SYNTHESIS AND CHARACTERISATION 3-CHLORO-SUBSTITUTED AZETIDIN-2-ONE

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Abstract

It was thought interesting to synthesized 3-chloro-substituted azetidin-2-one. A simple and efficient procedure for the synthesis of 3-chloro substituted azetidin-2-one.In this work some new substituted azetidin-2-one have been reported from Schiff base. The Schiff bases in turn were obtained from substituted aldehyde and substituted aniline in presence of H_2SO_4. The five variedly substituted compounds were prepared by this method. 3-chloro-substituted azetidin-2-one nucleus play a vital role as Antimicrobial, Antibacterial, Anticancer, Anti-inflammatory activity. The characterization of this compound was made by chemical property, elemental analysis, as well as spectral analysis (like IR, H^1-NMR)

Keywords: Substituted aldehyde, substituted aniline, Schiff base, 3-chloro-substituted azetidin-2-one.

Introduction

The heterocyclics compounds have great importance in medicinal chemistry. One of the most important heterocycle is β-Lactum. β-Lactumclass of compounds has served as an important and highly successful role in the pharmaceutical chemistry. 2-azetidinone, commonly known as β-Lactum. Miracle drugs such as penicillin's and cephalosporins have significantly improved the human health and life expectancy. Developments in the field of β-Lactums during the last decades have shown that the only essential feature for the antimicrobial activity in these compounds is the presence of β-Lactum ring. Much attention was therefore focussed on this four membered cyclic amide and also the various substituents attached directly to this system. The 2-azetidinone have also been recognised as TACE inhibitor[7] and agent with new biological activity such as anticancer[8], anticoccocidal[9], cardiovascular[10], antiviral[11], and anti-inflammatory[12].

The biological importance of the above heterocycles led us to introduce 2-azetidinone ring with aim to increase their biological activity.

Materials and Methods:-

Substituted aldehyde, substituted aniline, Triethylamine, Chloroacetylchloride, Dioxane are required chemicals purchased from s-d fine chemicals. All the used chemicals were A.R grade, melting point were measured in open capillary tube and are uncorrected. The purity of the compounds was check by TLC on silica gel in petroleum ether and ethyl acetate [80:20] and the spots were located under iodine vapours as visualised agent. The IR spectra were recorded on Agilent technology. H^1-NMR was recorded on Bruker AVANCE 400 MHZ spectrometer using TMS as an internal standard.

Experimental Methods:-

In this work, several variedly substituted Schiff base were prepared by condensation of the substituted aldehyde and substituted aniline in ethanol in presence of H_2SO_4. Schiff base thus obtained were further condensed with chloroacetylcloride and Triethylamine in dioxane to afford the formation of 3-chloro-substituted azetidin-2-one.

Scheme-I

Synthesis of N-[(E)-furan-2-ylmethylidene]-3-nitroaniline:

Furfural and 3-nitroaniline were taken in equimolar (0.02mol) proportion and dissolved in ethanol. To this solution added 2-3 drops of H_2SO_4. The reaction mixture was refluxed for four hour. Solid mass obtained was filtered and

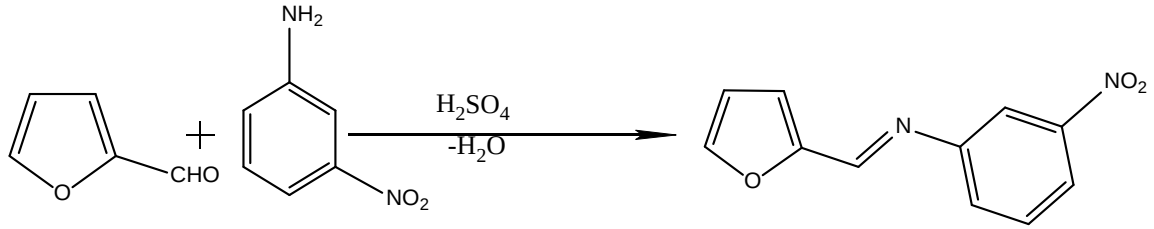
recrystalised from ethanol.Yield ofcompound64%,Melting point- 136^{0}C.

