino;

R^3 and R^4 are each directly bonded to a ring carbon and are each independently

(a) hydrogen;

(b) alkyl alkenyl, alkynyl, alkoxy, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, aryloxy, aralkyl or aralkoxy, any of

which may be substituted with Z^1, Z^2 and Z^3;

(c) halo;

(d) hydroxyl;

(e) cyano;

(f) nitro;

(g) $-C(O)H$ or $-C(O)R^5$;

(h) $-CO_2H$ or $-CO_2R^5$;

(i) $-Z^4-NR^6R^7$;

(j) $-Z^4-N(R^{10})-Z^5-NR^8R^9$; or

(k) R^3 and R^4 together may also be alkylene or alkenylene, either of which may be substituted with Z^1, Z^2 and Z^3, completing a 4- to 8-membered saturated, unsaturated or aromatic ring together with the carbon atoms to which they are attached;

and the remaining symbols are as defined in the specification.