IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 2, April 2023
Impact Factor: 7.301

Synthesis and Characterization of a Novel Azetidine Derivative

Garima Varule[1], Rekha Birle[2], Kavita Sahukare[3], Nandu Kayande[4]
Thakur Shivkumar Singh Memorial Pharmacy College, Burhanpur, MP, India

Abstract: *Azetidine represent one of the most important four membered heterocycles used in organic synthesis and medicinal chemistry .The reactivity of azetidines is more stable than that of related aziridines .Azetidine are useful substrates in organic chemistry for the design and preparation of biologically active compounds .New series of 3 phenyl 1-(2 phenyl -H, 1-3,benzodiazole -yl) amino azetidine -2one derivative were synthesized by the reaction ofSchiff base with 2 chloro acetyl chloride. Synthesized compounds were evaluated for their physical properties including Solubility, Melting point, RF value of derivative and % yield of product. Which highlights recent improvement and the discovery of new reaction and derivative that have overcome some longstanding challenges with in this field of research.*

Keywords: Alzheimer's disease; analgesic activity; anticancer activity; azaPaternò-Büchi reaction; Azetidine; dopamine receptors; fungicidal activity; pharmacological activities; recent development; ring strain

I. INTRODUCTION

The four membered heterocyclic ring compound are heterocyclic analogues of Cyclobutane N, O, S containing heterocyclic are known as Azetidine, Oxetane. These are relatively less strained then the three membered heterocyclic rings[1], but are most difficult to prepare by different intermolecular cyclization procedure. This difficulty, in part arise due to the change in the position of the atoms undergoing reactions. As the result direct cyclization occur only if the atoms combining are present in some appropriate orientation. The preference for ring closure,[2] understandably is because of their presence in close proximity. But as the chain length increase so does the total number of confirmations which do not allow easy ring closure.[3] 2.1 Azetines and AzetidinesAzacyclobutadiene is known formally as Azete and is the isomeric structure as azetine. Azetidine is the name given to the completely saturated 4 membered nitrogen containing compound, it is also design as Trimethylamines. Azete is anti aromatic and unstable. [4]The benzazetes such as phenylbenzaete are more stable and have been prepared. Not very many compounds are known to occur in nature which contains the Azetidine ring structure. synthetic Azetidine derivative has also not yet any useful results for pharmacological evaluation.[5] However L Azetidine 2 carboxylic acid naturally occurring antimetabolite of proline has been isolated from Liliaceae .Its 3 isomer has been prepared in laboratory[6]

Compounds with the Azetidine moiety display an important and diverse range of pharmacological activities, such as anticancer, antibacterial, antimicrobial, antischizophrenic, antimalarial, antiobesity,[7] anti-inflammatory,[8]antidiabetic, antiviral, antioxidant, analgesic, and dopamine antagonist activities, and are also useful for the treatment of central nervous system disorders and so forth. Owing to its satisfactory stability, molecular rigidity, and chemical and biological properties, Azetidine has emerged as a valuable scaffold and it has drawn the attention of medicinal The present review sheds light on the traditional method of synthesis of Azetidine and advancements in synthetic methodology over the past few years, along with its application with various examples, and its biological significance.(9)

II. MATERIAL AND METHOD

Method 1-. Synthesis of 2 phenyl 1-H, 1-3 benzodiazole

Take a round bottom flask and add O phenyldiamine10.8gm(0.1mole) was refluxed with 10ml of (0.1mole) benzaldehyde in the presence of 4N HCl (37.18)ml , and add 10ml of ethanol. Solution was refluxed for 4-5 hour at temperature 80 to 120°c , rpm 320. Obtained mixture was cooled in ice bath allowed to stand for 5min to obtain

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 2, April 2023
Impact Factor: 7.301

precipitate. The product was filtered, dried and recrystallized from ethanol. The completion of the reaction was tested solubility, melting point, TLC (Acetone :Acetic acid, 7:3) , percentage yield.

Method 2. Synthesis of 1Hydrazinyl 2phenyl 1H 1-3 benzodiazole

Take a round bottom flask and add.Obtained product (9.71) gm .. Now it is reacted with hydrazine hydrate 0.05M (2.5gm) In the presence of ethanol was refluxed for 4hour at temperature 80- 120°c . The mixture was carried out in beaker on the megnetic stirrer for 2hour .4.The mixture was cooled in ice bath allowed to stand for 5min to obtain precipitate..The product was filtered , dried and recrystallization was done with ethanol, water or, chloroform. The product is tested by solubility, TLC ,melting point percentage yield of product

Method 3. Synthesis of N (2 phenyl 1-H , 1-3 benzodiazole -yl) benzamide

Take a round bottom flask and add 2 nd intermediate product is reacted with benzaldehyde in the presence of H2SO4 and ethanol in reflux for 4hour at temperature 90°c . Solvent were partially evaporated then poured into water. The precipitates were collected by filtration, washed with ether, dried and compound were recrystallized from ethanol..The obtain product were tested solubility, melting point, TLC and percentage yield of product.

Method 4. Synthesis of 3 phenyl 1-(2phenyl -H, 1-3 benzodiazole-yl) amino azetidine -2one .

