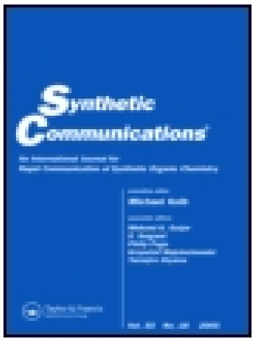


Taylor & Francis
Taylor & Francis Group

Synthetic Communications

An International Journal for Rapid Communication of Synthetic Organic Chemistry

ISSN: 0039-7911 (Print) 1532-2432 (Online) Journal homepage: http://www.tandfonline.com/loi/lsyc20

# Titanium Aminophosphates as Efficient, Economic and Recyclable Catalysts for the Synthesis of Xanthenediones

A. Rajini, C. Suman, A. Ajay kumar, S. Suresh & N. Venkatathri

**To cite this article:** A. Rajini, C. Suman, A. Ajay kumar, S. Suresh & N. Venkatathri (2016): Titanium Aminophosphates as Efficient, Economic and Recyclable Catalysts for the Synthesis of Xanthenediones, Synthetic Communications, DOI: 10.1080/00397911.2016.1220578

**To link to this article:** http://dx.doi.org/10.1080/00397911.2016.1220578

# Titanium aminophosphates as efficient, economic and recyclable catalysts for the synthesis of xanthenediones

A. Rajini[1], C. Suman[1], A. Ajay kumar[1], S. Suresh[1], N. Venkatathri[1]

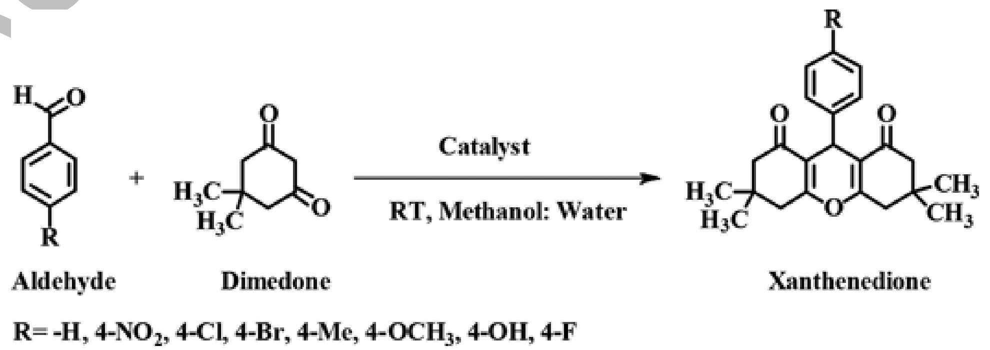
[1]Department of Chemistry, National Institute of Technology, Warangal, Telangana, India

Corresponding author to N. Venkatathri, E-mail : venkatathrin@yahoo.com

## Abstract

The titanium aminophospates have been used as catalysts in the synthesis of xanthenediones at room temperature. Among the three catalysts tested, titanium n-propyl aminophosphate (TNPAP) was found to be more efficient catalyst towards the synthesis of xanthenediones. The solvents screening studies for this catalytic reaction reveals us, MeOH: $H_2O$ was found to be suitable solvent system, yielding higher amounts (89 %) of products. The TNPAP catalyst was found to be reusable for five successive cycles. The optimized reaction conditions are, benzaldehyde (1.0 mmol), dimedone (2.0 mmol,), solvent (Methanol: water (5.0 mL)), temperature (RT) and TNPAP dosage (100 mg). A plausible mechanism for the catalytic reactions has been proposed.

