

Maltose as a green catalyst for the synthesis of 3,4,5-substituted furan-2(5H) ones in water

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ABSTRACT

Maltose as an efficient, available, cheap and eco-friendly catalyst has been applied for the synthesis of 3,4,5-substituted furan-2(5H)one derivatives via a one-pot three-component reaction of arylamines, aromatic aldehydes and dialkyl acetylenedicarboxylates in water. This method has notable advantages in terms of simple workup, no need for column chromatography, short reaction time and high yields.

Keywords: Maltose, 3,4,5-Substituted furan-(5H), Three-component reaction.

1. Introduction

Green chemistry is a vast field that provides us a proactive path to perform chemical processes in a very controlled way, so as to reduce drastically, or to eliminate completely, all the environmental impact. One important aspect of green chemistry is the replacement of hazardous solvents and catalysts with environmentally benign ones and one of the most challenging tasks in organic synthesis is the efficient preparation of reaction mixture from easily available raw materials. In this investigation we use of maltose as a green, cheap and available catalyst for the synthesis of 3,4,5-substituted furan-2(5H) one derivatives in water in good yields.

Heterocycles containing furan-2(5H)-one fragment generally named as butenolides are a key moiety of natural molecules. For example, some natural products such as acetogenins, muconolactones, leptospharin, and strigol have butenolide cores [1-6]. These compounds show a wide range of biological activities, such as antimicrobial [7-8], antifungal [9-10], anti-inflammatory [11], anticancer [12,13] and anti-viral HIV-1 [14-16]. A number of synthetic methods have been reported to prepare this class of compounds in the past few years [17-24].

Among the available methods for the construction of butenolides, the nucleophilic reaction between zwitterions of amine and dialkyl acetylenedicarboxylates with aldehyde is the most convenient [25-29]. However, most of the reported methods suffer from hazardous solvents and catalysts and often from low yields. Therefore, simpler, greener and high yield approaches towards this valuable nucleus is much desirable.

In this study we report an efficient method for the synthesis of 3,4,5-substituted furan-2(5H)one derivatives via a one-pot three-component reaction of amines, aldehydes and dialkyl acetylenedicarboxylates in water using maltose as a green catalyst.

2. Experimental

Melting points and IR spectra of all compounds were measured on an Electrothermal 9100 apparatus and a JASCO FTIR 460 Plus spectrometer, respectively. The ¹HNMR and ¹³CNMR spectra were obtained on Bruker DRX-400 Avance instruments with CDCl₃ as a solvent. All reagents and solvents obtained from Fluka and Merck were used without further purification.

2.1. General procedure for the synthesis of 3,4,5-substituted furan-2(5H)-ones derivatives

The mixture of aldehyde (1.0 mmol), amine (1.0 mmol), dialkylacetylenedicarboxylate (1.0 mmol) and

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maltose (40 mol %) were stirred at room temperature in water. After completion of the reaction (monitored by thin-layer chromatography, TLC), the reaction mixture was filtrated and washed with water:ethanol (1:1) (3×3 mL) to separate the catalyst, and then washed with ethanol to obtain the pure product.

Selected spectral data

t-Butyl-2,5-dihydro-5-oxo-2-(4-bromophenyl)-4-(phenylamino)furan-3-carboxylate (**4o**):

White powder. m.p.= 169-172 °C. IR (KBr): $\bar{\nu}$ = 3208, 1716, 1677, 1596, 1499 cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ = 1.39 (s, 9H, 3×Me), 5.65 (s, 1H, $\text{H}_{\text{benzylic}}$), 7.09-7.14 (m, 3H, H_{Ar}), 7.27-7.31 (m, 2H, H_{Ar}), 7.38-7.41 (m, 2H, H_{Ar}), 7.34-7.45 (m, 2H, H_{Ar}), 9.32 (brs, 1H, NH) ppm. ^{13}C NMR (CDCl_3 , 100 MHz): δ = 28.0 (3×Me), 61.0 ($\text{C}_{\text{benzylic}}$), 83.5 (OCMe_3), 114.0, 122.3, 122.4, 125.9, 129.0, 129.3, 131.6, 134.5, 136.0 and 156.9 (C_{Ar} and C=C), 162.7 and 164.8 (C=O) ppm.

