Tetrahedron Letters 55 (2014) 1006–1010

Contents lists available at ScienceDirect

Tetrahedron Letters

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

$Co_2(CO)_8$ as a convenient in situ CO source for the direct synthesis of benzamides from aryl halides (Br/I) via aminocarbonylation

Poongavanam Baburajan, Kuppanagounder P. Elango *

Department of Chemistry, Gandhigram Rural Institute (Deemed University), Gandhigram 624302, India

ARTICLE INFO

Article history:
Received 29 October 2013
Revised 13 December 2013
Accepted 17 December 2013
Available online 21 December 2013

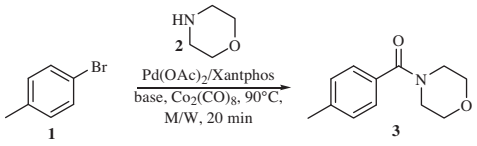
Keywords:
Benzamide
Aryl halide
Carbonylation
Microwave

ABSTRACT

A fast, mild, and functional group tolerant method for the direct synthesis of benzamides from aryl halides (Br, I) via aminocarbonylation, using solid $Co_2(CO)_8$ as a convenient CO source, has been demonstrated. The developed method is applicable to a wide variety of 1° and cyclic and acyclic 2° amines. Nitro substituted (*o*, *m* and *p*) aryl halides have easily been converted to the corresponding benzamides, without the reduction of the nitro group, in high yields using this in situ carbonylation methodology under microwave irradiation.

The aromatic carbonyl derivatives namely esters and amides are important building blocks in the synthesis of valuable organic compounds including pharmaceuticals and agrochemicals.[1] In carbonyl derivatives, the benzamide derivatives possess important biological activities. Several methods have been published for the synthesis of benzamides.[2] Also, a variety of carbonyl derivatives have been synthesized by atom economy and functional group tolerant methods using easily available starting materials based on the palladium catalyzed carbonylation developed by Heck[3] in 1970s through the three-component coupling reaction using $CO_{(g)}$, aryl halides and a nucleophile (O^-, N^-, C^-). Such carbonylation methods, using CO gas, is based on the excellent ability of CO to act as pi-acid ligand toward transition metals.[4] However, CO is a highly toxic and flammable gas. Also, these reactions require special pressure reaction setups, and these methods are inconvenient in laboratory (small scale) and library (analogous) syntheses. To overcome this inconvenience to some extent, in 2002 Mats and coworkers have developed an in situ carbonylation method using non-gaseous CO precursors (transition metal carbonyls) employing a fast and furious microwave instrument. Subsequently, many reports have been published based on this methodology.[5] Although, they are able to overcome the inconvenience to some extent, using this methodology, higher temperatures (>120 °C) and/or higher equivalence of CO source are required to get good yields. Recently, a new ex situ method of generation of CO from $Mo(CO)_6$ using a bridged two-vial system has

Table 1
Condition optimization of aminocarbonylation



1 3

Entry	Carbonyl source	Base	Solvent[a]	Temp (°C)	Time (min)	Yield[b] (%)
1	$Co_2(CO)_8$[c]	DMAP	Toluene	90	30	81
2	$Co_2(CO)_8$[c]	DMAP	DMSO	90	30	70
3	$Co_2(CO)_8$[c]	DMAP	DMF	90	30	77
4	$Co_2(CO)_8$[c]	DMAP	DME	90	30	69
5	$Co_2(CO)_8$[c]	DMAP	THF	90	30	64
6	$Co_2(CO)_8$[c]	DMAP	Dioxane	90	30	91
7	$Co_2(CO)_8$[c]	DMAP	Dioxane	90	20	92
8	$Co_2(CO)_8$[c]	DMAP	Dioxane	90	15	88
9	$Mo(CO)_6$[d]	DMAP	Dioxane	90	30	72
10	$Cr(CO)_6$[d]	DMAP	Dioxane	90	30	35
11	$W(CO)_6$[d]	DMAP	Dioxane	90	30	30
12	$Co_2(CO)_8$[e]	DMAP	Dioxane	90	30	69

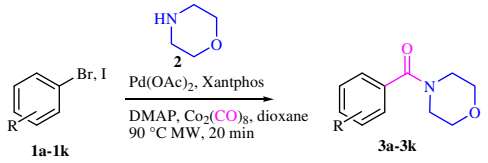
All the reactions were executed with 0.5 mmol of 4-bromotoluene, 5 mol % of $Pd(OAc)_2$, 5 mol % of ligand (4,5-bis(diphenylphosphanyl)-9,9-dimethylxanthene), 1 mmol of morpholine and 0.25 mmol of $Co_2(CO)_8$ at microwave irradiation.

