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(54) Title: NOVEL NICKEL CATALYST, PROCESS FOR PREPARATION AND USE THEREOF

(57) Abstract: The present invention disclosed to a novel nickel catalyst of formula (I) process for preparation of the same and use of nickel catalyst of formula (I) for C-H bond alkylation, and benzylolation of heteroarenes.



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**“NOVEL NICKEL CATALYST, PROCESS FOR PREPARATION AND USE
THEREOF”**

5 The following specification particularly describes the invention and the manner in which it is to be performed.

FIELD OF THE INVENTION:

10 The present invention relates to a novel nickel catalyst of formula (I). More particularly, the present invention relates to a novel nickel catalyst of formula (I), process for preparation of the same and use of nickel catalyst of formula (I) for C-H bond alkylation or benzylation of heteroarenes.

BACKGROUND AND PRIOR ART:

15 Heteroarenes are the very important building blocks in many pharmaceutically relevant compounds and biologically active natural products; hence the efficient and regioselective functionalization of heteroarenes like, indoles, pyrazoles and imidazoles are highly desirable. Indoles are indispensable substructures of various natural products, drugs, and biologically active compounds. Thus, there is a growing interest in the efficient and selective functionalization of indoles, particularly by
20 developing the strategies based on transition-metal-catalyzed direct C–H bond activation. While various effective methods were devised for the regioselective arylations and alkenylations of indoles, significantly more challenging C–H bond alkylation with unactivated alkyl halides containing β -hydrogen is very scarce, which is mainly due to the difficulty in oxidative addition of alkyl halides onto the transition
25 metals and their tendency to β -hydride eliminations. Indeed, only a few methods for direct alkylation of indoles with alkyl halides have been reported with a precious Pd-metal catalyst. In light of the beneficial features of earth-abundant 3d transition metals, Ackermann et al. described an inexpensive co-catalyzed C-2 alkylation of indoles with primary alkyl chlorides. However, the use of a strong base, the Grignard reagent CyMgCl, is the major limitation associated with this method.
30

A variety of nickel-catalyzed C–H functionalization have been established and found beneficial for organic synthesis. In general, Ni-catalyzed regioselective C–H functionalization has thus far been limited, with few exceptions, to the (hetero)arenes containing a N,N-bidentate auxiliary, (quinolin-8-yl)amide or (pyridin-2-yl)isopropyl amide. Along those lines, Ackermann et al. reported a Ni-catalyzed alkylation of indole-3-carboxamide with secondary alkyl halides through bidentate-chelate assistance, only with a limited scope. The bidentate directing group largely binds the Ni center more tightly and lowers the C–H activation barrier to facilitate the (hetero)arene C–H installation of an expensive bidentate auxiliary on each substrate before the C–H functionalization, which are the major disadvantages associated with it.

The regioselective direct C-H arylation and alkenylation at either the C2- or C3-position of indole have been successfully achieved by using palladium, rhodium, or copper catalysis. However, attempts to perform direct C-H alkylation reactions of indoles have been less successful so far. Although the 3-alkylation of indole can be achieved by catalytic methods such as Friedel-Crafts alkylation, allylic alkylation, and conjugate addition. A general protocol for the regioselective direct C-H alkylation at the C2-position of free N-H indoles has not yet been established. Given the limited availability of synthetic routes toward 2-alkylindoles, a straight-forward approach is highly demanded.

Article titled “8-Aminoquinoline: A Powerful Directing Group in Metal-Catalyzed Direct Functionalization of C-H Bonds” by M Corbet et al. published in *Angew Chem Int Ed Engl.*, 2013 ;52(38); pp 9896-9898 reports the 8-aminoquinoline auxiliary has recently gained much attention because of its versatility as a directing group in many metal-catalyzed direct CH bond functionalizations. Its chelating ability, its rigid backbone, and relatively acidic NH bond have proven to be critical in most transformations.

Article titled “Nickel-Catalyzed Direct Alkylation of C–H Bonds in Benzamides and Acrylamides with Functionalized Alkyl Halides via Bidentate-Chelation Assistance”

by Y Aihara published in *J. Am. Chem. Soc.*, 2013, 135 (14), pp 5308–5311 reports the alkylation of the ortho C–H bonds in benzamides and acrylamides containing an 8-aminoquinoline moiety as a bidentate directing group with unactivated alkyl halides using nickel complexes as catalysts.

5

Article titled “Ruthenium-Catalyzed Heteroatom-Directed Regioselective C–H Arylation of Indoles Using a Removable Tether” by VK Tiwari et al. published in *Org. Lett.*, 2015, 17 (7), pp 1766–1769 reports a new approach to C-2 arylated indoles has been developed by utilizing a ruthenium-catalyzed, heteroatom-directed regioselective C–H arylation. The reaction is highly site-selective and results in very good yields.

10

Article titled “Cobalt-Catalyzed C–H Bond Functionalizations with Aryl and Alkyl Chloride” by B Punji et al. published in *Chem. Eur. J.*, 2013, 19, pp 10605 – 10610 reports. Inexpensive cobalt catalysts derived from N-heterocyclic carbenes (NHC) allowed efficient catalytic C–H bond arylations on heteroaryl-substituted arenes with widely available aryl chlorides, which set the stage for the preparation of sterically hindered tri-*ortho*-substituted biaryls. The cobalt-catalyzed C–H bond functionalizations occurred efficiently at ambient reaction temperature with excellent levels of site-selectivities and ample scope.

15

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Review article titled “Transition Metal-Catalysed, Direct and Site-Selective N1-, C2- or C3-Arylation of the Indole Nucleus: 20 Years of Improvements” by L Joucla et. al. published in *Adv. Synth. Catal.*, 2009, 351, pp 673 – 714 reports a review of transition Metal-Catalysed, Direct and Site-Selective N1-, C2- or C3-Arylation of the Indoles.

25

Article titled “The Nickel/Copper-Catalyzed Direct Alkylation of Heterocyclic C–H Bonds” by O Vechorkin et al. published in *Angewandte Chemie International Edition*, 2010, 49 (17), pages 3061–3064 reports a general and straightforward protocol for the cross-coupling of non-activated alkyl halides with heterocyclic C–H bonds. The method employs cheap nickel/copper catalysts, and expands significantly the scope of C–H functionalization.

30

Article titled “Transition Metal-Catalyzed C-H Activation of Indoles” by AH Sandtorv et al. published in *Adv.Synth.Catal.*, 2015, 357, pp 2403–2435 discusses recent advances and strategies for transition metal-catalyzed C-H activation of
5 indoles.

Article titled “Rhodium-catalyzed regioselective direct C–H arylation of indoles with aryl boronic acids” by L Wang et al. published in *Tetrahedron Letters*, 2015, 56 (24), pp 3754–3757 reports a highly efficient Rh(III)-catalyzed direct C–H arylation of
10 indoles with aryl boronic acids under mild conditions. The methodology features wide substrate scope and excellent functional group compatibility (34 examples, up to 99% yield). The arylated products can also be conveniently transformed into biologically active polycyclic indole derivatives.

15 Article titled “Palladium- and nickel-catalyzed direct alkylation of azoles with unactivated alkyl bromides and chlorides’ by T Yao et al. published in *Chemistry - A European Journal*, 2010, 16 (41), pp 12307–12311 reports the catalytic direct C[BOND]H alkylation of azoles with unactivated alkyl bromides and chlorides. A palladium catalyst enables the alkylation of oxazoles, whereas a nickel one shows
20 unique activity for thiazole. The catalyses allow a straightforward access to azole motifs bearing long, functional alkyl side chains.

Article titled “Nickel catalyzed alkylation of N-aromatic heterocycles with Grignard reagents through direct C–H bond functionalization” by PY Xin et al. published in
25 *Chem. Commun.*, 2012,48, 6717-6719 reports a novel protocol for nickel-catalyzed direct sp² C–H bond alkylation of N-aromatic heterocycles. This new reaction proceeded efficiently at room temperature using a Grignard reagent as the coupling partner.

30 Article titled “Regioselective Direct C–H Alkylation of NH Indoles and Pyrroles by a Palladium/Norbornene-Cocatalyzed Process” by L Jiao et al. published in *Synthesis*; 2014; 46(01); pp 35-41 reports nitrogen-containing heterocycles, including 1H-

indoles and electron-deficient 1H-pyrroles, undergo a palladium/norbornene-cocatalyzed regioselective alkylation at the C–H bond adjacent to the NH group. A primary alkyl halide is used as the electrophile and the reaction proceeds smoothly under mild conditions to give 2-alkyl-1H-indoles and 2-substituted or 2,3-disubstituted 5-alkyl-1H-pyrroles in good yields.

