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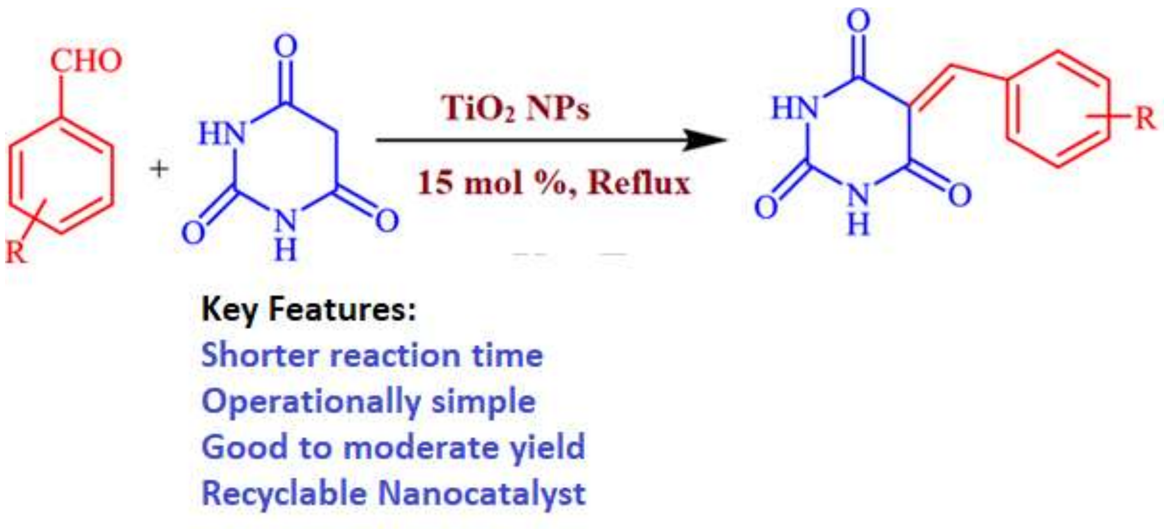
Catalytical Applications Of Tio2nanoparticles For Knoevenagel Condensation Between Barbituric Acid And Aromatic Aldehydes

Dr. Jay A. Tanna (Assistant Professor) PG Department of Chemistry, VMV College, Wardhaman Nagar, Nagpur -440008, Maharashtra (India) E-mail: jaytanna9999@gmail.com

Dr. Nilesh V. Gandhare (Assistant Professor) PG Department of Chemistry, NabiraMahavidhalaya, Katol Dist. Nagpur -441302, Maharashtra (India) E-mail: nilkanth81@gmail.com

Abstract:
The TiO_2Nanoparticles as an efficient catalyst was used for the synthesis of 5-arylidine barbituric acid derivatives by condensation reaction of barbituric acid and various aromatic aldehydes at room temperature with high speed stirring. The present protocol especially favoured because it offers advantages of high yields, short reaction times, simplicity and easy workup. Moreover the catalyst is inexpensive, stable, can be recycled and reused for four cycles without loss of its activity.

Graphical Abtract:



1. Introduction

Barbituric acid or 6-hydroxyuracil is an organic compound based on a pyrimidine heterocyclic skeleton. It is an odorless powder soluble in water. Barbituric acid is the parent compound of barbiturate drugs, although barbituric acid itself is not pharmacologically active. The derivatives of barbituric acid (2, 4, 6-trioxypyrimidine) are known as barbiturates. They are a class of drugs that have diverse applications such as sedatives, hypnotics and anticonvulsants under a variety of conditions and are also employed for anesthesia [1-2]. They are also used for the treatment of anxiety, epilepsy and other psychiatric disorders and possess effects on the motor and sensory functions [3]. Owing to the wide range of biological and medicinal activities, the synthesis of 5-arylidine barbituric acid compounds by the use of barbituric acid and 2-thio barbituric acid as starting compound have become an important target in recent years.

Solvent free organic reaction have drawn great interest, particularly from the viewpoint of green chemistry as organic solvent are toxic and flammable. Solid state reactions are simple to handle, reduce pollution and comparatively cheaper to operate. Heterogeneous catalysts offer several intrinsic advantages over their homogeneous counterparts such as easy removal of catalyst, operational simplicity and reusability [4].

