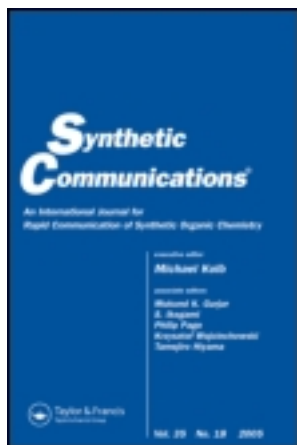


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## A Novel and Simple Solvent Free Method for Nucleophilic Aromatic Substitution of Inactive Aryl Halides

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### ABSTRACT

A simple, high yield, and short time method for nucleophilic displacement reaction of inactive aryl halides is reported. The reaction is performed in microwave oven under thermal condition with montmorillonite supported  $\text{AgNO}_3$ .

*Key Words:* Aryl halides; Nucleophilic substitution; Solvent free; Montmorillonite K10.

### INTRODUCTION

Nucleophilic aromatic substitution ( $\text{S}_{\text{N}}\text{Ar}$ ) reactions constitute an active field of organic chemistry, which is very important from the viewpoints of both practical applications<sup>[1]</sup> and the theory of nucleophilic reaction mechanisms.<sup>[2,3]</sup>

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It has long been known that an *ortho*- or *para*-nitro group strongly activates the condensation of a halobenzene with a nucleophilic reagent such as a hydroxide<sup>[4]</sup> or an alkoxide ion,<sup>[5]</sup> a halide ion,<sup>[6]</sup> a mercaptide ion<sup>[7]</sup> or an amine.<sup>[4,8]</sup>

It has been found that the order of activation in this reaction is  $\text{NO}_2 \gg \text{CH}_3\text{SO}_2 > \text{CN} > \text{CH}_3\text{CO}$ .<sup>[8]</sup>

In absence of the electron withdrawing groups the proposed mechanism is elimination–addition (Aryne mechanism).<sup>[9]</sup>

The nucleophilic substitution of inactive aryl halides is a very difficult reaction and the reported methods require vigorous conditions such as high pressure<sup>[10]</sup> and temperature,<sup>[11]</sup> very active nucleophiles<sup>[9,12]</sup> or special solvents,<sup>[5,7,13]</sup> give low yields,<sup>[5,13]</sup> or long reaction time.<sup>[13]</sup>

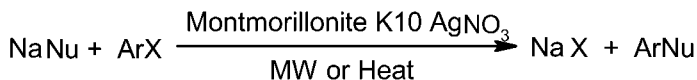
Solid-phase organic reactions have found widespread utility in organic synthesis.<sup>[14–16]</sup> A simple filtration allows the products to be recovered in these reactions.

Microwave-assisted rapid organic reactions constitute an emerging technology that makes experimentally and industrially important organic synthesis more effective and more eco-friendly than conventional reactions.<sup>[17,18]</sup> In continuation of our studies on microwave-assisted organic reactions,<sup>[17,19]</sup> we developed a very simple and convenient procedure for nucleophilic aromatic substitution reactions catalyzed by montmorillonite K10 supported  $\text{AgNO}_3$  under microwave irradiation and solvent-free condition (Sch. 1). The tendency of  $\text{Ag}^+$  cation to react with halides makes this cation a suitable candidate for these reactions, which is in accord with experimental results (Table 1).

The polarity of the reagents and the intermediates makes them good candidates for reaction in a microwave oven, and the interaction of the surface with halides and counter ion of  $\text{Ag}^+$  facilitate the reaction.

It is interesting that in spite of the previously known methods,<sup>[1–4,6]</sup> *para*- and *ortho*-nitro, aryl halides do not react in these conditions.

Although we have not experimentally established the mechanism of the reactions, according to Table 1, it seems that the attack of nucleophile does not play an important role before leaving the halide ion, and probably  $\text{Ag}^+$  cation with absorption of halide ion, makes an active intermediate from aryl halides which can react with even weak nucleophiles such as hydroxide and



*Scheme 1.*

**Table 1.** Nucleophilic substitution of aryl halides and phenyl tosylate.

Entry	Ar	X	Nu	Time		Yield (%)	
				a (hr)	b (sec)	a	b
1	Ph	Br	$^-OH$	2.0	5	68	78
2	Ph	Cl	$^-OH$	2.2	5	63	69
3	4-Methyl, phenyl	Cl	$^-CN$	2.3	8	70	63
4	Ph	Cl	$^-CN$	2.3	4	54	72
5	Ph	F	$^-CN$	1.5	6	54	77
6	4-Nitro, phenyl	Cl	$^-CN$	2.5	10	10	5
7	4-Nitro, phenyl	Cl	$^-OH$	2.5	12	10	22
8	2-Nitro, phenyl	Cl	$^-OH$	3.0	20	0	0
9	1-Naphtyl	Br	$^-OH$	2.5	9	48	73
10	2-Naphtyl	Br	$^-OH$	1.5	9	53	81
11 <sup>a</sup>	Ph	Br	( $S^{2-}$ )	1.0	5	62	71

Note: a, Thermal condition. b, Microwave irradiation.

<sup>a</sup>The yield refers to diphenyl sulfide.

benzoate anions. Therefore, the presence of a strong electron withdrawing group decreases the yield and increases the time of the reaction (entries 6–8).

In the case of  $S^{2-}$ , the product is diphenyl sulfide and thiophenol was not observed.

Using solvents in these types of reactions reduces the activity of some nucleophiles and causes the rate to drop.<sup>[7]</sup>

Elimination of solvent, simple experimental procedure and work-up, high yields, and mild conditions are the most significant aspects of this method.

## EXPERIMENTAL

Aryl halides were purchased from Fluka, Meck and Aldrich. Phenyl tosylate was prepared by treatment of phenol with tosyl chloride in acetonitrile. All products are known compounds and identified by their IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR data, and mps.

### Preparation of Supported AgNO<sub>3</sub>

To a solution of AgNO<sub>3</sub> (3.38 g in 100 mL of water), montmorillonite K10 (15 g) was added and the mixture stirred for 30 min, water was evaporated in

vacuum and the residue dried in an oven at 100°C for 1 hr to give 13.2 g of AgNO<sub>3</sub>/montmorillonite reagent.

### Reaction of Nucleophiles with Aryl Halides. General Procedure

Aryl halide (2 mmol), sodium salt of nucleophile (2–3 mmol), and 2 g of supported AgNO<sub>3</sub> were mixed thoroughly in a mortar. The reaction mixture was then irradiated in a domestic microwave oven for the indicated time, at 850 W or heated in a bath water in 96°C (Table 1). The progress of reaction was monitored by TLC using ethyl acetate/petroleum ether as eluent. The mixture was extracted first with chloroform and then with methanol, and the solvent was removed by rotary evaporation. Further purification by column chromatography and recrystallization (for solid products) gave the desired products.

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