Article

JOURNAL OF THE CHINESE CHEMICAL SOCIETY

An Efficient Microwave Assisted Eco-friendly Synthesis of 6-Chloro-3-(3-arylacryloyl)-2-methyl-4-phenylquinolines and their Conversion to 6-Chloro-3-(1-phenyl-5-aryl-4,5-dihydro-1H-pyrazol- 3-yl)-2-methyl-4-phenylquinolines

S. Sarveswari and V. Vijayakumar

Organic Chemistry Division, School of Advanced Sciences, VIT University, Vellore-632014, Tamil Nadu, India

(Received March 21, 2011; Accepted July 14, 2011; Published Online July 27, 2011; DOI: 10.1002/jccs.201100162)

An eco-friendly basic alumina catalyzed protocol for the synthesis of some new quinolinyl chalcones has been developed by microwave assisted methods which in turn are converted to pyrazoline derivatives.

Keywords: Microwave assisted synthesis; Chalcones; Reusable alumina catalyst; Pyrazolines.

INTRODUCTION

The most common and widespread compounds of chalconoid group are the chalcones, which possess a 1,3-diaryl-2-propen-1-one carbon framework. The importance of these compounds is due not only to their colours but also to their chemical in addition to biological activities and the fact that they are good accessible starting materials for construction of various heterocyclic derivatives.[1] They are naturally occurring plant metabolites can be regarded as open-chain flavonoids possess a broad spectrum of biological activities, including antimalarial, antituberculosis, antibacterial, anthelmintic, amoebicidal, antiulcer, antimicrobial, antiprotozoal, cytotoxic, immuno suppressive activities,[1-4] antiviral, insecticidal, antioxidant, antiinflammatory and several anticancer activities such as inhibitors of cancer cellproliferation, carcinogenesis and metastasis.[5-8] Natural and synthetic chalcones have shown strong anti proliferative effects in both primary and established ovarian cancer cells[9] and in gastric cancer HGC-27 cells.[10] Because of α,β-unsaturated ketones in their structures, chalcones have a preferential reactivity towards thiols in contrast to amino and hydroxyl groups. Therefore, chalcones are less likely to interact with nucleic acids and hence avoid the problems of mutagenicity and carcinogenicity associated with certain alkylating agents in cancer chemotherapy.[11] In addition, chalcones are susceptible to the Michael addition at enone (CH=CHCO), which can cause binding to particular receptors and lead to the induction of phase II enzymes against carcinogens.[12]

Chalcones are the intermediate precursors for all flavonoids in the phenyl propanoid pathway in plants and are unique in the flavonoid family[13] for example kava extracts are used for bladder cancer prevention that has kavalactones and flavokawains (chalcones) as the major constituents. Hydroxychalcone derivatives are also reported to have cytotoxic, anti-HIV properties.[14,15] Heme oxygenase activity[16] has been significantly increased by 2-hydroxychalcone, 2,2′-hydroxychalcone and 2,2′,4′-trihydroxy chalcone. The xanthohumol is a potent inhibitor of apo-β-secretion for the prevention of atherosclerosis.[17] Hence there is a continuing interest in efficient synthesis of quinolines and chalcones to get the derivatives with improved activities.[18,19] In continuation of our interest in the synthesis of quinolinyl chalcones,[20] Herein we report the eco-friendly synthesis of chalcones and their conversion to biologically important pyrazolines. Mamolo *et al.*, have synthesized[21] a series of 5-aryl-1-*iso*nicotinoyl-3-(pyridin-2-yl)-4,5-dihydro-1*H*-pyrazoles in a three-step process, in low yields, which involved an aldol condensation, cyclocondensation with hydrazine and N-acylation with *iso*nicotinoyl chloride. Powers *et al.*, reported[22] the synthesis pyrazoline through the reaction of chalcones on phenyl hydrazine hydrochloride in presence of sodium hydroxide in absolute ethanol at 70 °C, but it requires longer reaction time (8 h). Levai *et al.,* synthesized[23] 3,5-diaryl-2-pyrazolines through the reaction of chloro chalcones on phenyl hydrazine in acetic acid under refluxing conditions for 3 h., by keeping the ratio of chlorochalcones and phenyl hydrazine 1:5 ratio, but these reaction conditions suffer economic and environmental concerns. Carter *et al.*, reported[24] the synthesis of pyrazoline esters as an intermediate in the process α,β-diamino acids. Sahu *et al.,* reported[25] the syn-

