



# An Environmentally Route for Synthesis of Triarylmethanes Catalyzed by Heteropolyphosphotungstic Acid in Water

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## Abstract

An efficient and environmentally benign procedure for synthesis of triarylmethanes is developed via condensation of aromatic aldehydes and *N,N*-dimethylaniline using small quantity of heteropolyphosphotungstic acid (HPW) as catalyst in water. Good functional group tolerance, simple green experimental procedure, and good to excellent yields of products are the most advantages of this work.

**Keywords:** *Baeyer condensation, Triarylmethanes, Aldehyde, Dimethylaniline, Heteropolyphosphotungstic acid (HPW).*

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## Introduction

Organic reactions in water have attracted considerable attention in recent years due to their potential of great economic rewards and green benefits [1-2]. In this context, much attention has been focused on Lewis acid or solid acid catalyzed organic reactions in water. Heteropoly acids (HPAs) are used as homogeneous and heterogeneous acid due to their strong acidity, selectivity and safety in handling in comparison to conventional mineral acids [3-6]. Heteropolyphosphotungstic acid (HPW), the strongest HPA in the Keggin-

series, have been used as efficient catalyst in several reactions such as esterification, etherification, Friedel-Crafts alkylation and acylation, isomerisation, hydrolysis, Michael addition, protection of carbonyl compounds and alcohols, oxidation, and etc. [7-10]. Recently, we have shown that HPW is an efficient catalyst for Michael-type Friedel-Crafts alkylation of *N,N*-dialkylanilines with nitroalkenes in water [11].

The acid-catalyzed Friedel-Crafts alkylation of arenes with aromatic aldehydes has been known since 1886 [12]. In this context, synthesis

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of diaminotriphenylmethanes (DTMs) has received considerable attention due to their wide applications in biological and analytical fields [13-14]. These compounds are used as dyes for detection of hydrogen peroxide in medical diagnostic kits and biotechnology process control [15]. Also, they are used in medicinal chemistry as antifungal [16], anti-tubercular [17], anti-infective, and anti-microbial agents [18]. Due to the importance of DTM compounds, several reviews have emerged on di- and triphenylmethane derivatives [18-19]. Furthermore, DTMs are useful precursors for the preparation of printing inks, coloration of ceramics, drugs and leather, and dyeing of fibers [20-21].

One of the most applied procedures for the synthesis of triarylmethanes is the Baeyer condensation, which involves the direct reaction of aryl aldehydes with *N,N*-dialkylanilines in the presence of a catalyst. Recently, several novel homogeneous and heterogeneous catalytic systems were developed for this transformation [22-25]. It is notable that the main drawbacks of the reported works are using a toxic catalyst or an organic solvent. Therefore, there is a need for the alternative procedures to overcome the drawbacks of the current works and address the goals of green chemistry.

## Experimental

### *Reagents and equipments*

All reactions were carried out in an atmosphere

of air. All chemicals and solvents except water (tap water) were purchased from Merck or Fluka and used as received. All reactions were monitored by TLC on silica gel 60 F254 (0.25 mm), visualization being effected with UV. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker AMX 300-MHz spectrometer in  $\text{CDCl}_3$  with TMS as internal standard. Melting points were determined with a Branstead-Electrothermal 9200 apparatus and are uncorrected. Elemental analyses were conducted with a Perkin-Elmer 2004 (II) CHN analyzer.

### *Synthesis of 4,4'-dimethylaminotriarylmethane derivatives; A general procedure*

In a test tube equipped with a magnetic stirrer bar, benzaldehyde (2 mmol), *N,N*-dimethylaniline (4.5 mmol), and water (5 mL) were added. To this mixture, HPW (80 mg, 0.0278 mmol, 0.0139 mol %) was added and stirred at reflux temperature for overnight. After completion, the mixture was cooled to room temperature and the product was collected by filtration or extraction with ethyl acetate ( $2 \times 10$  mL, in the case of oily products). Purification was accomplished by crystallization in ethanol or using column chromatography [silica gel and petroleum ether–ethyl acetate (4:1)].

### *Characterization data for unknown products:*

4-((4-(dimethylamino)phenyl)(3-methoxy-

phenyl)methyl)-*N,N*-dimethylbenzenamine (Table 1, entry 6). Yield: 0.504 g (70%); mp 112-114 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ (ppm) 2.92 (12H, s, 4CH<sub>3</sub>), 3.75 (3H, s, -OCH<sub>3</sub>), 5.36 (1H, s, CH), 6.67-6.76 (7H, m), 6.99 (4H, d, *J* = 8.7 Hz), 7.19 (1H, m); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ (ppm) 40.7, 55.0 (2C), 110.9, 112.5, 115.3, 121.9, 128.9, 129.9, 132.7, 147.1, 148.9, 159.4; Anal. Calcd. (%) for C<sub>22</sub>H<sub>28</sub>N<sub>2</sub>O: C, 79.96; H, 7.83; N, 7.77; Found: C, 80.08; H, 7.87; N, 7.81.

