Catalysis Communications 148 (2021) 106170

Contents lists available at ScienceDirect

Catalysis Communications

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

Short communication

Nickel-catalyzed carbonylative synthesis of dihydrobenzofurans

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ARTICLE INFO

Keywords:
Nickel catalyst
Carbonylation
Alkyl halide
Dihydrobenzofurans
Cyclization
Carbonylative coupling

ABSTRACT

A nickel-catalyzed carbonylative synthesis of dihydrobenzofurans has been developed. With $Mo(CO)_6$ as the CO source and manganese metal as the reductant, alkyl halides were reacted with aryl iodides to give the desired products in moderate to good yields.

Transition metal-catalyzed carbonylative transformations have been well recognized by the synthetic community nowadays and has already been accepted as a powerful tool for the construction of carbonyl-containing chemicals [1–3]. However, concerning the catalysts applied, palladium- and rhodium-based complexes are more frequently studied compared with the other metal catalysts [4]. Among the various transition metal catalysts, nickel is attractive due to its abundancy and diversity in accessible oxidation states [5]. Nickel catalysts were originally studied to replace palladium catalysts in cross-coupling reactions. During these studies, nickel was found to show exceptional activities in some inert bonds' activation, including C─O, C─F, etc. [6,7] Then comes the term ‘Nickel is not just a replacement of palladium’.

However, in the topic of carbonylation chemistry, nickel catalysts are far less explored compared with palladium. The main reason is the high affinity of carbon monoxide with nickel metal. This specific property will cause two consequences: i) inhibit the catalytic reactivity of nickel catalysts; ii) forms $Ni(CO)_4$, which is a high toxic colorless liquid with low boiling point (43 °C) and hence known as ‘liquid death’. These phenomena, especially the later one, make chemists reluctant to study nickel catalysts in CO chemistry. Nevertheless, strategies still have been established: 1) perform the reaction under carbon monoxide atmosphere without stirring, to control the concentration of CO in the reaction solution [8,9]; 2) using pincer ligand coordinated nickel complexes as the catalyst, to pre-block three of the four coordination sites in advance and avoid CO over coordinating [10,11]; 3) avoid Ni(0) intermediate formation during the catalytic cycle [12,13]; 4) using CO surrogates, such as $Mo(CO)_6$, the CO can be released slowly or via ligand exchange with the catalyst directly [14–20]. We are more interested in the strategy with CO surrogates.

1-Iodo-2-((2-methylallyl)oxy)benzene and related derivatives have been found an class of attractive compounds in cyclization transformations [21–33]. Dihydrobenzofurans and analogues can be prepared in an efficient and straightforward manner. Although numerous transformations have been established, reductive carbonylative coupling with alkyl halides using nickel as the catalyst has not been realized yet. Here, our new results on nickel-catalyzed carbonylative synthesis of dihydrobenzofurans will be described. With $Mo(CO)_6$ as the CO source and manganese metal as the reductant, alkyl halides were reacted with 1-iodo-2-((2-methylallyl)oxy)benzenes to give the corresponding dihydrobenzofurans in moderate to good yields.

Initially, 1-iodo-2-((2-methylallyl)oxy)benzene and iodocyclopentane were selected as the model substrates to establish the catalytic system using nickel as the catalyst. With $NiCl_2$ and 4,4′-di-*tert*-butyl-2,2′-dipyridyl (dtbbpy) as the catalytic system, using $Mo(CO)_6$ as the CO source, in THF at 100 °C, the target product **3aa** was obtained in 8% yield (Table 1, entry 1). Then various organic solvents were checked (Table 1, entries 1–6), surprisingly, 36% of **3aa** was formed when the reaction was performed in DMF (Table 1, entry 4). In the case of 1,4-dioxane, the reaction temperature was varied as well, the reaction outcome could not be improved (for details, see Supporting Information). In the testing of the nickel catalyst precursors, $Ni(acac)_2$ could give the best yield of **3aa** (47%; Table 1, entry 9). The influences from ligands were studied subsequently, the other tested nitrogen ligands were all gave inferior results (Table 1, entries 11–15). Phosphine ligands were checked as well, the yield of **3aa** dropped dramatically and only trace amount of the target product could be detected with monophosphine ligands, such as PPh_3 or PCy_3 (Table 1, entry 16). The loading of manganese was fixed at 2 equivalents and no reaction

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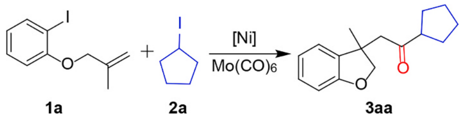
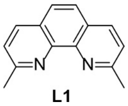
https://doi.org/10.1016/j.catcom.2020.106170
Received 25 August 2020; Received in revised form 10 September 2020; Accepted 11 September 2020

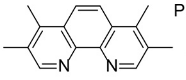
Table 1
Optimization of the catalyst system.[a]



