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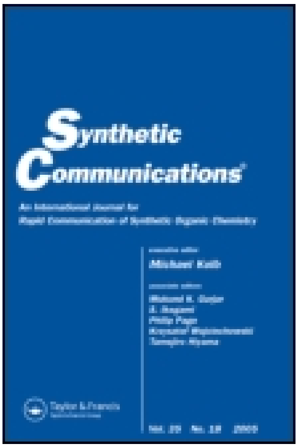

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SOLVENT-FREE KNOEVENAGEL CONDENSATION OVER COBALT HYDROXYAPATITE

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The Knoevenagel condensation between various aldehydes (benzaldehyde, 1-naphthaldehyde, p-bromobenzaldehyde and p-methoxybenzaldehyde) and esters (ethylcyanoacetate, ethylacetoacetate and diethylmalonoester) was carried out under solvent free condition in the presence of cobalt hydroxyapatite (CoHAp), as a catalyst. Good to excellent yields (35–96%) were obtained. The catalyst is found to be superior over fluorapatite and several other heterogeneous catalysts. The catalyst can be recycled at least 3 times.

Keywords: Cobalt hydroxyapatite; environment friendly; Knoevenagel condensation; solvent-free condition

INTRODUCTION

The Knoevenagel condensation is an important carbon-carbon double bond forming reaction and used widely in the synthesis of intermediates or end products for pharmaceuticals, perfumes, polymers, etc.[1] The reaction is usually catalysed by bases such as ammonia, primary and secondary amines,[2] quaternary ammonium salts[3,4] Lewis acids,[5–7] catalysis containing acid-base sites,[8] etc. and usually carried out under homogeneous conditions, which require organic solvent and this generates a large volume of solvent waste. For the standpoint of sustainable environment and minimising pollution, solvent free heterogeneous catalysts have been receiving increasing attention. Since, these heterogeneous catalysts not only avoid the use of organic solvent but also suppress side reactions such as self condensation, oligomerisation etc. resulting in better selectivity and product yield.[9] In recent years, therefore, the use of heterogeneous catalysts,[10–13] their recovery and reusability are very much sought after in industry. The use of fluorapatite was reported earlier as a heterogeneous catalyst for Knoevenagel condensation.[14] We have synthesized and characterized several hydroxyapatite catalysts and used them for the oxidation of pentane, n-hexane, etc.[15] We envisioned that cobalt hydroxyapatite, CoHAp could be extended for Knoevenagel condensation to form various alkenes and the results of

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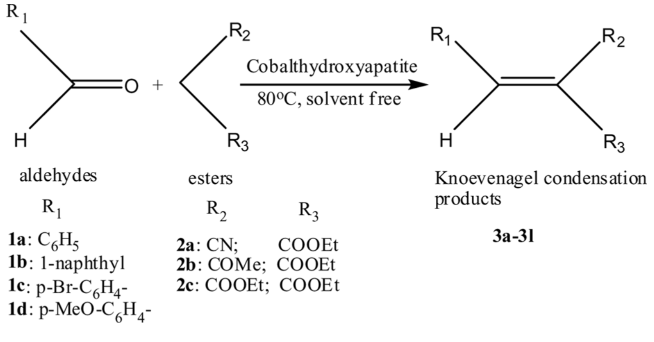
that study are communicated herewith. CoHAp was synthesised by the procedure as described in the literature.[16]

RESULTS AND DISCUSSION

In the present study, we report the Knoevenagel condensation between various aldehydes (benzaldehyde, **1a**; 1-naphthaldehyde, **1b;** p-bromobenzaldehyde, **1c** and p-methoxybenzaldehyde, **1d**) and esters (ethylcyanoacetate, **2a;** ethylacetoacetate, **2b** and diethylmalonoester, **2c**) under solvent free condition in the presence of CoHAp as a catalyst (Scheme 1). To investigate the effect and the role of catalyst on the yield of products, each one of the reactions was carried out in triplicate by varying the amounts of catalyst as 0.025, 0.05 and 0.100 g. For example, the reaction of **1a** with **2a** was carried out by the use of 0.025, 0.05 and 0.100 g of catalyst and respectively 45, 91 and 96% of yields of product **3a** (Table 1) were obtained. The same reaction was carried out under the similar reaction conditions without the catalyst and it did not give product in the stipulated time period (5 min). These results confirm the necessity of CoHAp as catalyst for the proposed reaction. Further, it was also observed that a maximum yield of 96% of product **3a** was obtained by the use of 0.10 g of catalyst; however, the yield 91%, which was very close to the maximum yield, was obtained by the use of 0.05 g of catalyst (Table 1). This observation was noticed in all cases, (Table 1, Entry 2–12) and the percentage yields of other condensation products, **3b–3l**, under similar condition and the time duration are given in Table 1.

