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SYNTHESIS AND PHYSICO-CHEMICAL CHARACTERIZATION OF NOVEL OXAZOLINES

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ABSTRACT

The aim of present work is to synthesize novel oxazoline compounds and its characterization. The title compounds synthesized with the use of catalyst Pyridinium Hydrobromide PerBromide. Synthesis accomplished in two steps. Aaromatic aldehydes and Pyridinium Hydrobromide PerBromide added in l water and mixed well with constant stirring. The resultant solution poured to dimethyl amine or diethyl amine stirred well and added ethyl acetate. Solution stirred well for 6 hrs. at room temperature. The resultant mixture is washed with 0.5 M acq. sodium thiosulfate solution. And then successively washed with saline. Remove the solvent by evaporation. Collect the product and recrystallize from alcohol. All resultant compounds are characterized by IR, NMR and CHN analysis. Physico-chemical characters also profiled. CHN analysis of all compounds done and results are incorporated.

KEYWORDS: Oxazolines, Aromatic aldehydes, Pyridinium Hydrobromide Per Bromide.

INTRODUCTION

Oxazole is a heterocyclic organic compound that has a five-member ring molecular structure, C3H3ON, containing three carbon atoms, one oxygen atom and one nitrogen atom. The double bond can be located in any of the three possible locations in the ring, thus three different oxazolines can exist. Oxazoles are basic in nature. Oxazolines are present in natural as well as in synthetic compounds. Oxazole derivatives have become increasingly important because of their use as intermediates for the preparation of new biological materials. Oxazolone plays very vital role in the manufacturing of various biologically active drugs. The wide range of biological activities of oxazoles includes anti- inflammatory, analgesic, antibacterial, antifungal, hypoglycemic, antiproliferative, anti- tuberculosis, muscle relaxant

and HIV inhibitor activity. In addition, oxazole derivatives are useful synthetic intermediates and can be used as diversity scaffolds in combinatorial chemistry and as peptidomimetics. Oxazolines can be polymerized to polyoxazolines have fruitful uses in coating, pigment dispersion and even in gene delivery.

MATERIALS AND METHODS

0.25mmol aromatic aldehydes and 0.75 mmol Pyridinium Hydrobromide PerBromide added in 10 ml water and mixed well with constant stirring. The resultant solution poured to 10 ml dimethyl amine or diethyl amine stirred well and added 5 ml ethyl acetate. Solution stirred well for 6 hrs. at room temperature. The resultant mixture is washed with 0.5 M acq. sodium thiosulfate solution. And then successively washed with acq. sodium chloride. Remove the solvent by evaporation. Collect the product and recrystallize from alcohol.

RESULTS AND DISCUSSION

Twenty five compounds are synthesized. For first fifteen compounds LJ1-LJ15 dialkyl amine used is Dimethyl amine whereas other 10 compounds LJ16-LJ25 diethyl amine used.

Physico-chemical properties of synthesized compounds are given below;