Article titled “A General Palladium-Catalyzed Method for Alkylation of Heteroarenes Using Secondary and Tertiary Alkyl Halides” by X Wu et al. published in *Angew Chem Int Ed Engl*; 2014; 53 (49); pp 13573–13577 reports a general alkylation of heterocycles using a simple palladium catalyst. Most classes of heterocycles, including indoles and pyridines, efficiently coupled with unactivated secondary and tertiary alkyl halides. An alkyl radical addition to neutral heteroarenes.

Article titled “C–H arylation and alkenylation of imidazoles by nickel catalysis: solvent-accelerated imidazole C–H activation” by K Muto et al. published in *Chem. Sci.*, 2015, 6, 6792-6798 reports the first nickel-catalyzed C–H arylations and alkenylations of imidazoles with phenol and enol derivatives. Under the influence of Ni(OTf)₂/dcype/K₃PO₄ (dcype: 1,2-bis(dicyclohexylphosphino)ethane) in *t*-amyl alcohol, imidazoles can undergo C–H arylation with phenol derivatives. The C–H arylation of imidazoles with chloroarenes as well as that of thiazoles and oxazoles with phenol derivatives can also be achieved with this catalytic system.

Article titled “Ruthenium-Catalyzed Direct C-H Bond Arylations of Heteroarenes” by L Ackermann et al. published in *Org. Lett.*, 2011, 13 (13), pp 3332–3335 reports Ruthenium-catalyzed C–H bond arylations of indoles, thiophenes, and pyrroles were accomplished in a highly chemo- and site-selective manner through the use of removable directing groups.

Article titled “Nickel-catalyzed C-H alkylations: direct secondary alkylations and trifluoroethylations of arenes” by W Song et al. published in *Angew Chem Int Ed Engl.*; 2014; 53(9); pp 2477-2480 reports a versatile nickel catalyst allowed for C-H alkylations of unactivated arenes with challenging secondary alkyl bromides and

chlorides. The high catalytic efficacy also set the stage for direct secondary alkylations of indoles as well as C-H trifluoroethylations with ample substrate scope.

Article titled “User-Friendly [(Diglyme)NiBr₂]-Catalyzed Direct Alkylations of Heteroarenes with Unactivated Alkyl Halides through C—H Bond Cleavages” L Ackermann et al. published in *Adv. Synth. Catal.*; 2011, 353, pp 3325-3329 reports reports a nitrogen and phosphorus ligand-free catalytic system derived from inexpensive [(diglyme)NiBr₂] allowed for efficient direct C—H bond alkylations of heteroarenes with unactivated β-hydrogen-containing alkyl halides under basic reaction conditions.

Article titled “Rh(III)-Catalyzed C–H Alkylation of Arenes Using Alkylboron Reagents” by H Wang et al. published in *Org. Lett.*, 2015, 17 (11), pp 2812–2815 reports Rhodium(III)-catalyzed direct alkylation of arenes using commercially available alkyltrifluoroborates. Oximes, heteroarenes, azomethines, N-nitrosoamines, and amides are viable directing groups to entail this transformation. The alkyl group in the boron reagent can be extended to primary alkyls, benzyl, and cycloalkyls, and the reaction proceeded with controllable mono- and dialkylation selectivity when both ortho C–H sites are accessible.

Article titled “Transition Metal-Catalysed, Direct and Site-Selective N1-, C2- or C3-Arylation of the Indole Nucleus: 20 Years of Improvements” by L Joucla et al. published in *Advanced Synthesis*, 2009, 351 (5), pp.673-714 reports the direct and site-selective transition metal-catalysed N1-, C2- or C3-arylations of indoles have been the subject of almost continuous improvements.

Article titled “Metal-catalyzed direct alkylations of (hetero)arenes *via* C–H bond cleavages with unactivated alkyl halides “ by L Ackermann et al. published in *Chem. Commun.*, 2010,46, pp 4866-4877 reports a valuable asset of these methodologies is represented by their excellent regio- and chemoselectivities, along with remarkable mild reaction conditions, rendering this approach an attractive alternative to traditional alkylation strategies.

The prior art reports expensive catalysts such as palladium and rhodium for selective C-H bond alkylation, benzylation and arylation of these heteroarenes. These noble metal catalysts are very expensive because of the scarcity of these metal precursors in earth-crust. Further, the reported benzylation process of indoles via C(sp²)-H/C(sp³)-H oxidative coupling with toluene derivatives uses strong oxidants, such as peroxides or secondary transition- metal.

Therefore there is need in the art to develop an inexpensive nickel (earth-abundant) catalyst system which performs the alkylation and benzylation of various heteroarenes under mild reaction conditions.

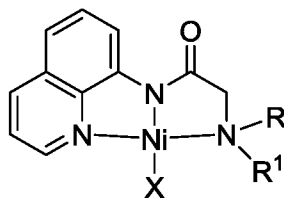
OBJECTIVE OF INVENTION:

The main objective of the present invention is to provide a nickel catalyst of formula (I) and process for preparation thereof.

Another objective of the present invention is to provide a process for the alkylation or benzylation - of heteroarenes with selectively at C2 position.

SUMMARY OF THE INVENTION:

Accordingly, the present invention provides a novel nickel catalyst of formula (I);



Formula I

Wherein;

R and R¹ are the same and are selected from the group consisting of alkyl, aryl, benzyl, heteroaryl, -(CH₂)₂O(CH₂)₂-, -(CH₂)₂N(Me)(CH₂)₂-, -(CH₂)₄-, -(CH₂)₅-, etc.

X is selected from the group consisting of hydrogen, halogen, OC(O)CH₃, OC(O)^tBu, OC(O)Ph, OC(O)admantyl, OSO₂CF₃, BF₄, SbF₆, etc.

In preferred embodiment, said nickel catalyst of formula (I) is selected from (R^2NNN^{8-Quin})-H, [2-(diethylamino)-N-(quinolin-8-yl)acetamide] (Et_2NNN^{8-Quin})NiCl, [2-(diethylamino)-N-(quinolin-8-yl)acetamide](NiCl) (Et_2NNN^{8-Quin})Ni(OAc), [2-(diethylamino)-N-(quinolin-8-yl)acetamide]Ni(OAc).

5

In another embodiment, the present invention provides a process for the preparation of nickel catalyst of formula (I), wherein said process comprising the steps of:

- a) Refluxing the reaction mixture of 2-bromo-N-(quinolin-8-yl) acetamide and amino compound in solvent for the period ranging from 20 to 24 hrs at temperature ranging from 60 to 80 °C afford (R^2NNN^{8-Quin})-H Ligands;
- b) Adding triethylamine to the mixture of compound of step (a), nickel compound and solvent followed by refluxing the reaction mixture for the period in the range of 3 to 12 hrs at a temperature ranging from 60 to 70 °C to afford compound of formula (I).

15

In preferred embodiment, said amino compound is selected from diisopropyl amine, diethylamine, dimethyl amine, morpholine, N-methyl piperazine, cyclopentyl amine, cyclohexyl amine.

- 20 In another preferred embodiment, said nickel compound is selected from (DME)NiCl₂, (THF)NiBr₂, Ni(OAc)₂.

In yet another preferred embodiment, said solvent in step (a) and (b) is selected from Acetone or Tetrahydrofuran (THF).

25

- In yet another embodiment, the present invention provides a process for the alkylation or benzylation of heteroarene in presence of novel nickel catalyst of formula (I), comprising stirring the reaction mixture of heteroarene, organic halide compound or benzyl compound, catalyst of formula (I), base and solvent at temperature ranging from 120 to 160 °C for the period ranging from 6 to 36 hrs to afford desired compound of formula (II).

30

In preferred embodiment, said heteroarene is selected from 1-(pyridine-2-yl)-1*H*-indole, 5-methyl-1-(pyridine-2-yl)-1*H*-indole, 5-methoxy-1-(pyridine-2-yl)-1*H*-indole, 5-fluoro-1-(pyridine-2-yl)-1*H*-indole, 5-bromo-1-(pyridine-2-yl)-1*H*-indole, 1-(pyridine-2-yl)-1*H*-indole-5-carbonitrile, 3-methyl-1-(pyridine-2-yl)-1*H*-indole, 1-(pyrimidin-2-yl)-1*H*-indole or 5-methoxy-1-(pyrimidin-2-yl)-1*H*-indole.

In another preferred embodiment, said organic halide compound is selected from 1-iodobutane, 1-iodopentane, 1-bromohexane, 1-bromodecane, 1-iodododecane, 1-bromotridecane, 1-bromotetradecane, 1-bromohexadecane, 1-bromooctadecane, 1-bromo-2-methylpropane, 1-bromo-3-methylbutane, (bromomethyl)cyclohexane, (2-bromoethyl)cyclohexane, 1-bromo-2,2-dimethylpropane, (3-bromopropyl)benzene, 1-(3-bromopropyl)-4-methoxybenzene, 1-chloro-4-iodobutane, 5-bromopent-1-ene, 9-(4-iodobutyl)-8a,9a-dihydro-9*H*-carbazole, 2-iodopropane, (1-bromoethyl)benzene, (bromoethylene)dibenzene, 2-iodobutane, bromocyclopropane, iodocyclopentane, bromocyclohexane, bromocycloheptane or 6-bromo-1-hexene.

