

## Synthesis of 4', 4''-Dihydroxytriphenylmethane derivatives using Montmorillonite K10 clay

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**Abstract:** An efficient and very simple method for the synthesis of 4', 4''-dihydroxy triphenylmethane and its derivatives has been achieved *via* condensation reaction of various substituted aromatic aldehydes containing both electron donating and electron withdrawing groups with phenol in the presence of montmorillonite K10 clay. The reaction proceeds with shorter reaction time and higher yield compared to the other conventional acid catalysts reported in the literature. The one pot reaction, simple workup, high yields, use of efficient, ecofriendly, inexpensive stable catalyst are the advantages of the proposed method.

**Keywords:** Montmorillonite, Condensation, Dihydroxytriphenyl methane.

### INTRODUCTION

4', 4''-Dihydroxytriphenylmethane derivatives have attracted considerable attention due to their various biological activities such as antitumor, antitubercular, antifungal, antioxidant activity<sup>1,2</sup> anticancer activity<sup>3</sup> antiviral<sup>4</sup>, inhibition activity for histidine protein kinases<sup>5</sup> and anti-inflammatory agents. Moreover, these classes of compounds have found widespread application in the chemical industry (Figure 1) as leuco dyes, phytochromic agents<sup>6</sup>, suitable building blocks for generating dendrimers, and substrates for theoretical and biological studies.

Numerous methods of construction of triphenylmethanes have been developed. Most of the methods are multistep or require harsh reaction conditions. As a result, there still exists a need for the development of new methods for the synthesis of triphenylmethane derivatives.

All the methods known in the literature for the synthesis of triphenylmethanes are protic acid catalysed<sup>7-10</sup> and the catalysts have to be used in higher concentration and in large excess. These catalysts entail problems of corrosion, workup and cause effluent pollution. We have synthesized the 4', 4''-dihydroxytriphenylmethane derivatives using montmorillonite K10 clay which offer several advantages over classical acids.

We have established the generality of the condensation reaction of pyridine-2-aldehyde with phenol by use of Montmorillonite K10 clay as a catalyst to prepare bisacodyl<sup>11</sup> (Scheme 1). We have further generalized the reaction by carrying out condensation on various aromatic aldehydes substituted at ortho, meta and para positions to give the corresponding triphenyl methanes. The strong acidity, non-corrosive properties, cheapness, mild reaction conditions, high yields and the ease of setting and working-up the reaction make an excellent method for the preparation of triphenylmethanes.

Herein, we report an efficient and convenient procedure for the synthesis of dihydroxytriphenylmethane derivatives in the presence of K10 clay as catalyst.

## EXPERIMENTAL

All chemicals were purchased from Sigma-Aldrich and employed without further purification. The identity of triphenylmethane products was confirmed by <sup>1</sup>H NMR, mass, IR spectra. The <sup>1</sup>H NMR spectra were recorded on Varian Mercury 300 MHz using DMSO-d<sub>6</sub> and tetramethylsilane (TMS) as solvent and internal standard, respectively. Fourier transform Infrared spectra were recorded in KBr disc on Shimadzu 8300 spectrophotometer. All melting points were recorded using open capillary tube and uncorrected. Thin layer chromatography was performed on silica gel as a stationary phase, hexane and ethyl acetate as eluent.

