USING AN IMIDAZOLE-BASED COMPOUND TO SPEED UP SEVERAL ORGANIC REACTIONS

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ABSTRACT

In this work, 1,4-di(1H-imidazol-1-yl)butane or [Bisim] is identified as an imidazole-based base compound with multiple Lewis centers for catalytic processing to accelerate the new synthesis. with a variety of techniques including FT-IR, ^{1}H and ^{13}C NMR. After identification, this compound was used as an economical and recyclable catalyst in the synthesis of arylidene malononitrile derivatives, 5-arylidene barbituric acid in the presence of 4,1-di(H1-imidazol-yl)butane Bisim. This method had several advantages, including excellent efficiency, simple operation, short reaction time, and the use of a low-cost and non-toxic compound as a catalyst. In addition, the prepared [Bisim] can be recycled and reused without significant reduction in its catalytic activity in the studied reactions.

Keywords: Organo catalyst, Imidazole, 1,4-di(1*H*-imidazol-1-yl)butane [Bisim], Arylidene malononitriles, 5 arylmethylene-pyrimidine-2,4,6-tri-ones, pyrano[2,3-*d*]pyrimidinones, Dihydropyrano[3,2-*c*]chromenes.

1) Introduction

Chemistry has played a fundamental role in the development of human civilization and its position in economy, politics and daily life has become more colorful day by day. However, during its progress, chemistry, which has always benefited people, has also caused significant damage to human health and the environment. During years of effort, chemists have taken raw materials from nature that are very compatible with human health and environmental conditions and have transformed them into other materials that have damaged human health and the environment. Also, in most cases, these materials do not easily return to the natural cycle of materials and remain as stable waste in nature for many years [1].

In the meantime, enzymes, non-homogeneous catalysts and organocatalysts are known as the most important part of this great

goal [2]. These compounds have a direct effect in reducing the harm of chemical processes [3].

In addition to their synthetic range, organocatalysts have many economic benefits. The absence of metal in the structure of these compounds is important from an economic point of view, in addition to complying with the principles of green chemistry. This has caused organocatalysts to become an attractive subject in organic research and to be considered as a suitable alternative to organometallic catalysts that have been widely used in industries. Organocatalysts are mostly non-toxic organic compounds that originate from biological materials. These compounds can be Lewis or Bronsted acid or base. Of course, most of the organocatalysts that have been reported so far are Lewis bases such as 4,1-diazabi-cyclo[2,2,2]octane, L-proline, 4-(dimethylamino)pyridine, McMillan catalyst. and quinine (Figure 1).

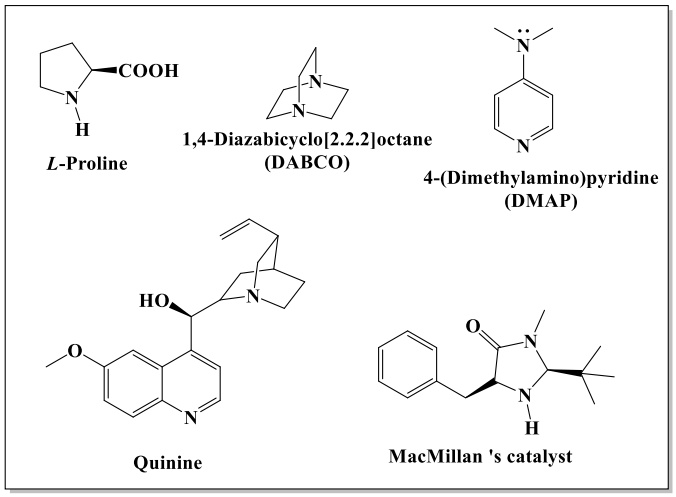

Figure (1): A number of famous organocatalysts.

Among the benefits of using organocatalysts are:

1. Reactions that are accelerated by organocatalysts have the ability to be used on a large scale for mass production in industries.

2. The range of application of these compounds is wide and many reactions catalyzed by organocatalysts cannot be performed by other catalysts.

3. A large number of organocatalysts such as L-proline, alkaloids, tartaric acid and natural amine compounds are available, which are economically viable to use.

4. Immobilization of organocatalysts on the substrate gives these compounds the ability to be reused.

5. Since a large number of organocatalysts are derived from nature, their return to nature does not cause environmental problems.

6. These compounds speed up the reaction even in mild conditions.

2) Some organic reactions catalyzed in the presence of DMAP

In 2010, Bogarin and Connell used DMAP to perform the Bayles-Hillman reaction. In this study, it was found that the DMAP catalyst accelerates the Morita-Biles-Hillman asymmetric reaction quite effectively and efficiently from the interaction of cyclopentanone with various aldehydes in the presence of MgI2 as a co-catalyst (Figure 2).