In yet another preferred embodiment, said base is selected from Lithium bis(trimethylsilyl)amide [LiHMDS], Lithium tert-butoxide (LiOtBu) or mixture thereof.

In still another preferred embodiment, said benzyl compound is selected from toluene, *p*-xylene, *m*-xylene, 1-methoxy-4-methylbenzene, 1-fluoro-4-methylbenzene, 1-chloro-4-methylbenzene, 1-bromo-4-methylbenzene, *ortho*-xylene, 1-fluoro-2-methylbenzene, 1-chloro-2-methylbenzene, 1-bromo-2-methylbenzene, 1-methyl-2-(trifluoromethyl)benzene, mesitylene, 2,4-difluoro-1-methylbenzene, 1-methylnaphthalene, 1-(*p*-tolyl)-1*H*-indole toluene.

In yet still another preferred embodiment, said solvent is selected from toluene, chlorobenzene or mixture thereof.

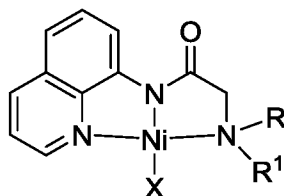
DETAILED DESCRIPTION OF THE INVENTION:

The invention will now be described in detail in connection with certain preferred and optional embodiments, so that various aspects thereof may be more fully understood and appreciated.

5

In the view of above, the present invention provides a novel nickel catalyst of formula (I), process for preparation of the same and use of these nickel catalyst of formula (I) for C-H bond alkylation and, benzylation of heteroarenes.

10 In an embodiment, the present invention provides novel nickel catalyst of formula (I);



Formula I

Wherein;

R and R¹ are the same and are selected from the group consisting of alkyl, aryl, benzyl, heteroaryl, -(CH₂)₂O(CH₂)₂-, -(CH₂)₂N(Me)(CH₂)₂-, -(CH₂)₄-, -(CH₂)₅-, etc.

15 X is selected from the group consisting of hydrogen, halogen, OC(O)CH₃, OC(O)^tBu, OC(O)Ph, OC(O)admantyl, OSO₂CF₃, BF₄, SbF₆, etc.

In preferred embodiment, said nickel catalyst of formula (I) is selected from (R²NNN^{8-Quin})-H, [2-(diethylamino)-N-(quinolin-8-yl)acetamide] (Et₂NNN^{8-Quin})NiCl [2-(diethylamino)-N-(quinolin-8-yl)acetamide](NiCl), (Et₂NNN^{8-Quin})Ni(OAc) [2-(diethylamino)-N-(quinolin-8-yl)acetamide].

20

In another embodiment, the present invention provides a process for the preparation of nickel catalyst of formula (I), wherein said process comprising the steps of:

25 a) Refluxing the reaction mixture of 2-bromo-N-(quinolin-8-yl) acetamide and amino compound in solvent for the period ranging from 20 to 24 hrs at temperature ranging from 60 to 80 °C afford (R²NNN^{8-Quin})-H Ligands;

b) Adding triethylamine to the mixture of compound of step (a), nickel compound and solvent followed by refluxing the reaction mixture for the period in the range of 3 to 12 hrs at a temperature ranging from 60 to 70 °C to afford compound of formula (I).

5

In preferred embodiment, said amino compound is selected from diisopropyl amine, diethylamine, dimethyl amine, morpholine, N-methyl piperazine, cyclopentyl amine, cyclohexyl amine.

10 In another preferred embodiment, said nickel compound is selected from (DME)NiCl₂, (THF)NiBr₂, Ni(OAc)₂.

In yet another preferred embodiment said solvent in step (a) and (b) is selected from Acetone or Tetrahydrofuran (THF).

15

In yet another embodiment, the present invention provides a process for the alkylation or benzylation of heteroarene in presence of novel catalyst of formula (I), comprising stirring the reaction mixture of heteroarene, organic halide compound or benzyl compound, catalyst of formula (I), base and solvent at temperature ranging from 120
20 to 160 °C for the period ranging from 6 to 36 hrs to afford desired compound of formula (II).

In preferred embodiment, said heteroarene is selected from 1-(pyridine-2-yl)-1*H*-indole, 5-methyl-1-(pyridine-2-yl)-1*H*-indole, 5-methoxy-1-(pyridine-2-yl)-1*H*-
25 indole, 5-fluoro-1-(pyridine-2-yl)-1*H*-indole, 5-bromo-1-(pyridine-2-yl)-1*H*-indole, 1-(pyridine-2-yl)-1*H*-indole-5-carbonitrile, 3-methyl-1-(pyridine-2-yl)-1*H*-indole, 1-(pyrimidine-2-yl)-1*H*-indole, 5-methoxy-1-(pyrimidine-2-yl)-1*H*-indole.

In another preferred embodiment, said organic halide compound is selected from 1-
30 iodobutane, 1-iodopentane, 1-bromohexane, 1-bromodecane, 1-iodododecane, 1-bromotridecane, 1-bromotetradecane, 1-bromohexadecane, 1-bromooctadecane, 1-bromo-2-methylpropane, 1-bromo-3-methylbutane, (bromomethyl)cyclohexane, (2-

bromoethyl)cyclohexane, 1-bromo-2,2-dimethylpropane, (3-bromopropyl)benzene, 1-(3-bromopropyl)-4-methoxybenzene, 1-chloro-4-iodobutane, 5-bromopent-1-ene, 9-(4-iodobutyl)-8a,9a-dihydro-9*H*-carbazole, 2-iodopropane, (1-bromoethyl)benzene, (bromoethylene)dibenzene, 2-iodobutane, bromocyclopropane, iodocyclopentane,
 5 bromocyclohexane, bromocycloheptane, 6-bromo-1-hexene.

In yet another preferred embodiment, said base is selected from Lithium bis(trimethylsilyl)amide [LiHMDS], Lithium tert-butoxide (LiOtBu) or mixture thereof.

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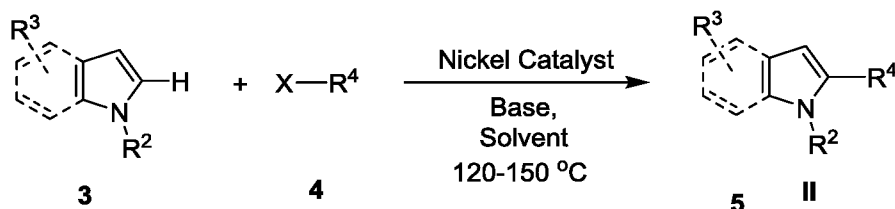
In still another preferred embodiment, said benzyl compound is selected from toluene, *p*-xylene, *m*-xylene, 1-methoxy-4-methylbenzene, 1-fluoro-4-methylbenzene, 1-chloro-4-methylbenzene, 1-bromo-4-methylbenzene, *ortho*-xylene, 1-fluoro-2-methylbenzene, 1-chloro-2-methylbenzene, 1-bromo-2-methylbenzene, 1-methyl-2-(trifluoromethyl)benzene, mesitylene, 2,4-difluoro-1-methylbenzene, 1-methylnaphthalene, 1-(*p*-tolyl)-1*H*-indoletoleuene.

15

In yet still another preferred embodiment, said solvent is selected from toluene, chlorobenzene or mixture thereof.

20

The process for the alkylation of heteroarenes is as shown in scheme 1:



Scheme: 1

Wherein,

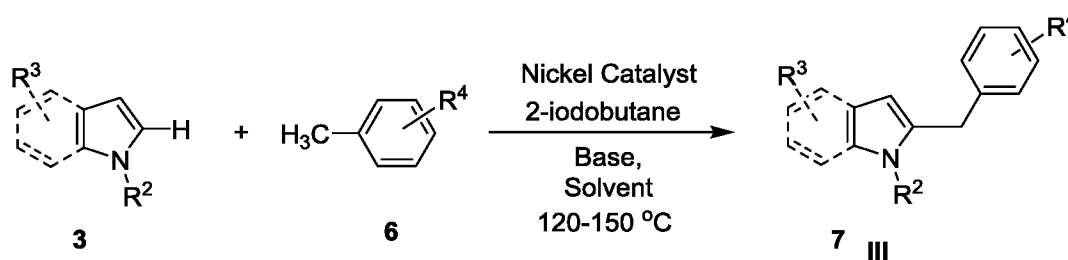
25 X is halogen selected from chlorine, bromine, iodine.

R² is selected from 2-pyridine, 2-pyrimidine, 2,4-pyrazine, , etc.

R³ is selected from hydrogen, alkyl, alkoxy, substituted alkoxy, phenoxy, halogens, trifluoromethyl, etc.

