J IRAN CHEM SOC (2012) 9:805–813
DOI 10.1007/s13738-012-0097-0

ORIGINAL PAPER

Light-induced dehydrogenation of 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides

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Received: 6 January 2012 / Accepted: 17 April 2012 / Published online: 4 May 2012

Abstract The light sensitivity of various 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides (THPMs) was investigated by exposing them to UV light in order to elucidate the effects of the nature of the substituents located on the 4- and 5-positions of the heterocyclic ring and also the effect of an oxygen or argon atmosphere on the rate of reaction. The rate of reaction is faster under argon than under oxygen and is influenced by the nature of the substituent on the 4- and 5-positions of the THPM ring. Furthermore, it is found that the dehydrogenation of THPM-amides is faster than that of the corresponding 5-ethoxycarbonyl- and 5-acetyl-THPMs. In contrast to the solution photochemistry, no changes have been observed by irradiation in the solid state. A mechanism concerning an electron transfer from excited THPM to acetonitrile has been proposed for this reaction.

Keywords Biginelli compounds · 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides · Photooxidation · Photodehydrogenation · Electron transfer

Introduction

In 1893, a multi-component reaction was discovered by Pietro Biginelli [1] which involves condensation of an aldehyde, a ketoester and urea in acidic medium. The products of this reaction were 2-oxo-1,2,3,4-tetrahydropyrimidines (THPMs), known also as 3,4-dihydropyrimidinones or Biginelli compounds which, based on their biological activities such as calcium channel blockers [2], as antihypertensive [3, 4], antitubercular [5], antitumor [6], antiviral [7] and anticancer [8] agents are important compounds. Efficient methods of their synthesis, their chemical and photochemical behavior, and their pharmacological properties are still under investigation. Dehydrogenation of the title compounds to the corresponding 2-oxo-1,2-dihydropyrimidines (DHPMs) or pyrimidin-2(1*H*)-ones may be useful for the preparation of the parent unsaturated heterocycles. Several oxidants have been applied in connection with thermal, microwave and ultrasound activation for this conversion [9–13]. Recently, we have investigated the effect of the nature of the substituent on 4-position of various 5-ethoxycarbonyl- and 5-acetyl-2-oxo-1,2,3,4-tetrahydropyrimidines in the dehydrogenation of these compounds by potassium peroxydisulfate ($K_2S_2O_8$) under thermal [10, 13], microwave [11], and ultrasound [12, 13] activation. The results of these studies indicated that the ethoxycarbonyl derivatives are oxidized faster than the corresponding acetyl compounds. In continuation to these works, we have synthesized various 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides [14] and investigated also their sensitivity towards dehydrogenation by tetrabutylammonium peroxydisulfate [$(n\text{-}Bu_4N)_2S_2O_8$] in order to elucidate the effects of the substituent on the 4-position and especially the effects of the substituent in the 5-carboxamide group on the rate of reaction in comparison to the ethoxycarbonyl and the acetyl derivatives [15]. The new results support our suggestion of a rate enhancement by the presence of the less electron withdrawing amide group compared with the acetyl and ethoxycarbonyl groups.

Electronic supplementary material The online version of this article (doi:10.1007/s13738-012-0097-0) contains supplementary material, which is available to authorized users.

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When evaluating the suitability of the title compounds as pharmaceuticals, the knowledge of any light sensitivity may be important, because they can easily lose their biological activities due to some molecular changes by exposing them to UV light. One class of these compounds is 1,4-dihydropyridines (DHPs) and their pharmaceutical properties such as their activity as calcium channel blockers are well known [16]. Our experience concerning the photochemistry of these compounds either in solution phase [17] or in the solid state [18], especially to elucidate the effect of the nature of the substituents located on 3-, 4- and 5-positions of dihydropyridine ring on the rate of photoreactions [17, 18], led us to extend our investigation to another class of heterocyclic compounds with pharmaceutical properties, namely Biginelli compounds. Recently, we have reported on the electron transfer-induced photodehydrogenation of various 4-aryl-substituted tetrahydropyrimidinones bearing carboethoxy or acetyl groups on 5-position of the heterocyclic ring [19, 20]. The results indicated that the presence of the ethoxycarbonyl or the acetyl groups on 5-position has a larger effect on the rate of reaction than the nature of 4-substituent. These results also indicated that due to the bathochromic shift of the acetyl group in 5-acetyl-THPMs, the rate of photodehydrogenation has been increased compared with those of the 5-ethoxycarbonyl derivatives. This can be attributed to the higher light absorbance of the acetyl derivatives compared to the ethoxycarbonyl derivatives. The obtained photochemical findings and also the recent publications concerning the pharmaceutical properties of 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides [5, 8] led us to investigate the photoreaction of these compounds in solution under oxygen and argon atmosphere and also in the solid state.

