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An Efficient and Facile Synthesis of Polyhydroquinolines through Hantzsch Reaction Catalyzed by a Novel and Reusable Cu (II) Complex

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Abstract

Usually, polyhydroquinolines have prepared effectively in a four-component Hantzsch reaction using a novel Cu (II) complex. This green and reusable Catalyst is used in one case condensation reaction of dimedone, various aldehyde, ammonium acetate and ethyl acetoacetate under solvent and free-solvent conditions. This method offers many advantages such as simple work-up procedure, mild reaction conditions, easy isolation of product, environmentally benign and high product yield.

Keywords: Polyhydroquinoline, Hantzsch Condensation, Cu (II) Complex, Dimedone, Reusable Catalyst.

Introduction

During the last decades, t the application of heterogeneous reusable catalysts attracted great attention in modern chemical composition because easy work-up, easy filtration and reusability (Zeinali-Dastmalbaf *et al*., 2011). Furthermore, an increasing interest directed to development and guidance new methods for the synthesis of heterocyclic compounds due to their significant biological and pharmaceutical activity.

Multicomponent reactions (MCRs) are the powerful tools that allow the formation of several bonds in a single action and are known as an eco-friendly method for the synthesis of organic molecules. Also, this way is very rapid and efficient without isolating any intermediary (Domling and Ugi, 2000). Multicomponent reactions have appeared as valuable tools for the supplied of heterocyclic compounds with biological activities (Ugi *et al*., 1994; Ugi *et al*., 2000).

Polyhydroquinolines are a class of fused 1,4-dihydropyridine contains a variety of Biological activities like antimicrobials (Murthy *et al*., 2012), antitubercular (Trivedi *et al*., 2011) and antioxidant agents (Vijesh *et al*., 2011).

Polyhydroquinolines are generally synthesized by one-pot Hantzsch reaction of dime done, ethyl acetoacetate, aldehydes and ammonium acetate use various catalysts such as montmorillonite (Song *et al*., 2005), ionic liquids (Ji *et al*., 2004), Yb(OTf)3 (Wang *et al*., 2005), Ni nanoparticles (Sapkal *et al*., 2009) and carbon nanotubes support cobalt catalyst (Trepanier *et al*., 2011).

Many of these methodologies they suffer from certain problems including, long reaction times, harsh conditions of reaction and unsatisfactory yields. Therefore, the development of efficient, high-yielding and environmentally benign method is desired.

It is therefore of interest to the review behavior of new Cu(II) complex (CuL) as catalyst for the synthesis a some of polyhydroquinolines. In continution of our studies toward the development of new routes to the synthesis of heterocyclic compounds (Allameh *et al*., 2011; Khoshdast *et al*., 2017), herein we report the catalytic effects of Cu (II) complex (CuL) for the synthesis polyhydroquinoline derivatives (Fig. 1).

In order to optimaze the reaction conditions, the reaction of dimedone, ammonium acetate, benzaldehyde, ethyl acetoacetate (1 mmol each) and various amounts of the catalyst (CuL) In various solvents and in non-solvent conditions selected as a model reaction (Table 1).

The best result is 0.03 g of catalyst under solven-free conditions at 100°C (Table1, Entry 7). In the absence of catalyst, the product 5a was obtained in trace amount after 150 min.

The generality of this protocol under optimized conditions was demonstrated by different aryl aldehydes to synthesize he products are good at good returns (Table 2).

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Experimental

All the reagents were commercially available from Merck company. Melting point was determined on Stuart SMP3 apparatus. The IR spectra were obtained on a Tensor 27 Bruker spectrophotometer as KBr disks. The 1H NMR spectra (300 MHz) were obtained using Bruker 300 spectrometer. The compounds were indentified by the Comparison of the melting point and their spectral data with known compounds. All products were known by spectral data and comparision of their melting points with those of authentic sample (Table 2).

Synthesis of the new schiff base

4-amino-3-methyl-1H-1,2,4-triazole-5(4H)-thione (1mmol, 0.130 g) and 2,4-dihydroxybenzaldehyde (1 mmol, 0.138 g) was added to a solution of ethanol (2ml) and 2 drop of hydrochloric acid. The reaction mixture was It was mixed up for 80 min at reflux condition (Raouf et al., 2019). After this time, the light pink product was filtered and washed with ethanol to give the Schiff base (M.p: 280-282 °C, yield: 90%) (Fig. 2).

Synthesis of the Cu (II) complex

A solution of methanolic ligand (1mmol, in 3 mL) was added dropwise to a solution of CuCl2. 2H2O (1mmol, in 3 mL methanol). The mixture has refluxed for 4 h to give the new complex. After completion of reaction, the copper (II) complex was filtered and washed with cold ether.