## GRAPHICAL ABSTRACT



R= -H, 4-$NO_2$, 4-Cl, 4-Br, 4-Me, 4-$OCH_3$, 4-OH, 4-F

**KEYWORDS:** titanium; aminophosphates; xanthenediones

## INTRODUCTION

A large variety of xanthenediones have been used as anti-malarial, anti-inflammatory, antiasthmatic, antibacterial, antihypertensive due to their interesting biochemical significance. Xanthenediones form structural units in many of the natural products [1]. Xanthenediones and its derivatives have received much importance in various applications including fragrances, pharmaceuticals, food additives, cosmetics and tunable dye lasers [2,3]. Benzoxanthenes are important biological heterocycles possessing therapeutic properties such as anti-viral [4], anti-inflammatory [5], anti-bacterial [6] and antimalarial activities. They act as antagonists for drug resistant leukemia and also for paralyzing the action of zoxazolamine [7]. A number of catalysts such as $NaHSO_4.SiO_2$ [8], amberlyst-15 [9], PPA-$SiO_2$ [10], DBSA [11], *p*-TSA [12], silica sulfuric acid [13], $Al(HSO_4)_3$ [14], TCCA [15] and alumina sulphuric acid [16] have been employed for synthesizing xanthenedione derivatives [17]. Most of the reported synthetic methods have limitations such as strong acidic media, high temperatures, inert atmosphere, stoichiometric amounts of reaction promoters, moisture sensitiveness of the catalysts and difficulty in the separation of the products. Thus, there is ample scope for the development of new synthetic protocols to assemble such scaffolds.

Phosphate based materials are important in several industrial acid catalysed reactions [18]. In recent years inorganic phosphorous containing materials have received much attention on account of their ability to selectively uptake specific ions, resistance to oxidation, high thermal and chemical stability. In addition, the presence of phosphate in materials seems to enhance catalytic properties, stabilize surface area, crystal phase, improve surface acidity and make the material porous [19]. Research on phosphate based materials with open frameworks is currently in progress due to their applications in catalysis and gas separation [20]. Study of phosphates of transition metals has received great attention in recent years. Phosphate frameworks stabilize reduced oxidation states, due to its high charge ($PO_4^{3-}$) and hence favour the formation of anionic frameworks with a high degree of chemical, mechanical and thermal stability.

Aminophosphates are having the organic functionality in aminophosphate framework enhances hydrophobicity and shows high activity in base catalyzed reactions [21]. Incorporation of transition metals such as titanium or  vanadium or palladium in aminophosphates leads to novel materials with redox properties. In particular, titanium cation $Ti^{4+}$ in framework positions is found to exhibit good activity in shape selective redox reactions.   This manuscript  deals with the synthesis of biologically active heterocyclic compounds like xanthenediones  at room temperature using  titanium aminophosphates. Owing to the presence of titanium that has Lewis acid , redox site, Lewis and Bronsted acidity nitrogen donor alkyl groups in titanium aminophosphates, the materials are expected to have catalytic  applications.

## RESULTS AND DISCUSSION

The catalytic applications of titanium  aminophosphates deals with one pot multi component synthesis of xanthenediones over titanium  aminophosphates (Scheme 1).

To explore the efficacy of the titanium aminophosphate catalysts and to establish the optimum conditions required, the reaction was investigated at room temperature by varying solvents, aromatic aldehydes and catalyst dosage. Among TNPAP, TNOAP and TNDDAP catalysts used for the synthesis of xanthenediones, TNPAP is found to exhibit higher catalytic activity with respect to short reaction time and yield of the product (Table 1).

In order to examine the influence of various solvents, model reaction of benzaldehyde and dimedone was carried out in different solvents using TNPAP as catalyst (Table 2). Solvents acetonitrile, chloroform, water, tetrahydrofuran did not favour the formation of product even after stirring the reaction mixture for 4 h. This may be due to solubility difference as the reaction mixture becomes triphasic with the organic substrate, solvent and catalyst. In the presence of solvents dimethyl formamide (DMF) and dimethyl sulfoxide (DMSO) the reaction requires more time due to their nature of adsorption on the active sites of catalyst surface and reported that these solvents may retard the condensation of the intermediates [25]. Methanol: water mixture was found to be most suitable solvent for the reaction. The results reveal that methanol and water solubilize the organic substrates and bring the reactants onto the surface of the catalyst, thus reducing phase separation and enhancing the yield [12]. The merit of the co-solvent is attributed to the good solubility of the organic reactants and the inorganic base.

