

Clean synthesis of 1,8-dioxo-dodecahydroxanthene derivatives catalyzed by polyaniline-*p*-toluenesulfonate salt in aqueous media

Amalraj John, Palamari Jaya Prakash Yadav, Srinivasan Palaniappan*

Organic Coatings and Polymers Division, Indian Institute of Chemical Technology, Hyderabad, India

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Abstract

An efficient and straightforward procedure for the synthesis of 1,8-dioxo-dodecahydroxanthene was achieved through one-pot condensation of arylaldehyde and 1,3-cyclohexanedione in the presence of polyaniline-*p*-toluenesulfonate salt as polymeric solid acid catalyst. For the first time it is demonstrated that polyaniline salt could be used as catalyst in aqueous medium also. This method provides several advantages such as easy synthesis, simple work up, versatility, reusability.

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1. Introduction

Xanthenes and benzoxanthenes are important classes of compounds that find use as dyes, fluorescent materials for visualization of bio-molecules and laser technologies due to their useful spectroscopic properties [1]. Xanthene-based compounds have also been investigated for agricultural bactericide activity [2], photodynamic therapy [3], anti-inflammatory effect [4] and antiviral activity [5]. Various literatures are available to synthesis xanthenes including palladium catalyzed cyclization of polycyclic aryltriflate esters [6], intramolecular trapping of benzynes by phenols [7] and reaction of aryloxymagnesium halides with triethylorthoformate [8]. However, these methodologies suffer from one or more disadvantages such as low yield, lack of easy availability or preparation of the starting materials, prolonged reaction time (16 h to 5 days), use of toxic organic solvents, requirement of excess of reagents or catalysts, special apparatus and harsh reaction conditions. Recently, synthesis of xanthene was reported by Tong-Shou Jin et al. using *p*-dodecylbenzenesulfonic acid in aqueous media and Khosropour et al. reported synthesis of benzoxanthene using *p*-toluenesulfonic acid in organic solvent [9].

Acid catalysts are often being used in organic syntheses and industrial processes. For example, sulfuric acid, fluorohydric acids are used in alkylation, esterification, hydrolysis reactions, etc. [10]. However, these acid catalysts are toxic, corrosive and in addition, are hard to remove from the reaction medium. The environmental care is one of the worldwide increasing problems. The replacement of environmental hazardous catalysts existing processes, by the use of solid acid catalysts such as zeolites, alumina, resins, etc., is one of the innovative trends. Each catalyst has its own advantages and disadvantages. It is always interesting to develop a new environmental benign catalyst for organic transformations.

Polyaniline supported metal catalysts in organic syntheses are reported in literature [11]. Recently, we have reported several organic transformations using polyaniline salts as polymer-based solid acid catalyst in organic solvents [12]. In this report, we are demonstrating the use of PANI-PTSA salt as polymeric solid acid catalyst in aqueous medium for the first time. Synthesis of 1,8-dioxo-dodecahydroxanthene was achieved using polyaniline salt catalyst.

2. Experimental

2.1. Materials

Aniline (reagent grade) from E. Merck was distilled prior to use. Reagent grade *p*-toluenesulfonic acid, sodium persul-

* Corresponding author. Tel.: +91 40 27160124x2474;

fax: +91 40 27193991/60757.

E-mail addresses: palani74@rediffmail.com, palaniappan@iict.res.in (S. Palaniappan).

fate and aldehydes were purchased from BDH, India, 1,3-cyclohexanedione and aldehydes were purchased from Fluka and used without further purification. Solvents were distilled by reported procedure prior to use.

2.2. Preparation of polyaniline-*p*-toluenesulfonate salt catalyst

Polyaniline-*p*-toluenesulfonate (PANI-PTSA) salt was synthesized by chemical oxidative method using sodium persulfate as oxidizing agent by our earlier reported procedure [13a,b].

2.2.1. Preparation of polyaniline salt

In a typical reaction, 1.0 ml of aniline, 2.1 g of *p*-toluene sulfonic acid and 75 ml of distilled water were taken in 250 ml round bottomed flask. The solution was kept under constant stirring at ambient temperature. To the above reaction mass, solution of 2.6 g of sodium persulfate in 35 ml water was added drop wise for 15–20 min. The reaction mass was maintained under constant stirring at ambient temperature for 4 h. The precipitated polyaniline was recovered from the polymerization vessel by filtration and then washed with distilled water until the washing liquid was colorless. In order to remove oligomers and other organic by products, the precipitate was washed with acetone until the acetone was colorless and subsequently dried at 100 °C till a constant mass.

