Microwave-Assisted Studies on the Reactions of the 4-Benzoyl-5-Phenyl-2,3-Dihydro-2,3-Furandione and Derivatives

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Abstract: Varieties of heterocyclic compounds were prepared in good yield from 4-benzoyl-5-phenyl-2,3-dihydro-2,3-furandione under microwave irradiation conditions. The reaction revealed much shorter reaction times with comparable yields comparison to the corresponding thermal conditions.

Keywords: Microwave-assisted, 2,3-furandione, synthesis, cyclic oxalyl compounds.

The interest in substituted 2,3-dihydro-2,3-furandiones is caused by their high reactivity and the possibility of using them as starting compounds for preparing various carbonyl compounds of acyclic and heterocyclic series [1-4].

The reactions of substituted 2,3-dihydro-2,3-furandiones have been studied with several semi/thiosemicarbazones, ureas, thioureas, oximes, various hydrazines, some acetanilides and amides under different conditions [5-13]. Most of these obtained compounds in general are well known for their potential biological activities [14].

In the last few years there has been an increased interest in the use of microwave heating in organic synthesis and it forms now the basis of a number of commercial systems. Some interesting features of this method are the rapid reaction rates, simplicity, solvent-free conditions, and the case of work-up after the reaction, and better selectivity. Also, microwave irradiation generates rapid intense heating of polar substances, which result in the reduction of reaction time compared to conventional heating [15-18].

Another improvement that can be made in the cyclic oxalyl compound derivatives synthesis is the diminution of the reaction time by using microwave technology. Indeed, most published conventional synthetic procedures required long reaction times that vary between 1-24 hours or more time. Microwave heating is an area of increasing interest in both industrial and academic studies because it can increase the rate of reaction and in many cases improve product yields [19].

The purpose of the present work is to extend the 2,3-dihydro-2,3-furandione reactions in order to synthesize some heterocyclic derivatives. The reported method is suggested a fast and efficient route for the preparation of cyclic oxalyl compound derivatives.

A survey of the literature reveals several reports on reactions of the 4-benzoyl-5-phenyl-2,3-dihydro-2,3-furandione (**1**), but no literature precedent exists on the microwave-promoted of this compound.

We now report that the synthesis of pyrazole-3-carbonylurea, aminobenzoates, pyrimidines [8], pyrazole carboxylic acids [13,14], pyridazines [13,14] and pyrazolopyridazine [20] derived from compound **1** were equally effective in solvent both under thermal as well as under microwave-induced conditions Scheme **1**.

A variety of substrates were successfully reacted under microwave condition; results are summarized in Table **1**.

The time of 45-360 min was chosen for thermal heating whereas microwave-induced reactions were performed at 50 W for 5–10 min with internal reaction temperatures. Under both sets of conditions, the desired compounds were obtained in good yield and in excellent purity by a simple crystallization.

We selected the synthesis of these compounds as a model reaction to study the effects of irradiation power and time on the yields. The best yields obtained are 56% (**5a**) after 5 min of irradiation using benzene as solvent.

In summary, the synthesis of cyclic oxalyl compound derivatives has been accomplished followed by the nucleophilic addition of urea, amines, and hidrazines under microwave irradiation. The main advantages of this method are short reaction times.

DATA FOR THE SELECTED COMPOUNDS

Compound 2

IR(KBr): 3324 and 3060(2NH), 1704, 1686, 1658(C=O); ^{1}H-NMR ($CDCl_3$): 10.13 (1H, bs, NH, NH⇆OH), 8.13-8.10 (1H, t, -NH), 7.77-7.15 (15H, m, ArH), 5.84-5.77 (1H, m, =CH), 5.08-5.01 (2H, t, CH_2), 3.77-3.75 (2H, t, $=CH_2$); ^{13}C-NMR ($CDCl_3$): 190.93, 162.04 and 152.75 (C=O), 144.38, 144.21, 139.08, 138.00, 135.71, 134.21, 130.38, 130.12. 129.79, 129.78, 129.55, 129.29, 129.17, 128.21, 126.37, 122.73, 115.89, 42.07 (CH_2). Microanalyses: C, 72.01; H, 4.90; N, 12.49%.