The effect of amount of catalyst on the model reaction has been studied by varying the amount of TNPAP catalyst in the range 10 – 100 mg to determine the optimum amount of catalyst and the obtained results are shown in Table 3. It was found that 100 mg is able to catalyze the reaction efficiently. The results indicate that the yield increases with the increase in amount of catalyst. With increase in dosage of TNPAP catalyst from 10 to 100 mg, the products yields were increased from 40% to 90% with the reaction times as detailed in the Table 3. Hence, the catalyst amount of 100 mg has been chosen as optimum amount to carry out the reaction.

After establishing the optimum reaction conditions, the protocol was extended to different substituted aromatic aldehydes. The results of the % yield of products are shown in Table 4. The nature of the substituent's on the aromatic aldehydes shows some effects on the  yields and reaction times. The *p*-bromo and *p*-nitro benzaldehydes was reacted faster and produced the corresponding products at higher yields in short reaction times. The *p*-hydroxy, *p*-methoxy and *p*-methyl benzaldehydes need long reaction times to get good yields. It was observed that all the aromatic aldehydes have reacted in short reaction times. It was found that *p*-fluoro benzaldehyde  and p-fluoro benzaldehyde is more reactive than *p*-chloro and *p*-methyl benzaldehydes. This may be attributed to the smaller size of fluorine atom, which allows the reactant molecules to gain closer proximity to the active centres of the titanium species compared to the larger chlorine and methyl groups. However, the differences in the reactivity of various substituted aldehydes are dependent on the synergetic effect of molecular parameters such as mesomeric (+M), inductive (+I/-I) and steric effect of substituents.

The reaction of benzaldehyde and dimedone to give xanthenediones was chosen as a model reaction to test the reusability of TNPAP catalyst (Table 5). After completion of the reaction, methanol was added to dissolve the product. The catalyst was filtered off, washed with ether and dried under vacuum and reused for the reaction under same reaction conditions.

A plausible mechanism for the synthesis of xanthenediones over TNPAP catalyst is depicted in Fig. 1. The mechanism follows a Knoevenagel condensation, Michael addition and cyclodehydration reactions. The aldehyde (I) forms an oxygen bonded complex through titanium of TNPAP. The first molecule of dimedone (II) undergoes Knoevenagel condensation reaction with the aldehyde to form an intermediate (III). The intermediate (III) thus formed successfully looses water molecule to give Knoevenagel product (IV) which inturn undergoes Michael addition with second molecule of dimedone. Then Michael adduct (V) underwent hemiketal formation, followed by dehydration gave xanthenedione (VI).

## CONCLUSION

The titanium aminophospates were investigated in the synthesis of xanthenediones at room temperature. TNPAP acts as an efficient catalyst towards the synthesis of xanthenediones. Methanol: water was found to be suitable solvent system for the reaction, yielding higher amounts (89 %) of products. The TNPAP catalyst were found to be reusable for five successive cycles. The optimized reaction conditions are, benzaldehyde (1.0 mmol), dimedone (2.0 mmol,), solvent (Methanol: water (5.0 mL)), temperature (RT) and TNPAP dosage (100 mg). A plausible mechanism for the catalytic reaction has been proposed.

## EXPERIMENTAL

Titanium n-propyl aminophosphate (TNPAP), Titanium n-octyalaminophosphate (TNOAP) and Titanium n-dodecylaminophosphate (TNDDAP) are synthesized and characterized by various procedures reported elsewhere [22-24]. The $^{1}H$ Nuclear magnetic resonance (NMR) spectroscopy was performed at room temperature on a DSX-300 Avance-III 400(L) NMR spectrometer with a spinning rate of 10-12 KHz operating at 75.47 MHz using a 5 mm dual probe. Titanium aminophosphates TNPAP, TNOAP and TNDDAP synthesized in our studies were tested for their catalytic activity in the synthesis of xanthenediones. A mixture of aromatic aldehyde (1.0 mmol), dimedone (2.0 mmol) and methanol: water (1:1) (5.0 mL) was taken in a round bottom flask. 50 mg of catalyst was added to the reaction mixture and contents were stirred at room temperature. The products formed were authenticated by their melting points, $^{1}H$ NMR, $^{13}C$ NMR and MASS spectra.

