



Zinc oxide Nanobelts: An Efficient Catalyst for Knoevenagel Condensation in Aqueous Media

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ABSTRACT:

Zinc oxide nanobelts (ZnO nanobelts) are prepared by chemical precipitation method and used as catalysts in the Knoevenagel condensation of a variety of aldehydes and active methylene compounds using distilled water as a green reaction media. Furthermore, Knoevenagel condensation products were characterized by their spectral analysis. The obtained results will contribute to our understanding of nanotechnology in catalysis and enable a green and efficient protocol for developing olefines.

Introduction

In the present period, metal nanoparticles have attracted much attention because of their many significant applications in various areas such as catalysis,¹⁻² water purification,³ electroanalysis,⁴ treatment of breast cancer,⁵⁻⁶ formation and stabilization of food emulsions,⁷ photocatalysis,⁸ tissue engineering and regenerative medicine,⁹ transcutaneous vaccine delivery,¹⁰ biosensors,¹¹⁻¹² optoelectronics,¹³ spintronics,¹⁴ piezoelectric transducers,¹⁵ ultraviolet optoelectronics.¹⁶ As a result, several methods have been developed for producing metal nanoparticles solvothermal, hydrothermal, self-assembly and template assisted sol-gel.¹⁷⁻²² In this present protocol we used very simple and low temperature fabrication method to produce nanobelts of Zinc oxide and used as a catalyst in Knoevenagel condensation of a variety of aldehydes and active methylene compounds using distilled water as a green reaction medium.

Further, Knoevenagel condensation²³ reaction for olefination of carbonyl compounds is one of the most important reactions due to its wide range of applicability in organic synthesis. In the beginning, organic bases and their salts are used for this condensation reaction. Recently, highly toxic Lewis acids like TiCl₄, ZnCl₂, NbCl₅, carcinogenic I₂ have been used.²⁴ Previously, reported procedures for

olefination of carbonyl compounds suffer several drawbacks thus, green and efficient protocol is highly desirable. In this present protocol zinc oxide nanoparticles are inexpensive, effective catalyst for Knoevenagel condensation and require only mild reaction conditions to produce high yields in short reaction time.

This protocol is also applicable to condense Chromone-3-carbaldehyde with various active methylene compounds. The chromone moiety is a subunit of various natural and synthetic bioactive molecules of medicinal importance.²⁵⁻²⁶ The chemical modification of Chromone-3-carbaldehyde scaffold led to the formation of a variety of biologically active heterocycles.

Experiment

Reagent-grade chemicals were purchased from a commercial source and used without further purification. Melting points were determined in labotech melting point apparatus MPA350. Infrared (IR) spectra were recorded in KBr discs on a Perkin-Elmer 240C analyzer. ¹H NMR spectra were recorded on a BRUKER AVANCE II 400 NMR spectrometer in CDCl₃/DMSO-d₆ using tetramethylsilane (TMS) as internal standard. The progress of the reaction was



monitored by thin-layer chromatography (TLC) using silica gel G (Merck).

Preparation of ZnO nanobelts:

0.1M solution of zinc acetate in absolute ethanol was having Zn^{2+} was prepared and it was refluxed for 3 hours with stirring at 80 °C. After that, the precursor obtained was mixed with 0.1M LiOH prepared in 100 ml triply deionized water. Precipitates were formed immediately and separated out using centrifugal machine at room temperature. Finally, precipitates were dried in oven at 100 °C.

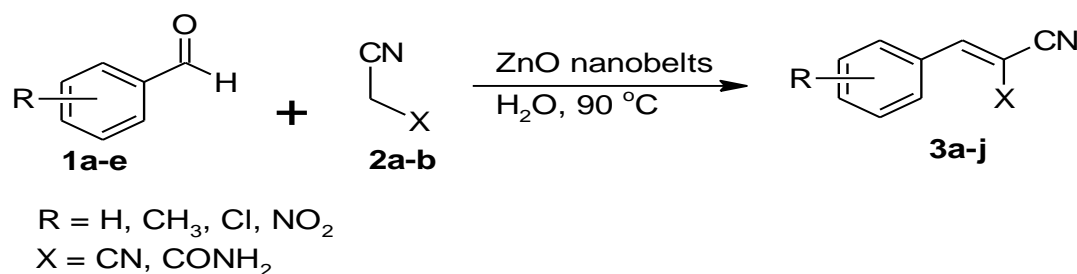
Synthesis of Knoevenagel condensation:

A mixture of aldehyde (**1a-e** or **4a-d**) (1.0 mmol), active methylene compound (**2a-c**) (1.0 mmol), ZnO nanobelts (5 mg) in 10.0 ml distilled water were stirred (at 90°C for **3a-j**/at 95°C for **5a-l**/at 95°C) on water bath (for appropriate time see table-1 and 2). The progress of reaction was monitored via thin layer chromatography. After the completion of reaction, reaction mass was cooled (15-20°C) and filtered the

isolated Knoevenagel product. The obtained products were recrystallize in DMF:ethanol. Then reaction mass was centrifuged for 10 min at 5,000 rpm. The supernatant was collected and reduced under pressure. During centrifugation obtained pellet was ZnO nanoparticles, which was dried in the oven at 100 °C to recover and reuse of catalyst. The products were further confirmed by their spectral analysis (IR, 1H NMR, mass spectra) and melting points.

Results and Discussion

In present protocol ZnO nanobelts were used to catalyse Knoevenagel reactions of benzaldehyde **1a** (1 mmol) with malononitrile **2a** (1 mmol) in 10 ml distilled water were stirred at 90°C on water bath for 5 minute and Knoevenagel adducts **3a** isolated with 98% yield (**Table 1**). The best results obtained when reaction was catalyzed by 5 mg of zinc oxide nanobelts. It was observed that, large amount of catalyst did not affect the rate of reaction as well yield but amount less than 5 mg catalyst considerably decrease the product yield.



Scheme 1 ZnO nanobelts catalysed Knoevenagel reaction of **1** and **2**.

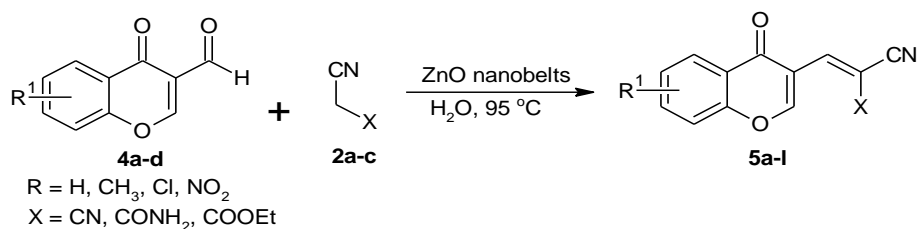
Table 1 : ZnO nanobelts catalysed Knoevenagel reaction of **1** and **2**.

Entry	R	X	Product	Time (min)	Yield (%) ^a
1	H	CN	3a	5	98
2	OMe	CN	3b	9	94
3	Cl	CN	3c	7	96
4	Br	CN	3d	11	92
5	NO ₂	CN	3e	12	91
6	H	CONH ₂	3f	6	95
7	OMe	CONH ₂	3g	8	96
8	Cl	CONH ₂	3h	8	97



9	Br	CONH ₂	3i	10	92
10	NO ₂	CONH ₂	3j	11	90

^aIsolated yields after recrystallization.



Scheme 2 : ZnO nanobelts catalysed Knoevenagel reaction of **4** and **2**.

Table 2 : ZnO nanobelts catalysed Knoevenagel reaction of **4** and **2**.

Entry	R ¹	X	Product	Time (min)	Yield (%) ^a
1	H	CN	5a	11.0	93
2	CH ₃	CN	5b	12.0	91
3	Cl	CN	5c	13.0	94
4	NO ₂	CN	5d	15.0	92
5	H	CONH ₂	5e	14.0	93
6	CH ₃	CONH ₂	5f	15.0	92
7	Cl	CONH ₂	5g	12.0	94
8	NO ₂	CONH ₂	5h	14.0	91
9	H	COOEt	5i	12.0	94
10	CH ₃	COOEt	5j	13.0	93
11	Cl	COOEt	5k	14.0	94
12	NO ₂	COOEt	5l	18.0	92

^aIsolated yields after recrystallization.

