

Borate Zirconia Mediated Knoevenagel Condensation Reaction in Water

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요 약. 4-Oxo-(4H)-1-benzopyran-3-carbaldehydes, 1,3-diphenyl-1H-pyrazol-4-carboxaldehyde 및 방향족 알데하이드와의 3-methyl-1-phenylpyrazolin-5-(4H)-one의 Borate Zirconia (B_2O_3/ZrO_2) 산을 촉매로 사용하여 수용액 상에서 Knoevenagel 축합 반응을 수행하여 생성물을 높은 수득율로 얻을 수 있었다. 각각의 반응에서 촉매는 수거되었고, 수거 후에 수득률과 선택성에서의 손실없이 재 사용을 하였다.

주제어: Knoevenagel 반응, B_2O_3/ZrO_2 , 3-포르밀 크로몬, 포밀 피라졸, 방향족 알데하이드, 물, 불균일 촉매

ABSTRACT. Knoevenagel condensation of 4-oxo-(4H)-1-benzopyran-3-carbaldehydes, 1,3-diphenyl-1H-pyrazol-4-carboxaldehyde and aromatic aldehyde has been carried out with 3-methyl-1-phenylpyrazolin-5-(4H)-one as condensing agent in moderate to good yields by using Borate Zirconia (B_2O_3/ZrO_2) solid acid catalyst in water medium. In each conversion, the catalyst was successfully recovered and recycled without significant loss in yield and selectivity.

Keywords: Knoevenagel Reaction, B_2O_3/ZrO_2 , 3-Formyl Chromone, Formyl Pyrazole, Aromatic Aldehyde, Water, Heterogeneous Catalysis

1. INTRODUCTION

Knoevenagel reaction¹ is one of the most important C-C bond forming reactions practiced by the synthetic chemists. It is widely used in the synthesis of important intermediates or end products for perfumes,² pharmaceuticals³ and polymers.⁴ Bases, acids, or catalysts containing both acid-base sites⁵ catalyze the reactions. Several homogeneous and heterogeneous catalysts such as $CuCl_2$,⁶ SmI_2 ,⁷ Al_2O_3 ,⁸ anionic resins,⁹ clays¹⁰ and calcined hydrotalcites¹¹ have been documented in the literature for Knoe-

nagel condensation. Recently we have also studied the Knoevenagel condensation reactions under different conditions.¹²

The enhancement of rate of several organic reactions due to hydrophobic effect of water, as a solvent was rediscovered by Breslow in 1980.¹³ Water is unique solvent due to easy availability, non-inflammable, non-toxic and negligible cost. To develop eco-efficient processes, selection of the solvent is critical. Although various catalysts have been developed to realize organic transformations in water,¹⁴ it is still difficult to achieve recovery and reuse of the

catalyst in many cases.

Boron oxide supported on zirconium oxide containing 30 mol% of boron has been reported as a superacid catalyst (acidic strength $H_0 = -13$) efficient for decomposition of ethanol to ethylene.¹⁵ Xu *et al.*¹⁶ has used B_2O_3/ZrO_2 catalyst for the selective synthesis of ϵ -caprolactum by gas phase Beckman Rearrangement of cyclohexanone oxime. Recently we have also studied the acidic properties of this catalyst for Friedel-Craft benzoylation of anisole to 4- and 2-methoxybenzophenones using benzoyl chloride¹⁷ and selective *C*-methylation of phenol to *o*-cresol and 2,6-xyleneol using methanol.¹⁸ It showed the comparable performance with conventional homogenous $AlCl_3$ catalyst, as well as heterogeneous catalysts such as zeolite H-beta and sulphated-zirconia¹⁷ and which is also found an efficient catalyst for selective *C*-methylation of phenol to *o*-cresol and 2,6-xyleneol using methanol as an alkylating agent.¹⁸ This prompted us to test its activity for Knoevenagel condensation reaction and to our knowledge borate zirconia has not been used as a catalyst for this reaction.

EXPERIMENTAL SECTION

The starting materials 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde,¹⁹ 3-methyl-1-phenylpyrazolin-5(4*H*)-one²⁰ and 1, 3-diphenyl-1*H*-pyrazol-4-carboxaldehyde²¹ were prepared by the reported method. The progress of reactions was monitored by TLC [silica, light petroleum-EtOAc (8:2)]. Melting points were measured in open capillaries in a paraffin bath. IR spectra were recorded as Nujol mulls on FTIR instrument. ¹H NMR spectra were recorded at 300 MHz with $CDCl_3$ as solvent and TMS as an internal standard. Elemental analysis was consistent with the structures. Spectral data matched with the authentic samples.²²

Synthesis and characterization of the catalyst

Borate zirconia containing 30 mol% boron oxide catalyst was prepared by impregnation method. Zirconyl oxychloride was dissolved in distilled water and aqueous ammonia was added dropwise to it with constant stirring (pH=10). The resultant pre-

cipitate was filtered and washed with distilled water till free from chloride ions. The residue was dried overnight at 85 °C in an oven. Boric acid was dissolved in distilled water. The zirconium hydroxide obtained above was added to the boric acid solution with stirring to obtain slurry. It was air dried, heated in an oven at 110 °C for 5 h and calcined overnight at 650 °C. The powder X-ray diffraction analysis (XRD) of the catalyst was carried out using Rigaku X-ray diffractometer (Rigaku miniflex) equipped with a Ni filtered Cu-K α (1.542 Å) radiation and a graphite crystal monochromator. X-ray Photoemission spectra (XPS) were recorded on VG Microtech Multilab ESCA 3000 spectrometer using non-monochromatized Mg-K α x-ray source ($h\nu=1253.6$ eV). Temperature Programmed Desorption (TPD-ammonia) profile of the catalyst was recorded on a Micromeritics Autochem 2910 apparatus. Scanning electron microscope JEOL JSM 500 was used to obtain SEM image and determination of specific surface area was carried out by BET (Brunner-Emmett-Teller) N_2 adsorption using NOVA 1200 Quanta chrome.

