



Zinc Oxide Suspension in Photocatalytic Oxidation of Dihydropyrimidinones

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Zinc oxide has been used for the photocatalytic oxidation of some ethyl 3,4-dihydropyrimidin-2(1H)-one-5-carboxylates to their corresponding ethyl pyrimidin-2(1H)-one-5-carboxylates under UV irradiation by 400W high pressure mercury lamp in oxygen atmosphere in acetonitrile. The effects of some physicochemical parameters such as amount of photocatalyst, solvent and time of irradiation were studied. The pyrimidinone compounds were attained from the related dihydropyrimidinone after 4-8 h. The results showed the photostability of this type of compounds.

Key Words: Zinc oxide, Photocatalytic, Photooxidation, Dihydropyrimidinone.

INTRODUCTION

3,4-Dihydropyrimidin-2(1H)ones are important class of compounds which are becoming increasing consideration due to their therapeutic and pharmacological properties¹⁻⁵. They have emerged as the integral backbones of several calcium channel blockers, antihypertensive agents, α -1a-antagonism⁶, neuropeptide Y (NPY) antagonism, antitumor, antibacterial and antiinflammatory activities⁷⁻¹².

In oxidation of 3,4-dihydropyrimidin-2(1H)ones and formation of pyrimidine-2(1H)-ones core such as MKC-442, a HEPT (1-[(2-hydroxyethoxy)methyl]-6-(phenylthio)thymine) analogue finds application in clinical trials and similar compounds are also expected to inhibit the HIV virus¹³. Several nucleosides containing 5-substituted pyrimidine moiety have been shown to inhibit the growth of murine mammary carcinoma virus¹⁴. Pyrimidine-cores with extended *p*-systems have interesting fluorescent properties and similar compounds are useful in the development of advanced electronic and photonic materials¹⁵. Furthermore, it is of interest to synthesize structurally diverse pyrimidines by the oxidation of 3,4-dihydropyrimidin-2(1H)ones¹⁶.

In contrast to facile oxidation of typical Hantzsch dihydropyridines by various oxidative methods¹⁷⁻¹⁹, the dehydrogenation of 3,4-dihydropyrimidin-2(1H)ones is known to be nontrivial^{20,21}.

Oxidants such as HNO₃²², PCC, Chloranil, KMnO₄/clay²³, DDQ²⁴, Co(NO₃)₂·6H₂O/K₂S₂O₈²⁵, electrochemical oxidation²⁶ and Pd/C²⁷ as well as Sono-thermal oxidation have been used²⁸.

None of these oxidations are efficient, particularly for use of excess corrosive or harmful reagents, hard reaction conditions, difficulty in product isolation and/or mostly low yields. Therefore, it is needed to search an alternative procedure.

The heterogeneous photocatalysis reaction with various semiconductors TiO₂, ZnO, CdS, ZnS, *etc.* has been studied extensively over the last decades^{29,30}. The semiconductor particle has also been used as sensitizer for organic photosynthetic processes³¹. Zinc oxide is close to being one of ideal photocatalysts due to being relatively nontoxic, cheap and its holes of strong oxidizing power.

Zinc oxide is a well-known semiconductor with a wide band gap and high exciton binding energy at room temperature, having many applications, such as being a photocatalyst, transducer, varistor, phosphor and transparent conductor³². ZnO as a photocatalyst has received much attention due to its low cost and high photo-activity in several photochemical and photo-electro-chemical processes^{33,34}. ZnO is a semiconductor with a wide and direct band gap of 3.37 eV and a large excitation binding energy of 60 meV³⁵.

When absorption of light is occurred by a semiconductor particle such as ZnO or TiO₂ with equal to or higher than the band gap energy, an electron from the valence band (VB) is excited to the conduction band (CB) with simultaneous generation of a hole (h⁺) in the valence band^{36,37} (Fig. 1).