Similarly, a variety of carbonyl compounds such as aromatic aldehydes **1a-e**, and heterocyclic aldehydes i.e. Chromone-3-carbaldehydes **4a-d** were condensed with malononitrile, ethylcyanoacetate and cyanoacetamide in presence of ZnO nanobeltes at 90-95°C in distilled water to provide Knoevenagel products **3a-j** and **5a-l** in very good to excellent yields (**Scheme 1 and 2**). Aromatic aldehydes **1a-e** afforded excellent yields in shorter reaction time, whereas

heterocyclic aldehydes **4a-d** gives high yields in slightly long reaction time (**Table 2**).

Active methylene compounds **2a-b** afforded the Knoevenagel products selectively with *exo* double bond without the formation of other side-products (**Scheme 1**). Electron withdrawing and donating groups on aromatic aldehyde **1a-e** as well heterocyclic aldehyde **4a-d**, were shown slightly diversion in rate of reaction and yields.



Further, the recyclability of the catalyst was studied by using **1a** and **2a** as the model reaction. It was observed that catalysts could be recovered and reused for a new set of reaction. The reaction mixture with minimum quantity of solvent was centrifuged for 10 min at 5,000 rpm. The supernatant was collected and the centrifuged pellet, which is ZnO nanoparticles. Finally, ZnO nanoparticles were dried in oven at 100 °C. The recovered catalyst was successfully recycled and reused for five runs without further purifications.

Physical and spectral data of compounds:

Benzylidenemalononitrile (**3a**): mp 84-85 °C; IR (KBr): 3015, 2216, 1591 cm^{-1} ; $^1\text{H NMR}$ (DMSO- d_6): δ 8.55 (s, 1H), 7.95 (d, $J=7.91$ Hz, 2H), 7.70- 7.54 (m, 3H).

p-chlorobenzylidenemalononitrile (**3c**): mp 160-161 °C; IR (KBr): 3032, 2227, 1585 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3): δ 8.54 (s, 1H), 8.01-7.65 (AA'BB' system, 4H).

p-bromobenzylidenemalononitrile (**3d**): mp 159-160 °C; IR (KBr): 3105, 2229, 1585 cm^{-1} ; $^1\text{H NMR}$ (DMSO- d_6): δ 8.54 (s, 1H), 7.86 (AA'BB' system, 4H).

Benzylidenecyanoacetamide (**3f**): mp 123-124°C; IR (KBr) 3402, 3166, 2220, 1690, 1598 cm^{-1} ; $^1\text{H NMR}$ (DMSO-): δ 8.21 (s, 1), 7.95 (d, $J=8.11$, 2H). 7.85 (br d, 2H), 7.57 (m, 3H).

p-nitrobenzylidenecyanoacetamide (**3j**): mp 236-237 °C; IR (KBr): 3438, 3198, 2222, 1690, 1600 cm^{-1} ; $^1\text{H NMR}$ (DMSO- d_6): δ 8.30 (AA'BB' system, 4H), 8.32 (s, 1H), 8.11-7.90 (br d, 1H).

[(6-chloro-4-oxo-4H-chromen-3-yl)methylidene]propanedinitrile (**5c**): mp: 207-208 °C; IR (KBr): 3170, 3030, 2228, 1660, 1608, 1550, 1460 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ : 8.11-7.71 (m, 3H), 8.20 (s, 1H), 9.12 (s, 1H); Mass (m/z): 256 (M^+).

(2Z)-2-cyano-3-(4-oxo-4H-chromen-3-yl)prop-2-enamide (**5e**): mp: 201-202 °C; IR (KBr): 3400, 3169, 3060, 2226, 1680, 1630, 1560, 1465 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ : 7.62 (br-s, 1H, N-H), 7.75 (br-s, 1H, N-H), 8.14-7.44 (m, 4H, Ar-H), 8.24 (s, 1H), 9.01 (s, 1H); Mass (m/z): 240 (M^+).

(2Z)-3-(6-chloro-4-oxo-4H-chromen-3-yl)-2-cyanoprop-2-enamide (**5g**): mp: 219-220 °C.

IR (KBr): 3400, 3311, 3192, 3035, 2800, 2211, 1688, 1656, 1590, 1463 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ : 7.51 (br-s, 1H, N-H), 7.60 (br-s, 1H, N-H), 8.07-7.56 (m, 3H, Ar-H), 8.25 (s, 1H), 8.98 (s, 1H); Mass (m/z): 274 (M^+).

ethyl (2Z)-2-cyano-3-(4-oxo-4H-chromen-3-yl)prop-2-enoate (**5i**): mp: 131-132 °C; IR (KBr): 3075, 3035, 2991, 2210, 1735, 1655, 1602, 1555, 1458 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ : 1.32 (t, 3H), 4.30 (q, 2H), 8.13-7.55 (m, 4H, Ar-H), 8.42 (s, 1H), 9.12 (s, 1H); Mass (m/z): 269 (M^+).