The use of metal nanoparticles in the field of catalysis is of great interest, since they have a large surface-to-volume ratio compared to bulk materials. Recently, there has been growing interest in using bismuth sulfide nanoparticles in organic synthesis because of their potent catalytic activity, high stability and non toxic. Herein, we were reported a simple, easy and convenient protocol for the microwave assisted synthesis of5-Arylidene Barbituric Acids derivatives catalyzed efficiently by TiO_2 NPs.

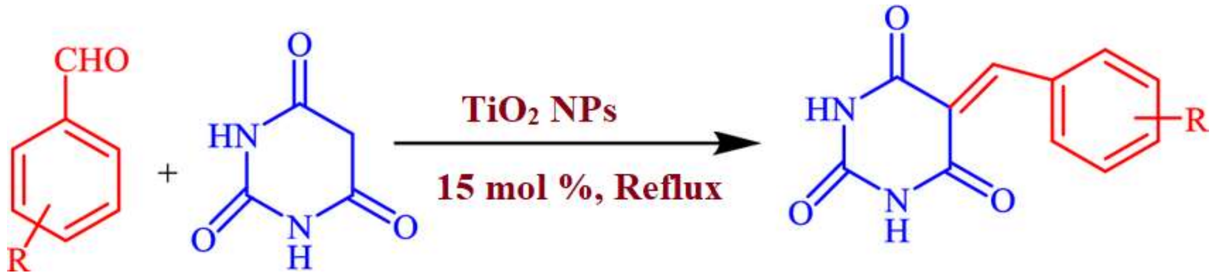
2. Experimental Section:

a. Preparation of titanium oxide nanoparticles (TiO_2 NPs)

The titanium oxide (TiO_2) nanoparticles were the promising material as semi-conductor having high photochemical stability. The well-dispersed TiO_2 NPs with very fine sizes are promising in many applications such as pigments, adsorbents and catalytic supports [5]. The TiO_2 NPs were synthesized by dissolving titanium isopropoxide in absolute ethanol and distilled water was added to the solution in terms of a molar ratio of 1:4. The few drops of nitric acid were used to adjust the pH and for restrain the hydrolysis of the solution. The solution was stirred vigorously for 30 min in order to form sols. After for 24 hrs, the sols were transformed into gels. In order to obtain NPs, the gels were dried under 120 °C for 2 h to evaporate water and organic material to the maximum extent. Then the dry gel was sintered at 450 °C for 2 h were subsequently carried out to obtain desired TiO_2nanocrystalline.

b. Synthesis of 5-arylidene barbituric acids by TiO_2 nanoparticles:

A mixture of aromatic aldehydes (1 mmol), barbituric acid(1 mmol) (solid aromatic aldehyde wetted with ethanol) andTiO_2 nanoparticles (15 mol %) (Scheme 1) was kept in microwave having voltage 340 V till the completion of reaction monitored by TLC (ethyl acetate and n-hexane 7:3). After completion of reaction solid product obtained was dissolved in 10ml ethyl acetate, filter and allow evaporating the filtrate. Finally pure product was obtained by recrystallization and authentic samples were characterized by FTIR, ^1H NMR.



Scheme 1: Synthesis of 5-arylidene barbituric acids by TiO_2 nanoparticles

Spectral data of some selected compounds:

1. **5-Benzylidene barbituric acid** (Table 1, 3a): FTIR (KBr): 3100-3060, 1730, 1670, 1540, 1430 cm^{-1}; ^1H NMR (DMSO d_6/TMS):11.40 (s, 1H, NH), 11.22 (s, 1H, NH), 8.35 (s, 1H, CH=C), 8.13 (d, 2H), 7.44(m, 3H).
2. **5(4-Cl-Benzylidene) barbituric acid** (Table 1, 3b): FTIR (KBr): 3404, 3214, 2970, 1755, 1703, 1570 cm^{-1}; ^1H NMR (DMSO d_6/TMS):7.53(d, 2H, Ar-H), 8.08(2d, 2H, Ar-H), 8.25(s, 1H, HC=C), 11.25(s, H, NH), 11.40(S, 1H, NH).
3. **5(2-Cl-Benzylidene) barbituric acid** (Table 1, 3c): FTIR (KBr): 3460, 3120, 2981, 1754, 1569, 1454, 1079, 910, 782 cm^{-1}; ^1H NMR (DMSO d_6/TMS):7.36 (t, 1H Ar-H), 7.47 (t, 1H, Ar-H), 7.53 (d, 1H, Ar-H), 7.73 (d, 1H, Ar-H), 8.29 (s, 1H, HC=C), 11.25(s,1H, NH), 11.47(s, 1H,NH).
4. **5(4-OH-Benzylidene) barbituric acid** (Table 15, 3i): FTIR (KBr) 3420, 3214, 2970, 1755, 1703, 1570 cm^{-1}; ^1H NMR (DMSO d_6/TMS):6.86(d, 2H, Ar-H), 8.32(2d, 2H, Ar-H), 8.24(s, 1H, HC=C), 10.68(S, 1H, OH), 11.13(s, H, NH), 11.25(S, 1H, NH).

