**Note**

ZrOCl$_2$.8H$_2$O as a new solid phase and recyclable catalyst for an efficient Knoevenagel condensation under solvent-free microwave irradiation conditions†

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A new solid phase and recyclable catalyst for an efficient Knoevenagel condensation under solvent-free microwave irradiation conditions has been developed for universal applications in C-C bond formation.

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The Knoevenagel condensation reaction is considered as an important reaction in C-C bond formation and has several applications in the synthesis of fine chemicals, carbocycles and heterocycles. In general, the reaction is carried by the condensation of carbonyl compounds with active methylenes by conventional heating, catalysed by organic bases such as primary, secondary, tertiary amines, ammonia and ammonium salts. Wherever organic base along with catalyst is used, the by-products are formed to some extent, however more specifically in presence of piperidine as a base, the formation of by-products are major which results in low yield and problem of separating the desired product. More recently the catalysts such as Al$_2$O$_3$, silica gel/base, TiCl$_4$/base, doped xenoliths, AlPO$_4$-Al$_2$O$_3$, ZnCl$_2$, solid-phase resins, CdI$_2$, EDDA, MW, potassium triiodide, an ion exchange resins, CaO and BiCl$_3$ have been used for the reaction. Thus each process has its own disadvantages with respect to high conversion and selectivity to the desired products. Our continued interest on metal oxides, oxyfluorides and chlorides prompted us to identify a new catalyst based on metal oxides or oxychlorides for the Knoevenagel condensation reaction to minimize the formation of by-products.

Earlier studies reveal that the Knoevenagel condensation requires a base to catalyse the reaction. It is known that the metal oxides and oxychlorides are highly basic in nature and considered to act as a catalyst for the Knoevenagel condensation reaction. In order to shorten the reaction time and operation simplicity with special attributes such as enhanced reaction rates, higher yields, greater selectivity and ease of manipulation of Knoevenagel condensation, microwave irradiation condition has been adopted. However the reaction with catalyst in combination with microwave irradiation conditions has not been exploited so far.

The most and readily available important “Zirconyl” salt is ZrOCl$_2$.8H$_2$O which crystallizes from dilute hydrochloric acid solutions and contains the ion [Zr$_4$ (OH)$_8$(H$_2$O)$_{16}$]$_{8+}$. Each Zr atom is in distorted square, linked by pairs of hydroxy bridges and also bound to four water molecules, so that the Zr atom is co-ordinated by eight oxygen atoms. Each oxygen atom acts as a Lewis base, which facilitates the Knoevenagel condensation. Based on our investigation, ZrOCl$_2$.8H$_2$O was found to be a suitable and recyclable catalyst for the efficient Knoevenagel condensation of various active methylene compounds such as malononitrile, ethyl cyanoacetate, cyanoacetamide, dimethyl malonate, methyl ethyl malonate, acetylacetone and aromatic aldehydes under solvent-free microwave irradiation conditions (Scheme I). The reaction is complete in 2-6 min with facile recovery of product in high yields and no Michael product was observed. The catalyst need no activation and is recycled four times with fresh reactants under same conditions and gave similar results without significant loss of activity. In order to determine the scope of the reaction, various aromatic aldehydes bearing electron-withdrawing and electron-releasing groups and active methylene compounds were studied and found that in all the cases high yield of product is formed except in the case of compound 31 where acetyl acetone is used as active methylene reactant. Alternately, the same reaction was performed with specific example under thermal conditions in the presence of ZrOCl$_2$.8H$_2$O
and reaction was completed in 2 hr and the yield of 3a was only 45%. The same reaction was unsuccessful with ketones such as acetophenone and also substituted ketones like 4-methylacetophenone and 4-chloroacetophenone. The number of products formed and yields obtained in this study is given in Table I.

In conclusion the new solid phase catalyst has been developed for an efficient Knoevenagel condensation for universal application of C-C bond formation with various substituents in aromatic aldehydes and active methylene compounds and is recyclable.

**Experimental Section**

Melting points were determined in open glass capillaries on a Fisher-Johns melting point apparatus and were uncorrected. Catalyst was procured from an Indian industry (Loba Chemie). IR spectra were recorded on a FT-IR Schimadzu Perkin-Elmer 1310 infrared spectrophotometer. ¹H NMR spectra were obtained on a Varian Gemini (200 MGz) spectrometer and TMS was used as an internal standard. Mass spectra were determined on a VG-micromass 7070H instrument at 70 eV. Elemental analysis were carried out on a Elemental Vario EL (Germany) apparatus.

**General Procedure**

In a typical experiment, benzaldehyde (0.2g, 1.9 mmol) and malononitrile (0.1g, 1.9 mmol) were dissolved in CH₂Cl₂ (5 mL) and ZrOCl₂·8H₂O (0.1 g, 0.4 mmol) added. The CH₂Cl₂ was thus evaporated and reaction was completed in 2 hr and the yield of 3a was only 45%. The same reaction was unsuccessful with ketones such as acetophenone and also substituted ketones like 4-methylacetophenone and 4-chloroacetophenone. The number of products formed and yields obtained in this study is given in Table I.

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and the dried solid mixture was subjected to microwave irradiation in a domestic microwave oven (BPL microwave cooking system model 700T) for 2-4 min with 100% power corresponding to 600 watts. The reaction mixture was cooled to room temperature and the product was extracted with CHCl3 (20 mL). The organic extract was concentrated to give a crude solid which was purified by column chromatography using silica gel (60-120 mesh) and chloroform/n-hexane mixture (20/80) as eluent to yield the product in 98%. The residue of the used catalyst was dried, weighed and further reacted four times with fresh reactants under similar conditions and the product was obtained.

4-Fluoroxybenzylidene malononitrile 3d: IR (KBr): 1615-1639 (C=C), 2221cm –1(CN); 1H NMR (CDCl 3): δ 2.2 (s, 6H, COCH3), 2.2 (s, 3H, Ar-H, 1H, CH); MS: m/z 172 (M+).

4-Methoxybenzylidene acetylacetone 3l: IR (KBr): 1620-1635 (C=C), 1650-1700 (C=O), 1028-1068 cm-1; 1H NMR (CDCl3): δ 2.2 (s, 6H, COCH3), 3.7 (s, 3H, OCH3), 6.65-6.75 (m, 2H, Ar-H), 7.2-7.35 (m, 2H, Ar-H, 1H, CH); MS: m/z 248 (M+).

4-Methoxybenzylidene ethyl acetoacetate 3m: IR (KBr): 1610-1640 (C=C), 1650-1700 (C=O), 1022-1065 cm-1; 1H NMR (CDCl3): δ 7.2-7.3 (m, 2H, Ar-H, 1H, CH), 7.9 (m, 2H, Ar-H); MS: (m/z) 172 (M+).

4-Methoxybenzylidene methyl acetoacetate 3n: IR (KBr): 1600-1635 (C=C), 1600-1700 (C=O), 1028-1060 cm-1(OCH3); 1H NMR (CDCl3): δ 1.2 (t, 3H, CH3), 2.4 (s, 3H, COCH3), 3.7 (s, 3H, OCH3), 4.23 (q, 2H, CH2) 6.65-6.75 (m, 2H, Ar-H), 7.2-7.35 (m, 2H, Ar-H, 1H, CH); MS: m/z 248 (M+).

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