

## Directed efficient and rapid bromination of phenols and anilines with *N*-bromosaccharin using tungstophosphoric acid as a heterogeneous recyclable catalyst under solvent-free conditions

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**Abstract:** *N*-Bromosaccharin in the presence of tungstophosphoric acid converts phenols and anilines to the corresponding bromides in high to excellent yields at room temperature under solvent free conditions.

**Keywords:** *N*-Bromosaccharin; Tungstophosphoric acid; Phenol; Aniline; Bromination.

### Introduction

A consequence of the necessity to minimize the amount of toxic waste and by-products from chemical processes is a need for the development of new, more environmentally friendly synthetic methods in which fewer toxic substances are used [1]. Many organic solvents are ecologically harmful, and their use should therefore be minimized as far as possible or even avoided altogether.

It has been studied how molecules move quite easily and even selectively in the solid state [2]. When the molecular movements in the solid state are applied to organic reactions, selective and efficient solvent-free organic reactions can be designed [2]. These solvent-free reactions are important not only for their efficiency and simplicity, but also as green and sustainable procedures.

Halogenations have not been extensively studied under solvent-free conditions [3], while recently the important role of solvent vapor [4] in the efficiency of bromination in comparison to solvent-free conditions [5] has been reported.

Bromination of phenols and anilines belong to an important class of organic intermediates that are used as precursors of organometallic reagents in synthetic organic chemistry [6]. Brominated anilines and phenols can be used as potent, antitumor, antibacterial, antifungal, antineoplastic, antiviral, antioxidizing agents and also as industrial intermediates in the

manufacture of pharmaceuticals and agrochemicals [7]. Additional problems arise from using brominated solvents and the release of corrosive HBr as a by-product [8]. Alternative brominating reagents such as *N*-bromosuccinimide [9] and pyridinium or tetraalkylammonium tribromides [10] make for easier handling and result in improved selectivity, but are unfortunately limited by their low atom efficiency and the need to remove the reagent's residue. Also, molecular bromine is required for their preparation [11].

Saccharin has been used as a sweetening agent in food and drug industries as a cheap and easily available compound [12]. *N*-Halosaccharins are more electrophilic than their analogues such as *N*-haloamides. *N*-halosaccharin is an oxidizing [13] and halogenating agent which is often employed for the halogenation of alkenes, activated aromatic compounds, enol acetates, 1, 3-diones and *etc* [14]. NBSac is easily prepared from the readily available sodium salt of saccharin [15].

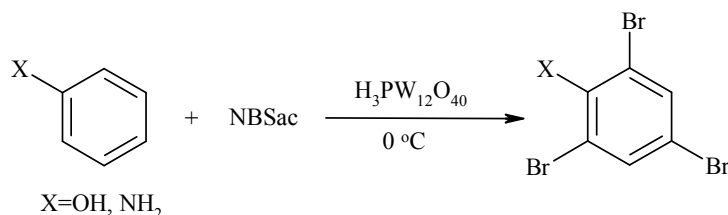
Heteropolyacids (HPAs) are solid superacids that catalyze a variety of organic transformations [16]. The Keggin structures, especially 12-tungstophosphoric acids (TPAs), exhibit high acidity and stability and have been investigated for a variety of acid-catalyzed reactions.

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Furthermore, HPA catalysis lacks side reactions, such as sulfonation and chlorination, which frequently occur with mineral acids [17]. HPAs have been reported as efficient homogeneous and/or heterogeneous catalysts for reactions such as hydration and acetoxylation of monoterpenes and camphene [18-19], Friedel-Crafts acylation and Fries rearrangement [20-22],

etherification [23-24], isomerization of alkanes [25-26] and alkenes [26-27].

Now, we wish to report efficient, operationally simple, and cost-effective procedure for the synthesis of tribromo phenol and aniline derivatives using NBSac in the presence of a catalytic amount of  $H_3PW_{12}O_{40}$  (Scheme 1).



**Scheme 1.** Bromination of phenol and aniline derivatives using NBSac catalyzed by  $H_3PW_{12}O_{40}$ .

## Experimental

*Typical procedure for the bromination of phenol with NBSac catalyzed by tungstophosphoric acid*

NBSac was prepared according to the literature procedure [15]. To a mixture of phenol (0.094 g, 1 mmol) and  $H_3PW_{12}O_{40}$  (0.0116 g, 1 mol %) under solvent-free condition at 0 °C, NBSac (0.588 g, 2 mmol) was added and the mixture was stirred. Completion of the reaction is indicated by TLC. Column chromatography of the crude mixture on silica gel using *n*-hexane:EtOAc (10:1) gave the tribromophenol (0.321 g, 95 % yield, Table 2, entry 1).

## Results and discussion

First, we tried the bromination of phenol (1 mmol) with NBSac (2 mmol) in various amounts of tungstophosphoric acid under solvent free condition. The reaction performed in the presence of 1 mol% catalyst predominantly gave tribromo phenol. As shown in Table 1, this reaction performed in longer reaction time in the absence of catalyst or lesser amounts of it.

**Table 1.** Effect of  $H_3PW_{12}O_{40}$  amounts on the synthesis of bromophenol

Entry	Catalyst (mol %)	Time (min)	Conversion%
1	–	30	80
2	0.5	15	85
3	0.75	10	90
4	1	Immediately	100

In order to show the generality and applicability of this procedure, we have treated a wide variety of phenols and anilines with NBSac in the presence of a catalytic

amount of tungstophosphoric acid at 0 °C and were obtained the desirable products in high to excellent yields (Table 2).

