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Research Article

GREEN SYNTHESIS OF BETA ACETAMIDO KETONES

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ABSTRACT

The multicomponent condensation of an aryl aldehyde, acetyl chloride, acetonitrile, and enolizable ketone as one-pot synthesis of β-acetamido ketones in high yields was investigated using commercial, non-corrosive, and environmentally benign Keggin and Wells-Dawson heteropolyacid catalysts. The best catalyst was H 5PW10 V 2O 40. The methodology used simple experimental conditions, and the short reaction times and high yields indicate it is a useful strategy for the large scale synthesis of β-acetamido ketones.

Keywords: Homogeneous Catalysis, Heteropolyacid, Keggin, Wells-Dawson, Dakin-West, B-Acetamido Ketones.

INTRODUCTION

Multi-component reactions (MCRs) have emerged as one of the most useful synthetic transformations in organic synthesis because of their wide applications in pharmaceutical chemistry for production of structural scaffolds and combinatorial libraries for drug discovery. They are preferred over other reactions as it provides useful products in a single step by the creation of several new bonds without isolation of any intermediate and thus reduces time and saves both energy and raw materials[1]. β-Acetamido carbonyl compounds are valuable intermediates for a large number of pharmaceutically[2] important compounds examples being for the preparation of 1,3-aminoalcohols[3,4] antibiotic nikkomycin or neopolyoximes[5,6]. Through multicomponent reactions used catalysts such as $CoCl_2$[7] montmorillonite K10 clay[8] $BiCl_3$[9], silica sulfuric acid[10], transition metal and main group tri-flates, BF_3, $CuCl_2$ $BiCl_3$ $LaCl_3$, $LiClO_4$, $InCl_3$[11-19] heteropolyacids[20], and solid acid Hβ-zeolite[21]. Although these methods are valuable, most of them suffer from one or more of the disadvantages of employing expensive catalysts, high temperature, long reaction times or harsh reaction conditions, and tedious work up. Although, a large number of methods are reported for this transformation, some of them lack the generality in producing β-amido ketones as they are restricted to acetonitrile giving the corresponding β-acetamido ketones 9-16. Furthermore, many of these methods require either a long reaction time or harsh reaction conditions or the reaction has to be carried out under an inert atmosphere or the use of expensive catalyst. Therefore, the development of simple, efficient and general methodology for this three-component reaction is still desirable.

MATERIALS AND METHODS

General procedure for synthesis of β-acetamido ketones
A mixture of aromatic aldehyde (1 mmol), acetophenone (1 mmol), and acetyl chloride (2 mmol) in acetonitrile (4 ml) was treated with a catalytic amount of the desired heteropolyacid at 80 ^{0}C. The progress of the reaction was monitored by TLC. The work up procedure of this reaction was very simple. After completion of the reaction, the mixture was filtered to separate the catalyst. The solid crude product was washed with petroleum ether and filtered. The pure product was obtained, if needed, by re-crystallization from an ethanol-water mixture. Silica gel 60 (70–230 mesh) was used for column chromatography. Infrared spectra were run on a 8700 Shimadzu Fourier transform spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE 200-MHz instrument using TMS as an internal reference. All products were identified by comparing their NMR and IR data with those reported in the literature.

RESULTS AND DISCUSSION

1) β-Acetamido-β-(phenyl)propiophenone
IR (KBr) νmax/cm-1: 3286, 1693, 1650; 1H NMR (300 MHz; CDCl3; Me4Si) δH 2.04 (s, 3H, CH3), 3.45 (dd, J = 6.0 and 16.9; Hz,1H, CH2), 3.77 (dd, J = 5.2 and 16.9 Hz, 1H, CH2), 5.58 (m, 1 H, methyne H), 6.90 (br, d, J= 6.3Hz, 1H, NH), 7.24-7.60 (m, 8H, Ar-H), 7.91 (d, J =7.5 Hz, 2H, Ar-H).

2) β-Acetamido-β-(4-methylphenyl)propiophenone

IR (KBr) νmax/cm-1: 3290,1675, 1645; ^{1}H NMR (300 MHz; CDCl3; Me4Si) δH 2.17 (s, 3H, CH3), 2.23 (s, 3H, CH3), 3.55(dd, J= 6.2 and 16.7 Hz, 1H, CH2), 3.82 (dd, J=5.1 and 16.7 Hz, 1H, CH2), 5.56 (m, 1H, methyneH), 7.05 (d, J=7.7 Hz, 2H, Ar-H), 7.28-7.58 (m, 5H, Ar-H), 7.88 (d, J=7.6 Hz, 2H, Ar-H),8.70(br, d, J = 7.5 Hz, 1H, NH).

