An Efficient, Simple and Green $\text{Zn(Phen)}_2\text{Cl}_2$ Complex Catalyzed Synthesis of 4-*H*-Benzo[b]pyrans in Water at Ambient Temperature

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Abstract: An efficient method for the synthesis of 4-*H*-benzo[b]pyrans has been developed by the use of $\text{Zn(Phen)}_2\text{Cl}_2$ (2 mol%) as an ecofriendly catalyst. The mixture of an appropriate aldehyde, malononitrile and dimedone in the presence of the $\text{Zn(Phen)}_2\text{Cl}_2$ as an inorganic catalyst in water at room temperature resulted excellent yields of the corresponding products in 5 min. Very short experimental time of the reaction, excellent yields, use of water as a green solvent, simple work-up and uses no extra catalyst and purification are the advantages of this method.

Keywords: $\text{Zn(Phen)}_2\text{Cl}_2$, 4-*H*-Benzo[b]pyrans, Malononitrile, Transition metal, Green chemistry.

Introduction

4-*H*-Benzo[b]pyrans and their derivatives are of considerable interest due to their pharmacological activities¹, such as spasmolytic, diuretic, anti coagulant, anti-cancer, anti-ancaphylactia activity²⁻⁵. In addition, they have been shown to act as cognitive enhancers, for the treatment of neurodegenerative disease, including Huntington's disease, Alzheimer's disease, amyotrophic lateral Sclerosis, AIDS associated dementia and Down's syndrome as well as for the treatment of Schizophrenia and myoclonus^{6,7}. Also several biologically active

natural products contain these subunits⁸. A number of 2-amino-4*H*-pyrans are useful as photoactive materials⁹, pigments¹⁰ potential biodegradable agrochemicals¹¹. Thus a synthetic interest has that included methodological improvements of the original reaction conditions. The titled compounds are synthesized by reaction of malononitrile with dimedone in the presence of an appropriate aldehyde. A variety of reagents such as hexadecyltrimethylammonium bromide (HTMAB)¹², NaBr^{13,14}, rare earth perfluorooctanoate RE(PFO)₃, (S)-proline^{15,16}, Na₂SeO₄, Ce(SO₄)₂·4H₂O¹⁷, the use of microwave irradiation¹⁸, KF-basic alumina under ultrasound irradiation¹⁹, tetramethylammonium hydroxide (TMAH)²⁰, electrolysis²¹, tetrabutylammonium bromide (TBABr)²² and amino-functionalized ionic liquid²³ were employed to catalyze these reactions.

In spite of potential utility of aforementioned routes for the synthesis of 4-*H*-benzo[b]pyran derivatives many of these methods involve expensive reagents, acidic conditions, long reaction times, low yields, use of excess of reagents/catalyst and use of toxic organic solvents and complicated work-up methods. The lack of facile and general synthetic methodology under essentially natural, practical and mild reaction condition has promoted us to develop an efficient, convenient and practical procedure for the one-pot green synthesis of 4-*H*-benzo[b]pyrans reaction under aqueous media. to the best of our knowledge a complex catalyst has not been used in the synthesis of 4-*H*-benzo[b]pyrans.

Green chemistry emphasizes the development of environmentally benign chemical processes and technologies²⁴. According to the principle of safe chemistry, synthetic method should be designed to use substances that exhibit little or no toxicity to human health and environment²⁵. In this regard and in continuation of our interest on application of heterogeneous catalysts in organic reactions²⁶, we wish to report herein, a new, simple, mild and ecofriendly method for the synthesis of 4-*H*-benzo[b]pyrans *via* a one-pot three-component tandem Knoevenagel-cyclo condensation reaction using Zn(Phen)₂Cl₂ (2 mol%) as environmentally friendly homogeneous complex catalyst with high catalytic activity and reusability in very short reaction time in water base media (Scheme 1).

Scheme 1

Experimental

Melting points were determined on a gallenkamp melting point apparatus and are uncorrected. NMR spectra were recorded at 500 (¹H) and 125.77 (¹³C) MHz on Bruker DRX-500 avance spectrometer at 500 and 125.77 MHz, respectively. All compounds were known in the literature, the NMR and IR spectra of the products were in agreement with earlier data.

