Solid Supported Reaction of Substituted 2-Oxazoline with Amines under Microwave Irradiation

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1,2-Diaryl-4-phenylmethylene-2-imidazolin-5-ones were obtained by the interaction of primary amines with 2-phenyl-4-phenylmethylene-2-oxazolin-5-one using acidic alumina or montmorillonite K10 clay under microwave irradiation (MWI). The same reaction over basic alumina gave arylamides of α -arylamido- β -arylacrylic acids in good yield. Usage of acidic alumina for cyclization gave better results in comparison with clay. This procedure highlights the versatility of various solid supports.

Keywords: Oxazoline; Amines; Microwave irradiation; Solid support; Imidazoline.

INTRODUCTION

The reaction of amines with 2-aryl-4-arylmethylene-2-oxazolin-5-ones using a variety of reagents have been described in the literature.^{1,2} It has been reported that interaction of amines with 2-aryl-4-arylmethylene-2-oxazolin-5ones generally leads to ring opening at C5 to give the arylamides of α -arylcarboxamido- β -aryl acrylic acids³ which could be recyclized in some cases to corresponding 1,2-diaryl-4-arylmethylene-2-imidazolin-5-ones, either by heating at 200 °C under vaccum or under the influence of acetic acid and sodium acetate.^{4,5}

The increasing environmental consciousness throughout the world has enforced the application of solventless conditions⁶ into practice. In this endeavour, the use of inorganic solid supports (alumina, zeolite, bentonite, montmorillonite K10 clay) have become a landmark as the reactions can be performed in "dry media"⁷ or solvent-free conditions.^{8,9} The coupling of microwave irradiation (MWI)¹⁰ with the use of inorganic solid support¹¹ offers benefits of shorter reaction time, milder reaction conditions, yield enhancement, and high catalytic activity with optimum utilization of energy. In addition, this methodology also provides an opportunity to work with open vessels and an enhanced possibility of upscaling the reaction on a preparative scale.

In view of the eco-friendly role of dry media using microwaves and our ongoing endeavour towards green synthesis, the reaction of 2-phenyl-4-phenylmethylene-2-oxazolin-5-one with primary amines was carried out under microwave irradiation using various solid supports viz. acidic alumina, basic alumina and montmorillonite K10 clay.

RESULTS AND DISCUSSION

2-Phenyl-4-phenylmethylene-2-oxazolin-5-one (1) was prepared according to the literature method.¹² The reaction of 1 with amines 2a-f was carried out using basic alumina under MWI (Scheme I). Arylcarboxamides of α-arylcarboxamides- β -arylacrylic acid **3a-f** were obtained in good yield (Table 1). The products were characterized by their spectral (Table 3) and analytical data. In IR spectra the appearance of a band at 3300-3200 cm⁻¹ due to N-H and the disappearance of a band at 1780 cm⁻¹ due to C=O of lactone, confirmed the formation of **3a-f**. However, when the reaction was carried out over acidic alumina under MWI, 1,2-diaryl-4-phenylmethylene-2-imidazolin-5-ones 4a-f (Scheme I) were obtained (Table 2), indicating the requirement of acidic conditions for the formation of cyclized product. The structures of the products were established on the basis of their spectral (Table 3) and analytical data. In IR spectra, the bands at 1720 and 1640 cm⁻¹ due to -CONR and C=N, respectively, confirmed the formation of product.

The above reactions were also carried out over montmorillonite K10 clay giving **4a-f** in good yield. This can be attributed to the ditopic¹³ nature of montmorillonite K10 clay. However, the reaction took more time for completion in comparison with acidic alumina. In addition, compounds **4a-f** were also obtained on subjecting compounds **3a-f** to microwave irradiation using acidic alumina/montmorillonite K10 clay as solid supports.

Thus, we have developed a simple, economical and environmentally benign synthesis keeping modernization and simplification of classical procedures, and avoiding volatile

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Scheme I



Table 1. Reaction Times and Yield for the Compounds 3a-f

Compd. No.	R	mp (°C)	Microwave Heating Basic alumina		
		_	Time (min)	Yield (%)	
3a	phenyl	232-234*	2.0	92	
3b	3-chloro-4-fluorophenyl	250-252	2.5	91	
3c	2-pyridyl	175-177	3.5	92	
3d	2-furfuryl	220-224	3.5	90	
3e	5-methyl-1,3,4-thiadiazolyl	185-187	4.0	89	
3f	5-phenyl-1,3,4-thiadiazolyl	178-180	4.5	88	

* Lit. m.p. 230⁴

and toxic organic solvents. In comparison with classical methodology, the reaction time has been brought down from hours to minutes with improved yield. The solid supports used not only act as catalysts but also as an energy transfer medium resulting in very rapid and homogeneous heating.

EXPERIMENTAL

Melting points were determined on a Thomas Hoover

melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer FTIR-1710 spectrophotometer. ¹H NMR spectra were recorded on a Bruker Avance (300 MHz) spectrometer using tetramethylsilane as an internal standard. Microwave irradiation was carried out in a Kenstar Microwave Oven, Model No. OM9925E (2450 MHz, 800 watts). Elemental analysis were performed by means of a Heraeus CHN-Rapid Analyzer and their results agreed satisfactorily with the calculated values. The purity of the compounds were checked on silica gel coated Al plates (Merck). Solid Supported Reaction of 2-Oxazoline

Compd. No.	R	mp (°C)	Acidic* Alumina		Montmorillonite* K10 Clay		Acidic** Alumina		Montmorillonite** K10 Clay	
		_	Time (min)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)	Time (min)	Yield (%)
4a	phenyl ^a	172-174	3.0	94	3.5	93	2.5	94	3.0	93
4b	3-chloro-4- fluorophenyl	265-269	3.5	93	4.0	92	3.0	92	3.5	93
4c	2-pyridyl	175-178	4.5	93	5.5	93	3.5	92	4.0	92
4d	2-furfuryl	184-186	5.0	91	6.0	90	4.0	90	5.0	89
4 e	5-methyl-1,3,4- thiadiazolyl	160-162	6.0	89	6.5	89	5.0	88	5.5	87
4f	5-phenyl-1,3,4- thiadiazolyl	149-151	6.5	87	7.0	88	5.5	88	6.0	87

	Table 2.	Reaction	Time and	Yield for	Compounds	4a-f	under	MWI
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* for conversion of 1 to 4a-f.