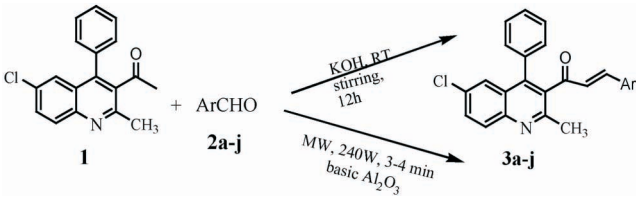
* Corresponding author. Tel: 04162202332; E-mail: sarveswari@gmail.com

thesis of few pyrazoline derivatives with *p*-nitro and *p*-hydroxy group in aryl moiety of pyrazoline analogs. Sayed Amr *et al.*, synthesized[26] the fused pyrazolines with steroidal moieties and evaluated them as 5α-reductase inhibitors, which are found to be comparable to standard drug anastrozole. Hence based on the above literature here in we report the synthesis some new pyrazoline derivatives.

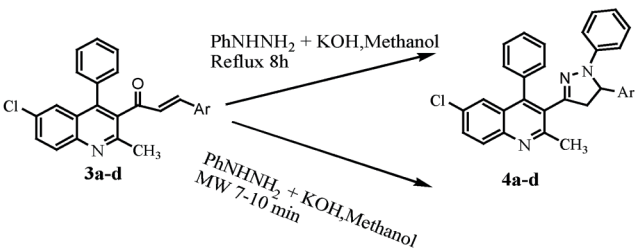
RESULTS AND DISCUSSION

In the present work compound **1** has been converted into its corresponding chalcones namely 6-chloro-3-(3-arylacryloyl)-2-methyl-4-phenylquinolines (**3a-j**) (Scheme I) by stirring the mixture of compound **1** and arylaldehydes in presence of potassium hydroxide in ethanol for 12 h. The completion of the reaction has been monitored by TLC. After completion of the reaction, the reaction mixture was concentrated, poured onto cold water and acidified with acetic acid. The crude product was purified by column chromatography using 8:2 mixture of petroleum ether-ethylacetate. Equimolar mixture of **1** and various arylaldehydes adsorbed on basic alumina was irradiated under the microwave for 2-4 minutes with the power level of 240 W to afford the product **3a-j**. After completion of the reaction, the product was recovered by washing with $CHCl_3$ and the washings were distilled to reuse the chloroform using rotary evaporator. This protocol eliminates useage of excess of alkali and the subsequent neutralisation procedures. The crude product was purified by column chromatography using 8:2 mixture of petroleum ether ethylacetate. The same reaction could be achieved without alumina catalyst with excess of KOH base, the product recovery in this involves neutralization with acetic acid, after evaporation the residue washed with petroleum ether and purified by column chromatography using 8:2 mixture of petroleum ether-ethylacetate. The reaction involved in synthesis of chalcones is Aldol condensation, is normally carried out in presence of bases and acidic work up to avoid the usage of bases, we tried the same reaction with basic alumina catalyst it results in the same chalcone formation. All the synthesized 6-chloro-3-(3-arylacryloyl)-2-methyl-4-phenylquinolines (**3a-j**) have been characterized by IR, ^{1}H NMR spectral data. The compound **3e** has been taken as representative example and its spectral characterization has been described below. The IR spectrum of **3e** shows the following characteristic absorption frequencies: 1657 cm^{-1} (α,β-unsaturated carbonyl), 1573 cm^{-1} (conjugated alkene function). The proton NMR spectrum of **3e** displayed two doublets at δ 6.28 ppm, δ 7.15 ppm with characteristic coupling constant of (*J*) 15.6 Hz, which confirms the formation of chalcones (α,β-unsaturated ketone). This higher coupling constant value indicates, the α,β-unsaturated protons are trans to each other, it also confirmed by single crytal structure of some of similar derivatives. In a similar way, proton chemical shift values of other members in the series are assigned. The compounds **3f**, **3h**, **3l** were recrystallized using ethanol and the obtained single crystals subjected to the X-ray diffraction studies and reported.[27] The compounds (**3a-d**) in turn are converted into pyrazoline derivatives (**4a-d**)[28] (Scheme II).

