Oriental Journal of Chemistry Vol. **26**(2), 743-746 (2010)

Synthesis of 1-(substituted phenyl)-4-(4-N,N-dimethyl amino phenyl)-azetidine-2-ones and its antimicrobial activity

TUSHAR W. THAKARE*, A.S. RATHOD[1], A.G. DOSHI and A.W. RAUT

P.G.Department of Chemistry, Shri Shivaji Science College,
Morshi Road, Amravati - 444 603 (India).
[1]Vidya Bharati Mahavidyalaya, Amaravati, Rural Institute, Amaravati (India).

(Received: April 12, 2010; Accepted: June 04, 2010)

ABSTRACT

Azomethine condenses with acetyl chloride in presence of triethyl amine in benzene gives 1-(substituted phenyl)-4-(4"N,N-dimethyl amino phenyl)-azetidine-2-ones, The azotidinones structure were confirmed by spectral and chemical data. These azetidinones were studied for their antimicrobial activity using cup plate diffusion method. The bacterial organism used included Bacillus Megatherium, Proteus valgaris, Bacillus subtilis and Escherichia coli. These compound were found effective against both Gram positive and Gram negative bacteria.

Key words: Synthesis, Antimicrobial activity, Azitidine-2-ones.

INTRODUCTION

Azetidine-2-ones have been known to exhibit interesting biological activities like anti-inflammatory, sedative hypotonic and anticovalant Azetidine-2-ones posses antimicrobial activity[2] and found to be potential antimicrobial agent[3]. Azetidinones have also known wide range of pharmaceutical activities[4-6]. Azetidine-2-ones and its corresponding derivative have been synthesized by a number of workers[7-9]. The powerful antibiotic activity shown by monocyclic â-lactum of Azetidine -2-ones [10-11].

2-Thiophenylidine substituted aniline were prepared by known method[12]. We reported synthesis of N-substituted phenyl-4-thiophenyl-2-azetidionones and its antimicrobial activity[13]. Azetidinones and thiazolidine-4-ones shows antimicrobial activity[14-15], as potential antitubercular agent[16], antimicrobial antitubercular agent[17], antimicrobial activity HMQC study and HMBC study[18], 2-Azetidinones derivative as antimicrobial[19].

In present communication we are reporting the synthesis of 1- (substituted phenyl)-4-(4"- N, N-dimethyl) amino phenyl) Azetidine-2-ones and its Antimicrobial activity.

EXPERIMENTAL

Preparation of 1-(4-chloro phenyl)-4-(4"-N, N-dimethyl) amino phenyl) azetidine – 2 – ones (A_1)

A mixture of N-(4-chloro pheny)-4 -(N, N – dimethyl) amino) phenyl azomethine (T_1) (0.01 M, 2.58g) and acetyl chloride (0.01 M, 1ml) was taken in 20 ml benzene in presence of 2ml trimethyl amine. The maxture was refluxed for 6 hours. It was then cooled, sticky mass was obtainedk, when the solvent was evaporated on hot water bath. The product was triturated with petroleum ether and crystallized from 40 % ethanol to yield 1 – (4 – chloro phenyl) – 4 - (4"- N, N – dimethyl) amino phenyl) azetidine – 2 – ones (A_1), m.pt. 140 ^{o}C, yield 70%

Properties of (A_1)

- It is brownish coloured crystalline compound m.p. 140°C.
- Analytical data shows molecular formaula C_{17} H_{17} N_2 OCL having molecular weitht 300.5
- UV – VIS –us – vis are recorded in methanol solvent. The ëmax values 326 nm and 240 nm corresponding to n-π-π* and π-π* transition azetidinones.
- IR – The IR spectrum was recorded in Nujol
  C – H str in CH_3 - 2921 cm^{-1}.
  C – H str in CH_2 - 2800 cm^{-1}.

Aromatic

C – H str - 3068 cm^{-1}.
C = C str - 1487 cm^{-1}.
C – N str - 1165 cm^{-1}.

Azetidinone

C = O str - 1704 cm^{-1}.
C – Cl str - 748 cm^{-1}.