t-Butyl-2,5-dihydro-5-oxo-2-phenyl-4-(3-nitrophenyl amino)furan-3-carboxylate (**4p**):

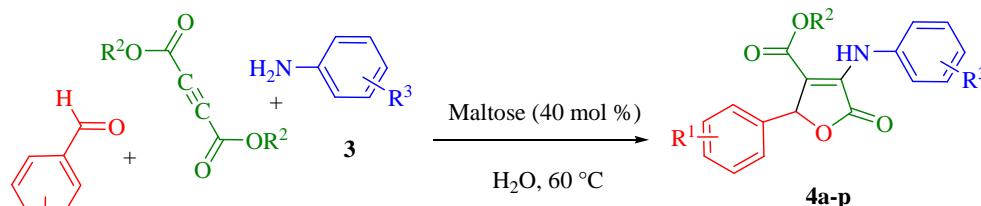
White powder. m.p.= 165-168 °C. IR (KBr): $\bar{\nu}$ = 3142, 1715, 1681, 1531, 1456 cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ = 1.37 (s, 9H, 3×Me), 5.76 (s, 1H, $\text{H}_{\text{benzylic}}$), 7.24-7.32 (m, 5H, H_{Ar}), 7.64 (t, 1H, J =8.0 Hz, H_{Ar}), 7.93 (ddd, J = 8.0, 2.0, 0.8 Hz, 1H, H_{Ar}), 8.09 (ddd, J = 8.4, 2.4, 0.8 Hz, 1H, H_{Ar}), 8.32 (t, 1H, J = 2.4 Hz, H_{Ar}), 9.40 (brs, 1H, NH) ppm. ^{13}C NMR (CDCl_3 , 100 MHz): δ = 27.9 (3×Me), 61.3 ($\text{C}_{\text{benzylic}}$), 83.8 (OCMe_3),

115.1, 115.9, 119.9, 127.3, 127.5, 128.8, 128.9, 129.8, 134.4, 137.6, 148.3 and 156.9 (C_{Ar} and C=C), 163.1 and 164.9 (C=O) ppm.

3. Results and Discussion

Presently, green reactions have received considerable attention for all chemists. In continuation of our investigation [30-33], we describe a green reaction between arylamines, aromatic aldehydes and dialkyl acetylenedicarboxylates for the synthesis of 3,4,5-substituted furan-2(5H) one derivatives in water (Scheme1).

In order to optimize the conditions, first we studied the reaction of aniline (1.0 mmol), benzaldehyde (1.0 mmol) and dimethyl acetylenedicarboxylate (1.0 mmol) with maltose as catalyst simple model substrate in various conditions. Continually assess of catalysts were investigated. When the reaction was carried out in the absence of any catalyst the product was not detected. In the presence of maltose, the reaction was possible, and in order to determine the appropriate concentration of the catalyst used, we investigated the model reaction at different concentrations of catalyst. The product was formed in different yield, respectively. It was observed that 40 mol % loading of maltose provided the maximum yield. Higher amount of the catalyst increased the reaction time (Table 1).



Scheme 1. Synthesis of 3,4,5-substituted furan-2(5H)one derivatives in water using maltose.

Table 1. Optimization amount of maltose for the synthesis of furan-2(5H)-one under temperature conditions.

Entry	Maltose/mol %	Time/h	Isolated Yield/%
1	5	3.5	37
2	10	3	52
3	20	3	60
4	30	2	68
5	40	2	80
6	50	2.5	74

^aReaction conditions: benzaldehyde (1.0 mmol), aniline (1.0 mmol), dimethyl acetylenedicarboxylate (1.0 mmol) and maltose as a catalyst at 60 °C.

Continually, a mixture of amines, aldehydes and dialkyl acetylenedicarboxylates in water was stirred at different temperatures to afford the products in high yields. It was observed that yield was a function of temperature, since the yield increased as the reaction temperature rose, at 60 °C, the product was obtained in a good yield and at the higher temperature did not increase the reaction yield (Table 2).

Encouraged by this result, in order to build the generality of the reaction, our attention moved to the

reactions of other aromatic aldehydes, and the results are summarized in Table 3. As expected, this reaction proceeded smoothly and the desired products were obtained in good to excellent yields (Table 3).

