Tetrahedron Letters 58 (2017) 4855–4858

Contents lists available at ScienceDirect

Tetrahedron Letters

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

CuI catalyzed sulfamidation of arylboronic acid using $TsNBr_2$ at room temperature

Dineshwori Chanu Loukrakpam, Prodeep Phukan *

Department of Chemistry, Gauhati University, Guwahati, 781014 Assam, India

ARTICLE INFO

Article history:
Received 17 October 2017
Revised 12 November 2017
Accepted 14 November 2017
Available online 15 November 2017

Keywords:
$TsNBr_2$
CuI
Arylboronic acid
Arylsulfonamide

ABSTRACT

An expeditious protocol for amidation arylboronic acid has been developed using $TsNBr_2$ as the nitrogen source in presence of a CuI as catalyst. Various arylboronic acids could be transformed into corresponding *N*-arylsulfonamide derivatives within a very short time using CuI as catalyst in presence of DBU at room temperature.

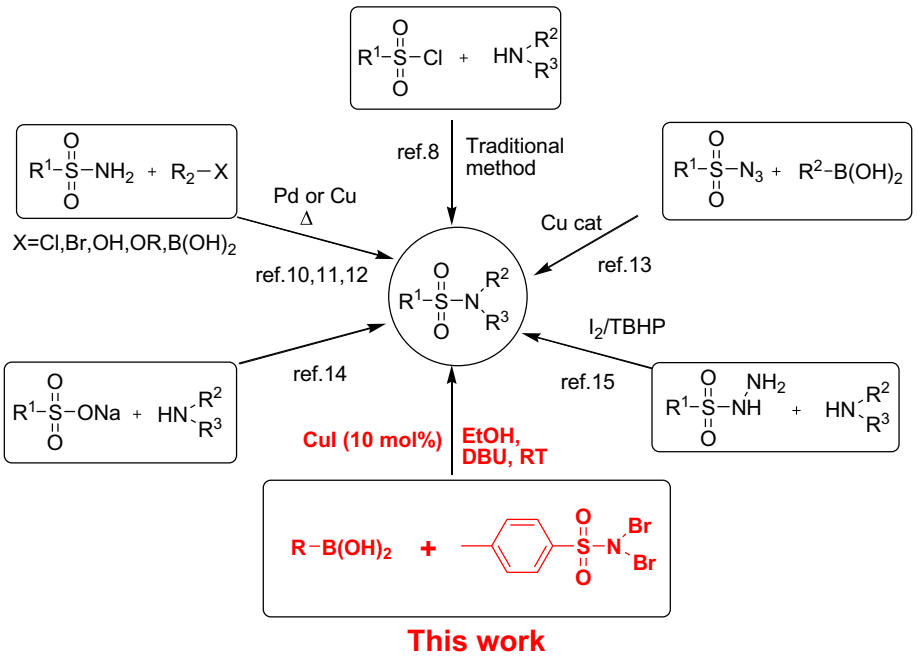
Introduction

Sulfonamides are important structural motif which is frequently encountered in pharmaceuticals, bioactive compounds and natural products.[1] Sulfonamide derivatives became popular ever since the discovery of their activities like anticancer,[2] HIV protease inhibitor,[3] anticonvulsant,[4] antimicrovial,[5] antibacterial and antifungal,[6] HCV NS5B polymerase inhibitors for acute hepatitis and chronic liver disease.[7] Pharmaceutically important examples of sulfonamides include celecoxib (analgesic), amprenavir (HIV protease inhibitor), pazopanid (antitumor), sildenafil (anti-impotence) and sulfamethoxazole (antibiotic).[1–7] Owing to their wide range of applications, various methods have been developed for the synthesis of sulfonamides (Scheme 1).