2.2.2. Preparation of polyaniline base

Polyaniline salt was dedoped by aqueous sodium hydroxide solution. Polyaniline salt (1.0 g) was stirred in 100 ml of 1.0 N sodium hydroxide solution for 12 h at ambient temperature. The solution was filtered, washed with sodium hydroxide (1.0 N) solution followed by distilled water and finally with acetone. The sample was dried at 100 °C till a constant weight was reached.

2.2.3. Preparation of redoped polyaniline salt from polyaniline base

Polyaniline base (1.0 g) was stirred with 3.8 g (0.2 M) of *p*-toluene sulfonic acid solution in 100 ml of dry acetone for 12 h at ambient temperature. The reaction mixture was filtered, washed with ample amount of acetone. The sample was dried at 100 °C till a constant weight was reached.

2.3. Synthesis of 1,8-dioxo-dodecahydroxanthene

In a typical reaction, 250 mg 4-methylbenzaldehyde, 513 mg 1,3-cyclohexanedione and 20 ml of distilled water were taken in a 50 ml round bottomed flask, which was arranged in reflux mode. To the above reaction mixture 62.5 mg of polyaniline-*p*-toluene sulfonate was added (25 wt.% with respect to aldehyde). The reaction mass was maintained under constant stirring at reflux condition for 6 h. Then the reaction mass was allowed to cool to room temperature, 20 ml of dichloromethane was added and catalyst was separated by simple filtration. The filtrate was collected, organic layer was separated and the solvent was distilled of completely under vacuum. The crude product

was isolated and recrystallized from ethanol. The products were authenticated by NMR and melting point.

2.4. Characterization

2.4.1. Resistance measurement

Polyaniline sample was pressed into disk of 16 mm diameter and ca. 2-mm thickness under a pressure of 400 MPa. Resistance measurement of the pellet was carried out on a four probe connected to a digital multimeter (Keithley model –2010). Resistance was calculated based on the average of at least three pairs of consistent readings at different points on the pressed pellet (total error involved is <1%).

2.4.2. Infrared spectrum

The polyaniline sample was mixed with KBr powder and compressed into pellet, wherein; the polyaniline powder was evenly dispersed. Fourier transform infrared spectrum was recorded using GC-FTIR spectrometer (Model 670 Nicolet Nexus, USA spectra).

2.4.3. NMR

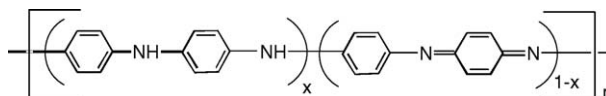
The NMR spectra for the products were recorded using Gemini-Varion 200 MHz equipment with CDCl₃ as solvent and TMS as internal reference.

2.4.4. Melting point

Melting point of 1,8-dioxo-dodecahydroxanthene compounds were checked in Shital Scientific Industries, India melting point apparatus.

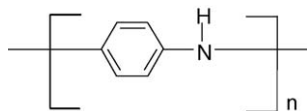
3. Results and discussion

Polyanilines are particularly attractive based on their easy preparation, excellent electrical properties, number of intrinsic redox states, possible processability and stability. The structure of polyaniline (PANI) is known as a *para*-linked phenylene amineimine. The base form of polyaniline can, in principle, be described by the following general formula:

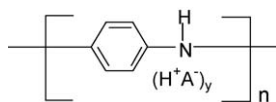


In the generalized base form $(1-x)$ measures the fraction of oxidized units. When $(1-x)=0$, the polymer has no such oxidized groups and is commonly known as a leucoemeraldine base. The fully oxidized form, $(1-x)=1$ is referred to as a pernigraniline base. The half-oxidized polymer, where the number of reduced units and oxidized units are equal, i.e. $(1-x)=0.5$, is of special importance and is termed as the emeraldine oxidation state or the emeraldine base. Partially oxidized emeraldine base is shown to be an alternating copolymer of reduced and oxidized repeat units. The value of x varies from 0 to 1, but the percentage of carbon, hydrogen and nitrogen will be almost the same. Taking these points into consideration, the following formula of polyaniline base and polyaniline salt is considered for simplicity.