R⁴ is selected from octyl, butyl, decyl, dodecyl, tetradecyl and others alkyl group

The process for the benzylation of heteroarenes is as shown in scheme 2:



Scheme: 2

Wherein,

R² is selected from 2-pyridine, 2-pyrimidine, 2,4-pyrazine, 2-oxazole, etc.

R³ is selected from hydrogen, alkyl, alkoxy, substituted alkoxy, phenoxy, halogens, trifluoromethyl, etc.

R⁴ is selected from hydrogen, methyl, alkoxy, etc.

The following examples, which include preferred embodiments, will serve to illustrate the practice of this invention, it being understood that the particulars shown are by way of example and for purpose of illustrative discussion of preferred embodiments of the invention.

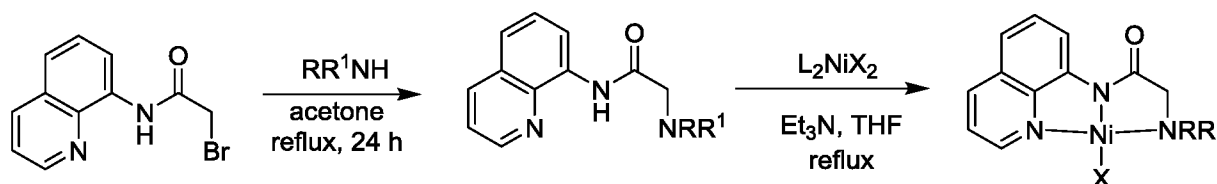
Examples:

Example 1: Synthesis of 2-Bromo-N-(quinolin-8-yl)acetamide:

To a solution of 8-aminoquinoline (1.0 g, 6.94 mmol) in CH₂Cl₂ (40 mL), Et₃N (1.02 mL, 7.32 mmol) was added at 0°C and stirred for 20 min. To the resulted reaction mixture, bromo acetyl chloride (1.20 g, 7.64 mmol) was added dropwise *via* a syringe. The reaction mixture was then allowed to warm to room temperature and continued stirring for 24 h. At ambient temperature, the reaction mixture was quenched with water (20 mL) and extracted with CH₂Cl₂ (15 mL x 3). The combined organic phase was washed with H₂O (15 mL x 3) and dried over Na₂SO₄. After filtration and evaporation of the solvents in *vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/EtOAc: 5/1) yielded the desired product as

light yellow solid. Yield: 1.30 g (71%). $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 10.89 (br s, 1H, N-H), 8.85 (dd, J = 4.2, 1.5 Hz, 1H, Ar-H), 8.74 (dd, J = 6.1, 2.9 Hz, 1H, Ar-H), 8.17 (dd, J = 8.3, 1.5 Hz, 1H, Ar-H), 7.57-7.54 (m, 2H, Ar-H), 7.47 (dd, J = 8.3, 4.2 Hz, 1H, Ar-H), 4.32 (s, 2H, CH_2). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ = 164.6 (CO), 148.8 (CH), 138.8 (C_q), 136.6 (CH), 133.7 (C_q), 128.1 (C_q), 127.4 (CH), 122.7 (CH), 121.9 (CH), 116.9 (CH), 43.5 (CH_2). HRMS (ESI): m/z Calcd for $\text{C}_{11}\text{H}_9\text{BrN}_2\text{O}+\text{H}^+$ [M+H] $^+$ 264.9971 and 266.9953; Found 264.9966 and 266.9945.

Example 2: General Procedure for the Synthesis of ($\text{R}^2\text{NNN}^8\text{-Quin}$)-H Ligands:



A mixture of 2-bromo-*N*-(quinolin-8-yl)acetamide (1.0 g, 3.77 mmol) and Et_2NH (0.83 g, 11.35 mmol) in acetone (30 mL) was refluxed for 24 h. The reaction mixture was then cooled to room temperature and quenched with distilled H_2O (20 mL). The crude aminated product was extracted with EtOAc (15 mL x 3), and the combined organic extract was washed with H_2O (15 mL x 3) and dried over Na_2SO_4 . After filtration and evaporation of the volatiles in *vacuo*, the crude product was purified by column chromatography on silica gel (*n*-hexane/ EtOAc / Et_3N : 5/1/0.5) yielded the desired product ($\text{Et}^2\text{NNN}^8\text{-Quin}$)-H.

($\text{Et}^2\text{NNN}^8\text{-Quin}$)-H: Yield: 0.95 g, 98%. $^1\text{H-NMR}$ (200 MHz, CDCl_3): δ = 11.56 (br s, 1H, N-H), 8.85-8.79 (m, 2H, Ar-H), 8.12 (dd, J = 8.3, 1.6 Hz, 1H, Ar-H), 7.57-7.46 (m, 2H, Ar-H), 7.41 (dd, J = 8.3, 4.2 Hz, 1H, Ar-H), 3.29 (s, 2H, CH_2), 2.70 (q, J = 7.2 Hz, 4H, CH_2), 1.16 (t, J = 7.2 Hz, 6H, CH_3). $^{13}\text{C-NMR}$ (100 MHz, CDCl_3): δ = 171.3 (CO), 148.6 (CH), 139.3 (C_q), 136.2 (CH), 134.7 (C_q), 128.2 (C_q), 127.4 (CH), 121.7 (CH), 121.6 (CH), 116.6 (CH), 59.2 (CH_2), 48.9 (2C, CH_2), 12.7 (2C, CH_3).

(Morph $\text{NNN}^8\text{-Quin}$)-H: Yield: 92%. $^1\text{H-NMR}$ (400 MHz, CDCl_3): δ = 11.45 (br s, 1H, N-H), 8.85 (dd, J = 4.2, 1.6 Hz, 1H, Ar-H), 8.76 (dd, J = 6.9, 1.8 Hz, 1H, Ar-H), 8.14 (dd, J = 8.3, 1.6 Hz, 1H, Ar-H), 7.55-7.48 (m, 2H, Ar-H), 7.44 (dd, J = 8.3, 4.3 Hz,

1H, Ar-H), 3.89 (t, $J = 4.5$ Hz, 4H, CH₂), 3.27 (s, 2H, CH₂), 2.68 (t, $J = 4.5$ Hz, 4H, CH₂). ¹³C-NMR (100 MHz, CDCl₃): $\delta = 168.9$ (CO), 148.7 (CH), 139.1 (C_q), 136.3 (CH), 134.4 (C_q), 128.2 (C_q), 127.4 (CH), 121.9 (CH), 121.7 (CH), 116.7 (CH), 67.4 (2C, CH₂), 62.9 (CH₂), 53.9 (2C, CH₂).

- 5 (PiperNNN⁸-Quin)-H: ¹H-NMR (400 MHz, CDCl₃): $\delta = 11.43$ (br s, 1H, N-H), 8.85 (dd, $J = 4.3, 1.8$ Hz, 1H, Ar-H), 8.76 (dd, $J = 6.1, 2.8$ Hz, 1H, Ar-H), 8.15 (dd, $J = 8.3, 1.8$ Hz, 1H, Ar-H), 7.55-7.49 (m, 2H, Ar-H), 7.44 (dd, $J = 8.3, 4.3$ Hz, 1H, Ar-H), 3.29 (s, 2H, CH₂), 2.73 (br s, 4H, CH₂), 2.64 (br s, 4H, CH₂), 2.38 (s, 3H, CH₃). ¹³C-NMR (100 MHz, CDCl₃): $\delta = 169.3$ (CO), 148.6 (CH), 139.2 (C_q), 136.3 (CH), 134.5 (C_q),
10 128.2 (C_q), 127.5 (CH), 121.8 (CH), 121.7 (CH), 116.7 (CH), 62.5 (CH₂), 55.5 (2C, CH₂), 53.5 (2C, CH₂), 46.2 (CH₃).

Example 3: Synthesis of (Et²NNN⁸-Quin)NiCl:

- To a schlenk flask equipped with magnetic stir bar was introduced (Et²NNN⁸-Quin)N-H
15 (0.3 g, 1.166 mmol) and (DME)NiCl₂ (0.27 g, 1.229 mmol), and THF (20 mL) was added into it. Then, the Et₃N (0.16 mL, 1.148 mmol) was added and the reaction mixture was heated to reflux for 3 h. The reaction mixture was cooled to ambient temperature and all the volatiles were evaporated under vacuum. The resultant residue was washed with *n*-hexane (10 mL x 3) and the product was extracted with toluene
20 (10 mL x 2). The toluene extract was concentrated and *n*-hexane was added to precipitate the pure product of (Et²NNN⁸-Quin)NiCl complex. Yield: 0.375 g, 92%.