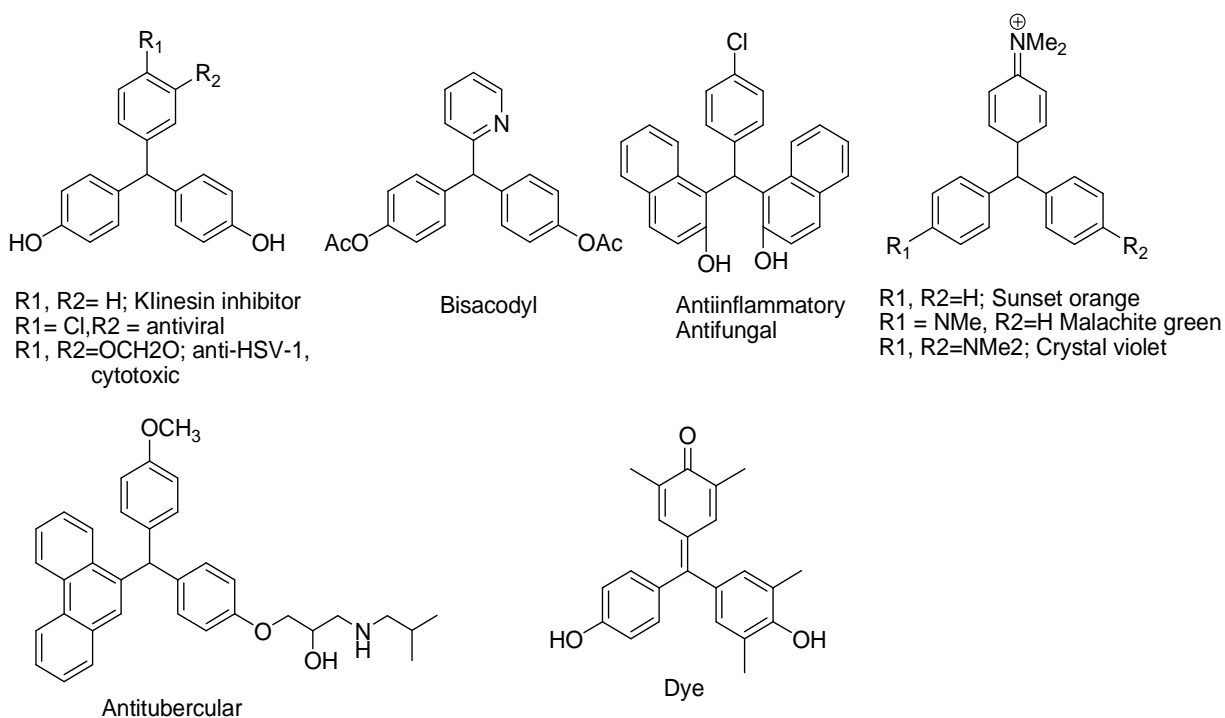
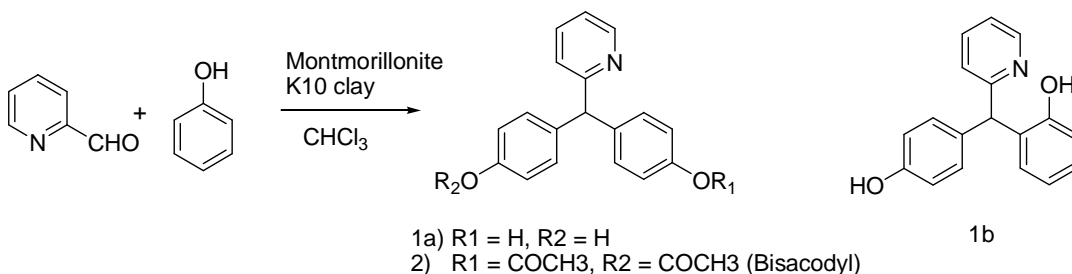
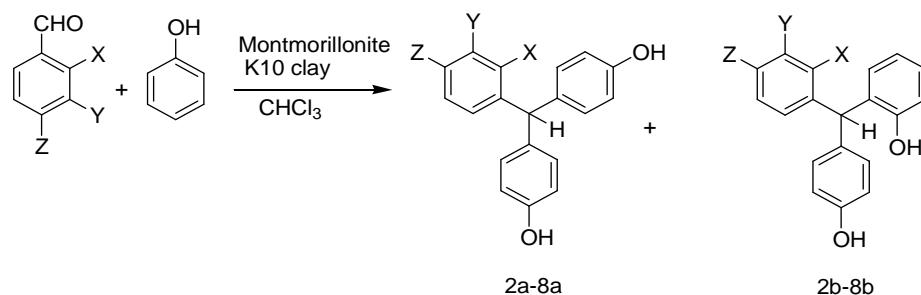