**Table 2.** Bromination of phenol and aniline derivatives with NBSac catalyzed by tungstophosphoric acid<sup>a</sup>

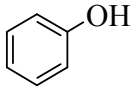
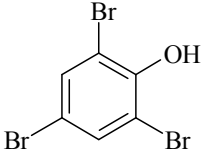
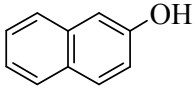
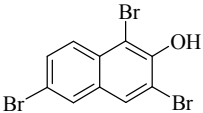
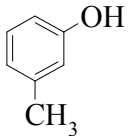
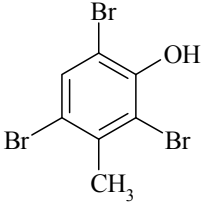
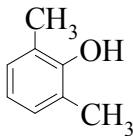
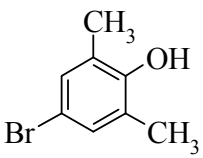
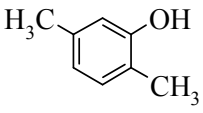
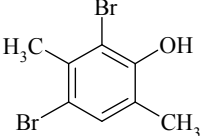
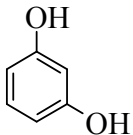
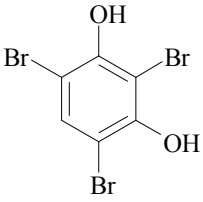
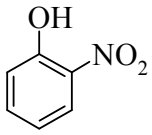
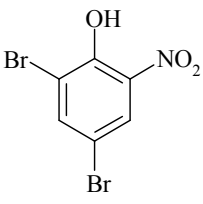
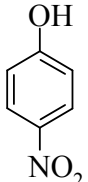
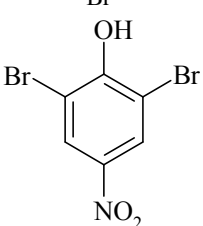
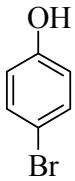
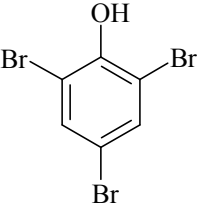
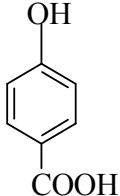
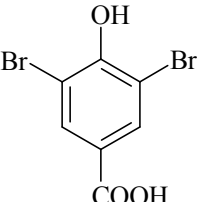
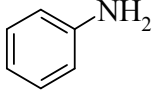
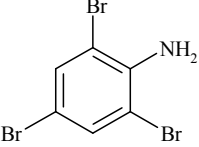
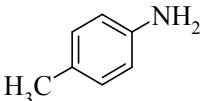
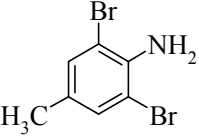
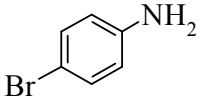
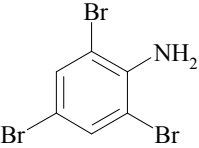
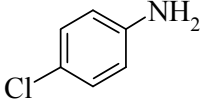
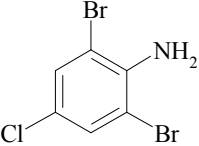
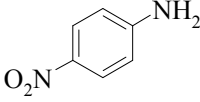
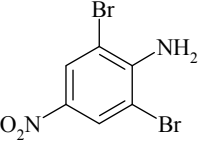
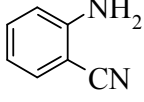
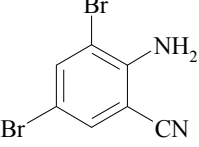
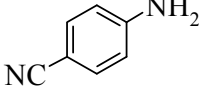
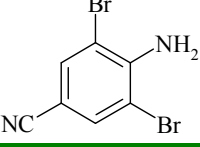
Entry	Substrate	Time (min)	Product <sup>b</sup>	Yield (%) <sup>c</sup>	Ref.
1		Immediately		95	[28]
2		Immediately		94	[29]
3		Immediately		91	[30]
4		Immediately		87	[28]
5		Immediately		90	[31]
6		Immediately		85	[32]
7		Immediately		92	[28]
8		Immediately		95	[28]

Table 1. continued

9		Immediately		94	[28]
10		Immediately		93	[33]
11		Immediately		84	[28]
12		Immediately		89	[28]
13		Immediately		97	[28]
14		Immediately		95	[34]
15		Immediately		90	[28]
16		5		93	[35]
17		3		91	[36]

<sup>a</sup>The molar ratio of phenol and aniline derivatives to NBSac was 1:2.

<sup>b</sup>All products were characterized spectroscopically (<sup>1</sup>H-NMR), and showed physical and spectral data in accordance with their expected structure and by comparison with authentic samples.

<sup>c</sup>Yields refer to isolated pure products.

On the basis of the results obtained so far, it seems that the functional groups on the aromatic ring would not affect obviously the reactivity.

In order to know whether the catalyst ( $H_3PW_{12}O_{40}$ ) would lose its catalytic activity during the reaction, we investigated the reusability of the catalyst. For this purpose we first carried out the bromination of phenol in the presence of the catalyst in the above reaction condition. After completion of the reaction, the catalyst was removed and washed with dichloromethane and subjected to a second run of the reaction process with the same substrate. The first experiment and subsequent experiments (2 runs) gave almost identical reaction times and yields. We have thus found that catalyst can be reused several times without any appreciable loss of activity, pointing to the stability and retention of catalytic capability of this useful catalyst.

### Conclusions

In conclusion, we have developed an efficient and versatile method for the bromination of phenol, aniline and their derivatives using simply prepared NBSac in the presence of tungstophosphoric acid as a heterogeneous and recyclable catalyst. The mild reaction conditions, simple experimental procedure, rapid conversion, high to excellent yields and reusability of the catalyst are notable advantages of the method. Also, Saccharin is a cheap and easily available compound for the preparation of reagent.

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