Substituent effect in photocatalytic oxidation of 2-oxo-1,2,3,4-tetrahydropyrimidines using TiO$_2$ nanoparticles

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A B S T R A C T

The semiconductor-sensitized oxidation of various 1-, 4- and 5-substituted 2-oxo-1,2,3,4-tetrahydropyrimidines was carried out in acetonitrile using TiO$_2$ anatase nanoparticles. The aims of this study were to elucidate the effects of the nature of the substituents on the 1-, 4- and 5-positions of the heterocyclic ring, the type of the photocatalyst and the nature of solvent on the rate of reaction. The proposed electron-transfer mechanism is supported by the experimental results and also by the computational studies.

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1. Introduction

Photochemical oxidation (PCO) is a promising technology which utilizes semiconductor powders; mainly metal oxides such as TiO$_2$, ZnO, WO$_3$ suspended in solution or as supported thin film to carry out a light-induced redox process for oxidation of various chemicals [1,2]. TiO$_2$ is the most extensively used semiconductor photocatalyst because of its photocatalytic activity, chemical stability, non-toxicity and low cost. TiO$_2$ has been widely used for degradation of various contaminants such as azo dyes [3–5], ammonia [6], cyanide [7], benzaton as a herbicide [8] or by photo-oxidation of aryl alcohols [9], α,β-dihydroxybenzyl derivatives [10–12] or organic sulfides [13]. When TiO$_2$ is subjected to UV light ($\lambda \geq 385$ nm), the primary step following the light absorption is the excitation of an electron from the TiO$_2$ valence band to the conduction band producing an electron/hole pair (e_{CB}^-/h_{VB}^+), which must be trapped somehow in order to avoid recombination (Scheme 1).
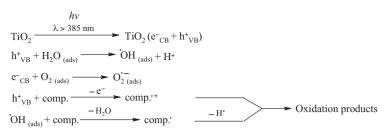
The redox process takes place primarily on the surface of TiO$_2$, where the photogenerated electrons and holes may interact with electron-acceptor or electron-donor species present in the medium [14]. The photogenerated holes are also able to accept an electron from adsorbed water producing hydroxyl radical (when the experiment is being carried out in aqueous media), or from the compound to be oxidized which is present in the solution. Meanwhile, oxygen dissolved in solution can scavenge the excited electrons, limiting the electron–hole recombination by formation of superoxide radical (O$_2$•$^-$), which acts as an active oxidant or reductant [15].

2-Oxo-1,2,3,4-tetrahydropyrimidines (THPMs) are important compounds due to their biological activities such as antitubercular [16], antihypertensive [17], antibacterial [18], anticancer agents [19], as calcium channel blockers [20] and inhibitors of the HIV virus [21]. Different activities of these compounds are related to the nature of the substituents located on the 4- and 5-positions of the heterocyclic ring. Recently, we studied the efficient oxidation of THPMs containing acetyl or carboethoxy groups on the 5-position of the heterocyclic ring by potassium peroxydisulfate (K$_2$S$_2$O$_8$) in aqueous acetonitrile under thermal [22], sono-thermal [23,24] and microwave [25] activations. According to the proposed mechanism and considering the results obtained in these studies, we found out that the removal of 4-hydrogen in the rate determining step occurs by *in situ* hydroxyl radical, an active hydrogen-abstracting species, formed in the reaction of potassium sulfate radical and water. This

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$$TiO_2 \xrightarrow[\lambda > 385 \text{ nm}]{h\nu} TiO_2 \, (e^-_{CB} + h^+_{VB})$$

$$h^+_{VB} + H_2O_{(ads)} \longrightarrow {}^{\cdot}OH_{(ads)} + H^+$$

$$e^-_{CB} + O_{2\,(ads)} \longrightarrow O^{\cdot-}_{2\,(ads)}$$

$$h^+_{VB} + \text{comp.} \xrightarrow{-e^-} \text{comp.}^{\cdot+}$$

$${}^{\cdot}OH_{(ads)} + \text{comp.} \xrightarrow{-H_2O} \text{comp.}^{\cdot} \qquad \xrightarrow{-H^{\cdot}} \text{Oxidation products}$$
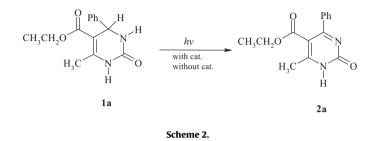
Scheme 1.

