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CONVENTIONAL SYNTHESIS AND CHARACTERIZATION OF SOME NOVEL CHALCONES AND THEIR HETEROCYCLIC DERIVATIVES

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ABSTRACT

In the present investigation a series of some novel chalcones **(2a-d)** and their heterocyclic analogs such as Isoxazolines **(3a-d)**, Pyrimidines **(4a-d)**, Pyrazolines **(5a-d)**, Benzodiazepines **(6a-d)** and Benzothiazepines **(7a-d)** respectively, have been conventionally synthesized and characterized by using physical and spectral analytical data.

KEYWORDS: Chalcone, Isoxazoline, Pyrimidine, Pyrazoline, Benzodiazepine, Benzothiazepine.

1. INTRODUCTION

Benzofuran and its derivatives have attracted the attention of chemists since the early 1960s mainly because of the broad spectrum of biological properties exhibited by this class of compounds.[1] The enormous amount of research work that has been conducted in the pharmaceutical laboratories on these compounds during the last few decades derives its inspiration from the discovery of clinically used coronary vasodilators such as Amiodarone and Benziodarone.[2]

Heterocyclic compounds are of immense importance due to their wide spectrum of bioactive properties. These compounds have attracted the attention of chemists and biologists due to their varied nature of potential pharmacological activities.[3] Since the compounds containing heteroatoms such as oxygen, nitrogen and sulfur were reported to possess diverse biological and pharmacological activities [4], as the most important study in the present research work focused on the synthesis of some novel benzofuran linked chalcones and their heterocyclic

derivatives [6-9] by conventional condensation reactions.[10-11] These compounds were further purified by chromatographic methods and identified by physical and spectral analytical data were reporting for the first time.

