



# Brevet canadien / Canadian Patent

Le commissaire aux brevets a reçu une demande de délivrance de brevet visant une invention. Ladite requête satisfait aux exigences de la *Loi sur les brevets*. Le titre et la description de l'invention figurent dans le mémoire descriptif, dont une copie fait partie intégrante du présent document.

Le présent brevet confère à son titulaire et à ses représentants légaux, pour une période expirant vingt ans à compter de la date du dépôt de la demande au Canada, le droit, la faculté et le privilège exclusif de fabriquer, construire, exploiter et vendre à d'autres, pour qu'ils l'exploitent, l'objet de l'invention, sauf jugement en l'espèce rendu par un tribunal compétent, et sous réserve du paiement des taxes périodiques.



The Commissioner of Patents has received a petition for the grant of a patent for an invention. The requirements of the *Patent Act* have been complied with. The title and a description of the invention are contained in the specification, a copy of which forms an integral part of this document.

The present patent grants to its owner and to the legal representatives of its owner, for a term which expires twenty years from the filing date of the application in Canada, the exclusive right, privilege and liberty of making, constructing and using the invention and selling it to others to be used, subject to adjudication before any court of competent jurisdiction, and subject to the payment of maintenance fees.

## BREVET CANADIEN

**2,738,045**

## CANADIAN PATENT

Date à laquelle le brevet a été accordé et délivré

**2019/02/19**

Date on which the patent was granted and issued

Date du dépôt de la demande

**2011/04/21**

Filing date of the application

Date à laquelle la demande est devenue accessible au public pour consultation

**2011/11/28**

Date on which the application was made available for public inspection

Commissaire aux brevets / Commissioner of Patents



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(54) Titre : COMPOSES CONJUGUES, LEURS PROCEDES DE FABRICATION ET LEURS UTILISATIONS

(54) Title: CONJUGATE COMPOUNDS, METHODS OF MAKING SAME, AND USES THEREOF

(57) Abrégé/Abstract:

The invention provides in part, conjugate compounds. The invention also provides synthesis methods for making the compounds, and uses of the compounds.

## CONJUGATE COMPOUNDS, METHODS OF MAKING SAME, AND USES THEREOF

### FIELD OF INVENTION

5 [0001] The present invention relates to conjugate compounds and methods of making and using same.

### BACKGROUND OF THE INVENTION

10 [0002] Prostaglandins are a sub-class of eicosanoids found in most body tissues and implicated in a variety of physiological functions in animals, including smooth muscle contraction, reproduction, autoimmunity, inflammation, reduction of intraocular pressure, *etc.* Prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) has been associated with various physiological and/or pathological conditions such as stimulation of bone formation, increase in bone mass, arthritis, pain, inflammation, cancer, multiple sclerosis, *etc.*

15 [0003] PGE<sub>2</sub> binds to four receptors (EP1, EP2, EP3 and EP4). The EP4 receptor is associated with intracellular cyclic adenosine monophosphate (cAMP) production, and is distributed in a wide variety of tissue types suggesting a major role in PGE<sub>2</sub>-mediated biological events, such as smooth muscle relaxation, intraocular pressure, pain (in particular inflammatory, neuropathic and visceral pain), inflammation, neuroprotection, lymphocyte differentiation, bone metabolic processes, allergic activities, promotion of sleep, renal regulation, gastric or enteric mucus secretion and duodenal bicarbonate  
20 secretion.

[0004] A variety of EP4 agonists have been described and include, without limitation, compounds as set forth in, for example, WO 02/24647, WO 02/42268, EP 1132086, EP 855389, EP 1114816, WO 01/46140, WO 01/72268, WO 05/116010, WO 03/047417, or  
25 US 7, 238,710. Many EP4 agonists have however been associated with systemic side effects.

[0005] Bisphosphonates are drugs used to strengthen bone and have been implicated in inhibiting bone resorption and bone targeting.

[0006] Prostaglandin-bisphosphonate conjugate compounds have been described in for example US 5,409,911 or US 6,121,253.