DOI: 10.1002/adsc.200700081

Synthesis of Symmetrical Bisquinolones *via* Nickel(0)-Catalyzed Homocoupling of 4-Chloroquinolones

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Received: February 2, 2007; Revised: August 3, 2007

Abstract: A method for the gram-scale preparation of functionalized 4,4′-bisquinolones using a microwave-assisted Ullmann-type homocoupling reaction is described. The method is catalytic in nickel(0) which is generated *in situ* by reduction from an inexpensive nickel(II) source and utilizes readily available 4-chloroquinolin-2(1*H*)-ones as starting materials. In contrast to the alternative palladium(0)-catalyzed one-pot borylation/Suzuki cross-coupling reaction, the new method avoids the use of an expensive catalyst and cross-coupling partner such as bis(pinacolato)diboron.

Keywords: homocoupling; homogeneous catalysis; microwave heating; nickel; quinolones; reduction

Introduction

The structural subunit of symmetrical biaryls plays an important role in organic and medicinal chemistry, and is found in a wide variety of natural products including alkaloids such as the anti-HIV alkaloid michellamine B,[1] coumarins (4,4′-biisofraxidin),[2] polyketides[3] and terpenes (Figure 1).[4] Compounds incorporating symmetrical biaryl moieties also find applications as conductors for thin film transistor applications (e.g., 2,2′-bidithieno[3,2-*b*:2′,3′-*d*]thiophene),[5] as electronic and optoelectronic materials (e.g., indenofluorenes),[6] as chiral ligands in catalysis (e.g., BINAP)[7] and in chiral or achiral liquid crystals (e.g., paracyclophanes).[8] The biaryl subunit also constitutes an important structural motif in several pharmaceuticals (e.g., in the laxative agent 4,4′-biphenol),[9] and in agrochemicals (e.g., in the non-selective broad-spectrum herbicide paraquat).[10] Related biaryl heterocycles are also well known in the literature and often display similarly interesting biological and physical properties.[11]

In view of the substantial interest and broad application of symmetrical biaryls,[1–11] considerable efforts have been undertaken to achieve efficient, economical, safe, and environmentally benign methods for their preparation in many academic and industrial laboratories.[12] Since the first biaryl couplings performed by Ullmann over a century ago applying stoichiometric amounts of copper metal,[13] the catalytic use of transition metals, especially of palladium and nickel, in the formation of symmetrical biaryls is now well established.[12] In this context we recently reported the first synthesis of 4,4′-bisquinolones of type **1**.[14] These novel, symmetrical bis-heterocycles are of considerable interest as aza-analogues of biscoumarin natural products (e.g., 4,4′-biisofraxidin),[2] because of their anticipated fluorescent properties as push-pull carbostyrils (**1**, $R^3 = R^4 = OMe$),[15] and as starting materials for the synthesis of novel aza-BINAP analogues (Figure 2).[16]

In our recent publication we have outlined the generation of 4,4′-bisquinolones **1**, employing both a palladium(0)-catalyzed one-pot borylation/Suzuki cross-coupling method, and a nickel(0)-mediated homocoupling protocol using the corresponding 4-chloroquinolin-2(1*H*)-ones **2** as precursors.[14] Both methods did in fact allow the successful, high-yielding preparation of a variety of bisquinolones of type **1**, in addition to 4,4′-biscoumarin and a range of other symmetrical bi(hetero)aryls. However, both procedures have severe disadvantages that make them impractical for a larger scale synthesis required for our purposes: most prominently, the borylation/Suzuki approach relied on the use of the rather expensive bis(pinacolato)diboron cross-coupling reagent[17] and additionally required 10 mol% of the costly palladium/ligand source $PdCl_2$(dppf).[17] While the alternative homocoupling method avoids the use of a cross-coupling partner and therefore appears to be more favorably from the standpoint of atom economy,[18] our original nickel-mediated method utilized stoichiometric amounts of a nickel(II) source (1.3 equivalents of $NiCl_2$) and required 4 equivalents of triphenylphosphine as ligand.[14] The