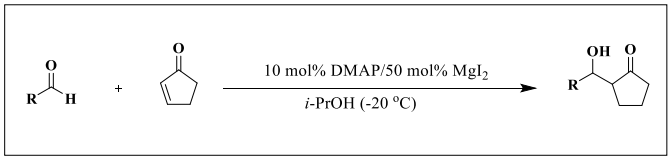

Figure (2): Morita-Biles-Hillman reaction.

Also, in 2011, Abu Khan and his colleagues synthesized the heterocyclic rings of pyran in the presence of DMAP. The remarkable features of this environmental compatibility project are simple work methods, high efficiency and the ability to recycle the catalyst [4], such as (Figure 3).

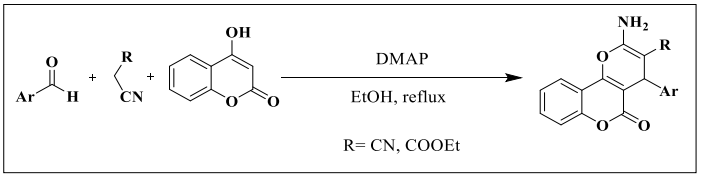

Figure (3): Synthesis of dihydropyrano[c-2,3] chromanes derivatives.

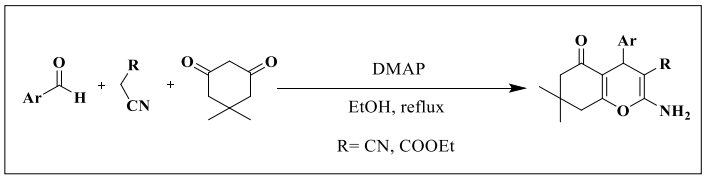

Figure (4): Synthesis of chromenes derivatives.

3) Imidazole

Imidazole was synthesized for the first time in 1858 by Henrich Debus [9], while various imidazole derivatives were prepared in 1840. Imidazole is a planar 5-membered heterocycle with slightly higher resonance energy than pyrrole [6,5], which has a melting point of 89-91 C˚, a boiling point of 255 C˚, a molecular weight of 6.80 g⁄mol and a density of g⁄It is 1/312 cm. The simplest member of this family is imidazole, which is a pale yellow crystalline solid. The molecular formula of this cyclic compound is C3H4N2. The unique feature of imidazole is its amphoteric property, which can act both as an acid and as a base in reactions, which can be justified due to its resonance structure [Figure (1-2)].

4) Two examples of organic reactions catalyzed in the presence of imidazole

4-1) Beales - Hillman reaction

In 2002, Cheng and his colleagues performed the Bills-Hillman reaction through the reaction of cyclopent-2-enone or cyclohex-2-enone and various aldehydes in the presence of imidazole as a catalyst at room temperature [Figure (14-1)].

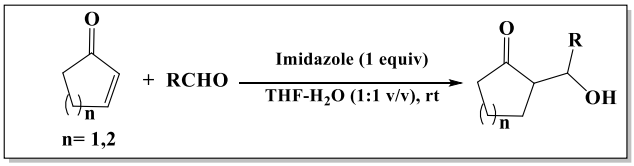

Figure (5): Beales-Hillman reaction in the presence of imidazole.

4-2) Artistic reaction

In 2009, Borah et al. used imidazole as a Lewis base catalyst in the reaction between nitroalkanes and different aldehydes under abrasive conditions and obtained significant results (Figure 6).

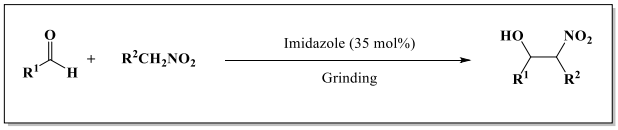

Figure (6): Art reaction in the presence of imidazole.

5) Preparation and identification of 1,4-di(H1-imidazol-yl)butane [Bisim]

By heating the mixture of imidazole and sodium hydroxide in DMSO solvent and then adding 1,4-dichlorobutane, a white fluffy precipitate was obtained, which after recrystallization in ethanol, obtained needle-shaped glass crystals. Then, several methods were used to identify it, which we will describe in the first part, Figure (7).

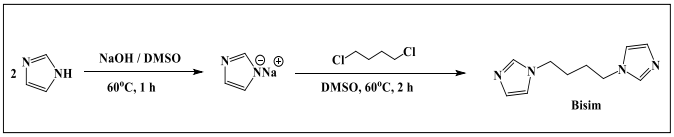

Figure (7): Preparation of -1,4-di(H1-imidazol-yl)butane Bisim.