These results indicate the effectiveness of electron-withdrawing and electron-donating groups on the time and yield of the reaction. Benzaldehydes with electron-withdrawing groups react with aniline better than electron-donating groups for generation of furan-2(5*H*)-ones in good to high yields.

Table 2. Optimization of temperature for the synthesis of furan-2(5*H*)-one by maltose.

Entry	Temp. (°C)	Time (h)	Isolated Yield %
1	25	6	-
2	30	3.5	37
3	40	3	60
4	50	2	69
5	60	2	80
6	70	3	57

^aReaction conditions: benzaldehyde (1.0 mmol), aniline (1.0 mmol), dimethyl acetylenedicarboxylate (1.0 mmol) and maltose (40 mol %).

Table 3. Synthesis of furan-2(5*H*)-one derivatives.

Entry	R ¹	R ²	R ³	Products	Time (h)	Yield% ^a	m.p. (°C)	Lit. m.p. (°C)	Ref.
1	H	CH ₃	H	4a	2	80	181-183	183-185	[30]
2	4-Me	CH ₃	H	4b	4.5	73	182-184	180-183	[30]
3	3-NO ₂	CH ₃	H	4c	5.5	74	169-170	168-169	[30]
4	4-NO ₂	CH ₃	H	4d	5	81	176-179	170-171	[31]
5	4-OMe	CH ₃	H	4e	7.5	80	177-179	170-173	[31]
6	H	CH ₃	4-F	4f	3	63	158-160	156-158	[31]
7	H	CH ₃	4-Cl	4g	2	64	168-166	165-166	[31]
8	H	CH ₃	3-NO ₂	4h	7.7	72	188-190	179-182	[31]
9	H	CH ₃ CH ₂	H	4i	3	81	177-178	179-181	[25]
10	H	CH ₃ CH ₂	4-Me	4j	3.5	82	179-180	179-181	[25]
11	4-Me	CH ₃ CH ₂	H	4k	4.5	78	197-196	195-197	[25]
12	4-Cl	CH ₃ CH ₂	H	4l	5.5	83	187-186	183-185	[25]
13	4-OMe	CH ₃ CH ₂	H	4m	7	82	197-195	197-199	[31]
14	1-naphtyl	CH ₃ CH ₂	H	4n	7.5	58	198-200	197-199	[25]
15	4-Br	<i>t</i> -Bu	H	4o	5	67	169-172	b	
16	H	<i>t</i> -Bu	3-NO ₂	4p	8	83	165-168	b	

^aIsolated yield.

^bThe new compounds synthesized in this work. All known products reported previously in the literature were characterized by comparison of m.p., IR and NMR spectra with those of authentic samples.

The proposed mechanism for the formation **4** is shown in Scheme 2. First, Michael nucleophilic addition of amine **3** to acetylenic ester **2**, generates the enaminone **A**. Next, nucleophilic attack of enaminone **A** to the aldehyde **1** would yield iminium-oxoanion intermediate **B**, that can be tautomerized to dialkyl 2-(hydroxy(phenyl)methyl)-3-(arylamino)-2-butenedioate **C**. γ -Lactonization of **C** would produce the alkyl-2,5-dihydro-5-oxo-2-aryl-4-(arylamino)furan-3-carboxylate derivatives **4** [34,35].

To compare the efficiency of maltose with the reported catalysts in the literature for the synthesis of 3,4,5-substituted furan-2(5*H*)-ones, we have tabulated the results of these catalysts in Table 4. As shown in Table 4, maltose can act as efficient catalyst with respect to reaction time and yield of products.

