

## Synthesis of Unsaturated 5(4H)-Oxazolone Derivatives in the Presence of Antimony Pentafluoride as Catalyst

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Unsaturated 2-phenyl-5(4H)-oxazolone derivatives (azlactons) are the important class of synthons. Antimony pentafluoride efficiently catalyzed the synthesis of unsaturated 2-phenyl-5(4H)-oxazolone derivatives under solvent-free conditions with microwave irradiation.

**Key Words:** Microwave irradiation, 5(4H)-Oxazolone, Catalyst.

### INTRODUCTION

Oxazoles and oxazolones are important synthons for the synthesis of several compounds such as amino acids, dyes, drugs and biological active compounds<sup>1-4</sup>. In recent years, new theory of the origin of life on earth in proposed by chemists. They reported that in hot water, methanethiol 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 they form peptides similar to those at under sea volcanic vents blasters<sup>5</sup>. Synthesis of these ring systems involves cyclization of 2-acylamino acids by various reagents, such as acetic anhydride with sodium acetate, acetic anhydride with lead acetate, polyphosphoric acid, sulphur trioxide/dimethyl formamide complex, perchloric acid and carbodiimides<sup>6-8</sup>.

In recent years the use of microwave irradiation in organic reactions has received considerable attention, this method can increase the purity of the resulting products, enhance the chemical yield and shorten the reaction time<sup>9-12</sup>. 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, *i.e.*, organic reactions using catalyst with microwave irradiation has been a field, which has shown excellent results leading to the development of many reaction procedures, which are environmental friendly falling in the domain of green chemistry<sup>12-14</sup>.

## EXPERIMENTAL

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Mass spectra were obtained on a Shimadzu QP 1100 EX. Infrared spectra were recorded with a Mattson 1000 FTIR spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Bruker DRX-500 Avance spectrometer using tetramethylsilane as an internal standard. All reaction were carried out in an unmodified domestic microwave oven BC380W having a maximum output of 900 W operating at 2450 MHz.

### 2-Phenyl-5(4H)-oxazolone derivatives (3a-j)

**Microwave method:** The appropriate aldehyde or ketone (**1**) (0.01 mol), hippuric acid (**2**) (0.01 mol), acetic anhydride (0.03 mol) and SbF<sub>5</sub> (1 mL) were introduced into a beaker. The paste was irradiated in a microwave oven at a power output of 300 W for the appropriate time (Table-1). After irradiation, the mixture was cooled to room temperature and was washed with cooled water, then crude product was recrystallized from ethanol 96 %.

TABLE-1  
SbF<sub>5</sub> CATALYZED SYNTHESIS OF UNSATURATED 5(4H)-  
OXAZOLONE DERIVATIVES UNDER SOLVENT-FREE CONDITION  
AND MICROWAVE IRRADIATION (POWER = 300 W)

Compounds	Time (min)	m.p. (°C)	Lit. m.p. (°C)	Yield (%)
<b>3a</b>	3	163-164	165-166 <sup>15</sup>	98
<b>3b</b>	5	198-199	197 <sup>16</sup>	89
<b>3c</b>	3	157-158	156 <sup>17</sup>	98
<b>3d</b>	5	174-171	175-176 <sup>16</sup>	98
<b>3e</b>	3	170-171	171 <sup>17</sup>	96
<b>3f</b>	4	151-152	153 <sup>17</sup>	92
<b>3g</b>	5	141-142	139 <sup>17</sup>	87
<b>3h</b>	5	85-86	84 <sup>17</sup>	79
<b>3i</b>	5	99-100	99 <sup>17</sup>	61

**Thermal heating method:** The appropriate aldehyde or ketone (**1**) (0.01 mol), hippuric acid (**2**) (0.01 mol), acetic anhydride (0.03 mol) and SbF<sub>5</sub> (1 mL) were introduced into a beaker. The mixture was heated with stirring until the mixture had gone from a pink, semi-solid mass to a deep orange liquid for the appropriate time (Table-2). The crude product was cooled and washed with cooled water then recrystallized from ethanol 96% (with using active carbon). The structure of the products were confirmed by IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, mass spectroscopy (Table-3).

TABLE-2  
SbF<sub>5</sub> CATALYZED SYNTHESIS OF UNSATURATED 5(4H)-  
OXAZOLONE DERIVATIVES UNDER FREE- SOLVENT CONDITION  
AND THERMAL HEATING (**3a-i**)

Compounds	Time (min)	Reaction Temperature (°C)	Yield (%)
<b>3a</b>	15	90-95	88
<b>3b</b>	23	90-95	80
<b>3c</b>	15	90-95	79
<b>3d</b>	30	90-95	87
<b>3e</b>	20	90-95	78
<b>3f</b>	20	90-95	77
<b>3g</b>	20	90-95	68
<b>3h</b>	35	42-45	63
<b>3i</b>	35	48-51	47

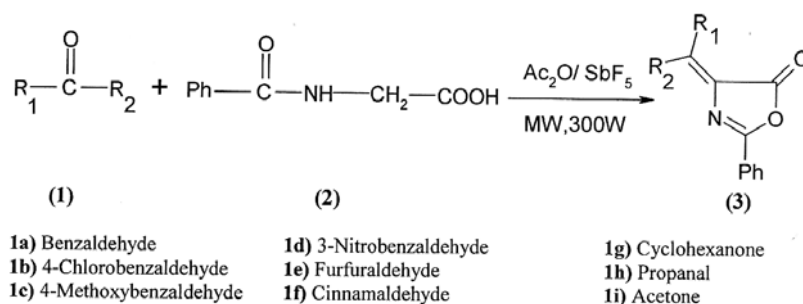
TABLE-3  
SPECTRAL DATA OF COMPOUNDS **3a-i**

