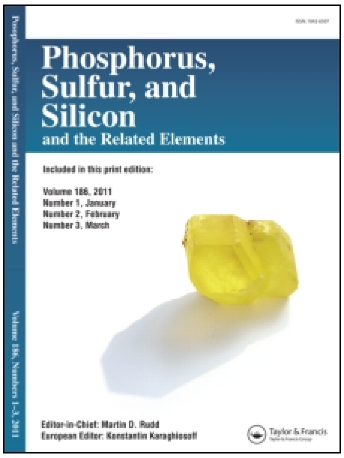

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$Ce(SO_4)_2 \cdot 4H_2O$ as a Recyclable Catalyst for an Efficient, Simple, and Clean Synthesis of 4H-Benzo[b]pyrans

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An efficient method for the synthesis of 4H-benzo[b]pyrans has been developed by the use of $Ce(SO_4)_2 \cdot 4H_2O$ *(2.5 mol%) as a catalyst. Heating the mixture of an appropriate aldehyde, malononitrile, and dimedone in the presence of the catalyst at 45°C in a mixture of water:ethanol (1:1) as solvent for about 9–55 min resulted excellent yields of the corresponding products. Short experimental time of the reaction, excellent yields, simple workup, not using cumbersome apparatus for purification of the products, and inexpensiveness and commercially availability of the catalyst are the advantages of this method.*

Keywords Aromatic aldehyde; 4-H-benzo[b]pyrans; $Ce(SO_4)_2 \cdot 4H_2O$; dimedone; malononitrile

INTRODUCTION

4H-Benzo[b]pyrans and their derivatives are of considerable interest due to their pharmacological activities,[1] such as spasmolytic, diuretic, anticoagulant, anticancer, and anti-anaphylactic activity.[2] In addition, they can be used as cognitive enhancers for the treatment of neurodegenerative diseases, 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.[3] Also 4H-pyrans constitute building blocks of a series of natural products.[4] A number of 2-amino-4H-pyrans are useful as photoactive materials,[5] pigments,[6] and potential biodegradable agrochemicals,[7] and consequently numerous methods have been reported for the synthesis of these compounds. The titled compounds are synthesized by the reaction of malononitrile with dimedone in the presence of an appropriate aldehyde. A variety of reagents such as HMTAB,[8] NaBr,[9]

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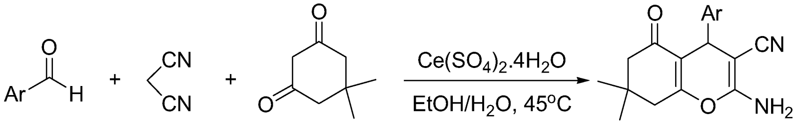
$RE(PFO)_3$,[10] TEBA,[11] (S)-proline,[12] Na_2SeO_4,[13] the use of microwave irradiation,[14] KF-basic alumina under ultrasound irradiation,[15] electrolysis,[16] and amino-functionalized ionic liquid[17] were employed to catalyze these reactions.

In spite of potential utility of the aforementioned routes for the synthesis of 4H-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 workup methods. We hoped to develop a more general protocol for the efficient synthesis of 4H-benzo[b]pyrans using $Ce(SO_4)_2 \cdot 4H_2O$ as a catalyst.

RESULTS AND DISCUSSION

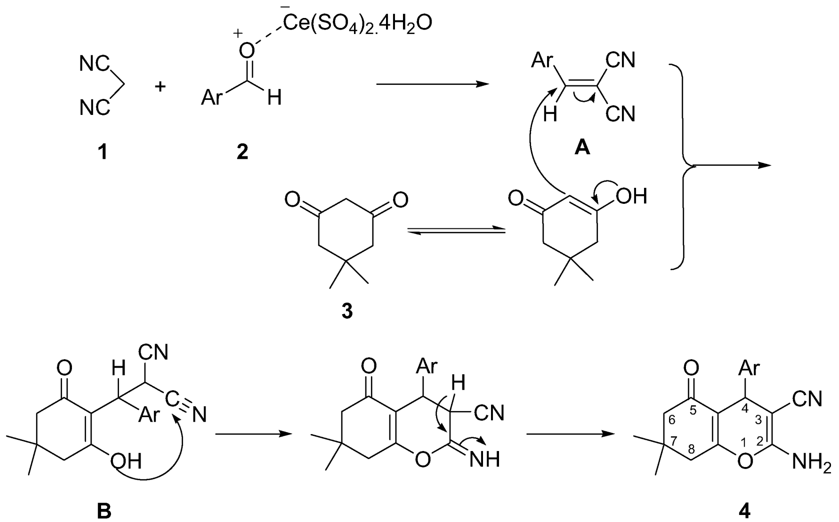
To the best of our knowledge, a Lewis acid catalyst has not been used in the synthesis of 4H-benzo[b]pyrans. In continuation of our interest on the application of heterogeneous catalysts for the development of useful synthetic methodology,[18] we wish to report herein a simple and highly efficient procedure for the preparation of 4H-benzo[b]pyrans via a one-pot three-component tandem Knoevonagel–cyclocondensation reaction using $Ce(SO_4)_2 \cdot 4H_2O$ (2.5 mol%) as environmentally friendly mild Lewis acid catalyst with high catalytic activity and reusability in H_2O-EtOH media (Scheme 1).



