RJC

RASĀYAN *J. Chem.*
Vol. 5 | No.2 | 148-151 | April-June | 2012
ISSN: 0974-1496 | CODEN: RJCABP
http://www.rasayanjournal.com

SYNTHESIS AND CHARACTERIZATION OF NEW SERIES SUBSTITUTED [1, 3-BROMOXAZINE]-4-ONE

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ABSTRACT
Substitute [1, 3-Bromoxazine]-4-one were readily prepared by the base catalyzed condensation of substituted dihydrobenzoxazones with acyl bromide in toluene. The synthesized compounds characterized by spectral analysis & elemental analysis.
Keywords: Substituted dihydrobenzoxazone, base catalyst like pyridine, 2-Bromopropionyl bromide.

INTRODUCTION

Bis-benzoxazines exhibit various biological activities including antibacterial[1, 2]. 1, 3-Benzoxazine are a group of compounds possessing a wide spectrum of biological activities such as antimicrobial, anti-inflammatory[3, 5]. Now a days there are lots of antibiotics are available in the market and are used as clinical agents but there are continuous fear and observation that when these drugs are constantly used their resistance towards gram positive and gram negative bacteria are decreased constantly with time. Therefore still continuous research work is on going for synthesize active pharmaceutical ingredients with better pharmaceutical properties and minimum side effects.

From the therapeutic point of view benzoxazones derivatives so far prepared on the most extensively and intensively studied are those containing heterocyclic moiety. Among these derivatives, bromoxazone have proved to be most successful against various bacterial infections in animal and human beings too.

Considering the biological and therapeutic activities of bromoxazones. It is proposed to synthesize substituted bromoxazones, which may produce pharmacologically more active compounds.

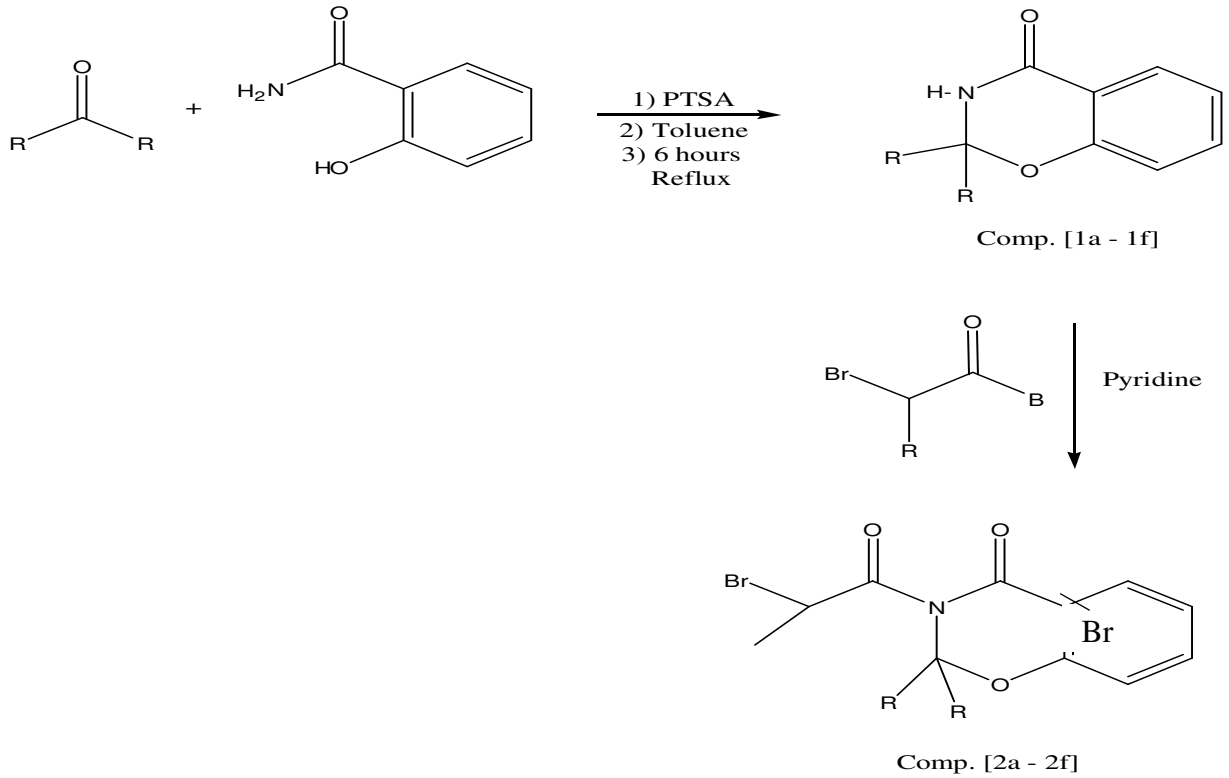
EXPERIMENTAL

General procedure for the synthesis of dihydrobenzoxazones compound [1a – 1f]

A mixture of salicylamide, appropriate ketone and PTSA in toluene was refluxed under condition to removal of water using dean stark apparatus for 6 hours at 105 – 110^{0}C, then cool at 0.5^{0}C and stir 2 hours filter and wash the toluene and dry at 45 – 50^{0}C under vacuum.