Generally, sulfonamides are prepared by the reaction of a primary amine (ammonia), or a secondary amine with sulfonyl chloride in presence of a base.[8] However, this methodology has limited application in pharmaceutical manufacturing since both the sulfonyl chloride and aromatic amine are genotoxic alerting structures having a very low threshold (ppm level) of residual tolerance in active pharmaceutical ingredients (API).[9] Alternative routes to *N*-arylsulfonamides are the transition metal catalyzed cross coupling reaction of sulfonamides with organohalides or boronic acids[10] and metal catalyzed aminosulfonation of benzylic and allylic hydrocarbons.[11] Sulfonamides can also be synthesized from arylthiols through an oxygen-activated radical protocol in presence of copper catalyst,[12] Chan-Lam coupling of sulfonyl azides and boronic acids under copper catalyst,[13] reaction of sodium sulfinates with amines under metal and metal free conditions.[14] Another synthetic approach include sulfonylation of amines or nitroarenes with arylsulfonyl hydrazides under metal-mediated or metal-free conditions.[15] Among the transition metals, palladium and copper have been generally used due to their efficiency and compatibility with functional groups. However, toxicity and high cost of palladium catalyst restrict their use on large scale industrial application. Thus, researchers have shifted their attention towards the used of less expensive, less toxic, and more efficient metals to replace palladium catalyst. Lam et al. (2001) reported the synthesis of *N*-arylsulfonamides employing sulfonamides and arylboronic acids.[10e] Since then, many extensions and modifications of the Chan–Lam coupling reaction of sulfonamides with arylboronic acids have been demonstrated.[16] Although, there are several existing methods for the synthesis of *N*-arylsulfonamides, yet certain significant drawbacks viz. use of non-stable, hazardous and mutagenic starting materials (e.g. sulfonyl chlorides and organic azides), generation of a large quantity of toxic waste, difficulty in handling and storing, the requirement of harsh reaction conditions and a prolonged reaction time are usually associated with them. While preparing this manuscript, we have come across a procedure for arylsulfonamide synthesis by coupling arylboronic acids with chloramine-T in presence of Cu $(OAc)_2$ as catalyst under the influence of potassium *tert*-butoxide.[17] Of late, various workers have reported the used of *N,N*-dibromo-*p*-toluenesulfonamide ($TsNBr_2$) as an efficient reagent for various organic transformation.[18] In continuation of our work on $TsNBr_2$,[19]

* Corresponding author.
E-mail address: pphukan@gauhati.ac.in (P. Phukan).

https://doi.org/10.1016/j.tetlet.2017.11.033
0040-4039/



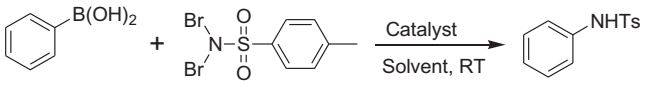
Scheme 1. Different synthetic approaches towards the synthesis of sulfonamides.

we report herein a new synthetic approach for the preparation of *N*-arylsulfonamide using $TsNBr_2$ as the nitrogen source in presence of CuI catalyst and base under mild reaction conditions within a short reaction time. To the best of our knowledge, the present study is the first to use $TsNBr_2$ as the nitrogen sources in the synthesis of *N*-arylsulfonamide.

Results and discussion

We began our studies by selecting phenylboronic acid as the model reactant to find out the optimized condition. The results are shown in Table 1. Initially, the reaction was carried out by treating phenyl boronic acid (1 mmol) with $TsNBr_2$ (1 mmol) in presence of 3 mol equivalent of cesium carbonate in methanol at room temperature under inert atmosphere. To our disappointment, the reaction did not proceed at all even after 24 h of reaction. Thereafter, the reaction was carried out using 10 mol% of Cu $(OAc)_2$ which resulted in a moderate yield of 68% after 4 h of reaction. When the reaction was carried out by using palladium acetate catalyst, biphenyl was formed instead of the desired *N*-arylated product. On modification of nature of the copper source, CuI was found to be the most efficient catalyst giving the desired *N*-arylated product in 75% yield. Further study with 1.2 equivalent of $TsNBr_2$ could impart a slight improvement in the result. However, when the reaction was examined in presence of DBU (3 mol equivalent based on the substrate) a dramatic improvement of yield and reaction rate was observed. The reaction produced the desired *N*-tosyl aniline in 86% yield within 5 min. The reaction was found to be marginally better in ethanol as a solvent. When the study was carried out in presence of K_2CO_3 instead of DBU, the reaction

Table 1
CuI catalyzed sulfamidation reaction under different conditions.[a]



Entry	$TsNBr_2$ (mmol)	Catalyst	Catalyst amount (mol%)	Base	Solvent	Time	Yield[b] (%)
1	1	Nil	–	Cs_2CO_3	MeOH	24 h	Nil
2	1	$Cu(OAc)_2$	10	Cs_2CO_3	MeOH	4 h	68
3	1	$Pd(OAc)_2$	10	Cs_2CO_3	MeOH	4 h	–[c]
4	1	$CuCl_2{\cdot}2H_2O$	10	Cs_2CO_3	MeOH	4 h	66
5	1	CuI	10	Cs_2CO_3	MeOH	4 h	75
6	1.2	CuI	10	Cs_2CO_3	MeOH	4 h	78
7	1.2	CuI	10	DBU	MeOH	5 min	86
8	**1.2**	**CuI**	10	**DBU**	**EtOH**	**5 min**	**88**
9	1.2	CuI	10	K_2CO_3	EtOH	8 h	80
10	1.5	CuI	10	DBU	EtOH	5 min	88
11	1.2	CuI	5	DBU	EtOH	10 min	80
12	1.2	CuI	15	DBU	EtOH	10 min	87

The bold letters signifies the optimized and final reaction condition.
[a] Reaction conditions: Phenylboronic acid (1 mmol), base (3 mmol), solvent (2 ml), room temperature.
[b] Isolated yield.
[c] Biphenyl was found as the sole product.