Scheme I Synthesis of *E*-(6-chloro-3-(3-arylacryloyl)-2-methyl-4-phenylquinolines



Scheme II Synthesis 6-chloro-3-(aryl)-4,5-dihydro-1*H*-pyrazol-3-yl)-2-methyl-4-phenylquinolines



Three doublet of doublets in aliphatic region of ^{1}H NMR spectrum of pyrazoline derivatives (**4a-d**) at δ 2.23 ppm (1H, dd, J_{AM} = 17.7 Hz and J_{AX} = 5.5 Hz), δ 3.26 ppm (1H, dd, J_{AM} = 17.7 Hz and J_{MX} = 12.3 Hz), δ 5.34 ppm (1H, dd, J_{MX} = 12.3 Hz and J_{AX} = 5.5 Hz) confirms the formation of pyrazoline ring. According to Ozdemir *et al.*, hydrozones may formed[28] as intermediate and subsequent addition of -NH on olefinic bond of propenone moiety led to the product. Condensation of chalcones with phenyl hydrazine. The formation of **4a-d** instead of its regioisomer is favored via hydrazone formation.[30] Under these reaction conditions, the product stereochemistry may be determined

by the stereoselective enamine-imine tautomerism take place giving rise to the preferred direction of the proton on C-4 *trans* to the phenyl group at C-5 (Fig. 1). While 3-pyrazoline isomerizes to the more stable 2-pyrazoline.[31]

The proton chemical shift values of other members of this series are assigned and given in experimental section. The yield time, and power level are given in Table 1. When the reaction durations were compared among microwave assisted synthesis and the conventional method for the synthesis of chalcones, present method requires much lesser duration with almost equal yield as in the conventional method. Hence the microwave assisted synthesis can be regarded as an efficient method for the synthesis of these compounds.

EXPERIMENTAL

Solvents and reagents were commercially sourced and used without further purification, which Melting points were taken on Elchem Microprocessor based DT apparatus in open capillary tubes and are corrected with benzoic acid. IR spectra were obtained on an Avatar-330 FTIR spectrophotometer (Thermo Nicolet) using KBr pellets, and only noteworthy absorption levels (reciprocal centimeters) are listed. The NMR spectra were recorded on a Bruker – 400 MHz spectrometer using TMS as internal standard (chemical shifts δ in ppm). Mass spectra were recorded on LCMS by Agilent 1200 series LC and Micromass zQ spectrometer. Microwave oven used is of synthetic microwave: CATA R with maximum power of 700W. Thin-layered chromatography (TLC) was performed on plates coated with TLC silica gel (s.d. fine). Visualization was made with iodine chamber. Column chromatography was performed by using silica gel (*60-120 mesh*). Elemental analysis was done in SAIF-CDRI-Luckow.

General procedure for the synthesis of *E*-(6-chloro-3-(3-arylacryloyl)-2-methyl-4-phenylquinolines) (3a-j)

(a) By microwave assisted method

A mixture of 6-chloro-2-methyl-4-phenylquinoline-3-yl-ethanone (2.95 g, 0.01 mol), aryl aldehyde (0.01 mol)

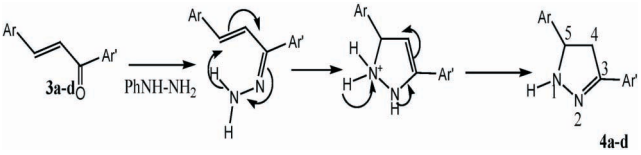


Fig. 1. Mechanism of formation of pyrazolines.

