EP112787 relates to new esters derived from substituted phenyl-cyclohexyl compounds, which are derived from tramadol.

WO2003/048113 relates to tramadol analogs useful for the treatment of CNS-related disorders, including pain, anxiety, depression and attention deficit disorder.

EP2022778 relates to a (R,R)-tramadol-(S)-naproxene salt, a crystalline form of (R,R)-tramadol-(S)-naproxene salt, their processes for preparation and uses as medicament for the treatment of pain.

GB997399 relates to phenol ethers that contain basic groups and to methods for preparing them.

US3564100 relates to cycloalkene compounds and processes for their manufacture.

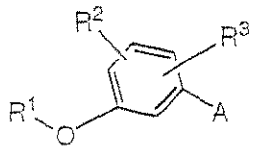
US3652589 relates to cycloalkanol-substituted phenol ethers having basic groups, to pharmaceutical compositions containing the compounds, processes for manufacturing the compounds, and methods of using the compounds.

Arzneimittel-Forschung/Drug Research, Vol. 28, No. 1a (1978), pages 107-113 relates to phenyl substituted aminomethylcycloalkanole compounds tested for analgesic properties.

Journal of the Mexican Chemical Society, Vol. 49, No. 4, (2005), pages 324-327 relates to tramadol and derivatives of tramadol, and processes for preparing them.

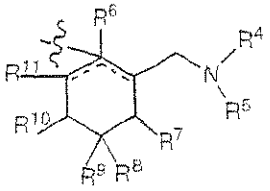
Summary

In a first aspect, there is provided a compound, or salt thereof, of formula I:



I

wherein A is



R^1 is hydrogen, C_1–C_5 alkyl, C_1–C_5 haloalkyl, C_1–C_5 alkanol, –(C_1–C_5 alkyl)phenyl, or phenyl, or a group of the formula –C(O)-R^{12}, where R^{12} is C_1–C_5 alkyl, C_1–C_5 alkoxy, C_1–C_5 haloalkyl, C_1–C_5 alkanol, –(C_1–C_5 alkyl)phenyl, or phenyl;

R^2 is hydrogen, C_1–C_5 alkyl, C_1–C_5 alkoxy, halogen, C_1–C_5 haloalkyl, or C_1–C_5 haloalkoxy;

R^3 is hydrogen, C_1–C_5 alkyl, C_1–C_5 alkoxy, halogen, C_1–C_5 haloalkyl, or C_1–C_5 haloalkoxy;

R^4 is hydrogen, C_1–C_5 alkyl, or –(C_1–C_5 alkyl)phenyl;

R^5 is hydrogen, C_1–C_5 alkyl, or –(C_1–C_5 alkyl)phenyl;

R^6 is hydrogen, hydroxy, or is absent;

R^7 is hydrogen;

R^8 is hydrogen or methyl;

R^9 is hydrogen or methyl;

R^{10} is hydrogen;

R^{11} is hydrogen or C_1–C_5 alkyl;

provided that one of I), II), and III) is present, wherein I), II) and III) are:

I) R^7 and R^{10} combine to form –CH_2- or –$(CH_2)_2$-;

II) R^8 and R^9 combine to form a cyclopropyl group with the carbon to which they are attached; and

III) R^{10} and R^{11} combine to form $-CH_2-$ or $-(CH_2)_3-$.

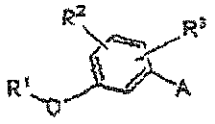
In a second aspect, there is provided a pharmaceutical formulation comprising a compound as defined herein and one or more pharmaceutically acceptable carriers.

In a third aspect, there is provided the use of an effective amount of a compound as defined herein in the manufacture of a medicament for controlling pain in a mammal.

In a fourth aspect, there is provided a compound or salt as defined herein for use in therapy.

Detailed Disclosure

Provided are analgesic compounds, and salts thereof, of formula I:



I

wherein A is