Asian Journal of Chemistry Vol, 4, No. 1, (1992), 166–170

A Novel Synthesis of Pyrazolyl Chromone Derivatives

M. S. S. SHANKER, R. B. REDDY, G. V. P. CHANDRA MOULI* AND Y. D. REDDY

Department of Chemistry
Regional Engineering College, Warangal–506 004, India

A new approach to synthesize pyrazolyl chromones (II and IV) by cyclisation of chalcones with hydrazine hydrate is reported. The behaviour of different chromones with hydrazine hydrate under different conditions is also studied. The biological activity of few selected compounds is evaluated.

INTRODUCTION

Survey of literature reveals that very few pyrazolyl chromones are reported though they have wide range of pharmacological activity[1-4]. The general methods of synthesis of these compounds involve either the cyclisation of the pyrazole analogues of chalcones or ring opening and simultaneous cyclisation of bichromones and benzodipyrones by the reaction of hydrazine. We have synthesised a few pyrazolyl chromones in a modified approach and tested the reactivity of chromone ring with hydrazine hydrate under different reaction conditions.

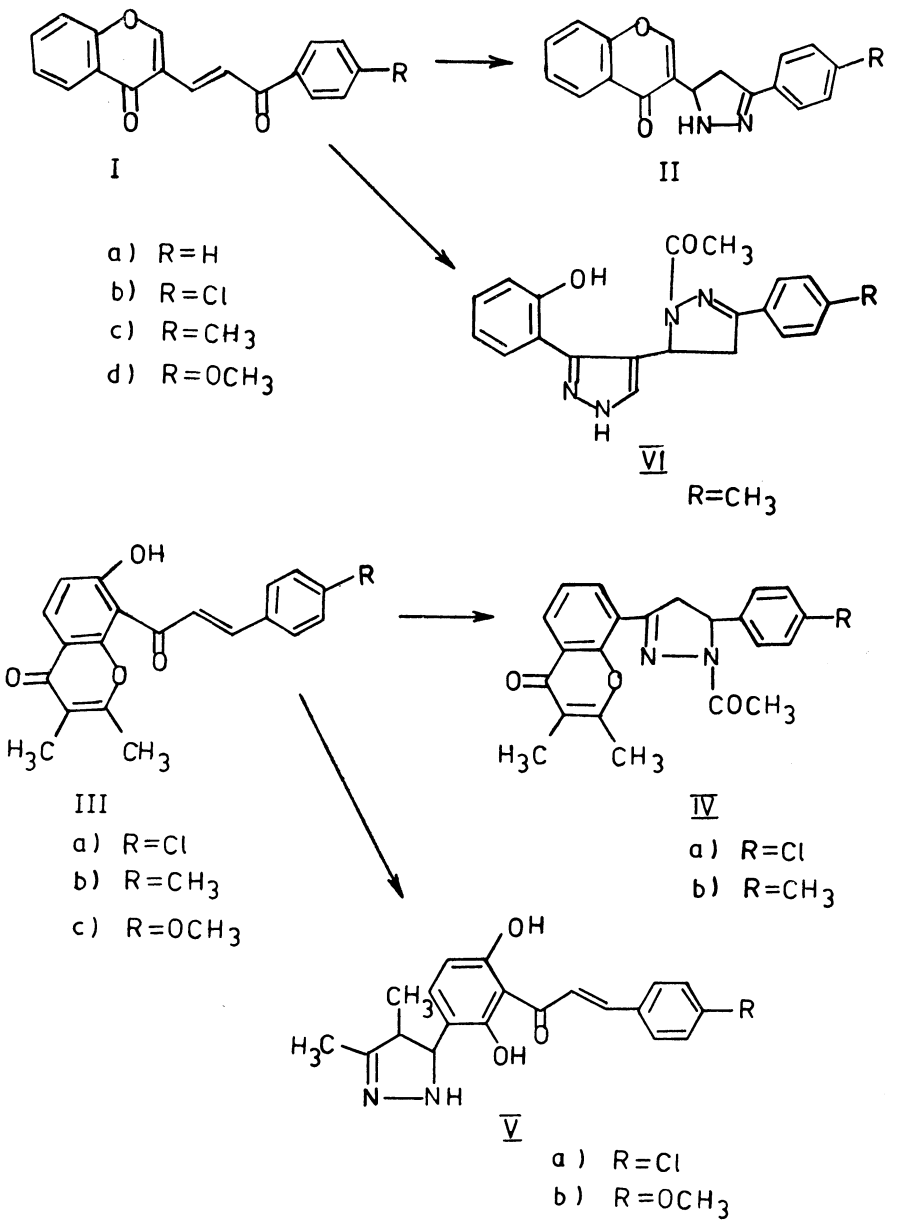
The α, β-unsaturated ketones (I & III), when heated with an equimolar quantity of hydrazine hydrate in glacial acetic acid afforded the corresponding dihydropyrazolyl chromones (II) and N-acetyl-dihyropyrazolyl chromones (IV).

