American Journal of Advanced Drug Delivery

www.ajadd.co.uk

Original Article

Eco-friendly Synthesis of 3-Chloro -4-(3-Nitrophenyl)-1-Phenyl-azetidin-2-One

Ruhi A. Khan*

Department of chemistry, Government Vidarbha Institute of Science and Humanities, Amravati (M.S) Pin-444604, India

Date of Receipt- 10/9/2014
Date of Revision- 17/9/2014
Date of Acceptance- 24/9/2014

Address for Correspondence

Department of chemistry, Government Vidarbha Institute of Science and Humanities, Amravati (M.S) PIN-444604, India

E-mail: ruhikhan.88.an@gmail.com

ABSTRACT

Recently in this laboratory a new route for the synthesis of azitidinones (6a-g) was developed by eco-friendly reactions to increase the yield of products by maintaining the purity of them. As well as the use of chloroacetyl chloride is a pungent, suffocating odor so, the Eco- friendly method for the synthesis of azetidinone was established. By considering this a novel synthesis of 3-chloro-4-3-nitrophenyl)-1-phenyl-azetidin-2-one (6a-g) were successfully carried out by interacting, N-[(E)-3-nitrophenyl) methylidene] aniline Schiff bases [3a] with triethylamine [4] and chloroacetyl chloride [5] in dioxane medium without any type of refluxion for the synthesis of the azetidinone.

The justification and identification of the structure of these newly synthesized compounds had been established on the basis of chemical characteristics, elemental analysis and through spectral data.

Keywords: Eco-friendly synthesis, Azetidinones, Ethanol.

INTRODUCTION

2-azetidinones, commonly known as β-lactams, are well-known heterocyclic compounds. 2-azetidinone is a β-lactam cyclic amide with four atoms in a ring. One of the fundamental milestones in medicinal chemistry is represented by the knowledge acquired during the studies carried out on a simple four-member ring, β-lactam[1-5]. A large number of 3-chloromonocylic β-lactam possess powerful anti-bacterial, anti-inflammatory, anti-fungal, analgesic, anti-convulscant and herbicidal activities[6].

The β-lactams also serve as synthons for many biologically important classes of organic compounds. Due to this, the investigation of chemistry and biology of these compounds continues to appeal the synthetic and medicinal organic chemists[7].

The present work is undertaken to explore more possibilities of finding a suitable derivative, which would exceed its activity more than the already known drugs containing β-lactam ring. Traditionally β-lactam is a part of structure of the broad

spectrum antibiotic class of drugs viz. penicillin and cephalosporin.

The β-lactam ring is the main feature of the most of the penicillins and another antibiotics[8-10]. The β-lactam ring shows various biological activities such as anti-fungal, anti-bacterial, anti-tubercular, anti-convulsant, analgesic, anti-inflammatory, synthetic precursor for amino acids, anti-viral, CNS, cholesterol absorption, etc[11,12].

The β-lactams nucleus is the key to the biological activity of a large class of compounds characterized by the presence of this four-member ring and differentiated by side chains, instauration, hetero atoms, and in many cases, by the presence of five or six-member rings[13-15]. The successful application of β-lactam antibiotics in the treatment of infectious diseases has been well documented for many years[16-18].

Azetidinones are of great biological interest, especially as anti-tubercular and anti-bacterial. Apart from this these possesses good anti-hypertensive activity[19,20].

Experimental

The melting points of all the synthesized compounds were recorded using hot paraffin bath. The carbon and hydrogen analysis were carried out on Carlo-Ebra 1106 analyzer[21]. Nitrogen estimation was carried out on Colman-N-analyzer-29. IR spectra were recorded on Perkin Elmer Spectrometer in the range 4000-400 cm^{-1} in KBr pellets. PMR spectra were recorded on Brucker Ac 400 F Spectrometer with TMS as internal standard using $CDCI_3$ and DMSO-d6 as a solvent[22,23]. The purity of compounds was checked on silica Gel-G Pellets by TLC with Layer thickness of 0.3 mm. All chemicals used were of AR-grade.

Synthesis of 3-chloro -4-(3-nitrophenyl)-1-phenyl–azetidin-2-one. [6a]

In 100ml beaker [3a], triethylamine [4] and chloroacetyl chloride [5] was taken in dioxane medium.The reaction mixture was stirred for 1 hrs by maintaining temperature 0-5^{0}C. After stirring the reaction mixture was stored for 24 hours at room temperature.It was pouring in water and stirred for 10 min the violet color crystal were filtered and dried. Yield 87%, M.P: 48^{0}C.

Properties

It gave a positive test for nitrogen. It is soluble in ethanol, methanol, benzene, acetone, chloroform and dioxane.

Elemental analysis

Carbon [(found 49.62%) calculated 59.68%], Hydrogen [(found 2.34%) calculated [03.65%]. Nitrogen [(found 8.30%) calculated 09.30%]. IR.

