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Synthesis and Characterization of Chalcones and Their New Pyrazolines Derivatives

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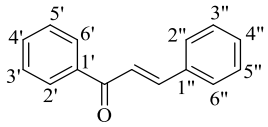
GRAPHICAL ABSTRACT



General structure of chalcone

ABSTRACT

Chalcones are open-chain flavonoids and considered to be the precursor of isoflavonoids and flavonoids which consist of two aromatic rings that linked by a three carbons consisting of a α, β-unsaturated carbonyl system. Besides, chalcones display a wide range of biological activities such as antibacterial, anticancer and antioxidant activity. In this study, the synthesis of several chalcones and their pyrazoline derivatives namely *(E)*-1-(5-methylfuran-2-yl)-3-phenylprop-2-en-1-one, *(E)*-3-(4-bromophenyl)-1-(5-methylfuran-2-yl)prop-2-en-1-one, *(E)*-1-(5-methylfuran-2-yl)-3-(*p*-tolyl)prop-2-en-1-one, 1-(5-(5-methylfuran-2-yl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one, 1-(3-(4-bromophenyl)-5-(5-methylfuran-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one and 1-(5-(5-methylfuran-2-yl)-3-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one has been carried out. These targeted compounds were synthesized *via* Claisen-Schmidt condensation of the respective aldehydes and ketones under basic condition to give the corresponding chalcones, *(E)*-1-(5-methylfuran-2-yl)-3-phenylprop-2-en-1-one, *(E)*-3-(4-bromophenyl)-1-(5-methylfuran-2-yl)prop-2-en-1-one, and *(E)*-1-(5-methylfuran-2-yl)-3-(*p*-tolyl)prop-2-en-1-one which were obtained as yellow precipitate with a percentage yield 76.98 %, 38.55 % and 66.33 % respectively. The pyrazoline derivatives which were 1-(5-(5-methylfuran-2-yl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one, 1-(3-(4-bromophenyl)-5-(5-methylfuran-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one and 1-(5-(5-methylfuran-2-yl)-3-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one were synthesized from *(E)*-1-(5-methylfuran-2-yl)-3-phenylprop-2-en-1-one, *(E)*-3-(4-bromophenyl)-1-(5-methylfuran-2-yl)prop-2-en-1-one, and *(E)*-1-(5-methylfuran-2-yl)-3-(*p*-tolyl)prop-2-en-1-one respectively with hydrazine hydrate in acetic acid. All pyrazoline derivatives obtain as white powder with a percentage yield of 40.29 %, 51.60% and 52.84 % respectively. The structures were confirmed spectroscopically by ATR-FTIR and ^{1}H NMR.

Keywords: chalcones, 2-acetyl-5-methylfuran, pyrazoline derivative

1. INTRODUCTION

Flavonoids are one of the large groups of abundant plant secondary metabolites which can be found in plants such as conifer, ferns and flowering plants [1]. These natural compounds are divided into several classes based on their molecular structure and one of them are chalcone. Chalcone is an important group in natural product and one of the major classes of flavonoids which can be found in vegetables, fruits, soy and tea [2]. Chalcone is also known as 1,3-dipheny-2-propene-1-one which consists of two aromatic rings that linked by a three carbons consisting of a α,β-unsaturated carbonyl system (Figure 1). This compound is abundant in most of the edible plants and are considered to be precursors of isoflavonoids and flavonoids [3]. Chalcone serves as a very good synthon for the synthesis and design of variety of novel heterocycles such as pyrazoline, hydroxyl pyrazoline and isoxazoles with good pharmaceutical profile [4].

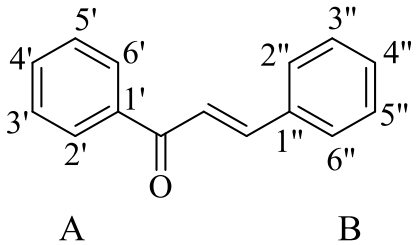


Figure 1 General structure of chalcones. A and B represent the order of ring formation in the synthesis. [2]

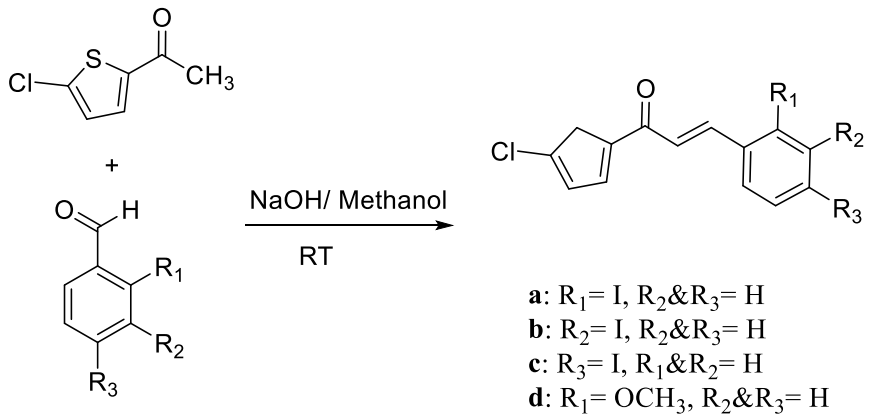
Chalcones are important precursors in the biosynthesis of flavones and flavones. Acetophenone and benzaldehyde are usually used for the synthesis of chalcone via Claisen-Schmidt condensation, using base in polar solvent. Besides, the synthesis of chalcone also reported to use other methods such as the palladium-mediated Suzuki-coupling between cinnamoyl chloride and phenyl boronic acids or the carbonylative Heck coupling with aryl halides and styrene in the presence of carbon monoxide [2].