Polyaniline base:



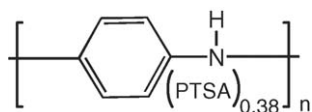
Polyaniline salt:



where H^+A^- is the acid group and y is the number of acid group per aniline unit.

3.1. Physical properties of PANI-PTSA salt

Amount of acid group present in the polyaniline chain was calculated based on the weight of redoped polyaniline salt obtained and weight of polyaniline base used. The amount of dopant was found as 43.5 wt.%, which corresponds to 0.38 dopant per aniline unit.



Yield of polyaniline was found to be 91.4% with respect to aniline used in the reaction or 51.4% based on PANI-PTSA formula. Conductivity of PANI-PTSA was found to be 1.0×10^{-2} S/cm. In our earlier report [13a], similar results were obtained for PANI-PTSA prepared from polyaniline base (polyaniline base was prepared from polyaniline-sulfate salt).

3.2. Infrared spectrum

Infrared spectrum of redoped PANI-PTSA salt is shown in Fig. 1. The spectrum shows the following five major vibration bands: 1585, 1480, 1300, 1115 and 805 cm^{-1} . These values are similar to the previously reported infrared spectrum for polyaniline salts [12a,b]. A broad band at 3440 cm^{-1} assigned to the free N–H stretching vibration. The bands at 2920 and 2850 cm^{-1} are assigned to vibration associated with NH part in $C_6H_4NH_2C_6H_4$ group or sum frequency. The ring stretching of

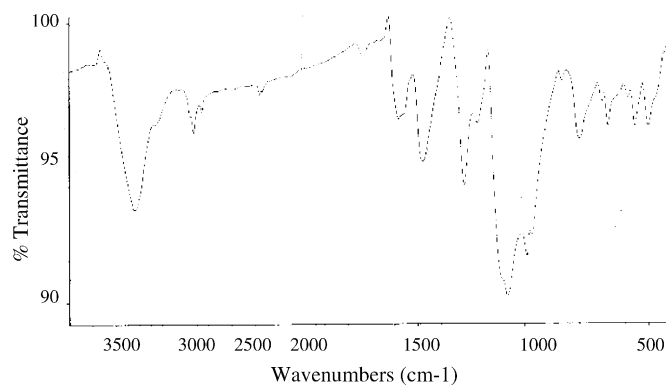


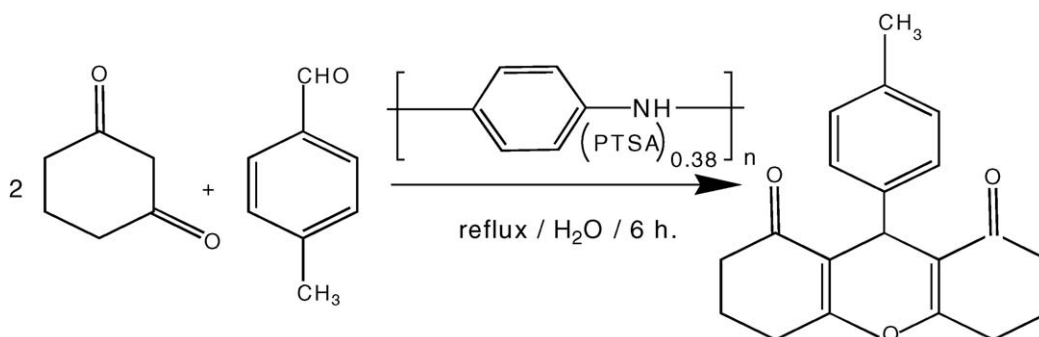
Fig. 1. Infrared spectrum of redoped PANI-PTSA salt.

quinoid and benzenoid form is observed at 1585 and 1480 cm^{-1} , respectively. The C–N stretching band of an aromatic amine appears at 1300 and 1225 cm^{-1} . Polyaniline shows a strong band at 1115 cm^{-1} , which has been explained as electronic like absorption of $N=Q=N$ (where Q denotes quinoid ring). The C–H out-of-plane bending mode has been used as a key to identifying the type of substituted benzene. For polyaniline salt, this mode was observed as a single band at 805 cm^{-1} , which was in the range $800\text{--}860\text{ cm}^{-1}$ reported for 1,4-substituted benzene. A band at 560 cm^{-1} is due to SO_3^- group of *p*-TSA. The bands at 695 and 580 cm^{-1} are assigned to ring C–C bending vibration and ring in plane deformation, respectively.