argument is supported by the influence of the steric and electronic effects of the substituents attached to C4- and C5-atoms of the heterocyclic ring on the rate of this step. In continuation, we have studied the light sensitivity of 5-carboethoxy- [26] and 5-acetyl-THPMs [27] in the electron-transfer induced photo-oxidation in chloroform. These results explain an electron-transfer process from excited THPMs to CHCl₃ and reconfirming the effect of the nature of these substituents on the rate of oxidation. The results of photochemical studies lead us to extend our investigations concerning the interaction of THPMs containing various substituents at 1-, 4- and 5-positions of the heterocyclic ring toward photo-excited TiO₂ anatase nanoparticles. The results should elucidate the effects of the nature and steric hindrance of the substituent on the rate of reaction.

2. Experimental

The THPMs were prepared according to the known procedure [28]. Titanium(IV) dioxide, anatase nanopowder (99.7%), anatase powder (99.9+%) and rutile powder (99.9+%) were purchased from Aldrich, and Degussa P-25 was purchased from Degussa, Germany. Melting points were determined on a Stuart Scientific SMP2 apparatus and are not corrected. IR spectra were recorded using KBr pellets on a Jasco FT/IR-6300 spectrometer. The ¹H and ¹³C NMR spectra (DMSO–d6) were recorded on a Bruker DRX-300 Avance and Bruker Avance III 400 spectrometers at 300, 400, 75.47, and 100.62 MHz. The ¹H NMR spectra are reported as follows: chemical shifts [multiplicity, number of protons, coupling constants J (Hz), and assignment]. Mass spectra were obtained on Platform II Mass Spectrometer from Micromass; EI mode at 70 eV. UV spectra were taken (in CH₃CN) with Shimadzu UV-160 spectrometer. All irradiations were carried out using a 400 W high-pressure Hg lamp from NARVA in Duran glass equipment, which was placed in a distance of 20 cm from light source.

The TiO₂ suspension (0.3 g TiO₂ anatase nanoparticles in 10 mL dry acetonitrile) was sonicated for 15 min to disperse TiO₂ uniformly in the solution. 100 μL of this suspension was added to solution of 0.01 mmol of THPM in 10 mL dry solvent, then the solution was magnetically stirred in the dark until a homogenous suspension was obtained. After that, the solution was irradiated with stirring until total disappearance of THPM. It should be noted that for the preparative scale, a solution of 0.1 mmol of THPMs and 12.5×10^{-2} mmol of TiO₂ anatase nanoparticles in 100 mL acetonitrile was irradiated until total disappearance of THPM. The mixture was centrifuged to remove TiO₂ effectively. The solution was separated by careful filtration; the solid material was washed with acetonitrile. Solvent was evaporated and the residue was recrystallized from n-hexane/ethyl acetate (otherwise is mentioned) to afford pure product. The known products were identified by comparison of their melting points and spectral data with those of the authentic samples. The physical and the spectral data of the new THPMs and the corresponding DHPMs are given as supplementary material.

Scheme 2.

3. Results and discussion

3.1. Photocatalyst activity and optimization of the reaction condition

In order to find a suitable form of TiO₂ for the electron-transfer induced oxidation of various THPMs, the solutions containing 0.01 mmol of ethyl 2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidin-5-carboxylate (**1a**) as a test substrate in dry acetonitrile in the absence of the photocatalyst or in the presence of 3.75×10^{-3} mmol of each of the photocatalysts anatase, rutile, Degussa P-25 (a mixture of 70% anatase and 30% rutile phases) and anatase nanoparticles were irradiated until maximum conversion of **1a** to **2a** (Scheme 2). The results shown in Fig. 1 indicated that the complete conversion of **1a** in shorter reaction time is observed using TiO₂ anatase nanoparticles, while irradiation in the presence of TiO₂ (anatase) and TiO₂ (rutile) resulted in 50% and 15% conversion of **1a**, respectively, and Degussa P-25 causes 90% conversion after the same irradiation time (3.75 h). Even though anatase should be the most active form of TiO₂, but some reports suggest that the presence of rutile phase with anatase introduces wider pore size distribution [29], this may be the cause of higher conversion observed using Degussa P-25. The effect of the particle size on the photocatalytic activity can be interpreted in terms of surface area. Generally, the smaller the particle size, the larger the surface area
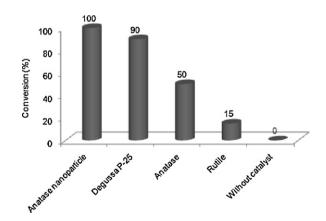