PMR – The PMR spectrum was recorded in $CDCl_3$.
3.05δ(S 6H N-$(CH_3)_2$)
2.15δ(d 2H CH_2-CO
2.9 δ(d,d 1H C-CH-N)
6.60 – 7.75 (m 8H Ar-H)

From the above chemical and spectral data it follows that compound 1-(4-chlor phenyl)– 4-(4"-N,N – dimethyl) amino phenyl) azetidine-2-ones(A_1),

Antimicrobial activities

All the synthesized compounds were studied for their antibacterial activity using cup-plate diffusion method[20].The bacterial organism used included both gram +ve and gram –ve strains such as *E. coli, B.subtilis, P.vulgaris and B.megatherium.*

Sensitivity plates were studied with their bacterial inoculum of 1 × 1^6 CIU/ml and each were diameter (100mm) was loaded with 0.1 of that compound solution (1000 ìg/ml) in DMF so that concertration was 100 ìg/ml. The zones of inhibition wre studied after incubation for 24 hours using vernier caliper.

Inhibition zone record of the compounds, clearly indicated that compound. No. A_3 were

Table 1 : Synthesis, m.pt. and yield of 2-azelidine (A_1)

Compound	Name of Compounds	M.Pt.	% Yield	Colour
A_1	1-(4-Chloro phenyl)-4-(4"-N,N-dimethyl amino phenyl) azetidine – 2 – one (A_1)	140°C	70	Golden Brown
A_2	1-(4'-Methoxy phenyl)-4-(4"-N,N-dimethyl amino phenyl) azetidine – 2 – one (A_2)	70°C	68	Mushroom
A_3	1-(4'-Nitro phenyl)-4-(4"-N,N-dimethyl amino phenyl) azetidine – 2 – one (A_3)	125°C	75	Black
A_4	1-(4'-Methyl phenyl)-4-(4"-N,N-dimethyl amino phenyl) azetidine – 2 – one (A_4)	64°C	74	Golden yellow
A_5	1-(3'-Methyl phenyl)-4-(4"-N,N-dimethyl amino phenyl) azetidine – 2 – one (A_5)	65°C	70	Deep Brown
A_6	1-(2'-Methyl phenyl)-4-(4"-N,N-dimethyl amino phenyl) azetidine – 2 – one (A_6)	55°C	70	Deep Orange
A_7	1-(1'-Naphthyl)-4-(4"-N,N-dimethyl amino phenyl) azetidine – 2 – one (A_7)	84°C	68	Yellow
A_8	1-(3-Nitro phenyl)-4-(4"-N,N-dimethyl amino phenyl) azetidine – 2 – one (A_8)	90°C	64	Mushroom
A_9	1- Phenyl-4-(4"-N,N-dimethyl amino phenyl) azetidine – 2 – one (A_9)	72°C	71	Sandstone
A_{10}	1-(2-Carboxy phenyl)-4-(4"-N,N-dimethyl amino phenyl) azetidine – 2 – one (A_{10})	88°C	62	Signal Red

Table 2 : Antimnicrobial activity of synthesized compounds (A_1-A_{10}) by cup plate method

Compound	Diameter of zones of inhibition in (mm)			
	Bacillus *magatherium*	**Bacillus *subtilis***	**Proteus *vulgaris***	**Escherichia *coli***
A_1	++	—	++	++
A_2	+	+	—	+
A_3	+++	—	++	+++
A_4	—	—	—	+
A_5	+	+	+	+
A_6	—	—	—	+
A_7	+	+	—	++
A_8	++	—	—	+++
A_9	+	+	—	—
A_{10}	+++	+++	+++	++