Spectrum

The IR spectrum was carried out in KBr pellets and The important absorption can be correlated as (cm^{-1}):- 3435.6cm^{-1} (Ar-NO_2 stretching),3043 cm^{-1} (Ar-N stretching), 3043cm^{-1}, 3038cm^{-1} (Ar-H stretching), 2968 cm^{-1} (Ar-CH stretching) 1693cm^{-1} (>C=O stretching), 1382cm^{-1} (-C-N-C stretching), 1319cm^{-1} (C-H stretching) 755cm^{-1}C-Cland DMSO-d_6. This spectrum distinctly displayed the signals due to the AR-NO2 proton at δ-8.218-8.7128ppm. The signal at δ-7.1095-7.7845ppm is due to Ar-N Protons, the signal at δ- 4.1212-4.8769 ppm is due to AR-CH protons and the signal at δ- 4.0967-4.1972ppm is due C=O proton, the signal at δ-3.1212-3.8769ppm is due to -C-N-C protons. The signal at δ -2.42ppm is due to CH protons attached to chlorine.

Similarly, Eco-friendly synthesis of 3-chloro -4 - (4methoxyphenyl) - 1- (3-nitro-phenyl) azetidin-2-one [6b], synthesis of 3-

chloro-1-(naphthalene-1-yl)-4-phenylazetidin-2-one [6c]. Synthesis of 3-chloro-4-[4-methoxyphenyl] -1-(3-methoxy-phenyl) azetidin-2-one [6d], synthesis of 3-chloro -1-[4-hydroxyphenyl]-4-(3-nitro-phenyl) azetidin-2-one [6e]. were synthesized by interaction of N-[(E)-(4-methoxy phenyl)methylidene] -3-nitro aniline Schiff Bases [3b], N-[(E)-phenyl methylidene] napthalene-1-amine Schiff bases [3c], N-(E)-(4-methoxyphenyl methylidene] -4-methyl aniline schiff bases [3d]., 4-{(E)-(3-nitrophenyl methylidene] amino} phenol Schiff Bases [3e], with triethylamine [4] and chloroacetyl chloride [5] was taken in dioxane medium respectively by the above mentioned method **Scheme -1.**

The result obtained are given in **Table No. 1.**

RESULTS AND DISCUSSION

The results are given in **Table No. 2.**

*Known literature medium. But as per literature survey the reaction mixture was must be reflux for minimum 4 hours in ethanol medium, but in our synthesis we did not use any type of refluxion or heating device during synthesis of 6a to 6g.

The Eco- friendly synthesis of various azetidin-2-one found to be a significant improvement over existing procedures and thus helps in the synthesis of variety of azetidin-2-one compounds.

Also, this simple technique of synthesis of azetidin-2-one required less time as well as good yields of product. These procedures also help in maintaining the green chemistry parameters. The yield for the synthesis of different azetidin-2-one compounds were found to be in the range of 80-90%. The characterization of these synthesized compounds was done on the basis of melting point and elemental analysis of compounds as well as spectral data.

CONCLUSION

This reaction was studied in various solvents for improving the yield and purity of the products as well as to maintain green chemistry parameters.

ACKNOWLEDGMENT

Authors are thankful to the Director, Mr. Avatar Singh and Mr. Manish Kumar of SAIF Punjab University Chandigarh for elemental and spectral analysis.

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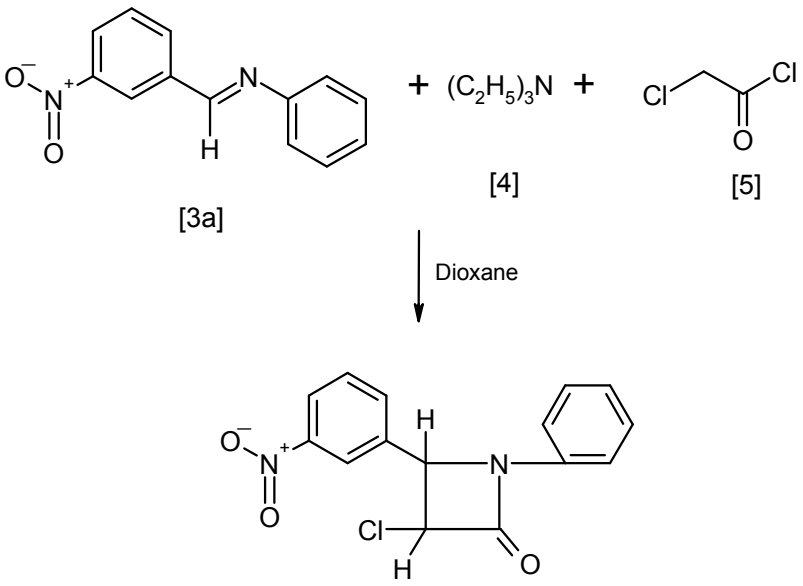
Table 1.

S. No.	Compound No.	Colour	Yield (%)	M.P. (^{0}C)
1.	6a	Yellow	92%	105^{0}c
2.	6b	Light brown	87%	235^{0}c
3.	6c	Dark brown crystal	87%	150^{0}c
4.	6d	Dark brown	87%	160^{0}c
5.	6e	Light brown crystal	87%	200^{0}c
6.	6f	Brown crystal	87%	130^{0}c
7.	6g	Light purple	87%	100^{0}c

Table 2.

S. No.	Solvent used	Quantity (ml)	Time spam (hours)	Yield (%)	Melting point (^{0}C)
1	Water	100	No reaction	--	--
2	Acetone	100	72	42	105
3	Ethanol*	20	48	92	105
4	Methanol	50	72	57	105
5	Isopropanol	50	72	35	105
6	Benzene	50	72	25	105
7	dioxane	50	72	20	105



3-Chloro-4-(3-nitrophenyl)-1-phenyl-azetidin-2-one

Scheme 1.