General procedure for the preparation of polyhydroquinolines (5a-5f)

A mixture of dimedone 1, aryl aldehydes 2a-f, ethyl acetoacetate 3 and ammonium acetate 4 (1 mmol of each) The existence of a catalytic amount was unpleasant (CuL) (0.05 g) was heated on the oil bath at 100°C for 29-35 min. In the end of the reaction (monitored by TLC), The reaction mixture was cooled to room temperature precipitate was filterated and washed with hot ethanol to give products 5a-f in high yields. Since the catalyst was soluble in ethanol, the filtrate was evaporated and catalyst was recycled by a simple filtration. The recycled catalyst used in model reaction without considerable reduction in the catalytic activity (92% for 1 st use, 90% for 2 nd use and 86% for 3 rd use).

Selected Spectral data

Ethyl 4-phenyl-2, 7, 7-trimethyl-5-oxo-1, 4, 5, 6, 7, 8-hexahydroquinoline-3-carboxylate (5a)

1H NMR (300 MHz, DMSO-d6): d 0.8 (s, 3H, CH3), 1.0 (s, 3H, CH3), 1.2 (t, 3H, CH3, OEt), 2.3 (s, 3H, CH3), 2.0 (m, 4H, 2CH2), 4.0 (q, 2H, OCH2), 4.9 (s, 1H, CH), 7.1-7.4 (m, 5H, arom-H), 9.1 (s, 1H, NH). IR (KBr disc):? 1617 (C=O, keton), 1699 (C= O, ester), 3290 (NH) cm-1.

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

1H NMR (300 MHz, DMSO-d6): d 0.9 (s, 3H, CH3), 1.0 (s, 3H, CH3), 1.2 (t, 3H, CH3, OEt), 2.1 (s, 3H, CH3), 2.3 (m, 4H, 2CH2), 2.5 (s, 3H, OCH3), 4.0 (q, 2H, OCH2), 4.8 (s, 1H, CH), 6.8-7.3 (m, 4H, arom-H), 9.1 (s, 1H, NH). IR (KBr disc):? 1607 (C=O, keton), 1700 (C= O, ester), 3277 (NH) cm^{-1}.

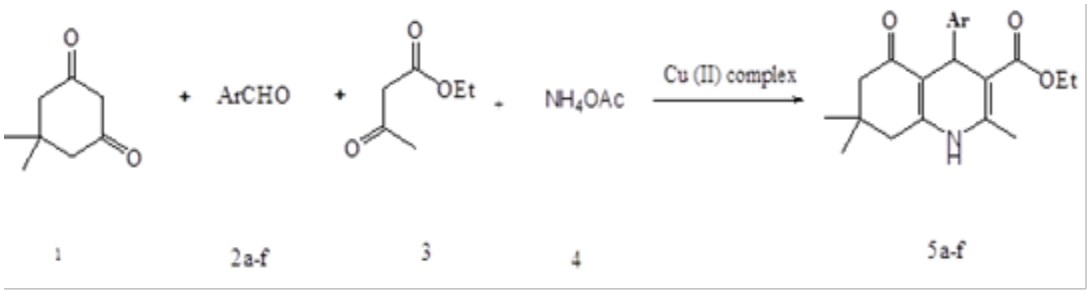

Figure 1: synthesis of polyhydroquinolines catalyzed by Cu(II) complex

Table 1- Optimization of model reaction conditions catalyzed Cu (II) complex

Entry	Catalyst (g)	Solvent	Temp (°C)	Time (min)	Yield (%)
1	----	----	110	150	----
2	0.01	----	80	45	52
3	0.02	----	80	45	58
4	0.03	----	80	45	61
5	0.01	----	90	30	72
6	0.02	----	90	30	80
7	0.03	----	100	30	92
8	0.03	----	110	30	94
9	0.03	----	120	30	94
10	0.10	H2O	Reflux	90	47

11	0.05	EtOH	Reflux	80	72
12	0.05	MeOH	Reflux	120	55
13	0.05	CHCl3	Reflux	100	52

Table 2- Synthesis of polyhydroquinolines under optimized conditions

Entry	Ar	Product	Time (min)	Yield (%)	Melting pint (°C) (Davoodnia *et al*., 2013)	
					Found	Reported
1	C_6H_5	5a	30	92	220-222	214-216
2	4-BrC_6H_4	5b	35	88	252-255	259-260
3	4-$MeOC_6H_4$	5c	32	87	260-262	257-259
4	4-$NO_2C_6H_4$	5d	31	95	241-242	245-247
5	4-MeC_6H_4	5e	29	87	263-266	257-260
6	4-HOC_6H_4	5f	34	85	234-236	239-241

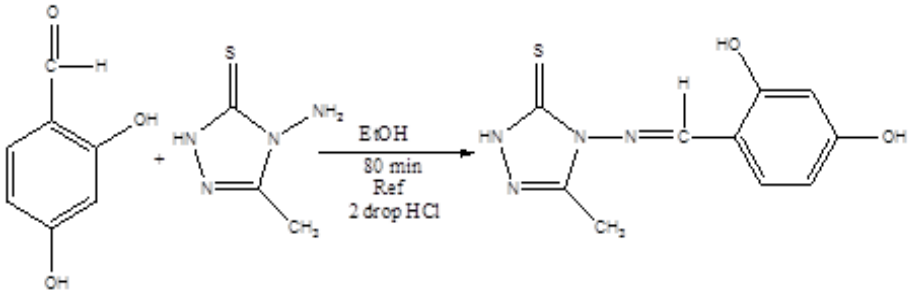

Figure 2: Synthesis of new schiff base

Results and Discussion

Treatment of dimedone, ammonium acetate, aromatic aldehydes and ethyl acetoacetate using a amount of new Cu(II) complex gave products which were identified as polyhydroquinolines. All prouducts gave satisfactory spectral data in accord with the assigned structures.

