International Journal of Chemical and Physical Sciences, ISSN:2319-6602
IJCPS Vol. 4 Special Issue – NCSC Jan-2015
www.ijcps.org

Synthesis and Characterization of Some 2-Azetidinones

S. S. THAKARE

P.G. Department of Chemistry, ShriShivaji Science College,Amravati-444603

Abstract

Synthesis of substituted 2-Azetidinones (4)have been synthesized by treatment of chloroacetyl chloridecontaining triethylamine with 4-chloro-N-(4-substituted benzylidene)-aniline (3) in 1,4-dioxane medium. The starting material 4-chloro-N-(4-substituted benzylidene)-aniline (3) were prepared by condensation of 4-chloroaniline(1) and different aromatic aldehyde (2)in ethanoic medium with H_2SO_4 in catalytic amount
The structure of newly synthesized compounds were established on the basis of their spectral data.

Introduction

2-Azetidinones, commonly known as β-lactams, are well-known heterocyclic compounds amongthe organic and medicinal chemists.[1] The activity of the famous antibiotics such as penicillins,cephalosporins and carbapenems are attributed to the presence of 2-azetidinone ring in them.Recently, some other types of biological activity besides the antibacterial activity have beenreported in compounds containing 2-azetidinone ring.[2,3] Such biological activities include

antifungal, antitubercular, antitumor, cholesterol absorption inhibition and enzyme inhibition

activity. The β-lactams also serve as synthons for many biologically important classes of organiccompounds.[4] Due to this, the investigation of chemistry and biology of these compoundscontinue to appeal the synthetic and medicinal organic chemists.[1-4]

The most common method for the synthesis of 2-azetidinones is the Staudinger keteneiminecycloaddition, which involves the reaction of imines with acid chloride in the presence of atertiary base.[5] This reaction, however, depends, on many factors including temperature, whichoften needs to be optimized.[6] We have been using α-diazoketones as precursors of diarylketenesandcarbenoids, and investigating the reactions of these intermediates with organic compoundscontaining nitrogen atom in different structural environments.[7] These reactions are simple tocarry out, versatile and don ot require the use of any acidic or basic reagent. Using 2-diazoketones as precursors of the diarylketenes, we have recently reported the synthesis of 2-azetidinones and spiro-2-azetidinones from the imines of the thiophene-2-carbaldehyde andindoline-2,3-dione, respectively, as possible antimicrobial agents.[8,9] The 2-azetidinones, obtainedfrom the imines of thiophene-2-carbaldehyde and diarylketenes, showed moderate antibacterialand antifungal activity.[8] The reactions of ketenes with ambident substrates, however, depend onthe structural environment of the particular functional group. For example, diphenylketeneaddson to the carbon-

nitrogen double bond of the benzilmonoimines and camphor monoiminesleaving the carbon-oxygen double bond on these compounds.[10,11] The reaction of diphenylketenewithisatin imines has been observed to occur at the amido nitrogen and not at imino nitrogen.[12]. The products, characterized on the basis of satisfactory analytical andspectraldata, have been screened for their antibacterial and antifungal activity.

Experimental

The melting points of all the products were determined in open capillary tubes and are uncorrected. IR spectra (cm^{-1}) were recorded using KBr on Shimadzu FT-IR 400 PC Spectrometer, ^1H NMR spectra ($CDCl_3$) were recorded on Brucker-Advance II-400 NMR Spectrometer using TMS as internal standard (chemical shift in δ ppm).

General procedure for the preparation of 4-Chloro-N-(4substitutedbenzylidene)-aniline(3a-e) :-

Reaction of 4 chloroaniline (1) and 4- methoxybenzaldehyde (2a):-

In the first step the 4-Chloro N-(4-methoxybenzylidene)-aniline (2a) prepared by the known method by the condensation of 4 chloroaniline (1) with 4- methoxybenzaldehyde(2a) Finally, the product are recrystallized from ethanol to give pure4-Chloro N-(4-benzylidene)-aniline (2a), yield 80-95 %, m.p.265-268 ^oc.