The aims of the present work were:

- To elucidate the effect of the nature of 4-substituent on the rate of reaction.
- To elucidate the effect of various 5-carboxamide groups as less electron withdrawing groups compared with 5-ethoxycarbonyl or 5-acetyl groups on the rate of reaction.
- To investigate the effect of oxygen or argon atmosphere on the rate of reaction.
- To compare the photochemical behavior of these compounds in solution phase and in the solid state.

Experimental

2-Oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides (**1a**–**p**) were synthesized according to the reported procedure [14]. All irradiations were carried out using a 400 W high-pressure Hg lamp from NARVA in Pyrex tubes and a Duran cell, which were placed in a distance of 20 cm from the light source. The UV reaction spectra were taken (in CH_3CN) with a Shimadzu UV-160 spectrometer.

The procedure for photodehydrogenation of 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides

Two separate Pyrex tubes (280 nm) containing 0.01 mmol of each of THPMs **1a**–**p** in 10 mL of dry acetonitrile ($c = 1$ mM) were irradiated while bubbling argon or oxygen through the solution during irradiation. The reaction was followed by thin layer chromatography (TLC) until maximum conversion of 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides. For the preparative work to obtain a large amount of products, a solution containing 0.1 mmol of THPMs in 100 mL of dry acetonitrile in a Duran cell is irradiated until maximum conversion of THPMs. The solvent was evaporated and the products were obtained by recrystallization from *n*-hexane/ethyl acetate. The photoproducts **2a–p** were identified by comparison of their melting points, UV, IR, ^{1}H NMR, and mass spectra with those reported earlier [15].

Irradiation of a solid sample

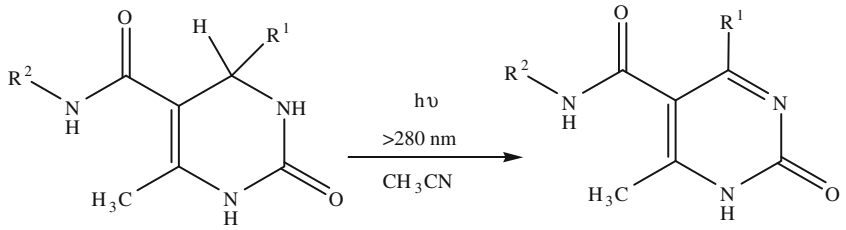
A sample of **1f** (113 mg) was ground in a mortar and strewn on a glass surface (15 cm × 15 cm) placed on a water cooled plate and exposed to the Pyrex-filtered light of a 400 W high-pressure mercury light source mounted inside a reflector at a distance of 40 cm from the glass surface.

Results and discussion

A solution of **1a**–**p** in CH_3CN was irradiated under oxygen and argon atmosphere until maximum conversion of **1a**–**p** (Scheme 1). The results are summarized in Table 1.

The characterization of the products **2a–p** was achieved by comparison of their IR, ^{1}H NMR, ^{13}C NMR, MS and UV data with those of the starting materials **1a**–**p** as follows:

- IR spectra showed a decrease in the intensity of the NH vibration with small shift to lower frequency in **2a–p** when compared with those in **1a**–**p**.
- ^{1}H NMR spectra of **2a–p** compared with those of **1a**–**p** showed following changes:
  - the lack of 3-NH and 4-H resonances,
  - the shifts of 1-NH and ArNH resonances to lower field, and



1a-p **2a-p**

Scheme 1 Photodehydrogenation of 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides

Table 1 Photodehydrogenation of 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides (**1a**–**p**) under oxygen and argon atmosphere