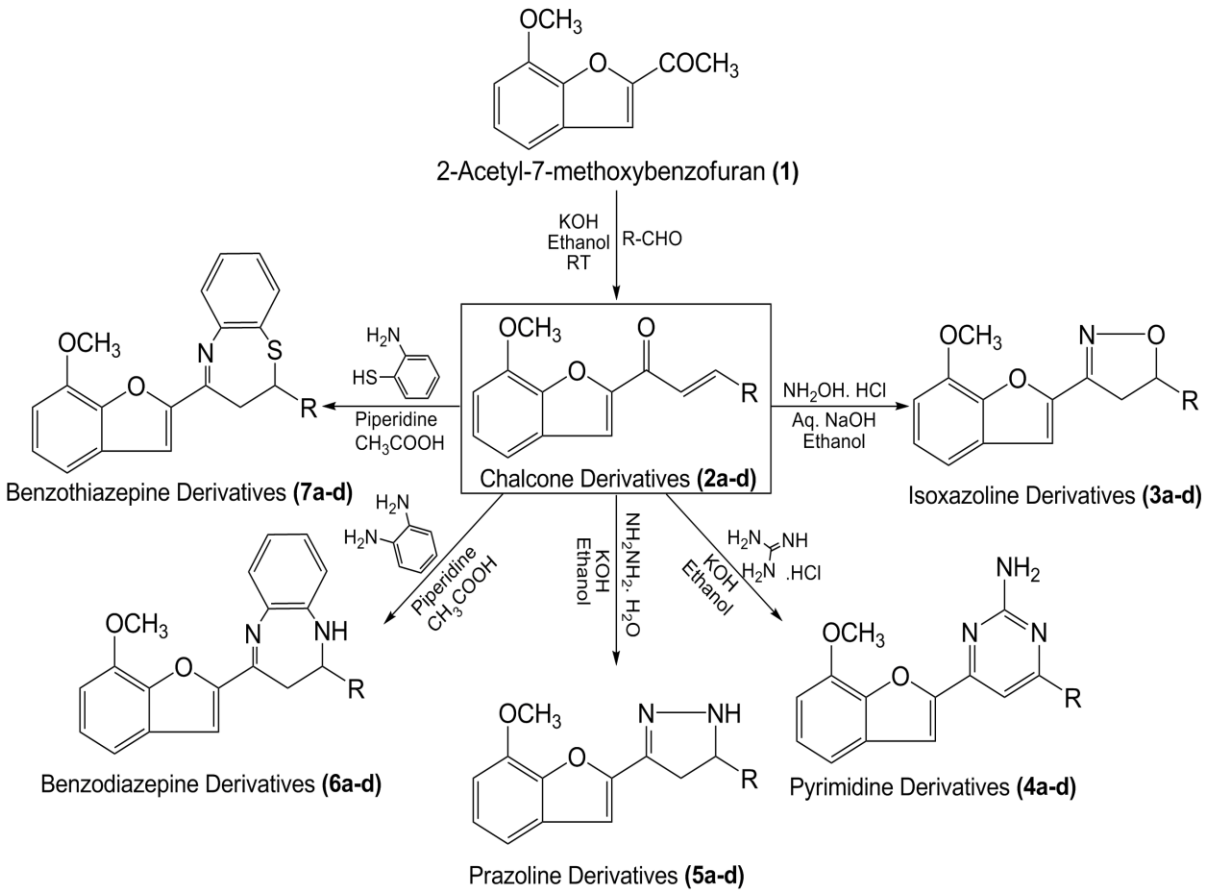
2. MATERIALS AND METHODS

2.1. Instrumentation

Melting points were taken in open capillary tubes and are therefore uncorrected. Purity of the compounds was checked on silica gel G TLC plates of 2 mm thickness using *n*-hexane and ethyl acetate as solvent system. The visualization of spot was carried out in an iodine chamber. The FT-IR spectra were recorded on Perkin-Elmer spectrometer. The ^{1}H NMR spectra were scanned on a Bruker 400 MHz. spectrometer in DMSO-d_6 using TMS as internal standard and chemical shifts are expressed in δ ppm.

2.2. Synthesis

The convention organic reaction sequence planned for the preparation of title compounds is shown in **Scheme 1**, and their physical and spectroscopic properties are depicted in **Table 1**.



Scheme 1. Reactions and reagents for the synthesis of titled compounds

2.2.1. General procedure for the synthesis of Chalcones (2a-d)

Chalcones were prepared by using standard Claisen-Schmidt condensation reaction between 2-acetyl-7-methoxylbenzofuran **(1)** and appropriate aromatic aldehydes **(a: Benzaldehyde, b: 4-Methoxybenzaldehyde, c: 4-Hydroxybenzaldehyde and d: 4-Fluorobenzaldehyde)** in the presence of 15% potassium hydroxide solution in ethanol afforded to give corresponding **1-(7-Methoxybenzofuran-2-yl)-3-(substituted)prop-2-en-1-ones (2a-d) in good yield.**

2.2.2. General procedure for the synthesis of Isoxazolines (3a-d)

Isoxazolines were prepared by subsequent condensation reaction of chalcone derivatives **(2a-d)** and hydroxylamine hydrochloride with catalytic amount of 20% sodium hydroxide in ethanol was taken in a round bottomed flask and refluxed for 6 hrs. Then reaction mixture was cooled to room temperature and treated with cold water. The solid separated was isolated by simple Buchner filtration; final purification was achieved by recrystallization from ethanol to give corresponding **3-(7-Methoxybenzofuran-2-yl)-5-substituted-4,5-dihydroisoxazoles (3a-d)** in good yield.

2.2.3. General procedure for the synthesis of Pyrimidines (4a-d)

Pyrimidines were prepared by subsequent condensation reaction of chalcone derivatives **(2a-d)** and guanidine hydrochloride with catalytic amount of 20% potassium hydroxide in ethanol was taken in a round bottomed flask and refluxed for 4 hrs. Then reaction mixture was cooled to room temperature and treated with cold water. The solid separated was isolated by simple Buchner filtration; final purification was achieved by recrystallization from ethanol to give corresponding **4-(7-Methoxybenzofuran-2-yl)-6- substituted-pyrimidin-2-amines (4a-d)** in good yield.

2.2.4. General procedure for the synthesis of Pyrazolines (5a-d)

Pyrazolines were prepared by subsequent condensation reaction of chalcone derivatives **(2a-d)** and guanidine hydrochloride with catalytic amount of 100% potassium hydroxide in ethanol was taken in a round bottomed flask and refluxed for 3 hrs. Then reaction mixture was cooled to room temperature and treated with cold water. The solid separated was isolated by simple Buchner filtration; final purification was achieved by recrystallization from ethanol to give corresponding **3-(7-Methoxybenzofuran-2-yl)-5- substituted -4,5-dihydro-1H-pyrazoles (5a-d)** in good yield.

2.2.5. General procedure for the synthesis of Benzodiazepines (6a-d)

Benzodiazepines were prepared by subsequent condensation reaction of chalcone derivatives **(2a-d)** and ortho-phenylenediamine with catalytic amount of acetic acid and piperidine in methanol was taken in a round bottomed flask and refluxed for 12 hrs. Then reaction mixture was cooled to room temperature and treated with cold water. The solid separated was isolated by simple Buchner filtration; final purification was achieved by recrystallization from ethanol to give corresponding **4-(7-Methoxybenzofuran-2-yl)-2-substituted-2,3-dihydro-1H-benzo[b][1,4]diazepines (6a-d)** in good yield.

