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Synthesis of Some Novel Imidazolinone Derivatives with Dibenzo(b,f)azepine Nucleus

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4-Arylidene-2-phenyl-5-(4*H*)-oxazolones (**1a–j**) were prepared by Erlenmeyer condensation. The 4-arylidene-2-phenyl-5-(4*H*)-oxazolones react with *p*-phenylene diamine in presence of dry pyridine to give corresponding 3-(4-amino-phenyl)-5-benzylidene-2-substituted phenyl-3,5-dihydro-imidazol-4-one (**2a–j**); this was further reacted with dibenzo (b,f) azepine-5-carbonyl chloride (**3**) in basic medium to give dibenzo(b,f)azepine-5-carboxylic acid [4-(4-substituted-5-oxo-2-phenyl-4,5-dihydro-imidazol-1-yl)-phenyl] amide (**4a–j**). The constitution of the selected products has been supported by elemental analysis, infrared spectra and ^1H NMR spectra. The purity of the compounds was checked by thin layer chromatography.

Key Words: **Imidazolinone, Derivatives, Dibenzo(b,f)azepine.**

INTRODUCTION

Oxazolones are a class of small heterocycles which are important intermediates in the synthesis of several small molecules, including amino acids, peptides[1–3], heterocyclic precursors[4–6] as well as biosensor couplings and/or photosensitive composition devices for proteins[7]. Some oxazolones have shown a wide range of pharmaceutical properties[8]. 4-Arylidene-2-phenyl-5-(4*H*)-oxazolones are usually prepared from benzoylglycine, acetic anhydride and sodium acetate[9–11].

Literature survey reveals that 4-arylidene-2-phenyl-5-(4*H*)-oxazolone on reaction with various heterocyclic amines[12], thiosemicarbazide derivatives[13] and sulphonamides[14], in the presence of dry pyridine, gave corresponding imidazolinone derivatives of significant importance.

Many analogues of dibenzo(c,e; b,e; b,f)azepines are known and exhibit biological activities[15–17]. The dibenzo(b,f)azepines are important as derivatives such as carbamazepine and oxcarbazepine, which have become established as effective agents in the treatment of epilepsy and affective disorders[18]. The

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heterocyclic precursor of carbamazepine and oxcarbazepine is dibenzo (b,f) azepine-5-carbonyl chloride and the synthesis has been reported by several authors[19, 20]. Here, the dibenzo(b,f)azepine-5-carbonyl chloride is used to condense in the basic medium with the prepared imidazolinones having amino group **(2a–j)**. A new class of compounds (4a–j) is thus synthesized and is characterized by usual spectral methods.

EXPERIMENTAL

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. Meck). The final products were purified by column chromatography using silica gel 60/120 mesh, by increasing percentage of ethyl acetate in carbon tetrachloride. IR (KBr, cm^{-1}) were recorded on a Shimadzu-8400 FT-IR spectrometer, ^1H NMR spectra on a Brucker spectrometer (300 MHz) using TMS as internal standard (chemical shift in δ ppm) in $CDCl_3$ and DMSO-d_6. All the synthesized compounds gave satisfactory C, H, N analyses on Perkin-Elmer (U.S.A.) 2400 Series.