1	R^1	R^2	2	Time/h (yield/%)[a]	
				Ar	O_2
a	C_6H_5–	C_6H_5–	**a**	6 (89)	8 (86)[b]
b	C_6H_5–	$C_6H_5CH_2$–	**b**	7.5 (91)	9 (88)[b]
c	C_6H_5–	*o*-ClC_6H_4–	**c**	4 (91)	5 (89)[b]
d	C_6H_5–	*p*-ClC_6H_4–	**d**	4.5 (89)	6.5 (86)[b]
e	C_6H_5–	*p*-BrC_6H_4–	**e**	5 (88)	7 (86)[b]
f	*o*-ClC_6H_4–	*o*-ClC_6H_4–	**f**	1.75 (92)	2.5 (92)
g	*m*-ClC_6H_4–	*o*-ClC_6H_4–	**g**	3.5 (89)	6 (87)[b]
h	*p*-ClC_6H_4–	*o*-ClC_6H_4–	**h**	2.5 (90)	5.5 (87)[b]
i	*o*-BrC_6H_4–	*o*-ClC_6H_4–	**i**	2 (93)	3.25 (91)
j	*p*-BrC_6H_4–	*o*-ClC_6H_4–	**j**	4.5 (89)	6.5 (84)[b]
k	*m*-$NO_2C_6H_4$–	*o*-ClC_6H_4–	**k**	10 (86)[c]	12 (85)[c]
l	*p*-$NO_2C_6H_4$–	*o*-ClC_6H_4–	**l**	2.5 (90)	4 (90)
m	*m*-$MeOC_6H_4$–	*o*-ClC_6H_4–	**m**	3 (87)[c]	6.5 (82)[b,c]
n	*p*-$MeOC_6H_4$–	*o*-ClC_6H_4–	**n**	2.5 (90)	5 (87)[b]
o	*p*-MeC_6H_4–	*o*-ClC_6H_4–	**o**	4.5 (88)	7 (84)[b]
p	$MeCHC_6H_5$–	*o*-ClC_6H_4–	**p**	2.5 (75)	3.5 (65)[b]

[a] Isolated yields

[b] The formation of trace amounts of unidentified products is observed

[c] The reactions were not complete in these cases and the times are given after maximum conversion of these THPMs

– the shift of the 6-CH_3 resonance to lower field due to the attachment of this group to the extended C=O conjugated aza-diene system.

- A comparison of the UV data of **2a–p** with those of **1a–p** indicates that the formation of the aza-diene system in **2a–p**, which is cross conjugated with 4-aryl substituent and also conjugated with 1-NH lone pair and 2-CO, causes a bathochromic shift in the UV spectra.

The results presented in Table 1 indicate that the rate of reaction is dependent on the following factors:

1. In all cases, the irradiation times are shorter by carrying out the experiments under argon atmosphere. It seems that both excited states (singlet and triplet) are involved in the reaction, since the reaction was not totally quenched by carrying out the experiment under oxygen purging during the irradiation. We have followed the photooxidation of compound **1c** as a representative example in argon saturated solution and also in oxygen saturated solution (each $c = 5.32 \times 10^{-5}$ M). Two isosbestic points were observed in each reaction spectrum. A comparison of the slope in the extinction versus time diagrams (ET diagrams) [19] at 335 nm equal to 119.5×10^{-4} (under argon) and 115.0×10^{-4} (under oxygen) showed that the reaction is faster under argon than under oxygen atmosphere, which supports the above-mentioned argument and also the required irradiation time of 4 and 5 h under argon and oxygen, respectively, by the experimental work (Fig. 1). The results of this experiment are also supported by plotting

of the ET diagrams for reaction of compound **1l** (with *p*-nitrophenyl) and **1n** (with *p*-methoxyphenyl) on C-4 in argon saturated solution. Total disappearance of **1l** and **1n** is observed after 2.5 h, which is in agreement with the values obtained for the slopes of the ET diagrams 149.0×10^{-4} and 150.0×10^{-4}, respectively.

2. The nature of both R^1 at C_4 and R^2 in the C_5-carboxamide function influences the rate of reaction.
3. Whereas a clean and faster reaction has been observed when irradiating under argon atmosphere, irradiation under oxygen atmosphere resulted in the formation of trace amounts of some hitherto unidentified by-products and in a retarded reaction.
4. Variation of the 4-aryl groups while keeping the 5-carboxamide group constant (in **1c, f–p**) influences the rate of reaction to a larger extent than varying the substitution in the N=aryl moiety of the 5-carboxamide while maintaining the 4-aryl group constant (as in **1a–e**). This clearly showed that the balance of the electronic (inductive and resonance) effects and the location of the additional substituent on the phenyl ring influences the rate of reaction.

Since we have observed a clean photodehydrogenation reaction of 5-ethoxycarbonyl- and 5-acetyl-2-oxo-1,2,3,4-tetrahydropyrimidines in chloroform solution under argon atmosphere [20, 21], we have also carried out the photoreactions of 5-carboxamide derivatives (**1c** and **1f**) as test substrates in chloroform under oxygen or argon atmosphere. TLC monitoring of the reaction mixtures showed that the reactions were completed under argon atmosphere after 3 and 1 h irradiations, respectively, whereas these dehydrogenations under oxygen atmosphere were completed after 4.5 and 2 h of irradiation, while the formation of the oxidation products **2c** and **2f** besides hitherto unidentified by-products was also observed under both atmospheres. Therefore, for better comparison of the results in our new study with those obtained by irradiation of 5-ethoxycarbonyl and 5-acetyl derivatives in chloroform [20, 21], we have carried out simultaneous irradiation of some 5-ethoxycarbonyl and 5-acetyl derivatives (Scheme 2) and some carboxamide derivatives with the same concentration in acetonitrile solution under argon atmosphere, to elucidate the nature of solvent on the rate of reaction. The results are presented in Table 2.