All other compounds (2b-e) were prepared in similar manner by the reaction of 4 chloroaniline with different 4- substituted aromatic aldehyde (1b-e) respectively Table No.1

Table No.1

Expt. No.	Product (3)	-R (3a-e)	Yield (%)	Melting Point^{0}C	Molecular Formula	Elemental analysis of N Found (Calcd.) (%)		
						C	H	N
1	3a	$-OCH_3$	86	265-268	$C_{14}H_{12}ClNO$	68.44 (68.40)	4.92 (4.88)	5.70 (5.65)
2	3b	-H	82	248-251	$C_{13}H_{10}ClN$	72.39 (72.30)	4.67 (4.58)	6.49 (6.40)
3	3c	-OH	76	215-218	$C_{13}H_{10}ClNO$	67.39 (67.30)	4.35 (4.28)	6.05 (5.98)
4	3d	-Cl	69	110-113	$C_{13}H_9Cl_2N$	62.42 (62.38)	3.63 (3.58)	5.60 (5.55)
5	3e	$N(CH_3)_2$	79	255-258	$C_{15}H_{15}ClN_2$	69.63 (69.56)	5.84 (5.79)	10.83 (10.78)

General producer for the synthesis of 4- Chloro-1-(4-chlorophenyl)-4-(4-methoxyphenyl)-azetidin-2-ones (4a).

4- Chloro-1-(4-chlorophenyl)-4-(4-methoxyphenyl)-azetidin-2-ones (4a)was prepared by mixture of triethylamine (0.01 mole) and chloroacetyl chloride (0.01 mole) in 1,4-doixane was drop wise added to the solution of 4-Chloro N-(4-methoxybenzylidene)-aniline (2a) (0.005 mole) at room temperature.

The reaction mixture was stirred for 30 minutes. Then reaction mixture was refluxed for 3 hr.

After cooling the reaction mixture was poured in crushed ice. The solid product4- Chloro-1-(4-chlorophenyl)-4-(4-methoxyphenyl)-azetidin-2-ones (4a) was collected by filtration and washed with water, The product was recrystallized from alcohol, the yellow coloured product (4a) was obtained, yield 95%, m.p. 150-153^{o}c.

IR(KBr) ν = 3106.33 (Ar-C-H)ν = 2951.78(Ali C-H),ν = 1670.97(C=O),ν =1554.16(C=C),ν =1040.38(C-N) cm^{-1}& ν =8156.31(-C-Cl).

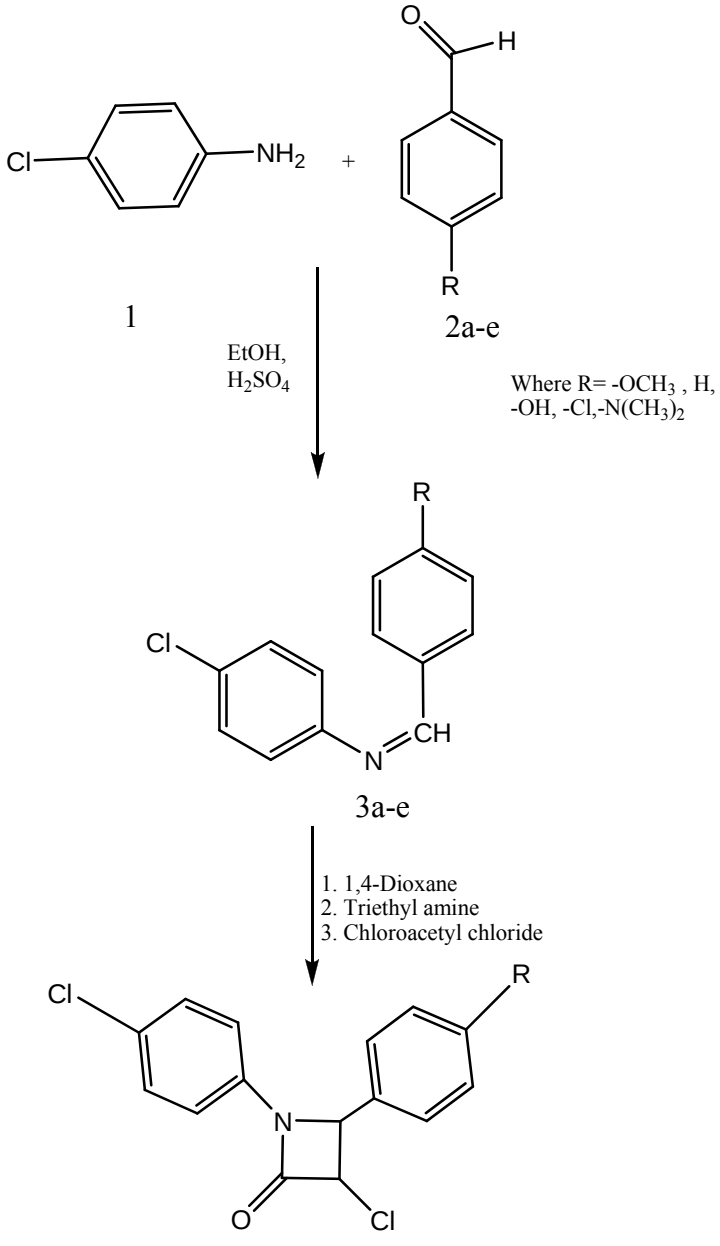
^{1}H NMR ($CDCl_3$) δ7.85-7.82 ppm (2H, m, Ar-H), δ7.30-7.25 ppm (6H, m, Ar-H), δ7.17-7.15ppm (2H, d, C-H), δ7.07-7.04ppm (2H, d, C-H), δ3.79 ppm (3H, s, O-CH_3).