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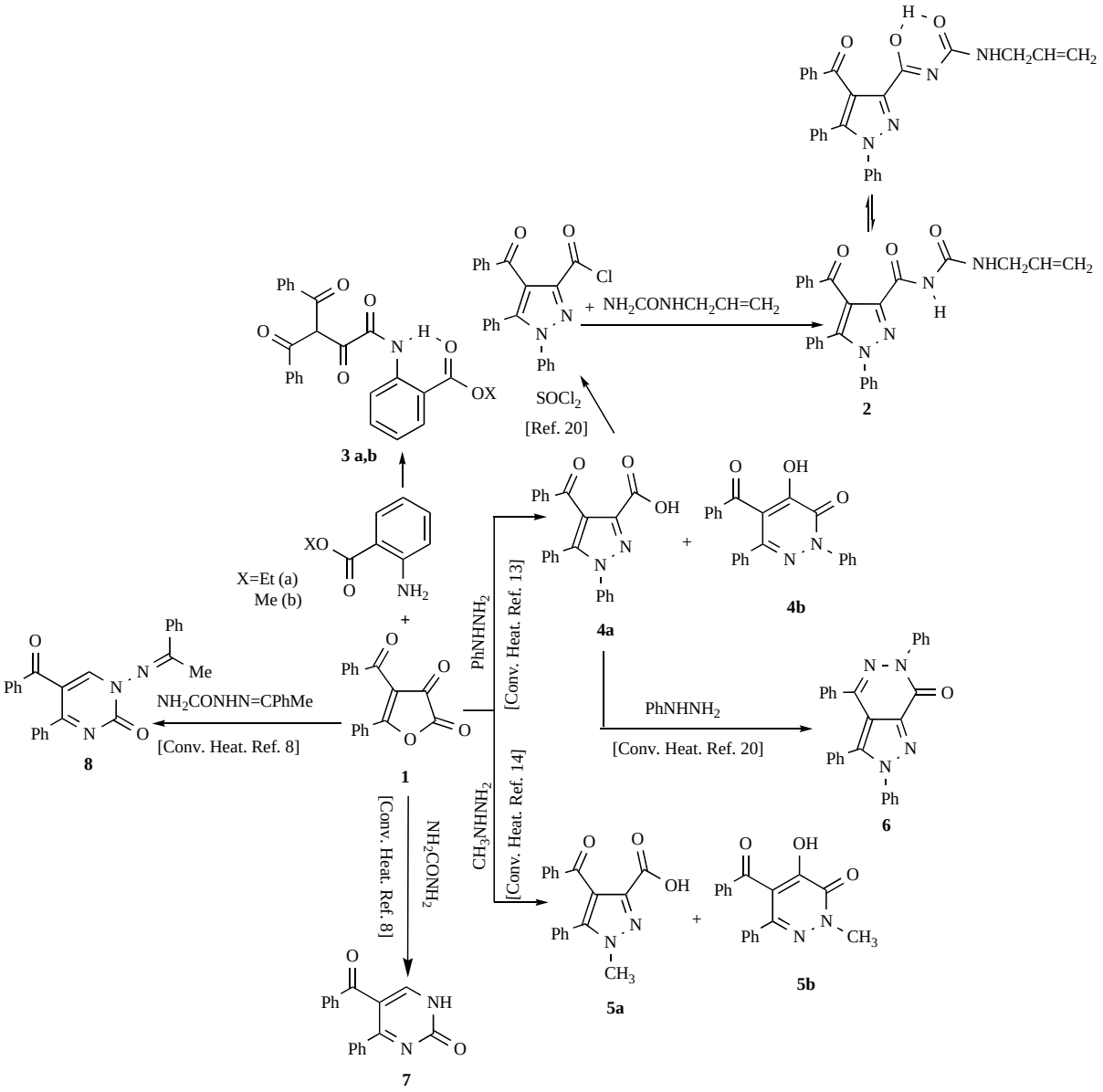
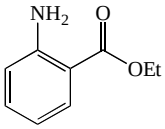
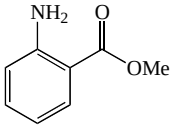


Scheme 1.

Table 1. Comparative Study of the Synthesis of 2-8

Compound	Substrate	[a]Yield (%)		Solvents used	[b]Reaction time/min	
		MW	CONV.		MW	CONV.
2	$NH_2CONHCH_2CH=CH_2$	38%	29%	xylene	5	360
3a		23%	20%	benzene	10	180
3b		28%	22%	*p*- xylene	10	180
4a	$PhNHNH_2$	33%	49%	benzene	5	60

(Table 1). Contd…..

Compound	Substrate	[a]Yield (%)		Solvents used	[b]Reaction time/min	
		MW	CONV.		MW	CONV.
4b	$PhNHNH_2$	11%	10%	benzene	5	60
5a	CH_3NHNH_2	56%	45%	benzene	5	60
5b	CH_3NHNH_2	36%	40%	benzene	5	60
6	$PhNHNH_2$	49%	70%	xylene	10	180
7	NH_2CONH_2	23%	36%	benzene	10	210
8	$NH_2CONHN{=}CPhMe$	34%	38%	benzene	5	45

[a]Isolated yield.
[b]Reaction times not optimized.

Compound 3a

IR(KBr): 3213 (NH), 1730, 1702, 1697, 1664, 1583 (C=O); ^{1}H-NMR ($CDCl_3$): 8.90 (1H, s, NH), 8.85 (1H, s, -CH), 8.15-7.15 (14H, m, ArH), 4.53-4.42 (2H, q, $-OCH_2$), 1.48-1.40 (3H, t, CH_3); ^{13}C-NMR ($CDCl_3$): 201.05, 189.54, 181.85 and 169.42 (C=O), 148.02, 141.59, 138.01, 137.08, 136.40, 133.12, 125.85, 122.47, 121.65, 118.87, 63.74($-OCH_2$), 16.25 (CH_3). Microanalyses: C, 70.44; H, 4.68; N, 3.18%.

Compound 3b

IR(KBr): 1732, 1707, 1673, 1668, 1591 (C=O); ^{1}H-NMR ($CDCl_3$): 8.71 (1H, s, NH), 8.67 (1H, s, -CH), 8.55-7.13 (14H, m, ArH), 3.02 (3H, s, CH_3). Microanalyses: C, 69.90; H, 4.41; N, 3.28%.

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