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A simpler and greener protocol for the preparation of β-acetylamino ketones by a one-pot reaction of aryl aldehydes, enolisable ketones, acetyl chloride and acetonitrile in the presence of zeolite Hβ as a reusable catalyst

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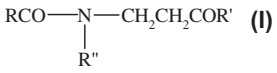
Abstract—β-Acetylamino ketones have been obtained in a one-pot coupling of an aldehyde with an enolisable ketone, acetyl chloride and acetonitrile in the presence of zeolite Hβ as catalyst at room temperature (26–28 °C). The procedure has the advantages of mild workup, circumvention of high temperature and inert atmosphere. The catalyst was found to be recyclable.

β-Acetylamino ketones **I** are fascinating compounds due to their multifunctional nature and are important synthons for a variety of speciality chemicals.[1] They are usually prepared through acylation of β-aminoketones,[2] Michael addition to α,β-unsaturated ketones[3] or photoisomerisation of phthalimides.[4]



(I)

The most interesting reaction for the synthesis of these compounds is by multicomponent coupling involving aldehyde, enolisable ketone, acetyl chloride and acetonitrile as first reported by Iqbal and co-workers.[5a–5d] Multicomponent one-pot reactions are always resource effective and environmentally acceptable and thus are greener compared to multistep reactions.[6] The multicomponent reactions leading to the formation of β-acetylamino ketones can be catalysed by catalysts such as $CoCl_2$, cobalt(II) acetate supported on polyaniline and Montmorillonite K10.[5a–5d] Recently, bismuth oxychloride has been reported as a procatalyst for the same reaction.[5e] However, the reported procedures have one or the other disadvantages and most of the catalysts are nonrecyclable. With increasing environmental concerns and regulatory constraints, the development of environmentally benign organic reactions has become mandatory.[7]

In recent years, the use of zeolites in the manufacture of fine chemicals and chemical intermediates has attracted interest owing to their special features such as shape selectivity, controlled variability and above all, their reusability and eco-friendly nature, the characters sought for in green chemistry.[8] Hβ is a strong Brønsted acid. It is easily available and in many cases reusable. This prompted us to use Hβ for the multicomponent coupling. As a part of our ongoing green technology program[9] we disclose here a more practical, one-pot, green alternative for the synthesis of β-acetylamino ketones (Scheme 1). In a typical procedure,[10,11] the reaction of methyl acetoacetate, acetophenone and propiophenone with substituted benzaldehydes proceeded smoothly at room temperature to afford good yields of β-acetylamino ketones (Table 1). The major advantage of this method is that the isolation of the products can be isolated without chromatography, that is, by simply washing with petroleum ether, affording β-acetylaminoketones in high purity. It is noteworthy that the reported $CoCl_2$ catalysed reaction, even though carried

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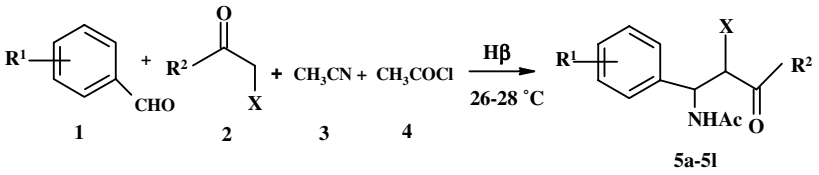

Scheme 1.

Table 1. Synthesis of β-acetylamino ketones using Hβ catalyst

No.	R^1	X	R^2	Time (h)	*syn*/*anti*	Yield (%)[a]
5a	2-NO_2	H	Ph	12	—	86
5b	3-NO_2	H	Ph	10	—	78
5c	2-Cl	H	Ph	9	—	80
5d	4-Cl	H	Ph	8.5	—	87
5e	4-OMe	H	Ph	8	—	90
5f	H	H	4-OMe-C_6H_4	8	—	88
5g	H	Me	Ph	11	3:97	72
5h	4-Me	COOMe	Me	8	8:92	75
5i	4-Cl	COOMe	Me	10	12:88	72
5j	4-F	COOMe	Me	9	3:97	63
5k	4-Br	COOMe	Me	9.5	12:88	69
5l	H	COOMe	Me	9	24:76	65

Reaction conditions: Enolisable ketone = 5 mmol, aldehyde = 5 mmol, acetyl chloride = 2 mL, acetonitrile = 12.5 mL, Hβ = 0.4 g, temp = 26–28 °C.
[a] Isolated and unoptimised yields of the mixtures of diastereomers.

out at room temperature, required longer periods, i.e., 5 days and also required a nonaqueous workup.[5b] The use of Montmorillonite K10 required a high temperature (70 °C).[5a] Polyaniline supported cobalt(II) acetate required a nitrogen atmosphere.[5c] Our protocol is advantageous as it does not need an inert atmosphere or a high temperature, involves an aqueous workup and above all short reaction times (8–12 h). The reaction involving acetophenone and substituted acetophenone gave products with only one asymmetric centre (**5a–f**). The reaction involving propiophenone (**5g**) and methyl acetoacetate (**5l**) however, led to diastereomeric mixtures. The ratio of these diastereomers was determined by ^{1}H NMR spectroscopy.[12] As can be seen from Table 1, the major diastereomer was *anti* in all cases. We also examined the reusability of the catalyst. The yields of **5c** were 78%, 75%, and 74%, respectively, in successive cycles.

In conclusion, we have demonstrated a simple one-pot procedure for the synthesis of β-acetylamino ketones by the reaction of aldehydes, enolisable ketones, acetonitrile and acetyl chloride at room temperature in the presence of the environmentally friendly, reusable and inexpensive zeolite Hβ as catalyst.

Acknowledgements

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10. Experimental procedure: To a stirred mixture of zeolite Hβ (0.4 g) in acetonitrile (12.5 mL) were added an aldehyde (5 mmol), an enolisable ketone (5 mmol) and acetyl chloride (2 mL). The reaction mixture was stirred at 26–28 °C for 8–12 h. The mixture was filtered to remove the catalyst and the filtrate was poured into ice-cold water

and stirred for 20 min. The precipitated solid was filtered, dried, washed with petroleum ether 60–80 °C to remove any residual starting material and dried. The products were characterised by their physical constants and spectral data.

11. Materials: the zeolite Hβ (Si/Al = 15), was supplied by Sud-Chemie India Ltd. ^{1}H NMR spectra were recorded using Varian 300 MHz spectrometer.
12. Representative spectral data: Compound **5c** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (m, 2H), 7.58–7.13 (m, 7H), 7.08 (d, J = 7.5 Hz, 1H), 5.83 (m, 1H), 3.79 (dd J = 16.8 and 6 Hz, 1H), 3.49 (dd, J = 16.8 and 5.4 Hz, 1H), 2.03 (s, 3H). FT-IR (KBr) ν_{max} 3290, 3065, 2362, 1688, 1546, 1367, 1202, 758, 685 cm^{-1}. Compound **5j** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29–7.24 (m, 2H), 7.03–6.97 (m, 2H), 6.94 (br s, 1H), 5.71 (dd, J = 8.7 and 5.4 Hz, 1H), 4.06 (d, J = 6 Hz, 1H), 3.72 (s, 3H), 2.16 (s, 3H), 2.01 (s, 3H). FT-IR (KBr) ν_{max} 3284, 1746, 1720, 1657, 1512 cm^{-1}. Mp of compounds (°C): **5a** 190–191, **5b** 114–115, **5c** 134–136, **5d** 150–152, **5e** 109–111, **5f** 128–130.