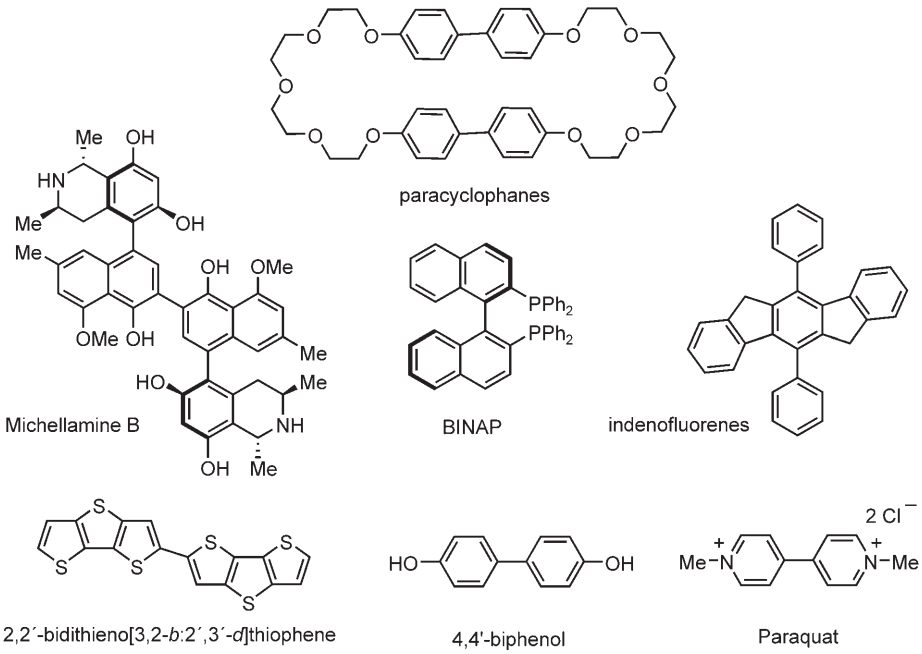


Figure 1. Important symmetrical biaryl products.

subsequent complex chromatographic separation of the desired product from triphenylphosphine and its oxide impurity in fact only allowed the preparation of quantities of bisquinolones **1** on a less than 50-mg scale.[19] We now report an improved method for the homocoupling of 4-chloroquinolin-2(1*H*)-ones **2** (see Table 1, Table 2 and Table 3) that utilizes a comparatively inexpensive combination of a nickel catalyst [25 mol% of $NiCl_2(PPh_3)_2$] and an additional bidentate ligand (25 mol% of DPEphos).[17] Importantly, using this method good isolated product yields can in many cases be obtained without purification by chromatography, allowing the preparation of bisquinolones **1** in gram-scale quantities.

Results and Discussion

The main problem in the reported cross- and homocouplings involving 4-chloroquinolin-2(1*H*)-ones[14] lies in the fact that these heteroaryl chlorides are comparatively unreactive as coupling partners. It is well known that aryl chlorides, despite the fact that those substrates would generally be the most useful ones because of their low cost and the wide availability,[20] are comparatively unreactive as coupling partners in transition metal-catalyzed processes when compared to aryl bromides and iodides.[20] General and efficient protocols employing aryl chlorides as starting materials in such transformations have only recently emerged in the literature.[20–23] The low reactivity of aryl chlorides is usually attributed to the strength of the C–Cl bond (bond dissociation energies for Ph–X: Cl = 96 kcal mol^{-1}; Br = 81 kcal mol^{-1}; I = 65 kcal mol^{-1}) which leads to a reluctance of aryl chlorides toward oxidative addition to transition metal centers, a critical step in many transition metal-catalyzed coupling reactions.[20]

In our original nickel-mediated reductive homocoupling, the active nickel(0) complex was generated