Table 1. Physical data of compound (**3a-j**, **4a-d**)

S. NO	Ar	Time [in min]	Yield[a]	Yield[b]
3a	2-methoxy-8-methylquinolin-3-yl	3	74	68
3b	2-naphthyl	3	78	74
3c	4-fluorophenyl	4	82	75
3d	Thiophen-2-yl	3	80	78
3e	Benzo[d][1,3]dioxo-6-yl	3	85	83
3f	4-ethoxyphenyl	3	73	67
3g	3,4-dimethoxy phenyl	4	85	83
3h	2-methoxyphenyl	4	70	68
3i	3-methoxyphenyl	4	77	63
3j	4-chlorophenyl	4	74	69
4a	2-methoxy-8-methylquinolin-3-yl	7	74	61
4b	2-naphthyl	10	65	62
4c	4-fluorophenyl	10	78	76
4d	Thiophen-2-yl	10	80	75

[a] Yield of microwave assisted synthesis at 240W.
[b] Yield by conventional method.

was dissolved in 3-4 mL chloroform-methanol (1:2) and adsorbed on 1 gm of basic alumina evaporated to dryness in ethanol was irradiated for 3-4 min. at 240 W. The dry solid obtained was cooled and extracted with little amount of chloroform, then the solution was distilled to afford the product as a solid. The crude product was purified by column chromatography using 8:2 mixture of petroleum ether ethylacetate.

(b) Conventional method

A mixture of 6-chloro-2-methyl-4-phenylquinoline-3-yl-ethanone (2.95 g, 0.01 mol), aryl aldehydes (0.01 mol) and 0.5 gm of KOH in ethanol was stirred 12 h at room temperature (The reaction was monitored by thin layer chromatography). The reaction mixture was concentrated and poured on to water and acidified with acetic acid to afford the product as a solid. The crude product was purified by column chromatography using 8:2 mixture of petroleum ether ethylacetate.

Synthesis of 6-Chloro-3-(1-phenyl-5-(3-methoxy-8-methylquinolin-4-yl)-4,5-dihydro-1*H*-pyrazol-3-yl)-2-methyl-4-phenylquinoline (4a)

(a) By conventional method

A mixture of corresponding 6-chloro-3-(3-(2-methoxy-8-methylquinolin-3-yl)acryloyl)-4-phenyl-2-methyl quinoline (**3a**) (0.5 g, 0.001 M) and phenyl hydrazine (0.76

g, 0.007 M) in distilled methanol was refluxed for about 8 h, the resulting mixture concentrated to remove methanol, then poured on to ice and neutralized with dil. HCl. The resultant solid was filtered, dried and purified by column chromatography using 1:1 mixture of chloroform and petroleum ether. The compound was recrystallized from methanol. The reproducibility of the synthetic procedure was checked with other acryloylquinolines (**3b-d**) to get the corresponding pyrazoline derivatives (**4b-d**).

(b) By microwave assisted method

A mixture of corresponding 6-chloro-3-(3-(2-methoxy-8-methylquinolin-3-yl)acryloyl)-4-phenyl-2-methyl quinoline (**3a**) (0.5 g, 0.001 M) and phenyl hydrazine (0.76 g, 0.007 M) in distilled methanol was irradiated for 7-10 min. at 240 W, the resulting mixture concentrated to remove methanol, then poured on to ice and neutralized with dil. HCl. The resultant solid was filtered, dried and purified by column chromatography using 1:1 mixture of chloroform and petroleum ether. The reproducibility of the synthetic procedure was checked with other acryloylquinolines (**3b-d**) to get the corresponding pyrazoline derivatives (**4b-d**).

The compound was recrystallized from methanol. Structural assignments of the products were made on the basis of spectral data.

(3a) Pale yellow solid; Mp: 240-241 °C; IR (KBr): 1656 (C=O), 1565 cm^{-1} (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.72 ppm (s, 3H), 2.88 (s, 3H), 4.06 (s, 3H), 6.77-6.95 (m, 3H), 7.05 (d, 1H, *J* = 16.0 Hz), 7.15 (d, 1H, *J* = 5.1 Hz), 7.39 (d, 2H, *J* = 7.8 Hz), 7.43 (d, 1H, *J* = 16.0 Hz), 7.48 (s, 1H), 7.57 (t, 1H, *J* = 7.5 Hz), 7.72 (d, 1H, *J* = 7.3 Hz), 7.82 (d, 1H, *J* = 8.1 Hz), 7.84 (dd, 1H, *J* = 9.0 Hz, 2.4 Hz), 8.14 (d, 1H, *J* = 9.0 Hz); ESMS: *m/z* 478 [M^+]; *Anal.* Calcd. for $C_{30}H_{23}ClN_2O_2$: C, 75.23; H, 4.84; N, 5.85. Found: C, 74.83; H, 5.04; N, 5.58.