2.2.6. General procedure for the synthesis of Benzothiazepines (7a-d)

Benzothiazepines were prepared by subsequent condensation reaction of chalcone derivatives **(2a-d)** and ortho-aminothiophenol with catalytic amount of acetic acid and piperidine in methanol was taken in a round bottomed flask and refluxed for 8 hrs. Then reaction mixture was cooled to room temperature and treated with cold water. The solid separated was isolated by simple Buchner filtration; final purification was achieved by recrystallization from ethanol to give corresponding **4-(7-methoxybenzofuran-2-yl)-2- substituted-2,3-dihydrobenzo[b][1,4]thiazepine (7a-d)** in good yield.

3. RESULTS AND DISCUSSION

3.1. Physical and spectral characterization of Chalcone (2a)

The titled compound 2a was analyzed for molecular formula $C_{18}H_{14}O_3$, m.p. 170 ^{0}C. The FT-IR (KBr, ν_{max}, cm^{-1}) and ^{1}H NMR (400 MHz, DMSO-d$_6$, δ, ppm) spectra of **2a** showed characteristic peaks **(Table 1)**. The results of elemental analysis were also in agreement with those of the calculated values. Based on the above spectral data and elemental analysis, the structure of the **2a** was confirmed as **1-(7-methoxybenzofuran-2-yl)-3-(phenyl)prop-2-en-1-one**. All the compounds synthesized in the present study **(2a-d)** were characterized based on the above mentioned physical and spectroscopic methods **(Table 1)**.

3.2. Physical and spectral characterization of Chalcone (3a)

The titled compound **3a** was analyzed for molecular formula $C_{18}H_{15}NO_3$, m.p. 182 ^{0}C. The FT-IR (KBr, ν_{max}, cm^{-1}) and ^{1}H NMR (400 MHz, DMSO-d$_6$, δ, ppm) spectra of **3a** showed characteristic peaks **(Table 1)**. The results of elemental analysis were also in agreement with those of the calculated values. Based on the above spectral data and elemental analysis, the structure of the **3a** was confirmed as **3-(7-methoxybenzofuran-2-yl)-5-phenyl-4,5-**

dihydroisoxazole (3a). All the compounds synthesized in the present study **(3a-d)** were characterized based on the above mentioned physical and spectroscopic methods **(Table 1)**.

3.3. Physical and spectral characterization of Chalcone (4a)

The titled compound **4a** was analyzed for molecular formula $C_{19}H_{15}N_3O_2$, m.p. 155 ^{0}C. The FT-IR (KBr, ν_{max}, cm^{-1}) and ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm) spectra of **4a** showed characteristic peaks **(Table 1)**. The results of elemental analysis were also in agreement with those of the calculated values. Based on the above spectral data and elemental analysis, the structure of the **4a** was confirmed as **4-(7-methoxybenzofuran-2-yl)-6- phenyl-pyrimidin-2-amine (4a)**. All the compounds synthesized in the present study **(4a-d)** were characterized based on the above mentioned physical and spectroscopic methods **(Table 1)**.

3.4. Physical and spectral characterization of Chalcone (5a)

The titled compound **5a** was analyzed for molecular formula $C_{18}H_{16}N_2O_2$, m.p. 233 ^{0}C. The FT-IR (KBr, ν_{max}, cm^{-1}) and ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm) spectra of **5a** showed characteristic peaks **(Table 1)**. The results of elemental analysis were also in agreement with those of the calculated values. Based on the above spectral data and elemental analysis, the structure of the **5a** was confirmed as **3-(7-methoxybenzofuran-2-yl)-5- phenyl -4,5-dihydro-1H-pyrazole (5a)**. All the compounds synthesized in the present study **(5a-d)** were characterized based on the above mentioned physical and spectroscopic methods **(Table 1)**.

3.5. Physical and spectral characterization of Chalcone (6a)

The titled compound **6a** was analyzed for molecular formula $C_{24}H_{20}N_2O_2$, m.p. 210 ^{0}C. The FT-IR (KBr, ν_{max}, cm^{-1}) and ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm) spectra of **6a** showed characteristic peaks **(Table 1)**. The results of elemental analysis were also in agreement with those of the calculated values. Based on the above spectral data and elemental analysis, the structure of the **6a** was confirmed as **4-(7-Methoxybenzofuran-2-yl)-2-phenyl-2,3-dihydro-1H-benzo[b][1,4]diazepine (6a)**. All the compounds synthesized in the present study **(6a-d)** were characterized based on the above mentioned physical and spectroscopic methods **(Table 1)**.