The results show that the three amide derivatives **1c**, **f**, **n** are dehydrogenated significantly faster than the corresponding ethoxycarbonyl and acetyl derivatives. A comparison of the UV data of 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides (Table 3) with those of 5-ethoxycarbonyl and 5-acetyl derivatives (given as supplementary materials and also reported earlier [20, 21]) indicates that almost all these compounds absorb the UV light in the same region with the same intensities. Since the same concentrations of these compounds were exposed to the UV light, either the extent of the possible deactivation processes of the molecules in the singlet or triplet excited states must be the reason for the observed different irradiation time required for maximum conversion, or the role of the nature of 5-substituent on the heterocyclic ring influences the time of reaction. Since the electron withdrawing character of the carbonyl group in the amide

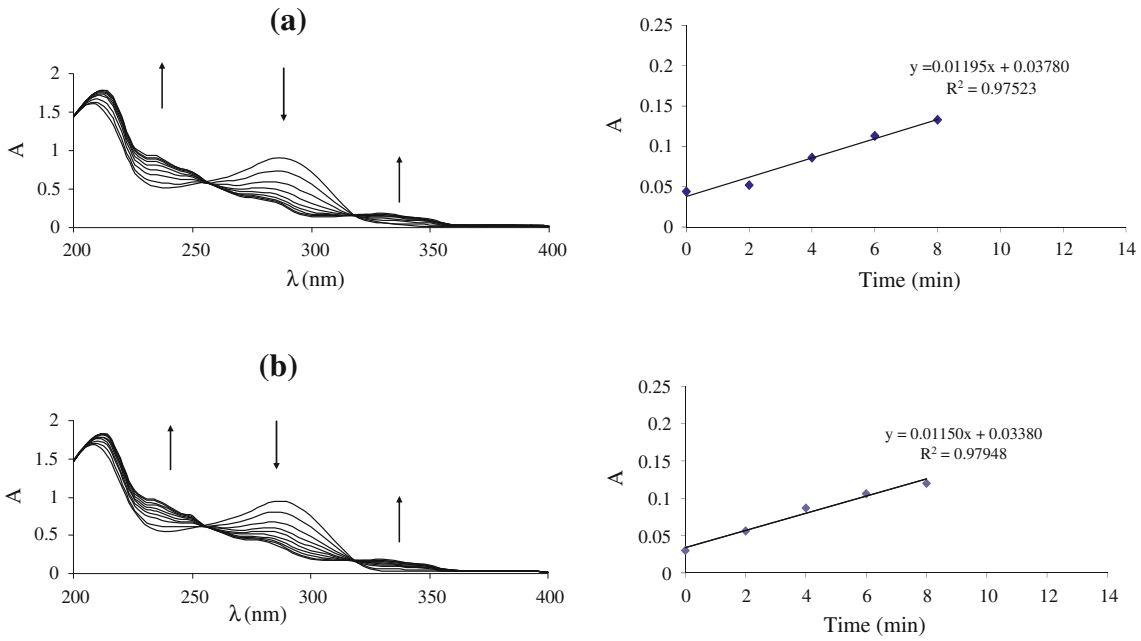
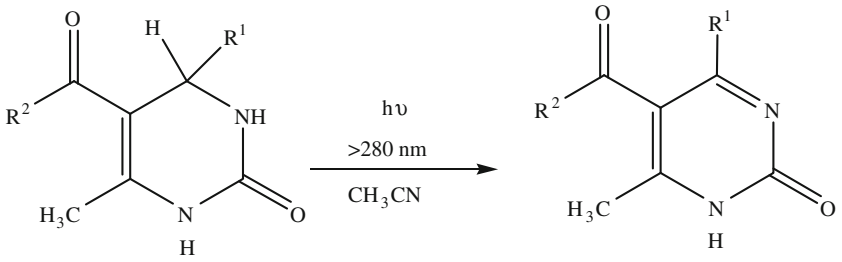


Fig. 1 The reaction spectra of (**a**) argon and (**b**) oxygen saturated solution of **1c** and the corresponding ET diagrams at 335 nm in acetonitrile



3: $R^2 = OC_2H_5$ **4**: $R^2 = OC_2H_5$

5: $R^2 = CH_3$ **6**: $R^2 = CH_3$

Scheme 2 Photodehydrogenation of 5-acetyl- and 5-ethoxycarbonyl-2-oxo-1,2,3,4-tetrahydropyrimidines to 5-acetyl- and 5-ethoxycarbonyl-2-oxo-1,2-dihydropyrimidines

