

Cellulose sulphuric acid as a biodegradable catalyst for conversion of aryl amines into azides at room temperature under mild conditions

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Abstract. This article describes simple and efficient method for the diazotization and azidation of different aromatic amines over cellulose sulphuric acid, sodium nitrite and sodium azide under mild conditions at room temperature. Various aryl amines possessing electron-withdrawing groups or electron-donating groups have been converted into the corresponding aryl azides with 71–99% yields. The use of mild reaction conditions, avoids the use of harmful acids and toxic solvents and short reaction times are advantages of this methodology. The selected catalyst is found to be highly efficient and recyclable.

Keywords. Cellulose sulphuric acid; aryl azides; diazotization; biodegradable.

1. Introduction

Aromatic azides are useful intermediates with various applications in organic and bioorganic chemistry.¹ Two important applications of these compounds are 1,3-dipolar cycloaddition to produce five-membered heterocycles² and their use as photoaffinity labelling agents for proteins.³ Thus, the synthesis of aryl azides is of prime importance.

A number of methods have been developed to synthesis of aryl azides, for example: reaction of *p*-tosyl azide with aryl grignard or lithium reagent derived from the corresponding aryl halides,⁴ reaction of arylamine with TfN₃, CuSO₄ and triethylamin,⁵ direct coupling of arylhalides⁶ or arylboronic acids⁷ with NaN₃ catalysed by copper salts, and combination of aryl amines with *t*-BuONO followed by addition of NaN₃ or TMSN₃. Furthermore, [ArN₂][BF₄] salts immobilized in [bmim][PF₆] ionic liquid have been shown to react with TMSN₃ to yield the desired azides.⁸ Although there are specific merits to each of these methods, different kinds of drawbacks include long reaction times, highly expensive reagents and use of toxic solvents commonly required. Hence, there is still a considerable interest in developing simple methods for synthesis of arylazides that requires a low manufacturing cost while minimizing environmental pollution are preferable.

Diazonium salts are multipurpose compounds in organic chemistry. However, their poor stability limits their applications. Recently, some methods on the

stabilization of diazonium salts are reported, such as synthesis of stable arenediazonium tosylate salts using *p*-TSOH⁹ or application of resin NO₂⁻ as nitrite source.¹⁰ Zarei and co-workers reported the use of grinding of ArNH₂/SSA/NaNO₂ in a mortar for the synthesis of very stable diazonium salts.¹¹ The reason for their increased stability of these salts relative to ArN₂⁺Cl⁻ is that, decomposition of a diazonium salt is dependent on the donor properties of the conjugated anion.¹² The sulphate anions are less nucleophile than free chloride anions therefore of increasing stabilization in diazonium salt.

Considering the new trends of science and technology towards using natural materials, in addition to the environmental hazards of some current methods, the research efforts on green and eco-friendly methods have become popular and desirable. One of the newly investigated alternatives which could fit in such standards is natural biopolymers and specially cellulose which could be used as a support for sulphuric acid.¹³

2. Experimental

Chemicals were purchased from the Fluka, Merck and Aldrich chemical companies. Melting points were determined on Electrothermal 9100 without further corrections. TLC on commercial aluminum-backed plates of silica gel 60 F254 was used to monitor the progress of reactions. Infrared spectra were recorded on a Shimadzu 8400s spectrometer with KBr plates. Only representative absorptions are given. NMR spectra were

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taken in CDCl₃ on a Bruker Avance3-400 MHz instrument at 20–25°C.

2.1 Preparation and recycling of cellulose sulphuric acid

CSA was prepared according to the procedure of Ahmad Shaabani *et al.*¹⁴ The catalyst was recovered by filtration and rinsed with EtOAc and MeOH thoroughly and dried in vacuum oven at 50°C for 24 h to give recycled CSA. The diazotization-azidation of 4-amino benzoic acid was repeated with recycled catalyst. The results indicate that the catalyst was recyclable three times without any significant loss of activity.