3.6. Physical and spectral characterization of Chalcone (7a)

The titled compound **7a** was analyzed for molecular formula $C_{24}H_{19}NO_2S$, m.p. 115 ^{0}C. The FT-IR (KBr, ν_{max}, cm^{-1}) and ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm) spectra of **7a** showed characteristic peaks **(Table 1)**. The results of elemental analysis were also in agreement with

those of the calculated values. Based on the above spectral data and elemental analysis, the structure of the **7a** was confirmed as **4-(7-methoxybenzofuran-2-yl)-2- phenyl-2,3-dihydrobenzo[b][1,4]thiazepine (7a)**. All the compounds synthesized in the present study **(7a-d)** were characterized based on the above mentioned physical and spectroscopic methods **(Table 1)**.

Table 1. Physical and spectral characterization of titled compounds.

S.No	Code	R	Molecular Formula	MW (g)	M.p. (^oC)	Yield (%)	FT-IR (KBr,ν_{max},cm^{-1})	^1H NMR (400 MHz, DMSO-d_6, δ, ppm)
1	**2a**	C_6H_5	$C_{18}H_{14}O_3$	278	170	75	Chalcone 1621 (C=O) 1506 (C=C)	Chalcone Hα (7.3) Hβ (6.9)
2	**2b**	4-$OMeC_6H_4$	$C_{19}H_{16}O_4$	308	163	69	Chalcone 1622 (C=O) 1505 (C=C)	Chalcone Hα (7.4) Hβ (6.7)
3	**2c**	4-OHC_6H_4	$C_{18}H_{14}O_4$	294	169	81	Chalcone 1622 (C=O) 1511 (C=C)	Chalcone Hα (7.1) Hβ (6.5)
4	**2d**	4-FC_6H_4	$C_{18}H_{13}FO_3$	296	141	69	Chalcone 1625 (C=O) 1507 (C=C)	Chalcone Hα (7.8) Hβ (7.1)
5	**3a**	C_6H_5	$C_{18}H_{15}NO_3$	293	182	77	Isoxazoline ring 1650 (C=N-O) 1230 (C-O-N)	Isoxazoline ring Ar-CH_2 (3.8, 3.2) Ar-CH (6.2)
6	**3b**	4-$OMeC_6H_4$	$C_{19}H_{17}NO_4$	323	174	64	Isoxazoline ring 1651 (C=N-O) 1231 (C-O-N)	Isoxazoline ring Ar-CH_2 (3.9, 3.2) Ar-CH (6.1)
7	**3c**	4-OHC_6H_4	$C_{18}H_{15}NO_4$	309	121	75	Isoxazoline ring 1653 (C=N-O). 1232 (C-O-N)	Isoxazoline ring Ar-CH_2 (3.9, 3.2) Ar-CH (6.1)
8	**3d**	4-FC_6H_4	$C_{18}H_{14}FNO_3$	311	139	85	Isoxazoline ring 1655 (C=N-O) 1232 (C-O-N)	Isoxazoline ring Ar-CH_2 (3.8, 3.2) Ar-CH (6.2)
9	**4a**	C_6H_5	$C_{19}H_{15}N_3O_2$	317	155	81	Pyrimidine ring 1621 (C=N)	Pyrimidine ring Ar-CH (5.95)
10	**4b**	4-$OMeC_6H_4$	$C_{20}H_{17}N_3O_3$	347	167	85	Pyrimidine ring 1622 (C=N)	Pyrimidine ring Ar-CH (5.92)
11	**4c**	4-OHC_6H_4	$C_{19}H_{15}N_3O_3$	333	182	74	Pyrimidine ring 1621 (C=N)	Pyrimidine ring Ar-CH (5.96)
12	**4d**	4-FC_6H_4	$C_{19}H_{14}FN_3O_2$	335	157	77	Pyrimidine ring 1621 (C=N)	Pyrimidine ring Ar-CH (5.92)
13	**5a**	C_6H_5	$C_{18}H_{16}N_2O_2$	292	233	67	Pyrazoline ring 1630 (C=N) 3241 (-NH-)	Pyrazoline ring Ar-CH_2 (3.8, 3.1) Ar-CH (5.9)
14	**5b**	4-$OMeC_6H_4$	$C_{19}H_{18}N_2O_3$	322	229	81	Pyrazoline ring	Pyrazoline ring