(3b) Yellow solid; Mp: 162-164 °C; IR (KBr): 1556 (C=C), 1689 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.58 (s, 3H), 2.61 (s, 3H), 6.94 (d, 1H, *J* = 16.6 Hz), 7.50 (d, 1H, *J* = 16.6 Hz), 7.53-7.55 (m, 1H), 7.57-7.51 (m, 6H), 7.76 (dd, 1H, *J* = 9.6 Hz, 1.6 Hz), 7.92-7.84 (m, 5H), 8.14 ppm (m, 2H); GCMS: *m/z* 433.2 [M^+].

(3c) Yellow solid; Mp: 145-147 °C; IR (KBr): 1556 (C=C), 1699 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.58 ppm (s, 3H), 6.70 (t, 1H, *J* = 6.2 Hz), 6.79 (d, 1H, *J* = 15.0 Hz), 6.92 (t, 1H, *J* = 8.9 Hz), 7.20 (d, 1H, *J* = 15.0 Hz), 7.22 (d, 1H, *J* = 7.3 Hz), 7.29 (d, 1H, *J* = 7.3 Hz), 7.38-7.45 (m, 5H), 7.39 (d, 1H, *J* = 2.4 Hz), 7.84 (dd, 1H, *J* = 9.0 Hz, 2.4 Hz), 8.11 (d, 1H, *J* = 9.0 Hz); GCMS: *m/z* 401.1 [M^+].

(3d) Very pale yellow solid; Mp: 210-212 °C; IR (KBr): 1657 (C=O), 1571 (C=C) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.63 (s, 3H), 6.28 (d, 1H, *J* = 15.6 Hz), 7.06 (d, 1H, *J* = 3.6 Hz), 7.15 (d, 1H, *J* = 15.6 Hz), 7.22 (t, 1H, *J* = 4.0 Hz), 7.32-7.36 (m, 5H), 7.34 (d, 1H, *J* = 3.2 Hz), 7.51 (d, 1H, *J* = 2.0 Hz), 7.62 (dd, 1H, *J* = 8.8 Hz, 2.4 Hz), 7.99 (d, 1H, *J* = 9.2 Hz), ms: *m/z*: 389.06.

(3e) Pale yellow solid; Mp: 152-53 °C; IR (KBr): 1634 (C=O), 1551 cm^{-1} (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.57 ppm (s, 3H), 6.06 (s, 2H), 6.70 (d, 1H, *J* = 16.2 Hz), 6.89 (d, 1H, *J* = 8.1 Hz), 7.13 (dd, 1H, *J* = 8.1 Hz, 1.5 Hz), 7.21 (d, 1H, *J* = 16.2 Hz), 7.28 (d, 1H, *J* = 1.6 Hz), 7.35-7.36 (m, 2H), 7.39 (d, 1H, *J* = 2.4 Hz), 7.43-7.45 (m, 3H), 7.84 (dd, 1H, *J* = 9.0 Hz, 2.4 Hz), 8.11 (d, 1H, *J* = 9.0 Hz); GCMS: *m/z*: 428.1[M+1]$^+$.

(3f) Yellow solid; Mp: 152-153 °C; IR (KBr): 1639 (C=O), 1599 cm^{-1} (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.3 (t, 3H), 2.58 (s, 3H), 4.05 ppm (q, 2H). 6.69 (d, 1H, *J* = 16.2 Hz), 6.90 (d, 2H, *J* = 8.8 Hz), 7.24 (d, 1H, *J* = 16.2 Hz), 7.34-7.36 (m, 3H), 7.39 (d, 1H, *J* = 2.2), 7.42-7.46 (m, 2H), 7.57 (d, 2H, *J* = 8.8 Hz), 7.85 (dd, 1H, *J* = 9.0, 2.2), 8.12 (d, 1H, *J* = 9.0 Hz), ESMS: *m/z* 427 [M^+].