Conclusion

In summary, we have developed a green, simple and rapid protocol for the synthesis of Knoevenagel condensation products using ZnO nanobelts as a reusable catalyst. Another merit of this procedure is the avoidance of volatile organic solvents and the use of distilled water as a green solvent. A variety of aldehydes can be employed and ZnO nanobelt has shown excellent catalytic activity for this condensation by activating both reactants without forming any by-products. Shorter reaction time and very good to excellent yields are another merit of this procedure.

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References:

- Xia, Y.; Yang, H.; Campbell, C. T. *Acc. Chem. Res.* **2013**, 46, 1671-1672. DOI: 10.1021/ar400148q.
- Polshettiwar, V.; Varma, R. S. *Green Chem.* **2010**, 12, 743-754. DOI: 10.1039/b927142c.
- Santhosh, C.; Velmurugan, V.; Jacob, G.; Jeong, S. K.; Grace, A. N.; Bhatnagar, A. *Chem. Eng. J.* **2016**. DOI: 10.1016/j.cej.2016.08.053.
- Campbell, F. W.; Compton, R. G. *Anal. Bioanal. Chem.* **2010**, 396, 241-259. DOI: 10.1007/s00216-009-3063-7.
- Yezhelyev, M. V.; Gao, X.; Xing, Y.; Al-Hajj, A.; Nie, S.; O'Regan, R. M. *Lancet Oncol.* **2006**, 7, 657-667. DOI: 10.1016/S1470-2045(06)70793-8.



