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Gowravaram Sabitha [a], R. SatheeshBabu [a] & J. S. Yadav [a]
[a] Indian Institute of Chemical Technology, Hyderabad, 500007, India
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ONE POT SYNTHESIS OF 4-(2-HYDROXYBENZOYL)-PYRAZOLES FROM 3-FORMYLCHROMONES UNDER MICROWAVE IRRADIATION IN SOLVENT FREE CONDITIONS

Gowravaram Sabitha,* R. Satheesh Babu and J.S. Yadav

Indian Institute of Chemical Technology, Hyderabad-500 007, India.

Abstract: The synthesis of 4-(-2-hydroxybenzoyl)pyrazoles (**3**) was achieved in a single step by the reaction of 3-formylchromones (**1**) with Phenylhydrazine or Tosylhydrazine under microwave irradiation without a solvent.

4-(2-Hydroxybenzoyl)pyrazoles (**3**)[1] are useful intermediates in the synthesis of biologically important systems such as benzofurans[2,3] and coumarins.[4] The synthesis of these pyrazoles was reported by either a Fries migration of pyrazolyl ester or a Friedel-Crafts reaction of phenyl ethers on 1-phenyl-pyrazol-4-carboxylic acid chloride. The preparation of the acid chloride or the corresponding acid involves more number of steps.[5] This has been overcome by the reaction of readily available substituted 3-formylchromones (**1**)[6] with hydrazines like phenylhydrazine, tosylhydrazine in ethanol furnishing initially hydrazones **2**. These have been further converted into corresponding 4-(2-hydroxybenzoyl)pyrazoles (**3**) by refluxing in acetic acid[7] or ethanolic potassium hydroxide[8] as shown in scheme 1.

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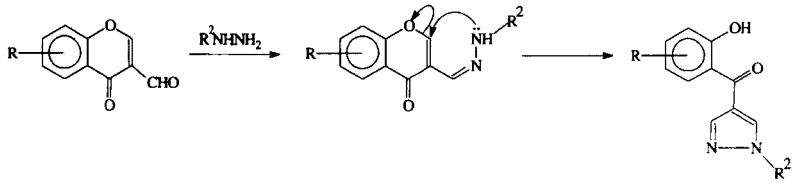
* To whom correspondence should be addressed.

The intermediate hydrazones **2** react further at the C-2 position with concomitant opening of the pyrone ring to give pyrazoles **3**. Ito et al[9] observed detosylation when tosylhydrazone of 3-formylchromone (**2**, R^2=Ts) was treated with aq. NaOH to give pyrazole **3**, where R^2=H.

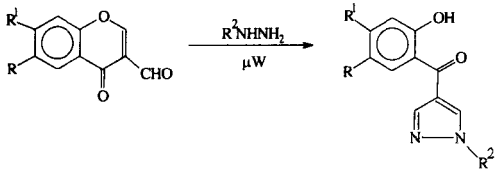
Reported method:



1 **2** **3**

Scheme - 1

3-Formylchromone (**1**) is a versatile synthon in heterocyclic chemistry and exploited in the synthesis of several heterocyclic systems[6] since a convenient synthesis of this molecule was reported by the Vilsmeier-Haack method.[10] Now, we wish to report a facile, one pot synthesis of 4-(2-hydroxybenzoyl)pyrazoles (**3**) from 3-formylchromones (**1**) with hydrazines under microwave irradiation in solvent free conditions (in dry media).



1 **3**

a) R=H, R^1=H
b) R=CH_3, R^1=H
c) R=Cl, R^1=H
d) R=Br, R^1=H
e) R=Cl, R^1=CH_3

R^2=Ph, Ts

Scheme - 2

Microwave assisted organic synthesis is a rapidly developing area in synthetic organic chemistry.[11] In many cases reactions that normally require many hours at reflux temperature under classical conditions can be completed within several minutes or even seconds in microwave. Here we have utilized this technique to the synthesis of pyrazoles in dry media.

Table 1 : Microwave-assisted one pot synthesis of 4-(2-hydroxybenzoyl)pyrazoles (3a-j)

Compd	R	R^1	R^2	Time (mins)	Yield (%)	M.P.(lit) (^{0}C)
3a	H	H	Ph	2.0	79	113(113)
3b	CH_3	H	Ph	1.5	84	119(121)
3c	Cl	H	Ph	2.5	89	146(145)
3d	Br	H	Ph	2.0	73	153(154)
3e	Cl	CH_3	Ph	4.5	71	158
3f	H	H	Ts	1.0	77	138
3g	CH_3	H	Ts	2.0	80	178
3h	Cl	H	Ts	3.0	82	144
3i	Br	H	Ts	1.5	69	125
3j	Cl	CH_3	Ts	4.0	67	127

a) All products were characterised by IR, ^{1}H NMR & Mass Spectra data.
b) Yields reported after crystallisation.

A mixture of equimolar amounts of 3-formylchromone (**1**) and tosylhydrazine was irradiated in a microwave oven for 1 minute to give 1-tosyl-4-(2-hydroxybenzoyl)pyrazole (**3f**) in 77% yield. Under similar conditions several substituted 3-formylchromones (**1**) were treated with phenylhydrazine or tosylhydrazine to give **3a-3j**. All the products were purified by recrystallisation from ethanol and characterised by IR, ^{1}H NMR and mass spectral data

and also by comparing with the authentic samples prepared according to reported procedure[1] by two steps. The compounds **3e-3j** were reported for the first time.