Fig. 1. The effect of TiO₂-type on the rate of photo-oxidation of **1a** after 3.75 h photolysis.
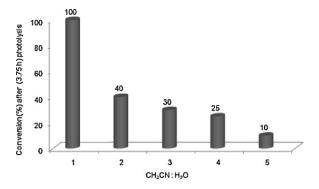
Fig. 2. The effect of the water content on photocatalytic oxidation of **1a** [CH_3CN/H_2O: (1) 10:0; (2) 9.5:0.5; (3) 9:1; (4) 8.5:1.5; (5) 8:2]; $TiO_2 = 3.75 \times 10^{-3}$ mmol.

Scheme 3.

and the higher the expected activity [30,31]. The important point of the presence of photocatalyst in this reaction is that **2a** was not formed in the absence of the photocatalyst even after 3.75 h irradiation.
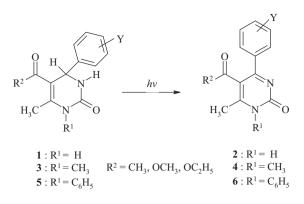
Since the amount of the photocatalyst has an important effect on the rate of reaction, irradiation of **1a** was carried out in dry acetonitrile in the presence of various amount of TiO_2 anatase nanoparticles. The results showed that the progress of reaction is influenced with increasing the amount of TiO_2 anatase nanoparticles up to an optimum loading of 12.5×10^{-3} mmol with simultaneous decrease of the irradiation time to 1.66 h. It should be noted that by further increasing the amount of TiO_2 anatase nanoparticles, the irradiation time did not decrease but a lower conversion of **1a** is observed. This may be possibly due to the screening effect by increasing the amount of the photocatalyst in solution and also due to self-quenching of the photocatalyst [32].

Due to solvent–solute interaction, especially in the electron-transfer induced reactions, the nature of solvent can also affect the rate of reaction. Therefore, irradiation of **1a** as test substrate in the presence of TiO_2 anatase nanoparticles was carried out in air saturated acetonitrile, ethanol and propan-2-ol. The results indicated that after 3.75 h irradiation, complete conversion of **1a** to **2a** was achieved in acetonitrile, whereas 45% conversion was observed in propan-2-ol. **1a** was obtained unchanged after the same irradiation time when carrying the experiment in ethanol.

Many TiO_2-sensitized photoreactions of organic compounds are carried out in water. According to the proposed mechanism (Scheme 1) the participation of hydroxyl radicals generated by the adsorbed water on the photogenerated hole is responsible for the oxidation process and also increasing the rate of reaction [15]. Based on our previous results concerning the oxidation of THPMs by $K_2S_2O_8$ in aqueous acetonitrile [22], the hydroxyl radical formed by reaction of water with potassium sulfate radical (obtained from thermal cleavage of $K_2S_2O_8$), acts as oxidizing agent in this oxidative process. Therefore, we have also carried out irradiation of **1a** in a mixture of CH_3CN/H_2O. The results presented in Fig. 2 indicated that by increasing the amount of water a decrease of the rate of conversion was observed.

Based on the above mentioned results and considering the optimization conditions, for better comparison of the effect of different substituents on the rate of reaction, the solutions of 0.01 mmol of various 4- and 5-substituted THPMs (**1a–q**), *N*1-methyl substituted THPMs (**3a–q**), *N*1-phenyl substituted THPMs (**5a,g,k**) and 3.75×10^{-3} mmol of TiO_2 anatase nanoparticles in 10 mL acetonitrile were irradiated until total disappearance of THPMs (Scheme 3). The results are presented in Table 1.

For a preparative work to obtain larger amount of oxidation products for the spectroscopic characterization, the solutions of 0.1 mmol of THPMs and 12.5×10^{-2} mmol of TiO_2 anatase nanoparticles in 100 mL acetonitrile were irradiated until total disappearance of THPMs. The TiO_2-sensitized oxidation of THPMs to their corresponding DHPMs was confirmed by comparison of the IR, UV, ^{1}H NMR, ^{13}C NMR and MS spectra of the products with those of starting THPMs based on the following observations:

I. A comparison of the IR spectra of the products **2a–q** with those of the reactants **1a–q** showed a decrease in the intensity of the NH vibration and a little shift to lower frequency, whereas in the cases of N1-substituted THPMs, **3a–q** and **5a,g,k**, disappearance of this vibration has been observed.

