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(62)	Divided application	EP3191470, 2016.06.30
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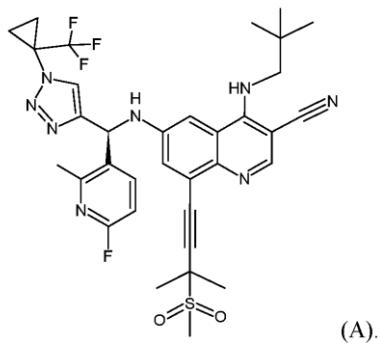
(54) Title **4,6-DIAMINO-QUINOLINE-3-CARBONITRILE DERIVATIVE AS CANCER OSAKA THYROID (COT) MODULATOR FOR TREATING INFLAMMATORY DISEASE**

(56) References  
 Cited: WO-A1-98/43960  
 KAILA ET AL: "Identification of a novel class of selective Tpl2 kinase inhibitors: 4-Alkylamino-[1,7]naphthyridine-3-carbonitriles", BIOORGANIC & MEDICINAL CHEMISTRY, PERGAMON, GB, vol. 15, no. 19, 4 July 2007 (2007-07-04), pages 6425-6442, XP022192446, ISSN: 0968-0896, DOI: 10.1016/J.BMC.2007.06.054  
 WU J ET AL: "Selective inhibitors of tumor progression loci-2 (Tpl2) kinase with potent inhibition of TNF-alpha production in human whole blood", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, PERGAMON, AMSTERDAM, NL, vol. 19, no. 13, 7 May 2009 (2009-05-07), pages 3485-3488, XP026155092, ISSN: 0960-894X, DOI: 10.1016/J.BMCL.2009.05.009 [retrieved on 2009-05-07]  
 RAKESH K GOYAL ET AL: "Models for anti-inflammatory activity of 8-substituted-4-anilino-6-aminoquinoline-3 -carbonitriles", MEDICINAL CHEMISTRY RESEARCH, BIRKHÄUSER VERLAG, BOSTON, vol. 21, no. 7, 19 March 2011 (2011-03-19) , pages 1044-1055, XP035060999, ISSN: 1554 -8120, DOI: 10.1007/S00044 -011-9613-5  
 NEAL GREEN ET AL: "Inhibitors of Tumor Progression Loci2 (Tpl2) Kinase and Tumor Necrosis Factor [alpha] (TNF-[alpha]) Production: Selectivity and in Vivo Antiinflammatory Activity of Novel 8-Substituted-4-anilino-6-aminoquinoline-3 -carbonitriles", JOURNAL OF MEDICINAL CHEMISTRY, vol. 50, no. 19, 2007, pages 4728-4745, XP055294201, US ISSN: 0022-2623, DOI: 10.1021/jm070436q

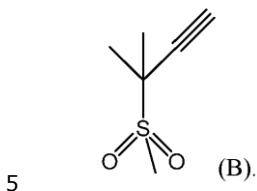
Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (<http://worldwide.espacenet.com>) or via the search engine on our website here: <https://search.patentstyret.no/>

**Patentkrav**

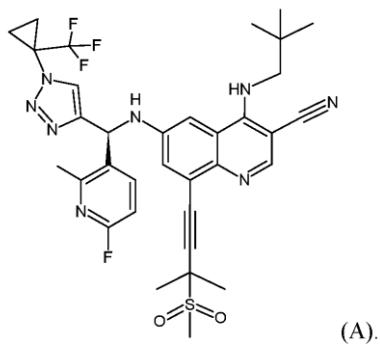
1. Forbindelse av formel (A):



2. Forbindelse av formel (B)

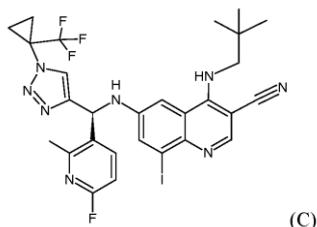


3. Fremgangsmåte for fremstilling av en forbindelse av formel (A):



omfattende trinnene:

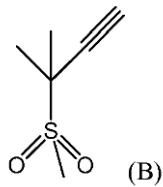
(i) å kontakte en forbindelse av formel (C)



10

(C)

Med en forbindelse av formel (B):



for å danne en blanding og

(ii) kombinere blandingen med  $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ .

4. Fremgangsmåte ifølge krav 3, hvor trinn (i) utføres ved å løse opp  
5 forbindelsene for formel (C) og (B) sammen med kobber(I) jodid i methyl-  
tetrahydrofuran (Me-THF).

5. Fremgangsmåte ifølge krav 3 eller 4, hvor fremgangsmåten omfatter det  
følgende trinn (iii) som utføres etter trinn (ii):

10 (iii) tilsetning av dietylamin.

6. Fremgangsmåte ifølge et hvilket som helst av kravene 3 til 5, hvor  
fremgangsmåten omfatter det følgende trinn (iv) som utføres etter trinn (iii), om til  
stede, eller etter trinn (ii) dersom trinn (iii) ikke er til stede:

(iv) oppvarming av reaksjonen til  $80^\circ\text{C}$  i en time og

15 så fortynne med  $\text{EtOAc}$  og saltlake.

7. Forbindelse av formel (E)

