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Synthesis and characterization of some novel biphenyl 4-carboxylic acid((3- chloro 2-(substituted phenyl) - 4-oxo azetidine-1-yl) amide

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ABSTRACT

Biphenyl 4- carboxylic acid hydrazide 2, which has been treated with different aromatic aldehydes to give Biphenyl 4- carboxylic acid(substituted benzylidene)- hydrazide 3a-j. The synthesis of Biphenyl 4-carboxylic acid((3- chloro 2-(substituted phenyl) - 4- oxo azetidine-1-yl) amide 4a-j , has been prepared by the reaction of 3a-j with chloro acetyl chloride in the presence of triethyl amine. The products have been characterized by elemental analysis,IR,^{1}H NMR and mass spectra.

Key words: Biphenyl carboxylic acid derivatives, synthesis.

INTRODUCTION

The ketene-imine cycloaddition reaction is one of the most common methods for constructing the β-lactam skeleton present in different antibiotic[1,2]. The Staudinger reaction is now widely employed in the preparation of β-lactams as it provides a direct access to such compounds from simple precursors[3]. Numerous β-lactams have been prepared by the reaction of acid chloride and imine in the presence of tertiary amine[4-7]. 2-azetidinones have been extensively explored for their antibacterial[8], antitubecular[9], anticancer[10], and anti-inflammatory[11] activities. Natural and synthetic azetidinone derivatives, especially those containing carbonyl group at C_2 occupy a central place among medicinally important compounds due to their diverse and interesting antibiotic activity[12-17].

EXPERIMENTAL

All the recorded melting points were determined in open capillary tubes and are uncorrected. All the chemicals and solvents used are of Laboratory Grade and solvents were purified. Completion of the reaction was monitored by TLC silica gel GF_{254} (E Merck). IR (KBr, cm^{-1}) were recorded on a Shimadzu-8400 FT-IR spectrometer, ^{1}H NMR spectra on a Brucker spectrometer (300MHz) using TMS as a internal standard (chemical shift in ä ppm) in $CDCl_3$ and DMSO d_6 and mass spectra were recorded on Hewlett-Packard 5989, All the synthesized compounds gave satisfactory C, H, N analyses on Perkin Elmer (U.S.A) 2400 Series.

General procedure for the preparation of Biphenyl 4- carboxylic acid (substituted benzylidene) hydrazide 3a-j

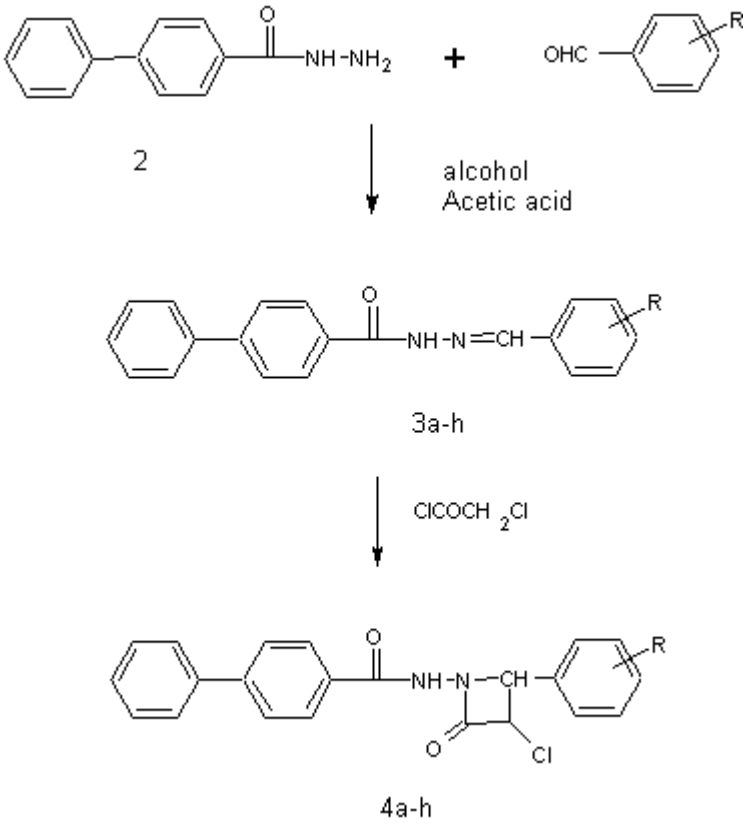
A mixture of 2 (0.01 moles) and different aromatic aldehydes (0.01moles) with a few drops of acetic acid in the ethanol was refluxed for 3 hr . Then reaction mass were cooled and the product obtained was filtered, dried and recrystallisation from suitable solvent.

