Tetrahedron Letters 53 (2012) 2218–2221

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

$NiCl_2·6H_2O$ as recyclable heterogeneous catalyst for N-arylation of amines and NH-heterocycles under microwave exposure

Amit Kumar Gupta, G. Tirumaleswara Rao, Krishna Nand Singh *

Department of Chemistry, Faculty of Science, Banaras Hindu University, Varanasi 221005, India

A R T I C L E I N F O

Article history:
Received 4 January 2012
Revised 15 February 2012
Accepted 16 February 2012
Available online 24 February 2012

Keywords:
Microwave
N-arylation
Ni-catalysis
Solvent-free

A B S T R A C T

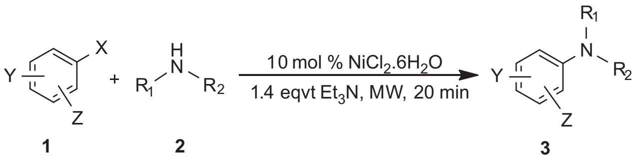
$NiCl_2·6H_2O$ has been proven to be an effective catalyst for the coupling of amines with aryl iodides without ligand under solvent-free conditions employing microwave irradiation. Reactions cleanly result in coupled products in a short reaction time. The catalyst, being heterogeneous, is recovered by filtration and is recyclable.

The use of microwave energy to heat chemical reactions has become an increasingly popular technique in the scientific community which is evidenced by a large number of review articles and books published on this subject.[1,2] In many instances, controlled microwave heating under sealed vessel conditions has been shown to dramatically reduce reaction times, increase product yields, and enhance product purities by reducing unwanted side reactions compared to conventional synthetic methods. The advantages of this technology have not only been exploited for organic synthesis and in the context of medicinal chemistry/drug discovery,[3] but have also penetrated the fields such as polymer synthesis,[4] material science,[5] nanotechnology,[6] and biochemical processes.[7]

Transition metal-catalyzed cross-coupling reactions of aryl halides with various nucleophilic compounds are now among the most prominent synthetic methods for the formation of carbon–heteroatom bonds. Among these, the formation of C–N bond has received much attention that finds wide applications in the synthesis of many substances such as drugs, materials, natural products, agrochemicals, and optical devices.[8] Exclusively, these reactions are performed under copper catalysis (Ullmann type reactions)[9] or palladium catalysis (Buchwald–Hartwig reactions).[10] Although significant progress has been made with regard to these reactions, there continues to be an increasing demand for low-cost and environment-friendly catalysts which have attracted other transition metals like iron and nickel in the field.

The first report regarding nickel catalyzed C–N coupling was produced by Buchwald in the form of cyclooctadiene complex of Ni(0) associated with 1,1′-bis(diphenylphosphino)ferrocene or 1,10-phenanthroline for the synthesis of aryl amines.[11] Till then a number of articles regarding nickel-catalysis for C–N bond formation have been published.[12] But nickel chemistry does not enjoy the fame as of palladium and copper and thus demands more studies to be made in the field. In view of the above and as a part of our ongoing research on the development of efficient protocols in organic synthesis,[13] we report herein a ligand and solvent-free Ni(II) catalyzed coupling of aryl halides with different aromatic, aliphatic and heterocyclic amines under controlled microwave protocol (Scheme 1).

As shown in Table 1, our experiments for the optimal conditions began with the coupling of iodobenzene with aniline taking various nickel salts as catalyst. The preliminary findings proved $NiCl_2·6H_2O$ to be the most effective for the reaction undertaken (Table 1, entries 1–4). Then, we probed the solvent effect on the reaction and to our delight we hit upon a solvent-free reaction which is far superior to any of the solvents used in the reaction (Table 1, entries 4–13). Some ligands were also incorporated in the reaction but surprisingly none of them could match the yield under



Scheme 1. Coupling of aryl halides with amines and NH-heterocycles.

---

* Corresponding author. Tel.: +91 542 6702485; fax: +91 542 2368127.
E-mail addresses: knsinghbhu@yahoo.co.in, knsingh@bhu.ac.in (K.N. Singh).