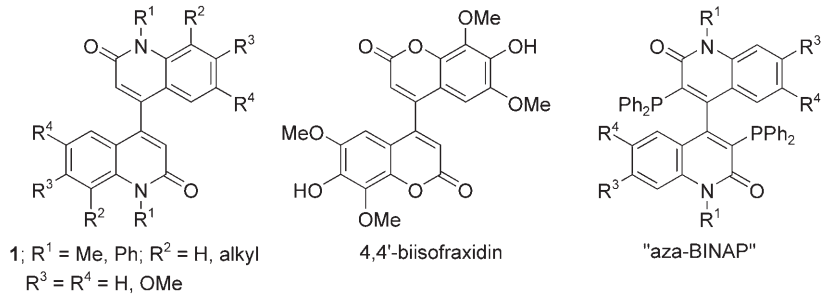
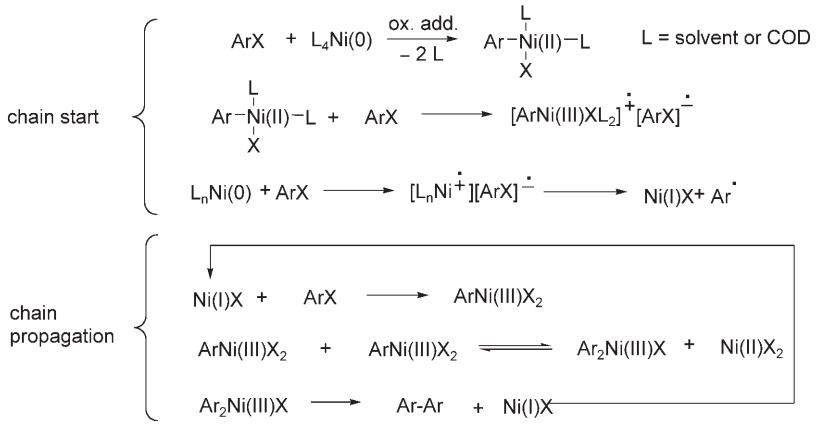


Figure 2. 4,4′-Bisquinolones and 4,4′-biscoumarins.

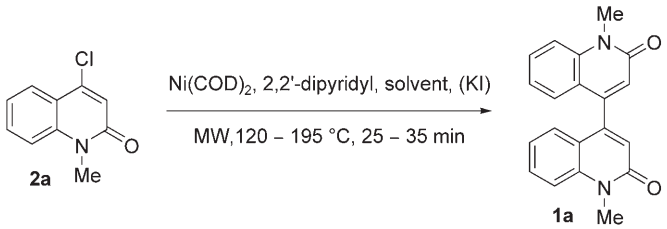


Scheme 1. Proposed mechanism of Ni(0)-mediated homocouplings of aryl halides using Ni(0) species.[26]

from a nickel(II) salt and Zn dust as reducing agent in the presence of triphenylphosphine as ligand.[14] In order to simplify and possibly to improve this procedure we have now considered the direct use of a nickel(0) source. The successful use of the commercially available zerovalent nickel complex $Ni(COD)_2$ (COD = 1,5-cyclooctadiene) in related homocoupling reactions of aryl bromides or iodides (Scheme 1)[24,25] prompted us to apply these conditions also to the homocoupling of 4-chloro-1-methylquinolin-2-(1*H*)-one **2a** as a model substrate (Table 1).[24,25]

All optimization studies were performed on a 0.25-mmol scale using sealed vessel microwave heating in order to extend the available temperature range above the boiling point of the individual solvent.[27] An extensive optimization of the reaction parameters included the amount of the nickel reagent, the type and concentration of additional ligands, the use of other additives, different solvents, reaction time and temperature. While aryl bromides and iodides have been shown to undergo this type of coupling with relative ease,[24,25] only one example of a reductive homocoupling which involves an aryl chloride is known,

Table 1. Reaction optimization for the nickel(0)-mediated reductive homocoupling of 4-chloroquinolone **2a** using $Ni(COD)_2$.[a]



Entry	$Ni(COD)_2$ (equivs.)	2,2'-Dipyridyl ligand (equivs.)	KI additive (equivs.)	Time [min]	Solvent/temperature [°C]	Product distribution (%)[b]
1	0.50	1.0	-	25	DMF/195	40/**52**/8
2	0.75	1.0	-	25	DMF/195	0/**97**/3
3	0.75	-	-	25	DMF/195	20/**75**/5
4	0.75	1.0	-	35	dioxane/130	10/**90**/0
5	0.75	1.0	0.5	35	dioxane/130	0/**99**/1[c]
6	0.75	0.5	0.5	35	dioxane/130	5/**94**/1
7	0.75	1.0	0.5	35	THF/120	9/**80**/11
8	0.75	1.0	0.5	55	DMSO/160	17/**73**/10

[a] *Reaction conditions:* 0.25 mmol chloroquinolone **2a**, $Ni(COD)_2$, 2,2′-dipyridyl, KI, 1.5 mL dry solvent, sealed vessel single mode microwave irradiation. See the Experimental Section for further information.

[b] Product distribution refers to relative peak area (%) ratios of crude HPLC-UV (215 nm) traces: starting material **2a**/product **1a**/dehalogenated product.