Table 2 Photodehydrogenation of 5-*N*-(2-chlorophenyl)-carboxamido-, 5-acetyl- and 5-ethoxycarbonyl-2-oxo-1,2,3,4-tetrahydropyrimidines in acetonitrile under argon atmosphere

THPM	R^1	Product	Time (h)	Conversion (%)
1c	Ph	**2c**	4	100
3a	Ph	**4a**	4	0
5a	Ph	**6a**	4	~5
1f	2-ClC_6H_4	**2f**	1.75	100
3b	2-ClC_6H_4	**4b**	1.75	~5
5b	2-ClC_6H_4	**6b**	1.75	~20
1n	4-$MeOC_6H_4$	**2n**	2.5	100
3c	4-$MeOC_6H_4$	**4c**	2.5	~20
5c	4-$MeOC_6H_4$	**6c**	2.5	~40

Table 3 UV-absorption [λ_{max}/nm] of 5-carboxamide derivatives (**1a–p**) and the corresponding photoproducts (**2a–p**) in ethanol solution

1	λ_{max} (log ε)	**2**	λ_{max} (log ε)
a	282.5 (4.01), 205.5 (4.31)	**a**	320 (3.61), 251 (4.13), 205 (4.31)
b	272.5 (3.69), 206.5 (4.32)	**b**	319 (3.71), 205.5 (4.32)
c	288 (4.26), 210 (4.56)	**c**	319 (4.05), 245 (4.48), 210.5 (4.59)
d	279 (4.32), 206 (4.40)	**d**	318 (3.87), 254.5 (4.40), 206 (4.45)
e	286 (4.16), 206 (4.37)	**e**	317 (3.76), 257.5 (4.36), 205.5 (4.39)
f	289 (3.84), 206 (4.33)	**f**	306 (4.05), 240 (4.41), 213 (4.62)
g	285 (3.80), 206.5 (4.22)	**g**	317 (3.52), 244 (4.02), 206.5 (4.31)
h	275 (4.11), 205 (4.24)	**h**	318 (3.37), 248.5 (3.84), 205.5 (4.09)
i	279 (4.27), 209 (4.53)	**i**	304 (3.67), 246 (4.01), 207.5 (4.37)
j	290 (4.08), 210 (4.49)	**j**	316 (4.06), 248 (4.51), 211 (4.61)
k	266 (4.21), 209.5 (4.47)	**k**	318 (3.68), 232.5 (4.34), 208.5 (4.42)
l	272 (4.22), 206 (4.38)	**l**	336 (3.88), 259.5 (4.32), 209 (4.51)
m	282 (3.86), 204.5 (4.31)	**m**	316 (3.43), 254 (3.78), 204 (4.08)
n	283 (4.35), 212 (4.32).	**n**	319.8 (4.13), 264.8 (4.10), 212.4 (4.16)
o	288.5 (4.15), 208.5 (4.49)	**o**	306 (3.90), 248 (4.23), 207.5 (4.48)
p	283.5 (4.04), 207.5 (4.44)	**p**	302 (3.50), 242 (3.91), 206.5 (4.26)

moiety compared to the ester or the acetyl moieties is expected to be lower, it should be expected that photodehydrogenation of the carboxamide derivatives be faster than that of corresponding ethoxycarbonyl and acetyl derivatives. It should be noted that due to very low solubility of the oxidation products in acetonitrile, these were precipitated during the irradiation and did not compete effectively with the THPMs by light absorption.

We have proposed earlier a rationale for the electron transfer-induced photooxidation of 5-ethoxycarbonyl and 5-acetyl derivatives in chloroform, in which chloroform was involved as an electron-acceptor species from excited THPMs [20, 21]. A comparison of the irradiation times required for compounds **1c, f** in acetonitrile (Table 1) with those obtained in chloroform clearly showed that the reaction is faster in chloroform. These results support also our suggestion to propose the same reaction mechanism by carrying the irradiation in acetonitrile. The slower reaction in acetonitrile relative to chloroform can be explained by comparison of the reduction potentials of both solvents. The reduction potentials of acetonitrile and chloroform are reported −3.1 and −1.77 V (vs. FC^+/FC, Ferrocene), respectively [22, 23]. Therefore, according to the proposed mechanism, the electron transfer from excited THPMs to $CHCl_3$ should occur faster than that to CH_3CN.