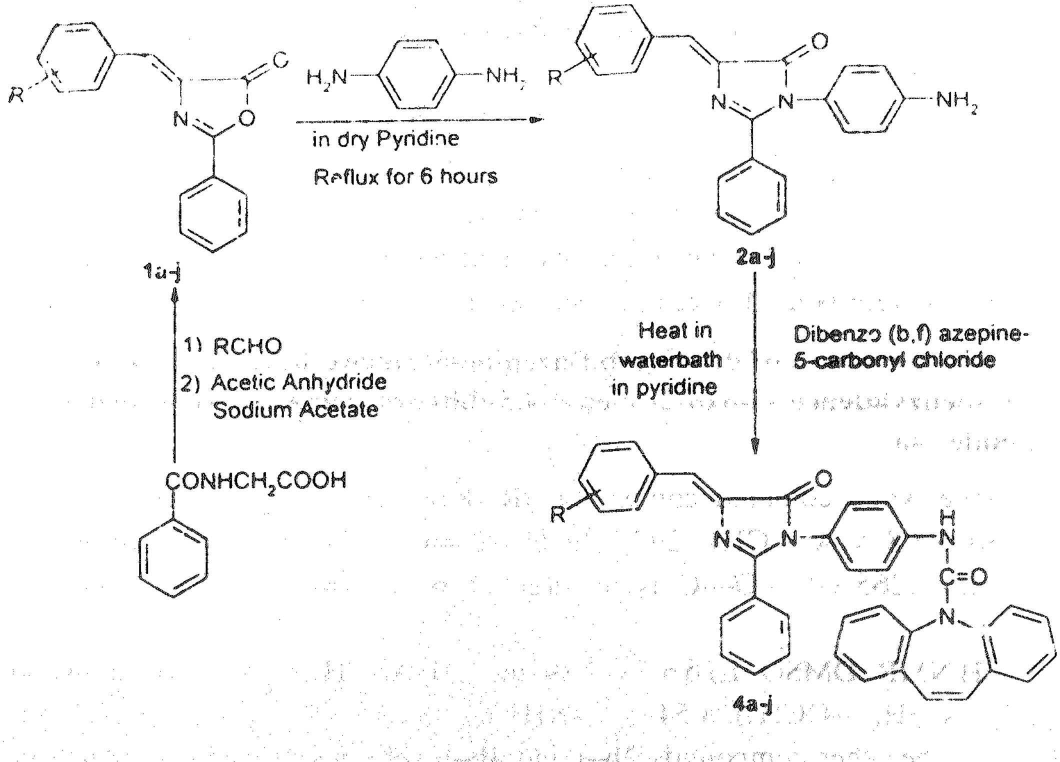

Fig. 1. **Reaction Scheme**

General procedure for the preparation of 4-arylidene-2-phenyl-5-(4*H*)-oxazolones (1a–j)

4-Arylidene-2-phenyl-5-(4*H*)-oxazolones were prepared according to the reported method[21].

General procedure for the preparation of 3-(4-amino-phenyl)-5-benzylidene-2-substituted phenyl-3,5-dihydro-imidazol-4-one (2a–j)

Equimolar amount of 4-arylidene-2-phenyl-5-(4*H*)-oxazolones and *p*-phenylene diamine were taken in a reaction flask attached with a reflux condenser and refluxed for 6 h with dry pyridine as solvent. The reaction was monitored by thin layer chromatography; on completion of the reaction the contents were poured in ice water to give coloured precipitates.

Characterization of 3-(4-amino-phenyl)-5-(4-methoxy-benzylidene)-2-phenyl-3,5-dihydro-imidazol-4-one (2a)

Dark coloured compound. IR (KBr, cm^{-1}) ν_{max}: 3300–3270 ν(—NH), 3100–3010 ν(Ar—CH), 2972–2916 ν(C═C), 1740 ν(C═O), 1251 ν(C—O—C asymmetric stretch), 1161 ν(C═C), 1026 ν(C—O—C sym. stret.).

^1H NMR ($CDCl_3$): δ 6.60–8.04 (m, 13H, Ar—H), 6.01 (s, 1H, Ar—C═CH), 4.61 (br, 2H, —NH_2), 3.78 (s, 3H, —OCH_3)

General procedure for the preparation of dibenzo(b,f)azepine-5-carboxylic acid [4-(4-substituted-5-oxo-2-phenyl-4,5-dihydro-imidazol-1-yl)-phenyl]-amide (4a–j)

Dibenzo(b,f)azepine carbonyl chloride (0.012) (**3**) was taken in 10 mL pyridine and added to the mixture of **2a–j** in pyridine at room temperature and then stirred for 30 min. Then the reaction mixture was heated in a water bath. The reaction was monitored by thin layer chromatography. On completion of the reaction the contents were poured in ice water to give coloured precipitates.

Characterization of dibenzo(b,f)azepine-5-carboxylic acid [4-{4-(4-methoxy-benzylidence)-5-oxo-2-pheny!-4,5-dihydro-imidazol-1-yl}-phenyl]-amide (4a)

Pale white coloured compound. IR (KBr, cm^{-1}) ν_{max}: 3326–3276 (—NH), 3080–3008 ν(Ar—CH), 2972–2916 ν(C═C), 1747 ν(C═O), 1650 ν(C═O amide), 1265 ν(C—O—C asym. stret.), 1161 ν(C═O), 1047 ν(C—O—C sym. stret.).

^1H NMR (DMSO-d_6) δ 6.58–7.89 (m, 23H, Ar—H), 6.18 (s, 1H, Ar—C═CH), 3.75 (s, 3H, —OCH_3), 8.54 (s, —NH).

All the other compounds **2b–j** and **4b–j** were prepared in a similar way; the reaction scheme is given in Fig. 1 and their physical and spectral data are recorded in Tables 1–4.