Table 1: Physical data for compounds 4a-h

Compd.	R	m.p. (°C)	Yield	Molecular Formula
4a	-OCH_3	179	66 %	$C_{23}H_{19}N_2O_3Cl$
4b	4-Cl	162	65 %	$C_{22}H_{16}N_2O_2Cl_2$
4c	4-OH	175	58 %	$C_{22}H_{17}N_2O_3Cl$
4d	4-F	180	62 %	$C_{22}H_{16}N_2O_2ClF$
4e	4-$N(CH_3)_2$	150	70 %	$C_{24}H_{22}N_3O_2Cl$
4f	3-OCH3,4-OH	188	64 %	$C_{23}H_{19}N_2O_4Cl$
4g	3,4,5-$(OCH_3)_3$	178	60 %	$C_{25}H_{23}N_2O_5Cl$
4h	H	132	63 %	$C_{22}H_{17}N_2O_2Cl$

Biphenyl 4- carboxylic acid (4- methoxy phenyl) hydrazide 3a

Light yellow colour, Yield 80 % , m.p. 151 °C, T.L.C. (Methanol:Toluene ; 1: 9) Analy. found : C 76.92 ; H, 5.36 ; N, 8.38 . C, H, N, requires C, 76.36; H, 5.45; N, 8.48. IR (KBr,cm^{-1}) : 3012 cm^{-1} (NH), 2983 cm^{-1} (Ar. C-H stretch), 2966 cm^{-1} and 2837 cm^{-1} (CH_3, C-H), 1620 cm^{-1} (N-C=O), 1508 cm^{-1} (C-N of N-CH-Ar.), 1355 cm^{-1} (C-N), 1251 cm^{-1} and 1026 cm^{-1} (C-O); ^{1}H NMR(CDCl3 and DMSO): d 8.58 (s, 1H, -NH), 7.79 (d, J= 8.86 Hz, 2H, 4-OCH_3 phenyl ring), 7.48-7.45 (m, 9H, Ar-H), 6.94 (d, J= 8.50 Hz, 2H, 4-OCH_3 phenyl protons). 6.24 (s, 1H,-N=CH-Ar), 3.85 (s, 3H, -OCH_3)



Scheme 1

General procedure for the preparation of Biphenyl 4- carboxylic acid (3- chloro 2- (4- substituted phenyl) 4- oxo azetidine 1- yl) amide 4a-j

A solution of 3a-j (0.01 moles) in dry DMF was added to a well stirred mixture of chloroacetyl chloride (0.012 moles) and triethyl amine (0.012 moles) at 0 °C temperature and than stirred for 12-20 hrs. and kept overnight at room temperature. The content were then poured into crushed ice with stirring and the product obtained was filtered, washed with water and dried and recrystallized from suitable solvent.