The molar absorption coefficient for compound **1c** at 300 nm in acetonitrile ($\varepsilon = 13{,}534$) and in chloroform ($\varepsilon = 11{,}466$) and also for compound **1f** at 300 nm in acetonitrile ($\varepsilon = 8{,}853$) and in chloroform ($\varepsilon = 12{,}105$) is obtained. Due to different values and irrespective of the reduction potential of solvent, we should expect a faster reaction for **1c** in acetonitrile than that in chloroform, but slower reaction for **1f** in acetonitrile than that in chloroform, because the excited **1c** and **1f** are formed better in acetonitrile and chloroform, respectively. The experimental results indicate that all photoreactions are faster in chloroform than in acetonitrile. This means, that independent of the efficiency of light absorption of THPM, the important factor is the reduction potential of solvent, as electron-acceptor molecule in our reaction. The UV spectra of **1c** and **1f** as the representative examples are shown in Fig. 2.

Furthermore, activation entropy for the electron transfer to $CHCl_3$ is expected to be lower than CH_3CN due to the threefold symmetry of the bridging atom (3 chlorine atoms) in the former as compared to onefold symmetry of the bridging atom (N on the CN group) in the latter for accepting an electron from excited THPMs. In other words, stereoselectivity of the electron transfer reaction [24, 25] to $CHCl_3$ is lower than that to CH_3CN. This supports more efficient electron transfer to chloroform as compared to that to acetonitrile. The involvement of acetonitrile as an electron-acceptor species, also proposed in our reaction, is supported by the following reactions:

- Photooxidation of some nickel(II) macrocyclic complexes caused by the electron transfer from excited molecule to acetonitrile [26, 27].
- Cyanation and cyanomethylation of kopsamine by the electrolysis of kopsamine in acetonitrile solution [28]. This is occurred in part by decomposition of the acetonitrile solvent after accepting an electron and following cyanation and cyanomethylation of kopsamine.

The proposed mechanism of photodehydrogenation of THPM-carboxamides in acetonitrile is illustrated in Scheme 3.

According to the proposed rationale for the electron transfer from excited THPM either in the singlet or triplet states to acetonitrile resulted in the occurrence of the ionic species, namely, tetrahydropyimidine radical cation ($THPM^{+}\cdot$) and acetonitrile radical anion ($CH_3CN^{-}\cdot$). Deprotonation at C4 resulted in the formation of 2-oxo-1,2,3-trihydropyrimidinyl radical (TrHPM·), which is simultaneously an allylic and a benzylic radical. Further electron detachment and the proton removal from TrHPM· resulted in the formation of the oxidation products, namely, the corresponding 2-oxo-1,2-dihydropyrimidines (DHPMs). The effect of the nature of the substituent especially in 4-position on the time of irradiation prompted us to carry the computational study to explain the obtained results by photodehydrogenation of these compounds and to compare them with those of 5-ethoxycarbonyl and 5-acetyl derivatives and finally to confirm the proposed mechanism.

Density functional theory at B3LYP/6-31++G** level has been applied to study structural, electronic and bonding characteristics of various 4-substituted 2-oxo-1,2,3,4-tetrahydropyrimidines containing acetyl, ethoxycarbonyl [29] or carboxamide groups [30] on 5-position. The results indicate that:

1. The six-membered heterocyclic ring in all series of compounds adopts a boat conformation, flatted at N1 towards an envelope conformation, with a *pseudoaxial* orientation of the C4-substituent (Fig. 3).