4-((4-(dimethylamino)phenyl)(5-methylfuran-2-yl)methyl)-*N,N*-dimethylbenzenamine (Table 1, entry 10). Yield: 0.4 g (60%) mp 109-111 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ (ppm) 2.24 (3H, s, CH<sub>3</sub>), 2.91 (12H, s, 4CH<sub>3</sub>), 5.22 (1H, s, CH), 5.72 (1H, d, *J* = 2.9 Hz), 5.84 (1H, d, *J* = 2.8 Hz), 6.67 (4H, d, *J* = 8.7 Hz), 7.03 (4H, d, *J* = 8.7 Hz); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ (ppm) 13.7, 40.7, 49.0, 105.7, 108.3, 112.6, 129.2, 130.9, 149.2, 150.9, 156.4; Anal. Calcd. (%) for C<sub>22</sub>H<sub>26</sub>N<sub>2</sub>O: C, 79.00; H, 7.84; N, 8.38; Found: C, 78.80; H, 7.68; N, 8.26.

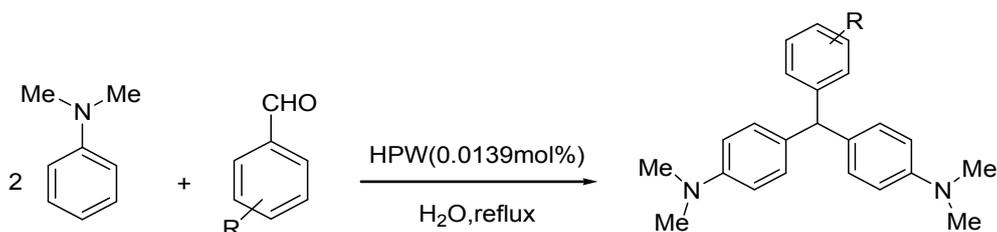
4-((4-(bis(4-(dimethylamino)phenyl)methyl)phenyl)(4-(dimethylamino)phenyl)methyl)-*N,N*-dimethylbenzenamine (Table 1, entry 15). Yield 0.757 g (65%); mp 249-250 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ (ppm) 2.92 (24H, s, 8CH<sub>3</sub>), 5.34 (2H, s, CH), 6.66 (8H, d, *J* = 8.6 Hz), 6.98 (8H, d, *J* = 8.6 Hz), 6.97 (4H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ (ppm) 40.7, 54.6,

112.5, 128.9, 129.9, 133.1, 142.6, 148.8; Anal. Calcd. (%) for C<sub>40</sub>H<sub>46</sub>N<sub>4</sub>: C, 82.43; H, 7.96; N, 9.61; Found: C, 81.95; H, 8.05; N, 9.50.

3-(bis(4-(dimethylamino)phenyl)methyl)-4H-chromen-4-one (Table 1, entry 16). Yield 0.636 g (80%); mp 140-141 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ (ppm) 2.91 (12H, s), 4.82 (1H, s), 5.33 (1H, s), 6.54 (1H, s), 6.62-6.74 (6H, m), 6.97 (4H, d, *J* = 8.6 Hz), 7.13 (1H, t, *J* = 7.8 Hz); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ (ppm) 40.8, 54.7, 112.6, 112.7, 116.2, 121.9 (2C), 129.2, 129.9 (2C), 132.6, 147.3, 148.9, 155.3, 203.2. Anal. Calcd. (%) for C<sub>26</sub>H<sub>26</sub>N<sub>2</sub>O<sub>2</sub>: C, 78.36; H, 6.58; N, 7.03; Found: C, 78.30; H, 6.45; N, 6.78.

## Results and discussion

The request for cheap and environmentally friendly catalysts and mild reaction conditions is still a major challenge in synthetic organic chemistry. To the best of our knowledge, there is not any report on the synthesis of DTMs in water. For this purpose, in continuation of our attempts to use water as solvent or catalyst for organic transformations [26], here we wish to describe an efficient and environmentally benign procedure for the synthesis of DTM derivatives in aqueous medium using small amount of HPW as catalyst as outlined in Scheme 1.



