Asian Journal of Biological and Life Sciences | Original Research

New Hg(II) complex : As a novel, green and efficient reusable catalyst for synthesis of polyhydroquinolines via Hantzschcondensation

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Submitted : 10.02.2018 Accepted : 24.04.2018 Published : 30.04.2018

Abstract

A novel Hg(II) complex based on5-nitro-N1- (pyridin-2-yl) methylene) benzene-1, 2-diamine (HgL_2) has been studied for catalytic performance in the synthesis of polyhydroquinoline derivatives. This efficient and eco-friendly catalyst has been utilized in a one-pot four-component Hantzschcondensation of dimedone, aromatic aldehydes, ethyl acetoacetate and ammonium acetate under solvent and free-solvent conditions. Mild reaction conditions, simple work-up procedure, being environmentally friendly and high product yields are advantageous feature of this method.

Key words : polyhydroquinoline, Hg(II) complex, aromatic aldehyde, Hantzschcondensation.

INTRODUCTION

In recent years, the application of reusable catalysts attracted muchattentionin modern organic synthesis owing their easy work-up, easy filtration and minimization of cost and waste generation [1-3].Furthermore, an increasing interest has beendirected toward the development of new methods for the synthesis ofheterocyclic compounds due to their significant biological and pharmaceutical activity.

Multi Component Reactions (MCRs) are known as an efficient and powerful tool for the synthesis of complex organic molecules from simple and readily available substrates. Also, this manner is very fast and impressive without the isolation of any intermediate [4-7].Multicomponent reactions have emerged as valuable tools for the preparation of structurally diverse chemical libraries of drug-like heterocyclic compounds [8-10].

Polyhydroquinolines contains a variety of biological activities such as antimicrobial [11], antitubercular[12] andantioxidant agents [13]. The general procedures for the preparation of polyhydroquinolines include a multicomponent condensation of dimedone, aldehydes, ethyl acetoacetate and ammonium acetate (Hantzsch reaction) in the presence of various catalysts such asmontmorillonite[14], ionic liquids [15], $Yb(OTf)_3$ [16], Ni nanoparticles [17] and carbon nanotubes supported cobalt catalyst [18].

However, most of these methodologies suffer from certain drawbacks such as long reaction times, harsh reaction conditions and unsatisfactory yields. Thus, the development of efficient, high-yielding and environmentally benign method is desired.It is therefore of interest to examine the behavior of new Hg(II) complex (HgL_2) as catalyst for the synthesis of *polyhydroquinolines*. In continuation of our studies toward the development of new routes to the synthesis of heterocyclic compounds [19-22], herein we report the catalytic effects of (HgL_2)for the synthesis *polyhydroquinoline* derivatives (Scheme 1).

In order to find the optimal conditions, we first selected a model reaction including the synthesis of 5c. Therefore, a mixture of dimedone, 4-Chlorobenzaldehyde, *ethyl acetoacetate and ammonium acetate*(1 mmol each), in the presence of various amounts of the catalyst (HgL_2)was heated in different solvents and under solvent-free conditions (Table 1).

The best result has been obtained at (0.05 g) of catalyst*under solven-free conditions* at 110°C (Table1, Entry 9). In the absence of catalyst, the product5c was obtained in trace amount after 150 min.The generality of this process was demonstrated by the wide range of aromatic aldehydes to synthesize the corresponding products in high yields (Table 2).

MATERIALAND METHODS

All chemicals were commercially available and used without further purification.Melting points were recorded using a Stuart SMP3 melting point apparatus. The IR spectra were recorded on a Tensor 27 Bruker spectrophotometer as KBr disks. The ^{1}HNMR spectra(300 MHz) were obtained using Bruker 300 spectrometer. The compounds were identified by the comparison of their physical and spectroscopic data with those of known compounds.All products were known by spectral data and comparison of their melting points with those of authentic sample (Table 2).

Synthesis of the Hg(II) complex

The schiff base ligand was synthesized according to earlier work [21]. A metanolic solution of the ligand (1 mmol in 3 mL) was added dropwise to a solution of $Hg(NO_3)_2.H_2O$ (1 mmol) in 3 mL methanol. The mixture was refluxed for 4 h. The products formed werefiltered and washed with diethyl ether.Finally, the complex was left to dry atroom temperature.

General procedure for the synthesis of polyhydroquinoline derivatives (4a-4f)

A mixture ofdimedone1 (1 mmol),aromatic aldehydes 2a-g (1 mmol), *ethyl acetoacetate 3* (1 mmol), *ammonium acetate 4*(1 mmol)andcatalyst (HgL_2)(0.05 g) was heated on the oil bath at 110°Cfor 13-25 min. After completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and precipitate was filterated and washed with cold ethanol to give products 5a-g in high yields.

Because of solubility of the catalyst in ethanol, the filtrate was evaporated under reduced pressure and catalyst was recycled by a simple filtration.The separated catalyst reused in model reaction without appreciable reduction in the catalytic activity. The results of the first experiment and subsequent experiments were almost consistent in yields (90, 87 and 83%).

Selected Spectral data

Ethyl4-(4-chlorophenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5c)

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.84 (s, 3H, CH_3), 1.02-1.04 (s, 3H, CH_3), 1.12-1.15 (t, 3H, CH3, OEt), 2.27 (s, 3H, CH_3), 1.96-2.21 (m, 4H, $2CH_2$), 3.94-4.02 (q, 2H, OCH_2), 4.85 (s, 1H, CH), 7.15-7.18 (d, 2H, arom-H), 7.25-7.28 (d, 2H, arom-H), 9.14 (s, 1H, NH).