Figure 1

### Scheme 1:



**Scheme 2:**

2 = X, Y = H, Z = F

3 = X, Y = H, Z = Me

4 = X = Cl, Y, Z = H

5 = X = H, Y = Cl, Z = H

6 = X, Y = H, Z = OCH<sub>3</sub>

7 = X = Cl, Y = H, Z = Cl

8 = X, Y = H, Z = NO<sub>2</sub>

**Typical Procedure for Synthesis of 4', 4''-Dihydroxydiphenyl (2-pyridyl) methane (1a):**

To a solution of pyridine-2-carbaldehyde (1 g, 9.3 mmol) and phenol (1.75 g, 18.69 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added clay (0.1 g) and heated to reflux. After completion of the reaction, the reaction mixture was filtered and washed with water, dried and concentrated to yield a syrup which was chromatographed [SiO<sub>2</sub> 60-120 mesh, hexane:ethylacetate) (3:7)] to obtain 4',4''-dihydroxydiphenyl (2-pyridyl) methane **1a** in 65.4% yield and 2',4''-dihydroxydiphenyl (2-pyridyl) methane **1b** as white solid in 18.5% yield. <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ 5.40 (s, 1H, Ph<sub>3</sub>C-H), 6.60 (d, 4H, *J* = 10.0 Hz, H-3',5',3'',5''), 6.92 (d, 4H, *J* = 10.0 Hz, H-2',6',2'',6''), 7.15-7.28 (m, 2H, H-3,5), 7.72, (t, 1H, H-4), 8.42 (d, 1H, *J*<sub>5,6</sub> = 8.0 Hz, H-6), 9.32 (brs, -OH). EIMS: *m/z* 277 (M<sup>+</sup>). IR. (KBr): ν<sub>max</sub> 763, 825 & 3086 cm<sup>-1</sup>.

**RESULTS AND DISCUSSION**

During the first part of the study, we have planned the condensation reaction of pyridine-2-carbaldehyde **1**. The compound **1a** was characterized from the <sup>1</sup>H NMR by the appearance of two AB type doublets at δ 6.60 and 6.92 and the methine hydrogen at δ 5.28 as a singlet. Appearance of *m/z* at 295 in the mass spectrum was also in agreement with structure. IR spectrum showed absorption at 825 cm<sup>-1</sup> and 3086 cm<sup>-1</sup> indicating presence para substituted benzene and the hydroxyl group.

Compound **1b** showed complex aromatic signals and the methine hydrogen appeared at δ 5.40 (1H). We have continued our studies on several other aromatic aldehydes bearing halogen substituents at *ortho* and *para* position eg. 2-chloro benzaldehyde **4**, 4-nitrobenzaldehyde **8**, 3-chloro benzaldehyde **5**, 2, 4-dichloro benzaldehyde **7**, and aldehydes bearing electron donating substituents eg. 4-methyl benzaldehyde **3** and 4-methoxy benzaldehyde **6**.

It was observed that these reactions resulted in the formation of the 4', 4'' – linked product as a major product and the 2', 4''-linked product was obtained as the minor product, except in the case of 2', 4''-dichloro benzaldehyde which gave only the 4', 4'' – linked product

**Characterisation of 4', 4'' and 2', 4''-products:**

<sup>1</sup>H NMR spectrum of the 4',4''-substituted product showed two AB type doublets while the 2',4''-substituted product showed a complex aromatic pattern and the methine hydrogen appeared comparatively down field in the case of 2', 4'' – product. IR spectrum showed an absorption at 825 cm<sup>-1</sup> indicating a para substitution in case of 4',4'' -linked product and the 2',4''-linked product showed an absorption at 755 cm<sup>-1</sup>.

In conclusion we have demonstrated an easy and efficient procedure for the preparation of triphenylmethane.