[c] Product isolation by filtration through Celite, evaporation, and subsequent recrystallization furnished a 93% yield of bisquinolone **1a**.

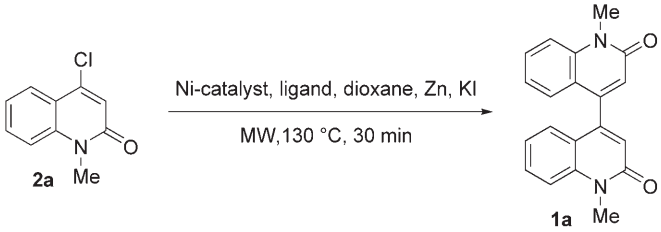
providing a mere 14% product yield.[24] In these transformations, the oxidative addition generally is the rate-limiting step (Scheme 1). Aryl halides which have comparatively small dissociation energies (e.g., aryl iodides) will undergo faster oxidative addition to the metal center and ultimately will show a higher reactivity in the reductive homocoupling.[24] Since there is no regeneration mechanism in this homocoupling, stoichiometric amounts of $Ni(COD)_2$ have to be employed in order to achieve full conversion. In the case of 4-chloro-1-methylquinolin-2-(1*H*)-one **2a** the use of 0.75 equivs. of the sensitive $Ni(COD)_2$ reagent (1.5 equivs. per biaryl product) provided the best results. Lowering the amount of $Ni(COD)_2$ led to incomplete conversions (Table 1, entry 1), with the only observed by-product being the dehalogenated quinolone.[14] Nickel(0)-mediated homocoupling reactions routinely rely on additional ligands,[12,24–26,28] which stabilize the catalyst and the arylnickel species during the reaction sequence and restrict decomposition. In the present case, 1.0 equivalent of 2,2′-dipyridyl exhibited an optimum effect on the observed conversion (compare entries 2 and 3). Close to quantitative conversions were observed by heating the reaction mixture in DMF at 195 °C for 25 min. Under these conditions, only very small amounts of the dehalogenated side-product, 1-methylquinolin-2-(1*H*)-one, were observed by HPLC monitoring. Ultimately, we found that optimum results were achieved by switching to anhydrous dioxane as a solvent, which allowed reduction of the reaction temperature to 130 °C. Further improvements were made by adding 0.5 equivalents of potassium iodide as an additive since it is known that iodide ions enhance the reaction rate of nickel-catalyzed homocoupling reactions (compare entries 4 and 5).[28] Under optimized reaction conditions (Table 1, entry 5), full conversion to bisquinolone **1a** was observed within a 35 min reaction time with only 1% of the dehalogenated by-product formed. Gratifyingly, product isolation in this case did not require chromatography and simply involved filtration through a Celite pad, evaporation of solvent, and recrystallization of the crude product from acetonitrile to provide a 93% isolated product yield of the desired bisquinolone **1a**. This protocol could be scaled to 1.0 mmol to provide **1a** in *ca.* 100 mg quantity. Despite this fact, the high cost and pronounced air sensitivity of the $Ni(COD)_2$ reagent,[17] employed in almost stoichiometric amounts, precluded this method from being used for the preparation of larger quantities of bisquinolones.

We therefore turned our attention again to our original reductive homocoupling protocol starting from a nickel(II) source in the hope to turn the stoichiometric method into a catalytic version that would require less metal, and therefore also a smaller amount of the reducing agent and, most importantly, less ligand which would greatly simplify the purification process and thus make this method scalable. A number of examples involving the Ni-mediated homocoupling of aryl chlorides to biphenyls have been reported in the literature.[29,30] In this context, several sources of nickel(II) were evaluated under the originally reported *in situ* reductive conditions using zinc dust.[14] In addition, in light of the results obtained with $Ni(COD)_2$, the solvent system was changed from DMF to dioxane. In our originally reported protocol requiring stoichiometric amounts of an Ni source using DMF as solvent,[14] we assume that the reductive elimination step is not favorable, therefore not allowing the regeneration of the active Ni(0) species. The use of DMF or other coordinating dipolar aprotic solvents will likely lead to de-coordination of ligands from the Ni(0) complex and to the formation undesired side products.[30] Employing dioxane as solvent, most of the tested nickel(II) salts/complexes such as $NiCl_2$, $NiCl_2(PPh_3)_2$, $NiCl_2$(dppe), $NiCl_2$(dppf) and Ni(acac)$_2$ were effective in the desired homocoupling (Table 2). In all cases the only by-product was the dehalogenated quinolone. By adding an additional amount of a bidentate ligand (see mechanistic discussion below), such as bis(2-diphenylphosphinophenyl) ether (DPEphos) or diphenylphosphinoferrocene (dppf) (Figure 3) to the reaction mixture, the amount of the required nickel(II) complex could be reduced to 20 mol% and the dehalogenation pathway could be largely suppressed (entries 3 and 7).