TABLE-1
PHYSICAL DATA FOR COMPOUNDS 2a–j

Compd.	R	m.p. (°C)	Yield (%)	m.f.	Recrystallization solvent
2a	4-OCH3	128	62.0	$C_{23}H_{19}N_3O_2$	Acetone
2b	4-Cl	142	62.6	$C_{22}H_{16}ClN_3O$	Acetone
2c	4-OH	158	65.1	$C_{22}H_{17}N_3O_2$	Methanol
2d	4-N(CH3)2	174	66.2	$C_{24}H_{22}N_4O$	Dioxane
2e	4-F	148	70.1	$C_{22}H_{16}FN_3O$	Methanol
2f	3-OCH3, 4-OH	160	65.3	$C_{23}H_{19}N_3O_3$	Ethanol
2g	2-OH, 3-OCH3	138	60.1	$C_{23}H_{19}N_3O_3$	Methanol
2h	1-Naphthyl	190	64.1	$C_{32}H_{24}N_4O_4$	DMF
2i	2-Cl-Quinoline	175	67.1	$C_{25}H_{17}ClN_4O$	DMF
2j	H	112	66.0	$C_{22}H_{17}N_3O$	Acetone

TABLE-2
PHYSICAL DATA FOR COMPOUNDS 4a–j

Compd.	R	m.p. (°C)	Yield (%)	m.f.	Recrystallization solvent
4a	4-OCH3	128	62.0	$C_{38}H_{28}N_4O_3$	Dioxane/water
4b	4-Cl	160	66.6	$C_{37}H_{25}ClN_4O_2$	Acetone
4c	4-OH	158	60.1	$C_{37}H_{26}N_4O_3$	Methanol/DMF
4d	4-N(CH3)2	167	61.2	$C_{39}H_{31}N_5O_2$	Dioxane/water
4e	4-F	178	70.1	$C_{37}H_{25}FN_4O_2$	Methanol/DMF
4f	3-OCH3, 4-OH	146	61.3	$C_{38}H_{28}N_4O_4$	Dioxane/water
4g	2-OH, 3-OCH3	138	60.1	$C_{38}H_{28}N_4O_4$	Dioxane/water
4h	1-Naphthyl	126	65.1	$C_{41}H_{28}N_4O_2$	Methanol/DMF
4i	2-Cl-Quinoline	155	68.1	$C_{40}H_{26}ClN_5O_2$	Methanol/DMF
4j	H	172	60.0	$C_{37}H_{26}N_4O_2$	DMF

RESULTS AND DISCUSSION

The structures of all compounds were confirmed by IR, ^{1}H NMR and elemental analyses. The IR spectrum of compound **2a** showed the NH bands at 3326 and 3276 cm^{-1} and the ν(C═O) band at 1740 cm^{-1}. The infrared spectrum of **4a** gave two bands at 1747 ν(C═O) and 1161 ν(C═O) which correspond to the carbonyl in 5-imidazolone and the carbonyl of amide at 1650, which indicates the presence of two carbonyl groups.

The ^{1}H NMR spectrum of **2a** shows broad peak at 4.63 ppm and was assigned the —NH_2 group. The benzylidene proton of **2a** (Ar—C═CH) was found in downfield region at 6.01 ppm. In the spectra of **4a** the —NH proton shifted downfield at 8.28 ppm which is due to the C═O and heterocyclic ring system in close vicinity. Such downfield shift of the —NH proton is reported by several researchers[22]. The benzylidene proton gave a singlet at 6.18 ppm; the other entire proton was obtained in the aromatic region.

The NMR data and elemental content of all the prepared compounds, *viz*. **2a–j** and **4a–j**, are shown in Tables 3 and 4.