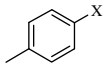
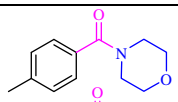
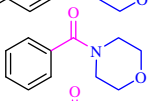
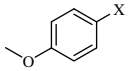
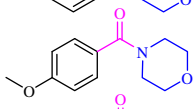
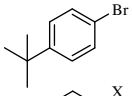
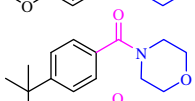
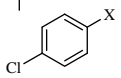
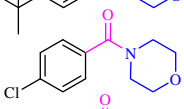
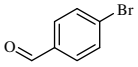
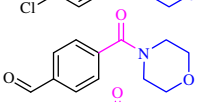
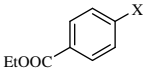
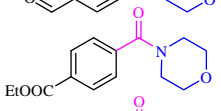
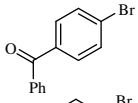
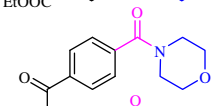
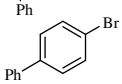
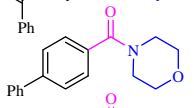
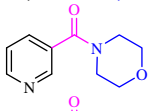
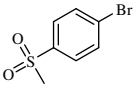
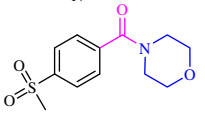
[a] All the solvents were freshly distilled and used.
[b] Yield of the isolated product by column chromatography.
[c] 0.25 equiv of $Co_2(CO)_8$ were used.
[d] 0.5 equiv of metal carbonyls (Mo, Cr, W) were used.
[e] The reaction was performed with oil bath heating at 90 °C for 1 h.

* Corresponding author. Tel.: +91 451 2452371; fax: +91 451 2454466.
E-mail address: drkpelango@rediffmail.com (K.P. Elango).

0040-4039/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2013.12.062

Table 2
Synthesis of morpholine amides of aryl halides



Entry	Arylhalide (1a-k)	$Co_2(CO)_8$ (eqv.)	Product (3a-k)	Yields (%)[a]
1		0.25		X=Br, 91 X=I, 88
2		0.25		X=Br, 89 X=I, 93
3		0.25		X=Br, 95 X=I, 83
4		0.30		82
5		0.25		X=Br, 92 X=I, 84
6		0.25		93
7		0.25		X=Br, 90 X=I, 86
8		0.30		82
9		0.25		X=Br, 87 X=I, 91
10		0.30		75
11		0.30		80

[a] Yield of isolated product.

been reported for the carbonylation of nitro substituted aryl halides.[6] The major advantage of this method (i.e., carbonylation of nitro substituted aryl halides without affecting the nitro group) is based on the fact that the reduction of nitro group to aniline by $Mo(CO)_6$ is known in the literature.[7] Recently, we have described the synthesis of esters directly from aryl halides by using $Co_2(CO)_8$ as a simple and successful in situ CO source.[8] In continuation of this work, herein we report a simple and convenient protocol for the synthesis of benzamides in excellent yields through aminocarbonylation of different aryl halides including nitro substituted ones at low temperatures and at lower equivalents of CO source.

As part of our on-going work on carbonylation reactions using $Co_2(CO)_8$ as CO source, in this Letter we report a convenient method of amino carbonylation of aryl halides. With an aim to optimize the reaction conditions, 4-bromotoluene and morpholine were chosen as model substrates using microwave irradiation. As in the previous case, $Pd(OAc)_2$/xantphos in the presence of DMAP base was found to be the effective catalytic system in the present reaction also. The effect of various reaction conditions such as solvent, transition metal carbonyl, reaction time and equivalence of metal carbonyl on the isolated yield of the product is shown in Table 1.

The results given in Table 1 indicate that, among the various solvents investigated, 1,4-dioxane (Entry 4) was found to be the best solvent. Further, based on the reaction time variation studies (Entries 6–8), 20 min was fixed as the optimum time as the reaction gets completed within this period with excellent yields (Entry 7). With these stabilized reaction conditions (Entry 7), we have carried out the CO source variation study (Entries 9–11). The results showed that molybdenum hexacarbonyl (Entry 9) gave good yields (72%) and the rest of the metal carbonyls