Conclusion

It should be noted that, we reported an efficient and green method for synthesis a some of polyhydroquinolines using a new Cu (II) complex as a catalyst from the Hantzsch condensation. The catalyst showed high activity for the synthesis polyhydroquinolines. Some advantaes of this method are high yields, short reaction times and recyclability of the catalyst.

References

Allameh S, Heravi MM, Hashemi MM, Bamoharram FF. Synthesis of 3-(aryl)-2-thioxo-2,3-dihydroquinazolin-4(1H)-one derivatives using heteropolyacids as green, heterogeneous and recyclable catalysts. Chines Chemical Letters. 2011; 22: 131-134.

Domling. A, Ugi I. Multiple reactions with isocyanides. Angewandte Chemie. 2000; 39(18): 3168-3210.

Davodnia A, Khashi M, Tavakoli-Hoseini N. Tetrabutylammonium hexatungsate [TBA]2[W6O19]: Novel and reusable heterogeneous catalyst for rapid withought solvent synthesis of polyhydroquinolines via unsymmetrical Hantzsch reaction. Chinese Journal of Catalysis. 2013; 34: 1173-1178.

Ji SJ, Jiang ZQ, Lu J, JUN L, Loh TP. Ionic liquids-promoted one-pot synthesis of polyhydroquinoline derivative under solvent free conditions. Synlett, 2004; 5: 831-835.

Khoshdast A, Allameh S, Beyramabadi SA, Khashi M, Morsali A, Pordel M. Synthesis, new experimental and theoretical properties Cu(II) complex based on 3-hydroxy-2-naphtoic acid. Bulgarian Chemical Communications. 2017; 49: 35-49.

Murthy NLM, Rajack A, Taraka Ramji M, Jeson Babu J, Praveen C, Aruna Lakshmi K. Design, free solvent synthesis and antimicrobial evaluation 1,4-dihydropyridines. Bioorganic and Medicinal Chemistry Letter. 2012; 22: 6016-6023.

Song G, Wang B, Wu X, Kang Y, Yang L. An effective solid catalyst for one-pot synthesis of polyhydroquinoline derivatives. Synthetic communications. 2005; 35 (22):2875-2880.

Raouf H, Beyramabadi SA, Allameh S, Morsali A. Synthesis, experimental and theoretical characteristics a 1,2,4-triazole Schiff base and its nickel(II) complex. Journal of molecular structure. 2019; 1179: 779-786.

Sapkal. SB, Shelke. KF, Shingate. BB, Shingare. MS. Nickel nano particle-catalyzed efficient one-pot synthesis of polyhydroquinoline derivative via Hantzsch condensation under solvent conditions. Tetrahedron Lett. 2009; 50(15) 1754-1756.

Trivedi A, Dodiya D, Dholariya B, Kataria V, Bhuva V, Shah V. Synthesis and biological evaluation of some novel 1,4-dihydropyridines as potent antitubercular agents. Chem Biol Drug Des, 2011; 78(5) 881-886.

Trepanier M, Tavasoli A, Anahid S, Dalai AK. Deactivation Behavior of Carbon Nanotubes Supported catalysts in Fischer-Tropsch Synthesis Iranian Journal of Chemistry and Chemical Engineering. 2011; 30 (1) 37-47.

Ugi I, Domling A, Horl W. Multicomponent reactions in organic chemistry. Endeavour. 1994; 18(3): 115-122.

Ugi I, Domling A, Werner B. Since 1995 the new chemistry of multicomponent reactions and their libraries, including their heterocyclic chemistry. Journal of heterocyclic Chemistry. 2000; 32(3): 647-658 .

Vijesh AM, Isloor AM, Peethambar SK, Shivananda KN, Arulmoli T, Isloor AN. Hantzsch reaction: synthesis and characterization of some new 1,4-dihydropyridine derivatives as potent antimicrobial and antioxidant agents. Eur. J. Med. Chem. 2011; 46(11): 5591-5597 .

Wang LM, Sheng J, Zhang L, Han JW, Fane ZY, Tian H, Qian CT. Facile Yb(OTf)3 promoted pot synthesis of polyhydroquinoline derivatives through Hantzsch reaction. Tetrahedron. 2005; 61: 1539-1543.

Zeinali- Dastmalbaf M, Davoodnia A, Heravi. MM. A Highly efficient and fast method for the synthesis of biscomarins using tetrabutylammonium hexatungstate [TBA]3[W6O19] as green and reusable heterogeneous catalyst. Bullten of Korean Chemical Society. 2011; 32(12): 4286-4290.