General procedure for the preparation of 4-H-Benzo[b]pyran4-H-Benzo[b]pyrans (4c)

In a typical general procedure, a mixture of aromatic aldehyde (1 mmol), malononitrile (1 mmol) and dimedone (1 mmol) in H₂O (3 mL) at room temperature, were stirred thoroughly in the presence of catalytic amount of Zn(Phen)₂Cl₂ (10 mg, 2 mol%) about 5 min to afford the 4-*H*-benzo[b]pyrans in excellent yields. Completion of the reaction was confirmed by TLC. Then the mixture was filtered. The solid product was separated by filtration from the soluble catalyst after washing with H₂O. Pure 4-*H*-benzo[b]pyran4-*H*-benzo[b]pyrans (**4**) was obtained in 94% yield without any use of more purification. Structures of the products were confirmed from physical and spectroscopic data (IR and ¹H NMR) in comparison with the literature data.

General procedure for the synthesis of $\text{Zn}(\text{phen})_2\text{Cl}_2$

To a 20 mL ethanolic solution of ZnCl_2 (0.136 g, 1 mmol), 10 mL ethanolic solution of the 1,10-phenanthroline (0.360 g, 2 mmol) was added drop wise. The resulting white suspension was stirred at 70 °C for 24 h. The suspension was cooled, filtered and then dried at room temperature. White colored zinc complex, $\text{Zn}(\text{phen})_2\text{Cl}_2$, was obtained in 89% yield. Structure of the zinc complex was confirmed from spectroscopic data (IR and Anal. Calc) in comparison with those reported literature²⁷: Anal. Calc. For $\text{C}_{24}\text{H}_{16}\text{N}_4\text{Cl}_2\text{Zn}$: C, 58.05; H, 3.22; N, 11.28. Found: C, 58.10; H, 3.19; N, 11.26%; FT-IR (KBr, cm^{-1}): 3046(br), 1622(m), 1579(m), 1515(s), 1427(s), 1345(m), 1223(m), 1143(s), 1092(m), 846(s), 725(s), 638(s), 577(m) and 418(m).

Results and Discussion

To show that $\text{Zn}(\text{Phen})_2\text{Cl}_2$ is an efficient catalyst, we accomplished the reaction at room temperature in the absence of catalyst for 4 h. The reaction just produced alkene (**a**) and no benzo[b]pyran was formed (Figure 1.).

Figure 1

This prove the essential effect of $\text{Zn}(\text{Phen})_2\text{Cl}_2$ as a mild and efficient catalyst in the progressing of the reaction. In order to improve yield, we performed reaction using different quantities of reagents. The best results was obtained with a 0.02:1:1:1.5 ratio of $\text{Zn}(\text{Phen})_2\text{Cl}_2$ complex, aldehyde, dimedone and malononitrile. Also, we carried out a controlled reaction in different solvents (Table 1).

Table 1. Effect of solvents in the synthesis of 4-*H*-benzo[b]pyran4-*H*-benzo[b]pyrans (**4c**) using 2 mol% of $\text{Zn}(\text{Ph})_2\text{Cl}_2$ complex at room temperature.

Entry	Solvent	Time	Yield, %
1	H ₂ O	5 min	94
2	EtOH	18 h	82
3	CH ₂ Cl ₂	24 h	—
4	Ethylacetate	24 h	—
5	1,2-Dichloroethane	24 h	—

As shown in Table 1, for this type of reaction, a polar solvent is generally needed to obtain high yields with low mole percentages of catalyst in mild reaction conditions. The result suggests that H₂O at room temperature condition is the better reaction system than the organic solvents media.

To investigate the versatility of the catalyst, the reaction of dimedone, malononitrile and various aromatic aldehydes was carried out in H₂O at room temperature using 2 mol% of $\text{Zn}(\text{Phen})_2\text{Cl}_2$ (Table 2).

4-*H*-Benzo[b]pyrans derivatives containing electron-withdrawing groups such as nitro and halide groups or electron-donating groups such as hydroxyl and alkoxy groups (Table 2) were formed in a short experimental time (5 min) with excellent yields (90%-100%).

It is also noticed that the condensation using $\text{Zn}(\text{Ph})_2\text{Cl}_2$ complex proceeds rapidly and is superior to the reported procedures. This claim is justified through the representative examples, illustrated in Table 3.