II. Due to the formation of 1-aza-1,3-diene (imino-diene) system in the heterocyclic ring which is cross-conjugated with 4-aryl substituent, this system benefits also from extended conjugation with the 2-CO π-bond and N-1 lone pair, therefore, the bathochromic shift in the UV spectra of photoproducts has been observed.

III. Analysis of ^{1}H NMR spectra of all THPMs considered in this study shows the lack of 3-NH and 4-H peaks due to being eliminated upon oxidation. Formation of the imino-diene system causes a shift of 1-NH peak in **2a–q** and also 1-NCH$_3$ peak in **4a–q** to lower fields due to the attachment to this conjugated system. In consistent with these observations, due to anisotropic effect of the semi-aromatic heterocyclic ring, the methyl group in 6-position, especially in **2a–q** is shifted downfield. Interestingly, in **4a–q**, no significant changes in the chemical shift of 6-CH$_3$ compared with those in **3a–q** has been observed. This is possibly due to gauche interaction of both methyl groups in 1- and 6-positions leading to an increase in the deviation of N-1 from planarity and consequent diminished aromatic character of the heterocyclic ring.

IV. Analysis of the ^{13}C NMR spectra supported also the changes as are also observed in the ^{1}H NMR spectra.

3.2. Mechanistic aspects

The results obtained in the present study concerning effects of the solvent, the presence of water and the nature of the substituents on the 1-, 4- and 5-positions of the heterocyclic ring on the rate of reaction are discussed separately.

The mechanism of TiO_2-sensitized oxidation of many organic compounds is illustrated in Scheme 1. As mentioned above, the excitation of TiO_2 by photons with energy equal to or larger than its band gap energy leads to the promotion of an electron from the valence band to the conduction band. This process results in the occurrence of an electron in the conduction band and leaving a positive hole in the valence band. Without any electron or hole trapping agent, recombination of e_{CB}^-/h_{VB}^+ occurs in a few nanoseconds and loses the excitation energy as heat [33]. Generally, molecular oxygen can act as an e_{CB}^- trapping agent, leading to the formation of

Table 1
Light induced oxidatiaon of THPM (**1a–q**; R^1 = H), *N*1-methyl substituted THPM (**3a–q**; R^1 = CH$_3$) and *N*1-phenyl substituted THPM (**5a,g,k**; R^1 = Ph).[a]

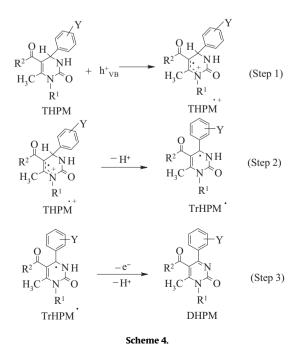| 1	Y	R^2	hν/h[b]	3	Y	R^2	hν/h[b]	5	Y	R^2	hν/h[b]
a	H	OCH$_2$CH$_3$	3.75	**a**	H	OCH$_2$CH$_3$	2	**a**	H	OCH$_2$CH$_3$	8.75
b	4-Br	OCH$_2$CH$_3$	2.5	**b**	4-Br	OCH$_2$CH$_3$	2				
c	4-F	OCH$_2$CH$_3$	3.5	**c**	4-F	OCH$_2$CH$_3$	2.5				
d	2-OCH$_3$	OCH$_2$CH$_3$	3.5	**d**	2-OCH$_3$	OCH$_2$CH$_3$	3				
e	3-OCH$_3$	OCH$_2$CH$_3$	4.25	**e**	3-OCH$_3$	OCH$_2$CH$_3$	3.25				
f	4-OCH$_3$	OCH$_2$CH$_3$	3.0	**f**	4-OCH$_3$	OCH$_2$CH$_3$	2.5				
g	4-NO$_2$	OCH$_2$CH$_3$	7.5	**g**	4-NO$_2$	OCH$_2$CH$_3$	4	**g**	4-NO$_2$	OCH$_2$CH$_3$	16
h	H	OCH$_3$	3.0	**h**	H	OCH$_3$	2.25				
i	4-Br	OCH$_3$	2.5	**i**	4-Br	OCH$_3$	2				
j	4-F	OCH$_3$	3.5	**j**	4-F	OCH$_3$	2.5				
k	H	CH$_3$	3.17	**k**	H	CH$_3$	2.5	**k**	H	CH$_3$	6.5
l	4-F	CH$_3$	1.75	**l**	4-F	CH$_3$	1.5				
m	2-OCH$_3$	CH$_3$	3.08	**m**	2-OCH$_3$	CH$_3$	2.75				
n	3-OCH$_3$	CH$_3$	3.08	**n**	3-OCH$_3$	CH$_3$	2.67				
o	4-OCH$_3$	CH$_3$	2.5	**o**	4-OCH$_3$	CH$_3$	2				
p	4-NO$_2$	CH$_3$	5.5	**p**	4-NO$_2$	CH$_3$	5.17				
q	H	Ph	4.17	**q**	H	Ph	3.42				