One of the best sets of conditions (entry 3) employed 20 mol% of $NiCl_2(PPh_3)_2$ as Ni(II) complex and 20 mol% of dppf as ligand employing the traditional reductive environment (1.3 equivs. Zn dust, 1.8 equivs. KI). Microwave heating of the reaction mixture at 130 °C for 30 min provided full conversion to the bisquinolone product with less than 10% of the dehalogenated by-product being formed (86% isolated yield by flash chromatography). Equally high selectivity and efficiency toward homocoupling was displayed employing DPEphos as a ligand system, albeit using a 25 mol% catalyst and ligand loading (entry 7).

While both methods required only 0.20–0.25 equivs. of the relatively inexpensive nickel(II) complex $NiCl_2(PPh_3)_2$ as catalyst,[17] the true advantage lies in the fact that here chromatography is not required to separate triphenylphosphine and the additional dppf/DPEphos ligands from the bisquinolone product. Notably, the use of DPEphos (entry 7) provides equally high conversions as dppf (entry 3), but is the ligand of choice due to the significantly lower cost.[17] We have therefore performed a *ca.* 40-fold scale-up of the experiment described in entry 7 employing 11 mmol of chloroquinolone **2** as starting material employing a larger microwave process vial (11-mL reaction volume). Gratifyingly, monitoring the crude reaction

Table 2. Catalyst/ligand screening for the nickel(0)-mediated reductive homocoupling of 4-chloroquinolone using Ni(II) complexes.[a]



Entry	Catalyst (mol%)	Additive (mol%)	Product distribution (%)[b]
1	$NiCl_2(PPh_3)_2$ (10)	dppf (20)	0/**61**/39
2	$NiCl_2(PPh_3)_2$ (20)	dppf (10)	0/**87**/13
3	$NiCl_2(PPh_3)_2$ (20)	dppf (20)	0/**91**/9[c]
4	$NiCl_2$(dppe) (20)	dppf (20)	0/**68**/32
5	$NiCl_2$(dppf) (25)	dppf (25)	0/**71**/29
6	$Ni(acac)_2$ (25)	dppf (25)	1/**65**/34
7	$NiCl_2(PPh_3)_2$ (25)	DPEphos (25)	0/**91**/9[d]

[a] *Reaction conditions:* 0.25 mmol chloroarene **2a**, Ni catalyst, ligand, 1.3 equivs. Zn dust, 1.8 equivs. KI, 1 mL dry dioxane, sealed vessel single mode microwave irradiation at 130 °C for 30 min.

[b] Product distribution refers to relative peak area (%) ratios of crude HPLC-UV (215 nm) traces: starting material **2a**/product **1a**/dehalogenated product.

[c] Product isolation by flash chromatography provided a 86% yield of bisquinolone **1a**.

[d] For an 11-mmol run, product isolation by an extractive work-up and recrystallization led to a 74% yield of isolated pure product.

mixture by HPLC demonstrated the full scalability of this process: again, less than 10% of the unwanted dehalogenated quinolone was observed, with HPLC traces being nearly identical to those of the small-scale experiment. In the purification procedure, the dioxane solvent was evaporated under reduced pressure. After addition of acetonitrile and warming to *ca.* 80 °C the crude reaction mixture was filtered through a pad of Celite. Since DPEphos is nearly insoluble under those conditions, most of the ligand material could be removed. Evaporation of the acetonitrile solvent furnished the crude bisquinolone product which was subsequently dissolved in dichloromethane and washed three times with saturated aqueous ammonium chloride solution. Evaporation of dichloromethane and recrystallization of the crude material from acetonitrile provided bisquinolone **1a** in 74% yield (purity > 99% by HPLC at 215 nm).

