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Synthesis of Various Heterocycles from 3-(Naphthylene-3-yl)-1H-pyrazol-4-carbaldehyde

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Various substituted *o*-hydroxy acetophenone (**1**), on condensation with 3-(naphthylene-3-yl)-1H-pyrazol-4-carbaldehyde (**2**) yields 1-(2-hydroxyphenyl)-3-(3-naphthalen-3-yl)-1-(phenyl-1H-pyrazol-4-yl)prop-2-en-1-one (**3**), which on treatment with hydrazine and catalytic amount of iodine in presence DMSO gives pyrazoline (**4**) and chromone derivatives (**5**), respectively. Compound **5** reacts with hydrazine in ethanol to afford the pyrazole **6**. The constitution of these compounds was elucidated on the basis of spectral studies.

Key Words: Chalcone, Pyrazoline, Chromone and Pyrazole.

INTRODUCTION

Chalcones or 1,3-diaryl-2-propen-1-ones are natural or synthetic compounds belonging to the flavonoid family. Literature survey revels that chalcones have attracted considerable attention as they are endowed with wide spectrum of activities like, antiviral[1], insecticidal[2] and antimicrobial[3].

Pyrazolines are well known and important nitrogen-containing five-membered heterocyclic compounds. Several pyrazoline derivatives have been found to posses considerable biological activities including anti-inflammatory[4], antomicrobial[5], antiviral[6] and anti-HIV[7]. Chromones have broad spectrum of application in the field of synthetic chemistry[8], pharmocological[9] and physiological processes[10].

2-Phenyl chromone and 5-styrylchromones are a group of flavonoid type compounds widely occurring in plants, where they play several biological function[11]. Last decade 5-hydroxy-2-strylchromones were obtained from the blue-green algae[12] *Chrysophaeum taylari*. These compounds show potent *in vitro* cytotoxic activity against leukemia cells[12]. Pyrazole, an important class of compounds in medicinal chemistry, constitute the basic framework of drugs such as celecoxib and are well recognized for their multifaceted pharmacological[13] and medicinal applications[14]. Pyrazole derivatives have been associated with various biological activities such as antiinflammatory[15], fungicidal[16] and antibacterial activity[17].

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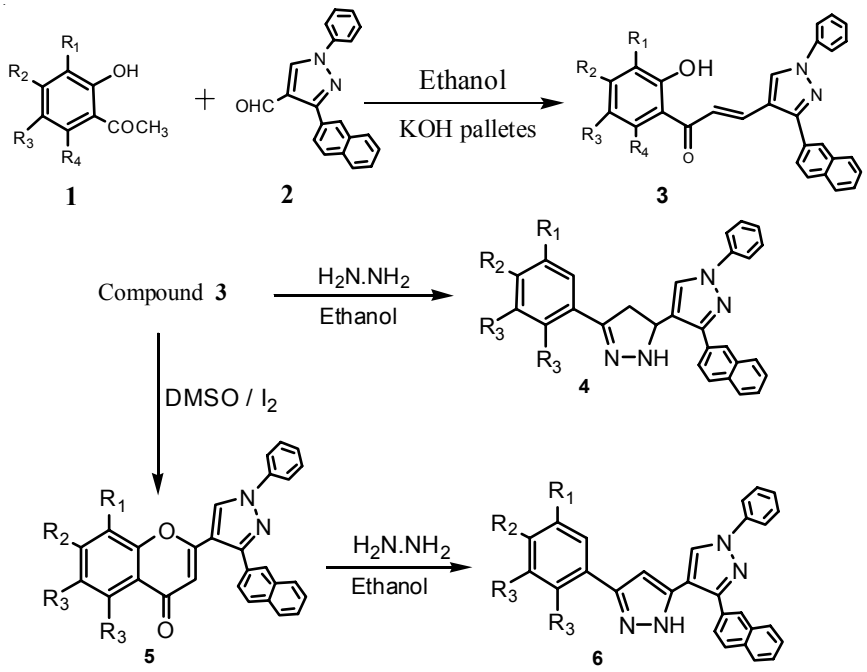
Keeping in view of these observations and in continuation of our work on chalcone[18], pyrazoline[19], chromone[20] and pyrazole[21] derivatives, herein we wish to report synthesis of these heterocycles (**Scheme-I**) containing naphthalene moiety.