Chromonyl chalcones (III), upon reaction with hydrazine hydrate in alcohol medium, gave the corresponding pyrazole derivatives (V) by the opening of pyrone ring, in which the chalcone portion however remained unaffected.

A mixture of 3-[3-(4-methylphenyl)-3-oxo-1-propenyl]-4H-1-benzopyran-4-one (Ic) and hydrazine hydrate in 1 : 2 molar ratio, when treated with alcohol, followed by the excess addition of glacial acetic acid yielded 1-acetyl-3-(4-methylphenyl)-5-[3-(2-hydroxyphenyl)-1H-pyrazol-4-yl]-4,5-dihydropyrazole (VI).

In excess amount of acetic acid the chalcone part participated in the reaction resulting iu the formation of VI and also the product underwent N-acetylation on the dihydropyrazole nucleus as evidenced by the mass spectrum. It may be probably due to the higher basicity of N—H of dihydropyrazole ring when compared to the N—H of the pyrazole system.

SCHEME 1


I
II
a) R=H
b) R=Cl
c) R=CH3
d) R=OCH3
VI
R=CH3
III
a) R=Cl
b) R=CH3
c) R=OCH3
IV
a) R=Cl
b) R=CH3
V
a) R=Cl
b) R=OCH3

EXPERIMENTAL

Melting points reported were uncorrected. IR data were obtained for KBr discs with Perkin-Elmer Model 283 instrument. PMR spectra were measured at 90 MHz on Varian A–90 spectrometer using TMS as an internal standard (chemical shifts in δ ppm). The mass spectra were recorded on JMS–D 300 mass spectrometer at 70 eV.

3-(3-Aryl-4,5-dihydro-1H-pyrazol-5-yl)-4H-1-benzopyran-4-ones (II) and 8-[1-acetyl-5-(4-aryl)-4,5-dihydropyrazol-3-yl]-7-hydroxy-2,3-dimethyl-4H-1-benzopyran-4-ones (IV): A mixture of the compound (I or III) (0.01 mol), acetic acid (25 ml) and hydrazine hydrate (1 ml) was refluxed for 8 hrs and poured over crushed ice. The solid separated was filtered, washed and dried. Crystallisation was done from methanol.

2-1-Oxo-3,4-aryl-prop-2-en-1-yl]-4-[3,4-dimethyl-1H-pyrazol-5-yl]-1,3-benzenediols (V): Compound III (0.01 mol) in ethyl alcohol (30 ml) was treated with hydrate (99%; 1 ml) and refluxed for 1 hr. It was concentrated and poured over crushed ice. The solid was filtered and purified from benzene.

1-Acetyl-3-(4-methylphenyl)-5-[3-(2-hydroxyphenyl)-1H-pyrazol-4-yl)-4,5-dihydropyrazole (VI): The compound Ic (2.9 g) was treated with hydrazine hydrate (5 ml) in alcohol (20 ml) and refluxed for ½ hr. and then glacial acetic acid (20 ml) was added and continued the heating for 6 hrs. It was cooled and poured over crushed ice. The solid that separated was filtered and purified from dioxan.

RESULTS AND DISCUSSION

Screenlng for Antibacterial Activity

A few selected compounds (IIa, IIb, IVa and Va) were assayed against *Bacillus megaterium* and *Proteus vulgaris* following Vincent and Vincent filter paper disc method[5]. The compounds were tested at 400 and 600 μg/ml concentrations. Almost all the compounds tested were less toxic towards the above two bacteria. But compound IIb was moderately active against *B. megaterium* at 600 μg/ml concentration.

Screening for Antifungal Activity

Compounds used for antibacterial activity were also screened for their antifungal property by adopting glass slide humid chamber technique[6]. The fungi employed were *Dreschlera speciferum* and *Fusarium solani*. The testing was carried out at 360, 600 and 840 μg/ml concentrations. The activity was determined by measuring the zone of inhibition in mm. Compound IIa was found to be highly toxic to both the fungi at 360 μg/ml.