3) β-Acetamido-β-(3-nitrophenyl)propiophenone

IR (KBr) νmax/cm-1: 3291, 1689, 1653; ^{1}H NMR (300 MHz; CDCl3; Me4Si) δH 2.11 (s, 3 H, CH3), 3.54 (dd, J= 5.5 and 17.6Hz, 1 H, CH2), 3.83 (dd, J=5.0 and 17.5 Hz, 1 H, CH2), 5.68 (m, 1H, methyne H), 7.18 (d, J=7.8Hz, 1H, NH), 7.45-7.53 (m, 3H, Ar-H), 7.61 (t, J=7.5 Hz, 1H, Ar-H), 7.74 (d, J=7.7 Hz, 1H, Ar-H), 7.91(d, J =8.2 Hz, 2H, Ar-H), 8.10(d, J =8.2 Hz, 1H, ArH), 8.24(s, 1H, Ar-H).

4) β-Acetamido-β-(4-nitrophenyl)propiophenone

IR (KBr) νmax/cm-1: 3291,1689, 1653; ^{1}H NMR (300 MHz; CDCl3; Me4Si) δH 2.01 (s, 3 H, CH3), 3.38 (dd, J= 5.6 and17.4Hz, 1 H, CH2), 3.85 (dd, J=7.1 and 17.4 Hz, 1 H, CH2), 5.60 (m, 1H, methyne H), 7.19-7.54(m,7H, Ar-H) 7.87 (d, J =7.7 Hz, 2H, Ar-H), 9.18 (br, 1H, NH).

Mechanism of reaction

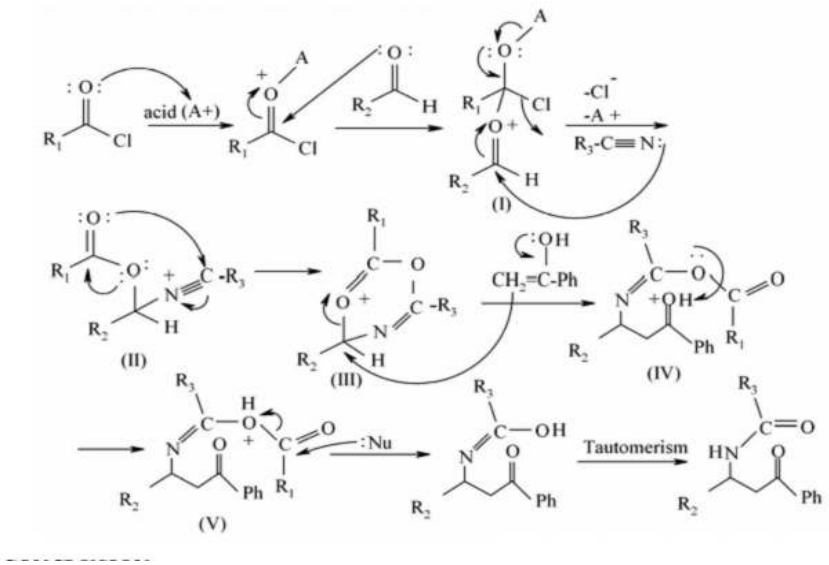

Table 1: Physicochemical data of synthesized compounds

Sr.No	Carbonyl compound	Aldehyde	Physical constant	Yield	Time
1	Acetophenonne	C6H5	20	86	291
2	Acetophenonne	2-ClC6H4	22	87	131
3	Acetophenonne	3- ClC6H4	23	89	233
4	Acetophenonne	4- MeOC6H4	22	88	224
5	Acetophenonne	2-NO2C6H4	24	89	256
6	Acetophenonne	3- NO 2C6H4	25	87	307
7	Acetophenonne	4-NO2C6H4	23	88	314
8	Acetophenonne	4-MeC6H5	22	89	266
9	Acetophenonne	4-Me2NC6H4	23	90	238
10	Acetophenonne	2-Furanyl	24	91	283
11	Acetophenonne	3,4-OCH 2OC6H3	25	92	247

CONCLUSION

In conclusion, Cu4)2.nH2O has demonstrated to be a mild and efficient catalyst for the three-component coupling of aldehydes, enolizable ketones or β-ketoesters and nitriles to produce β-amido ketones and ketoesters. The yields are generally high to quantitative, though moderate selectivity. This method is useful especially to the preparation of β-amido ketones from benzonitrile, benzyl cyanide and acrylonitrile under extremely mild conditions.

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