Serialno	sample	Mole. Formula	Mol. Weight	Melting point	yield	Rf value	Mol. volume (MV) cm^3	Mol.ref(MR) cm^3	Ref.IntexIn cm^3	Surface tension	Density In g/cm^3
1	L J1	C 9 H8 ClNO	181.618g	113^{0}C	88%	0.86	140.8	47.96	1.546	42.6	1.28
2	LJ2	C9 H8 N2 O8	192.17g	105^{0}C	81%	0.81	137	49.02	1.634	57.1	1.4
3	LJ3	C9 H8 N2 O8	192.17 g	98^{0}C	78%	0.86	137	49.02	1.6	57.1	1.4
4	LJ4	C16 H13 NO2	251.28 g	115^{0}C	69%	0.78	210.7	50.92	1.603	48.0	1.56
5	LJ5	C9 H8 ClNO	181.61 g	79^{0}C	83%	0.83	140.8	47.96	1.596	42.6	1.28
6	LJ6	C15 H10 N2 O4	282.25 g	150^{0}C	73%	0.72	206.2	74.25	1.639	59.3	1.368
7	LJ7	C9 H8 BrNO	226.06 g	90^{0}C	78%	0.79	144.1	50.92	1.624	45.7	1.56
8	LJ8	C10 H11 NO	161.2 g	88^{0}C	79%	0.83	146.7	47.78	1.564	37.1	1.09
9	LJ9	C11 H14 N2 O	190.24 g	115^{0}C	68%	0.85	172.8	56.16	1.563	37.3	1.10
10	LJ10	C9 H9 NO3	179.17g	113^{0}C	81%	0.78	126.1	45.06	1.633	54.3	1.42
11	LJ11	C11 H13 NO3	207.22 g	80^{0}C	90%	0.81	175.1	54.99	1.540	36.9	1.18
12	LJ12	C11 H13 NO3	207.22 g	97^{0}C	88%	0.88	175.1	54.99	1.60	49.7	1.250
13	LJ13	C12 H15 NO4	237.25g	68^{0}C	83%	0.81	196.8	60.80	1.529	35.9	1.20
14	LJ14	C9 H8 FNO	165.164g	112^{0}C	78%	0.82	134.4	43.23	1.556	36.8	1.22
15	LJ15	C9 H8 Cl2 NO	216.06 g	70^{0}C	83%	0.79	134.4	43.23	1.556	36.8	1.22
16	LJ16	C14 H18 Cl NO	251.7 g	82^{0}C	79%	0.81	222.9	71.26	1.55	40.4	1.129
17	LJ17	C14 H17 NOCl2	286.1 g	90^{0}C	84%	0.80	234.8	76.15	1.561	42.4	1.218
18	LJ18	C14 H18 N2 O8	262.3 g	71^{0}C	86%	0.78	222.8	72.91	1.568	46.6	1.177
19	LJ19	C14 H18 FNO	235.29 g	68^{0}C	76%	0.83	215.2	66.35	1.528	37.5	1.093
20	LJ20	C16 H23 NO3	277.35 g	73^{0}C	76%	0.86	258.9	79.72	1.527	37.8	1.070
21	LJ21	C17 H 25 NO4	307.38 g	85^{0}C	85%	0.83	283.0	86.40	1.522	37.6	1.086
22	LJ22	C16 H24 N2 O	260.37 g	96^{0}C	87%	0.76	248.9	80.67	1.562	40.9	1.045
23	LJ23	C14 H18 N2 O3	262.3 g	89^{0}C	76%	0.81	222.8	72.97	1.568	46.6	1.77
24	LJ24	C16 H23 NO3	277.35 g	93^{0}C	91%	0.8	258.9	79.72	1.527	37.8	1.070
25	LJ25	C14 H18 Cl NO	251.75 g	70^{0}C	88%	0.85	222.9	71.26	1.552	40.4	1.129

NMR and IR features of synthesized compounds are as follows.