3. Characterization of TiO_2 nanoparticles

The X-ray diffraction pattern of the synthesized titanium dioxide nanoparticles have shown in Figure 1. The Keiteb et al. reports that absence of spurious diffractions indicates the crystallographic purity [6]. The experimental XRD pattern agrees with the JCPDS card no. 21-1272 (anatase TiO_2) and the XRD pattern of TiO_2 nanoparticles other literature [7]. The 2θ at peak 25.4° confirms the TiO_2 anatase structure. There was no any spurious diffraction peak found in the sample. The intensity of XRD peaks of the sample reflects that the formed nanoparticles were crystalline and broad diffraction peaks indicate very small size crystallite. The crystallite size obtained using Debye-Scherrer formula was 10 nm for sol-gel derived particles.

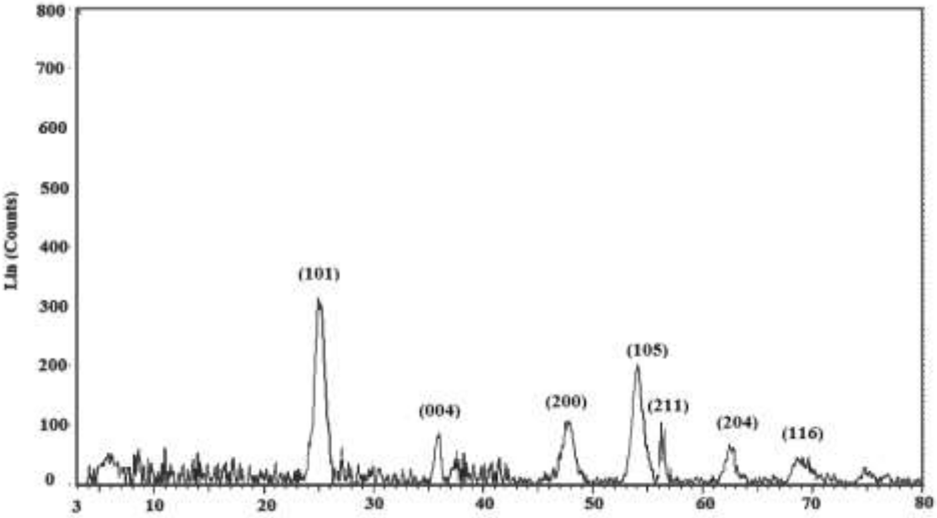


Figure 1: XRD spectra of TiO_2 nanoparticles

Figures 2 show SEM micrographs powder prepared by the sol-gel method calcined at 500 °C for 2 h. The SEM micrograph of the TiO_2 NPs shows agglomerate of fine powder which was irregular in shape. The TEM images of sol-gel derived nanoparticles have shown in Figure 3.69. Selected area diffraction was shown in inset of Figure 3 which clearly indicates that the TiO_2 nanoparticles were highly crystalline in nature. No clear spherical structures were seen in the TEM image. Nanoparticles obtained in this case were adhering to one another. Agglomeration of nanoparticles was more in this case than the former one. As can be seen from the TEM image that the average particle size was around 9 nm, which was in agreement with the crystallite, size obtained from XRD.