2.2 Experimental procedure for synthesis of 4-azido benzoic acid

4-Aminobenzoic acid (2 mmol, 0.274 g) and CSA (1.5 g) were charged into a 25 mL round-bottom flask, then 0.2 mL of water was added and the mixture was magnetically stirred to afford a homogeneous mixture, subsequently NaNO₂ (4 mmol, 0.138 g) was added. The reaction mixture was stirred for 5 min. In this period of time the starting amine disappeared. The solution of NaN₃ (5 mmol, 0.326 g) in H₂O (6 ml) was added gradually to the diazonium salt and stirring was continued for 5 min. The mixture was diluted with EtOAc (10 mL) and after vigorous stirring, was filtered. The filtrate was extracted with EtOAc (3 × 10 mL) and combined organic layer was treated with 5% NaOH solution

(15 mL) (if a substrate has a carboxyl group, the reaction mixture should be acidified to pH = 1), then dried over anhyd Na₂SO₄. The solvent was evaporated *in vacuo* and the 4-azidobenzoic acid was obtained as yellow crystalline product with an yield of 99%, 0.32 g, mp 180°C. The other products were purified by flash chromatography (*n*-hexane-EtOAc, 95:5). *The most of the products were kept away from direct sunlight.*

2.3 Spectroscopic data

2.3a *Table 1, entry 1*: ¹H NMR (CDCl₃, 400 MHz) δ 8.28–8.24 (m, 1H); 7.18–7.14 (m, 1H); IR (KBr, cm⁻¹): 2129.

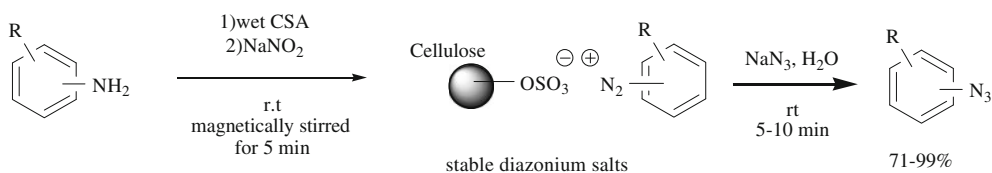
2.3b *Table 1, entry 10*: M. P. 180°C; ¹H NMR (CDCl₃, 400 MHz) δ 8.14 (d, *J* = 8.4 Hz, 1H); 7.14 (d, *J* = 8.4 Hz); ¹³CNMR (CDCl₃, 100 MHz) δ 167.92, 149.27, 132.24, 131.17, 129.02; IR (KBr, cm⁻¹): 2400–3400 as a broad band (OH), 2106 (N₃), 1681 (CO); Anal. Calcd. for C₇H₅N₃O₂: C, 51.53; H, 3.06; N, 25.76%, Found: C, 51.59; H, 3.10, N, 25.69%.

2.3c *Table 1, entry 8*: ¹H NMR (CDCl₃, 400 MHz) δ 7.5 (d, *J* = 3 Hz, 1H); 7.34 (dd, *J* = 8.4 Hz, 1 H); 7.19 (d, *J* = 8.4 Hz, 1H); ¹³CNMR (CDCl₃, 100 MHz) δ 144.1, 133.5, 133.3, 130.7, 130.2, 128.6; IR (KBr, cm⁻¹): 2113. Anal. Calcd. for C₆H₃Cl₂N₃: C, 38.29; H, 1.59; N, 22.34%, Found: C, 38.21; H, 1.64, N, 22.28%.

Table 1. Azidation of aromatic amines with wet CSA/NaNO₂/NaN₃ (solution in H₂O) at room temperature.

Entry	ArNH ₂ ^a	Product ^b	Yield (%) ^c	IR (KBr, cm ⁻¹)
1	4-NO ₂ C ₆ H ₄ NH ₂	4-NO ₂ C ₆ H ₄ N ₃	87	2129 ¹⁶
2	2-NO ₂ C ₆ H ₄ NH ₂	2-NO ₂ C ₆ H ₄ N ₃	85	2150 ¹⁶
3	4-MeC ₆ H ₄ NH ₂	4-MeC ₆ H ₄ N ₃ (oily)	82	2130; 2106 ⁶
4	4-MeOC ₆ H ₄ NH ₂	4-MeOC ₆ H ₄ N ₃ (oily)	86	2260; 2106 ⁶
5	2-MeOC ₆ H ₄ NH ₂	2-MeOC ₆ H ₄ N ₃	85	2016 ¹⁷
6	4-BrC ₆ H ₄ NH ₂	4-BrC ₆ H ₄ N ₃ (oily)	91	2249, 2291 ⁶
7	4-ClC ₆ H ₄ NH ₂	4-ClC ₆ H ₄ N ₃ (oily)	83	2133; 2096 ⁸
8	3,4-Cl ₂ C ₆ H ₃ NH ₂	3,4-Cl ₂ C ₆ H ₃ N ₃ (oily)	79	2113
9	2,4-Cl ₂ C ₆ H ₃ NH ₂	2,4-Cl ₂ C ₆ H ₃ N ₃	71	2113 ¹⁷
10	4-NH ₂ C ₆ H ₄ COOH	4-N ₃ C ₆ H ₄ COOH	99	2106
11	3-NH ₂ C ₆ H ₄ COOH	3-N ₃ C ₆ H ₄ COOH	99	2129 ⁶
12	2-NH ₂ C ₆ H ₄ COOH	2-N ₃ C ₆ H ₄ COOH	93	2106 ⁶
13	2-I C ₆ H ₄ NH ₂	2-I C ₆ H ₄ N ₃ (oily)	89	2125, 2088 ¹⁶
14	C ₆ H ₅ NH ₂	C ₆ H ₅ N ₃ (oily)	79	2101 ⁸