Table 2: Spectral and elemental data for 4a-h

Compd.	R	Found (Calcd.) (%)			^{1}H NMR ($CDCl_3$ and DMSO-d_6)
		C	H	N	
4a	4 -OCH_3	67.23 (67.89)	4.62 (4.67)	6.82 (6.88)	δ 8.67(s,1H,-NH),7.73(d,J=7.61 Hz,2H,4-OCH_3 phenyl ring),7.68-7.20 (m, 9H,Ar-H),6.90(d,J=7.74 Hz,2H,4-OCH_3 phenyl proton),6.72(s,1H,Ar-CH- N),4.85(d,J=10.19 Hz, 1H, N-CH-Cl),3.84(s,3H,-OCH_3)
4b	4 -Cl	64.19 (64.23)	3.85 (3.89)	6.79 (6.81)	δ 8.55(s,1H,-NH),7.80-6.91(m,9H Ar-H+4H, 4-Cl phenyl ring),6.61(d, J=10.50 Hz, 1H, Ar-CH- N),4.83 (d,J=10.20 Hz, 1H, N-CH-Cl)
4c	4 -OH	67.24 (67.26)	4.34 (4.33)	7.12 (7.13)	δ 8.64(s,1H,-NH),7.79-6.88(m,9H,Ar-H+4H, 4-OH phenyl ring),6.72(d, J=10.50 Hz, 1H, Ar-CH-N),4.84(d, J=10.23 Hz, 1H, N-CH-Cl),3.41 (s,1H,-OH)
4d	4 -F	67.05 (67.09)	4.04 (4.06)	7.10 (7.11)	δ 8.52 (s,1H,-NH),7.80-6.90(m,9H, Ar-H + 4H , 4-F phenyl ring), 6.71 (d, J=10.46 Hz, 1H, Ar-CH-N), 4.86 (d, J=10.20 Hz, 1H, N-CH-Cl)
4e	4 -$N(CH_3)_2$	68.61 (68.65)	5.20 (5.24)	10.0 (10.01)	δ 8.72(s,1H,-NH),7.94-6.95(m,9H, Ar-H + 4H, 4-N,N,dimethyl amino phenyl ring),4.88(d, J=10.51 Hz, 1H, N-CH-Cl),3.63(s,6H, -$N(CH_3)_2$)
4f	3 -OCH_3, 4 -OH	65.30 (65.32)	4.45 (4.49)	6.61 (6.62)	δ 8.52(s,1H,-NH),7.81-6.87(m,9H, Ar-H + 3H,3-OCH_3 4-OH phenyl ring), 6.70 (d, J=10.51 Hz,1H, Ar-CH-N), 4.82 (d, J=10.20 Hz, 1H,N-CH Cl),3.84 (s,3H,-OCH_3),3.42(s,1H, -OH).
4g	3,4,5 -OCH_3	64.28 (64.30)	4.91 (4.93)	5.97 (6.00)	δ 8.50(s,1H,-NH),7.83-7.18(m,9H, Ar-H + 2H 3,4,5-OCH_3 phenyl ring), 6.70(d, J=10.52 Hz, 1H, Ar-CH-N), 4.86 (d, J=10.19 NHz, 1H, N-CH-Cl),3.83(s,9H,-OCH_3)
4h	H	70.10 (70.12)	4.49 (4.51)	7.41 (7.43)	δ 8.66(s,1H,-NH),7.78(m,14H,Ar-H) 6.70(d, J=10.44 Hz, 1H, Ar-CH-N), 4.82(d, J=10.21 Hz, 1H, N-CH-Cl)

Bipheyl 4- carboxylic acid (3- chloro 2- (4- methoxy phenyl) 4- oxo azetidine 1-yl) amide 4a

light yellow colour. Yield 65 % , m.p. 189 ^{o}C ; TLC (Ethyl acetate:Carbon tetrachloride, 6:4) Anal. Found: C, 67.23 ; H, 4.62 ; N, 6.82 . C, H, N, requires C, 67.89 ; H,4.67 ; N,6.88 ; IR(KBr, cm^{-1}): 3358 cm^{-1} (NH), 3070 cm^{-1} (Ar-C-H), 2960 cm^{-1}, 2839 cm^{-1} (CH_3, C-H), 1745 cm^{-1} and 1714 cm^{-1} (C=O, β- lactam ring), 1514 cm^{-1} and 1344 cm^{-1} (C-N), 1261 cm^{-1} and 1027 cm^{-1} (C-O), 699 cm^{-1} (C-Cl);^{1} H NMR ($CDCl_3$ and DMSO): d 8.67 (s, 1H, -NH), 7.73 (d, J= 7.60 Hz, 2H, 4-OCH_3 phenyl ring), 7.68-7.19 (m, 9H, Ar-H), 6.91 (d, J= 7.75 Hz, 2H, 4-OCH_3 phenyl protons). 6.72 (d, J=10.51 Hz, 1H, Ar-CH-N), 4.87 (d, J= 10.19 Hz, 1H,N-CH-Cl), 3.84 (s, 3H, -OCH_3).

RESULTS AND DISCUSSION

The structures of all compounds were confirmed by IR, ^{1}H NMR and Elemental analyses. The IR spectra of 4a showed the –NH band at 3358 cm^{-1}, carbonyl (C=O) of â- lactam at 1745 cm^{-1} and 1714 cm^{-1}, (C-N) band at 1514 cm^{-1} and 1344 cm^{-1}, (C-Cl) band at 699 cm^{-1}, (C-O) band at 1261 cm^{-1} and 1027 cm^{-1}.

The ^{1}H NMR spectra of 4a the –NH proton shifted downfield at ä 8.67, Ar-CH-N proton shifted at δ 6.72, and methoxy proton gave a singled at δ 3.84. The other entire proton was obtained in the aromatic region.

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