6) Synthesis of 5-arylidene barbituric acid derivatives in the presence of Bisim

Derivatives of 5-aryl-methylene-pyrimidine-2,4,6-trione are prepared by a very simple method, by condensation of barbituric acid and aldehyde derivatives. In continuation of the aforementioned studies and investigations, the synthesis of these compounds was chosen as a suitable option to investigate the catalytic properties of Bisim. To optimize the conditions, the reaction of 4-chlorobenzaldehyde and barbituric acid was chosen as a sample reaction and the effect of changes in temperature, solvent and catalyst amount on the

reaction time and efficiency was investigated. According to the obtained results which can be seen in table (1), the best result is obtained when 5 mol percent of catalyst is used at 80°C temperature and water solvent (table 1).

Table (1): Effect of temperature, solvent and amount of catalyst in the synthesis of 5-(4-chlorobenzylidene)pyrimidine-2,4.6-(H1,H3,H5)-trione

conversion percentage	Time (minutes)	Temperature (°C)	Solvents	Catalyst (mol %)	Row
The reaction was not complete	90	Reflux	chloroform	5	1
The reaction was not complete	90	Reflux	ethanol	5	2
The reaction was not complete	90	Reflux	Acetonitrile	5	3
The reaction was not complete	90	دمای اتاق	Water	5	4
[a]](89)100	20	Water/60°C	Water	5	5
[a] **(97)100**	**9**	Water/80°C	**Water**	**5**	**6**
[a](92)100	6	Water/80°C	Water	8	7
[a] (90)100	17	Water/80°C	Water	3	8
[a] (86)100	5	Reflux	Water	5	9
[a] (90)100	22	Reflux	ا :Water Ethanol (1:1)	5	10

[a] Eleven isolated products

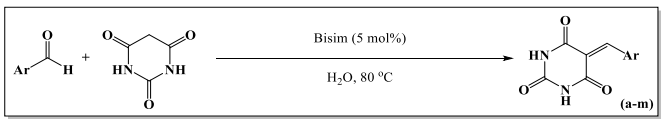

Figure (8): Synthesis of 5-arylmethylene-pyrimidine-2,4,6-trione derivatives in the presence of Bisim

After determining the optimal conditions, the desired reaction was investigated on different types of aromatic

aldehydes. The results showed that by using this method, desired products are obtained with excellent yields and in very suitable times (Table 2).

Table (2): Synthesis of 5-arylmethylene-pyrimidine-2,4,6-trione derivatives in the presence of Bisim

Reference	Melting point (°C)		Yield (%) [a]	Time (minutes)	The Product		Aldehyde	Row
	Reported	Observed						
[7]	-263 262	259-261	88	15	a	$C_6H_5CHC_4H_2O_3N_2$	C_6H_5CHO	1
[8]	-230 227	222-224	90	12	b	$3OMeC_6H_4CHC_4H_2O_3N_2$	3-$MeOC_6H_4CHO$	2
[7]	-298 296	299-300	96	9	c	$4ClC_6H_4CHC_4H_2O_3N_2$	4-ClC_6H_4CHO	3
[7]	-252 250	245-247	93	10	d	$2ClC_6H_4CHC_4H_2O_3N_2$	2-ClC_6H_4CHO	4
[7]	-270 268	265-268	91	18	e	$4NO_2C_6H_4CHC_4H_2O_3N_2$	4-$NO_2C_6H_4CHO$	5
[7]	-231 230	230-232	94	15	f	$3NO_2C_6H_4CHC_4H_2O_3N_2$	3-$NO_2C_6H_4CHO$	6
[9]	-275 277	275-273	83	17	g	$4MeOC_6H_4CHC_4H_2O_3N_2$	4-$MeOC_6H_4CHO$	7
[10]	-276 274	271-273	95	8	h	$2NO_2C_6H_4CHC_4H_2O_3N_2$	2-$NO_2C_6H_4CHO$	8
[11]	-274 276	272-270	92	15	i	$4MeC_6H_4CHC_4H_2O_3N_2$	4-MeC_6H_4CHO	9
[12]	>300	>300	96	10	j	$4FC_6H_4CHC_4H_2O_3N_2$	4-FC_6H_4CHO	10
[9]	-291 292	294-293	94	15	k	$4BrC_6H_4CHC_4H_2O_3N_2$	4-BrC_6H_4CHO	11
[9]	>300	>300	93	20	l	$4OHC_6H_4CHC_4H_2O_3N_2$	4-OHC_6H_4CHO	12
[13]	-295 294	294-296	93	12	m	$3OMe4OH5NO2C_6H_2CHC_4H_2O_3N_2$	3-$OCH_{3.4}$-OH.5-$NO_2C_6H_3CHO$	13

[a] Eleven isolated products

The proposed mechanism for the synthesis of 5-arylidene barbituric acid derivatives is shown in Figure (9). In the presented mechanism, it is assumed that barbituric acid is first activated through the basic sites of bisimidazole and then it is attacked by barbituric acid (activated

methylene) and then the intermediate produced from this process is lost Water becomes the final product.