Table 2. Synthesis of **4** catalyzed by $\text{Zn(Phen)}_2\text{Cl}_2$ at ambient temperature in water as solvent

Product	Ar	yield (%) ^a	mp, °C	Mp., reported ^[Ref]
4a	C_6H_5	90	222-224	226-228 ^[19]
4b	4-Br- C_6H_4	91	207-209	203-205 ^[18]
4c	4-Cl- C_6H_4	94	208-209	207-209 ^[17]
4d	2,4- Cl_2 - C_6H_3	96	178-179	180-182 ^[16]
4e	3- O_2N - C_6H_4	97	207-209	208-211 ^[19]
4f	3-OH- C_6H_4	93	231-233	236-238 ^[19]
4g	3- H_3C - C_6H_4	99	212-214	214-216 ^[19]
4h	2-Cl- C_6H_4	100	209-210	200-202 ^[17]
4i	3- H_3CO - C_6H_4	93	188-190	186-187 ^[17]
4j	4- H_3CO - C_6H_4	90	122-124	122-125 ^[28]

^aYields refer to the isolated products**Table 3.** Synthesis of 2-amino-4-(4-chlorophenyl)-3-cyano-7,7-dimethyl-5-oxo-4H-5,6,7,8-tetrahydrobenzopyran using different reagents and reaction conditions

Entry	Reagent	Conditions	Time	yield(%) ^{ref}
1	NaBr, 0.4 mmol	MW(Power: 60), 70 °C	10 min	90 ^[12]
2	Na_2SeO_4 , 0.1 g	EtOH/ H_2O , reflux	3h	90 ^[16]
3	TMAH, 10 mol%	H_2O , r.t	0.5-2 h	83 ^[20]
4	—	electrolysis (10 mA)	4-5 h	95 ^[17]
5	TBABr, 10 mol%	H_2O , reflux	2 h	91 ^[22]
6	$\text{Ce}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$, 2.5 mol%	EtOH/ H_2O , 45°C	30 min	90 ^[17]
7	$\text{Zn(Phen)}_2\text{Cl}_2$	H_2O , r.t	5 min	94 ^{Present work}

^aYields refer to the isolated products; r.t: room temperature

Reusability of $\text{Zn(Phen)}_2\text{Cl}_2$

The reusability of the catalysts is one of the most important benefits and makes them useful for commercial applications. Thus the recovery and reusability of $\text{Zn(Phen)}_2\text{Cl}_2$ was investigated. Fortunately, the precipitated material in the reaction shown in Scheme 1 was successfully recycled three times. The catalyst could be recycled in two ways.

Method A

In the first method, the reaction mixture was filtered and washed with H_2O . The soluble catalyst was easily reused after distillation of solvent, washing with CHCl_3 and drying at room temperature. The recycled catalyst could be examined in next run in the reaction between 4-chlorobenzaldehyde, malononitrile and dimedone.

Method B

In the second method, the reaction mixture was filtered and the solid product was washed with H_2O . $\text{Zn(Phen)}_2\text{Cl}_2$ complex is soluble in water. The remaining solution including soluble catalyst could be reused as such for subsequent experiments (up to 3 cycles). In the next run, 4-chlorobenzaldehyde, malononitrile and dimedone was added to the filtered solution to afford the comparable yields of the product as shown in Figure 2.

Figure 2. The reusability of the catalyst in the synthesis of 4-*H*-benzo[b]pyran4-*H*- benzo [b]pyrans (**4c**).

It was interesting to note that the $\text{Zn}(\text{Ph})_2\text{Cl}_2$ could be reused in three cycles via this method without any loss of its activity, more purification, distillation of solvent and dry catalyst. Thus the remained mixture of the reaction could be used several times to produce the 4-*H*-benzo[b]pyran derivatives with simple work-up and not using cumbersome apparatus for recycling of the catalyst. A little increase in reaction time is attributable to the mechanical loss of some of the 10 mg of catalyst used, increase in volume of solvent or some combination of these factors. Also, a little increase was observed in the product yields. It could be because of the soluble and remaining products from the previous run. So, this improved procedure could be used to obtain the products with more efficiency. The presented procedure is continual, very simple and clean, environmentally friendly due to use water as green solvent, cost effective, more efficient and easier work-up than reported methods. Also, the product could be obtained continual in the same solvent environment.