The e_{CB}⁻ and h_{VB}⁺ can recombine on the surface or in the bulk of the particle or can be separated under the built-in electric field to transfer to different positions on the surfaces, further being trapped to react with donor or acceptor species

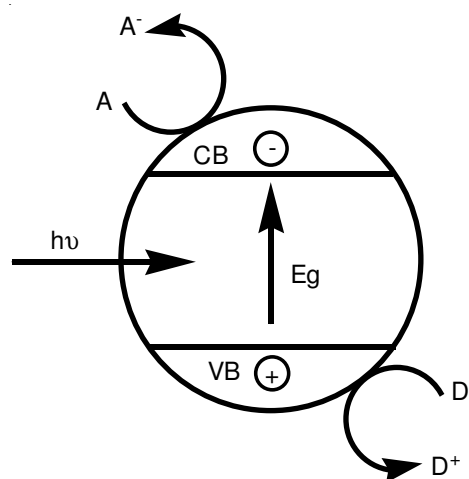


Fig. 1. Schematic diagram of function of a semiconductor in photocatalytic reaction

adsorbed on or close to the surfaces. The separation and recombination of photoinduced charge carriers are in competition process and the photocatalytic reaction is effective only when photoinduced electrons and holes are trapped on the surfaces, respectively.

A chemical acceptor species can be photocatalytically reduced by e_{CB} only if the conduction band potential of the photocatalyst is more negative than the redox potential of the acceptor species. In the same way, a chemical donor species can be photocatalytically oxidized by h_{VB} only if the valence band potential of the photocatalyst is more positive than the redox potential of the donor species. Both reactions should occur simultaneously because electro neutrality has to be maintained^{38,39}. The surface oxygen species can play important roles in photocatalytic reactions. Most often, oxygen play the role of electron trap^{40,41}.

In continuation of our previous studies on photochemical reactions⁴²⁻⁴⁶, in this research we report the photocatalytic oxidation of 3,4-dihydropyrimidin-2(1H)ones.

EXPERIMENTAL

Chemicals were purchased from Merck, Fluka and Aldrich chemical companies. The ZnO was purchased from Aldrich Chemical Co. The ZnO powder was used as received as a photocatalyst without further purification. 3,4-Dihydropyrimidin-2(1H)ones were prepared according to the reported procedure⁴⁷. The reactions were monitored by TLC. The products were isolated and identified by comparison of their physical and spectral data with those reported in the literature. IR spectra were recorded on FT-IR 680-Jasco-instrument model. ¹H NMR data were obtained on 300 MHz DPX-Brucker model.

Photochemical set containing 400W high pressure mercury lamp as shown in Fig. 2 was used for photooxidation experiments.

General procedure for the photocatalytic oxidation of 3,4-dihydropyrimidin-2(1H)ones: Zinc oxide (40 mg) was added to a solution containing 3,4-dihydropyrimidin-2(1H)ones (1 mmol) in 20 mL acetonitrile under oxygen bubbling. The mixture was stirred at room temperature under irradiation of UV light (400 W high pressure mercury lamp)

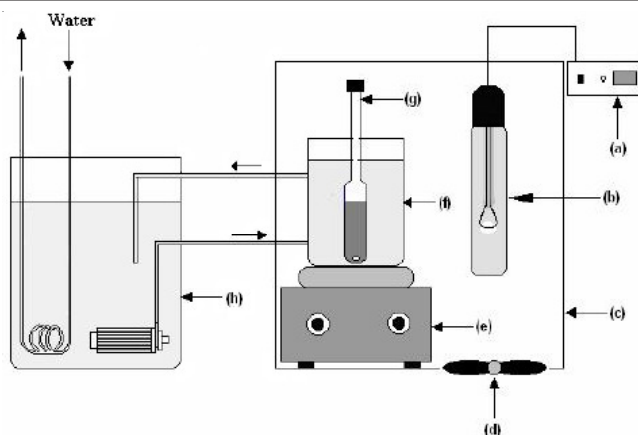


Fig. 2. Photocatalytic setup for photooxidation experiments; (a) power supply; (b) 400-W high pressure Hg lamp; (c) photoreactor with aluminium foil as reflector for a full irradiation of catalyst; (d) fan; (e) magnetic stirrer; (f) 2L pyrex beaker; (g) photolytic cell; (h) water thermostat

