Asian Journal of Chemistry; Vol. 27, No. 5 (2015), 1698-1700

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2015.17551

Copper Catalyzed Synthesis of Aryl Azides from Aryl Bromides and Sodium Azide

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Received: 4 March 2014; *Accepted*: 13 May 2014; *Published online*: 20 February 2015; AJC-16872

Aryl azides were synthesized using heterogeneous porous Cu catalyst *via* a coupling reaction of aryl bromides with sodium azide under mild conditions. The catalyst can be recycled in five times without significant loss of their catalytic activity.

Keywords: Porous copper, Aryl bromides, Sodium azide, Aryl azides.

INTRODUCTION

Aryl azides are important building blocks in organic synthesis, especially for the assembly of various heterocycles[1-5]. The most common method reported in the literature for synthesis of aryl azides involves the replacement of diazonium salts or some activated aryl halide with sodium azide[6-7]. Recently, syntheses of aryl azides have also been reported using coupling of aryl halides with sodium azide catalyzed by CuI[8-9]. However, it is worth noting that other copper catalysts have not been used in this coupling reaction, especially Cu (0) metal. On the other hand, porous Cu, which has excellent structural characteristics and is basically harmless to the human body, has mostly been used as filter material. It is commercially available and can also be prepared according to published methods[10,11]. Recently, it has been reported that fabricated nanoporous Cu materials were highly efficient heterogeneous catalysts for Click reactions and exhibited high reusability[12]. We have recently reported the Click reaction to afford 1,2,3-triazoles using porous Cu catalyst[13]. In continuation of our studies, herein, we report an efficient method for the preparation of aryl azides from the corresponding aryl bromides with sodium azide in the presence of porous Cu catalyst.

EXPERIMENTAL

All the chemicals were obtained from commercial suppliers and used without further purification. N-sulfonyl imines were prepared by the procedures in the literature. Thin layer chromatography (TLC) was performed using silica gel 60 F254 and visualized using UV light. Column chromatography was performed with silica gel (mesh 300-400). ^{1}H NMR spectra was recorded on a Bruker Avance 500 MHz spectrometer in $CDCl_3$ with Me_4Si as an internal standard.

General procedure for aryl azides (2a-i): To a reactor containing aryl bromides (1 mmol), sodium azide (2 mmol), iPr_2NH (20 mol %), L-proline (20 mol %), EtOH (3 mL) and H_2O (1 mL) was added porous Cu (0.05 mmol). The mixture was then sealed and stirred at 100 °C until the reaction was completed as judged by TLC, filtered. The recovered Cu catalyst was washed with water and methanol with no further purification before reuse. The filtrate was extracted with ethyl acetate (3 × 10 mL). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography to give the pure product.

4-Methoxyphenylazide (**2a**)[14]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.98 (d, J = 9.0 Hz, 2H), 6.91 (d, J = 9.0 Hz, 2H), 3.81 (s, 3H).

4-Ethoxyphenylazide (**2b**)[15]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (d, J = 9.0 Hz, 2H), 6.89 (d, J = 9.0 Hz, 2H), 4.02 (q, J = 7.0 Hz, 2H), 1.43 (t, J = 7.0 Hz, 3H).

2-Methoxyphenylazide(**2c**)[14]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14-7.10 (m, 1H), 7.04-7.02 (m, 1H), 6.97-6.94 (m, 1H), 6.92-6.90 (m, 1H).

4-Methylphenylazide (**2d**)[16]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, J = 8.0 Hz, 2H), 6.94 (d, J = 8.0 Hz, 2H), 2.35 (s, 3H).

4-Aminophenylazide (**2e**): m.p. 50-52 °C (lit.[8] 65-66 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (d, J = 8.7 Hz, 2H), 6.69 (d, J = 8.7 Hz, 2H), 3.66 (s, 2H).

4-Acetylaminophenylazide (**2f**): m.p. 126-127 °C (lit.[17] 122-123 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.8 Hz, 2H), 7.30 (s, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 2.19 (s, 3H).

Phenylazide (**2g**)[18]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.36 (m, 2H), 7.18-7.15 (m, 1H), 7.06-7.05 (m, 2H).

4-Trifluoromethylphenylazide (**2h**)[19]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.5Hz, 2H), 7.72 (d, *J* = 8.5Hz, 2H).

4-Chlorophenylazide (**2i**)[15]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 8.7 Hz, 2H).

RESULTS AND DISCUSSION

In an initial attempt to prepare aryl azides using Cu porous material as a catalyst, we investigated the coupling reaction of 4-methoxy phenyl bromide (**1a**) with sodium azide. It was found that under the action of 5 mol % porous Cu (5 μm), 20 mol % L-proline and 20 % diisopropylamine in DMSO, this reaction gave 4-methoxyphenyl azide (**2a**) in only 7 % yield at 80 °C for 34 h, even when the reaction time was longer or the reaction temperature was raised. (Table-1, entries 1-3). Different solvents were screened, replacement of DMSO by EtOH or H_2O along gave lower yield (Table-1, entries 9-10). The coupling reaction of 4-bromoanisole (**1a**) with sodium azide provided 4-azidoanisole (**2a**) in 73 % yield at 100 °C when a mixed solvent ($EtOH/H_2O$ = 3:1) was used (Table-1, entry 11). Other bases, such as Et_3N, NaOH, LiOH, Cs_2CO_3 and K_3PO_4 were ineffective (Table-1, entries 4-8). Furthermore, a decreased yield was observed using Cu with larger pores (Table-1, entry 12).

