NOVEL SYNTHESIS OF UNSATURATED 5(4H)-OXAZOLONE DERIVATIVES WITH USING PALLADIUM(II) ACETATE AS A CATALYST AND MICROVAWE IRRADIATION IN SOLVENT-FREE CONDITION

Hooshang Hamidian and Ahmad Momeni Tikdari*
Department of Chemistry, Shahid Bahonar University of Kerman, Kerman 76175-133, Iran. Fax: (+98)3413222033, E-Mail: amomeni@mail.uk.ac.ir

Abstract: Unsaturated 5(4H)-oxazolones have emerged as an important class of synthons. These compounds have prepared with using palladium(II) acetate under free-solvent conditions with excellent yields and microwave irradiation.
Keywords: Palladium, Heterocycles, Unsaturated 5(4H)-oxazolone, Microwave method

Introduction

Ever since the initial discovery of the Waker process,[1] i.e. the Pd/Cu-catalyzed oxidation of ethylene to acetaldehyde in water, methods for the palladium(II)-mediated oxidative functionalization of alkenes have found widespread application in the synthesis of complex molecules.[2]

The basic principle of this chemistry is that η^2-alkene-Pd(II) complexes, usually generated in situ, which is form σ-alkyl-Pd specie by nucleophiles, then in turn are able to react further in a variety of ways. In general, several kinds of nucleophiles are able to attack the alkene complex intermediates in an intra- or intermolecular fashion. This article, however, focusses on intramolecular and intermolecular reactions.

Their application of the 5(4H)-oxazolone derivatives are important synthetic intermediates and interest in their chemistry.5(4H)-Oxazolone derivatives are important synthons because synthesis of drugs, dyes, aminoacids and biologically active compounds.[3-6] Especially in recent years, new theory of the origin of life on earth is proposed by chemists.They reported that in hot water, methanthiol and carbon monoxide react in the presence of mixed iron-nickel sulfides to give 5(4H)-oxazolone.First of all 5(4H)-oxazolone link up and then they from peptides similar to those at under sea volcanic vents blasters.[7]

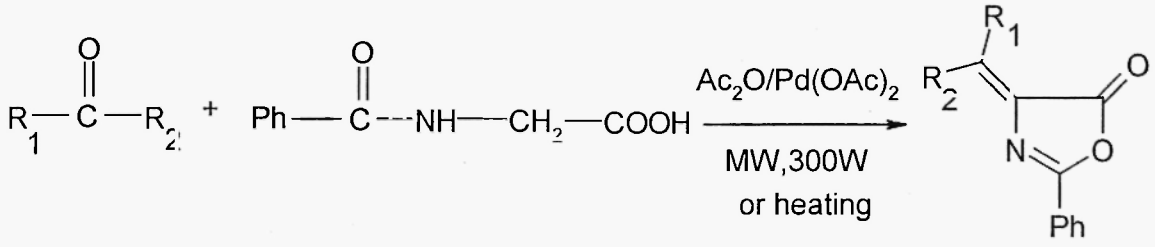
Synthesis of these ring systems involves cyclisation of 2-acylaminoacids by various reagents, such as acetic anhydride with sodium acetate,[8] acetic anhydride with lead acetate,[9] polyphosphoric acid,[10] bismuth(III) acetate,[11] anhydrous zinc chloride.[12]

Microwave irradiation is a nonconventional energy source whose popularity and synthetic utility in organic chemistry has increased considerably in recent years.[13-15] The rapid heating induced by such radiation avoids harsh classical conditions and the decomposition of the reagents, leading to the formation of products under mild reaction conditions, thus increasing the yield.

The elimination of toxic organic solvents and use of catalysts is one of the most important goals in green chemistry. Coupling of these two techniques, that is, organic reactions using catalyst with microwave irradiation has been a filed, which has shown excellent results leading to the development of many reaction procedures, which are environmental friendly falling in the domain of green chemistry.

Results and Discussions

We selected palladium(II) acetate as the catalyst, which gives the excellent yield of product and has not been reported to use this compound as a catalyst for such synthesis. 5(4H)-oxazolones are important synthons for biologically compounds and the advantages of these reactions offered by solvent-free media reactions, we report here a solvent-free procedure for the synthesis of 2-phenyl-5(4H)-oxazolones **3a-i** (Table-1) from appropriate aldehydes or ketones (**1**) with hippuric acid (**2**) in the presence of palladium(II) acetate under microwave irradiation and thermal condition (Scheme-1).