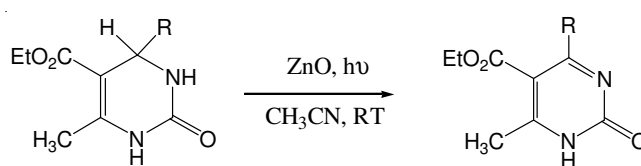
for the appropriate time (4-8 h). The progress of the reaction was monitored by TLC. After completion of the reaction as monitored by TLC (CCl_4 : EtOAc), zinc oxide was separated by centrifugation. Evaporation of the solvent followed by chromatography on a silica-gel plate afforded the pure products.

Ethyl 6-methyl-4-(2,6-dichlorophenyl)pyrimidin-2(1H)-one-5-carboxylate (4): Pale yellow solid; m.p. 185-186 °C. IR (KBr, ν_{max} , cm^{-1}): 3235, 2930, 1700, 1670, 1430, 1200. ¹H NMR ($DMSO-d_6$): δ = 0.85 (t, 3H, J = 7.3 Hz), 2.50 (s, 3H), 3.94 (q, 2H, J = 7.3 Hz), 7.17-7.29 (m, 3H), 12.73 (s, 1H). Anal. calcd. (%) for $C_{14}H_{12}N_2O_3Cl_2$: C 51.40, H 3.70, N 8.56; found (%): C 51.5, H 3.8, N 8.7.

Ethyl 6-methyl-4-(3-bromophenyl)pyrimidin-2(1H)-one-5-carboxylate (10): Pale yellow solid; m.p. 167-168 °C. IR (KBr, ν_{max} , cm^{-1}): 3230, 2900, 1700, 1650, 1470, 1226. ¹H NMR ($DMSO-d_6$): δ = 0.92 (t, 3H, J = 7.2 Hz), 2.41 (s, 3H), 3.88 (q, 2H, J = 7.2 Hz), 7.20-7.45 (m, 3H), 9.25 (s, 1H). Anal. calcd. (%) for $C_{14}H_{13}N_2O_3Br$: C 49.87, H 3.89, N 8.31; found (%): C 50, H 3.8, N 8.4.

RESULTS AND DISCUSSION

Present investigation during the controlled reactions showed to us that UV irradiation is necessary for the effective progress of the oxidation reactions and without oxygen, the oxidation reactions were not done at all even with prolonged reaction times. With this preliminary results, the optimization of important operational parameters were performed in the photo-oxidation reaction of 3,4-dihydropyrimidin-2(1H)ones (**Scheme-I**).



Scheme-I

Amount of photocatalyst: To obtain the optimum amount of ZnO, a photocatalytic oxidation of 3,4-dihydropyrimidin-2(1*H*)-ones were run on a typical 3,4-dihydropyrimidin-2(1*H*)-one (1 mmol) using various amounts of ZnO. As shown in Table-1 oxidation times of the selected compounds were decreased by increasing the photocatalyst amounts, then reached the lowest time of completion of the oxidation and finally remain at constant value of 40 mg. It is interesting to note that this phenomenon has been observed previously in other photocatalytic reaction⁴⁸⁻⁵¹. This can be rationalized in terms of availability of active sites on ZnO surface and the light penetration of photoactivating light into the suspension. The availability of active sites increases with the suspension of photocatalyst loading, but the light penetration and hence the photoactivated volume of the suspension shrinks. Moreover, the increase in the time of oxidation at higher photocatalyst loading may be due to deactivation of activated molecules by collision with ground state molecules. Shielding by ZnO may also take place (eqn. 1).



where ZnO* is the ZnO with active species adsorbed on its surface and ZnO is the deactivated form.