Scheme-I

EXPERIMENTAL

All the recorded melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded on Perkin-Elmer FTIR spectrophotometer in KBr disc. ^{1}H NMR spectra were recorded on Varian 300 MHz spectrophotometer in DMSO as a solvent and TMS as an internal standard. Peak values are shown in δ ppm. Mass spectra were obtained by Finnigan mass spectrometer.

General procedure

1-(2-hydroxyphenyl)-3-(3-naphthalen-3-yl)-1-phenyl-1H-pyrazol-4-yl) prop-2-en-1-one (3): 3-(Naphthylene-3-yl)-1H-pyrazol-4-carbaldehyde (0.005 mol) **2** and *o*-hydroxy acetophenone **1** (0.005) were taken in 100 mL round bottom flask with 25 mL dioxane. To this reaction 2 g of KOH was added and resulting reaction was stirred at room temperature for 24 h. Then contents were poured over crushed ice and acidified

with conc. HCl, solid thus obtained were separated by filtration and crystallized from proper solvent to get compounds **3**. Products obtained were identified with the help of spectral data. Compounds **3a-l** was synthesized similarly. The physical data of **3a-l** are given in Table-1.

IR (ν_{max}, cm^{-1}) (**3a**): 3459(-OH), 1643(-C=O), 1574(Ar-C=O), 1574(C=N); NMR (in δ ppm) (**3a**): 2.37 (s, 3H, $-CH_3$), 6.88 (d, 1H, ethylene proton), 6.92 (d, 1H, ethylene proton), 7.26 to 8.77 (m, 15H, Ar-H), 9.64 (s, 1H, pyrazole proton), 12.71 (s, 1H,-OH); Mass (m/z) (**3a**): 331.

4-(4, 5-dihydro-3-phenyl-1H-pyrazol-5-yl)-3-(naphthalene-3-yl)-1-phenyl-1H-pyrazole (4): Compounds **3** (0.003 mol) were taken in 100 mL RBF with 15 mL dioxane. To this reaction mixture 1 mL hydrazine hydrate was added and the contents were heated under refluxed for 4 h. Then add to the reaction mixture 1 mL glacial acetic acid and heating was continued for further 3 h. After complete heating contents were cooled to room temperature and poured over crushed ice. The solid thus obtained was separated by filtration and crystallized with acetic acid to get compounds **4**. Products obtained were identified with help of spectral data. Their characterization data is given in the Table-1. Compounds **4a-l** was synthesized similarly. The physical data of **4a-l** are given in Table-1.

IR (ν_{max}, cm^{-1}) (**4a**): 1663(-C=N), 1597(-C=N group), 1499(-C-N group); NMR (in δ ppm) (**4a**): 2.17(s, 1H, $-CH_3$), 3.18(dd, 1H, One of the methylene proton), 3.64(dd, 1H, One of the methylene proton), 5.94(dd, 1H, C-H), 6.78 to 8.17(m, 19H, Ar-H), 10.01(s, 1H, -O-H).

2-(3-(Naphthalene-3-yl)-1-phenyl-1H-pyrazol-4-yl)-4H-chromon-4-one (5): 1-(2-hydroxyphenyl)-3-(3-naphthalen-3-yl)-1-phenyl-1H-pyrazol-4-yl) prop-2-en-1-one (0.005 mol) **3** and iodine crystal (0.005 mol) were taken in 100 mL RBF with 5 mL DMSO. Resulting reaction was refluxed for 3 h. Then contents were poured over crushed ice, solid thus obtained were separated by filtration and crystallized from proper solvent to get compounds **5**. Products obtained were identified with help of spectral data. Compounds **5a-l** was synthesized similarly. The physical data of **5a-l** are given in Table-1.

IR (ν_{max}, cm^{-1}) (**5a**): 3053(=C-H), 1644(-C=O chromone group), 1609 (-C=N), 1561(-C-N); NMR (in δ ppm) (**5a**): 2.44(s, 3H, -CH3), 6.44 (s, 1H,-C3-H Chromone), 7.19 to 8.19(m, 15H, Ar-H), 8.49(s, 1H, Pyrazole proton).