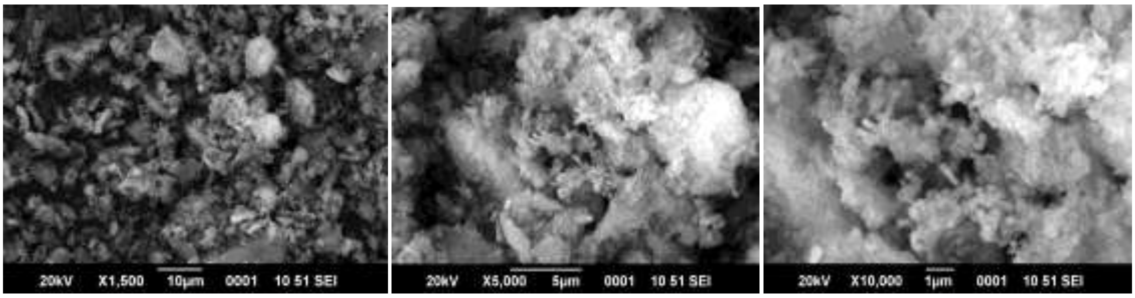


Figure 2: SEM image of TiO_2 nanoparticles at different magnification

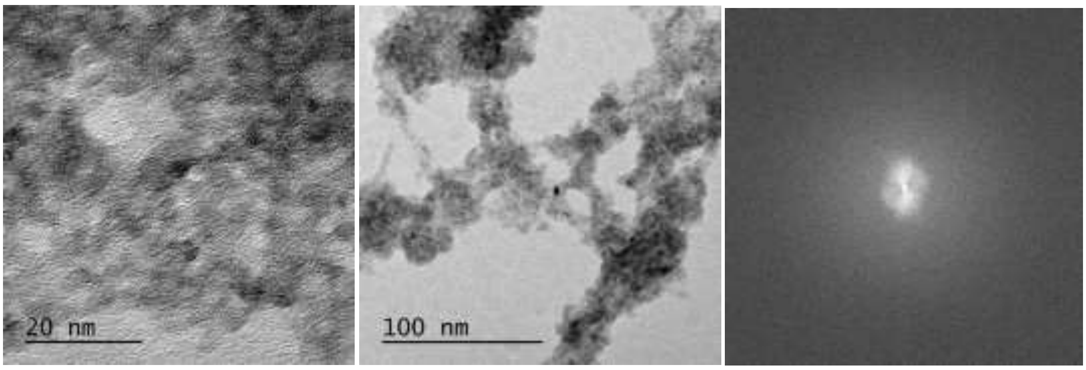


Figure 3: TEM image of TiO_2 nanoparticles

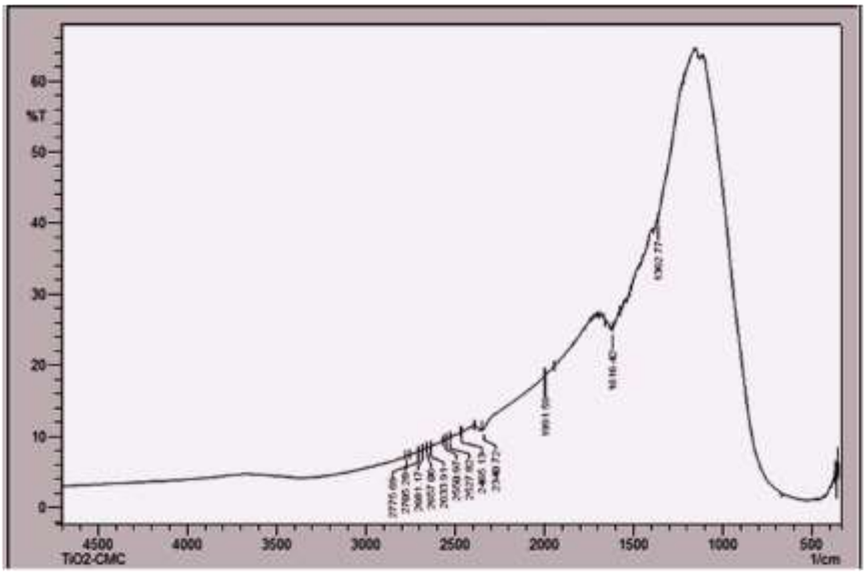


Figure 4: FTIR spectra of TiO_2 nanoparticles

The FTIR spectra of TiO_2 NPs in the wave number region from 200 to 4000 cm^{-1} are shown in Figure 4.The TiO_2 NPs shows a broad band centered around 600 cm^{-1} corresponding to the Ti–O–Ti stretching vibration in the TiO_2 lattice. The FTIR spectrum of TiO_2 rutile phase shows a broad band from 500 to 1000 cm^{-1}, which was attributed to the vibration mode of Ti–O in the anatase phase of TiO_2 NPs [8].