## ACKNOWLEDGEMENT

The authors are thankful to the MHRD, New Delhi for a fellowship.

## REFERENCES

[1] Wang, H. K.; Morris-Natschke, S. L.; Lee, K. H. *Med. Res. Rev*. **1997**, *17*, 367.

[2] Rakavishnikov, A.V.; Smith, M. P.; Birrell, G. B.; Keana, J. F. W.; Griffith, O. H. *Tetrahedron Lett.* **1998**, *39*, 6637.

[3] Chibale, K.; Visser, M. R.; Van Schalkwyk, D.; Smith, P. J.; Saravanamuthu, A.; Fairlamb, A. H. *Tetrahedron* **2003**, *59*, 2289.

[4] Lambert, R. W.; Martin, J. A.; Merrett, J. H.; Parkes, K. E. B.; Thomas, G. J. *Chem. Abstr.* **1997**, *126*, 212377; PCT Int. Appl. WO 9706178, 1997.

[5] Poupelin, J. P.; Saint-Rut, G.; Foussard-Blanpin, O.; Narcisse, G.; Uchida-Ernouf, G.; Lacroix, R. Eur. *J. Med. Chem.* **1978**, *13*, 67.

[6] El Ashry, E. S. H.; Awada, L. F.; Ibrahim, E. S. I.; Bdeewy, O. K.; *Arkivoc* **2006**, *2*, 178.

[7] Nguyen, H. T.; Lallemand, M. C.; Boutefnouchet, S.; Michel, S.; Tillequin, F. *J. Nat. Prod.* **2009**, *72*, 527.

[8] Das, B.; Thirupathi, P.; Reddy, K. R.; Ravikanth, B.; Nagarapu, L. *Cat. Commun.* **2007**, *8*, 535.

[9] Das, B.; Thirupathi, P.; Mahender, I.; Reddy, V. S.; Rao, Y. K. *J. Mol. Catal. A: Chem.* **2006**, *247*, 233.

[10] Kantevari, S.; Vuppalapati, S. V. N.; Biradar, D. O.; Nagarapu, L. *J. Mol. Catal. A: Chem.* **2007**, *269*, 53.

[11] Jin, T. S.; Zhang, J. S.; Guo, T. T.; Wang, A. Q.; Li, T. S. *Synlett.* **2004**, *5*, 866.

[12] Venkatesan, K.; Pujari, S. S.; Lahoti, R. J.; Srinivasan, K. V. *Ultrason. Sonochem.* **2008**, *15*, 548.

[13] Seyyedhamzeh, M.; Mirzaei, P.; Bazgir, A. *Dyes. Pigments*. **2008**, *76*, 836.

[14] Srinivasa, A.; Varma, P. P.; Hulikal, V.; Mahadevan, K. M. *Monatsh. Chem.* **2008**, *139*, 111.

[15] Bigdeli, M. A.; Nemati, F.; Hossein Mahdavinia, G.; Doostmohammadi, *H. Chin. Chem. Lett.* **2009**, *20*, 1275.

[16] Pramanik, A.; Bhar, *S. Catal. Commun.* **2012**, *20*, 17.

[17] Jing-Ju, M.; Chun, W.; Qiu-Hua, W.; Ran-Xiao, T.; Hai-Yan, Liu.; Qing, L. *Heteroatom Chemistry*. **2008**, *19*, 609.

[18] Samantaray, S. K.; Mishra, T.; Parida, K. M. *J. Mol. Catal. A: Chem*. **2000**, *156*, 267.

[19] Samantaray, S. K.; Parida, K. M. *J. Mol. Catal. A: Chem.* **2001**, *176*, 151.

[20] Cheetham, A. K.; Ferey, G.; Loiseau, T. *Angew. Chem. Int. Ed. Engl*. **1999**, *38*, 3268.

[21] Berlini, C.; Guidotti, M.; Moretti, G.; Psaro, R.; Ravasio, N. *Catal. Today*. **2000**, *60*, 219.