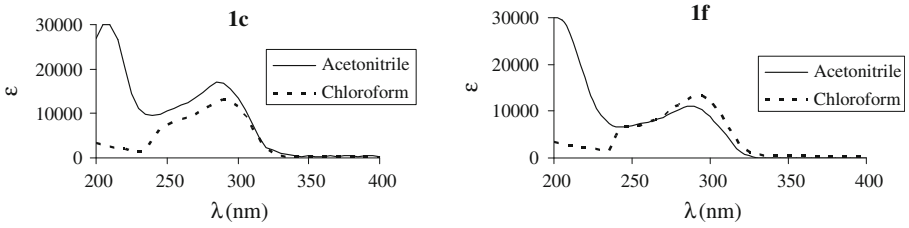
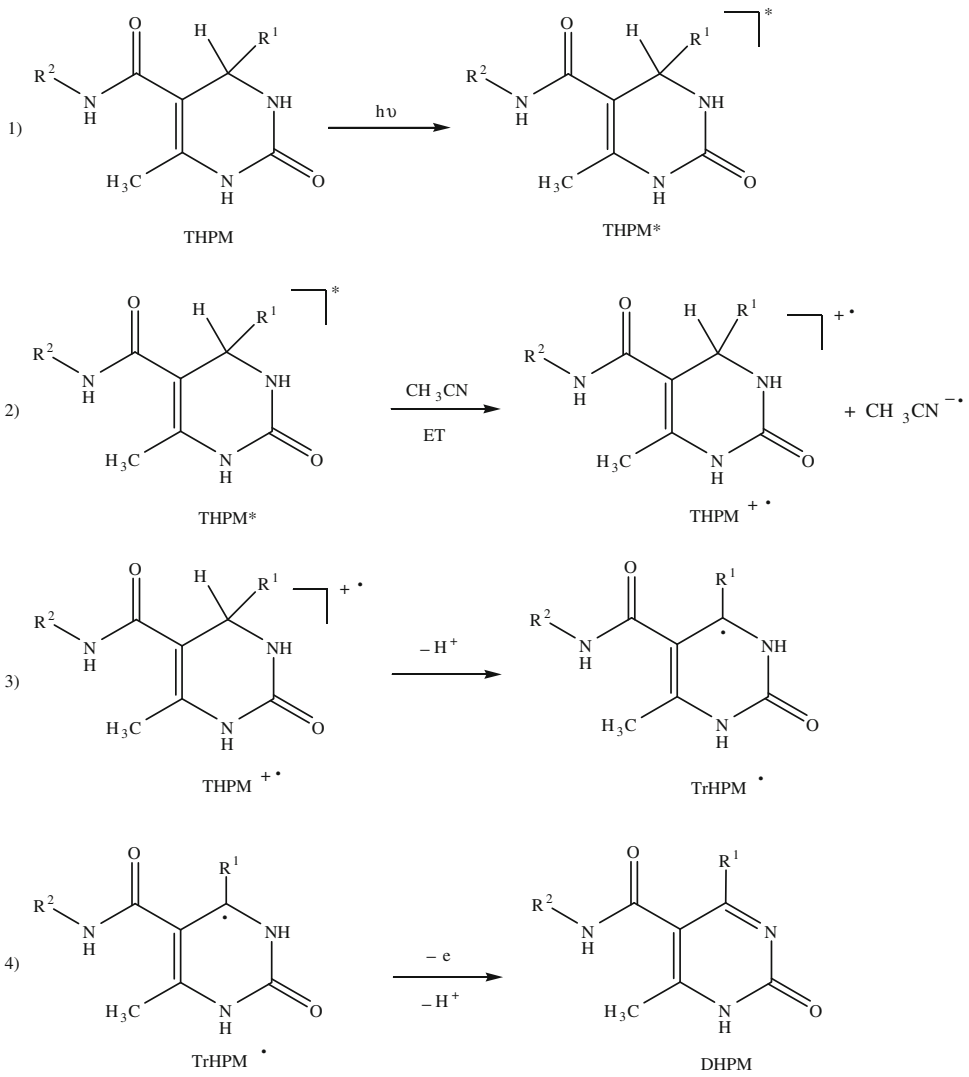


Fig. 2 UV spectra of compounds **1c** and **1f** in acetonitrile and chloroform

Scheme 3 The proposed rationale for photodehydrogenation of 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides



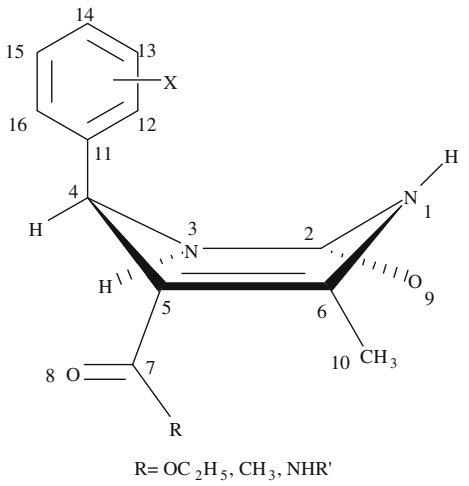


Fig. 3 Boat conformation of the heterocyclic ring of THPMs **1** with *pseudoaxial* orientation of the C4-substituent

2. The aryl and THPM rings are not co-planar and deviation of the dihedral angle between both rings from co-planarity are dependent on the additional substituent on the aryl group on 4-position and also on the presence of the ethoxycarbonyl, acetyl or amide groups on 5-position.
3. The dihedral angle between CO group (C^7=O^8) with respect to C^5=C^6 is dependent on its attachment to the ethoxy, methyl or the aryl/alkylamino substituents. Whereas the angles in **3a** and **5a** are -173.9^o and -175.0^o, respectively, the angle in **1c** is 148.7^o. This indicates the reduced electron withdrawing character (via conjugation) of the amide group in comparison to that of ethoxycarbonyl and the acetyl groups.
4. The calculated dihedral angles for the CO group in the corresponding oxidation products **4a**, **6a** and **2c** (which are, respectively, −128.0, −122.9 and 51.4) explain