In general the reactions were fast and the products were obtained in short reaction time of 2 to10 min, except for the reaction of **1b** with **2a–2c** in which cases it took about 60–90 min. Among the condensation reactions investigated, the catalyst was very efficient towards i) the reactions of **1a** with **2a**, **2b** and **2c** which gave the products **3a**, **3e**, and **3i** in an excellent yields of 96%, 87%, and 92% respectively; and ii) the reactions of **1d** with **2a**, **2b**, and **2c**, which gave the products **3d**, **3h**, and **3l** in an excellent yield of 91%, 88%, and 93% respectively. The reactions of **1b** with **2a**, **2b**, and **2c** were moderately accelerated by the CoHAp which gave the products **3b, 3f** and **3j** with a yield of 76, 62 and 82%, respectively. The catalyst



Scheme 1. Knoevenagel condensation.

Table 1. Synthesis of various alkenes, **3a-3l**, by Knoevenagel condensation using CoHAp under solvent-free condition

				Amount of catalyst and yields		
Entry	Aldehydes	Esters	Products	0.025 g yield (time)	0.05 g yield (time)	0.100 g yield/(time)
1	benzaldehyde, **1a**	**2a**	**3a**	45 (5)	91 (5)	96 (5)
2	1-naphthaldehyde, **1b**	**2a**	**3b**	42 (90)	72 (90)	76 (90)
3	p-bromobenzaldehyde, **1c**	**2a**	**3c**	35 (5)	44 (5)	49 (5)
4	p-methoxybenzaldehyde, **1d**	**2a**	**3d**	47 (2)	85 (2)	91 (2)
5	benzaldehyde, **1a**	**2b**	**3e**	61 (10)	80 (10)	87 (10)
6	1-naphthaldehyde, **1b**	**2b**	**3f**	41 (60)	55 (60)	62 (60)
7	p-bromobenzaldehyde, **1c**	**2b**	**3g**	39 (8)	56 (8)	60 (8)
8	p-methoxybenzaldehyde, **1d**	**2b**	**3h**	47 (5)	84 (5)	88 (5)
9	benzaldehyde, **1a**	**2c**	**3i**	51 (2)	85 (2)	92 (2)
10	1-naphthaldehyde, **1b**	**2c**	**3j**	53 (70)	78 (70)	82 (70)
11	p-bromobenzaldehyde, **1c**	**2c**	**3k**	46 (10)	49 (10)	56 (10)
12	p-methoxybenzaldehyde, **1d**	**2c**	**3l**	48 (2)	87 (2)	93 (2)

Yields are in mol %; time is in minutes.

poorly accelerated the reactions of **1c** with **2a**, **2b**, and **2c** which gave the products **3c**, **3g**, and **3k** with a yield of 49%, 60% and 56%, respectively.

In order to test the reusability of CoHAp, the Knoevenagel condensation of **1a** with **2a** was carried out in the presence of 0.100 g of catalyst. The catalyst was tested for a total of five successive usages and the yields were very satisfactory for three successive usages and gave the product **3a** with a yield of 92%, 90%, and 86% respectively. Thereafter, the yields were drastically lowered such that for the fourth and fifth successive usages it gave only 62 and 44% of yields, respectively. In the fourth usage, the recovered catalyst was about 50% (0.054 g) and if the catalyst is as efficient as fresh it would have to yield as much as of 91%. However, the obtainment of 62% of yield implied that the catalyst has lost its efficiency from the fourth usage onwards. The probable reasons for this can be of twofold: i) apparently, the amount of catalyst played an important role in the yield of products i.e., higher the amount of catalyst, the higher is the yield of products. During recovery, a loss of about 10–15% of catalyst was observed in every successive cycle and that would be