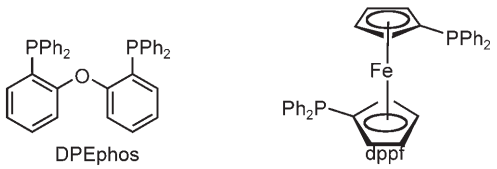
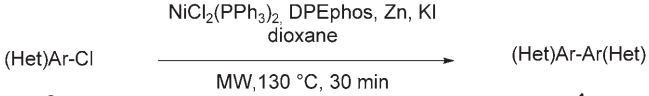
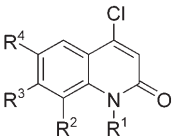


Figure 3. Structures of bidentate ligands DPEphos and dppf.

In order to evaluate the general applicability of this homocoupling protocol, a number of different 4-chloroquinolone substrates (in addition to 4-chlorocoumarin)[14] were subjected to the optimized coupling protocol outlined above (Table 2). Utilizing the optimized catalytic method detailed in Table 2 (entry 7), all substrates did undergo homocoupling to the respective biaryl derivatives in > 98% conversion and with very high selectivity. The amount of dehalogenated by-products in most cases was below 5% In fact, we find that this new protocol involving catalytic amounts of $NiCl_2(PPh_3)_2$ in combination with DPEphos as ligand provides equally high isolated product yields (71–92%) compared to our previously published method employing stoichiometric amounts of a Ni(II) source.[14] In most cases, the extractive work-up/purification elaborated above specifically for bisquinolone **1a** was also successful for other biaryl de-

Table 3. Nickel(0)-mediated reductive homocoupling of 4-chloroquinolone using $NiCl_2(PPh_3)_2$ and DPEphos.[a]



Substrate	Yield [%][b]
	
2a; R^1 = Me, R^2 = R^3 = R^4 = H	85 (69)
2b; R^1-R^2 = $(CH_2)_3$, R^3 = R^4 = H	92 (39)
2c; R^1 = Me, R^2 = R^3 = H, R^4 = OMe	71 (–)[c]
2d; R^1 = Me, R^2 = R^4 = H, R^3 = OMe	79 (45)
2e; R^1 = Me, R^2 = H, R^3 = R^4 = OMe	83 (34)
2f; 4-chlorocoumarin	92 (73)

[a] *Reaction conditions:* 0.50 mmol chloroarene **2**, 25 mol% $NiCl_2(PPh_3)_2$, 25 mol% DPEphos, 1.3 equivs. Zn dust, 1.8 equivs. KI, 0.8 mL dry dioxane, sealed vessel single mode microwave irradiation at 130 °C for 30 min.

[b] Isolated yields of pure product using flash chromatography. In parenthesis, isolated yields obtained by extractive work-up and recrystallization (see Experimental Section).

[c] Due to the insolubility of this material in acetonitrile, the extraction procedure was not successful in this case.

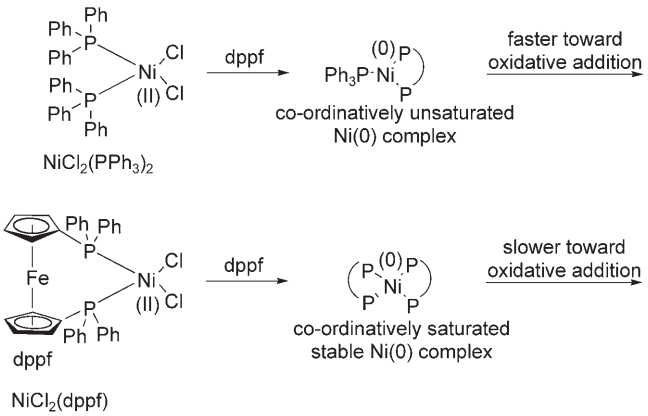


Figure 4. Difference in catalytic activity of coordinatively unsaturated and saturated Ni(0) complexes.

rivatives, although the isolated yields using this non-chromatographic method were not always as high as when using standard flash chromatography (Table 3).