General procedure for the synthesis of Bromoxazones compound [2a – 2f]

Take a mixture of compound [1a – 1f] dihydrobenzoxazones, pyridine in toluene and 2 – charged bromopropionyl bromide in 30 – 40' slowly at 26 – 28^{0}C, exotherm observed upto 50 – 52^{0}C. Stir 2 hours at 45 – 50^{0}C, then cool at room temperature, wash with water, 5% $NaHCO_3$, 25% Brine solution and organic layer distilled out completely under vacuum at 45 – 50^{0}C, charged methanol stir 60' at room temperature then cool 0 – 5^{0}C. Stir 2 hours and filter and wash with methanol. Dry 2 – 3 hours under vacuum at room temperature.



Scheme-1

Melting points were determined in open capillary tubes were found uncorrected. IR spectra were recorded on fourier transform IR spectrophotometer (Shimadzu) using KBr disc methods. PMR spectra in $CDCl_3$ were recorded on Burker advance DPx 200 MHz spectrophotometer. Mass spectra was recorded on JEOL JMS DX303 mass spectrophotometer with electron impact ionization at 70eV. The purity of the test compounds was determined by TLC. A single spot obtained confirmed the purity of substituted Bromozaxones[6-11].

Physical data and spectral analysis are recorded in the following Table-1.

Table-1

Comp.	R.	Yield	M.P.	Mass (M/Z)	IR (KBr) cm^{-1}	NMR ($CDCl_3$) δ
2a	Me	72%	63-66^{0}C	313 (M^++1)	1730 (C=O) 1683 (CO-NH) 1360 (C-N)	1.75 δ (S, 3H), 1.90 (S,3H) 1.92 (d, J = 6Hz, 3H), 5.22 (q, J = 6Hz, 1H), 6.94 – 6.98 (M, 1H), 7.07 – 7.16 (M, 1H), 7.50 – 7.59 (M, 1H), 7.92 – 7.96 (M, 1H)
2b	Bu	75%	Colourless oil	397 (M^++1)	1725 (C=O) 1686 (CO-NH) 1320 (C-N)	0.70-0.96 (M, 6H), 1.1 – 1.07 (M, 8H), 1.96 (d, J = 6.6Hz, 3H), 2.0 - 2.5 (M, 4H), 5.25 (q, J = 6Hz, 1H), 6.90 - 7.0 (M, 1H), 7.04 - 7.12 (M, 1H), 7.48 – 7.57 (M, 1H), 7.91 – 7.95 (M, 1H)
2c	$C_{15}H_{31}$	64%	Yellow oil	205 (M^++1)	1722 (C = O) 1685 (CO-NH) 1335 (C-N)	0.80 (t, J = 6.4 Hz, 6H), 1.0 – 2.5 (M, 6H), 1.96 (d, J = 6.7 Hz, 3H), 5.26 (q, J = 6.6 Hz, 1H), 6.91 – 6.97 (M, 1H), 7.04 – 7.12 (M,