- ¹H-NMR (400 MHz, CDCl₃): $\delta = 8.59$ (d, $J = 7.9$ Hz, 1H, Ar-H), 8.54 (dd, $J = 5.2, 0.9$ Hz, 1H, Ar-H), 8.17 (dd, $J = 8.2, 1.2$ Hz, 1H, Ar-H), 7.43 (vt, $J = 7.9$ Hz, 1H, Ar-H), 7.29-7.25 (m, 2H, Ar-H), 3.20 (s, 2H, CH₂), 3.15 (app sextet, $J = 4.9$ Hz, 2H, CH₂),
25 2.38 (t, $J = 7.0$ Hz, 6H, CH₃), 2.06 (app sextet, $J = 5.5$ Hz, 2H, CH₂). ¹³C-NMR (100 MHz, CDCl₃): $\delta = 176.3$ (CO), 151.4 (CH), 145.9 (C_q), 143.7 (C_q), 138.8 (CH), 129.4 (CH), 128.7 (C_q), 121.2 (CH), 119.6 (CH), 119.3 (CH), 63.5 (CH₂), 57.8 (2C, CH₂), 13.7 (2C, CH₃).

Example 4: Synthesis of (^{Et2}NNN^{8-Quin})Ni(OAc):

This complex was synthesized following the procedure similar to the synthesis of (^{Et2}NNN^{8-Quin})NiCl, using (^{Et2}NNN^{8-Quin})N-H (0.3 g, 1.166 mmol), Ni(OAc)₂ (0.216 g, 1.222 mmol) and Et₃N (0.16 mL, 1.148 mmol).

- 5 ¹H-NMR (400 MHz, CDCl₃): δ = 8.46 (d, *J* = 7.5 Hz, 1H, Ar-H), 8.19 (d, *J* = 7.8 Hz, 1H, Ar-H), 7.55 (d, *J* = 4.5 Hz, 1H, Ar-H), 7.42 (vt, *J* = 7.9 Hz, 1H, Ar-H), 7.32-7.22 (m, 2H, Ar-H), 3.22 (s, 2H, CH₂), 2.86 (app sextet, *J* = 5.1 Hz, 2H, CH₂), 2.34 (t, *J* = 6.7 Hz, 6H, CH₃), 2.21 (app sextet, *J* = 6.1 Hz, 2H, CH₂), 1.98 (s, 3H, CH₃). ¹³C-NMR (100 MHz, CDCl₃): δ = 178.6 (CO), 175.2 (CO), 148.7 (CH), 145.6 (C_q), 143.4 (C_q), 138.7 (CH), 129.4 (CH), 128.8 (C_q), 121.4 (CH), 119.7 (CH), 119.0 (CH), 62.6 (CH₂), 56.1 (2C, CH₂), 24.5 (COCH₃), 13.1 (2C, CH₃).
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Example 5: Representative procedure for the alkylation of indoles:**a) Synthesis of 2-octyl-1-(pyridine-2-yl)-1*H*-indole:**

- 15 To a flame-dried screw-capped tube equipped with a magnetic stir bar were introduced 1-pyridine-2-yl-1*H*-indole (0.58 g, 0.3 mmol), 1-iodooctane (0.144 g, 0.6 mmol), (^{Et2}NNN^{8-Quin})Ni(OAc) (0.0056 g, 0.015 mmol, 5.0 mol%), LiHMDS (0.010 g, 0.06 mmol, 20 mol%) and LiOtBu (0.048 g, 0.60 mmol), and toluene (0.15 mL) was added into it. The resultant reaction mixture was stirred at 150 °C in a preheated oil
- 20 bath for 16 h. At ambient temperature, H₂O (5 mL) was added and the reaction mixture was extracted with CH₂Cl₂ (20 mL x 3). The combined organic layers were dried over Na₂SO₄ and the solvent was evaporated in vacuo. The remaining residue was purified using column chromatography on neutral alumina (*n*-hexane–EtOAc 50/1) to yield desired compound (0.075 g, 82%) as an oily liquid. ¹H-NMR (500
- 25 MHz, CDCl₃): δ = 8.68 (d, *J* = 5.0 Hz, 1H, Ar-H), 7.88 (td, *J* = 7.6, 1.8 Hz, 1H, Ar-H), 7.60-7.58 (m, 1H, Ar-H), 7.44 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.35-7.31 (m, 2H, Ar-H), 7.16-7.12 (m, 2H, Ar-H), 6.47 (s, 1H, Ar-H), 2.85 (t, *J* = 7.6 Hz, 2H, CH₂), 1.61-1.55 (m, 2H, CH₂), 1.31-1.24 (m, 10H, CH₂), 0.89 (t, *J* = 6.9 Hz, 3H, CH₃). ¹³C{¹H}-NMR (125 MHz, CDCl₃): δ = 151.8 (C_q), 149.8 (CH), 141.9 (C_q), 138.4 (CH), 137.4 (C_q), 128.8 (C_q), 122.1 (CH), 121.7 (CH), 121.3 (CH), 120.7 (CH), 120.0 (CH), 110.2 (CH), 102.2 (CH), 32.0 (CH₂), 29.5 (2C, CH₂), 29.3 (CH₂), 28.7 (CH₂), 27.6 (CH₂),
- 30

22.8 (CH₂), 14.3 (CH₃). HRMS (ESI): m/z Calcd for C₂₁H₂₆N₂+H⁺ [M+H]⁺ 307.2169; Found 307.2172.

b) 2-Octadecyl-1-(pyridin-2-yl)-1H-indole (5aj):

- 5 The representative procedure was followed, using substrate **3a** (0.058 g, 0.3 mmol), 1-bromooctadecane (**4j**; 0.20 g, 0.6 mmol) and KI (0.1 g, 0.6 mmol), and the reaction mixture was stirred for 20 h. Purification by column chromatography on neutral alumina (Pet ether/EtOAc/Et₃N: 50/1/0.5) yielded **5aj** (0.075 g, 56%) as a light yellow solid. ¹H-NMR (400 MHz, CDCl₃): δ = 8.68 (dd, J = 5.0, 1.8 Hz, 1H, Ar-H), 7.92-7.87 (m, 1H, Ar-H), 7.61-7.57 (m, 1H, Ar-H), 7.44 (d, J = 8.2 Hz, 1H, Ar-H), 7.35-7.32 (m, 2H, Ar-H), 7.15-7.12 (m, 2H, Ar-H), 6.46 (s, 1H, Ar-H), 2.85 (t, J = 7.3 Hz, 2H, CH₂), 1.60-1.58 (m, 2H, CH₂), 1.36-1.24 (m, 30H, CH₂), 0.91 (t, J = 6.4 Hz, 3H, CH₃). ¹³C{¹H}-NMR (100 MHz, CDCl₃): δ = 151.8 (C_q), 149.8 (CH), 142.0 (C_q), 138.4 (CH), 137.4 (C_q), 128.8 (C_q), 122.2 (CH), 121.7 (CH), 121.3 (CH), 120.7 (CH), 120.0 (CH), 110.2 (CH), 102.2 (CH), 32.1 (CH₂), 29.9 (8C, CH₂), 29.8 (CH₂), 29.7 (CH₂), 29.6 (2C, CH₂), 29.5 (CH₂), 28.8 (CH₂), 27.6 (CH₂), 22.9 (CH₂), 14.3 (CH₃). HRMS (ESI): m/z Calcd for C₃₁H₄₆N₂+H⁺ [M+H]⁺ 447.3734; Found 447.3730.
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c) 2-Dodecyl-5-methyl-1-(pyridin-2-yl)-1H-indole (5bf):

- 20 The representative procedure was followed using, 5-methyl-1-(pyridine-2-yl)-1H-indole (**3b**; 0.062 g, 0.3 mmol) and iodide **4f** (0.178 g, 0.6 mmol), and the reaction mixture was stirred for 16 h. Purification by column chromatography on neutral alumina (Pet ether/EtOAc/Et₃N: 20/1/0.5) yielded **5bf** (0.105 g, 93%) a light yellow liquid. ¹H-NMR (500 MHz, CDCl₃): δ = 8.67 (dd, J = 5.0, 1.5 Hz, 1H, Ar-H), 7.87 (td, J = 7.6, 1.9 Hz, 1H, Ar-H), 7.42 (d, J = 8.0 Hz, 1H, Ar-H), 7.37 (s, 1H, Ar-H), 7.31-7.29 (m, 1H, Ar-H), 7.24 (d, J = 8.4 Hz, 1H, Ar-H), 6.96 (dd, J = 8.3, 1.1 Hz, 1H, Ar-H), 6.38 (s, 1H, Ar-H), 2.84 (t, J = 7.6 Hz, 2H, CH₂), 2.45 (s, 3H, CH₃), 1.59-1.53 (m, 2H, CH₂), 1.34-1.23 (m, 18H, CH₂), 0.91 (t, J = 6.9 Hz, 3H, CH₃). ¹³C{¹H}-NMR (125 MHz, CDCl₃): 152.0 (C_q), 149.7 (CH), 142.0 (C_q), 138.3 (CH), 135.8 (C_q), 129.9 (C_q), 129.1 (C_q), 123.1 (CH), 121.9 (CH), 121.1 (CH), 119.8 (CH), 109.9 (CH), 101.9 (CH), 32.1 (CH₂), 29.8 (CH₂), 29.8 (CH₂), 29.8 (CH₂), 29.7 (CH₂), 29.5 (2C, CH₂),
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29.5 (CH₂), 28.8 (CH₂), 27.7 (CH₂), 22.9 (CH₂), 21.5 (CH₃), 14.3 (CH₃). HRMS (ESI): *m/z* Calcd for C₂₆H₃₆N₂+H⁺ [M+H]⁺ 377.2946; Found 377.2951.

