A Recyclable and Highly Effective ZnO-beta Zeolite as a Catalyst for One-pot Three-Component Synthesis of Tetrahydrobenzo[*b*]pyrans

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4*H*-Benzo[*b*]pyrans was synthesized under reflux condition in ethanol via condensation of benzaldehyde, malononitrile and dimedone with ZnO-beta zeolite as an inexpensive and effective catalyst. The key features of the reported protocols are good to excellent yields, short reaction time and recovery and reusability of catalytic material.

Keywords heterogeneous, 4*H*-benzo[*b*]pyrans, ZnO-beta zeolite, multicomponent, cyclocondensation

Introduction

Multi-component reactions (MCRs) are important for the achievement of high levels of shortness and diversity. They allow more than two simple and flexible building blocks to be combined in practical, time-saving one-pot operations, giving rise to complex structures by simultaneous formation of two or more bonds, according to the domino principle.[1] MCRs contribute to the requirements of an environmentally friendly process by reducing the number of synthetic steps, energy consumption and waste production. Researchers have transformed this powerful technology into one of the most efficient and economic tools for combinatorial and parallel synthesis.[2] 4*H*-Benzo[*b*]pyrans represent a medicinally and pharmaceutically important class of compounds, because of their diverse range of biological activities, such as anticoagulant, spasmolytic, diuretic, anticancer and antianaphylactin activities.[3] Some 2-amino-4*H*-pyrans can be employed as photoactive materials.[4] In addition, polysubstituted 4*H*-benzopyrans also constitute a structural unit of a series of natural products.[5]

4*H*-Benzo[*b*]pyrans are useful in organic synthesis because of their biological importance. Therefore, various synthetic methods are reported, using microwave,[6] ultrasonic irradiation,[7] organic solvents, such as acetic acid or DMF[8] and in aqueous media,[9,10] also reported by tetrabutylammonium bromide,[11] (*S*)-proline,[12] rare earth perfluorooctanoates,[13] hexadecyltrimethylammonium bromide,[14] diammonium hydrogen phosphate[15] and iodine.[16] However, most of the methods to prepare 4*H*-benzo[*b*]pyran derivatives suffer from certain drawbacks including long reaction times, unsatisfactory yields, higher temperatures and use of expensive non reusable catalyst.

To avoid these limitations, the discovery of a mild and efficient catalyst with high catalytic activity, short reaction time, simple work-up procedure and recyclability of catalyst is still being actively pursued for the synthesis of 4*H*-benzo[*b*]pyrans. In order to overcome these problems, zeolite seems to be an excellent candidate to take over the catalytic job, since the use of a zeolite as the catalyst will be very promising not only from an economical point of view but also from an ecological viewpoint because of their suitable acidity, thermal stability, easy work-up, recyclability and environment-friendly nature. Zeolites have been used as catalyst in the petroleum refining and chemical industries.[17,18] Their properties and thus their performance as catalyst can be adjusted by modification by ion exchange with metal ions, acid treatment and hydrothermal treatment.[19,20] There have been extensive efforts to utilize the zinc loaded zeolites in organic transformations such as Heck reaction,[21] propane aromatization,[22] dehydrogenation of small paraffins,[23] aromatization of *in situ* generated ethylene[24] and the hydration of acetylene.[25,26] To the best of our knowledge the use of ZnO-beta zeolite as a catalyst in the synthesis of 4*H*-benzo[*b*]pyrans has not been reported yet. In view of the importance of heterogeneous solid acids as reusable catalyst in organic synthesis and in continuation of our ongoing work using zeolite as a solid acid catalyst for developing new synthetic methodologies,[27] we would like to report herein an efficient synthesis of 4*H*-benzo[*b*]pyrans using ZnO-beta zeolite as catalyst.