IIb showed zero toxicity against both the fungi even at 840 μg/ml. Compound IVa registered a moderate action against *F. solani* and *D. speciferum*. Rest were inactive towards both the fungi.

TABLE 1

PHYSICAL AND ANALYTICAL DATA OF THE COMPOUND

Compound No.	R	M.pt. °C	Yield %	Analyses % Found/(Calcd.) C	H	N	Formula
IIa	—H	235-6	63	77.29 (77.48)	4.65 (4.81)	9.40 (9.63)	$C_{18}H_{14}N_2O_2$
IIb	—Cl	255-6	68	66.40 (66.66)	4.00 (4.01)	8.60 (8.64)	$C_{18}H_{13}ClN_2O_2$
IIc	—CH_3	240-1	64	74.82 (74.98)	5.15 (5.26)	9.02 (9.20)	$C_{19}H_{16}N_2O_2$
IId	—OCH_3	228-9	60	71.08 (71.25)	4.91 (5.00)	8.67 (8.75)	$C_{19}H_{16}N_2O_3$
IVa	—Cl	220-1	72	63.25 (63.31)	4.60 (4.62)	6.75 (6.82)	$C_{22}H_{19}ClN_2O$
IVb	—CH_3	216-7	70	70.59 (70.76)	5.60 (5.64)	7.10 (7.17)	$C_{23}H_{22}N_2O_4$
Va	—Cl	177-8	80	65.00 (65.11)	4.55 (4.61)	7.40 (7.50)	$C_{20}H_{17}ClN_2O_3$
Vb	—OCH_3	220-1	70	69.01 (69.23)	5.33 (5.49)	7.58 (7.69)	$C_{21}H_{20}N_2O_4$
VI	—CH_3	266-7	60	69.60 (70.00)	5.66 (5.54)	15.51 (15.57)	$C_{21}H_{20}N_4O_2$

IIa : ν_{max} KBr : 3220 (N—H), 1640, 1600 (C=N), 1230 and 1060 (C—O—C) cm^{-1},

IVb : ν_{max} KBr : 3400 (O—H), 1655 (amide C=O), 1630 (pyrone C=O), 1600 (C=N) 1270, 1040 (C—O—C) cm^{-1}

m/z : 390 (M^+), 348, 331, 257, 231, 203, 195, 149, 133, 105, 91 and 71.

Va : ν_{max} KBr : 3315, 3290 (—OH, NH), 1620 (C=O) and 1590 (C=N) cm^{-1}.

m/z : 368 (M+2), 366 (M^+), 351, 257, 229, 216, 203 and 138.

VI : ν_{max} KBr : 3300, 3250 (—OH) and —NH), 2950 (C—H), 1635 (C=O amide) and 1580 (C=N) cm^{-1}.

δ($CDCl_3$) : 2.4 (3H, s, $COCH_3$), 3.8 (3H, s, $-C_6H_4-CH_3$), 5.7 (1H, —CH), 3.2 (2H, d, $-CH_2-$), 6.7-7.5 (8H, m, aromatic) and 7.8 (1H, s, —CH of pyrazole).

m/z : 360 (M^+), 318, 301, 273, 266, 226, 201, 184, 171, 160, 133, 117, 105, 91 and 77.

ACKNOWLEDGEMENTS

The authors are thankful to the Principal, C. K. M. Arts & Science College, Warangal and the Principal, Regional Engineering College, Warangal for providing necessary facilities.

REFERENCES

1. E. C. Hermann and J. Grablickes, *Cancer Chemotherapy Pept.*, **14**, 85 (1961).
2. E. L. Anderson, J. E. Casey Jr., L. C. Green and N. E. Reiff, *J. Med. Chem.*, **1**, 259 (1964).
3. R. Hirschmann, W. J. Palweda and Tishler Max, *J. Med. Chem.*, **1**, 352 (1964).
4. R. E. Orth, *J. Pharm. Sci.*, **57**, 537 (1968).
5. J. C. Vincent and H. W. Vincent, *Proc. Soc. Exp. Biol. Med.*, **55**, 162 (1964).
6. Anonymous, *Phytopath*, **37**, 354 (1947).
7. M. S. S. Shanker, R. B. Reddy, G. V. P. Chandra Mouli and Y. D. Reddy, *J. Indian Chem. Soc.*, **66**, 138 (1989).

[*Received* : 5 March 1990; *Accepted* : 15 November 1990] AJC-244