d) 5-Methoxy-2-octyl-1-(pyridin-2-yl)-1*H*-indole (5ca):

5 The representative procedure was followed, using 5-methoxy-1-(pyridine-2-yl)-1*H*-indole (**3c**; 0.067 g, 0.3 mmol) and iodide **4a** (0.144 g, 0.6 mmol), and the reaction mixture was stirred for 16 h. Purification by column chromatography on neutral alumina (Pet ether/EtOAc/Et₃N: 10/1/0.5) yielded **5ca** (0.053 g, 53%) as a light yellow liquid. ¹H-NMR (400 MHz, CDCl₃): δ = 8.63 (dd, *J* = 4.4, 1.0 Hz, 1H, Ar-H),
10 7.85 (td, *J* = 7.8, 1.8 Hz, 1H, Ar-H), 7.38 (d, *J* = 8.3 Hz, 1H, Ar-H), 7.29-26 (m, 1H, Ar-H), 7.22 (d, *J* = 8.8 Hz, 1H, Ar-H), 7.04 (d, *J* = 2.5 Hz, 1H, Ar-H), 6.76 (dd, *J* = 8.8, 2.5 Hz, 1H, Ar-H), 6.36 (s, 1H, Ar-H), 3.84 (s, 3H, CH₃), 2.81 (t, *J* = 7.3 Hz, 2H, CH₂), 1.58-1.50 (m, 2H, CH₂), 1.31-1.21 (m, 10H, CH₂), 0.86 (t, *J* = 6.6 Hz, 3H, CH₃). ¹³C{¹H}-NMR (100 MHz, CDCl₃): 154.9 (C_q), 151.9 (C_q), 149.7 (CH), 142.6
15 (C_q), 138.4 (CH), 132.6 (C_q), 129.4 (C_q), 121.9 (CH), 121.0 (CH), 111.2 (CH), 111.0 (CH), 102.3 (CH), 102.1 (CH), 56.0 (CH₃), 32.0 (CH₂), 29.5 (2C, CH₂), 29.3 (CH₂), 28.8 (CH₂), 27.7 (CH₂), 22.8 (CH₂), 14.3 (CH₃). HRMS (ESI): *m/z* Calcd for C₂₂H₂₈N₂O+H⁺ [M+H]⁺ 337.2274; Found 337.2273. The ¹H and ¹³C spectra are consistent with those reported in the literature.⁴

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e) 2-Octyl-1-(pyridin-2-yl)-1*H*-indole-5-carbonitrile (5fa):

The representative procedure was followed using, 1-(pyridin-2-yl)-1*H*-indole-5-carbonitrile (**3f**; 0.066 g, 0.3 mmol) and iodide **4a** (0.144 g, 0.6 mmol), and the reaction mixture was stirred for 16 h. Purification by column chromatography on
25 neutral alumina (Pet ether/EtOAc/Et₃N: 20/1/0.5) yielded **5fa** (0.038 g, 38%) a light yellow liquid. ¹H-NMR (400 MHz, CDCl₃): δ = 8.69 (dd, *J* = 4.4, 1.0 Hz, 1H, Ar-H), 7.95 (td, *J* = 7.8, 2.0 Hz, 1H, Ar-H), 7.90 (s, 1H, Ar-H), 7.43-7.39 (m, 2H, Ar-H), 7.36-7.29 (m, 2H, Ar-H), 6.50 (s, 1H, Ar-H), 2.78 (t, *J* = 7.3 Hz, 2H, CH₂), 1.56 (pent, *J* = 7.3 Hz, 2H, CH₂), 1.30-1.22 (m, 10H, CH₂), 0.86 (t, *J* = 6.9 Hz, 3H, CH₃).
30 ¹³C{¹H}-NMR (100 MHz, CDCl₃): 150.7 (CN), 150.2 (CH), 144.6 (C_q), 139.1 (C_q), 138.8 (CH), 128.6 (C_q), 125.3 (CH), 124.9 (CH), 123.2 (CH), 121.6 (CH), 120.9 (C_q), 111.1 (CH), 103.7 (C_q), 102.4 (CH), 32.0 (CH₂), 29.4 (2C, CH₂), 29.3 (CH₂), 28.5

(CH₂), 27.5 (CH₂), 22.8 (CH₂), 14.3 (CH₃). HRMS (ESI): *m/z* Calcd for C₂₂H₂₅N₃+H⁺ [M+H]⁺ 332.2121; Found 332.2119.

f) 2-Dodecyl-1-(pyridin-2-yl)-1*H*-indole-5-carbonitrile (5ff):

- 5 The representative procedure was followed using, substrate **3f** (0.066 g, 0.3 mmol) and iodide **4f** (0.178 g, 0.6 mmol), and the reaction mixture was stirred for 16 h. Purification by column chromatography on neutral alumina (Pet ether/EtOAc/Et₃N: 20/1/0.5) yielded **5ff** (0.052 g, 45%) a light yellow liquid. ¹H-NMR (500 MHz, CDCl₃): δ = 8.69 (d, *J* = 4.2 Hz, 1H, Ar-H), 7.94 (td, *J* = 7.6, 1.5 Hz, 1H, Ar-H), 7.89 (s, 1H, Ar-H), 7.42-7.38 (m, 2H, Ar-H), 7.34-7.29 (m, 2H, Ar-H), 6.49 (s, 1H, Ar-H), 2.78 (t, *J* = 7.6 Hz, 2H, CH₂), 1.56 (pent, *J* = 7.4 Hz, 2H, CH₂), 1.34-1.22 (m, 18H, CH₂), 0.88 (t, *J* = 6.9 Hz, 3H, CH₃). ¹³C{¹H}-NMR (125 MHz, CDCl₃): 150.7 (CN), 150.1 (CH), 144.6 (C_q), 139.1 (C_q), 138.8 (CH), 128.6 (C_q), 125.2 (CH), 124.8 (CH), 123.2 (CH), 121.5 (CH), 120.9 (C_q), 111.1 (CH), 103.7 (C_q), 102.3 (CH), 32.1 (CH₂), 29.8 (CH₂), 29.8 (CH₂), 29.7 (CH₂), 29.6 (CH₂), 29.5 (CH₂), 29.4 (CH₂), 29.4 (CH₂), 28.5 (CH₂), 27.5 (CH₂), 22.8 (CH₂), 14.3 (CH₃). HRMS (ESI): *m/z* Calcd for C₂₆H₃₃N₃+H⁺ [M+H]⁺ 388.2747; Found 388.2744.

g) 1-(Pyrimidin-2-yl)-2-tetradecyl-1*H*-indole (5hh):

- 20 The representative procedure was followed, using 1-(pyrimidin-2-yl)-1*H*-indole (**3h**; 0.039 g, 0.2 mmol), bromide **4h** (0.111 g, 0.4 mmol) and KI (0.067 g, 0.4 mmol), and the reaction mixture was stirred for 24 h. Purification by column chromatography on neutral alumina (Pet ether/EtOAc/Et₃N: 50/1/0.5) yielded **5hh** (0.044 g, 56%) as a light yellow liquid. ¹H-NMR (500 MHz, CDCl₃): δ = 8.80 (d, *J* = 5.0 Hz, 2H, Ar-H), 8.21 (d, *J* = 8.0 Hz, 1H, Ar-H), 7.53 (d, *J* = 7.2 Hz, 1H, Ar-H), 7.22-7.14 (m, 3H, Ar-H), 6.47 (s, 1H, Ar-H), 3.15 (t, *J* = 7.8 Hz, 2H, CH₂), 1.61 (pent, *J* = 7.6 Hz, 2H, CH₂), 1.39-1.33 (m, 2H, CH₂), 1.31-1.22 (m, 20H, CH₂), 0.88 (t, *J* = 6.9 Hz, 3H, CH₃). ¹³C{¹H}-NMR (125 MHz, CDCl₃): 158.5 (C_q), 158.3 (2C, CH), 142.6 (C_q), 137.1 (C_q), 129.6 (C_q), 122.5 (CH), 121.9 (CH), 119.8 (CH), 117.2 (CH), 113.7 (CH), 105.6 (CH), 32.1 (CH₂), 29.9 (3C, CH₂), 29.8 (2C, CH₂), 29.8 (CH₂), 29.7 (2C, CH₂), 29.6 (CH₂), 29.5 (CH₂), 29.2 (CH₂), 22.9 (CH₂), 14.3 (CH₃). HRMS (ESI): *m/z* Calcd for C₂₆H₃₇N₃+H⁺ [M+H]⁺ 392.3060; Found 392.3053.