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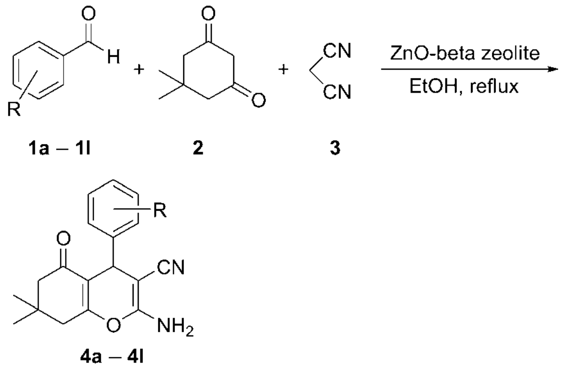
We have previously reported synthesis, characterization and catalytic applications of ZnO-beta zeolite in the synthesis of benzothiazoles, quinoxalines and polyhydroquinolines.[28,29] Since the ZnO-beta zeolite has been exploited in the organic synthesis, as a nontoxic, inexpensive, eco-friendly, easy handling and mild catalyst, we investigated ZnO-beta zeolite as a catalyst for the synthesis of 4*H*-benzo[*b*]pyrans by cyclocondensation of aldehyde, malononitrile and 5,5-dimethyl-1,3-cyclohexanedione (dimedone) at reflux condition in ethanol (Scheme 1).

Scheme 1



Experimental

All chemicals are purchased from Aldrich and Rankem chemical suppliers and used as received. The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. ^{1}H NMR spectra were recorded on an 400 MHz FT-NMR spectrometer in $CDCl_3$ as a solvent and chemical shifts (δ) values are recorded relative to tetramethylsilane (Me_4Si) as an internal standard. The X-ray powder diffraction patterns were recorded by using Bruker 8D X-ray diffractometer using Cu Kα radiation of wavelength 1.54056 Å. FT-IR spectra were recorded on JASCO FT-IR-4100, Japan. Scanning electron microscope image with energy dispersive X-ray spectroscopy (SEM-EDS) was obtained on JEOL, JSM-6330 LA operated at 20.0 kV 1.0000 nA. The surface area of catalyst was determined by the nitrogen adsorption on Quantachrome Autosorb Instrument.

General procedure for the synthesis of tetrahydrobenzo[*b*]pyran

A mixture of aldehyde (10 mmol), malononitrile (10 mmol), dimedone (10 mmol) and ZnO-beta zeolite (0.1 g) in ethanol (10 mL) was refluxed until the reaction completed (monitored by TLC). After completion of reaction, catalyst was separated by simple filtration, crude product was obtained and resulting solid was purified by recrystallization from hot methanol to afford the pure products **4a**—**4l**.

Spectroscopic data of typical compounds

2-Amino-3-cyano-4-(4-hydroxyphenyl)-7,7-dimethyl-5-oxo-4*H*-5,6,7,8-tetrahydrobenzo[*b*]pyran (4d) ^{1}H NMR δ: 0.94 (s, 3H), 1.03 (s, 3H), 2.10 (d, J=8 Hz, 1H), 2.23 (d, J=8 Hz, 1H), 2.48 (s, 2H), 4.04 (s, 1H), 6.63 (s, 1H), 6.89—6.92 (m, 4H), 9.25 (s, 1H); IR (KBr) v: 3350, 2957, 2176, 1658, 1399, 1218 cm^{-1}; EI-MS (m/z): 310 (M^+).

2-Amino-3-cyano-4-(3-nitrophenyl)-7,7-dimethyl-5-oxo-4*H*-5,6,7,8-tetrahydrobenzo[*b*]pyran (4e) ^{1}H NMR δ: 0.96 (s, 3H), 1.05 (s, 3H), 2.11 (d, J=8 Hz, 1H), 2.27 (d, J=8 Hz, 1H), 2.55 (s, 2H), 4.42 (s, 1H), 7.17 (s, 2H), 7.59—8.09 (m, 4H); IR (KBr) v: 3426, 2955, 2185, 1676, 1530, 1210 cm^{-1}; EI-MS (m/z): 339 (M^+).