IR (KBr disc): υ 1647 (C=O, keton), 1705 (C= O, ester),3270(NH) cm^{-1}.

Ethyl4-(4-methylphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (5f)

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.86 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 1.12-1.17 (t, 3H, CH_3, OEt), 2.27 (s, 3H, CH_3), 2.21-2.28 (m, 4H, $2CH_2$), 3.94-4.01 (q, 2H, OCH_2), 4.81 (s, 1H, CH), 6.97-7.00 (d, 2H, arom-H), 7.03-7.05 (d, 2H, arom-H),9.04 (s, 1H, NH).

IR (KBr disc): υ 1647 (C=O, keton), 1702 (C= O, ester), 3276 (NH) cm^{-1}.

RESULTS AND DISCUSSION

Due to the importance of polyhydroquinoline in the field of drug and therapeutics, the synthesis of these compounds has attracted many researchers in recent years.Methods for synthesizing these derivatives have been developed, although most of these methods have some disadvantages Such as low reactivity, long reaction time, high consumption of reagents, and use of expensive catalysts Price-sensitive air and safety issues. The purpose of this research is to investigate and find Healthier reactors are more suitable for the synthesis of polyhydinquinolins

Table 1: Effect of amount of catalyst, solvent and temperature in the model reaction

Entry	Catalyst (g)	Solvent	Temp (°C)	Time (min)	Yield (%)
1	----	----	120	150	----
2	0.01	----	100	40	50
3	0.03	----	100	40	55
4	0.05	----	100	35	60
5	0.07	----	100	30	64
6	0.10	----	100	30	68
7	0.01	----	110	30	70
8	0.03	----	110	22	75
9	0.05	----	110	15	90
10	0.07	----	110	15	92
11	0.10	----	110	15	93
12	0.01	----	120	15	75
13	0.03	----	120	15	77
14	0.05	----	120	15	91
15	0.07	----	120	15	91
16	0.10	----	120	15	92
17	0.05	EtOH	Reflux	50	60
18	0.05	MeOH	Reflux	50	60
19	0.05	$CHCl_3$	Reflux	60	45

Table 2: Synthesis of polyhydroquinolines under optimized conditions

Entry	Ar	Product	Time (min)	Yield (%)	Melting pint (°C) [23]	
					Found	Reported
1	4-OHC_6H_4	5a	25	82	237-239	239-241
2	4-BrC_6H_4	5b	15	92	256-258	259-260
3	4-ClC_6H_4	5c	15	90	243-245	246-248
4	3-$NO_2C_6H_4$	5d	13	91	178-180	181-183
5	4-$NO_2C_6H_4$	5e	13	93	244-246	245-247
6	4-MeC_6H_4	5f	23	88	255-257	257-260
7	4-$MeOC_6H_4$	5g	20	90	256-258	257-259

Table 3: Comparison of the present method with other reported methods for the synthesis of polyhydroquinoline

Entry	Catalyst (g)	Amount of Catalyst (g)	Time (h)	Yield (%)	References
1	FeCl3	200	12	48	[24]
2	ZnCl2	150	12	42	[24]
3	PTSA	10	1.5	92	[25]
4	Present method	0.1	15(min)	93	-

and their derivatives.

We have developed a simple and efficient method for the synthesis ofpolyhydroquinoline derivatives via Hantzsch condensation using an HgL_2catalyst. In this study, for the synthesis of polyhydroquinoline frombenzaldehyde, ethyl acetate, diamondon, ammonium acetate in the presence of a catalyst Hg (II) was used (Fig. 1)

Initially, in order to demonstrate the efficacy of the present method in comparison with other results reported so far for reactionsthe survey was done as shown in Table 3. The results of this study provide better time and efficiency for doing thisthe reaction provides (Table 3, row 4). It should be noted that this reaction without the presence of a catalyst and at a temperature of 120°C was also achieved with no efficiencies and with a long time (Table 1, row 1).

The results of this study showed that the Hg catalyst is very suitable for the synthesis of polyhydroquinoline because it is much less time consuming than other catalysts and less catalyst for synthesis, which is much more favorable than previous studies.Subsequently, the reaction was optimized under various reflux conditions with different solvents such as ethanol, methanol, and chloroform for 50 and 60 minutes (Table 1). In each case, the reactants plus the amount of 0.05 g of the catalyst was investigated. As shown in Table 1, the non-solvent condition is accelerated. Reaction and high output of products (Table 1, Rows 17, 18 and 19).

After the optimization conditions, we performed the reaction with ethyl acetate, ammonium acetate and various erythemicaldehydes.The result is shown in (Table 2) As expected for benzaldehyde with fossilized electron componentsThe reaction time was shorter and higher than the electrons subjected to benzaldehyde.The method used in this study to synthesize polyhydroquinoline derivatives in the presence of Hg in conditions No solvent has many advantages that can be used to make non-toxic and stable nanocatalysts Heat, short duration of reaction, very low catalyst consumption, optimal product efficiency and purity, The use of a simple method and lack of side reactions is due to the use of suitable catalysts.

Best results were obtained in the presence of 0.1 gr of catalysts and time 15 min at 110 C.

Treatment ofdimedone, aromatic aldehydes, *ethyl acetoacetateand ammonium acetate* in the presence of a catalytic amount of Hg(II) complex gave products which were identified as polyhydroquinolines. All products gave satisfactory spectral data

inaccord with the assigned structures.

CONCLUSION

In conclusion, a new solid acidic catalyst, Hg(II) complex was prepared. The catalyst showed high catalytic activity in the synthesis polyhydroquinolines. Someattractive features of this method are high yields, short reaction times and recyclability and reusability of the catalyst.

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