(1) **(2)** **(3)**

1a) Benzaldehyde
1b) 4-Chlorobenzaldehyde
1c) 4-Methoxybenzaldehyde
1d) 3-nitrobenzaldehyde
1e) 3,4-Dimethoxybenzaldehyde
1f) Furfuraldehyde
1g) Acetone
1h) Acetophenone
1i) Cyclohexanone

Scheme-1

Table-1: Palladium(II) acetate catalyzed synthesis of unsaturated 5(4H)-oxazolone derivatives under solvent-free condition and microwave irradiation (power = 300W)

Products	R_1	R_2	Yield(%)[a]	m.p.(°C)	m.p.(Lit)
3a	H	C_6H_5	98	160-161	158[16]
3b	H	4-ClC_6H_4	81	195-196	197[17]
3c	H	4-$MeOC_6H_4$	98	163-164	165[12]
3d	H	3-$NO_2C_6H_4$	96	195-196	195-196[18]
3e	H	3,4-$(OMe)_2C_6H_3$	97	152-153	151-152[12]
3f	H	C_4H_3O	89	170-171	171[16]
3g	CH_3	CH_3	51	100-101	98-99[16]
3h	CH_3	C_6H_5	66	106-107	104[19]
3i		-$(CH_2)_5$-	83	138-139	137-138[16]

[a]Yield of isolated products.

Table-2: Comparison of heating condition and microwave irradiation (MW) (power = 300W) in Cases of **3a-i.**

	Microwave irradiation		Conventional heating		
Product	Time(min)	Yield(%)[a]	Time(min)	Temp.(°C)	Yield(%)[a]
3a	4	98	15	90-95	81
3b	6	81	30	90-95	72
3c	3	98	20	90-95	83
3d	6	96	35	90-95	74
3e	4	97	20	90-95	80
3f	5	89	20	90-95	79
3g	4	51	40	46-50	41
3h	6	66	55	90-95	57
3i	5	83	20	90-95	71

[a]Yield of isolated products.

The activity of palladium(II) acetate for the synthesis of 5(4H)-oxazolones **3a-i** was carried out with two method, microwave irradiation and heating. The best results were obtained microwave irradiation (Table 2).It has been found that for 0.01mol of aldehyde or ketone, 0.01mol of hippuric asid and 0,03mol of acetic anhydride, 0.1g of palladium(II) acetate was required. A power setting of 300w appeared to be the best compromise between efficiency and safety (Higher power output leads to fumes and reduction in yields).

This effect can be attributed to the carbonyl complexation by palladium(II) acetate leading to electrophilic assistance during nucleophilic attack on this group. When the reaction was carried out by irradiation or heating hippuric acid (**2**) alone, oxazolone (**4**) was formed in 7 min for irradiation (yield 76%) and 35 min for thermal heating (80°C) (yield 61%).

In order to check the possibility of the existence of a specific microwave effect accelerating the reaction with respect to conventional heating, a water bath was used as a source of heat in comparative experiments. Lower yields were obtained with thermal heating under the same condition of time and temperature. This observation is consistent mechanism of the reaction as depicted in Scheme 2 and Scheme 3, which involves a polar transition state starting from a neutral ground state. This enhancement in polarity during the reaction progress can thus induce an improved stabilization of the transition state by microwave (dipole-dipole intraction), leading to a lowering in the activation energy[20].

Experimental Section

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Mass spectra were obtained on a SHIMADZU QP 1100 EX. IR spectra were recorded with a MATTSON 1000 FT-IR spectrophotometer. Nuclear magnetic resonance spectra were recorded on a BRUKER DRX-500 AVANCE spectrometer using tetramethylsilane (TMS) as an internal standard. All reaction were carried out in an unmodified demostic microwave oven BC380W having a maximum output of 900W operating at 2450MHz..