2-Amino-3-cyano-4-(3-hydroxyphenyl)-7,7-dimethyl-5-oxo-4*H*-5,6,7,8-tetrahydrobenzo[*b*]pyran (4f) ^{1}H NMR δ: 0.97 (s, 3H), 1.04 (s, 3H), 2.10 (d, J=8 Hz, 1H), 2.26 (d, J=8 Hz, 1H), 2.57 (s, 2H), 4.06 (s, 1H), 6.54 (s, 2H), 6.97—7.08 (m, 4H), 9.31 (s, 1H); IR (KBr) v: 3310, 2964, 2191, 1652, 1359, 1211 cm^{-1}; EI-MS (m/z): 310 (M^+).

2-Amino-3-cyano-4-(4-methoxyphenyl)-7,7-dimethyl-5-oxo-4*H*-5,6,7,8-tetrahydrobenzo[*b*]pyran (4i) ^{1}H NMR δ: 0.95 (s, 3H), 1.03 (s, 3H), 2.08 (d, J=8 Hz, 1H), 2.22 (d, J=8 Hz, 1H), 2.25 (s, 3H), 2.49 (s, 2H), 3.34 (s, 3H), 4.11 (s, 1H), 6.85 (s, 2H), 6.82—7.06 (m, 4H); IR (KBr) v: 3356, 2969, 2157, 1658, 1382, 1217 cm^{-1}; EI-MS (m/z): 324 (M^+).

Results and discussion

To optimize the reaction conditions, benzaldehyde, malononitrile and dimedone were employed as a model reaction to examine the effect of various solvent, such as acetone, toluene, chloroform, acetonitrile, methanol and ethanol and varying amounts of ZnO-beta zeolite (0.01, 0.05, 0.1 and 0.2 g). The use of acetone, toluene and chloroform gave the product **4a** in low yield (Table 1, Entries 2—4). Acetonitrile and methanol gave moderate yields (Table 1, Entries 5 and 6) in 60 min and 90 min. respectively. Finally, the reaction in ethanol with 0.1 g of catalyst afforded **4a** in 95% yield (Table 1, Entry 7)

Table 1 Optimization of various solvents and amount of catalyst for the reaction of benzaldehyde, malononitrile and dimedone

Entry	Solvent	Catalyst/g	Time[a]	Yield[b]/%
1	Ethanol	—	3 h	—
2	Acetone	0.1	2 h	35
3	Toluene	0.1	2.5 h	52
4	Chloroform	0.1	3 h	41
5	Acetonitrile	0.1	1 h	85
6	Methanol	0.1	1.5 h	79
7	Ethanol	0.1	35 min	95
8	Ethanol	0.05	45 min	87
9	Ethanol	0.2	35 min	95

[a] All reactions were carried out using ZnO-beta zeolite at reflux condition. [b] Isolated yields.

within 35 min. Therefore, we selected ethanol as a solvent and 0.1 g of catalyst for this reaction. As shown in Table 1, no desirable product could be detected in the absence of catalyst for 180 min (Table 1, Entry 1), which indicated that the catalyst should be absolutely necessary for this reaction.

Based on the above result, this process was then extended to variety of aldehydes containing electron-donating and electron-withdrawing groups to prepare corresponding 4*H*-benzo[*b*]pyrans. No significant substituent effect was observed on the yields of the products (Table 2, Entries 1—12). Further that 4*H*-benzo[*b*]pyran bearing nitro functionality on the aryl ring was obtained in good yields (Table 2, Entries 3 and 5). Encouraged by these results, we have also carried out the cyclocondensation of heterocyclic aldehyde, that is, furfuraldehyde with malononitrile and dimedone to obtain the respective tetrahydrobenzo[*b*]pyran (Table 2, Entry 12) in a better yield. A plausible mechanism for the synthesis of tetrahydrobenzo[*b*]pyran is shown in Scheme 2.

The reusability of the catalyst is one of the most important benefits and makes them useful for commercial applications, thus the recovery and reusability of ZnO-beta zeolite was investigated. The separated catalyst can be reused after washing with *n*-hexane and drying at 120 ℃ for 1 h. The reusability of the catalyst was checked by the reaction of benzaldehyde, malononitrile and dimedone under optimized reaction condition (Table 3). The results clearly indicate that the catalyst can be reused four times without loss of its activity.