Mechanistic Discussion

It is known that bidentate ligands such as dppf (Figure 3) increase the electron density on low-valent transition metals, making the metal more nucleophilic, thus facilitating oxidative addition and reducing the propensity for reductive elimination.[26,31] The use of $NiCl_2$(dppf) in the presence of an additional amount of dppf (Table 2, entry 5) may lead to the formation of a rather stable coordinatively saturated Ni(0) ligand complex (Figure 4) with tetrahedral geometry having large ligand bite angles (dppf = 96°). This reduces the accessibility for oxidative addition.[32] In contrast, a coordinatively unsaturated Ni(0) complex generated from $NiCl_2(PPh_3)_2$ and dppf (Figure 4) is more efficient toward oxidative addition and will enhance the overall efficiency of the catalytic cycle.[32] In the specific homocoupling reaction described in Table 2, $NiCl_2(PPh_3)_2$ has proven to be more efficient and selective than the bidentate ligand catalyst $NiCl_2$(dppf) (compare entries 3 and 5). $NiCl_2(PPh_3)_2$ is surrounded by monodentate ligands and is thus more efficient to generate coordinatively reactive Ni(0) *in situ* in the presence of an additional dppf ligand.

Conclusions

In summary, we have developed a Ni(0)-catalyzed reductive homocoupling reaction of easily accessible 4-chloroquinolin-2(1*H*)-ones that provides 4,4′-bisquinolones in good yields. In contrast to our previous protocol,[14] this new method only requires 0.25 equivalents of a comparatively inexpensive Ni source and does not rely on chromatography for product isolation. Key to the success was a change of solvent and the *combined use* of bidentate and monodentate ligands providing more active Ni(0) catalytic species. The method is therefore scalable and will allow us to further study the properties of these novel types of bisheterocylces.

Experimental Section

General Remarks

All homocoupling reactions involving air-sensitive reagents were carried out under an atmosphere of dry argon. Dry flash chromatography[33] was performed on Merck silica gel 60 H (<45 nm particle size). TLC analyses were performed on pre-coated (Merck Silica gel 60 HF_{254}) plates. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 360 MHz instrument at 360 and at 90 MHz, respectively. FT-IR spectra were recorded using KBr pellets. Low resolution mass spectra were obtained on an Agilent 1100 LC/MS instrument using atmospheric pressure chemical ionization (APCI) in positive or negative mode. Analytical HPLC analysis was carried out on a Merck C18 reversed-phase (RP) analytical column (119×3 mm, particle size 5 mm) or a Pathfinder-AS100 reversed-phase column (150×4.6 mm, particle size 5 mm) at 25 °C using mobile phase A [water/acetonitrile 90:10 (v/v) + 0.1 % TFA] and B (MeCN + 0.1 % TFA) at a flow rate of 0.5–1.0 mL min^{-1}. The following gradient was applied: linear increase from solution 30 % B to 100 % B in 7 min, hold at 100 % solution B for 2 min.

Zn powder (Merck 108789, <60 μm particle size) was used for the Ni(0)-catalyzed homocouplings. All anhydrous solvents, catalysts and ligands were obtained from Aldrich Chem. Co. and were used without any further purification. Microwave irradiation experiments were carried out on an Initiator Eight EXP or Emrys Synthesizer single-mode cavity instrument, producing controlled microwave irradiation at 2450 MHz (Biotage AB, Uppsala). Reaction times refer to hold times at the temperature indicated, not to total irradiation times. The temperature was measured with an IR sensor on the outside of the reaction vessel.

Homocoupling of 4-Chloro-1-methylquinolin-2(1*H*)-one 2a using Bis(1,5-cyclooctadiene)nickel(0)

A mixture containing 48.4 mg (0.25 mmol) of 4-chloro-1-methylquinolin-2(1*H*)-one (**2a**),[34] 51.7 mg (0.188 mmol, 0.75 equivs.) of $Ni(COD)_2$, 39.0 mg (0.25 mmol, 1.0 equiv.) of 2,2′-dipyridyl, and 20.8 mg (0.125 mmol, 0.50 equivs.) of KI was suspended in 1.0 mL of anhydrous dioxane under an argon atmosphere in a 5-mL Pyrex microwave vial equipped with a magnetic stirring bar. The vial was sealed, stirred for 4 min at room temperature, and then heated for 35 min at 130 °C. Thereafter, the solvent was removed under reduced pressure, the remaining residue dissolved in CH_2Cl_2 and filtered through a small pad of Celite. Evaporation of the solvent and recrystallization of the resulting crude material from acetonitrile delivered pure bisquinolone **1a**; yield: 36.8 mg (93 %).

The reaction was also performed on a 1.0-mmol scale (130 °C for 55 min) providing the same product yield.