Product	IR (KBr) / ν (cm <sup>-1</sup> )	<sup>1</sup> H NMR (CDCl <sub>3</sub> )/δ(ppm)	m/z (%)
<b>3a</b>	1790, 1650	7.24 (s, 1H, vinyl), 7.44-8.12 (m, 10H, ArH)	249 (M <sup>+</sup> , 15), 105 (100), 77 (70)
<b>3b</b>	1800, 1650	7.44 (m, 10H, vinyl and ArH)	285 (M <sup>+</sup> , 2) 283 (M <sup>+</sup> , 15), 105 (100), 77 (70)
<b>3c</b>	1790, 1660	4.02 (s, 3H, CH <sub>3</sub> ), 7.07 (s, 1H, vinyl), 7.25-8.22 (m, 9H, ArH)	279 (M <sup>+</sup> , 10) 105 (100), 77 (70)
<b>3d</b>	1800, 1660	7.42-8.29 (m, 10H, vinyl and ArH)	249 (M <sup>+</sup> , 15) 105 (100), 77 (70)
<b>3e</b>	1790, 1660	6.66 (q, 1H, 2-furyl), 7.17-8.28 (m, 8H, viny, furyl and ArH)	239 (M <sup>+</sup> , 5) 105 (100), 77 (70)
<b>3f</b>	1790, 1660	6.89-7.00 (m, 2H, vinyl), 7.28-8.19 (m, 11H, vinyl, ArH)	275 (M <sup>+</sup> , 10) 105 (100), 77 (70)
<b>3g</b>	1780, 1650	1.34-2.13 (m, 10H, cyclohexyl), 7.34-7.88 (m, 5H, ArH)	241 (M <sup>+</sup> , 10) 105 (100), 77 (70)
<b>3h</b>	1790, 1660	1.19 (t, 3H, CH <sub>3</sub> ), 2.19 (m, 2H, CH <sub>2</sub> ), 7.14 (t, 1H, vinyl), 7.45-7.98 (m, 5H, ArH)	201 (M <sup>+</sup> , 10) 105 (100), 77 (70)
<b>3i</b>	1780, 1660	2.04 (d, 6H, CH <sub>3</sub> ), 7.44-7.89 (m, 5H, ArH)	201 (M <sup>+</sup> , 10) 105 (100), 77 (70)

## RESULTS AND DISCUSSION

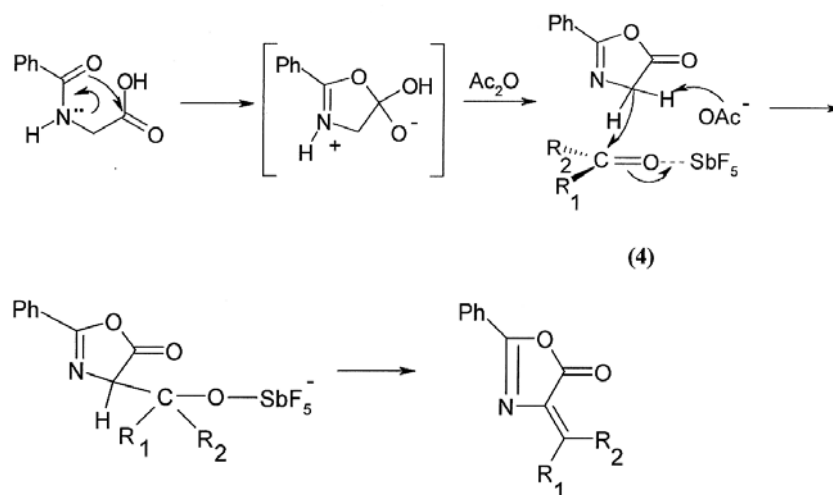
Antimony pentafluoride was used as the catalyst, which gives the excellent yield of product and has not been reported to use this compound as a catalyst for such synthesis. 5(4H)-Oxazolones are important synthons for biologically compounds and the advantages of these reactions offered by solvent-free media reactions. 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 antimony pentafluoride under microwave irradiation and thermal heating is reported (**Scheme-1**).



**Scheme-1**

The activity of antimony pentafluoride for the synthesis of 5(4H)-oxazolones (**3a-i**) was carried out with two methods, microwave irradiation and thermal heating. The best results were obtained in case of microwave irradiation (Table-2). It has been found that for 0.01 mol of aldehyde or ketone, 0.01 mol of hippuric acid and 0.03 mol of acetic anhydride, 1 mL of antimony pentafluoride was required. A power setting of 300 W appeared to be the best compromise between efficiency and safety (higher power output leads to fumes and reduction in yields).



**Scheme-2**

This effect can be attributed to the carbonyl complexation by antimony pentafluoride 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 80%) and 35 min for thermal heating (80°C) (yield 67%).

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**, 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 microwaves (dipole-dipole interaction), leading to a lowering in the activation energy<sup>17</sup>.

Consequently, antimony pentafluoride 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.

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