Conclusion

In conclusion, the present method is an operationally simple and environmentally friendly procedure for the synthesis of compound **4** using catalytic amount of $\text{Zn}(\text{Phen})_2\text{Cl}_2$ at ambient temperature. In addition recyclability and moderate Lewis acidity of the catalyst, safe conditions, cost effective, excellent yields of products without any use of more purification, very short reaction time and use of water as a green solvent make this methodology a valid contribution to the existing processes in the field of 4-*H*-benzo[b]pyrans derivatives synthesis. To the best of our knowledge, this procedure provides the first example of complex catalyzed the efficient synthetic method for 4-*H*-benzo[b]pyrans derivatives.

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References

1. Green G R, Evans J M and Vong A K, *Comprehensive Heterocyclic Chemistry II*; Katritzky A R, Rees C W, Scriven E F V, Ed., Pergamon Press: Oxford, 1995, **5**, 469.
2. Zhang Y L, Chen B Z, Zheng K Q, Xu M L, Zhang L Z and Lei X H, *Yao Xue Xue Bao.*, 1982, **17**(1), 17-22.

3. Zhang Y L, Chen B Z, Zheng K Q, Xu M L and Lei X H, *Chem Abstr.*, 1982, **96**, 135383e.
4. Andreani L L and Lapi E, *Bull Chim Fr.*, 1960, **99**, 583.
5. Witte E C, Neubert P and Roesch A, *Chem Abstr.*, 1986, **104**, 224915f.
6. Konkoy C S, Fick D B, Cai S X, Lan N C and Keana J F W, *PCT Int Appl WO*, 00, 75 2000, 123.
7. Konkoy S, Fick D B, Cai S X, Lan N C and Keana J F W, *PCT Int Appl WO 0075123 Chem Abstr.*, 2000, **134**, 29313a.
8. Hatakeyama S, Ochi N, Numata H and Takano S, *J Chem Soc Chem Commun.*, 1988, 1202-1204.
9. Arnesto D, Horspool W M, Martin N, Ramos A and Seaone C, *J Org Chem.*, 1989, **54**, 3069-3072.
10. Ellis G P, The Chemistry of Heterocyclic Compounds Chromenes, Chromanones and Chromones Vol. 31: Weissberger A, Taylor E C, Wiley; New York: 1977.
11. Hafez E A A, Elnagdi M H, Elagamey A G A and Eltaweel F M A A, *Heterocycl.*, 1987, **26**, 903-907.
12. Jin T S, Wang A Q, Wang X, Zhang J S and Li T S, *Synlett.*, 2004, 871-873.
13. Devi I and Bhuyan P J, *Tetrahedron lett.*, 2004, **45**, 8625-8627.
14. Wang L M, Shao J H, Tian H, Wang Y H and Liu B, *J Fluorine Chem.*, 2006, **127**, 97-100.
15. Balalaie S, Bararjanian M, Amani A M and Movassagh B, *Synlett.*, 2006, 263-266.
16. Hekmatshoar R, Majedi S and Bakhtiari K, *Catal Commun.*, 2008, **9**, 307-310.
17. Islami M R and Mosaddegh E, *Phosphorus, Sulfur Silicon Relat Elem.*, 2009, **184**, 3134-3138.
18. Tu S J, Gao Y, Guo C, Shi D and Lu Z, *Synth Commun.*, 2002, **32**, 2137-2141.
19. Wang X S, Shi D Q, Tu S J and Yao C S, *Synth Commun.*, 2003, **33**, 119-126.
20. Balalaie S, Sheikh-Ahmadi M and Bararjanian M, *Catal Commun.*, 2007, **8**, 1724-1728.
21. Fotouhi L, Heravi M M, Fatehi A and Bakhtiari K, *Tetrahedron Lett.*, 2007, **48**, 5379-5381.
22. Gurumurthi S, Sundari V and Valliappan R, *E-J Chem.*, 2009, **6(S1)**, S466-S472.
23. Peng Y Q and Song G H, *Catal Commun.*, 2007, **8**, 111-114.
24. Anastas P T and Warner J C, *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, UK, 1998.
25. Anastas P T and Williamson T, *Green Chemistry: Frontiers in Benign Chemical Synthesis and Process*; Oxford University Press: Oxford, UK, 1998.
26. Mosaddegh E, Islami M R and Hassankhani A, *Lett Org Chem.*, 2007, **4**, 524-529.
27. Gyoryova K, Baiek V, Melnik M and Nour El-Dien F A, *J Therm Anal.*, 1998, **53**, 577-584.
28. Kumar S, Sharma P, Kapoor K and Hundal S M, *Tetrahedron*, 2008, **64(3)**, 536-542.