[a] A solution contains 0.01 mmol of THPMs and 3.75×10^{-3} mmol of TiO$_2$ anatase nanoparticles in 10 mL acetonitrile.

[b] Irradiation times (hours) are given after total disappearance of THPMs.

the superoxide anion radical. This process extends the lifetime of h$_{VB}^+$; therefore, the oxidation step is more likely to occur. In the present study and based on the obtained results, we will propose that the oxidation of THPMs should start by the donation of an electron from nitrogen lone pair (N1) to photogenerated hole producing the 2-oxo-1,2,3,4-tetrahydropyrimidinyl radical cation (THPM$^{+•}$), in which the positive charge and the electron is delocalized as being heteroallylic radical cation (Scheme 4). In the next step, the proton detachment from this species leads to the formation of 2-oxo-1,2,3-trihydropyrimidinyl radical (TrHPM$^•$), as a simultaneously stabilized allylic and benzylic radical. The second electron donation and proton detachment accomplish the reaction by the formation of the final product, namely, 2-oxo-1, 2-dihydropyrimidines (DHPMs).

The observed fast reaction in acetonitrile, as compared to that in ethanol or propan-2-ol, indicates that THPM as an electron-donor species should not be effectively solvated in acetonitrile, which is a polar aprotic solvent, whereas in alcoholic solvents, due to solvation phenomenon, hydrogen bonding can occur between the NH and the OH groups which leads to enhancement of the

effective volume of THPMs. This hinders facile electron donation from THPMs to photogenerated holes. This is also supported by the observed dimeric form in the crystal structure of THPMs, mediated by the interaction between 3-NH and 2-CO of the heterocyclic ring [34]. On the other hand, alcohols can compete with THPM in adsorption at TiO$_2$ surface *via* electron donation and undergoing oxidation [35,36]. It is expected that due to different sizes of solvent molecules, the steric hindrance affects the attraction between non-bonding electrons in the solvent molecule and photogenerated holes; therefore, ethanol can be better adsorbed at TiO$_2$ surface than propan-2-ol. Thus, the effective occupation of TiO$_2$ holes and better solvation of THPMs by ethanol molecules result in a faster oxidation of THPM in propan-2-ol than ethanol, which is also observed in this study. In the aqueous media, H$_2$O molecule is typically adsorbed at TiO$_2$ h$_{VB}^+$, generating a hydroxyl radical which is a powerful oxidant [37]. It has been expected that by adding water to the acetonitrile solution, the rate of reaction should be increased. Surprisingly, the results shown in Fig. 2 indicated that by increasing the water content, the oxidation rate is decreased. The observed behavior of water in decreasing the rate of reaction in this study is like those observed and discussed for ethanol and propan-2-ol, namely the solvation of THPM molecules and competing with THPMs by electron donation to photogenerated holes. The participation of holes in the photocatalytic oxidation can be evaluated using iodide ion acting as a scavenger and reacting with the valence band holes to suppress the oxidation of compounds [14]. By adding potassium iodide (KI) to the reaction mixture of **1a** and TiO$_2$ anatase nanoparticles in acetonitrile:water (8.5:1.5) (KI is not soluble in pure acetonitrile), the yield of oxidation is decreased approximately to 10% after 3.75 h irradiation. As an evidence of the competitive oxidation of I$^-$ to I$_2$, colour of the reaction mixture became yellow.