^aIn the all substrates the time of reactions were between 10 and 15 minutes. ^bThe products were characterized from their spectral data especially IR, ¹H NMR or mp by comparison with reported samples. ^cThe yields refer to isolated products



Scheme 1. The synthesis of arylazides under mild condition.

3. Results and discussion

As a continuation of our interest in the area of environmentally benign reactions,¹⁵ we present here the application of green catalyst and simple synthesis of aromatic azides from their corresponding amines using biodegradable and reusable catalyst: cellulose sulphuric acid (scheme 1).

In a model reaction, 4-aminobenzoic acid was homogenized by mixing by CSA and 0.2 mL of water into a round-bottom flask and magnetically stirred. Then NaNO_2 was added, the diazotization, proceeded in few minutes. The amount of water present in the reaction mixture was very important for the successful diazotization. In the absence of water, the most of arylamine was not converted to the corresponding diazonium salt even after longer reaction time. Then, the solution of NaN_3 in H_2O was added to the diazonium salt and thoroughly mixed at room temperature. The reaction proceeded smoothly and rapidly to afford 4-azidobenzoic acid in 99% yield.

Based on the above results, this process was then extended to other structurally varied amines to investigate its scope and generality. The results are presented in table 1. In contrast to the related SSA procedure,¹¹ arylamines including electron-withdrawing groups (e.g., entry 1), electron-rich groups (e.g., entry

4) as well as ortho-substituted anilines (e.g., entry 2) were found to react well to give the corresponding arylazides in high yields and no undesirable side reactions, although, the yields and the time of the reaction were dependent on the substituent (table 1). Interestingly, amino benzoic acid derivatives afforded the corresponding azides in excellent yield and did not require further purification.

Our attention was then directed toward the possibility of recycling the catalyst since the recovery and reuse of catalyst are superior for a greener process. After completion of the reaction, the catalyst was recovered as follows: the reaction mixture was extracted with ethyl acetate. The ethyl acetate layer was then dried over sodium sulphate and evaporated under reduced pressure and aromatic azides were purified by flash chromatography. The aqueous layer was filtrate to recover the cellulose sulphuric acid, which its reusability was investigated by using 4-amino benzoic acid as a model substrate. It has been observed that the recovered catalyst was reused three times consecutively with a minimum variation of the yields of the products (table 2). It was observed that with increase in the number of usage of the CSA, its activity is slightly decreased. This could probably be due to the gradual loss of the catalyst during filtration and washing.

It should be noted that the aryldiazonium salts supported on cellulose sulphuric acid were stable to be kept at room temperature and could be stored for 48 h in a desiccator without any loss of activity.

Table 2. Reuse of cellulose sulphuric acid for synthesis of 4-azido benzoic acid.^a

Entry	Use	Yield ^{b,c} (%)
1	1st	99
2	2nd	94
3	3rd	87
4	4th	81
5	5th	73

^aReaction condition: first step: 4-aminobenzoic acid (2 mmol, 0.274 g), CSA (1.5 g), 0.2 mL H_2O , NaNO_2 (4 mmol, 0.138 g); second step: NaN_3 (5 mmol, 0.326 g) in H_2O (6 ml).

^bAfter each experiment the CSA was recovered and the recovered CSA was used for the subsequent entry of reaction.

^cIsolated yield of 4-azido benzoic acid

4. Conclusions

In summary, we have established a practical and simple method for the preparation of arylazides. The procedure offers several advantages including high reaction yields, broad application scope and simple experimental process. On the other hand, the selected catalyst is biodegradable, easily available and recyclable. Therefore, the present method is expected to serve as an alternative process for the preparation of arylazide derivatives.

Supplementary information

Supplementary data associated with this article can be found in the online version at www.ias.ac.in/chemsci.

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