4. Conclusions

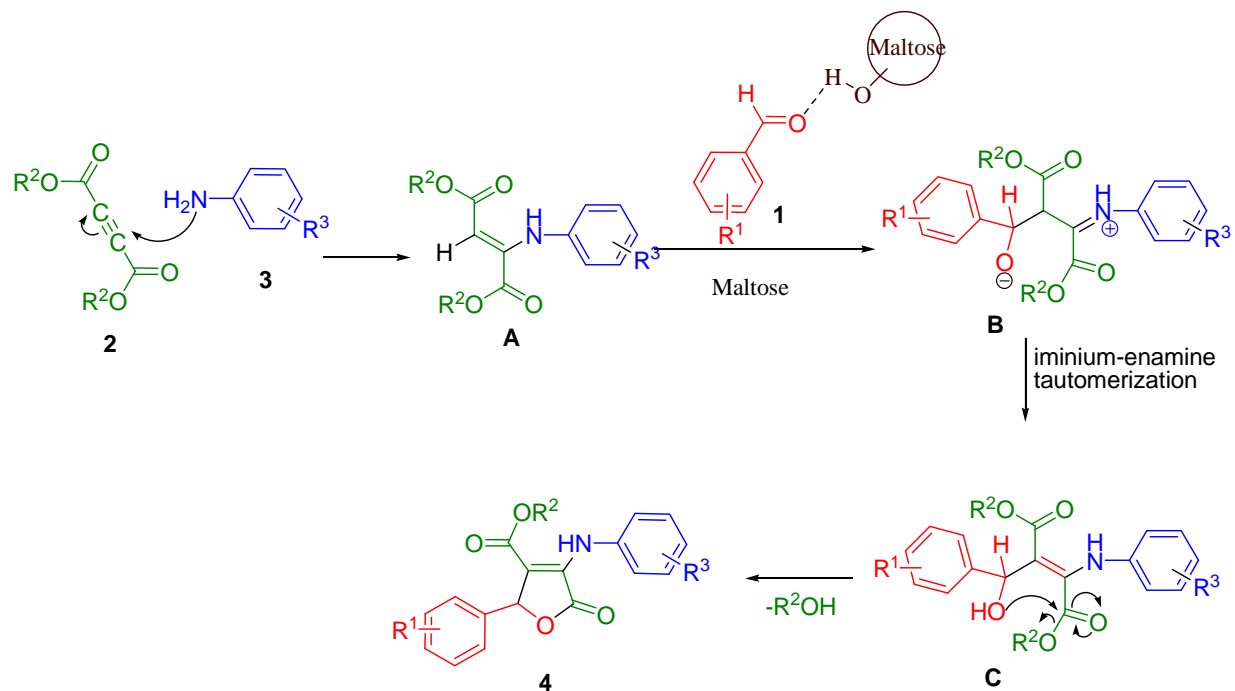
In conclusion, we have presented here our methodology for the synthesis of 3,4,5-substituted furan-2(5*H*) one derivatives with water as green solvent in the presence of maltose as a green catalyst. We have shown that maltose is an efficient and green catalyst for the synthesis of these compounds.

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Scheme 2. The proposed mechanism for the formation of furan-2(5*H*)-one derivatives.

Table 4. Comparison result comparison result of maltose with the reported catalysts in literature for the synthesis of 3,4,5-substituted furan-2(5*H*)-ones **4a** and **4i**.

Entry	Product	Catalyst	Conditions	Time	Yield (%)	Ref.
1	4a	β -Cyclodextrin	H ₂ O/ 60-70 °C	-	-	[25]
2		Nano-ZnO	EtOH: H ₂ O/ 90 °C	2.5 h	94	[27]
3		Al(HSO ₄) ₃	EtOAc, r.t.	8 h	84	[28]
4		SnCl ₂ .2H ₂ O	EtOH/ Reflux	6.5 h	90	[26]
5		AcOH	r.t.	-	-	[30]
6		[Bu ₄ N][HSO ₄]	EtOH, r.t.	5 h	92	[32]
7		PPA/SiO ₂	EtOH, r.t.	1 h	90	[31]
8		Sucrose	H ₂ O/ 65 °C	9 h	97	[33]
9		Maltose	H ₂ O/ 60 °C	2 h	80	This work
10	4i	β -Cyclodextrin	H ₂ O/ 60-70 °C	12 h	85	25
11		Nano-ZnO	EtOH: H ₂ O/ 90 °C	-	-	27
12		Al(HSO ₄) ₃	EtOAc, r.t.	9 h	77	28
13		SnCl ₂ .2H ₂ O	EtOH/ Reflux	-	-	26
14		AcOH	r.t.	1 h	95	30
15		[Bu ₄ N][HSO ₄]	EtOH, r.t.	2 h	90	32
16		PPA/SiO ₂	EtOH, r.t.	1 h	91	31
17		Sucrose	H ₂ O/ 65 °C	4.5 h	85	33
18		Maltose	H ₂ O/ 60 °C	3 h	81	This work

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