(3g) Yellow solid; Mp: 181-182 °C; IR (KBr): 1641 (C=O), 1597 cm^{-1} (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.58 (s, 3H), 3.74 (s, 3H), 3.77 (s, 3H), 6.77 (d, 1H, *J* = 15.8 Hz), 6.93 (d, 1H, *J* = 8.8 Hz), 7.18 (d, 1H, *J* = 2.0 Hz), 7.22 (d, 1H, *J* = 15.8 Hz), 7.37-7.35 (m, 3H), 7.40 (d, 1H, *J* = 2.2 Hz), 7.47-7.43 (m, 3H), 7.86 (dd, 1H, *J* = 9.0 Hz, 2.2 Hz), 8.12 (d, 1H, *J* = 8.8 Hz). ESMS: *m/z* 443 [M^+].

(3h) Pale yellow solid; Mp: 150-53 °C; IR (KBr): 1554 (C=C), 1637 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.58 (s, 3H), 3.78 ppm (s, 3H, -OCH_3), 6.68 (d, 1H, *J* = 16.5 Hz), 6.88 (d, 1H, *J* = 16.5 Hz), 7.31 (d, 1H, *J* = 2.7 Hz), 7.69-7.58 (m, 9H), 7.70 (dd, 1H, *J* = 8.9 Hz, 2.3 Hz), 8.08 (d, 1H, *J* = 8.9 Hz); Es ms: *m/z* 413 [M^+].

(3i) Pale yellow solid; Mp: 124-126 °C; IR (KBr): 1636 (C=O), 1552 cm^{-1} (C=C); ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.71 (s, 3H), 3.78 (-OCH_3), 6.58 (d, 1H, 16.2 Hz), 6.83 (d, 1H, *J* = 1.7 Hz), 6.92 (dd, 2H, *J* = 8.7 Hz, 2.4 Hz), 7.06 (d, 1H, *J* = 16.2 Hz), 7.31-7.22 (m, 3H) 7.44-7.39 (m, 3H), 7.59 (d, 1H, *J* = 2.2 Hz), 7.69 (dd, 1H, *J* = 8.9 Hz, 2.4 Hz), 8.09 (d, 1H, *J* = 8.9 Hz); GCMS: *m/z* 414

[M+1], 413 [M^+].

(3j) Pale yellow solid; Mp: 184-186 °C; IR (KBr): 1649 (C=O), 1555 cm^{-1} (C=C); ^1H NMR (400 MHz, $CDCl_3$): δ 3.32 ppm (s, 3H), 6.88 (d, 1H, *J* = 16.2 Hz), 7.30-7.34 (m, 2H), 7.38 (d, 1H, *J* = 16.2 Hz), 7.41-7.51 (m, 7H), 7.83 (d, 1H, *J* = 2.4 Hz), 7.85 (dd, 1H, *J* = 9.0, 2.4 Hz), 8.10 (d, 1H, *J* = 9.0 Hz); GCMS: *m/z* 417 $[M]^+$.

(4a) Deep yellow solid (with greenish yellow florescence in $CHCl_3$); Mp 183-85 °C; IR (KBr): 1629 (C=N), 1492 (C=C), 2923 (CH aliphatic) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.23 (dd, 1H, *J* = 17.7 Hz, 5.5 Hz), 2.72 (s, 3H), 2.88 (s, 3H), 3.26 (dd, 1H, *J* = 17.7 Hz, 12.3 Hz), 4.06 ppm (s, 3H), 5.34 (dd, 1H, *J* = 12.3 Hz, 5.5 Hz), 6.77-6.95 (m, 5H), 7.17-7.30 (m, 5H), 7.18 (d, 1H, *J* = 5.1 Hz), 7.43-7.49 (m, 4H), 7.62 (d, 1H, *J* = 9.3 Hz), 8.06 (d, 1H, *J* = 8.7 Hz), ms: *m/z* 568.2 (M^+).