All other compounds (4b-e) were synthesized in similar manner by treatment of (3b-e) with mixture of triethylamine (0.01 mole) and chloroacetyl chloride (0.01 mole) Table No.2

Table No.1

Expt. No.	Product (4)	-R (1a-e)	Yield (%)	Melting Point^{0}C	Molecular Formula	Elemental analysis of N Found (Calcd.) (%)		
						C	H	N
1	4a	-OCH_3	95	150-153	$C_{16}H_{13}Cl_2NO_2$	59.65 (59.60)	4.07 (4.00)	4.35 (4.31)
2	4b	-H	92	170-173	$C_{15}H_{11}Cl_2NO$	61.67 (61.60)	3.79 (3.70)	4.79 (4.71)
3	4c	-OH	89	169-172	$C_{15}H_{11}Cl_2NO_2$	58.46 (58.40)	3.60 (3.55)	4.55 (4.48)
4	4d	-Cl	80	155-158	$C_{15}H_{10}Cl_3NO$	55.16 (55.10)	3.09 (3.00)	4.29 (4.19)
5	4e	$N(CH_3)_2$	90	95-100	$C_{17}H_{16}Cl_2N_2O$	60.91 (60.88)	4.81 (4.77)	8.36 (8.29)

Reaction Scheme :-



4a-e

Results and Discussion

In present worksubstituted 2-Azetidinones (4)have been synthesized by treatment of chloroacetyl chloride containing triethylamine with 4-chloro-N-(4-substituted benzylidene)-aniline (3) in 1,4-dioxane medium. The starting material 4-chloro-N-(4-substituted benzylidene)-aniline (3) were prepared by condensation of

4-chloroaniline(1) and different 4-substituted aromatic daldehyde (2) in ethanoic medium with H_2SO_4 in catalytic amount

The structure of newly synthesized compounds were established on the basis of their spectral data.

Reference

[1]. (a) Singh, G. S. *Tetrahedron* **2003**, *59*, 7631. (b) De Kimpe, N. In *Comprehensive Heterocyclic Chemistry II*, Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V.: Eds.,
[2]. Pergamon: Oxford, 1996; p 507. (c) Brown, M. J. Heterocycles1989, 29, 2225. (d) Isaacs,
[3]. N. S. Chem. Soc. Rev. 1976, 5, 181. (e) Mihovilovic, M. D.; Spina, M.; Stanetty, P. Arkivoc
[4]. 2005, 43. (f) Shirode, N. M.; Kulkarni, K. C.; Gumatse, V. K.; Deshmukh, A. R. A. S.
[5]. Arkivoc2005, 53.
[6]. Singh, G. S. Mini-Rev. Med. Chem. 2004, 4, 69.
[7]. Singh, G. S. Mini-Rev. Med. Chem. 2004, 4, 93.
[8]. Reviews: (a) Deshmukh, A. R. A. S.; Bhawal, B. M.; Krishnaswami, D., Govande, V. V.;
[9]. Shinkre, B. A.; Jayanthi, A. Curr. Med. Chem. 2004, 11, 1889; b) Alcaide, B.; Almendros,
[10]. P. Curr. Med. Chem. 2004, 11, 1921.
[11]. Staudinger, H. Liebigs. Ann. Chem. 1907, 356, 51.
[12]. Banik, B. K., Becker, F. F. Tetrahedron Lett. 2000, 41, 6551
[13]. Singh, G. S. Curr. Org. Synth. 2005, 2, 377.
[14]. Singh, G. S.; Mmolotsi, B. J. IlFarmaco2005, 60, 727.
[15]. Singh, G. S.; Mmolotsi, B. J. J. Heteocycl. Chem., 2006, in press.
[16]. Singh S, B.; Mehrotra, K. N. Can. J. Chem. 1982, 60, 1901.
[17]. Singh, G. S.; Mehrotra, K. N. Ind. J. Chem. 1985, 24B, 129.
[18]. Singh, G. S.; Singh, T.; Lakhan, R. Nat. Acad. Science Lett. 1997, 20, 49.