3.3. Synthesis of 1,8-dioxo-dodecahydroxanthene

Product was not obtained when 4-methylbenzaldehyde was allowed to react with 1,3-cyclohexanedione in water solvent in the absence of the catalyst and 84% yield was obtained with the use of PANI-PTSA catalyst (25 wt.% with respect to aldehyde used). For comparison, the reaction was carried out only with *p*-toluene sulfonic acid (10 mmol) and obtained the product in 80% yield. *p*-Toluene sulfonic acid as catalyst cannot be reused and however, PANI-PTSA can be reused.

As a model reaction, the reaction of 4-methylbenzaldehyde with 1,3-cyclohexanedione catalyzed by PANI-PTSA in various solvents such as water, ethanol, trichloromethane, cyclohexane, propane-2-ol, 1,4-dioxane and acetonitrile was investigated and the results are reported in Table 1. Good yield of the product was obtained with the use of water as solvent (Scheme 1).



Scheme 1. Synthesis of 1,8-dioxo-dodecahydroxanthene.

Table 1
Synthesis of 1,8-dioxo-dodecahydroxanthene using various solvents

Entry	Solvent	Yield (%)
1	Ethanol	61
2	Water	84
3	Cyclohexane	75
4	Propane-2-ol	62
5	Dichloromethane	70
6	1,4-Dioxane	35
7	Acetonitrile	45

In order to optimize the synthetic procedure for synthesis of 1,8-dioxo-dodecahydroxanthene, reaction time and amount of the catalyst with respect to aldehydes were varied and the results are given in Table 2. Maximum yield (84%) was obtained in 6 h for the reaction of 4-methylbenzaldehyde with 1,3-cyclohexanedione catalyzed by PANI-PTSA in water. The yield of the product was found to be increased with increase of catalyst amount, attains a maximum yield (84%) with the use of 25 wt.% catalyst and then start decreases (Table 2).

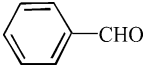

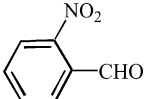
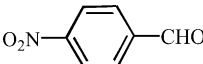
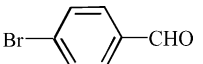
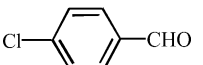
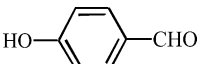
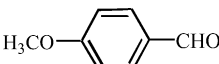
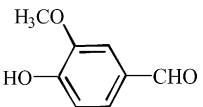
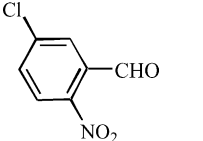
To investigate the versatility of the catalyst, the reaction of 1,3-cyclohexanedione was carried out with various aromatic

Table 2
Synthesis of 1,8-dioxo-dodecahydroxanthene with different time and amount of catalyst

Entry	Time (h)	Amount of catalyst (wt.%)	Yield (%)
1	2	25	65
2	4	25	78
3	6	25	84
4	6	10	57
5	6	15	68
6	6	20	72
7	6	30	74
8	6	35	71

aldehydes in water for 6 h using 25 wt.% of PANI-PTSA catalyst with respect to aldehyde and the results are reported in Table 3. Benzaldehyde and other aromatic aldehydes containing electron-withdrawing groups (such as nitro, halide group) or electron-donating groups (such as hydroxy, alkoxy group) were employed and gave the corresponding 1,8-dioxo-dodecahydroxanthene in good yields (84–73%). This result indicates that the nature of the substituents did not affect the yield much.