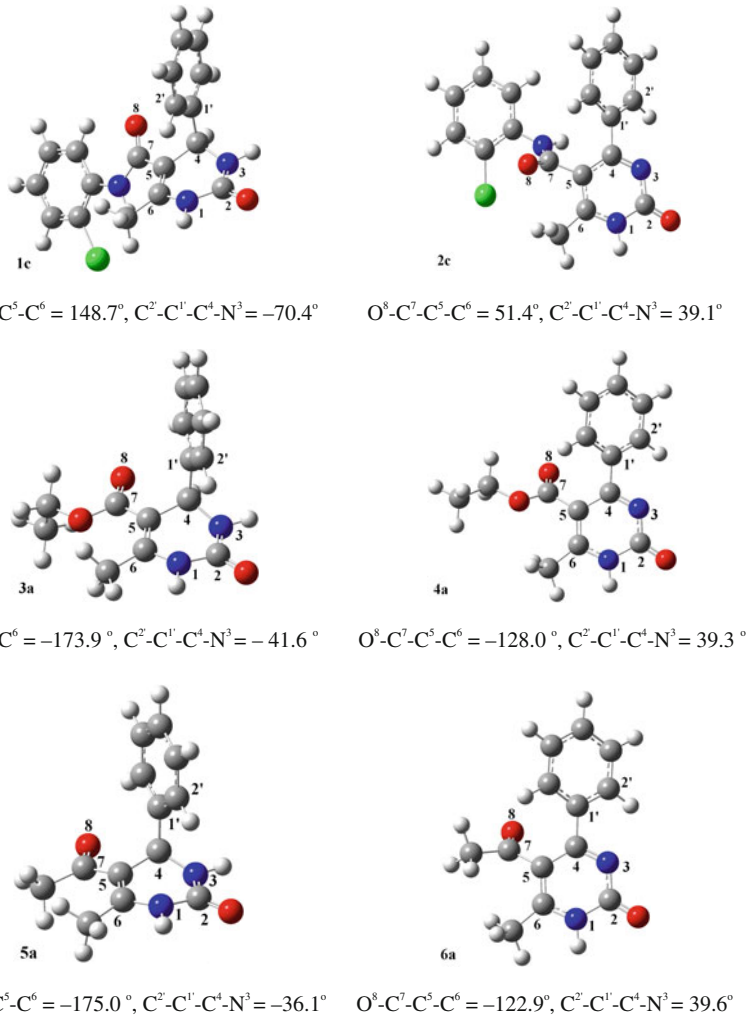


Fig. 4 The optimized structures of **1c**, **3a** and **5a** and the corresponding dehydrogenation products **2c**, **4a** and **6a** at the B3LYP/6-31 ++G** level of theory

clearly that the heterocyclic ring in the amide compounds tends to have more conjugative character, which explains a lower activation energy for its formation (Fig. 4). This results in faster oxidation of amides. The same trends have also been observed for the thermal and ultrasound-assisted oxidation of 5-carboxamide derivatives [15] compared with those for 5-ethoxycarbonyl- [10, 12] and 5-acetyl-THPMs [11, 13]. It should be noted that electron transfer-induced oxidation of THPM-esters by cerric ammonium nitrate (CAN) in acetic acid and acetone has also been reported [31].

Another point is the lake of light sensitivity of THPMs in the solid state. Whereas irradiation of **1f** as test substrate in acetonitrile under argon or oxygen resulted in the complete conversion of **1f** after 1.75 and 2.5 h, respectively, irradiation of **1f** in the solid state had not effected any reactions after 9 h.

The loss of the substituent in 4-position of Hantzsch 1,4-dihydropyridines has earlier been reported by the photoreaction of these compounds bearing carboxy [32], some heterocyclic [33], secondary alkyl and benzyl groups [33] in this position, but in the present study the loss of secondary and benzylic group such as $PhCHCH_3$ (**1p**) was not observed.

Conclusions

We investigated the photodehydrogenation of some 2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxamides to the corresponding 2-oxo-1,2-dihydrpyrimidine-5-carboxamide in acetonitrile under argon and oxygen atmospheres and also in the solid state. The rate of reaction is faster under argon than under oxygen and is influenced by the nature of the substituent on 4- and 5-positions of the THPM ring. Furthermore, it is found that dehydrogenation rates of THPM-amides are faster than for the corresponding THPM-esters and THPM-ketones. In contrast to the solution photochemistry, no changes have been observed by irradiation of **1f** in the solid state. Therefore, due to the pharmaceutical

activity of these compounds, protection of the reaction mixture from light during their preparation is necessary; however, protection during packing as a tablet or capsule is not important, which is important for drug design and manufacturing.

Acknowledgments We are thankful to the Center of Excellence (Chemistry), Research Council and Office of Graduate Studies of the University of Isfahan for their financial support.

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