Molecular formula: $C_{11}H_8N_2O_3$
IR : 3250 cm-1 (Ar,C-H str); 1452cm-1 (Ar, C=C str); 1521cm-1(C=N str); 1148 cm-1(C-O str) ; 1340-1451 cm-1 (-NO_2 asystr).
1H-NMR (DMSO) : 7.80 (s, 1H, Ar-H); 7.66(dd, 1H, Ar-H); 7.32(dd, 2H, Ar-H); 8.50(s, 1H, CH); 7.84(d, 1H, CH); 6.8(dd, 1H, CH) ; 6.93(d, 1H, CH)

Scheme-II
Synthesis of 3-chloro-4-(furan-2-yl)-1-(3-nitrophenyl)azetidin-2-one.
N-[(E)-furan-2-ylmethylidene]-3-nitroaniline and Triethylamine were taken in equimolar (0.02mol) proportion and dissolved in 1,4-dioxane. Maintained the temperature of the solution up to 5 to 10 □C, chloro (0.002mol) was added drop wise within a 20 minutes. The reaction mixture was then stirred for 3 hours then poured into ice cold water. The product was purified by column chromatography over silica gel coated plates by using ethyl acetate. Recrystallized the product from ethanol.Yield of compound is 77 %, Melting point 154^{0}C

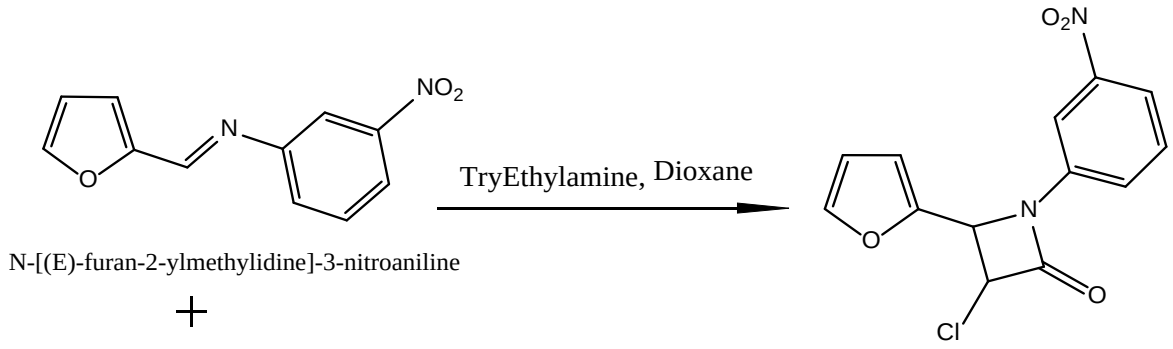
Molecular formula: $C_{11}H_8N_2O_3$
IR : 3277 cm-1 (Ar, C-H str); 1521cm-1 (Ar, C=C str); 599.86 cm-1 (C – Clstr) ; 1754cm-1(C=O str); 1244.09cm-1 (C-N str); 1186.68 cm-1(C-O str) ; 1344-1411 cm-1 (O=Nasystr).
1H-NMR (DMSO): 8.11 (s, 1H, Ar-H); 7.62(dd, 1H, Ar-H); 8.14(d, 1H, Ar-H); 5.44(d, 1H, CH); 7.56(d, 1H, CH); 6.39(dd, 1H, CH) ; 6.43(d, 1H, CH); 5.39(d, 1H, CH)

REACTION



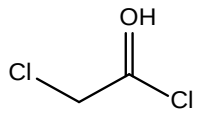
N-[(E)-furan-2-ylmethylidine]-3-nitroaniline

SCHEME 1 : Synthesis of schiff base



N-[(E)-furan-2-ylmethylidine]-3-nitroaniline

3-chloro-4-(furan-2-yl)-1-(3-nitrophenyl)azetidin-2-one



chloroacetyl chloride

SCHEME -II: Synthesis of 3-Chloro-substituted azetidin-2-one

RESULTS AND DISCUSSION

We synthesized here unreported 3-chloro-substituted azetidin-2-one by the condensation of Schiff base, triethylamine and chloroacetylchloride. Schiff base was obtained by the condensation of substituted aldehyde and substituted aniline inpresence of H_2SO_4. The target compounds are given in the following table.

Table: The list of synthesized compounds, their % yield and melting points.

Sr. No.	Compounds	Percent Yield (%)	Melting point(□C
1	3-chloro-4-(furan-2-yl)-1-(3-nitrophenyl)azetidin-2-one	77%	154 □C
2	3-chloro-1-(4-nitrophenyl)-4-phenylazetidin-2-one	66%	148 □C
3	3-chloro-4-(furan-2-yl)-1-(4-nitrophenyl)azetidin-2-one	60%	152 □C
4	3-chloro-4-(4-methoxyphenyl)-1-(4-methylphenyl)azetidin-2-one	70%	138 □C
5	3-chloro-4-(4-methoxyphenyl)-1-(4-nitrophenyl)azetidin-2-one	62%	136 □C

CONCLUSION

Thus it was possible for us to reduce reflux time and increase percent yield of new synthesized products. The use of triethylamine as a base afford rapid synthetic route to azetidin-2-one and also easy workup of the products. These newly synthesized compounds contain many bioactive substituents and therefore should be screened for their antibacterial activity.

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