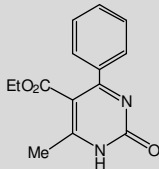
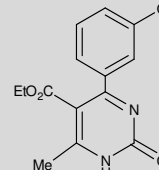
TABLE-1
EFFECTS OF PHOTOCATALYST AMOUNTS OF ZINC OXIDE ON THE OXIDATION OF TYPICAL 3,4-DIHYDROPYRIMIDIN-2(1*H*)-ONE AT ROOM TEMPERATURE^a

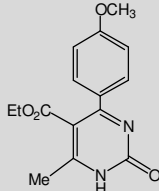
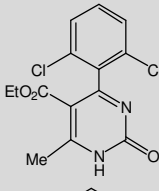
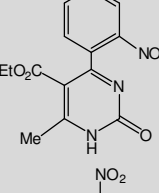
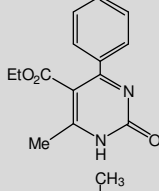
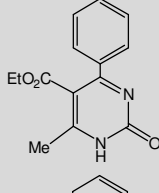
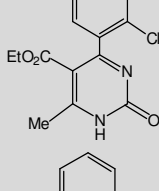
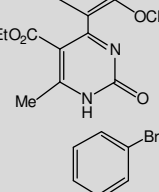
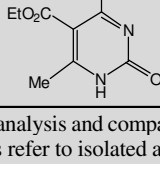
Entry	Amount of ZnO (mg)	Time (h)	Yields (%) ^b
1	10	7.0	86
2	20	5.5	88
3	40	4.5	90
4	60	6.5	85
5	80	8.0	83

^a5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one as typical DHPMs were used; ^bIsolated yields.

Photocatalytic oxidation of dihydropyrimidinones: In obtained optimum conditions, the photocatalytic reactions (**Scheme-1**) proceed efficiently in high yields. The results are summarized in Table-2. As shown in case of 3,4-dihydropyrimidin-2(1*H*)-ones including electron withdrawing substituents have longer reaction time than electron donor substituents.

TABLE-2
PHOTOCATALYTIC OXIDATION OF 3,4-DIHYDROPYRIMIDIN-2(1*H*)-ONES WITH ZnO/O₂ SYSTEM

Entry	R	Products ^a	Time, h (Yield, %) ^b	m.p. (°C)
1	C ₆ H ₅		6 (92)	133-134
2	3-OHC ₆ H ₄		5 (90)	182-184

3	4-OCH ₃ C ₆ H ₄		6.5 (80)	151-153
4	2,6-Cl ₂ C ₆ H ₃		4.5 (94)	185-186
5	2-NO ₂ C ₆ H ₄		8 (75)	184-186 (Ref. 52)
6	4-NO ₂ C ₆ H ₄		8 (70)	152-154
7	4-CH ₃ C ₆ H ₄		4 (92)	136-138 (Ref. 28)
8	2-ClC ₆ H ₄		5 (85)	165-167
9	2-OCH ₃ C ₆ H ₄		4 (85)	121-123
10	3-BrC ₆ H ₄		4 (94)	167-168

^aCharacterized by spectral analysis and comparison with those reported in the literature^{28,52}; ^bYields refer to isolated and purified products.

Conclusion

From the results obtained from photocatalytic oxidation of 3,4-dihydropyrimidin-2(1*H*)-ones with ZnO/O₂ system and compared with the results obtained by thermal oxidation, it concluded that photooxidation can effectively increase the rate of oxidation. Easy reaction progress, moderate reaction times and good to excellent yields are some of the advantages of this oxidative method.