The UV Visible absorption spectra of TiO_2 nanoparticles have shown in Figure 5. The absorption band edges were estimated around 351 nm and having band gap energy was found to be about 3.54 eV determined by using Tauc's equation.

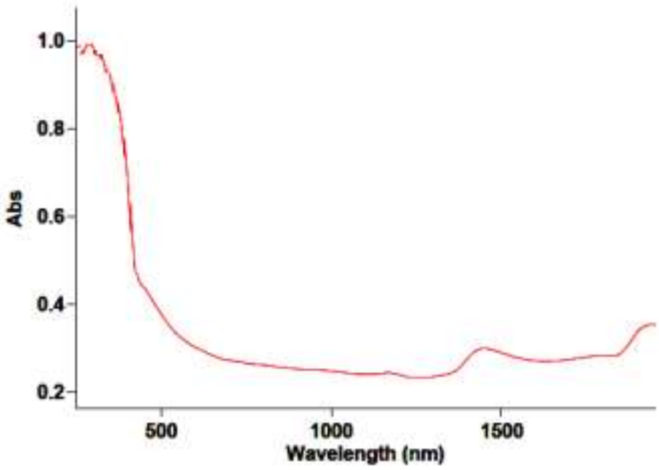


Figure 5: TheUV-Vis absorption spectra of titanium dioxide nanoparticles

The synthesis of biologically active of 5-arylidene barbituric acids and its derivatives were achieved by one-pot, two-component condensation of an aromatic aldehydes and barbituric acids in the presence of TiO_2 NPs under solvent free condition by microwave irradiation gives excellent yields of product. In our initial study on the efficiency of the titania nanocatalyst, benzaldehyde and barbituric acid were used as the model substrate. We carried out the reaction without any catalyst, but the product isolated gave poor yield (25 %). In optimizing the reaction conditions, the amount of catalyst was the major factor. The model reaction was studied using 5, 10, 15, 20 and 25 mol % of a reaction of benzaldehyde. The results revealed that best yield was obtained by using 100mg catalyst. With increase in the catalyst concentration, the yield of the desired product was found to be constant. Therefore, the catalyst plays a crucial role in the success of the reaction in term of yields of the product. The results obtained have summarized in Table 2. It is evident that the aromatic aldehydes carrying electron-donating or electron withdrawing groups reacted smoothly to produce high yield of products. The results with different aromatic aldehydes are summarized in Table 1.

In order to investigate the reusability of the catalyst, 15 mol % TiO_2 nanoparticles were used for condensation of benzaldehyde and barbituric acid. The catalyst was recovered by simple work-up using the reaction mixture was stirred until complete dissolution of product in ethyl acetate. The resulting solution was centrifuged for 5 min. The ethyl acetate solution was collected by simple decantation. The catalyst was washed with ethanol for 2-3 times. Then dried catalyst reused in same reaction for over four successive reaction corresponding yields for each cycle were mentioned in Table 3.

Product	Benzaldehyde	Time (min)	Yield (%)	Melting Point (°C)	
				Found	Reported[9-10]
3a	C_6H_5	10	94	264-266	253-265
3b	4-ClC_6H_4	10	89	298-299	298
3c	2-ClC_6H_4	15	89	250-252	253-255
3d	4-$NO_2C_6H_4$	12	94	268-270	272-274
3e	3-$NO_2C_6H_4$	10	90	230-231	231-233
3f	4-$CH_3C_6H_4$	15	85	290-291	297-298
3g	2,4-$Cl_2C_6H_3$	15	88	268-270	269-270
3h	4-$OCH_3C_6H_4$	15	90	296-298	298-299

Table 1: Synthesis of 5-arylidine barbituric acid catalysed by TiO_2 NPs

Entry	Amount of Catalyst (mol %)	Yield (%)
1	No catalyst	25
2	5	38
3	10	82
4	15	94
5	20	95
6	25	95

