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C07D 213/79 (2006.01)
C07D 213/803 (2006.01)

Norwegian Industrial Property Office

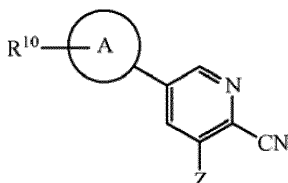
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(54)	Title	PROCESS FOR PREPARING [(5-(3-CHLOROPHENYL)-3-HYDROXYPYRIDINE-2-CARBONYL)-AMINO]ACETIC ACID FROM 5-((3-CHLOROPHENYL)-3-CHLORO-PYRIDIN-2-YL)-NITRILE, AND PROCESS FOR PREPARING 5-((HALOPHENYL)-3-HALO-PYRIDIN-2-YL)-NITRILE DERIVATIVES
(56)	References	
	Cited:	WO-A2-2008/002576

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/>

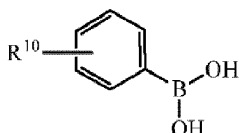
PATENTKRAV

1. Fremgangsmåte for fremstilling av en forbindelse med formel:

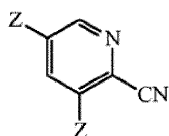


5 omfattende:

omsette en substituert arylboronsyre:



med 3,5-dihalogen-2-cyanopyridin:



10 i nærvær av en katalysator,

hvor

ring A er fenyl,

R¹⁰ representerer fra 1 til 5 uavhengig valgte substituenten for hydrogen som er halogen, og

15 hver Z er uavhengig klor eller brom.

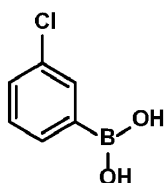
2. Fremgangsmåte ifølge krav 1, hvor katalysatoren er [1,1'-bis(difenylfosfino)ferrocen]diklorpalladium(II).

20 3. Fremgangsmåte ifølge krav 1, hvor reaksjonen utføres i nærvær av en base.

4. Fremgangsmåte ifølge krav 3, hvor basen er LiOH, NaOH, KOH, Ca(OH)₂, Li₂CO₃, Na₂CO₃, K₂CO₃ eller CaCO₃.

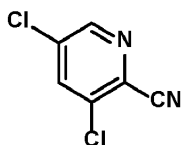
5. Fremgangsmåte ifølge krav 4, hvor basen er K_2CO_3 .

6. Fremgangsmåte ifølge krav 1, omfattende å omsette (3-klorfenyl)borsyre:

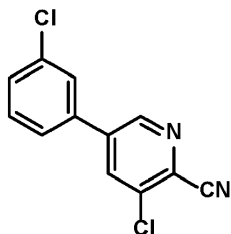


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med 3,5-diklor-2-cyanopyridin:

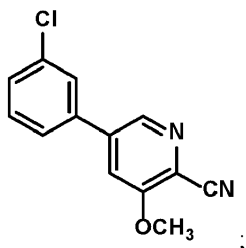


i nærvær av K_2CO_3 , [1,1'-bis(difenylfosfino)ferrocen]diklorpalladium(II), i DMF ved 45 °C for å danne 5-(3-klorfenyl)-3-klor-2-cyanopyridin:



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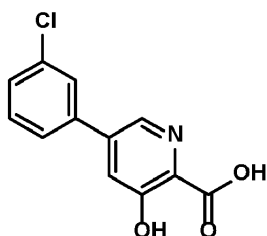
7. Fremgangsmåte ifølge krav 6, videre omfattende å omsette 5-(3-klorfenyl)-3-klor-2-cyanopyridin med natriummetoksyd og metanol under tilbakesløp for å danne 5-(3-klorfenyl)-3-metoksy-2-cyanopyridin:



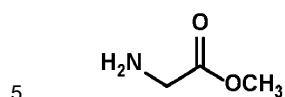
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omsetting av 5-(3-klorfenyl)-3-metoksy-2-cyanopyridin med 48 % hydrobromsyre ved tilbakesløp for å danne 5-(3-klorfenyl)-3-hydroksypyridin-2-karboksytsyre:

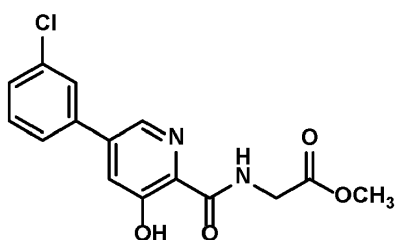
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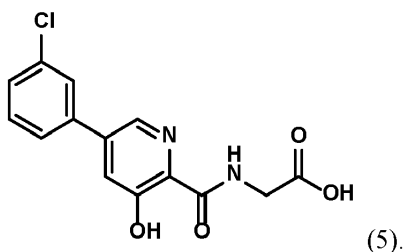
8. Fremgangsmåte ifølge krav 7, videre omfattende å omsette 5-(3-klorfenyl)-3-hydroksypyridin-2-karboksylysyre med glycinmetylester:



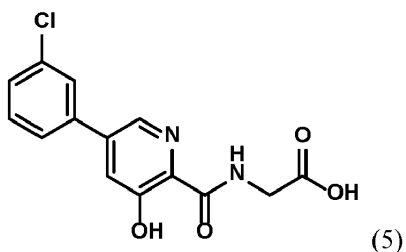
i nærvær av karbonyldiimidazol (CDI) og DIPEA i DMSO ved romtemperatur for å danne metyl {[5-(3-klorfenyl)-3-hydroksypyridin-2-yl]amino}acetat:



10 9. Fremgangsmåte ifølge krav 8, videre omfattende å omsette metyl {[5-(3-klorfenyl)-3-hydroksypyridin-2-yl]amino}acetat med natriumhydroksid i THF for å danne forbindelse (5):

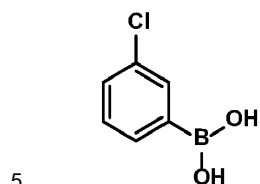


10. Fremgangsmåde for fremstilling af forbindelse (5):

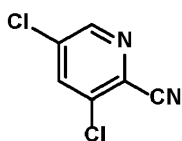


omfattende:

A. omsette (3-klorfenyl)borsyre:

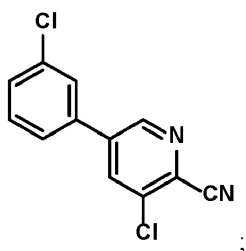


med 3,5-diklor-2-cyanopyridin:

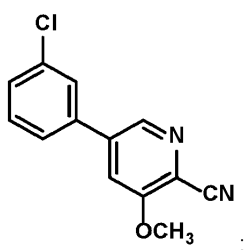


i nærvær af [1,1'-bis(difenylfosfino)ferrocen]diklorpalladium(II) og K_2CO_3 i DMF ved 45 °C for å danne 5-(3-klorfenyl)-3-klor-2-cyanopyridin:

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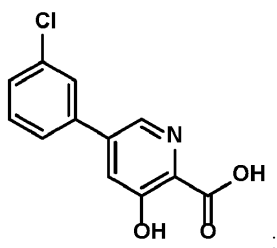
B. omsette 5-(3-klorfenyl)-3-klor-2-cyanopyridin med natriummetoksyd i metanol ved tilbakeløp for å danne 5-(3-klorfenyl)-3-metoksy-2-cyanopyridin:



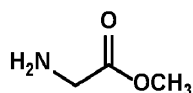
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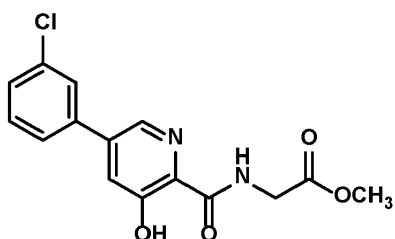
C. omsette 5-(3-klorfenyl)-3-metoksy-2-cyanopyridin med 48 % hydrobromsyre ved tilbakeløp for å danne 5-(3-klorfenyl)-3-hydroksypyridin-2-karboksylysyre:



5 D. omsette 5-(3-klorfenyl)-3-hydroksypyridin-2-karboksylysyre med glycinmetylester:



i nærvær av CDI og DIPEA i DMSO ved romtemperatur for å danne metyl {[5-(3-klorfenyl)-3-hydroksypyridin-2-yl]amino}acetat:



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E. omsette metyl {[5-(3-klorfenyl)-3-hydroksypyridin-2-yl]amino}acetat med natriumhydroksid i THF for å danne forbindelse (5):