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REFERENCES

1. K. Folker, H.J. Harwood and T.B. Johnson, *J. Am. Chem. Soc.*, **54**, 3751 (1932).
2. K.S. Atwal, B.N. Swanson, S.E. Unger, D.M. Floyd, S. Moreland, A. Hedberg and B.C. O'Reilly, *J. Med. Chem.*, **34**, 806 (1991).
3. K.S. Atwal, G.C. Rovnyak, B.C. O'Reilly and J. Schwartz, *J. Org. Chem.*, **54**, 5898 (1989).
4. C.O. Kappe, *J. Org. Chem.*, **62**, 7201 (1997).
5. P. Wipf and A. Cunningham, *Tetrahedron Lett.*, **36**, 7819 (1995).
6. G.C. Rovnyak, S.D. Kimball, B. Beyer, G. Cucinotta, J.D. DiMarco, J. Gougoutas, A. Hedberg, M. Malley, J.P. McCarthy, R. Zhang and S. Moreland, *J. Med. Chem.*, **38**, 119 (1995).
7. K.S. Atwal, G.C. Rovnyak, B.C. O'Reilly and J. Schwartz, *J. Org. Chem.*, **54**, 5898 (1989).
8. G.C. Rovnyak, S.D. Kimball, B. Beyer, G. Cucinotta, J.D. Dimarco, J. Gougoutas, A. Hedberg, M. Malley, J.P. McCarthy, R. Zhang and S. Moreland, *J. Med. Chem.*, **38**, 119 (1995).
9. C.O. Kappe, W.M.F. Fabian and M.A. Semones, *Tetrahedron*, **53**, 2803 (1997).
10. E.H. Hu, D.R. Sidler and U.H. Dolling, *J. Org. Chem.*, **63**, 3454 (1998).
11. K.S. Atwal, B.N. Swanson, S.E. Unger, D.M. Floyd, S. Moreland, A. Hedberg and B.C. O'Reilly, *J. Med. Chem.*, **34**, 806 (1991).
12. G.J. Grover, S. Dzwonczyk, D.M. McMullen, D.E. Normandin, C.S. Parham, P. G. Slep and S. Moreland, *J. Cardiovasc. Pharmacol.*, **26**, 289 (1995).
13. R.C. Rizzo, J. Tirado-Rives and W.L. Jorgensen, *J. Med. Chem.*, **44**, 145 (2001).
14. C. Chen, K.M. Wilcoxon, C.Q. Huang, Y.F. Xie, J.R. McCarthy, T.R. Webb, Y.F. Zhu, J. Saunders, X.J. Liu, T.K. Chen, H. Bozighian and D.E. Grigoriadis, *J. Med. Chem.*, **47**, 4787 (2004).
15. K. Itami, D. Yamazaki and J. Yoshida, *J. Am. Chem. Soc.*, **126**, 15396 (2004).
16. F.A. Kang, J. Kodah, O. Guan, X. Li and W.V. Murray, *J. Org. Chem.*, **70**, 1957 (2005).
17. M. Moghadam, M. Nasr-Esfahani, S. Tangestaninejad, V. Mirkhani and M.A. Zolfigol, *Can. J. Chem.*, **84**, 1 (2006).
18. M. Montazerzohori, B. Karami, M. Nasr-Esfahani and S.A. Musavi, *Heterocycl. Commun.*, **13**, 289 (2007).
19. M. Nasr-Esfahani, M. Moghadam and G. Valipour, *J. Iran. Chem. Soc.*, **5**, 244 (2008).
20. C.O. Kappe, *Tetrahedron*, **49**, 6937 (1993).
21. J.J. Vanden Eynde, N. Audiart, V. Canonne, S. Michel, Y. Van Haverbeke and C.O. Kappe, *Heterocycles*, **45**, 1967 (1997).
22. A. Puchala, F. Belaj, J. Bergman and C. O. Kappe, *J. Heterocycl. Chem.*, **38**, 1345 (2001).