Table 2: Optimizations of amount of TiO_2 NPs

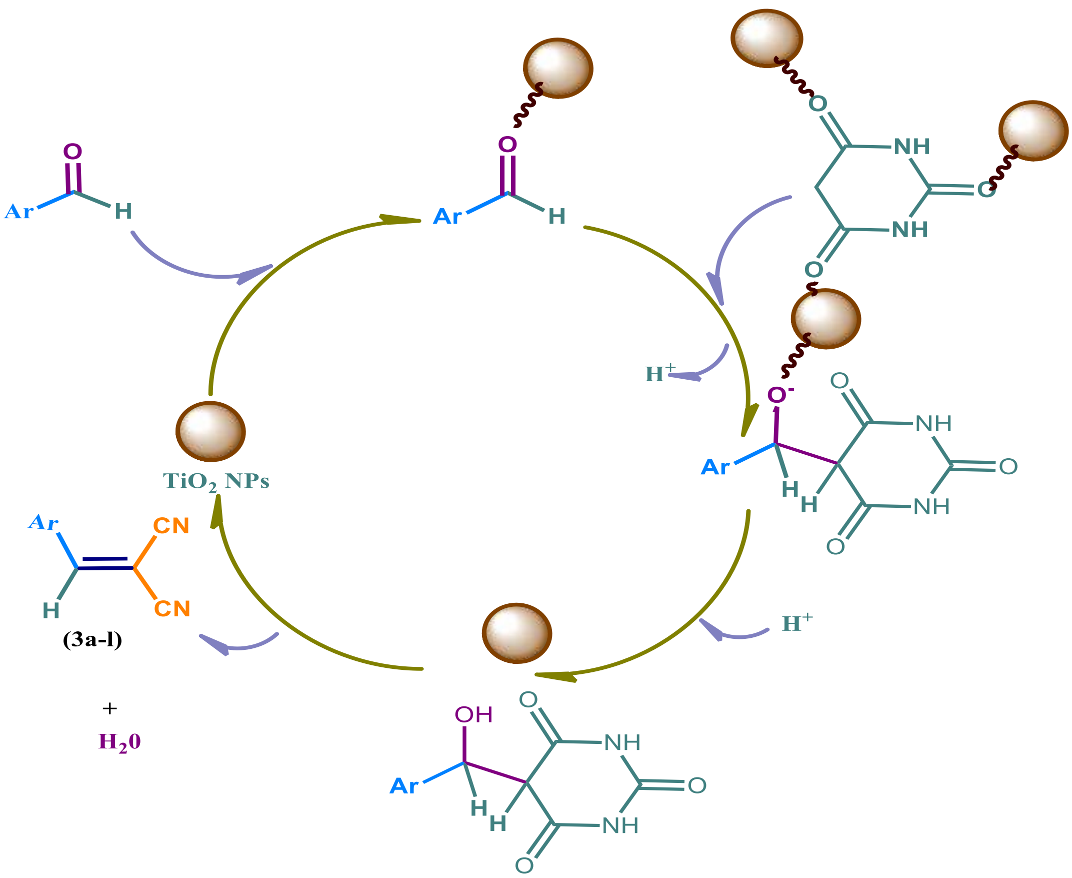
To compare the merits of our work to the other reported procedure; the results of the synthesis of arylidene barbituric acid derivatives in the presence of different reported catalysts with respect to time and yield of the product are listed in Table 4. These results show that our catalyst TiO_2 nanoparticles are more stable in air, nontoxic, give good yield in short time than other catalysts and there is no use of any hazardous solvent.

Run	Yield (%)	Recovery of TiO_2 NPs (%)
1	94	90
2	90	88
3	88	85
4	86	80

Table 3: Reusability of the TiO_2 nanoparticles

Sr. No.	Catalyst[9,10]	Reaction condition	Yield (%)
1	NH_2SO_3H	Grinding/10 min	47
2	KSF clay	MW. 560 W/7min	70
3	PVPNi NPs	Ethylene glycol, 50° C/ 10-15 min	91
4	CuO NPs	Solvent free/ R.T./ 7 min	95
5	TiO_2 NPs	Solvent free/ MW. 340 W/10 min	94

Table 4: Synthesis of 5-arylidine barbituric acid catalysed by different reported catalyst



Scheme 2: The proposed mechanism for 5-arylidine barbituric acid catalysed by TiO_2 NPs

The conceivable mechanisms for the formation of the products (3a-l) have been shown in Scheme 2. The more important is that TiO_2 NPs facilitate the Knoevenagel-type coupling by coordinated to the oxygen of carbonyl groups. On the other hand, Ni NPs can activate methylene compounds i.e. malononitrile so that deprotonation of the C-H bond occurs. As a result Knoevenagel condensation proceeds by activation of reactants by NPs.