							1630 (C=N) 3233 (-NH-)	Ar-CH_2 (3.5, 3.4) Ar-CH (5.8)
15	**5c**	4-OHC_6H_4	$C_{18}H_{16}N_2O_3$	308	215	72	Pyrazoline ring 1630 (C=N) 3230 (-NH-)	Pyrazoline ring Ar-CH_2 (3.3, 3.9) Ar-CH (5.8)
16	**5d**	4-FC_6H_4	$C_{18}H_{15}FN_2O_2$	310	199	77	Pyrazoline ring 1630 (C=N) 3213 (-NH-)	Pyrazoline ring Ar-CH_2 (3.7, 3.4) Ar-CH (5.8)
17	**6a**	C_6H_5	$C_{24}H_{20}N_2O_2$	363	210	71	Benzodiazepine ring 1630 (C=N) 3243 (-NH-)	Benzodiazepine ring Ar-CH_2 (3.7, 3.4) Ar-CH (5.4)
18	**6b**	4-$OMeC_6H_4$	$C_{25}H_{22}N_2O_3$	398	188	88	Benzodiazepine ring 1630 (C=N) 3226 (-NH-)	Benzodiazepine ring Ar-CH_2 (3.8, 3.4) Ar-CH (5.4)
19	**6c**	4-OHC_6H_4	$C_{24}H_{20}N_2O_3$	384	197	69	Benzodiazepine ring 1630 (C=N) 3216 (-NH-)	Benzodiazepine ring Ar-CH_2 (3.9, 3.1) Ar-CH (5.5)
20	**6d**	4-FC_6H_4	$C_{24}H_{19}FN_2O_2$	386	191	79	Benzodiazepine ring 1630 (C=N) 3221 (-NH-)	Benzodiazepine ring Ar-CH_2 (3.2, 3.9) Ar-CH (5.5)
21	**7a**	C_6H_5	$C_{24}H_{19}NO_2S$	385	115	67	Benzothiazepine ring 781 (C-S) 3240 (-NH-)	Benzothiazepine ring Ar-CH_2 (3.4, 3.2) Ar-CH (6.2)
22	**7b**	4-$OMeC_6H_4$	$C_{25}H_{21}NO_3S$	415	124	73	Benzothiazepine ring 782 (C-S) 3242 (-NH-)	Benzothiazepine ring Ar-CH_2 (3.4, 3.2) Ar-CH (6.3)
23	**7c**	4-OHC_6H_4	$C_{24}H_{19}NO_3S$	401	129	84	Benzothiazepine ring 782 (C-S) 3235 (-NH-)	Benzothiazepine ring Ar-CH_2 (3.4, 3.2) Ar-CH (6.1)
24	**7d**	4-FC_6H_4	$C_{24}H_{18}FNO_2S$	403	140	61	Benzothiazepine ring 783 (C-S) 3222 (-NH-)	Benzothiazepine ring Ar-CH_2 (3.4, 3.2) Ar-CH (6.0)

4. REFERENCES

1. Scammells, P. J.; Baker, S. P.; Beauglehole, A. R. Bioorg. Med. Chem. 1998; 6: 1517.
2. Tsai, I. L.; Hsieh, C. F.; Duh, C. Y. Phytochem. 1998; 48: 1371.
3. Lowig, C. J. Pogg. Ann. 1836; 37: 552.
4. Katritzky, A. R.; Cui, X.; Long, Q.; Yang, B.; Zhang, Y. K.; Wilcox, A. Org. Prep. Proced. Int. 2000; 32: 175.

5. YR Prasad; PR Kumar; CA Deepti; MV Ramana, E-Journal of Chemistry., 2006; 3(13): 236- 241.
6. EV Rao; YR Prasad, Phytochemistry., 1992; 31: 2121.
7. SK Kumar; E Hager; C Pettit; H Gurulingappa; NE Davidson; SR Khan, J. Med Chem., 2003; 46: 2813.
8. MR jayapal; KS Prasad; NY Sreedhar, J. Chem. Pharm. Res., 2010; 2(3): 127.
9. MS Cheng; RS Li; G Kenyon, Chin Chem Lett., 2000; 11(10): 851.
10. G Thinurayanan; G Vanangamudi, E-Journal of Chemistry., 2007; 4(1): 90.
11. M Zeng; L Wang; J Shao; Q Zhong, Synth Commun., 1997; 27(2): 351.