General Procedures

2-Phenyl-5(4H)-oxazolone derivatives (3a-h) :

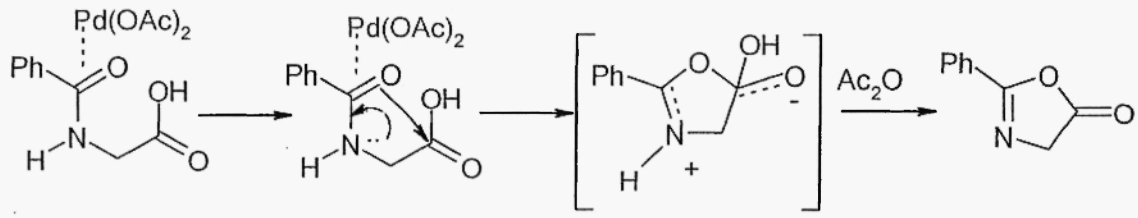
MW method) The appropriate aldehyde or ketone **(1)** (0.01 mol), hippuric acid **(2)** (0.01 mol), acetic anhydride (0.03mol) and palladium(II) acetate (0.1 g) were introduced into a beaker.The paste which

obtained was irradiated in a microwave oven at a power output of 300w for the appropriate time (Table 1). After irradiation, the mixture was cooled to room temperature and was washed with cold water,then crude product was recrystallized from ethanol 96% (with using active carbon).

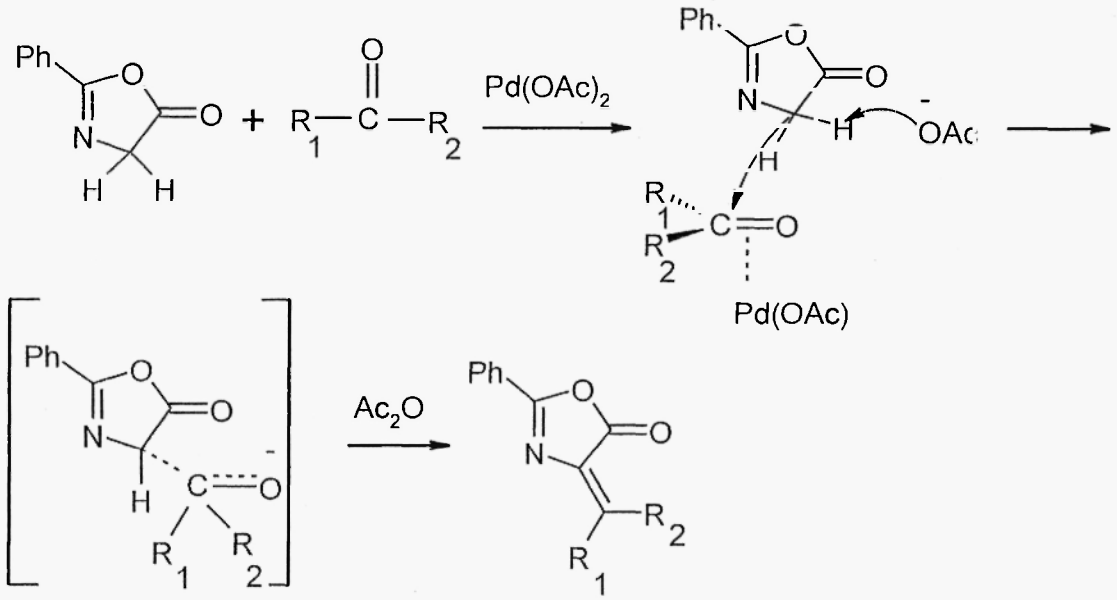
Thermal heating method) The appropriate aldehyde or ketone **(1)** (0.01 mol), hippuric acid **(2)** (0.01 mol), acetic anhydride (0.03mol) and palladium(II) acetate (0.1 g) were introduced into a beaker. The mixture was heated with stirring until the mixture had gone from semi- solid mass to liquid for the appropriate time (Table 2).The crude product was cooled and washed with cooled water then racrystallized from ethanol 96% (with using active carbon).The structure of the products were confirmed by IR, ^{1}HNMR, ^{13}CNMR, mass spectroscopy (Table 3).

Table-3: Spectral Data of Compounds **3a-i**.