6. Jeyaraj, M.; Sathishkumar, G.; Sivanandhan, G.; MubarakAli, D.; Rajesh, M.; Arun, R.; Kapildev, G.; Manickavasagam, M.; Thajuddin, N.; Premkumar, K.; Ganapathi, A. *Colloids Surf. B Biointerfaces* **2013**, 106, 86–92. DOI: 10.1016/j.colsurfb.2013.01.027.
7. Dickinson, E. *Trends Food Sci. Technol.* **2012**, 24, 4–12. DOI: 10.1016/j.tifs.2011.09.006.
8. Beydoun, D.; Amal, R.; Low, G. et al. *J. Nanopart. Res.* **1999**, 1, 439–458. DOI: 10.1023/A:1010044830871.
9. Vial, S.; Reis, R. L.; Oliveira, J. M. *Curr. Opin. Solid State Mater. Sci.* **2017**, 21(2), 92–112. <https://doi.org/10.1016/j.cossms.2016.03.006>.
10. Kohli, A. K.; Alpar, H. O. *Int. J. Pharm.* **2004**, 275, 13–17. DOI: 10.1016/j.ijpharm.2003.10.038.
11. Shi, X.; Gu, W.; Li, B. et al. *Microchim. Acta* **2014**, 181, 1–22. DOI: 10.1007/s00604-013-1069-5.
12. Warriner, K.; Reddy, S. M.; Namvar, A.; Neethirajan, S. *Trends Food Sci. Technol.* **2014**, 40(2), 183–199. DOI: 10.1016/j.tifs.2014.07.008.
13. Kong, X. Y.; Wang, Z. L. *Appl. Phys. Lett.* **2004**, 84(6), 975–977.
14. Sharma, P.; Gupta, A. K.; Rao, V.; Owens, F. J.; Sharma, R.; Ahuja, J. M.; Osorio, B.; Johansson, B.; Gehring, G. A. *Nat. Mater.* **2003**, 2(10), 673–677.
15. Catti, M.; Noel, Y.; Dovesi, R. *J. Phys. Chem. Solids* **2003**, 64(11), 2183–2190.
16. Wang, X.; Ding, Y.; Summers, C. J.; Wang, Z. L. *J. Phys. Chem. B* **2004**, 108(26), 8773–8777.
17. Lakshmi, B. B.; Patrissi, C. J.; Martin, C. R. *Chem. Mater.* **1997**, 9(11), 2544–2550. DOI: 10.1021/cm970268y.
18. Vayssieres, L.; Keis, K.; Hagfeldt, A.; Lindquist, S. E. *Chem. Mater.* **2001**, 13(12), 4395–4398. DOI: 10.1021/cm011160s.
19. Pacholski, C.; Kornowski, A.; Weller, H. *Angew. Chem. Int. Ed.* **2002**, 41(7), 1188–1191. DOI: 10.1002/1521-3773(20020402)41:7<1188::AID-ANIE1188>3.0.CO;2-5.
20. Vayssieres, L. *Adv. Mater.* **2003**, 15(5), 464–466. DOI: 10.1002/adma.200390108.
21. Liu, B.; Zeng, H. C. *J. Am. Chem. Soc.* **2003**, 125(15), 4430–4431. DOI: 10.1021/ja0299452.
22. Zhang, H.; Ma, X. Y.; Xu, J.; Niu, J. J.; Yang, D. R. *Nanotechnology* **2003**, 14(4), 423–426. DOI: 10.1088/0957-4484/14/4/303.
23. Surrey, A. R. *Name Reactions in Organic Chemistry (Second Edition)*, Academic Press, **1961**, pp 147–149. DOI: 10.1016/B978-1-4832-3227-0.50065-1.
24. (a) Prajapati, D.; Sandhu, J. S. *J. Chem. Soc. Perkin Trans 1* **1993**, 739; (b) Lehnert, W. *Tetrahedron Lett.* **1970**, 54, 4723; (c) Yang, Y-O.; Dong, D-W.; Pan, W.; Zhang, J.; Liu, Q. *Tetrahedron* **2006**, 62, 10111; (d) Shanthan, R-P.; Venkataratnam, R-V. *Tetrahedron Lett.* **1991**, 32, 5821; (e) Yadav, J-S.; Bhunia, D-C.; Singh, V-K.; Srihari, P. *Tetrahedron Lett.* **2009**, 50, 2470; (f) Ren, Y.; Cai, C. *Catal. Lett.* **2007**, 118, 134; (g) Li, Z-X.; Liu, X-P.; Qiu, Z.; Xu, D.; Yu, X-J. *J. Chem. Res.* **2011**, 35, 35; (h) Cruz, P.; Barra, E-D.; Loupy, A.; Langa, F. *Tetrahedron Lett.* **1996**, 37, 1113; (i) Cabello, J. A.; Campelo, J. M.; Garcia, A.; Luna, D.; Marinas, J. M. *J. Org. Chem.* **1984**, 49, 5159; (j) Rao, P. S.; Venkataratnam, R. V. *Tetrahedron Lett.* **1991**, 32, 5821; (k) Li, Y. Q. *J. Chem. Res. (S)* **2000**, 524; (l) Iranpoor, N.; Zeynizadeh, B.; Aghapour, A. *J. Chem. Res. (S)* **1999**, 554; (m) Zhang, X. Y.; Fan, X. S.; Niu, H. Y.; Wang, J. J. *Green. Chem.* **2003**, 5, 267; (n) Iranpoor, N.; Kazemi, F. *Tetrahedron* **1998**, 54, 9475; (o) Wang, L.; Sheng, J.; Tian, H.; Han, J.; Fan, Z.; Qian, C. *Synthesis* **2004**, 18, 3060; (p) Reddy, T. I.; Varma, R. S. *Tetrahedron Lett.* **1997**, 38, 1721; (q) Li, J. T.; Chen, G. F.; Wang, S. X.; He, L.; Li, T. S. *Aus. J. Chem.* **2005**, 58, 231; (r) Moison, H.; Texier-Bouillet, F.; Foucaud, A. *Tetrahedron* **1987**, 43, 537.
25. (a) Polykov, V. K.; Shevtsova, R. G. *Ukr. Khim. Zh.* **1981**, 47, 85; (b) Treibs, A.; William, R.; Grimm, D. *Liebigs Ann. Chem.* **1981**, 3, 306; (c) Jones, W. D.; Albrecht, W. L. *J. Org. Chem.* **1976**, 41, 706; (d) Gasparova, R.; Lacova, M. *Molecules* **2005**, 10, 937.
26. (a) Ellis, G. P. *Chromenes, Chromanones and Chromones*, Wiley, New York, **1977**, Chapters I, VII, IX, X and