(4b) Yellow solid (with greenish yellow florescence in $CHCl_3$); Mp: 168-170 °C; IR (KBr): 1625 (C=N), 1498 (C=C), 2900 cm^{-1} (CH aliphatic); ^1H NMR (400 MHz, $CDCl_3$): δ 2.43 (dd, 1H, *J* = 17.8 Hz, 7.4 Hz), 2.88 (s, 3H), 3.19 (dd, 1H, *J* = 17.8 Hz, 12.3 Hz), 5.66 (dd, 1H, *J* = 12.3 Hz, 7.4 Hz), 6.77 (t, 1H, *J* = 7.2 Hz), 6.98 (d, 1H, *J* = 8.1 Hz), 7.08-7.16 (m, 2H), 7.25-7.33 (m, 5H), 7.41-7.49 (m, 5H), 7.55 (s, 1H), 7.61 (dd, 1H, *J* = 9.1 Hz, 2.1 Hz), 7.71-7.82 (m, 3H), 8.01 ppm (d, 1H, *J* = 7.8 Hz); ms: *m/z* 523 (M^+).

(4c) Orange yellow solid (with greenish yellow florescence in $CHCl_3$); Mp: 160-162 °C; IR (KBr): 2914 (CH aliphatic), 1599 (C=N), 1566 cm^{-1} (C=C), ^1H NMR (400 MHz, DMSO-d_6): δ 2.80 (s, 3H), 3.68 (dd, 1H, *J* = 18.8 Hz, 8.0 Hz), 4.18 (dd, 1H, *J* =18.8 Hz, 12.3 Hz), 5.80 (dd, 1H, *J* = 12.3 Hz, 7.8 Hz), 6.88 (m, 1H), 7.98 (m, 1H), 7.00-7.45 (m, 12H), 7.50-7.60 ppm (m, 3H); ms: *m/z* 491 (M^+).

(4d) Yellow solid (with greenish yellow florescence in $CHCl_3$); Mp: 190-192 °C; IR (KBr) cm^{-1}: 1628 (C=N), 1479 (C=C), 2923 (CH aliphatic); ^1H NMR (400 MHz, $CDCl_3$): δ 2.50 (dd, 1H, *J* = 17.5 Hz, 6.9 Hz), 2.88 (s, 3H), 2.97 (dd, 1H, *J* = 12.0 Hz, 17.5 Hz), 5.22 (dd, 1H, *J* = 12.0 Hz, 6.9 Hz), 6.77-6.87 ppm (m, 3H), 7.01-7.41 (m, 10H), 7.49 (s, 1H), 7.63 (d, 1H, *J* = 8.7 Hz), 8.03 (d, 1H, *J* = 8.7 Hz); ms: *m/z* 479 (M^+).