The results presented in Table 1 do not clearly distinguish between the effect of 5-carboethoxy and 5-carbomethoxy groups (the ester groups) with the same substituent at 4-position of the heterocyclic ring on the rate of reaction, whereas increasing the rate of reaction is observed by replacing these ester groups with the acetyl group. The results of electron-transfer induced photo-oxidation of 5-carboethoxy- and 5-acetyl-THPMs in CHCl$_3$ (electron transfer from excited THPMs to CHCl$_3$) [26,27] indicated that the presence of the acetyl group in 5-acetyl-THPMs causes a bathochromic shift in the UV spectrum which results in higher light absorbance and consequently an increase in the rate of reaction compared with those of 5-carboethoxy derivatives. But in the present study and in contrast to the electron-transfer induced photo-oxidation in CHCl$_3$ solution, the reaction starts
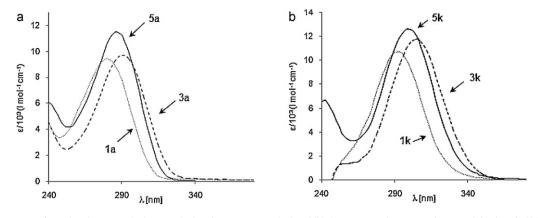

(Step 1)

(Step 2)

(Step 3)

Scheme 4.

Fig. 3. (a) UV spectra of 5-carboethoxy-NH- (**1a**), NCH$_3$- (**3a**) and NC$_6$H$_5$-THPMs (**5a**) and (b) the corresponding 5-acetyl-THPMs (**1k**, **3k** and **5k**) in acetonitrile.

by electron donation from THMPs in the ground state to photo-generated holes. Since under experimental conditions (irradiation at $\lambda \geq 280$ nm), the light absorption by THPMs cannot be totally excluded, therefore, due to higher reduction potential of acetonitrile compared with chloroform, only very low conversion of 5-acetyl-THPMs to the corresponding DHPMs is possible. This means that a maximum conversion of THPMs occurs by electron-transfer from THPMs in the ground state to photogenerated holes. A comparison of the irradiation times of 5-carboethoxy-THPMs (**a**–**g**), 5-carbomethoxy-THPMs (**h**–**j**) and 5-acetyl-THPMs (**k**–**p**) shows that, besides the effect of the nature of the 4-substituent, 5-acetyl-THPMs are reacted faster than the corresponding ester derivatives in the present study. Interesting results is the effect of introducing a methyl or a phenyl group instead of the hydrogen in position 1 of the heterocyclic ring. While *N*1-methyl substituted THPMs (**3a,g,k,q**) react faster than the *N*1-H derivatives (**1a,g,k,q**), *N*1-phenyl substituted THPMs (**5a,g,k**) cause a decrease in the rate of reaction. The UV spectra of 5-carboethoxy-NH-THPM (**1a**), 5-carboethoxy-NCH$_3$-THPM (**3a**) and 5-carboethoxy-NC$_6$H$_5$-THPM (**5a**) and the corresponding 5-acetyl-THPMs (**1k,3k,5k**), as representatives, are presented in Fig. 3. A bathochromic shift is observed
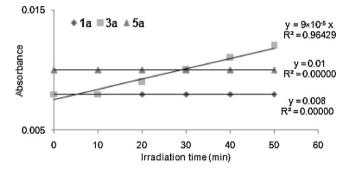

Fig. 4. Extinction time diagram obtained by direct irradiation of **1a**, **3a** and **5a** in acetonitrile.

by introducing the phenyl and methyl groups. This can be resulted in higher light absorption of the *N*1-substituted THPMs. Therefore, it is expected that if these compounds should be involved in the photo-oxidation reaction by absorption of the light photons (direct excitation), the order of **3a** > **5a** > **1a** should be obtained for their photochemical reactivity. Irradiations of **1a**, **3a** and **5a** in
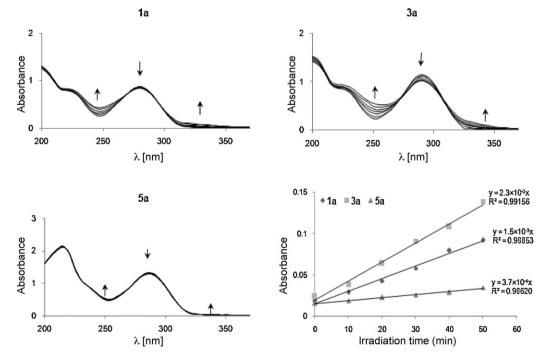