h) 2-Benzyl-1-(pyridin-2-yl)-1H-indole:

¹H-NMR (500 MHz, CDCl₃): δ = 8.66 (dd, J = 3.8, 0.8 Hz, 1H, Ar-H), 7.77 (td, J = 8.0, 1.7 Hz, 1H, Ar-H), 7.62-7.56 (m, 1H, Ar-H), 7.36-7.31 (m, 1H, Ar-H), 7.29-7.26 (m, 2H, Ar-H), 7.20-7.13 (m, 5H, Ar-H), 7.06 (d, J = 6.9 Hz, 2H, Ar-H), 6.40 (s, 1H, Ar-H), 4.28 (s, 2H, CH₂). ¹³C{¹H}-NMR (125 MHz, CDCl₃): δ = 151.5 (C_q), 149.7 (CH), 140.3 (C_q), 138.9 (C_q), 138.3 (CH), 137.6 (C_q), 129.0 (2C, CH), 128.6 (C_q), 128.3 (2C, CH), 126.3 (CH), 122.2 (CH), 122.0 (CH), 121.3 (CH), 120.8 (CH), 120.3 (CH), 110.2 (CH), 104.3 (CH), 34.2 (CH₂). HRMS (ESI): m/z Calcd for C₂₀H₁₆N₂+H⁺ [M+H]⁺ 285.1386; Found 285.1386.

Example 6: Representative Procedure for benzylation of indoles:**a) Synthesis of 2-Benzyl-1-(pyridin-2-yl)-1H-indole (7aa):**

Procedure A: To a flame dried screw-cap tube (5 mL) equipped with magnetic stir bar was introduced 1-pyridine-2-yl-1H-indole (**3a**; 0.058 g, 0.3 mmol), 2-iodobutane (0.083 g, 0.45 mmol), cat **1a** (0.0056 g, 0.015 mmol, 5.0 mol %), LiHMDS (0.010 g, 0.06 mmol, 20 mol %), LiO^tBu (0.048 g, 0.6 mmol) and toluene (**6a**; 0.96 mL, 9.0 mmol) inside the glove-box. The resultant reaction mixture was stirred at 150 °C in a preheated oil bath for 20 h. At ambient temperature, the reaction mixture was quenched with distilled H₂O (10 mL) and then neutralized with 2N HCl (0.5 mL). The crude product was then extracted with CH₂Cl₂ (20 mL x 3). The combined organic extract was dried over Na₂SO₄ and the volatiles were evaporated in *vacuo*. The remaining residue was purified by column chromatography on neutral alumina (petroleum ether/EtOAc/Et₃N: 20/1/0.5) to yield **7aa** (0.060 g, 70%) as a light yellow liquid.

Procedure B: This procedure was similar to procedure **A**, except the solvent chlorobenzene (0.304 mL, 3.0 mmol, 10 equiv) was added in addition to toluene (0.96 mL, 9.0 mmol, 30 equiv). The yield of the product **7aa** obtained by this procedure was 82% (0.070 g).

2-Benzyl-1-(pyridin-2-yl)-1H-indole (7aa): ¹H-NMR (500 MHz, CDCl₃): δ = 8.66 (dd, J = 3.8, 0.8 Hz, 1H, Ar-H), 7.77 (td, J = 8.0, 1.7 Hz, 1H, Ar-H), 7.62-7.56 (m, 1H, Ar-H), 7.36-7.31 (m, 1H, Ar-H), 7.29-7.26 (m, 2H, Ar-H), 7.20-7.13 (m, 5H, Ar-

H), 7.06 (d, $J = 6.9$ Hz, 2H, Ar-H), 6.40 (s, 1H, Ar-H), 4.28 (s, 2H, CH₂). ¹³C{¹H}-NMR (125 MHz, CDCl₃): $\delta = 151.5$ (C_q), 149.7 (CH), 140.3 (C_q), 138.9 (C_q), 138.3 (CH), 137.6 (C_q), 129.0 (2C, CH), 128.6 (C_q), 128.3 (2C, CH), 126.3 (CH), 122.2 (CH), 122.0 (CH), 121.3 (CH), 120.8 (CH), 120.3 (CH), 110.2 (CH), 104.3 (CH), 34.2 (CH₂). HRMS (ESI): m/z Calcd for C₂₀H₁₆N₂+H⁺ [M+H]⁺ 285.1386; Found 285.1386.

b) 2-(4-Methylbenzyl)-1-(pyridin-2-yl)-1H-indole (7ab):

The representative procedure **A** was followed, using substrate **3a** (0.058 g, 0.3 mmol) and *p*-xylene (**6b**; 1.1 mL, 9.0 mmol). Purification by column chromatography on neutral alumina (petroleum ether/EtOAc/Et₃N: 30/1/0.5) yielded **7ab** (0.074 g, 83%) as a light yellow liquid. ¹H-NMR (500 MHz, CDCl₃): $\delta = 8.68$ (d, $J = 4.2$ Hz, 1H, Ar-H), 7.78 (td, $J = 8.0, 1.3$ Hz, 1H, Ar-H), 7.60 (dd, $J = 5.7, 3.1$ Hz, 1H, Ar-H), 7.37-7.35 (m, 1H, Ar-H), 7.32-7.28 (m, 2H, Ar-H), 7.19-7.16 (m, 2H, Ar-H), 7.03 (d, $J = 8.0$ Hz, 2H, Ar-H), 6.99 (d, $J = 7.9$ Hz, 2H, Ar-H), 6.40 (s, 1H, Ar-H), 4.25 (s, 2H, CH₂), 2.32 (s, 3H, CH₃). ¹³C{¹H}-NMR (125 MHz, CDCl₃): $\delta = 151.5$ (C_q), 149.6 (CH), 140.6 (C_q), 138.3 (CH), 137.6 (C_q), 135.8 (C_q), 135.7 (C_q), 129.0 (2C, CH), 128.9 (2C, CH), 128.6 (C_q), 122.1 (CH), 121.9 (CH), 121.3 (CH), 120.8 (CH), 120.3 (CH), 110.2 (CH), 104.1 (CH), 33.7 (CH₂), 21.1 (CH₃). HRMS (ESI): m/z Calcd for C₂₁H₁₈N₂+H⁺ [M+H]⁺ 299.1543; Found 299.1542.

c) 2-(4-Methoxybenzyl)-1-(pyridin-2-yl)-1H-indole (7ac):

The representative procedure **B** was followed, using substrate **3a** (0.058 g, 0.3 mmol) and 1-methoxy-4-methylbenzene (**6c**; 1.13 mL, 9.0 mmol). Purification by column chromatography on neutral alumina (petroleum ether/EtOAc/Et₃N: 10/1/0.5) yielded **7ac** (0.062 g, 66%) as a light yellow liquid. ¹H-NMR (500 MHz, CDCl₃): $\delta = 8.65$ (dd, $J = 4.6, 0.8$ Hz, 1H, Ar-H), 7.77 (td, $J = 7.6, 1.9$ Hz, 1H, Ar-H), 7.57 (dd, $J = 5.7, 3.1$ Hz, 1H, Ar-H), 7.32 (dd, $J = 5.7, 3.1$ Hz, 1H, Ar-H), 7.29-7.25 (m, 2H, Ar-H), 7.15-7.12 (m, 2H, Ar-H), 6.97 (d, $J = 8.8$ Hz, 2H, Ar-H), 6.73 (d, $J = 8.8$ Hz, 2H, Ar-H), 6.37 (s, 1H, Ar-H), 4.19 (s, 2H, CH₂), 3.75 (s, 3H, CH₃). ¹³C{¹H}-NMR (125 MHz, CDCl₃): $\delta = 158.1$ (C_q), 151.5 (C_q), 149.6 (CH), 140.8 (C_q), 138.3 (CH), 137.6 (C_q), 130.9 (C_q), 130.0 (2C, CH), 128.6 (C_q), 122.2 (CH), 122.0 (CH), 121.4 (CH), 120.8 (CH), 120.3 (CH), 113.8 (2C, CH), 110.2 (CH), 104.1 (CH), 55.4 (CH₂), 33.3

(CH₃). HRMS (ESI): m/z Calcd for C₂₁H₁₈N₂O+H⁺ [M+H]⁺ 315.1492; Found 315.1489.

d) 2-(4-Fluorobenzyl)-1-(pyridin-2-yl)-1*H*-indole (7ad):