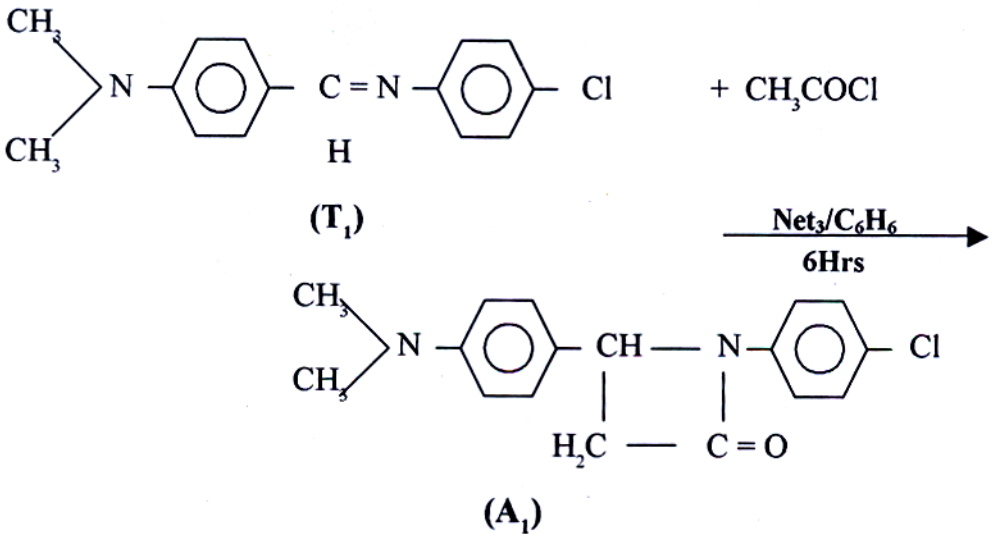
Control – DMF – No activity

(+++) : Highly active (21 – 30 mm) (++) : Moderately active (17 – 20 mm)

(+) : Weakly active (12 – 16 mm) (—) : Inactive (Less than 12 mm)

found to be highly active against *Bacillius magatherium* and *E. coli.* Compounds A_{10} is found highly active against Bacillius magatherim and *Bacillius subtilis,* A_3 and A_8 are found to be highly active against *E.coli.*

And majority of the compounds were found to moderately active and rest of the compounds are found to be resistant against the organisms given in the table 2.



Scheme 1.

REFERENCES

1. Tandon M, Kumar P, Tondon P, Bhalla T.N. and Bharathwal J.B. *Acta Pharm.Jugori* B, **93** (1963).
2. Rahatgaonkar A.M. *Asian J. Chem*. **11(3)**: 987-990(1990).
3. Shah M, Parikh K.and Parikh H, *Indian J.Chem*. **37**A: 73-77 (1998)
4. SendaiM,OchiarM.and Kishimoto,*Chem, PharmaBull*, **33**: 3798 (1985) *Chem, Abstr*. **105**: 152768f (1986).
5. Andrus A, *Heterocycles*, **22**: 1713 (1984), *Chem. Abstr*, **101**: 19145n (1984).
6. Ladva K, Dave U, Parikh H, *Indian Hetero. Chem*, **1:** 249 (1992)
7. Udapi R.H, Kasinath N. and Bhatt A.R. *Indian J. Heterocyclic. Chem*, 7: 221 (1998).
8. Udapi R.H, Jeeson M. and Bhatt A.R. *Indian J.Heterocyclic. Chem*, **6:** 99 (1990).
9. Berbeim P. *Science*, **92**: 204 (1940).
10. Durcheimer W, Blumbach J, Lattroll and Schenemann K.H, *Angew.Chem. Int. Ed*. **24**: 180 (1985).
11. Brown A.G. and Robert S.M. Recent advances in chemistry of â-lactum, antibiotics, The royal society of chemistry, Burlington House, London (1984).
12. Raut A.W.and Doshi A.G. *Orient J.Chem*, **1**: 93-94 (1996).
13. Md. Idress Md.Siddique *et al, Orient J,Chem*, **17**(1): 143-146(2001)
14. Suryawanshi J.D and Pai Nandini R.*Indian J.Chem*, **45B,**1227-1230(2006).
15. Vyas D.A, Chauhan N.A. and Parikh A.R *Indian J.Chem,* **46B:** 1699-1702(2007).
16. Naruti A.S.Khedekar P.B.and K.P.Bhusari. *Indian J.Chem.* **47**B: 586-591 (2008).
17. Patel R.B,Desai P.S.Desai K.R.and Chikhalia.*Indian J.Chem,***45B**: 773-778 (2006).
18. Singh G.S. and Pheko T.*Indian J.Chem*.**47B**: 159-162 (2008).
19. Jubie S, Gowramma, Muthal Nitin K.and *et al. International J.of Chem. Tech Researh*.**1(**2): 153-157 (2009).
20. Kavangh. F., Analytical Microbiology Academic Press, New York(1963).