Table 3
Synthesis of 1,8-dioxo-dodecahydroxanthene derivatives

Entry	Aldehyde	Yield (%)	Melting point (°C) found	Melting point (°C) reported [14]
1		75	201–203	204–205
2		84	216–218	
3		78	245–247	246–248
4		84	224–246	222
5		73	228–231	
6		79	231–233	
7		75	245–247	246
8		83	241–243	241–243
9		77	225–227	
10		73	231–233	

3.3.1. NMR details

9-Benzene-1,8-dioxo-dodecahydroxanthene (entry no. 1); $\delta = 2.0$ (m, 4H), 2.3 (m, 4H), 2.6 (m, 4H), 4.7 (s, 1H), 7.0–7.4 (m, 5H); 9-(4-methylphenyl)-1,8-dioxo-dodecahydroxanthene (entry no. 2) $\delta = 2.0$ (m, 4H), 2.3 (m, 4H), 2.6 (m, 4H), 4.7 (s, 1H), 7.0 (d, 2H), 7.2 (d, 2H); 9-(2-nitrophenyl)-1,8-dioxo-dodecahydroxanthene (entry no. 3) $\delta = 2.0$ (m, 4H), 2.3 (m, 4H), 2.6 (m, 4H), 5.1 (s, 1H), 7.2 (m, 2H), 7.4 (m, 2H), 7.7 (d, 1H); 9-(4-nitrophenyl)-1,8-dioxo-dodecahydroxanthene (entry no. 4) $\delta = 2.0$ (m, 4H), 2.3 (m, 4H), 2.6 (m, 4H), 4.8 (s, 1H), 7.4 (d, 2H), 8.1 (d, 2H); 9-(4-bromophenyl)-1,8-dioxo-dodecahydroxanthene (entry no. 5) $\delta = 2.0$ (m, 4H), 2.3 (m, 4H), 2.6 (m, 4H), 4.7 (s, 1H), 7.2 (d, 2H), 7.4 (d, 2H); 9-(4-chlorophenyl)-1,8-dioxo-dodecahydroxanthene (entry no. 6) $\delta = 2.0$ (m, 4H), 2.3 (m, 4H), 2.6 (m, 4H), 4.7 (s, 1H), 7.2 (s, 5H); 9-(4-hydroxyphenyl)-1,8-dioxo-dodecahydroxanthene (entry no. 7) $\delta = 2.0$ (m, 4H), 2.3 (m, 4H), 2.6 (m, 4H), 4.6 (s, 1H), 6.6 (d, 2H), 7.0 (d, 2H); 9-(4-methoxyphenyl)-1,8-dioxo-dodecahydroxanthene (entry no. 8) $\delta = 2.0$ (m, 4H), 2.3 (m, 4H), 2.6 (m, 4H), 3.7 (s, 3H), 4.7 (s, 1H), 6.8 (d, 2H), 7.2 (d, 2H); 9-(4-hydroxy-3-methoxyphenyl)-1,8-dioxo-dodecahydroxanthene (entry no. 9) $\delta = 2.0$ (m, 4H), 2.3 (m, 4H), 2.6 (m, 4H), 4.0 (s, 3H), 4.7 (s, 1H), 6.4 (d, 1H), 6.7 (d, 1H), 7.1 (s, 1H); 9-(5-chloro-2-nitrophenyl)-1,8-dioxo-dodecahydroxanthene (entry no. 10) $\delta = 2.0$ (m, 4H), 2.3 (m, 4H), 2.6 (m, 4H), 5.3 (s, 1H), 7.2 (d, 1H), 7.5 (d, 1H), 7.6 (s, 1H).

3.4. Reusability

Reusability of the catalyst was checked by the reaction of 4-methylbenzaldehyde and 1,3-cyclohexanedione in water medium at reflux temperature for 6 h using 25 wt.% of PANI-PTSA and obtained the product in 84% yield. PANI-PTSA salt catalyst was recovered and reused for further six consecutive reactions and obtained 74–84% yield. This results show that PANI-PTSA can be reusable for these condensation reactions of aldehyde and 1,3-cyclohexanedione.

4. Conclusion

In summary, synthesis procedure for 1,8-dioxo-dodecahydroxanthene was optimized using polyaniline-*p*-toluenesulfonate salt as solid acid catalyst in water as solvent.

Polyaniline-*p*-toluenesulfonate salt catalyst showed versatility and reusability in the synthesis of 1,8-dioxo-dodecahydroxanthene derivatives.

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