Homocoupling of 4-Chloro-1-methylquinolin-2(1*H*)-one 2a using Bis(triphenylphosphine)nickel(II) Dichloride and Diphenylphosphinoferrocene

A mixture containing 48.4 mg (0.25 mmol) of 4-chloro-1-methylquinolin-2(1*H*)-one (**2a**), 32.7 mg (0.05 mmol, 20 mol%) of $NiCl_2(PPh_3)_2$, 27.7 mg (0.05 mmol, 20 mol%) of diphenylphosphinoferrocene (dppf), 21.2 mg (0.324 mmol, 1.3 equivs.) of Zn powder and 74.7 mg (0.45 mmol, 1.8 equivs.) of KI was suspended in 1.0 mL anhydrous dioxane under an argon atmosphere in a 5-mL Pyrex microwave process vial equipped with a magnetic stirring bar. The vial was sealed, the mixture was stirred for 4 min at room temperature, and then heated by microwave irradiation for 30 min at 130 °C. Thereafter, the solvent was removed under reduced pressure. The product was isolated by gradient dry flash chromatography using EtOAc/acetone as solvent mixture to obtain pure bisquinolone **1a**; yield: 34.0 mg (86%).

Homocoupling of 4-Chloro-1-methylquinolin-2(1*H*)-one 2 using Bis(triphenylphosphine)nickel(II) Dichloride and DPEphos

A mixture containing 2.13 g (11 mmol) of 4-chloro-1-methylquinolin-2(1*H*)-one (**2a**), 1.8 g (2.75 mmol, 25 mol%) of $NiCl_2(PPh_3)_2$, 1.48 g (2.75 mmol, 25 mol%) of DPEphos, 935 mg (14.3 mmol, 1.3 equivs.) of Zn powder and 3.29 g (19.82 mmol, 1.8 equivs.) of KI was suspended in 11 mL anhydrous dioxane under an argon atmosphere in a 20-mL Pyrex microwave vial equipped with a magnetic stirring bar. The vial was sealed, the mixture was stirred for 4 min at room temperature, and then heated for 30 min at 130 °C. In the purification procedure, dioxane solvent was evaporated under reduced pressure. After addition of 60 mL of acetonitrile and warming to *ca.* 80 °C the crude reaction mixture was filtered through a pad of Celite to remove insoluble DPEphos ligand in addition to most of the triphenylphosphine ligand. Evaporation of the acetonitrile solvent furnished the crude bisquinolone product contaminated with small quantities of triphenylphosphine which was subsequently dissolved in 400 mL of dichloromethane and washed three times with 150 mL of saturated aqueous ammonium chloride solution (to remove inorganic potassium iodide). Drying of the organic phase over anhydrous $MgSO_4$, filtration through a pad of Celite, evaporation of dichloromethane and subsequent recrystallization (2 times) from acetonitrile provided bisquinolone **1a**; yield: 1.28 g (74%, purity > 99% by HPLC at 215 nm). For complete characterization data see the ref.[14]

Homocoupling of 4-Chloroquinolin-2(1*H*)-ones 2a–e and 4-Chlorocoumarin (2f) using Bis(triphenylphosphine)nickel(II) Dichloride and DPEphos

A mixture containing 0.50 mmol of the corresponding chloroarene **2a–f**, 81.8 mg (0.125 mmol, 25 mol%) of $NiCl_2(PPh_3)_2$, 67.3 mg (0.125 mmol, 25 mol%) of DPEphos, 42.5 mg (0.65 mmol, 1.3 equivs.) of Zn powder and 149.4 mg (0.90 mmol, 1.8 equivs.) of KI was suspended in 0.8 mL anhydrous dioxane under an argon atmosphere in a 5-mL Pyrex microwave process vial equipped with a magnetic stirring bar. The vial was sealed, the mixture was stirred for 4 min at room temperature, and then heated by microwave irradiation for 30 min at 130 °C. Thereafter, the solvent was removed under reduced pressure. The products were isolated by gradient dry flash chromatography using EtOAc/acetone as solvent mixture to obtain the pure biaryls **1a–f**; yield: 71–92%.

Alternatively, products were isolated using an extractive work-up/purification method as described above for compound **1a**. Yields for both protocols are given in Table 3. Spectroscopic and analytical data for biaryls **1a–f** were as previously reported in ref.[14]

Acknowledgements

J. H. thanks the Higher Education Commission of Pakistan for a Ph.D. scholarship. We also thank Biotage AB (Uppsala, Sweden) for the provision of microwave instrumentation.

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