Fig. 5. Reaction spectra of TiO$_2$-sensitized oxidation of **1a**, **3a** and **5a** in acetonitrile and the corresponding extinction time (ET) diagrams; time interval 10 min.

the absence of the photocatalyst have been followed by UV spectroscopy. The slopes in the extinction time (ET) diagram for these compounds (Fig. 4) derived from their UV reaction spectra indicate that no changes in the UV spectra of **1a** and **5a** are observed after 50 min irradiation, whereas a bathochromic shift in the UV reaction spectra of **3a** has been observed due to the formation of the corresponding product **4a**.

The different behavior of 1-CH$_3$ and 1-Ph groups on the rate of TiO$_2$-sensitized photo-oxidation reaction supports again our proposal concerning the interaction of THPMs in the ground state with the photogenerated holes. The photocatalytic oxidation reactions of **1a**, **3a** and **5a** have been followed by UV spectroscopy. Bathochromic shift in the UV spectra and increased absorption have been observed owing to the formation of the 4-amino-1-aza-1,3-diene system. The corresponding plots of the ET diagram of these reactions, illustrated in Fig. 5 compared with those presented in Fig. 4, show clearly the effect of the presence of the photocatalyst and comparative effect of hydrogen, methyl and phenyl substitutions on the rate of reaction.

3.3. Computational study

The observed comparative behavior of these compounds, especially the strong effect of the substitution in the 1-position of the heterocyclic ring on the rate of photochemical oxidation reaction, can be partially explained by the results obtained from *ab initio* calculations. Computational study on the geometries of various 1-, 4- and 5-substituted 2-oxo-1,2,3,4-tetrahydropyrimidines carried out at the B3LYP/6-31++G(d,p) level of theory elucidates the electronic and the steric effects of the substituents on the optimized structures of these compounds [38–41]. According to these results, the heterocyclic ring appears as quasi-planar structure (boat conformation), in which the aryl groups occupy a pseudo-axial position (Fig. 6). In this structure, the C-4 and N-1 atoms are not in the same plane as other remaining four atoms (C-2, N-3, C-5 and C-6). The important points in the computational studies of various 1-, 4- and 5-substituted THPMs were to find the factors which influence the following items:

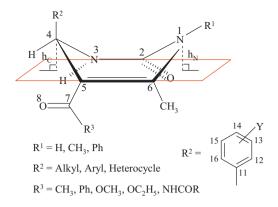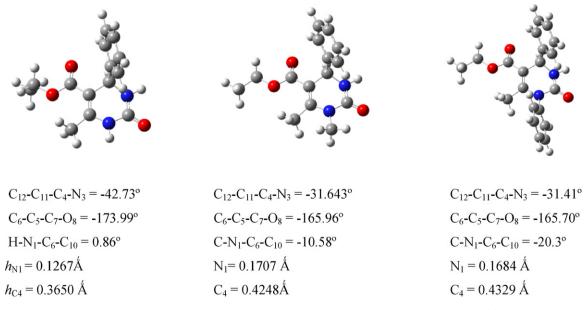i) The amounts of deviations of the C-4 and also N-1 centers from ring planarity.

R^1 = H, CH$_3$, Ph

R^2 = Alkyl, Aryl, Heterocycle

R^3 = CH$_3$, Ph, OCH$_3$, OC$_2$H$_5$, NHCOR

Fig. 6. General structures of 2-oxo-1,2,3,4-tetrahydropyrimidines (THPMs).

ii) The dihedral angles of 5-CO groups of the ester or the acetyl moiety with respect to the C$_5$=C$_6$ bond.
iii) The dihedral angles formed by C$_{12}$C$_{11}$C$_4$N$_3$ atoms (the angle of the aromatic ring on C$_4$ with the THPM ring).
iv) The electron density of the heterocyclic and also aromatic ring atoms and finally.
v) The additional effects of the substitution in the 1-position on the above mentioned items.

The results explained that the above mentioned items were influenced by the orientation of the aryl group attached to C-4 ring toward the heterocyclic ring, especially the position of the additional substituent on the phenyl ring, the stereoeletronic effect of the acetyl, carboethoxy and carbomethoxy groups located on C-5 and effectively by the substitution on N-1.