Experimental

Microwave irradiations were carried out using commercial microwave oven (BPL, BMO 700T), operating at a frequency 2450 MHz. Melting points were determined on a Fischer-John's apparatus and are uncorrected. IR and ^{1}H NMR spectra were recorded on NICOLET-740 and Gemini-200 instruments respectively. Mass spectra were recorded on mass 7070 H or Finnigan Mat 1020B mass spectrometer operating at 70ev.

General procedure: A mixture of 3-formylchromone (**1**, 2.85m.mol) and phenylhydrazine or tosylhydrazine (2.85 m.mol) was taken in 25mL conical flask and irradiated in microwave at an output of about 600 Watt for 1-4.5 minutes. The residue was recrystallised in boiling ethanol to give yellow crystalline products (**3a-3j**) in 67-89% yield.

1-Phenyl-4-(5-chloro-2-hydroxy-4-methylbenzoyl)pyrazole (3e):

IR (KBr) : 3126 (br OH), 1634 (CO); ^{1}H NMR($CDCl_3$) : δ 2.44(s,3H, CH_3), 6.94-7.88 (m, 7H, Ar-H), 8.32 (s, 1H, pyrazole H_5), 8.44 (s, 1H, pyrazole H_3), 11.88 (br.1H, ArOH); MS (m/z) M^+ : 344; Anal. Calcd. for $C_{17}H_{13}ClN_2O_2$: C, 59.22; H, 3.80; N, 8.12; O, 18.56; found : C, 59.01; H, 3.95; N, 8.14; O, 18.48.

1-Tosyl-4-(2-hydroxybenzoyl)pyrazole (3f):

IR (KBr) : 3120 (br OH), 1630 (CO); ^{1}H NMR($CDCl_3$) : δ 2.44(s,3H, CH_3), 6.95-7.98 (m, 8H, Ar-H), 8.08 (s, 1H, pyrazole H_5), 8.45 (s, 1H, pyrazole H_3), 12 (br.1H, ArOH); MS (m/z) M^+ : 342; Anal. Calcd. for $C_{17}H_{14}N_2O_4S$: C, 59.46; H, 4.40; N, 8.14; O, 18.63; S, 9.36; found : C, 59.57; H, 4.28; N, 8.08; O, 18.68; S, 9.47.

1-Tosyl-4-(2-hydroxy 5-methylbenzoyl)pyrazole (3g):

IR (KBr) : 3120 (br OH), 1634 (CO); ^{1}H NMR($CDCl_3$) : δ 2.44(s,3H, CH_3), 2.46 (s, 3H, CH_3), 7.25-7.92 (m, 8H, Ar-H), 8.08 (s, 1H, pyrazole H_5), 8.40 (s, 1H, pyrazole

H_3), 11.2 (br.1H, ArOH); MS (m/z) M^+ : 356; Anal. Calcd. for $C_{18}H_{16}N_2O_4S$: C, 60.66; H, 4.52; N, 7.86; O, 17.95; S, 8.99; found : C, 60.70; H, 4.46; N, 7.78; O, 17.91; S, 8.83.

1-Tosyl-4-(5-chloro-2-hydroxybenzoyl)pyrazole (3h):

IR (KBr) : 3124 (br OH), 1630 (CO); ^{1}H NMR($CDCl_3$) : δ 2.44(s,3H, CH_3), 6.96-7.84 (m, 8H, Ar-H), 8.08 (s, 1H, pyrazole H_5), 8.45 (s, 1H, pyrazole H_3), 11.7 (br.1H, ArOH); MS (m/z) M^+ : 376; Anal. Calcd. for $C_{17}H_{13}ClN_2O_4S$: C, 54.18; H, 3.47; N, 7.43; O, 16.98; S, 8.50; found : C, 54.22; H, 3.38; N, 7.41; O, 16.87; S, 8.31.

1-Tosyl-4-(5-bromo-2-hydroxybenzoyl)pyrazole (3i):

IR (KBr) : 3122 (br OH), 1633 (CO); ^{1}H NMR($CDCl_3$) : δ 2.44(s,3H, CH_3), 6.92-8.1 (m, 8H, Ar-H), 8.35 (s, 1H, pyrazole H_5), 8.40 (s, 1H, pyrazole H_3), 11.72 (br.1H, ArOH); MS (m/z) M^+ : 421; Anal. Calcd. for $C_{17}H_{13}BrN_2O_4S$: C, 48.46; H, 3.11; N, 6.64; O, 15.19; S, 7.61; found : C, 48.37; H, 3.15; N, 6.72; O, 15.26; S, 7.58.

1-Tosyl-4-(5-chloro-2-hydroxy-4-methylbenzoyl)pyrazole (3j):

IR (KBr) : 3126 (br OH), 1634 (CO); ^{1}H NMR($CDCl_3$) : δ 2.40(s,3H, CH_3), 2.45(s,3H,CH_3), 6.99-7.98 (m, 7H, Ar-H), 8.12 (s, 1H, pyrazole H_5), 8.42 (s, 1H, pyrazole H_3), 10.39 (br.1H, ArOH); MS (m/z) M^+ : 391; Anal. Calcd. for $C_{18}H_{15}ClN_2O_4S$: C, 55.31; H, 3.86; N, 7.16; O, 16.37; S, 8.20; found : C, 55.43; H, 3.89; N, 7.04; O, 16.41; S, 8.15.

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