Sample.ID	IR peaks(cm^{-1})	NMR peaks (ppm)
LJ1	1490(C-O-stretch),1243 (C-N Stretch)	11.663(alcoholic proton)8-421 (2H),-CH_2-5 membered ring,8.330, (1H)-isomer of isoxazole, 8.229, 8.2210,8.05,8.04-(4H),of Aro-H.
LJ2	1505(C-O stretch)1255(C-N- Stretch)	8.404-(2H),-CH2(5-membered ring).8.357-(1H)isomer of isoxazole,8.363,8.366,8.369-(4H,Ar-H)
LJ3	1545(C-O stretch),1255(C-N stretch.)	11.646-alcoholic proton. 8.424-(2H,CH2-5 membered ring),
LJ4	1550 (C-O stretch),1290 (C-N stretch)	8.337-(2H),CH2(5-membered ring)7.469-(4H) of Ar-H
LJ5	1490(C-O stretch),1275 stretch (C-N)	7.470 (4H)of Ar-H
LJ6	1510(C-O stretch), 1255(C-N stretch)	11.075 – alcoholic proton peak.8.141-(2H)CH2-5-membered ring,7.959,7.955,7.875 (4H,of Ar-H)
LJ7	1534(C-O stretch),1200(C-N stretch)	11.844 alcoholic proton,8.308-(2H)CH2-5 membered ring.7.872,7.850-(4H,Ar-H)
LJ8	1576(C-O-stretch),1245(C-N stretch)	10.966-alcoholic proton,8.306-(2H,CH2-5 membered ring),8.067,7.545,7.539 (4H of Ar-H)
LJ9	1537(C-O stretch),1245(C-N stretch).	11.186-alcoholic proton peak.7.526-(2H,CH2 5-membered ring)
LJ10	1501(C-O stretch),1260(C-N stretch).	8.176-(2H,CH2-5membered ring),8.170-OH isomer of isoxazole.8.157,8.152,8.149-Ar-H
LJ11	1560(C-O stretch),1249(C-N stretch).	8.170-(2H,CH2-5membered ring),8.080-OH isomer of isoxazole.6.834(-Ar-H)
LJ12	1520(C-O stretch),1297(C-N stretch)	8.078-(2H,CH2-5membered ring),7.793-OH isomer of isoxazole.7.286,6.836(-Ar-H)
LJ13	1500(C-O stretch),1234(C-N stretch)	7.953-(2H,CH2-5membered ring),7.950-OH isomer of isoxazole.7.932,7.929.7.704(-Ar-H)
LJ14	1556(C-O stretch), 1249(C-N stretch)	8.062-(2H,CH2-5membered ring),8.059-OH isomer of isoxazole.8.041,8.037,7.829(-Ar-H)
LJ15	1494(C-O-stretch) ,1292(C-N stretch)	8.159-(2H,CH2-5membered ring),8.154-OH isomer of isoxazole.7.671,7.648,7.456(-Ar-H)
LJ16	1550(C-O stretch) ,1272(C-N stretch)	8.079-(2H,CH2-5membered ring),7.752-OH isomer of isoxazole.6.837(-Ar-H)

CHN analysis of synthesized compounds are enumerated below.

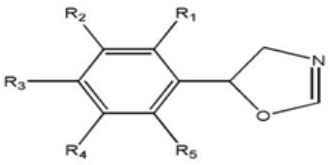
	CALCULATED			ANALYTICAL		
Sample	**N%**	**C%**	**H%**	**N%**	**C%**	**H%**
LJ1	7.71	59.52	4.44	4.65	66.76	3.86
LJ2	14.58	56.25	4.20	10.59	49.60	3.81
LJ3	14.58	56.25	4.20	7.67	77.11	8.42
LJ4	6.20	47.82	3.57	8.45	51.10	3.58
LJ5	7.71	59.52	4.44	4.65	66.50	3.67
LJ6	8.69	74.51	6.88	10.64	49.87	2.79
LJ7	6.20	47.82	3.57	5.20	67.00	4.02
LJ8	8.69	74.51	6.88	4.65	66.98	4.30
LJ9	14.73	69.45	7.42	5.61	67.46	5.80

LJ10	7.82	60.33	5.06	3.80	54.30	3.60
LJ11	6.76	63.76	6.32	6.20	63.45	6.73
LJ12	6.76	63.76	6.32	6.48	61.87	5.99
LJ13	5.90	60.75	6.37	5.10	60.31	5.49
LJ14	8.48	65.45	4.88	8.34	66.78	4.60
LJ15	6.48	50.03	3.27	6.94	54.48	3.25
LJ16	5.56	66.79	7.21	5.04	68.38	7.45
LJ17	4.89	58.75	5.99	4.32	55.44	5.30
LJ18	10.68	64.10	6.92	10.01	60.57	6.16
LJ19	5.95	71.46	7.71	5.90	79.12	7.03
LJ20	5.05	69	8.36	6.15	66.89	8.09
LJ21	4.56	66.43	8.20	4.23	64.71	8.86
LJ22	10.76	73.8	9.29	10.09	71.90	8.66
LJ23	10.68	64.1	6.92	10.13	64.02	6.75
LJ24	5.05	69.2	8.36	5.05	68.56	8.70
LJ25	5.56	66.79	7.21	5.10	65.85	7.39

Lipinsky Rule Analysis.