Recently, we reported the effect of the nature of the substituent on the electrochemical oxidation of various substituted 2-oxo-1,2,3,4-tetrahydropyrimidin-5-carboxamides [41]. These results and the data obtained from computational studies of these compounds [39] support the argument that the first electron donation occurs from N-1 which followed the first proton detachment forming 2-oxo-1,2,3-trihydropyrimidinyl radical (TrHPM$^\bullet$), as also represented in Scheme 4. The stability of this intermediate and also the value of the oxidation peak potential are dependent more on

C$_{12}$-C$_{11}$-C$_4$-N$_3$ = -42.73°

C$_6$-C$_5$-C$_7$-O$_8$ = -173.99°

H-N$_1$-C$_6$-C$_{10}$ = 0.86°

h_{N1} = 0.1267Å

h_{C4} = 0.3650 Å

C$_{12}$-C$_{11}$-C$_4$-N$_3$ = -31.643°

C$_6$-C$_5$-C$_7$-O$_8$ = -165.96°

C-N$_1$-C$_6$-C$_{10}$ = -10.58°

N$_1$ = 0.1707 Å

C$_4$ = 0.4248Å

C$_{12}$-C$_{11}$-C$_4$-N$_3$ = -31.41°

C$_6$-C$_5$-C$_7$-O$_8$ = -165.70°

C-N$_1$-C$_6$-C$_{10}$ = -20.3°

N$_1$ = 0.1684 Å

C$_4$ = 0.4329 Å

Fig. 7. The optimized structures of **1a**, **3a** and **5a** (from left) obtained at the B3LYP/6-31++G(d,p) level of theory.

the nature of C4 substitution, especially on the type and location of the additional substituent on the aromatic ring at C4 position. The important part of the photosensitized oxidation reaction of THPMs is the adsorption of the substrate at the semiconductor surface, as a key step in the electron-transfer process. The parameters, either electronic or steric, especially the substitution in position 1, which inhibits such adsorption, resulted in slower conversion of THPMs to the corresponding DHPMs. The UV reaction spectra of TiO_2 sensitized oxidation of compounds **1a**, **3a** and **5a**, as representative substrates, and the corresponding extinction time diagram shown in Fig. 5 indicate that the order of the oxidative ability of these compounds is **3a** > **1a** > **5a**. This explains that the enhanced reactivity of **3a** compared with **1a** is due to the positive inductive effect of the methyl group, whereas the presence of the large and electron-withdrawing phenyl group in **5a** causes decreasing rate of reaction. The influence of the steric hindrance on the lowering the rate of oxidation reaction is also reported on the photo-oxidative dealkylation of α-alkylbenzyl methyl ethers induced by TiO_2 [42]. Computational studies carried out on some of these compounds support this argument [40]. As representative, the characteristic data of the computational studies of compounds **1a**, **3a** and **5a** obtained from their optimized structures are presented in Fig. 7. These results explain that by changing the substitution in the 1-position from hydrogen to methyl or phenyl, the dihedral angle of the aromatic ring toward the heterocyclic ring (C_{12}–C_{11}–C_4–N_3), the dihedral angle of 5-CO with respect to the C_5=C_6 bond ($O_8C_7C_5C_6$), the dihedral angle formed by $H(C)N_1C_6C_{10}$ atoms and also deviation of the C_4- and N_1-atoms from ring planarity are affected. The interesting point is that these dihedral angles depend on the type of substituent in 1-position. This observation is possibly due to increased gauche interaction of 6-CH_3 with 1-H, 1-CH_3 and 1-C_6H_5.

4. Conclusion

In conclusion, the present study reports photo-sensitized oxidation of various 1-, 4-, and 5-substituted 2-oxo-1,2,3,4-tetrahydropyrimidines (THPMs) by TiO_2 anatase nanoparticles to their corresponding 2-oxo-1,2-dihydropyrimidines (DHPMs). The results explain the steric and the electronic effects of the substitutions especially at the 1-position on the rate of oxidation. These results also indicate that in comparison with the steric and the electronic effects of the 4-substituents on the rate of reaction, the type of the substituent on the 5-position has a little effect. All these facts support the argument that a key step of this oxidative reaction is the electron transfer from THPM molecule to photogenerated holes. In protic solvents, or in the presence of water, the oxidative reaction is retarded.

Acknowledgments

Appendix A. Supplementary data

References

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