The representative procedure **A** was followed, using substrate **2a** (0.058 g, 0.3 mmol) and 1-fluoro-4-methylbenzene (**6d**; 0.99 mL, 9.0 mmol). Purification by column chromatography on neutral alumina (petroleum ether/EtOAc/Et₃N: 20/1/0.5) yielded **7ad** (0.069 g, 76%) as a light yellow liquid. ¹H-NMR (500 MHz, CDCl₃): δ = 8.64 (dd, J = 5.7, 1.9 Hz, 1H, Ar-H), 7.77 (td, J = 7.6, 1.9 Hz, 1H, Ar-H), 7.59 (dd, J = 5.7, 3.1 Hz, 1H, Ar-H), 7.33-7.30 (m, 1H, Ar-H), 7.28-7.26 (m, 2H, Ar-H), 7.17-7.14 (m, 2H, Ar-H), 7.00-6.97 (m, 2H, Ar-H), 6.89-6.80 (m, 2H, Ar-H), 6.39 (s, 1H, Ar-H), 4.24 (s, 2H, CH₂). ¹³C{¹H}-NMR (125 MHz, CDCl₃): δ = 161.5 (d, ¹ J_{C-F} = 244.1 Hz, C_q), 151.4 (C_q), 149.7 (CH), 140.2 (C_q), 138.4 (CH), 137.6 (C_q), 134.6 (d, ⁴ J_{C-F} = 2.9 Hz, C_q), 130.4 (d, ³ J_{C-F} = 7.6 Hz, 2C, CH), 128.5 (C_q), 122.2 (CH), 122.2 (CH), 121.3 (CH), 120.9 (CH), 120.4 (CH), 115.1 (d, ² J_{C-F} = 21.0 Hz, 2C, CH), 110.2 (CH), 104.3 (CH), 33.4 (CH₂). ¹⁹F-NMR (377 MHz, CDCl₃): δ = -117.0 (s). HRMS (ESI): m/z Calcd for C₂₀H₁₅FN₂+H⁺ [M+H]⁺ 303.1292; Found 303.1293.

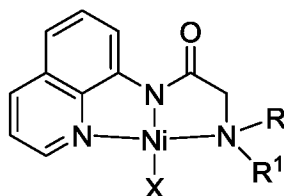
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Advantages of invention:

1. Novel and inexpensive nickel catalysts of formula (I) is provided.
2. Novel compounds of formula (II) provided.
3. The Novel and inexpensive nickel catalysts effectively used to performs the alkylation and benzylation indoles, pyrazoles, imidazoles, etc.

THE CLAIM:

1. A nickel catalyst of formula (I);

**Formula I**

Wherein;

- 5 R and R¹ are the same and are selected from the group consisting of alkyl, aryl, benzyl, heteroaryl, -(CH₂)₂O(CH₂)₂-, -(CH₂)₂N(Me)(CH₂)₂-, -(CH₂)₄-, -(CH₂)₅-, etc.

X is selected from the group consisting of hydrogen, halogen, OC(O)CH₃, OC(O)^tBu, OC(O)Ph, OC(O)admantyl, OSO₂CF₃, BF₄, SbF₆, etc.

- 10 2. The compound as claimed in claim 1, wherein said nickel catalyst of formula (I) is selected from (R²NNN^{8-Quin})-H [2-(diethylamino)-N-(quinolin-8-yl)acetamide], (Et₂NNN^{8-Quin})NiCl [2-(diethylamino)-N-(quinolin-8-yl)acetamide](NiCl), (Et₂NNN^{8-Quin})Ni(OAc) [2-(diethylamino)-N-(quinolin-8-yl)acetamide]Ni(OAc).

- 15 3. A process for the preparation of nickel catalyst of formula (I) as claimed in claim 1, wherein said process comprising the steps of:

a) Refluxing the reaction mixture of 2-bromo-N-(quinolin-8-yl) acetamide and amino compound in solvent for the period ranging from 20 to 24 hrs at temperature ranging from 60 to 80 °C afford (R²NNN^{8-Quin})-H [2-

- 20 (dialkylamino)-N-(quinolin-8-yl)acetamide] Ligand;

b) Adding triethylamine to the mixture of compound of step (a), nickel compound and solvent followed by refluxing the reaction mixture for the period in the range of 3 to 12 hrs at a temperature ranging from 60 to 70 °C to afford nickel catalyst of formula (I).

- 25 4. The process as claimed in claim 3, wherein said amino compound is selected from diisopropyl amine, diethylamine, dimethyl amine, morpholine, N-methyl piperazine, cyclopentyl amine, cyclohexyl amine and said nickel compound is selected from (DME)NiCl₂, (THF)NiBr₂, Ni(OAc)₂.

5. The process as claimed in claim 3, wherein said solvent in step (a) and (b) is selected from acetone or tetrahydrofuran (THF).
6. A process for the alkylation or benzylation of heteroarene using nickel catalyst of formula (I) as claimed in claim 1, comprising stirring the reaction mixture of heteroarene, organic halide compound or benzyl compound, catalyst of formula (I), base and solvent at temperature ranging from 120 to 160 °C for the period ranging from 6 to 36 hrs to afford desired compound of formula (II) or (III).
7. The process as claimed in claim 6, wherein said heteroarene is selected from 1-(pyridine-2-yl)-1*H*-indole, 5-methyl-1-(pyridine-2-yl)-1*H*-indole, 5-methoxy-1-(pyridine-2-yl)-1*H*-indole, 5-fluoro-1-(pyridine-2-yl)-1*H*-indole, 5-bromo-1-(pyridine-2-yl)-1*H*-indole, 1-(pyridine-2-yl)-1*H*-indole-5-carbonitrile, 3-methyl-1-(pyridine-2-yl)-1*H*-indole, 1-(pyrimidin-2-yl)-1*H*-indole, 5-methoxy-1-(pyrimidin-2-yl)-1*H*-indole.
8. The process as claimed in claim 6, wherein said organic halide compound is selected from 1-iodobutane, 1-iodopentane, 1-bromohexane, 1-bromodecane, 1-iodododecane, 1-bromotridecane, 1-bromotetradecane, 1-bromohexadecane, 1-bromooctadecane, 1-bromo-2-methylpropane, 1-bromo-3-methylbutane, (bromomethyl)cyclohexane, (2-bromoethyl)cyclohexane, 1-bromo-2,2-dimethylpropane, (3-bromopropyl)benzene, 1-(3-bromopropyl)-4-methoxybenzene, 1-chloro-4-iodobutane, 5-bromopent-1-ene, 9-(4-iodobutyl)-8a,9a-dihydro-9*H*-carbazole, 2-iodopropane, (1-bromoethyl)benzene, (bromoethylene)dibenzene, 2-iodobutane, bromocyclopropane, iodocyclopentane, bromocyclohexane, bromocycloheptane, 6-bromo-1-hexene,
9. The process as claimed in claim 6, wherein said benzyl compound is selected from toluene, *p*-xylene, *m*-xylene, 1-methoxy-4-methylbenzene, 1-fluoro-4-methylbenzene, 1-chloro-4-methylbenzene, 1-bromo-4-methylbenzene, *ortho*-xylene, 1-fluoro-2-methylbenzene, 1-chloro-2-methylbenzene, 1-bromo-2-methylbenzene, 1-methyl-2-(trifluoromethyl)benzene, mesitylene, 2,4-difluoro-1-methylbenzene, 1-methylnaphthalene, 1-(*p*-tolyl)-1*H*-indole, toluene.

10. The process as claimed in claim 6, wherein said base is selected from Lithium bis(trimethylsilyl)amide [LiHMDS], Lithium tert-butoxide (LiOtBu) or mixture thereof and said solvent is selected from toluene, chlorobenzene or mixture thereof.

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2017/050082

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D401/04 C07F15/04 C07D403/04
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WEIFENG SONG ET AL: "Nickel-Catalyzed CH Alkylations: Direct Secondary Alkylations and Trifluoroethylations of Arenes", ANGEWANDTE CHEMIE INTERNATIONAL EDITION, vol. 53, no. 9, 24 February 2014 (2014-02-24), pages 2477-2480, XP055382573, ISSN: 1433-7851, DOI: 10.1002/anie.201309584 scheme 3; compounds 5, 6 ----- -/--	1-10



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search

30 June 2017

Date of mailing of the international search report

07/07/2017

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2017/050082

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MATTHIEU CORBET ET AL: "8-Aminoquinoline: A Powerful Directing Group in Metal-Catalyzed Direct Functionalization of C-H Bonds", ANGEWANDTE CHEMIE INTERNATIONAL EDITION, vol. 52, no. 38, 16 September 2013 (2013-09-16), pages 9896-9898, XP055381700, ISSN: 1433-7851, DOI: 10.1002/anie.201303556 scheme 2	1-10
X,P	----- VINEETA SONI ET AL: "Unified Strategy for Nickel-Catalyzed C-2 Alkylation of Indoles through Chelation Assistance", ACS CATALYSIS, vol. 6, no. 9, 2 September 2016 (2016-09-02), pages 5666-5672, XP055381750, US ISSN: 2155-5435, DOI: 10.1021/acscatal.6b02003 schemes 1-6; table 1 -----	1-10