General experimental procedure for the Knoevenagel condensation

4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde (10 mmol) and 3-methyl-1-phenylpyrazolin-5(4*H*)-one (10 mmol) with acidic catalyst B_2O_3/ZrO_2 (0.2 g) in distilled water (10 mL) was heated in an oil bath at 90 °C for time given in Table 1. The progress of the reaction was monitored on TLC. After completion of the reaction, the reaction mixture was cooled and filtered to obtain solid product with catalyst, which was separated during crystallization. It was recrystallized from dioxane to get pure product. The similar procedure is applied for the condensation reactions of aromatic aldehyde and 1, 3-diphenyl-1*H*-pyrazol-4-carboxaldehyde. Compounds synthesized by above method are listed in Table 1 with their yields and physical constants. The separated catalyst was heated at 120 °C and used for the recycling experiments.

RESULTS AND DISCUSSION

In continuation of our work on the Knoevenagel

Table 1. B₂O₃/ZrO₂ catalyzed Knoevenagel condensation reaction in water.

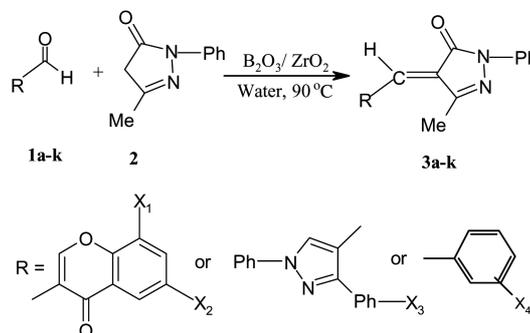
Entry	Product	Substituents	Time (mins)	Yield (%)	M.P. (°C)
1	3a	X ₁ - X ₂ - H	25	80	230
2	3b	X ₁ - H; X ₂ - Cl	30	85	240
3	3c	X ₁ - H; X ₂ - Br	30	84	324
4	3d	X ₁ - X ₂ - Cl	25	85	248
5	3e	X ₁ - H; X ₂ - Cl	25	88	238
6	3f	X ₃ - H	30	70	212
7	3g	X ₃ - Cl	30	75	238
8	3h	X ₃ - Me	30	72	235
9	3l	X ₄ - H	25	70	110
10	3j	X ₄ - Cl	30	70	108
11	3k	X ₄ - Me	30	73	138

condensation reactions of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde, 1,3-diphenyl-1*H*-pyrazol-4-carboxaldehyde and aromatic aldehyde with 3-methyl-1-phenylpyrazolin-5(4*H*)-one under several different conditions.²³ And as a part of our research programme aimed at developing new catalyst and subsequent application for various organic transformations, herein we wish to report the Borate zirconia mediated Knoevenagel condensation of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehydes, 1,3-diphenyl-1*H*-pyrazole-4-carboxaldehyde and aromatic aldehyde with 3-methyl-1-phenylpyrazolin-5(4*H*)-one as condensing agent at 90 °C, in moderate to good yields of the condensed product using water as an ecofriendly reaction solvent (Table 1, entries 1-11). The substrate 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde has three active sites: α, β-unsaturated carbonyl group, a carbon-carbon double bond and a formyl group. Of these, formyl has higher reactivity towards the active methylene compounds and we got exclusively single product.

The catalyst was characterized by several techniques like X-Ray diffraction (XRD), X-ray Photoelectron Spectroscopy (XPS), Temperature Programmed Desorption (TPD) of ammonia, Scanning Electron Microscopy (SEM) and BET surface area measurements. The XRD pattern B₂O₃/ZrO₂ calcined at 650 °C showed the formation of cubic phase of zirconia. The surface area of the catalyst was found to be 114 m²/g. XPS study showed the binding energy of 191.9 eV for B 1s, which is in good agreement with standard value of 192 eV for B³⁺ state. The acid site

Table 2. Recycling data of B₂O₃/ZrO₂ for the Knoevenagel condensation reaction of 4-chlorobenzaldehyde with 3-methyl-1-phenylpyrazolin-5(4*H*)-one

Entry	Cycles	Selectivity (%)	Yield (%)
1	Fresh	98	70
2	1 st	98	67
3	2 nd	98	67
4	3 rd	98	67



Scheme 1.

density of B₂O₃/ZrO₂ measured by TPD ammonia as a probe molecule was found to be 0.398 mmol/g, which is quite high for its use as an acid catalyzed reaction. SEM of the catalyst showed the particles of size ranging from 2 to 3 μm and the particles were observed in agglomerated form.

We have also examined the catalytic activity of recovered B₂O₃/ZrO₂ for the Knoevenagel condensation of 4-chlorobenzaldehyde with 3-methyl-1-phenylpyrazolin-5(4*H*)-one and the results of recycling experiments are given in Table 2. These results

clearly indicates that the catalytic activity of recovered B_2O_3/ZrO_2 was slightly decreased than the fresh catalyst and it remains constant for further two cycles without any influence on yield and selectivity.

CONCLUSIONS

In conclusion, we have developed an environmentally benign, economically viable and cleaner methodology for the Knoevenagel condensation of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde and 1,3-diphenyl-1*H*-pyrazol-4-carboxaldehyde, aromatic aldehyde with 3-methyl-1-phenylpyrazolin-5-(4*H*)-one in water using borate zirconia solid acid catalyst. We got the condensed product in moderate to good yield.

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