SCHEME 1

Although we have not established a mechanism for the formation of products in an experimental manner, a reasonable possibility is indicated in Scheme 2. The reaction occurs via initial formation of the cyano olefin (A) from the Knoevonagel condensation of aryl aldehyde **1** and malononitrile **2**. This compound reacts with **3** to give the intermediate **B**, which subsequently cyclizes to afford the desired compound **4** after proton transfer and tautomerization. The existence of $Ce(SO_4)_2 \cdot 4H_2O$ is essential for the reaction.

The three-component reaction of 2,6-dichlorobenzaldehyde, dimedone, and malononitrile at room temperature in a mixture of water:ethanol (1:1) as solvent for 2 h in the presence of $Ce(SO_4)_2 \cdot 4H_2O$ just yields benzo[b]pyran (entry 2) at (42%). In the absence of



SCHEME 2

$Ce(SO_4)_2 \cdot 4H_2O$, there was no reaction. We found that increasing the temperature to 45°C leads to a yield of 92%. In order to optimize the conditions, we refluxed this reaction, but increasing the temperature has not showed a particular effect on the formation of the products.

To show that $Ce(SO_4)_2 \cdot 4H_2O$ is an efficient catalyst, we accomplished the reaction at 45°C in the absence of catalyst for 4 h. The reaction just produced alkene **A**, and no benzo[b]pyran (entry 2) was formed. This proves the essential effect of $Ce(SO_4)_2 \cdot 4H_2O$ as a mild Lewis acid catalyst in the progress of the reaction.

To investigate the versatility of the catalyst, the reaction of dimedone, malononitrile, and various aromatic aldehydes was carried out in H_2O-EtOH at 45°C using 2.5 mol% of $Ce(SO_4)_2 \cdot 4H_2O$. 4H-Benzo[b]pyran derivatives containing electron-withdrawing groups such as nitro and halide groups or electron-donating groups such as hydroxyl and alkoxy groups (Table I) were formed in a short experimental time (9–55 min) with high yields (90%–98%).

The reusability of catalysts is a very important benefit and makes them useful for commercial applications. Thus the recovery and reusability of $Ce(SO_4)_2 \cdot 4H_2O$ was investigated. In these experiments, the reaction mixture was filtered and washed with H_2O. The soluble catalyst was easily reused after distillation of the solvent, washing with $CHCl_3$, and drying at 60°C. The recycled catalyst has been examined in the next run of the reaction between 2,6-dichlorobenzaldehyde,

TABLE I Synthesis of 4 Catalyzed by $Ce(SO_4)_2{\cdot}4H_2O$ at 45°C in Water/ Ethanol Media

Entry	Ar	Time (min)	Yield (%)[a]	Mp	[Mp reported][Ref]
1	C_6H_5	50	90	222–224	[226–228][15]
2	4-Br- C_6H_4	38	98	207–209	[203–205][14]
3	4-Cl- C_6H_4	30	90	208–209	[207–209][15]
4	4-O_2N- C_6H_4	34	96	179–181	[177–178][8]
5	2,4-Cl_2-C_6H_3	21	94	178–179	[180–182][12]
6	3-O_2N- C_6H_4	42	98	207–209	[208–211][8]
7	3-OH- C_6H_4	33	97	231–233	[236–238][12]
8	3-Cl- C_6H_4	13	92	228–230	[224–225][8]
9	3-Br- C_6H_4	15	98	289–291	[293–294][19]
10	4-H_3C-C_6H_4	55	90	212–214	[214–216][8]
11	4-$(CH_3)_2N$-C_6H_4	55	90	175–176	[198–200][16]
12	2-Cl- C_6H_4	9	97	209–210	[200–202][15]
13	3-H_3CO- C_6H_4	30	93	188–190	[186–187][20]
14	4-H_3CO- C_6H_4	25	96	122–124	[122–125][19]

[a] Yields refer to the isolated products.

malononitrile, and dimedone. The $Ce(SO_4)_2{\cdot}4H_2O$ catalyst could be reused three times without any loss of activity.

In conclusion, the present method is an operationally simple and environmentally friendly procedure for the synthesis of compound **4** using catalytic amount of $Ce(SO_4)_2{\cdot}4H_2O$. In addition, low cost, easy availability, recyclability, low toxicity, moderate Lewis acidity and moisture compatibility of the catalyst, excellent yields of products, and short reaction time make this methodology a valid contribution to the existing processes in the field of 4H-benzo[b]pyran derivatives synthesis.

EXPERIMENTAL

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. All compounds were known in the literature, and the NMR and IR spectra of the products were in agreement with earlier data.