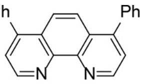
Entry	Nickel	Solvent	Ligand	Yield
1	$NiCl_2$	THF	dtbbpy	8%
2	$NiCl_2$	toluene	dtbbpy	1%
3	$NiCl_2$	MeCN	dtbbpy	4%
4	$NiCl_2$	DMF	dtbbpy	36%
5	$NiCl_2$	DMSO	dtbbpy	6%
6	$NiCl_2$	1,4-dixoane	dtbbpy	12%
7	$NiBr_2$	DMF	dtbbpy	8%
8	NiI_2	DMF	dtbbpy	15%
9	$Ni(acac)_2$	DMF	dtbbpy	47%
10	$Ni(OTf)_2$	DMF	dtbbpy	13%
11	$Ni(acac)_2$	DMF	bpy	11%
12	$Ni(acac)_2$	DMF	1,10-phen	16%
13	$Ni(acac)_2$	DMF	**L1**	13%
14	$Ni(acac)_2$	DMF	**L2**	28%
15	$Ni(acac)_2$	DMF	**L3**	10%
16	$Ni(acac)_2$	DMF	DPPP	6%
17	$Ni(acac)_2$	DMF	dtbbpy	52%[b]
18	$Ni(acac)_2$	DMF	dtbbpy	66%[c]
19	$Ni(acac)_2$	DMF	dtbbpy	94%[d]



L1



L2



L3

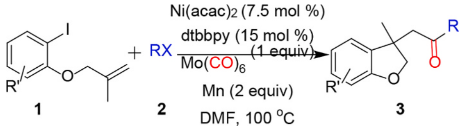
[a] Reaction condition: **1a** (0.2 mmol), **2a** (2 equiv), nickel (5 mol%), ligand (5 mol%), $Mo(CO)_6$ (1 equiv), Mn (2 equiv), DMF (1 mL), 100 °C, 16 h, GC yield with hexadecane as the internal standard. b. 10 mol% of ligand. c. $Ni(acac)_2$ (7.5 mol%), dtbbpy (15 mol%). d. **1a** (0.2 mmol), **2a** (2.5 equiv), Ni(acac) (7.5 mol%), dtbbpy (15 mol%), $Mo(CO)_6$ (1 equiv), Mn (2 equiv), DMF (1 mL), 100 °C, 16 h. dtbbpy: 4,4′-di-*tert*-butyl-2,2′-dipyridyl. Bpy: 2,2′-bipyridine. 1,10-phen: 1 10-phenanthroline.

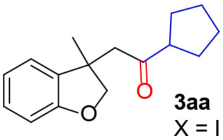
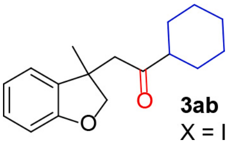
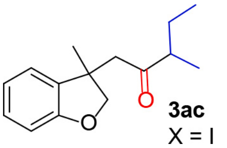
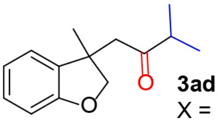
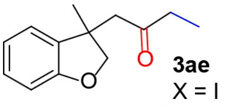
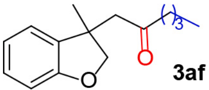
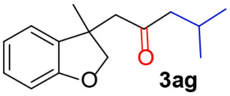
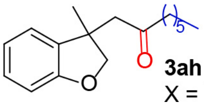
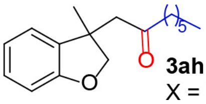
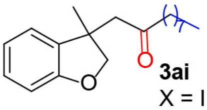
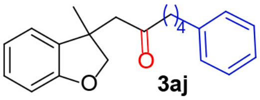
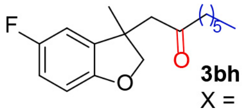
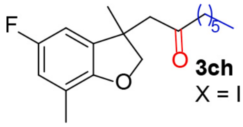
occurred when zinc was used instead of manganese (for details, see Supporting Information). The amount of $Mo(CO)_6$ added proved to be critical as well, the yield of **3aa** decreased with higher loadings of $Mo(CO)_6$ (for details, see Supporting Information). The yield can be further improved by increasing the ratio of ligand related to metal (Table 1, entry 17). Finally, 94% yield of **3aa** can be achieved with increased loading of catalyst and iodocyclopentane (Table 1, entry 19).

With the optimal reaction conditions in hand, we carried out the testing of substrates subsequently (Table 2). In general, various alkyl iodides can be applied successfully and gave the desired dihydrobenzofuran derivatives in moderate to good yields. In the case of alkyl bromide, the reaction efficiency decreased dramatically, and 38% yield of the corresponding product was isolated (Table 2, entry 9). In the case of benzyl iodides, only trace amount of the target products could be detected. Then some 1-iodo-2-((2-methylallyl)oxy)benzenes were tested, moderate yields can be obtained as well (Table 2, entries 12–13). However, under our standard conditions, no reaction occurred when 1-bromo-2-((2-methylallyl)oxy)benzene was applied as the substrate (for details, see Supporting Information). Finally, 2-iodo-*N*-methyl-*N*-(2-methylallyl)aniline was prepared and tested under our conditions, the corresponding indoline derivative was obtained in 43% yield without further optimization (Table 2, entry 14).