To further assess the scope of this process, we have examined the coupling reaction of different aryl bromides with sodium azide using the optimized reaction conditions as in entry 11 (Table-1). The results are summarized in Table-2 and **Scheme-I**. Aryl bromides with an *para*-substituted electron-donating group on the benzene ring all gave good isolated yields of the corresponding aryl azides (entries 1, 2, 4-6). In sharp contrast, aryl bromides with *ortho*-substituted groups

TABLE-1

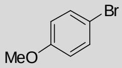
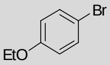
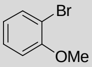
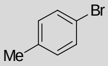
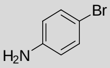
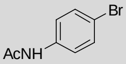
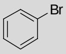
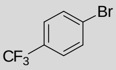
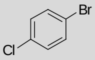
REACTION OF 4-METHOXY PHENYL BROMIDE (**1a**) WITH SODIUM AZIDE IN THE PRESENCE OF POROUS Cu CATALYST[a]

Entry	Base (20 mol %)	Additive (20 mol %)	Temperature (°C)	Solvent	Time (h)	Yield of **2a** (%)[b]
1	$(Me_2CH)_2NH$	L-proline	80	DMSO	34	7
2	$(Me_2CH)_2NH$	L-proline	80	DMSO	45	9
3	$(Me_2CH)_2NH$	L-proline	100	DMSO	34	10
4	Et_3N	L-proline	100	DMSO	34	0
5	NaOH	L-proline	100	DMSO	34	0
6	LiOH	L-proline	100	DMSO	35	0
7	Cs_2CO_3	L-proline	100	DMSO	35	0
8	K_3PO_4	L-proline	100	DMSO	34	0
9	$(Me_2CH)_2NH$	L-proline	100	EtOH	45	22
10	$(Me_2CH)_2NH$	L-proline	100	H_2O	45	29
11	$(Me_2CH)_2NH$	L-proline	100	$EtOH:H_2O$ = 3:1	45	73
12[c]	$(Me_2CH)_2NH$	L-proline	100	$EtOH:H_2O$ = 3:1	50	50

[a]Reactions were performed with **1a** (1 mmol), NaN_3 (2 mmol), base (20 mol %), ligand (20 mol %) and Cu (5 μm, 5 mol %) in solvent (4 mL), [b]Isolated yields, [c]Cu (15 μm) was used

TABLE-2

ARYL AZIDES 2 FROM ARYL BROMIDES WITH SODIUM AZIDE BY Cu[a]

Run	1	Time (h)	Temperature (°C)	2	Yield (%)[b]
1		45	100	2a	73
2		45	100	2b	85
3		50	100	2c	50
4		35	100	2d	75
5		20	100	2e	68
6		25	90	2f	88
7		40	90	2g	70
8		50	100	2h	58
9		50	100	2i	62

[a]Reactions were performed with **1** (1 mmol), NaN_3 (2 mol), $^iPr_2NH$ (20 mol %), L-proline (20 mol %) and Cu (5 μm, 5 mol %) in EtOH and H_2O (3 mL, 2:1), [b]Isolated yields

the corresponding coupling product was obtained in 50 % yield (entry 3). Phenyl bromide gave a good isolated yield of **2g** (entry 7). In addition, containing *p*-CF_3 or *p*-Cl groups on the benzene ring were tolerated for the reaction, obtaining the corresponding products **3h** and **3i** in 58 and 62 % yields, respectively (entries 8-9)

$$\underset{\mathbf{1}}{\mathrm{ArBr}} \quad + \quad \mathrm{NaN_3} \longrightarrow \underset{\mathbf{2a\text{-}i}}{\mathrm{ArN_3}}$$

Scheme-I: Aryl azides (**2a-i**) from aryl bromides with sodium azide

The reusability of porous Cu catalyst was studied for the coupling reaction of **1a** with sodium azide. The results are summarized in Table-3. The Cu catalyst was recovered using simple filtration and reused with consistent activity even after the fifth cycle.

TABLE-3
RECYCLING OF CATALYST[a]

Entry	1	2	3	4	5
Yield (%)[b]	73	75	69	71	67

[a]Reactions were performed with **1a** (1 mmol), NaN_3 (2 mol), $(Me_2CH)_2NH$ (20 mol %), L-proline (20 mol %) and Cu (5 µm, 5 mol %) in EtOH and H_2O (4 mL, 3:1) at 100 °C for 35 h, [b]Isolated yields

Conclusion

An efficient porous Cu catalyzed coupling reaction of aryl bromides with sodium azide to produce aryl azides under mild conditions with medium to good yield is reported. A wide range of aryl bromides can be tolerated. The heterogeneous porous Cu catalyst could be recycled.

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