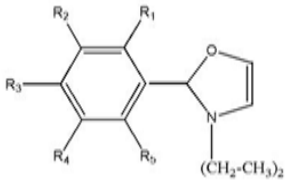
SAMPLE CODE	C log P	MW	nON	nOHNH	n rot b	n voi
LJ1	2.27	181.62	2	0	1	0
LJ2	1.50	192.17	5	0	2	0
LJ3	1.55	192.17	5	0	2	0
LJ4	2.40	226.07	2	0	1	0
LJ5	2.25	181.62	2	0	1	0
LJ6	2.38	226.07	2	0	1	0
LJ7	2.30	159.19	2	0	1	0
LJ8	2.02	161.20	2	0	1	0
LJ9	1.70	190.25	3	0	1	0
LJ10	0.62	179.18	4	2	1	0
LJ11	1.24	207.23	4	0	3	0
LJ12	1.64	207.23	4	0	3	0
LJ13	1.23	237.25	5	0	4	0
LJ14	2.88	216.07	2	0	1	0
LJ15	1.76	165.17	2	0	1	0
LJ16	2.27	181.62	2	0	1	0
LJ17	2.88	216.07	2	0	1	0
LJ18	1.50	192.17	5	0	2	0
LJ19	1.76	165.17	2	0	1	0
LJ20	1.64	207.23	4	0	3	0
LJ21	1.23	207.23	4	0	3	0
LJ22	1.70	190.25	3	0	2	0
LJ23	1.55	192.17	5	0	2	0
LJ24	1.24	207.23	4	0	3	0
LJ25	2.25	181.62	2	0	1	0

The structure of the synthesized compounds are summarized below.



Basic structure for compounds LJ1-LJ15.

SAMPLE	R1	R2	R3	R4	R5
LJ1	H	H	Cl	H	H
LJ2	NO_2	H	H	H	H
LJ3	H	H	NO_2	H	H
LJ4	H	H	H	Br	H
LJ5	H	H	H	Cl	H
LJ6	CH_3	H	H	H	H
LJ7	H	Br	H	H	H
LJ8	H	CH_3	H	H	H
LJ9	H	H	N-$(CH_3)_2$	H	H
LJ10	H	H	OH	OH	H
LJ11	H	H	OCH_3	OCH_3	H
LJ12	H	OCH_3	H	OCH_3	H
LJ13	H	OCH_3	OCH_3	OCH_3	H
LJ14	H	Cl	H	H	H
LJ15	H	H	F	H	H



Basic structure of compounds LJ16-LJ25.

SAMPLE	**R1**	**R2**	**R3**	**R4**	**R5**
LJ16	H	H	Cl	H	H
LJ17	H	Cl	H	H	H
LJ18	NO_2	H	H	H	H
LJ19	H	H	F	H	H
LJ20	OCH_3	H	OCH_3	H	H
LJ21	H	OCH_3	OCH_3	OCH_3	H
LJ22	H	H	N-$(CH_3)_2$	H	H
LJ23	H	H	NO_2	H	H
LJ24	H	OCH_3	OCH_3	H	H
LJ25	Cl	H	H	H	H

CONCLUSION

Twenty five compounds have been synthesized in the manner explained in methods. Physico-chemical characterestics of all compounds also given in the table. By IR and NMR analysis structures confirmed. CHN analysis also done since title compounds are heterocyclic in nature. Oral route suitability of synthesized compounds checked by Lipinsky rule. None of the compound showed violation. Structure of all compounds given in table. Most of all the compounds gave more than 75% yield.

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