						1H), 7.48 – 7.57 (M, 1H), 7.92 – 7.97 (M, 1H)
2d	$-(CH_2)_4^-$	67%	76 – 78^{0}C	339 (M^++1)	1722 (C = O) 1685 (CO-NH) 1320 (C – N)	1.7 – 2.6 (M, 8H), 1.97 (d, J = 8.7 Hz, 3H), 5.25 (q, J = 8.7 Hz, 1H), 6.90 – 7.02 (M, 2H), 7.5 – 7.6 (M, 1H), 7.91 – 7.95 (M, 1H)
2e	$-(CH_2)_5^-$	87%	74 – 76^{0}C	353 (M^++1)	1723 (C = O) 1682 (CO-NH) 1290 (C – N)	1.20 – 2.5 (M, 10H), 1.92 (d, J = 6.6 Hz, 3H), 5.14 (q, J = 6.6 Hz, 1H), 7.0 – 7.15 (M, 2H), 7.50 – 7.60 (M, 1H), 7.90 – 7.95 (M, 1H)
2f	$-(CH_2)_6^-$	92%	94 – 96^{0}C	367 (M^++1)	1717 (C = O) 1684 (CO-NH) 1469 (C – N)	1.5 – 1.9 (M, 8H), 1.92 (d, J = 6.6 Hz, 3H), 3.10 – 2.65 (M, 4H), 5.19 (q, J = 6.6 Hz, 1H), 6.97 – 7.03 (M, 1H), 7.06 – 7.15 (M, 1H), 7.5 – 7.6 (M, 1H), 7.89 – 7.95 (M, 1H)
2g	 Bn Bn Benzene	77%	114–115^{0}C	464 (M^+)	1715 (C = O) 1694 (CO-NH) 1350 (C – N)	1.4 (d, J = 6 Hz, 3H), 3.23 (d, J = 16 Hz, 1H), 3.40 (d, J = 16 Hz, 1H), 3.72 (d, J = 16 Hz, 2H), 5.25 (q, J = 6 Hz, 1H), 7.0 – 7.12 (M, 2H), 7.10 – 7.35 (M, 10H), 7.55 – 7.64 (M, 1H), 7.80 – 7.85 (M, 1H)

Elemental Analysis

Satisfactory elemental analysis were obtained on Carlo – Erba – 1108 analyzer and the values were found to be ± 0.4% of calculated values.Percentage of element are recorded by elemental analysis and described in Table-2.

Table-2

Comp.	Mol. Formula	Mol. Wt.	% of element					
			Found			Calculated		
			C	H	N	C	H	N
2a	$C_{13}H_{14}BrNO_3$	314.142	50.07	4.48	4.49	50.02	4.52	4.49
2b	$C_{19}H_{26}BrNO_3$	396.298	57.37	6.71	3.81	57.38	6.61	3.53
2c	$C_{41}H_{70}BrNO_3$	704.87	69.68	9.95	2.03	69.86	10.01	1.99
2d	$C_{15}H_{16}BrNO_3$	338.178	53.12	4.67	3.98	53.27	4.77	4.14
2e	$C_{16}H_{18}BrNO_3$	352.204	54.56	5.15	3.98	54.57	5.26	4.03
2f	$C_{17}H_{20}BrNO_3$	366.23	55.55	5.54	4.14	55.75	5.50	3.82
2g	$C_{25}H_{20}BrNO_3$	462.31	64.88	4.99	2.98	64.66	4.78	3.02

The antibacterial data of synthesized substituted 3-(2-Bromopropionyl) spiro [2H - 1, 3 – benzoxazine - 2, 1 - cyclohexane] – 4 (3H) – one are shown in Table-3.

RESULTS AND DISCUSSION

The acid catalyzed condensation of salicylamide and with corresponding ketone in toluene give benzoxazone which is on again bromopropionylation in the presence of base catalyst like pyridine give respective Bromoxazone.

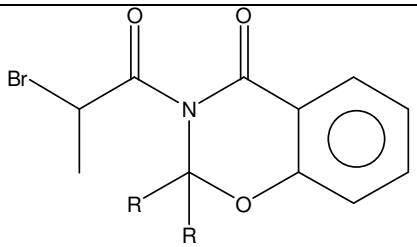
The IR spectra of compound 2a – 2g should extra vibration at near about 1684 cm^{-1} which are characteristics of carbonyl group present as an amido group.

H^1NMR data of synthesized compound confirm the formation of substituted bromoxazone.

CONCLUSION

We screened comp.(2a–2f) for antibacterial activity. All the synthesized compounds have shown mild to good activity against pathogenic bacteria. The synthesized compounds (2 e) have been shown to be more potent than other synthesize compounds.The overall impact of all the derivatives against Nor-Floxacin was inferior against all bacterial species.Substituted Bromoxazone and their derivatives are an important class of heterocyclic compounds with diverse biological effect and industrial uses.

Table-3

S. No.	 Bacteria	Zone of inhibition in (mm)			
		S. aureus	E. coli	B. subtilis	P. aeruginosa
1	Standard [Nor floxacin 100 µg/ml	25	24	24	24
2	Comp. 2 a	24	21	20	19
3	Comp. 2 b	26	-	21	20
4	Comp. 2 c	-	20	19	22
5	Comp. 2 d	24	24	22	-
6	Comp. 2 e	25	23	24	25
7	Comp. 2 f	23	19	-	22

ACKNOWLEDGEMENTS

We are thankful to Mr. Sai Somase who provides me spectral analysis of synthesized compounds.

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[RJC-902/2012]