Take a round bottom flask and add 3 rd intermediate compound is reacted with triethylamine in dioxan and mixture was stirred for 2 h. During stirring chloroacetyl chloride in dioxan was added dropwise.. The mixture was refluxed for 2 hour and kept for 24 hour on room temperature. The resulting mixture was poured in the water and filtered it to solid was separated out. Recrystallization was done with ethanol and chloroform to give the azetidine – 2one .

III. RESULT

C13H10N2 194.24 Acetone Acetic acid Reddish brown 293.0°c 0.93 71.42% 2. 1Hydrazinyl 2phenyl 1-H , 1-3 benzodiazole C13H`12N4 224.27 Acetone Acetic acid Methanol Dark brown 228°c 0.80 80.50% 3. N(2phenyl 1- H 1-3benzodiazole yl) benzamide C20H15ON3 313.36 Methanol Acetic acid Brownish orange 190- 192°c 0.5 53.3% 4. 3phenyl 1(2phenyl 1- H, 1-3 benzodiazoleyl) amino

S. N.	Compound name	Mol. Formula	Mol. WT	Solubility	Colour	M.P.	RF value	% yield
1	2phenyl 1-H, 1-3 benzodiazole	$C^{13}H^{10}N$	194.24	Acetone	Reddish broun	293	0.93	71.42%
2	1Hydrazinyl 2phenyl 1-H, 1-3 benzodiazole	$C^{13}H^{12}N^{4}$	224.27	Acetone acetic acid	Dark broun	228	0.80	80.50%
3	N(2phenyl 1- H 1-3benzodiazole yl) benzamide	$C^{20}H^{15}ON^{13}$	313.36	methanol	Brownish orange	190-192	0.5	53%
4	3phenyl 1(2phenyl 1- H, 1-3 benzodiazoleyl) amino azetidine-2 one	$C^{22}H^{15}ON^{3}$	354.41	Water	Brick brown	160	0.3	40.7%

IV. SUMMARY AND CONCLUSION

Synthesis of 3-phenyl -1 (2-phenyl -1H-1,3-benzodiazole-1-yl) amino azetidine-2-one derivative it is a final compound (d) which included four step scheme . Firstly the o- phenyldiamine was reacted with benzaldehyde in the presence of ethanol to form derivative (A) 2phenyl 1-H-1,3 benzodiazole .Now the second step first product is treated with hydrazine hydrate in the presence of ethanol to form derivative (B) 1Hydrazinyl -2 phenyl -1H-1,3 benzodiazole . Now

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 3, Issue 2, April 2023
Impact Factor: 7.301

the third step derivative (B) is also treated with benzaldehyde and in the presence of H2SO4 to form derivative (C) N(2-phenyl-H-1,3-benzodiazole-1-yl) benzamide. Obtained product also treated with triethylaminne and dioxane in the presence chloroacetyl chloride. Final product was obtained .All the synthesized compound were tested for their physical properties. Molecular formula , Molecular weight , Solubility of compound , colour of product ,Melting point of compound , RF value by the TLC, and final percentage(%) yield are calculated .

REFERENCES

[1]. Thomas Williams David A Foyes Principal of medicinal chemistry seventh edition published by wolterskluwer (India) private limited, New Delhi. Page no.1-5

[2]. Bansal R. K. Text book of heterocyclic chemistry fifth edition (2014) Published by new age international private limited publishers page no 15-30.\

[3]. Dr Jain Rashmi, Dr SahayAlok.Text book of Heterocyclic compound Published by pragatiprakashan edition (2016)page no 112-118..

[4]. S Brian Furniss, Hannaford J. Antony Text book of Practical Organic chemistry fifth edition Published by Pearson Publication (2018)page no 400-430.

[5]. Morrison Robert Thornton. Text book of organic chemistry 6th edition Published by Pearson's education in South Asia page no 145-160.

[6]. Dr. Kadam S. S. Dr.Mahadik K. R Volume -1Principles of medicinal chemistry eighteenth edition 2007 Published by NiraliPrakashan. Page no 180-190 .

[7]. Gupta L. Alka, Text book of Medicinal chemistry seventh edition 2016 Published by K. K Mittal for PragatiPrakashan.page no 304-335

[8]. Dr SiddiquiAnees Ahmad, Dr. R. Rajesh A Text book of medicinal chemistry volume 2 second edition 2010-2011 Published by Birla Publications Private limited 1/9185, Stret N. 5 Rohlas Nagar page no 600-615.

[9]. Jacob , Clement BaguiaHajar, 28 January (2022). A general synthesis of Azetidine by copper, catalyst Photoinduced antibacterial radical cyclization of ynamides 120-142.

[10]. Patel Rakesh, and Bhandari Anil, American Journal of Advanced Drug delivery, September 26-27, (2022). Synthesis and Antimicrobial Screening of Some Azetidine Derivatives 45-66

[11]. Han Yang, Zhen Chen (2022), Synthesis of 2-aryl Azetidines through Pd catalysed migration/coupling of 3-iodoazetidine and aryl boronic acid page no 76-85.,

[12]. Mughal Hasseb and Szostak Michal, issue -15, (2021), Recent Advance in the synthesis and reactivity of azetidine strain -driven character of the four membered Heterocycles page no 113 page no 145-155