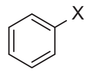
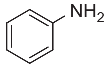
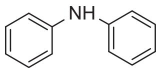
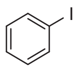
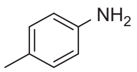
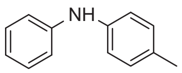
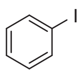
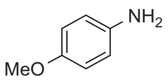
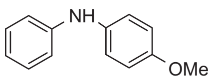
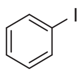
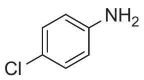
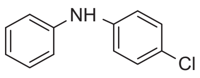
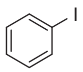
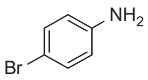
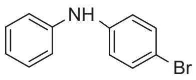
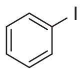
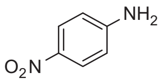
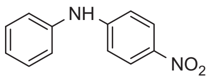
0040-4039/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2012.02.081

Table 1
Optimization of reaction conditions[a]

Entry	Catalyst (mol %)	Solvent	Ligand	Base	Temp (°C)	Time (min)	Yield [b] (%)
1	$Ni(OAc)_2.4H_2O$ (20)	DMSO	–	Et_3N	120	20	38
2	$NiSO_4$ (20)	DMSO	–	Et_3N	120	20	44
3	$Ni(NO_3)_2$ (20)	DMSO	–	Et_3N	120	20	35
4	$NiCl_2{\cdot}6H_2O$ (20)	DMSO	–	Et_3N	120	20	62
5	$NiCl_2{\cdot}6H_2O$ (20)	Toluene	–	Et_3N	120	20	16
6	$NiCl_2{\cdot}6H_2O$ (20)	Acetonitrile	–	Et_3N	120	20	23
7	$NiCl_2{\cdot}6H_2O$ (20)	Ethanol	–	Et_3N	120	20	nr
8	$NiCl_2{\cdot}6H_2O$ (20)	DMF	–	Et_3N	120	20	Trace
9	$NiCl_2{\cdot}6H_2O$ (20)	Water	–	Et_3N	120	20	nr
10	$NiCl_2{\cdot}6H_2O$ (20)	Dioxane	–	Et_3N	120	20	Trace
11	$NiCl_2{\cdot}6H_2O$ (20)	Ethylene glycol	–	Et_3N	120	20	38
12	$NiCl_2{\cdot}6H_2O$ (20)	NMP	–	Et_3N	120	20	32
13	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Et_3N	120	20	78
14	$NiCl_2{\cdot}6H_2O$ (20)	–	L-Proline	Et_3N	120	20	45
15	$NiCl_2{\cdot}6H_2O$ (20)	–	Ethylenediamine	Et_3N	120	20	54
16	$NiCl_2{\cdot}6H_2O$ (20)	–	1,10-Phenenthroline	Et_3N	120	20	32
17	$NiCl_2{\cdot}6H_2O$ (20)	–	Ethylacetoacetate	Et_3N	120	20	43
18	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Na_2CO_3	120	20	nr
19	$NiCl_2{\cdot}6H_2O$ (20)	–	–	KOH	120	20	nr
20	$NiCl_2{\cdot}6H_2O$ (20)	–	–	NaOH	120	20	nr
21	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Pyridine	120	20	24
22	$NiCl_2{\cdot}6H_2O$ (20)	–	–	–	120	20	nr
23	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Et_3N	120	20	77[c]
24	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Et_3N	120	20	68[d]
25	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Et_3N	120	20	78[e]
26	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Et_3N	110	20	57
27	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Et_3N	130	20	85
28	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Et_3N	140	20	83
29	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Et_3N	130	10	52
30	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Et_3N	130	30	82
31	$NiCl_2{\cdot}6H_2O$ (20)	–	–	Et_3N	130	40	76
32	$NiCl_2{\cdot}6H_2O$ (30)	–	–	Et_3N	130	20	85
33	**$NiCl_2{\cdot}6H_2O$ (10)**	–	–	**Et_3N**	**130**	**20**	**85**
34	$NiCl_2{\cdot}6H_2O$ (5)	–	–	Et_3N	130	20	81
35	–	–	–	Et_3N	130	20	nr
36	$NiCl_2{\cdot}6H_2O$ (10)	–	–	Et_3N	130	60	17[f]

The bold values in Table 1 signify the optimized reaction conditions.
[a] Reaction using 1 mmol iodobenzene, 1.5 mmol aniline and 1.4 equiv base.
[b] Isolated yield.
[c] Reaction performed with 2 equiv of Et_3N.
[d] Reaction using 1.2 mmol aniline.
[e] Reaction using 2 mmol aniline.
[f] Reaction by conventional heating.

Table 2
Coupling of aryl halides with various amines and NH-heterocycles[14]

Entry	Aryl halide	Amine	Product		Temp (°C)	Yield [a] (%)
1	 X= I, Br, Cl			**3a**	120 140 140 160	85 (X = I) 62 (X = Br) Trace (X = Cl) 34 (X = Cl)
2				**3b**	125	92[b] 89[c] 88[d] 86[e]
3				**3c**	125	88
4				**3d**	110	72
5				**3e**	120	70
6				**3f**	150	75

(continued on next page)