[22] Rajini, A.; Ajay Kumar, A.; Suman, C.; Suresh, S.; Venkatathri, N. *RSC Advances*. **2016**, *6*, 507.

[23] Rajini, A.; Nookaraju, M.; Suman, C.; Ajay Kumar, A.; Venkatathri, N. *RSC Advances*. **2015**, *5*, 106509.

[24] Rajini, A.; Ajay Kumar, A.; Suman, C.; Venkatathri, N. *RSC Advances*, **2015**, *5*, 87713.

[25] Karthikeyan, G.; Pandurangan, A. *J. Mol. Catal. A: Chem*. **2009**, *311*, 36.

**Table 1.** Synthesis of xanthenediones using titanium aminophosphate catalysts

**Reaction conditions:** benzaldehyde = 1.0 mmol, dimedone = 2.0 mmol, methanol: water = 5.0 mL, catalyst dosage = 100 mg.

| **S.No** | **Catalyst** | **Solvent/Temp. (°C)** | **Time (h)** | **Yield (%)** | **TOF (x $10^{-3}$ $s^{-1}$)** | **TON** |
|---|---|---|---|---|---|---|
| 1. | TNPAP | MeOH:$H_2O$ / RT | 0.5 | 89 | 1.55 | 5.6 |
| 2. | TNOAP | MeOH:$H_2O$ / RT | 1.0 | 74 | 1.29 | 4.6 |
| 3. | TNDDAP | MeOH:$H_2O$ / RT | 0.8 | 80 | 2.47 | 8.9 |

**Table 2.** Synthesis of xanthenediones using different solvents in the presence of TNPAP catalyst

**Reaction conditions:** Benzaldehyde = 1.0 mmol, Dimedone = 2.0 mmol, Solvent = 5.0 mL, Temperature = RT, TNPAP dosage = 100 mg, NR = No reaction.

| **S.No** | **Solvent** | **Time (h)** | **Yield (%)** | **TOF (x $10^{-3}$ $s^{-1}$)** | **TON ($h^{-1}$)** |
|---|---|---|---|---|---|
| 1. | Methanol | 2.0 | 75 | 0.3 | 1.2 |
| 2. | Chloroform | 4.0 | No reaction | - | - |
| 3. | Tetrahydrofuran | 5.0 | No reaction | - | - |
| 4. | Ethanol | 2.3 | 70 | 0.3 | 1.0 |
| 5. | Methanol: Water | 0.5 | 89 | 1.6 | 5.6 |
| 6. | Water | - | No reaction | - | - |
| 7. | DMF | 2.3 | 72 | 0.3 | 1.0 |
| 8. | DMSO | 3.0 | 74 | 0.2 | 0.8 |

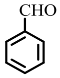
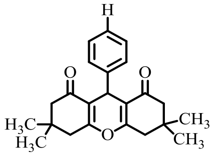
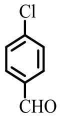
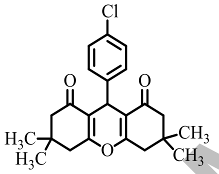
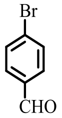
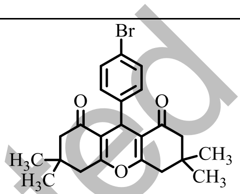
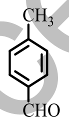
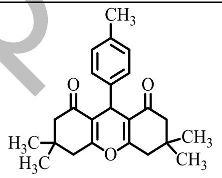
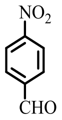
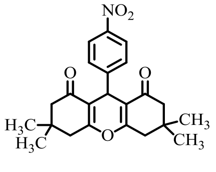
**Table 3.** Effect of TNPAP catalyst dosage on the synthesis of xanthenediones

**Reaction conditions:** Benzaldehyde = 1.0 mmol, Dimedone = 2.0 mmol, Methanol: Water = 5.0 mL, Temperature = RT.

| **S.No** | **Amount of catalyst (mg)** | **Time (h)** | **Yield (%)** | **TOF (x $10^{-3}$ $s^{-1}$)** | **TON (x $h^{-1}$)** |
|---|---|---|---|---|---|
| 1. | 10 | 1.5 | 40 | 0.2 | 0.8 |
| 2. | 30 | 1.0 | 55 | 0.5 | 1.7 |
| 3. | 50 | 0.7 | 70 | 0.9 | 3.1 |
| 4. | 70 | 0.6 | 80 | 1.2 | 4.2 |
| 5. | 100 | 0.5 | 90 | 1.6 | 5.6 |