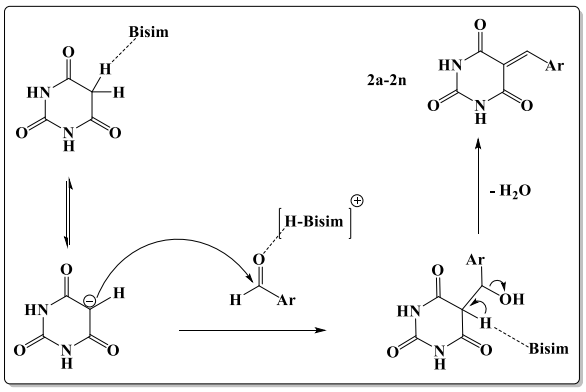

Figure (9): Synthesis mechanism of 5-aryl-methylene-pyrimidine-2,4,6-trione derivatives in the presence of [Bisim]

In this section, to check the ability to recover the catalyst, the preparation reaction of 5-(4-chlorobenzylidene)pyrimidine-2,4,6-(H1,H3,H5)-trione derivative was selected as a sample reaction. After the end of the reaction, the product was separated by filter paper. The reaction was carried out again in the filtered solution without increasing the catalyst. The recycled catalyst was able to accelerate the reaction of the sample for at least three more times with little change in yield and reaction time (Figure 10).

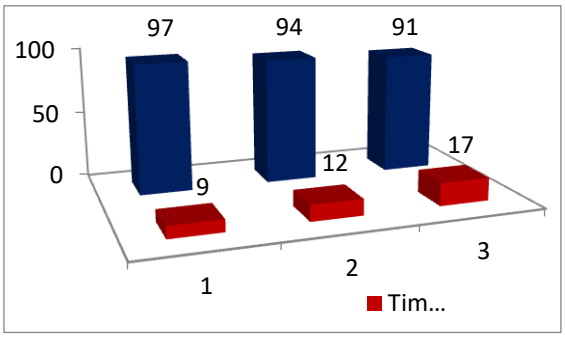

Figure (10): Catalyst recycling diagram [Bisim] in the synthesis of 5-(4-chlorobenzylidene)pyrimidine-2,4,6-(H1,H3,H5)-trione.

The comparison of the performance of the [Bisim] catalyst in the synthesis of 5-arylidene derivatives of barbituric acid with other catalysts and the methods used in similar reactions shows the proper performance of this catalyst in the synthesis of the target compounds (Table 3).

Table (3): Comparison of performance of different catalysts [Bisim] in the synthesis of 5-(4-chlorobenzylidene)pyrimidine-2,4,6-(H1,H3,H5)-trione

Reference	Yield (%)	Time (minutes)	Conditions	Catalyst (amount)	Row
[11]	93	180	Abrasion	NH_2SO_3H (100 mol%)	1
[14]	82	30	Water / room temperature	CTMAB (50 mol%)	2
[9]	91	10	Abrasion	CH_3COONa (100 mol%)	3
[15]	85	60	Ethanol/60-70 °C	mg) CMZO (200	4
[16]	84	30	Ethanol/Room temp	BF_3/nano-γ-mg) Al_2O_3 (60	5
Present work	**96**	**9**	**Water / 80 °C**	**[Bisim] (5 mol%)**	**6**

(CTMAB) cetyltrimethylammonium bromide
(CMZO) mixture of CeO_2/MgO/ZrO_2 5:3:2 oxides

As can be seen in table (3), the present method is superior to most previous methods in terms of efficiency, time and amount of catalyst used.

7) CONCLUSION

Barbituric acids have special importance in medicinal and medical chemistry due to their important medicinal and biological properties. Barbituric acid is used as a precursor in the synthesis of compounds with antitumor and antibacterial properties. With all the positive characteristics, barbituric acid in small amount can increase the weight of liver and kidney in humans.

One of the most important derivatives of barbituric acids are pyrano[d-3,2]-pyrimidinones, which in addition to anti-allergic, antibacterial, blood pressure lowering, vasodilator, bronchodilator properties (compounds that are effective in the treatment of asthma) They protect the liver against hepatitis and regulate heart rate. The great influence of these compounds in the manufacture of various drugs has caused many methods and catalysts to be used for the synthesis of these compounds [17-18].

Pyrano[d-3,2]-pyrimidinone derivatives are prepared simply through a three-component one-pot reaction between barbituric, aldehydes and malonitrile.

For the synthesis of these compounds in the presence of Bisim in the first step, to find the optimal conditions, the reaction between 4-chlorobenzaldehyde, malonitrile and barbituric acid in the presence of this catalyst was chosen as a model reaction to change the amount of catalyst, temperature and solvent, the best conditions for To achieve the reaction with the highest efficiency in the shortest time (Table 3).

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