Conclusion

In summary, we have demonstrated a new and important catalytic activity of ZnO-beta zeolite as an inexpensive, effective, reusable and non-corrosive catalyst for the synthesis of tetrahydrobenzo[*b*]pyrans in high to excellent yields. Compared to the existing method, it has the several advantages, such as simple experimental procedure combined with the easy work-up, high to excellent yields of products and reusability of catalyst.

Table 2 Synthesis of tetrahydrobenzo[*b*]pyran derivatives catalyzed by ZnO-beta zeolite[a]

Entry	Ar	Product	Time/min	Yield[b]/%	m.p./℃	
					Found	Reported
1	C_6H_5	**4a**	35	95	227—228	226—228[13]
2	4-$CH_3C_6H_4$	**4b**	40	93	215—216	214—216[13]
3	4-$NO_2C_6H_4$	**4c**	50	87	177—178	178—179[14]
4	4-OHC_6H_4	**4d**	40	89	213—214	214—215[14]
5	3-$NO_2C_6H_4$	**4e**	48	86	213—214	213—217[15]
6	3-OHC_6H_4	**4f**	40	88	234—235	230—235[15]
7	4-BrC_6H_4	**4g**	42	91	207—208	207—209[15]
8	4-ClC_6H_4	**4h**	35	95	209—210	209—211[12]
9	4-$OMeC_6H_4$	**4i**	45	91	200—201	199—201[14]
10	2-ClC_6H_4	**4j**	40	95	217—218	217—218[14]
11	2,4-$Cl_2C_6H_3$	**4k**	40	89	115—116	115—117[13]
12	Furyl	**4l**	52	91	219—220	218—220[8b]

[a] All reactions were carried out at reflux condition using aldehyde (10 mmol), malononitrile (10 mmol) and dimedone (10 mmol). [b] Yield refer to isolated products, which were characterized by comparing IR, ^1H NMR, mass spectral data and melting points with those reported in literature.

Scheme 2 Plausible mechanism for the synthesis of tetrahydrobenzo[*b*]pyran catalyzed by ZnO-beta zeolite

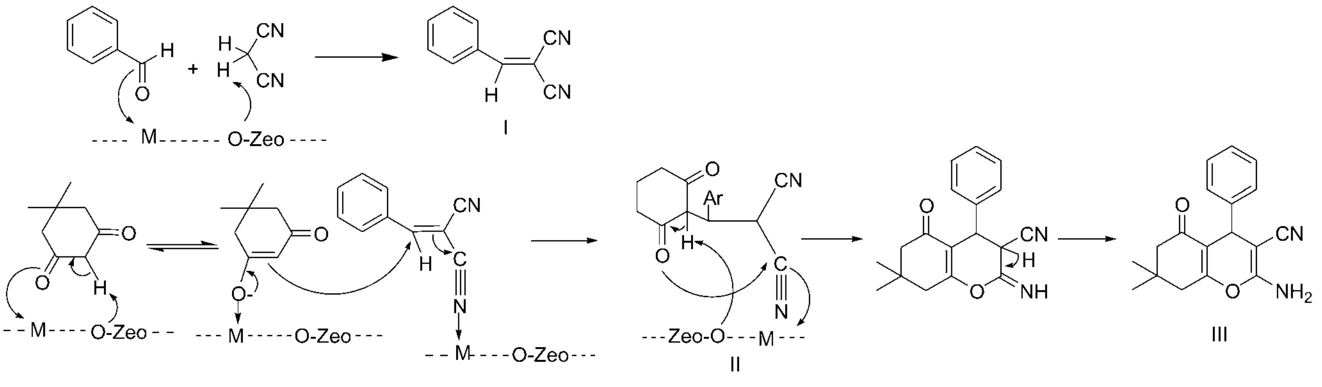


Table 3 Reusability of catalyst for the reaction of benzaldehyde, malononitrile and dimedone (Table 2, Entry 1)[a]

Entry	1	2	3	4
Cycle	Fresh	First	Second	Third
Yield[b]/%	95	95	94	93

[a] Reaction were carried out at reflux condition. [b] Isolated yields.

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