TABLE-3
SPECTRAL AND ELEMENTAL DATA FOR **2a–j**

Compd.	R	Found (Calcd.) (%)			^{1}H NMR ($CDCl_3$ and DMSO-d_6) (δ ppm)
		C	H	N	
2a	4-OCH_3	74.65 (74.78)	5.08 (5.18)	11.12 (11.37)	δ 6.60–8.04 (m, 13H, Ar—H), 6.01 (s, 1H, Ph—C═CH), 4.63 (br, 2H, —NH_2), 3.78 (s, 3H, —OCH_3)
2b	4-Cl	70.85 (70.68)	4.21 (4.31)	11.10 (11.24)	δ 6.80–7.85 (m, 13H, Ar—H), 6.25 (s, 1H, Ph—C═CH), 4.60 (br, 2H, —NH_2)
2c	4-OH	74.45 (74.35)	4.62 (4.82)	11.64 (11.82)	δ 6.65–7.80 (m, 13H, Ar—H), 6.30 (s, 1H, Ph—C═CH), 4.54 (s, —OH), 4.63 (br, 2H, —NH_2)
2d	4-$N(CH_3)_2$	75.01 (75.37)	5.62 (5.80)	14.31 (14.65)	δ 6.90–7.84 (m, 13H, Ar—H), 6.36 (s, 1H, Ph—C═CH), 3.65 (s, 6H, $(NCH_3)_2$), 4.63 (br, 2H, —NH_2)
2e	4-F	74.19 (73.94)	4.34 (4.51)	11.51 (11.76)	δ 6.63–7.89 (m, 13H, Ar—H), 6.34 (s, 1H, Ph—C═CH), 4.63 (br, 2H, —NH_2)
2f	3-OCH_3, 4-OH	71.07 (71.27)	4.90 (4.97)	10.81 (10.90)	δ 6.60–7.78 (m, 12H, Ar—H), 6.22 (s, 1H, Ph—C═CH), 4.60 (br, 2H, NH_2), 4.44 (s, —OH), 3.79 (s, 3H, —OCH_3)
2g	2-OH, 3-OCH_3	71.32 (71.67)	4.90 (4.97)	10.81 (10.90)	δ 6.67–7.84 (m, 12H, Ar—H), 6.28 (s, 1H, Ph—C═CH), 4.54 (s, OH), 4.60 (br, 2H, —NH_2), 3.79 (s, 3H, —OCH_3)
2h	1-Naphthyl	72.58 (72.72)	4.40 (4.58)	10.39 (10.60)	δ 6.60–7.88 (m, 16H, Ar—H), 6.25 (s, 1H, Ph—C═CH), 4.60 (br, 2H, —NH_2)
2i	2-Cl-Quinoline	71.02 (70.67)	4.18 (4.03)	13.02 (13.19)	δ 6.69–7.81 (m, 15H, Ar—H), 6.30 (s, 1H, Ph—C═CH), 4.63 (br, 2H, —NH_2)
2j	H	77.14 (77.36)	4.92 (5.05)	12.18 (12.38)	δ 6.90–7.84 (m, 14H, Ar—H), 6.21 (s, 1H, Ph—C═CH), 4.60 (br, 2H, —NH_2)

TABLE-4
SPECTRAL AND ELEMENTAL DATA FOR **4a–j**

Compd.	R	Found (Calcd.) (%)			^{1}H NMR (CDCl$_3$ and DMSO-d$_6$) (δ ppm)
		C	H	N	
4a	4-OCH$_3$	77.20 (77.53)	4.60 (4.79)	9.30 (9.52)	δ 6.58–7.89 (m, 23H, Ar—H), 6.18 (s, 1H, Ar—C=CH), 3.85 (s, 3H, —OCH$_3$), 8.28 (s. —NH)
4b	4-Cl	74.85 (74.93)	4.06 (4.25)	9.30 (9.45)	δ 6.80–7.85 (m, 23H, Ar—H), 6.21 (s, 1H, Ar—C=CH), 8.52 (s, —NH)
4c	4-OH	77.65 (77.34)	4.32 (4.56)	9.49 (9.75)	δ 6.65–7.80 (m, 23H, Ar—H), 4.54 (s, OH, 6.21 (s, 1H, Ar—C=CH), 8.50 (s, —NH)
4d	4-N(CH$_3$)$_2$	78.18 (77.85)	5.05 (5.19)	11.29 (11.64)	δ 6.90–7.84 (m, 23H, Ar—H), 3.65 (s, 6H, —NCH$_3$)$_2$), 6.21 (s, 1H, Ar—C=CH), 8.52 (s, —NH)
4e	4-F	77.49 (77.07)	4.04 (4.37)	9.51 (9.72)	δ 6.63–7.89 (m, 23H, Ar—H), 6.21 (s, 1H, Ar—C=CH), 8.55 (s, —NH)
4f	3-OCH$_3$, 4-OH	75.88 (75.48)	4.50 (4.67)	9.18 (9.27)	δ 6.60–7.78 (m, 22H, Ar—H), 3.85 (s, 3H, —CH$_3$), 4.60 (s, —OH), 6.21 (s, 1H, Ar—C=CH), 8.54 (s, —NH)
4g	2-OH, 3-OCH$_3$	75.92 (75.48)	4.69 (4.67)	9.21 (9.27)	δ 6.67–7.84 (m, 22H, Ar—H), 3.85 (s, 3H, —OCH$_3$), 4.60 (s, —OH), 6.21 (s, —1H, Ar—C=CH), 8.62 (s, —NH)
4h	1-Naphthyl	81.28 (80.90)	4.40 (4.64)	9.39 (9.20)	δ 6.60–7.88 (m, 26H, Ar—H), 6.21 (s, 1H, Ar—C=CH), 8.50 (s, —NH)
4i	2-Cl-Quinoline	74.95 (74.59)	3.99 (4.07)	10.69 (10.87)	δ 6.69–7.81 (m, 25H, Ar—H), 6.21 (s, 1H, Ar—C=CH), 8.44 (s, —NH)
4j	H	78.98 (79.55)	4.40 (4.69)	10.38 (10.03)	δ 6.90–7.84 (m, 24H, Ar—H), 6.21 (s, 1H, Ar—C=CH), 8.60 (s, —NH)

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