5-(3-(Naphthalene-3-yl)-1-phenyl-1H-pyrazol-4-yl)-3-phenyl-1H-pyrazole (6): Compounds **5** (0.003 mol) were taken in 100 mL round bottom flask with 15 mL ethanol. To this reaction mixture 1 mL hydrazine hydrate was added and the contents were heated under refluxed for 4 h. Then to the reaction mixture 1 mL glacial acetic acid and heating was continued for further 3 h. After complete heating contents were cooled to

TABLE-1
CHARACTERIZATION DATA OF SYNTHESIZED COMPOUNDS **3**, **4**, **5** AND **6**

Compd.	R_1	R_2	R_3	R_4	m.p. (ºC) [Yield (%)]	Elemental analysis: Found (Calcd.) %		
						C	H	N
3a	H	H	CH_3	H	198 [62]	88.85 (80.91)	5.12 (5.15)	6.49 (6.51)
3b	H	H	Cl	H	184 [65]	74.50 (74.58)	4.21 (4.25)	6.20 (6.21)
3c	Cl	H	Cl	H	236 [68]	69.20 (69.29)	3.78 (3.75)	5.80 (5.77)
3d	CH_3	H	Cl	H	200 [66]	74.78 (74.81)	4.56 (4.55)	6.02 (6.03)
3e	CH_3	H	CH_3	H	248 [59]	81.00 (81.06)	5.40 (5.44)	6.28 (6.30)
3f	H	CH_3	H	CH_3	186 [61]	81.00 (81.06)	5.41 (5.44)	6.29 (6.30)
3g	H	H	H	H	250 [58]	80.70 (80.75)	4.82 (4.84)	6.75 (6.73)
3h	H	CH_3	H	H	196 [63]	80.77 (80.91)	5.21 (5.15)	6.50 (6.51)
3i	CH_3	H	H	H	252 [59]	80.89 (80.91)	5.22 (5.15)	6.50 (6.51)
3j	H	H	C_2H_5	H	210 [55]	81.00 (81.06)	5.41 (5.44)	6.27 (6.30)
3k	H	H	Br	H	196 [65]	67.80 (67.89)	3.86 (3.87)	5.64 (5.66)
3l	H	H	F	H	215 [67]	77.35 (77.41)	4.43 (4.41)	6.42 (6.45)
4a	H	H	CH_3	H	185 [56]	78.30 (78.36)	5.42 (5.44)	12.61 (12.60)
4b	H	H	Cl	H	170 [62]	78.30 (72.33)	4.53 (4.55)	12.04 (12.05)
4c	Cl	H	Cl	H	210 [65]	67.30 (67.34)	4.06 (4.04)	12.25 (11.22)
4d	CH_3	H	Cl	H	178 [68]	72.65 (72.72)	4.86 (4.84)	12.72 (11.70)
4e	CH_3	H	CH_3	H	210 [61]	78.50 (78.58)	5.73 (5.72)	12.18 (12.22)
4f	H	CH_3	H	CH_3	165 [63]	78.52 (78.58)	5.74 (5.72)	12.19 (12.22)
4g	H	H	H	H	230 [59]	78.00 (78.12)	5.12 (5.15)	13.04 (13.01)
4h	H	CH_3	H	H	208 [59]	78.30 (78.36)	5.43 (5.44)	12.62 (12.60)