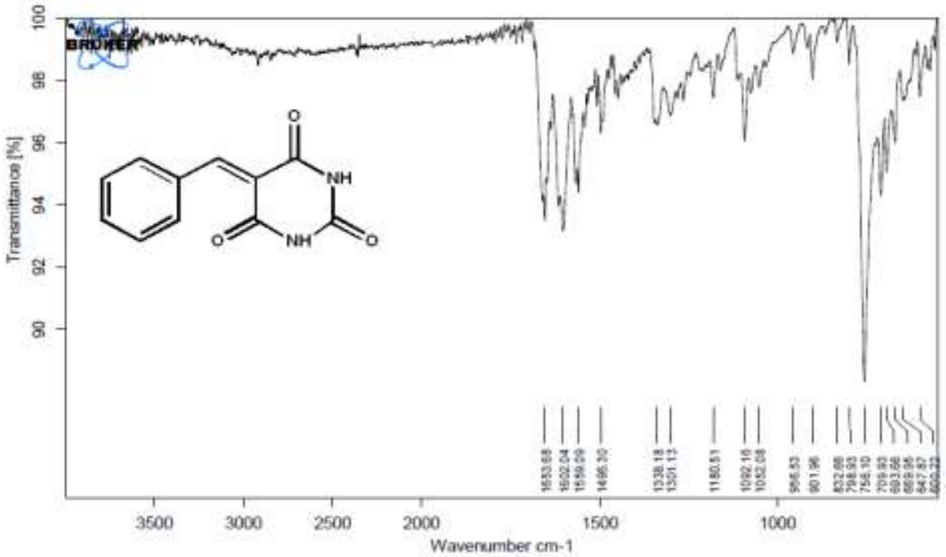


Figure 5: FTIR spectra of spectra of 5-Benzylidene barbituric acid (Table 1, 3a)

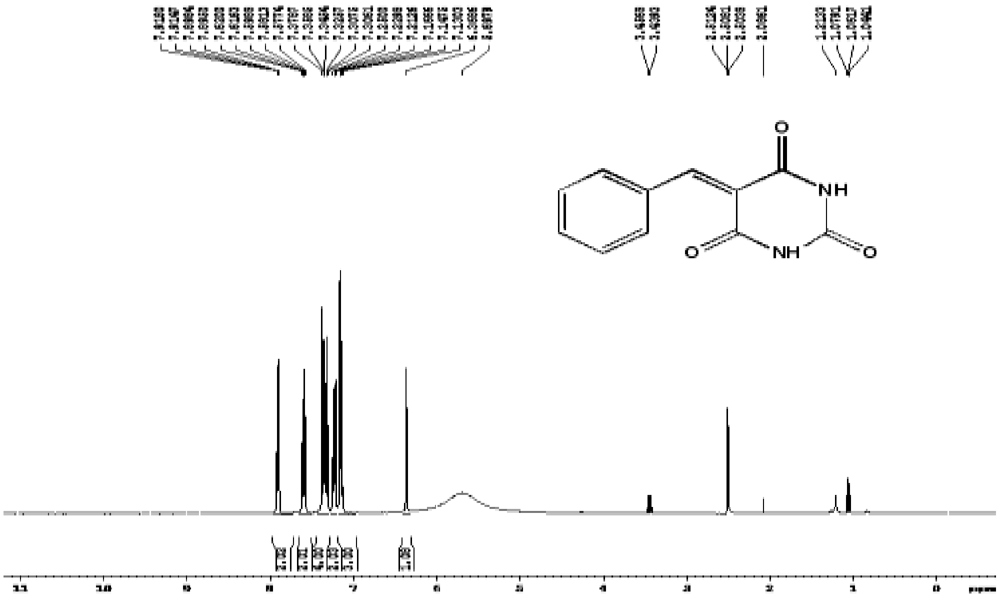


Figure 6: [1]H NMR spectra of 5-Benzylidene barbituric acid (Table 1, 3a)

5. Conclusion

In conclusion, TiO_2 nanoparticles were used as catalyst for the solvent free green synthesis of 5-arylidine barbituric acid and its derivatives. The TiO_2 nanoparticles were found to be most efficient catalyst being inexpensive, stable, can be recycled and reused for three cycles without loss of its activity. The obtained products from the catalytical application of nanoparticles were characterized by various spectroscopy techniques such as ^{1}H NMR, FTIR and Mass analyses and then compared their melting point with authentic samples in the literature.

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