Product	IR(KBr) / υ [cm^{-1}]	^{1}H NMR ($CDCl_3$) / δ[ppm]	MZ/ m/z(%)
3a	1790, 1650	7.24 (s, 1H, Vinyl);7.44-8.12 (m, 10H, ArH)	249 (M^+, 15), 105 (100), 77 (70)
3b	1800,1650	7.44-8.12 (m,10H, Vinyl and ArH)	285(M+2), 283 (M^+, 15), 105 (100), 77 (70)
3c	1790,1660	4.02 (s, 3H, CH_3);7.07 (s, 1H, Vinyl);7.25-8.22 (m,9H, ArH)	279 (M^+, 10), 105 (100), 77 (70)
3d	1800,1660	7.42-8.29 (m, 10H, Vinyl and ArH)	294 (M^+, 15), 105 (100), 77 (70)
3e	1780, 1650	3.86 (s, 6H, CH_3);7010 (s, 1H, Vinyl, 7.31-8.14 (m, 8H,ArH)	307 (M^+, 5), 105 (100), 77 (70)
3f	1790,1660	6.66 (q, 1H, 2-furyl);7.17-8.28 (m, 8H, Vinyl , Furyl And ArH)	239 (M^+, 5), 105 (100), 77 (70)
3g	1780, 1660	2.04 (d, 6H, CH_3);7.44-7.89 (m,5H, ArH)	201 (M^+, 10), 105(100) 77 (70)
3h	1790,1640	2.67 (s, 3H, CH_3);7.41-8.18 (m, 10H, ArH)	263 (M^+, 10), 105 (100), 77 (70)
3i	1780,1650	1.34-2.13 (m, 10H,Cyclohexyl);7.34-7.88 (m, 5H, ArH)	241 (M^+, 10), 105 (100), 77 (70)



Intramolecular catalysis by palladium(II) acetate
Scheme-2



Intermolecular catalysis by palladium(II) acetate
Scheme-3

Conclusions

Palladium(II) acetate is a suitable catalyst for synthesis of unsaturated 5(4H)-oxazolones, because of excellent yields of the products, short reaction time and ease of work-up make the above method advantageous in comparison to the other methods. In addition, this method is environmentally and involves relatively nontoxic reagents.

Acknowledgments

The authors appreciate to the Department of Chemistry of Shahid Bahonar University of Kerman for its supporting this investigation.

References

1. J. Smidt, W. Hafner, R. Jira, R. Sieber, J. Sedlmeier and A. Sabel, *Angew. Chem.* **71**, 176 (1959).
2. (a) L. S. Hegedus, *Tetrahedron* **40**, 2415 (1984). (b) T. Hosokawa, S. Murahashi, *Acc.Chem.Res.* **23**, 49 (1990).
3. J. D. Fissekis, C. G. Skinner and W. Shive, *J. Am. Soc. Chem.* **81**, 2715 (1959).
4. J. M. Stewart and D. V. Woolley, *J. Am. Chem. Soc.* **78**, 5336 (1956).
5. V. Benedetti-Doctrovich, E. M. Burgess, J. Lambropoulos, D. Lednicer, D. V. Derveer and L. H. Zalkow, *J. Med. Chem.* **37**, 710 (1994).
6. G. Viti, R. Namnicine, R. Ricci, V. Pestelline, L. Abeli and M. Furio, *Eur. J. Med. Chem.* **29**, 401 (1994).
7. G. Wachtershauser, *C& EN* April, 6 (1996).
8. H. E. Carter, *Org. React.* **3**, 198 (1946).
9. E. Baltazzi and R. Robinson, *Chem. Ind.* 191 (1954).
10. Y. S. Rao, *J. Org. Chem.* **41**, 722 (1976).
11. K. A. Monj, D. Sarapa and R. S. Mohan, *Synth. Commun.* **30**, 3167 (2000).
12. R. P. Shantham and R. V. Venkatratnam, *Indian J. Chem.* **33B**, 984 (1998).
13. S. Caddick, *Tetrahedron.* **51**, 10403 (1995).
14. C. R. Strauss and R.W. Trainor, *Aust. J. Chem.* **48**, 1665 (1995).
15. F. Langa, P. de la Cruz, A. de la Hoz, A. Diaz-Oritz and E. Diez-Barra, *Contemp. Org. Synth.* **4**, 373 (1979).
16. M. Crawford and W. T. Little, *J. Chem. Soc.* 729 (1959).
17. F. M. Bautista, J. M. Campelo, A. Garcia, D. Luna, J. M. Marinas and A. A. Romero, *J. Chem. Soc. Perkin Trans. 2* **(2)**, 227 (2002).
18. R. L. Doulglas and J. M. Gulland, *J. Chem. Soc.* 2893 (1931).
19. C. Cativiela and E. Melendez, *Synthesis* 833 (1978).
20. L. Perreux and A. Loupy, *Tetrahedron.* **57**, 9199 (2001).

Received on July 25, 2005.