**Scheme 1.** HPW promoted synthesis of 4,4'-diaminotriarylmethanes in water.

We initially examined the Baeyer condensation of *N,N*-dimethylaniline with benzaldehyde in refluxing water without using any catalyst. We have found that only a trace amount of product was obtained. In continuation, we have focused our attempt to improve the reaction yield in water. Encouraged by the work of Saidi *et al.* [8-10] on using heteropoly acids in water as efficient homogenous catalyst, and our experience on using HPW for Friedel-Crafts alkylation of *N,N*-dialkylanilines with nitroalkenes in water, we have found that by using a small quantity of heteropolyphosphotungstic acid in water at reflux temperature, good to excellent yield of product was obtained. Lower yield was obtained when the reaction was carried out at lower temperatures. Also, performing the reaction in organic solvents or solvent-free condition gave lower yield compare to water.

With optimized conditions in hand, the generality of the reaction was investigated using different aromatic aldehydes (Table 1). The results show that electron-donating and electron-withdrawing groups on the phenyl ring of aldehydes in various positions (*o*, *m*, *p*) do not have significant effect on the yield of reaction. Highly electron-rich aldehydes such as 2,4-dimethoxybenzaldehyde and *N,N*-dimethyl-4-aminobenzaldehyde gave 85 and 70% yield respectively. (entries 8 and 14) Heterocyclic aldehydes such as furfural, 5-methylfurfural and thiophene 2-carbaldehyde were successfully used in this reaction to give the corresponding diaryl heteroaryl methanes (entries 9, 10 and 11) with potent biological activity as antibacterial and antitumor activities [27]. Terephthalaldehyde gave the corresponding *bis* adduct in 65% yield. (entry 15).

**Table 1.** Diversity in the synthesis of diaminotriarylmethanes.

Entry	Aldehyde	Product	Yield(%) <sup>a,b</sup>	mp (°C) (Reported)	Entry	Aldehyde	Product	Yield(%) <sup>a,b</sup>	mp (°C) (reported)
1			80	100-101 (97-99) <sup>22-23</sup>	9			62	87-89 (89-90) <sup>24</sup>
2			85	150-151 (152-153) <sup>25</sup>	10			60	109-111
3			81	151-152 (152-154) <sup>24</sup>	11			50	93-94 (92-93) <sup>24</sup>
4			90	165-167 (169-171) <sup>25</sup>	12			80	91-93 (95-96) <sup>25</sup>
5			88	144-146 (142-144) <sup>22-23</sup>	13			75	98-100 (99-100) <sup>25</sup>
6			70	112-114	14			70	165-167 (167-168) <sup>25</sup>
7			80	103-105 (101-103) <sup>22-23</sup>	15			65	249-250
8			85	142-145 (147-149) <sup>24</sup>	16			80	140-141

<sup>a</sup>Isolated yield. <sup>b</sup> Reaction condition: *N,N*-dimethylaniline (4.5 mmol), aldehyde (2 mmol), water (5 mL) and HPW (80 mg, 0.0278 mmol, 0.0139 mol%) at reflux temperature.

In addition, 3-formylchromone gave high yield of products (entry 16). Using 1,2-dimethoxy benzene as electron-rich arene did not

afford any products and the starting materials were recovered. Aliphatic aldehydes are not suitable starting materials for this reaction.

Work-up procedure for this reaction was very simple; involving filtration of the solid products or decanting the water in most of the cases. Further purification was accomplished by crystallization in ethanol or using column chromatography. Structures of the products were confirmed by  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and CHN analysis. The  $^1\text{H}$  NMR spectra of the products showed a characteristic singlet signal between 5.00-5.50 ppm for the aliphatic CH resonance in the products. The carbon of this group was observed between 49.0-56 ppm in  $^{13}\text{C}$  NMR spectra.

This procedure provide a simple route for synthesis of the well-known Leucomalachite Green (entry 1, Table 1) and Crystal Violet (entry 14, Table 1) and many other industrial dyes which are some of the oldest synthetic dyes.

### Conclusion

In conclusion, we have developed an efficient, mild and environmentally benign procedure for the synthesis of diamino-triarylmethanes catalyzed by heteropolyphosphotungstic acid in water via a Baeyer condensation of substituted aryl aldehydes and *N,N*-dimethylaniline under reflux condition. This work is devoted to extend the scope of the available leuco based of diamino-triphenylmethane dyes, and to describe the application of a new green catalyst in their synthesis. Also, other advantages of this work include using green and low-loading

catalyst, green solvent, simple work-up and high to excellent yield of products. In addition, water may play dual roles as a solvent or as a co-catalyst to provide a homogenous medium for HPW with highly acidic strength.

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