Based on our results and literatures, a possible reaction mechanism is proposed (Scheme 1). Firstly, the active nickel catalyst will be generated from $Ni(acac)_2$ in the presence of Mn and ligand. Then Ni^0L complex oxidative adds into the C—I bond of 1-iodo-2-((2-methylallyl)oxy)benzenes and forms arylNi^{II} complex **A**. After an intramolecular addition step, alkylNi^{II} complex **B** will be formed which will be

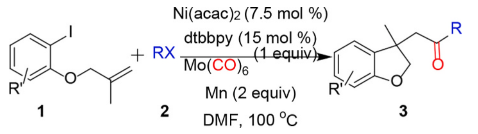
Table 2
Nickel-catalyzed carbonylative synthesis of dihydrobenzofurans.[a]

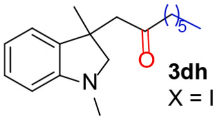


Entry	Product	Yield
1	 **3aa** X = I	87%
2	 **3ab** X = I	58%
3	 **3ac** X = I	45%
4	 **3ad** X = I	53%
5	 **3ae** X = I	59%
6	 **3af** X = I	56%
7	 **3ag** X = I	64%
8	 **3ah** X = I	71%
9	 **3ah** X = Br	38%
10	 **3ai** X = I	45%
11	 **3aj** X = I	54%
12	 **3bh** X = I	67%
13	 **3ch** X = I	65%

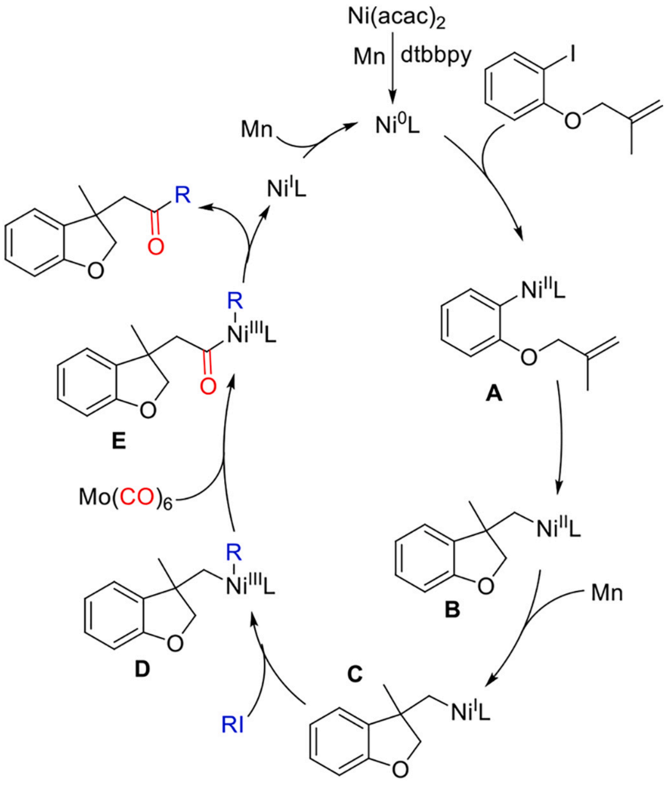
(*continued on next page*)

Table 2 (*continued*)



Entry	Product	Yield
14	 **3dh** X = I	43%

[a] **1** (0.2 mmol), **2** (2.5 equiv), Ni(acac) (7.5 mol%), dtbbpy (15 mol%), Mo(CO)$_6$ (1 equiv), Mn (2 equiv), DMF (1 mL), 100 ˚C, 16 h, isolated yields.



Scheme 1. Proposed reaction mechanism.

immediately reduced to alkylNi^{I} complex **C** in the presence of Mn. Oxidative addition of alkyl iodides with complex **C** will occur to give the alkylNi^{III} intermediate **D** which will release the final product after reductive elimination step. The Ni^{I} intermediate will be further reduced by Mn to regenerate the active Ni^{0}L complex for the next catalytic cycle.

In summary, an interesting procedure on nickel-catalyzed carbonylative synthesis of dihydrobenzofurans from 1-iodo-2-((2-methylallyl)oxy)benzenes and alkyl halides has been developed. By using Mo(CO)$_6$ as the CO source and manganese metal as the reductant, the desired dihydrobenzofurans were produced in moderate to good yields.

Declaration of Competing Interest

None.

Acknowledgment

We thank the generous supports from Zhejiang Sci-Tech University.

Credit Author Statement

X.W. directed the project and prepared the manuscript. H.Q.G. and W. W. performed all the experiments.

Declaration of Competing Interest

We have no conflict of interest to declaration!

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.catcom.2020.106170.

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