**Table 4.** Synthesis of xanthenediones from various aromatic aldehydes by employing TNPAP

**Reaction conditions:** Benzaldehyde = 1.0 mmol, Dimedone = 2.0 mmol, Methanol: Water = 5.0 mL, Temperature = RT, TNPAP dosage = 100 mg.

| S.No | Reactant | Product | Time (h) | Yield (%) | TOF (x 10$^{-3}$ s$^{-1}$) | TON (h$^{-1}$) |
|---|---|---|---|---|---|---|
| 1. |  |  | 0.5 | 89 | 1.6 | 5.6 |
| 2. |  |  | 0.7 | 70 | 7.9 | 2.8 |
| 3. |  |  | 0.5 | 74 | 1.1 | 3.8 |
| 4. |  |  | 0.5 | 72 | 1.2 | 4.3 |
| 5. |  |  | 0.6 | 75 | 1.0 | 3.5 |

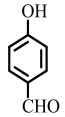
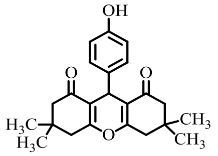
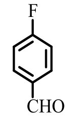
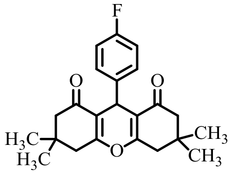
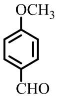
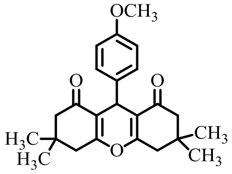
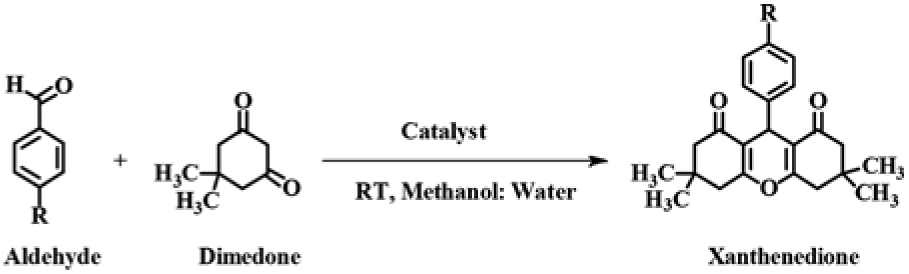
| | | | | | | |
|---|---|---|---|---|---|---|
| 6. |  |  | 1.0 | 69 | 0.6 | 2.1 |
| 7. |  |  | 0.6 | 74 | 1.0 | 3.7 |
| 8. |  |  | 1.0 | 60 | 0.5 | 1.7 |

**Table 5.** Reusability of TNPAP catalyst towards the synthesis of xanthenediones

**Reaction conditions:** Benzaldehyde = 1.0 mmol, Dimedone = 2.0 mmol, Methanol: Water = 5.0 mL, Temperature = RT, TNPAP dosage = 100 mg.

| **S.No** | **Catalyst** | **Time (h)** | **Yield (%)** |
|---|---|---|---|
| 1. | Fresh | 0.5 | 89 |
| 2. | Recycle 1 | 0.5 | 88 |
| 3. | Recycle 2 | 0.5 | 87 |
| 4. | Recycle 3 | 0.5 | 86 |
| 5. | Recycle 4 | 0.5 | 85 |

**Scheme 1.** Synthesis of xanthenediones over titanium aminophosphates.



R= -H, 4-$NO_2$, 4-Cl, 4-Br, 4-Me, 4-$OCH_3$, 4-OH, 4-F

Catalyst uses: TNPAP or TNOAP or TNDDAP

**Figure 1.** A plausible mechanism for the synthesis of xanthenediones over TNPAP catalyst.