** for conversion of **3a-f** to **4a-f**.

^a lit. m.p. 175.⁴

Table 3.	Spectral	Data of	Compound	s 3a-f	f and 4a-f
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Compd.	IR (v cm ⁻¹) / ¹ H NMR δ (ppm)
3b	1614 (CO), 3343 (N-H); (DMSO-d ₆): δ 6.6 (s, 1H, CH=C), 7.2-7.8 (m, 13H, Ar-H),
	9.3 (s, 1H, N-H), 9.4 (s, 1H, N-H)
3c	1612 (CO), 3267 (N-H); (DMSO-d ₆): δ 6.8 (s, 1H, CH=C), 7.2-8.3 (m, 14H, Ar-H),
	9.4 (s, 1H, N-H), 9.5 (s, 1H, N-H)
3d	1620 (CO), 3268 (N-H); (DMSO-d ₆): δ 3.2 (s, 2H, CH ₂), 6.7 (s, 1H, CH=C), 6.3-7.4
	(m, 13H, furan & Ar-H), 9.3 (s, 1H, N-H), 9.4 (s, 1H, N-H)
3e	1624 (CO), 3243 (N-H); (DMSO-d ₆): δ 2.6 (s, 3H, 5'CH ₃), 6.9 (s, 1H, CH=C), 7.2-
	7.4 (m, 10H, Ar-H), 9.5 (s, 1H, N-H), 9.6 (s, 1H, N-H)
3f	1628 (CO), 3248 (N-H); (DMSO-d ₆): δ 6.8 (s, 1H, CH=C), 7.2-7.8 (m, 15H, Ar-H),
	9.6 (s, 1H, N-H), 9.7 (s, 1H, N-H)
4b	1642 (C=N), 1715 (CO); (CDCl ₃): δ 6.9 (s, 1H, CH=C), 7.0-7.4 (m, 13H, Ar-H)
4 c	1640 (C=N), 1720 (CO); (DMSO-d ₆): δ 7.0 (s, 1H, CH=C), 6.9-7.6 (m, 14H, Ar-H
	& pyridyl)
4d	1652 (C=N), 1710 (CO); (DMSO-d ₆): δ 3.2 (s, 2H, CH ₂), 6.9 (s, 1H, CH=C), 6.3-
	7.4 (m, 13H, furyl & Ar-H)
4e	1649 (C=N), 1720 (CO); (DMSO-d ₆): δ 2.7 (s, 3H, 5'CH ₃), 7.2-7.5 (m, 10H, Ar-H)
4f	1650 (C=N), 1725 (CO); (DMSO): δ 7.2-7.8 (m, 15H, Ar-H)

Melting points, yields and spectroscopic data are given in Tables 1, 2 and 3.

2-Phenyl-4-phenylmethylene-2-oxazolin-5-one (1)

Compound 1 was prepared according to the literature method. $^{\rm 12}$

Arylcarboxamides of $\alpha\mbox{-}arylcarboxamido\mbox{-}\beta\mbox{-}arylacrylic acids (3a-f) from (1)$

To the solution of 1 (0.05 mole) and primary amine **2a-f** (0.05 mole) in ethanol (10 mL), basic alumina¹⁴ (20 g) was added. The reaction mixture was stirred well, air dried and

subjected to MWI. On completion of reaction, as monitored by TLC (at an interval of 30 s), the product was extracted into ethanol (3×15 mL). Recovery of solvent under reduced pressure gave the product **3a-f** which was recrystallized from ethanol.

1,2-Diaryl-4-phenylmethylene-2-imidazolin-5-ones (4a-f) from (1)

To the solution of **1** (0.05 mole) and primary amines **2a-f** (0.05 mole) in ethanol, acidic alumina or montmorillonite K10 clay¹⁴ was added. The reaction mixture was stirred well, dried in air and subjected to MWI for a specified time (Table 2). On completion of reaction, as monitored by TLC examination (at an interval of 30 s), the product was extracted into ethanol (3×15 mL). Recovery of solvent gave the required product **4a-f** which was recrystallized from ethanol.

1,2-Diaryl-4-phenylmethylene-2-imidazolin-5-ones (4a-f) from (3a-f)

To the solution of **3a-f** (0.05 mole) in ethanol, acidic alumina (20 g) or montmorillonite (20 g) was added. The reaction mixture was stirred well, dried in air and subjected to MWI for a specified time (Table 2). On completion of reaction, as followed by TLC examination (at an interval of 30 s), the product was extracted into ethanol (3×10 mL). Removal of solvent under reduced pressure gave the required product **4a-f** which was recrystallized from ethanol.

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- 14. (a) Aluminium oxide, Basic Brockmann 1 (Aldrich Chem. Co., Cat No. 19, 944-3, ~ 150 mesh, 58 Å, surface area 155 m²/g) was used. (b) Aluminium oxide, acidic, Aldrich 26, 774-0, Brockmann 1, ~ 150 mesh, 58 Å CAMAG 506-C-1, surface area 155 m²/g was used. (c) Montmorillonite K10 clay, Aldrich 11, 6168, surface area 220-270 m²/g, Bulk density 300-370 g/l.