Compd.	R_1	R_2	R_3	R_4	m.p. (ºC) [Yield (%)]	Elemental analysis: Found (Calcd.) %		
						C	H	N
4i	CH_3	H	H	H	240 [58]	78.28 (78.36)	5.42 (5.44)	12.59 (12.60)
4j	H	H	C_2H_5	H	180 [60]	78.50 (78.58)	5.70 (5.72)	12.21 (12.22)
4k	H	H	Br	H	220 [63]	66.01 (66.02)	4.12 (4.16)	10.98 (11.00)
4l	H	H	F	H	235 [66]	74.90 (74.98)	4.71 (4.72)	12.46 (12.49)
5a	H	H	CH_3	H	244 [59]	81.20 (81.29)	4.69 (4.70)	6.52 (6.54)
5b	H	H	Cl	H	280 [62]	74.90 (74.92)	3.85 (3.82)	6.21 (6.24)
5c	Cl	H	Cl	H	270 [66]	69.50 (69.58)	3.36 (3.34)	5.79 (5.80)
5d	CH_3	H	Cl	H	270 [65]	75.15 (75.24)	4.11 (4.14)	6.01 (6.05)
5e	CH_3	H	CH_3	H	240 [61]	81.40 (81.43)	5.04 (5.01)	6.30 (6.33)
5f	H	CH_3	H	CH_3	178 [64]	81.35 (81.43)	5.03 (5.01)	6.31 (6.33)
5g	H	H	H	H	240 [60]	81.10 (81.14)	4.32 (4.38)	6.79 (6.76)
5h	H	CH_3	H	H	142 [62]	81.20 (81.29)	4.73 (4.70)	6.53 (6.54)
5i	CH_3	H	H	H	267 [62]	81.20 (81.29)	3.38 (4.70)	6.51 (6.54)
5j	H	H	C_2H_5	H	252 [61]	81.41 (81.43)	5.04 (5.01)	6.30 (6.33)
5k	H	H	Br	H	288 [65]	68.10 (68.17)	3.46 (3.47)	5.62 (5.68)
5l	H	H	F	H	260 [68]	77.70 (77.77)	3.94 (3.96)	6.43 (6.48)
6a	H	H	CH_3	H	170 [61]	78.65 (78.71)	5.01 (5.01)	12.65 (12.66)
6b	H	H	Cl	H	165 [65]	72.60 (72.65)	4.14 (4.14)	12.12 (12.10)
6c	Cl	H	Cl	H	294 [67]	67.55 (67.61)	3.65 (3.65)	11.22 (11.26)
6d	CH_3	H	Cl	H	172 [64]	72.90 (73.03)	4.44 (4.44)	11.72 (11.75)
6e	CH_3	H	CH_3	H	178 [59]	79.80 (78.92)	5.30 (5.30)	12.26 (12.27)
6f	H	CH_3	H	CH_3	150 [57]	78.80 (78.92)	5.30 (5.30)	12.25 (12.27)

Compd.	R_1	R_2	R_3	R_4	m.p. (ºC) [Yield (%)]	Elemental analysis: Found (Calcd.) %		
						C	H	N
6g	H	H	H	H	195 [58]	78.45 (78.49)	4.70 (4.70)	13.03 (13.08)
6h	H	CH_3	H	H	120 [61]	78.48 (78.51)	5.01 (5.01)	12.63 (12.66)
6i	CH_3	H	H	H	192 [58]	78.45 (78.51)	5.01 (5.01)	12.62 (12.66)
6j	H	H	C_2H_5	H	160 [59]	78.85 (78.92)	5.30 (5.30)	12.24 (12.27)
6k	H	H	Br	H	198 [63]	66.25 (66.28)	3.77 (3.77)	11.03 (11.04)
6l	H	H	F	H	128 [62]	75.30 (75.32)	4.29 (4.29)	12.51 (12.55)

room temperature and poured over crushed ice. The solid thus obtained was separated by filtration and crystallized with acetic acid to get compounds **6**. Products obtained were identified with help of spectral data. Their characterization data is given in the Table-1.

IR (ν_{max}, cm^{-1}) (**6c**):3336 (-O-H), 3053(=C-H), 1698(Ar-C=N), 1598 (C=N), 1501(C-N), 546 (C-Cl); NMR (in δ ppm) (**6c**): 6.66 to 8.77 (m, 15H, Ar-H), 7.88(s, 1H, Pyrazole proton), 8.15 (s, 1H, -NH), 8.59 (s, 1H, -OH).

RESULTS AND DISCUSSION

In present investigation differently substituted *o*-hydroxy acetophenone (**1**) were condensed with 3-(naphthalene-3-yl)-1H-pyrazol-4-carbaldehyde (**2**) to get compounds 1-(2-hydroxyphenyl)-3-(3-naphthalen-3-yl)-1-phenyl-1H-pyrazol-4-yl) prop-2-en-1-one (**3**).

Compound **3** when treated with hydrazine hydrate and were refluxed in DMSO with catalytic amount of iodine to obtain 4-(4,5-dihydro-3-phenyl-1H-pyrazol-5-yl)-3-(naphthalene-3-yl)-1-phenyl-1H-pyrazole (**4**) and 2-(3-(naphthalene-3-yl)-1-phenyl-1H-pyrazol-4-yl)-4H-chromon-4-one (**5**) respectively.

Differently substituted 2-(3-(naphthalene-3-yl)-1-phenyl-1H-pyrazol-4-yl)-4H-chromon-4-one (**5**) were refluxed with hydrazine hydrate in ethanol to get compounds 5-(3-(naphthalene-3-yl)-1-phenyl-1H-pyrazol-4-yl)-3-phenyl-1H-pyrazole (**6**).

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