**Table 1: Synthesis of Triphenyl methanes (2a-8a)**

Entry	Aldehyde	Product	m.p. % yield		Product	m.p. % yield	
i.	2	1a	150	56.5	1b	Syrup	18.5
ii.	3	2a	140	44.5	2b	Syrup	22.5
iii.	4	3a	162	57.7	3b	Syrup	20.2
iv.	5	4a	160	47.8	4b	Syrup	25.1
v.	6	5a	125	52.5	5b	Syrup	15.5
vi.	7	6a	164	56.9	6b	-	-
vii.	8	7a	210	57.5	7b	Syrup	8.5

**Table 2: Spectral data of 4',4''-substituted product (2a-8a)**

Compd No	IR (KBr) $\nu(\text{cm}^{-1})$	$^1\text{H NMR}$ (DMSO- $d_6$ ) $\delta$ in ppm
2a	820 & 3319 $\text{cm}^{-1}$ .	$^1\text{H NMR}$ (200MHz, $\text{CDCl}_3 + \text{DMSO}$ ) $\delta$ 5.28 (s, 1H, $\text{Ph}_3\text{C-H}$ ), 6.71 (d, 4H, 2', 6', 2'', 6''), 6.85 (d, 4H, H-3', 5', 3'', 5''), 7.02-7.15 (m, 4H, H-2, 3, 6, 5), 8.60 (s, 1H, -OH).
3a	817 & 3330 $\text{cm}^{-1}$ .	$\delta$ 5.25 (s, 1H, $\text{Ph}_3\text{C-H}$ ), 6.62 (d, 4H, H-2', 6', 2'', 6''), 6.85 (d, 4H, H-3', 5', 3'', 5''), 6.85-7.30 (m, 4H, H-2, 3, 5, 6), 8.62 (s, 1H, -OH).
4a	825 & 3320 $\text{cm}^{-1}$ .	5.65 (s, 1H, $\text{Ph}_3\text{C-H}$ ), 6.64 (d, 4H, 2', 6', 2'', 6''), 6.81 (d, 4H, H-3', 5', 3'', 5''), 6.90-7.38 (m, 4H, H-3, 4, 5, 6), 8.58 (brs, 1H, OH).
5a	825, 3309 $\text{cm}^{-1}$ .	5.28 (s, 1H, $\text{Ph}_3\text{C-H}$ ), 6.62 (d, 4H, H-2', 6', 2'', 6''), 6.82 (d, 4H, H-3', 5', 3'', 5''), 6.90-7.22 (m, 4H, H-2, 4, 5, 6), 8.72 (brs, 1H, OH).
6a	827, 1220, 3330 $\text{cm}^{-1}$ .	3.72 (s, 1H, OMe), 5.25 (s, 1H, $\text{Ph}_3\text{C-H}$ ), 6.62-7.20 (m, 12H, Ar-H), 8.45 (brs, 1H, -OH)
7a	820 & 3350 $\text{cm}^{-1}$ .	5.62 (s, 1H, $\text{Ph}_3\text{C-H}$ ), 6.65 (d, 4H, H-3', 5', 3'', 5''), 6.82 (d, 4H, H-2', 6', 2'', 6''), 6.92 (d, 1H, H-6), 7.38 (d, 1H, H-5), 7.56 (d, 1H, H-3), 9.18 (brs, 1H, -OH).
8a	815 & 3340 $\text{cm}^{-1}$ .	5.40 (s, 1H, $\text{Ph}_3\text{C-H}$ ), 6.71 (d, 4H, H-2', 6', 2'', 6''), 6.85 (d, 4H, H-3', 5', 3'', 5''), 7.25 (d, 2H, H-2, 6), 8.10 (d, 2H, H-3, 5), 9.08 (brs, -OH).

## CONCLUSIONS

In this study, we have described an effective and very simple method for preparation of dihydroxy triphenylmethane derivatives using K10 clay. The one-pot reaction, simple work up, high yields, use of efficient and eco-friendly reagent with no special handling techniques are the notable advantages of the proposed method.

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