23. J.J. Vanden Eynde, N. Audiart, V. Canonne, S. Michel, Y. Van Haverbeke and C.O. Kappe, *Heterocycles*, **45**, 1967 (1997).
24. M. Watanabe, H. Koike, T. Ishiba, T. Okada, S. Seo and K. Hirai, *Bioorg. Med. Chem.*, **5**, 437 (1997).
25. P. Shanmugam and P.T. Perumal, *Tetrahedron*, **63**, 666 (2007).
26. V. Kadysh, J. Stradins, H. Khanina and G. Duburs, *Electrochim. Acta*, **34**, 899 (1989).
27. C.O. Kappe and P. Roschger, *J. Heterocycl. Chem.*, **26**, 55 (1989).
28. H.R. Memarian and A. Farhadi, *Ultrason. Sonochem.*, **15**, 1015 (2008).
29. A. Henglein, *Top. Curr. Chem.*, **143**, 113 (1988).
30. P.V. Kamat, *Chem. Rev.*, **93**, 267 (1993).
31. B. Kraeutler and A.J. Bard, *J. Am. Chem. Soc.*, **100**, 2239 (1978).
32. D.C. Look, *Mater. Sci. Eng. B*, **80**, 383 (2001).
33. J. Domenech and A. Prieto, *Electrochim. Acta*, **31**, 1317 (1986).
34. J.R. Harbour and M.L. Hair, *J. Phys. Chem.*, **83**, 652 (1979).
35. D.C. Reynolds, D.C. Look, B. Jogai, J.E. Hoelscher, R.E. Sherriff, M.T. Harris and M.J. Callahan, *J. Appl. Phys.*, **88**, 2152 (2000).
36. M.I. Litter, *Appl. Catal. B: Environ.*, **23**, 89 (1999).
37. M.R. Hoffmann, S.T. Martin, W. Choi and D.W. Bahnemann, *Chem. Rev.*, **95**, 69 (1995).
38. J.M. Herrmann, *Top. Catal.*, **34**, 49 (2005).
39. M.I. Litter, *Appl. Catal. B: Environ.*, **23**, 89 (1999).
40. J.R. Harbour, J. Tromp and M.L. Hair, *Can. J. Chem.*, **63**, 204 (1985).
41. H. Gerischer and A. Heller, *J. Phys. Chem.*, **95**, 5261 (1991).
42. H.R. Memarian, M. Nasr-Esfahani and D. Dopp, *New J. Chem.*, **25**, 476 (2001).
43. H.R. Memarian, M. Nasr-Esfahani and D. Dopp, *New J. Chem.*, **25**, 1605 (2001).
44. H.R. Memarian, M. Nasr-Esfahani, R. Böese and D. Dopp, *Liebigs Ann.*, 1023 (1997).
45. M.H. Habibi, A.Z. Isfahani, A. Mohammadkhani and M. Montazerzohori, *Monatsh. Chem.*, **135**, 1121 (2004).
46. M.H. Habibi, S. Tangestaninejad, I. Mohammadpoor-Baltork and M. Montazerzohori, *Phosphorus Sulfur Silicon Rel. Elem.*, **179**, 597 (2004).
47. M. Nasr-Esfahani, B. Karami, M. Montazerzohori and K. Abdi, *J. Heterocycl. Chem.*, **45**, 1183 (2008).
48. S. Sakthivel, B. Neppolian, M.V. Shankar, B. Arabindoo, M. Palanichamy and V. Murugesan, *Solar Energy Mater. Solar Cells*, **77**, 65 (2003).
49. T. Ohno, K. Sarukawa and M. Matsumura, *J. Phys. Chem. B*, **105**, 2417 (2001).
50. R.J. Davis, J.L. Gainer, G. O'Neal and I.W. Wu, *Water Environ. Res.*, **66**, 50 (1994).
51. J. Saïen, R.R. Ardjmand and H. Iloukhani, *Phys. Chem. Liq.*, **41**, 519 (2003).
52. P. Shanmugam and P.T. Perumal, *Tetrahedron*, **62**, 9726 (2006).