REFERENCES

1. Dhar, D. N. *The Chemistry of Chalcones and Related Compounds*; Wiley: New York, 1981; p 201.
2. Grayer, R. J. In *Methods in Plant Biochemistry*; Dey, P. M.; Harborne, J. B.; Eds.; Academic Press: London, 1989; pp 283-323.
3. Fabiane, L.; Guzela, M.; Rodrigues, A. T.; Iriane Eger-Mangrich, R. C.; Steindel, M.; Grisard, E. C.; Assreuy, J.; Calixto, J. B.; Santos, A. R. S. *Antimicrob. Agents Chemother.* **2003**, *4*, 1449.
4. Dimmock, J. R.; Elias, D. W.; Beazely, M. A; Kandepu, N. M. *Curr. Med. Chem.* **1999**, *6*, 1125.
5. Baba, M.; Asano, R.; Takigami, I. *Biol. Pharm. Bull.* **2002**, *25*, 247.
6. Yamazaki, S.; Morita, T.; Endo, H.; Hamamoto, T.; Baba, M.; Joichi, Y.; Kaneko, S.; Okada, Y.; Okuyama, T.; Nishino, H.; Tokue, A. *Cancer Lett.* **2002**, *183*, 23.
7. Gerhauser, C.; Alt, A.; Heiss, E.; Gamal-Eldeen, A.; Klimo, K.; Knauft, J.; Neumann, I.; Scherf, H. R.; Frank, N.; Bartsch, H.; Becker, H. *Mol. Cancer Ther.* **2002**, *1*, 959.
8. Kimura, Y.; Baba, K. *Int. J. Cancer* **2003**, *106*, 429.
9. De Vincenzo, R.; Scambia, G.; Mancuso, S. *Anticancer Drug Des.* **1995**, *10*, 481.
10. Shibata, S. *Stem Cells* **1994**, *12*, 44.
11. Baluja, A.; Municio, A. M.; Vega, S. *Chem. Ind.* **1964**, *3*, 2053.
12. Dinkova-Kostova, A. T.; Holtzclaw, W. D.; Cole, R. N.; Itoh, K.; Wakabayashi, N.; Katoh, Y.; Yamamoto, M.; Talalay, P. *Proc. Natl. Acad. Sci. U. S. A.* **2002**, *99*, 11908.
13. Xiaolin, Zi.; Simoneau, A. R. *Cancer Res.* **2005**, *65*, 3479.
14. Wu, X.; Wilairat, P.; Lin-Go, M. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 2299.
15. Barsoum, F. F.; Hosni, H. M.; Girgis, A. S. *Bioorg. Med. Chem.* **2006**, *14*, 3929.
16. Foresti, R.; Hoque, M.; Monti, D.; Green, C. J.; Motterlini, R. *J. Pharmacol. Exp. Ther.* **2004**, *312*, 686.
17. Tomoda, H.; Ômura, S. *Pharmacol. Ther.* **2007**, *115*, 375.
18. Zhang, X.-L.; Hu, Q.-S.; Sheng, S.-R.; Xiao, C.; Cai, M.-Z. *J. Chin. Chem. Soc.* **2011**, *58*, 18.
19. Misra, S. S. *J. Chin. Chem. Soc.***1977**, *24*, 45.
20. Sarveswari, S.; Vijayakumar, V. *Arabian J. Chem*. 2011, doi:10.1016/j.arabjc.2011.01.032.
21. Mamolo, G. M.; Zampieri, D.; Falagiani, V.; Vio, L.; Banfi, E. *Farmaco* **2001**, *56*, 593.
22. Powers, D. G.; Casebier, D. S.; Fokas, D.; Ryan, W. J.; Troth, J. R.; Coffen, D. L. *Tetrahedron* **1998**, *54*, 16, 4085.
23. Lévai, A.; Kövér, E. K.; Jekö, J. *ARKIVOC* **2007**, *viii*, 26.
24. Carter, H. E.; Van Abeele, F. R.; Rothrock, J. W. *J. Biol. Chem*. **1949**, *178*, 325.
25. Sahu, S. K.; Banerjee, M.; Samantray, A.; Behera, C.; Azam, M. A. *Trop. J. Pharm. Res.* **2008**, *7*, 961-968.

26. Sayed Amr, A. G.; Abdel-Latif, N. A.; Abdella, M. M. *Acta Pharm.* **2006**, *56*, 203.
27. (a) Loh, W. S.; Fun, H. K.; Sarveswari, S.; Vijayakumar, V.; Palakshi Reddy, B. P. *Acta Cryst.* **2010**, *E66*, o91. (b) Loh, W. S.; Fun, H. K.; Sarveswari, S.; Vijayakumar, V.; Palakshi Reddy, B. P. *Acta Cryst.* **2010**, *E66*, o353. (c) Shahani, T.; Fun, H. K.; Sarveswari, S.; Vijayakumar, V.; Ragavan, R.V. *Acta Cryst.* **2010**, *E66,* o374.
28. (a) Fun, H. K.; Quah, C. K.; Sarveswari, S.; Vijayakumar, V.; Prasath, R. *Acta Cryst.* **2009**, *E65*, o2707. (b) Fun, H. K.; Yeap, C. S.; Sarveswari, S.; Vijayakumar, V.; Prasath, R. *Acta Cryst.* **2009**, *E65*, o2665. (c) Loh, W. S; Fun, H.-K.; Sarveswari, S.; Vijayakumar, V.; Reddy, B. P. *Acta Cryst.* **2010**, *E66*, o304.
29. Ozdemir, A.; Turan-Zitouni, G.; Kaplancikli, Z. A. *Turk. J. Chem.* **2008**, *32*, 529.
30. Wiley, R. H.; Jarboe, C. H.; Hayes, F. N.; Hansbury, E.; Nielsen, J. T.; Callahan, P. X.; Sellars, M. C. *J. Org. Chem.* **1958**, *23*, 732.
31. Gökhan, N.; Ye silada, A.; Ucar, G., Erol, K.; Bilgin, A. A. *Arch. Pharm.* **2003**, *336*, 362.