Table 2. The catalytic activity of recycled CoHAP catalyst (0.100 g) for the Knoevenagel condensation of **1a** with **2a**

Cycle	Time (min)	Yield (mol%)	Recovery of catalyst (wt%)
1	5	93	84
2	5	90	75
3	5	86	62
4	5	62	54
5	5	44	40

Table 3. Comparison of CoHAp catalysed Knoevenagel condensation of **1a** with **2a** for the yields of product **3a** with other heterogeneous catalysts

Entry	Catalyst	Time (min)	Yield (mol%)
1	CoHAp (0.100 g)	5	96
2	CoHAp (0.050 g)	5	91
3	Flourapatite (1.25 g) [14]	15	37
4	Flourapatite (1.25 g) [14]	90	95
5	Nickel hydroxyapatite (0.083 g) [15]	1200	55
6	Zeolite (Znβ) (0.100 g) [1]	360	72
7	KF/Al_2O_3 [17]	150	86
8	$AlPO_4/Al_2O_3$ [18]	15	80
9	Resin [19]	300	32
10	Zeolite [20]	720	78
11	$ZnCl_2$ [6]	10	91

one of the reasons for the lower in yield in every successive cycle ii) another plausible reason would be that the active sites on the surface of the catalyst might have slowly poisoned due to interaction with products. The poisoning effect might have been much more pronounced from fourth cycle onwards. Therefore, only 62% of yield was obtained from 0.054 g of the recovered catalyst in fourth cycle which was much lower than the yield of 91% obtained from 0.05 g of fresh catalyst, i.e., about the same quantity of catalyst. Table 2 shows the percentage yield in every cycle and the corresponding loss of an average of about 10–15% of catalyst in every successive usage.

A literature survey of the yields reported for Knoevenagel condensation reaction of **1a** with **2a** to give **3a** using various heterogeneous catalyst materials and solvent free conditions shows that CoHAp catalysed system proves superior than many others.[1,14,15,17–20] Table 3 summarises the literature values of yields with different catalysts under varied temperature conditions. The fluorapatite catalyst required 1.25 g (>1 mmol) to produce 37 and 95% yields of product **3a** in 15 and 90 min,[14] respectively. A meager quantity, 0.100 g (<0.1 mmol) and 0.05 g, of CoHAp is required for producing, respectively, 96 and 91% yields of product **3a** in 5 min times.

EXPERIMENTAL

An equimolar quantity (2.0 mmol) of aldehydes (**1a–1d**) and esters (**2a–2c**) were taken in a flask and the mixture was heated at 80 °C for a while and then CoHAp catalyst was added and stirred vigorously and left to stand. The products (**3a–3l**) were extracted with chloroform and the catalyst was removed by simple filtration. The products were separated by isolation method using column chromatography using a 40 cm column packed with silica gel 60 (Merck, 0.063–0.200 micron) and eluted the product mixture with solvents of increasing polarity, in the order hexane, chloroform and acetone. Each fraction was monitored through TLC. The pure compound factions were isolated and were identified by ^1H NMR spectroscopy, and then the yields were calculated. The yields reported in the communication are in mol%;

the amount of the recovered catalyst is reported in wt%. All reagents used were of Analytical grade reagents; p-methoxybenzaldehyde and 1-naphthaldehyde were purchased from Sigma-Aldrich; benzaldehyde, ethylacetoacetate, p-bromobenzaldehye, ethylcyanoacetate and diethylmalonoester were purchased from Merck. Silica gel 60 TLC plates were obtained from Merck, Darmstadt, Germany.

CONCLUSIONS

We have demonstrated the efficiency of CoHAp as catalyst for the Knoevenagel condensation between various aldehydes (**1a–1d**) and esters (**2a–2c**) giving good to excellent yields. The reactions were fast and carried under solvent free conditions. CoHAp can replace the existing homogeneous catalyst as well as many of the heterogeneous catalysts with reasonable recovery and reusability and therefore ideal for industrial applications.

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