In a typical general procedure, a mixture of aromatic aldehyde (1 mmol), malononitrile (1 mmol), and dimedone (1 mmol) in H_2O:EtOH (1:1, 5 mL) at 45°C was stirred thoroughly in the presence of catalytic amount of $Ce(SO_4)_2{\cdot}4H_2O$ (10 mg, 2.5 mol%) to afford the 4H-benzo[b]pyrans in excellent yields. After completion of the reaction confirmed by TLC, the mixture was filtered. The solid product was washed with H_2O and finally was recrystallized from ethanol and characterized. The structures of the products were confirmed from physical and spectroscopic data (IR and ^{1}H NMR) in comparison with the data in the literature.

REFERENCES

[1] G. R. Green, J. M. Evans, and A. K. Vong, In *Comprehensive Heterocyclic Chemistry II*, A. R. Katritzky, C. W. Rees, and E. F. V. Scriven, Eds. (Pergamon Press, Oxford, 1995), vol. 5, pp. 469.

[2] (a) L. L. Andreani and E. Lapi, *Bull. Chim. Fr.*, **99,** 583 (1960); (b) Y. L. Zhang, B. Z. Chen, K. Q. Zheng, M. L. Xu, and X. H. Lei, *YaoXue XueBao.*, **17,** 17 (1982); (c) Y. L. Zhang, B. Z. Chen, K. Q. Zheng, M. L. Xu, and X. H. Lei, *Chem. Abstr.*, **96,** 135383e (1982); (d) L. Bonsignore, G. Loy, D. Secci, and A. Calignano, *Eur. J. Med. Chem.*, **28,** 517 (1983); (e) E. C. Witte, P. Neubert, and A. Roesch, *Ger. Offen. De.*, 3427985 (1986); (f) E. C. Witte, P. Neubert, and A. Roesch, *Chem. Abstr.*, **104,** 224915f (1986).

[3] C. S. Konkoy, D. B. Fick, S. X. Cai, N. C. Lan, and J. F. W. Keana, PCT Int. Appl., WO, 00,75,123 (2000); *Chem. Abstr.*, **134,** 29313a (2000).

[4] (a) S. Hatakeyama, N. Ochi, H. Numata, and S. Takano, *J. Chem. Soc., Chem. Commun.*, 1202 (1988); (b) R. Gonzalez, N. Martin, C. Seoane, and J. Soto, *J. Chem. Soc., Perkin Trans., 1*, 1202 (1985).

[5] D. Arnesto, W. M. Horspool, N. Martin, A. Ramos, and C. Seaone, *J. Org. Chem.*, **54,** 3069 (1989).

[6] G. P. Ellis, In *The Chemistry of Heterocyclic Compounds*, A. Weissberger and E. C. Taylor, Eds. (Wiley, New York, 1977), vol. 31, p. 13.

[7] (a) E. A. A. Hafez, M. H. Elnagdi, A. G. A. Elagamey, and F. M. A. A. Eltaweel, *Heterocycles*, **26**, 903 (1987); (b) F. M. Abdelgalil, B. Y. Riad, S. M. Sherif, and M. H. Elnagdi, *Chem. Lett.*, **8,** 1123 (1982).

[8] T. S. Jin, A. Q. Wang, X. Wang, J. S. Zhang, and T. S. Li, *Synlett*, 871 (2004).

[9] I. Devi and P. J. Bhuyan, *Tetrahedron Lett.*, **45,** 8625 (2004).

[10] L. M. Wang, J. H. Shao, H. Tian, Y. H. Wang, and B. Liu, *J. Fluorine Chem.*, **127,** 97 (2006).

[11] D. Q. Shi, S. Zhang, Q. Y. Zhuang, S. J. Tu, and H. W. Hu, *Chin. J. Org. Chem.*, **23,** 877 (2003).

[12] S. Balalaie, M. Bararjanian, A. M. Amani, and B. Movassagh, *Synlett*, 263 (2006).

[13] R. Hekmatshoar, S. Majedi, and K. Bakhtiari, *Catal. Commun.*, **9,** 307 (2008).

[14] S. J. Tu, Y. Gao, C. Guo, D. Shi, and Z. Lu, *Synth. Commun.*, **32,** 2137 (2002).

[15] X. S. Wang, D. Q. Shi, S. J. Tu, and C. S. Yao, *Synth. Commun.*, **33,** 119 (2003).

[16] L. Fotouhi, M. M. Heravi, A. Fatehi, and K. Bakhtiari, *Tetrahedron Lett.*, **48,** 5379 (2007).

[17] Y. Penjg and G. Song, *Catal. Commun.*, **8,** 111 (2007).

[18] E. Mosaddegh, M. R. Islami, and A. Hassankhani, *Lett. Org. Chem.*, **4,** 524 (2007).

[19] S. Kumar, P. Sharma, K. Kapoor, and M. Singh. Hundal, *Tetrahedron*, **64,** 536 (2008).

[20] A. H. Gheath and N. M. Al-Orffi, *J. Sci. & Its Appl.*, **2,** 60 (2008).