Moreover, chalcone has been reported to have various chemotherapeutic effects including antifungal, antituberculosis and antitumor activities [5]. Based on the previous study, polymethoxy chalcone derivatives such as Nobiletin, Combrestatin A-4 (CA-4) and Tangeretin were found to be highly cytotoxic against a variety of human cancer cell lines. In addition, pyrazole-containing compounds are considerable for their diverse chemotherapeutic potentials, besides of their capability to exert remarkable anticancer effects by inhibiting different types of enzymes that play important role in cell division. The introduction of pyrazole nucleus between the two aryl rings of chalcone was found to increase the cytotoxic potential [5].

Chalcones are a good synthon for a variety of synthesis involving heterocyclic compounds. The synthesis of chalcone with heterocyclic pyrazoline involve the Claisen-Schmidt reaction. In the initial step reaction, chalcone was synthesized by condensing 3,4,5-trimethoxylbenzaldehyde with the acetophenone in the presence of potassium hydroxide. Then, chalcone underwent cycloaddition reaction using hydrazine hydrate in boiling formic or acetic acid to give dihydropyrazole-1-carbaldehyde [6]. This research will focus on synthesis and characterization of furan-based chalcones **(1)** and their pyrazoline derivatives **(2)**.

In 2014, Kulathooran *et al.* has reported the synthesis of chalcones and their evaluation for in vitro antimicrobial activity against various pathogenic bacterial and fungal strains. Chalcone which contain methyl substituted thiophene shows significant antibacterial activity against bacteria strain such as *Klebsiella pneumonia, Staphylococcus aureus, Escherichia coli, Rhizopus arrhizus and Candida* albicans with minimum inhibitory concentration (MIC) range between 4.1-16.5. From the study, methyl substituted thiophene derivative in 2,5-dimethylfuran ring was found to be the most active compounds against all the microbial strains except *Aspegillus niger* [7].

Kumar *et al.* has reported the synthesis and antioxidant activity of a series of new 5-chlorothiophene chalcones. The compounds synthesized were reported to displayed mild to good antioxidant properties. This is due to the presence of electron donating $–OCH_3$ and electronegative –I substituent at different positions on the phenyl rings. From the study, the antioxidant activity of the synthesized compounds can be shown as the following order f > d > e > b > a > c (Scheme 1). Their studies revealed that the influence of the nature of the functional linkage (electron donating or electron withdrawing groups) and the position of the substituent on the phenyl ring of 5-chlorothiophene chalcone play the role in determining the antioxidant activities [8].



a: R_1= I, R_2&R_3= H
b: R_2= I, R_2&R_3= H
c: R_3= I, R_1&R_2= H
d: R_1= OCH_3, R_2&R_3= H
e: R_2= OCH_3, R_1&R_3= H
f: R_3= OCH_3, R_1&R_2= H

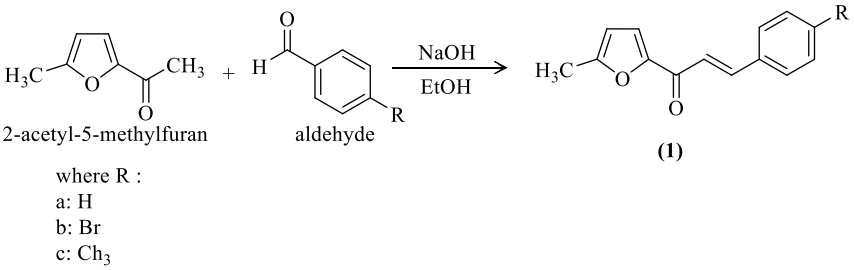
Scheme 1 Synthesis of 5-chlorothiophene chalcone.

2. EXPERIMENTAL

The experiment was divided into three main stages. The first stage was focused on the synthesized of furan-based chalcones by base catalyzed Claisen- Schmidt condensation. Next, the second stage was synthesized of pyrazolines derivatives *via* the reaction of chalcones with hydrazine hydrate in glacial acetic acid. The last stage was the characterization of the chalcones and their pyrazoline derivatives by ATR-FTIR and ^{1}H NMR.

2.1 Synthesis of Chalcones

Chalcones 1 (a, b and c) were synthesized from 2-acetyl-5-methylfuran with aldehyde which were benzaldehyde, 4-bromobenzaldehyde and 4-methylbenzaldehyde. The synthesis of chalcones as shown in Scheme 2. 2-acety-5-methylfuran (1mmol) and aldehyde (1 mmol) were mixed together with ethanol (10 mL) as solvent. The mixture was stirred at room temperature until the reaction completed. The progress of reaction was monitored using TLC. Then, it was filtered by vacuum filtration, washing with cold distilled water and dried. The recrystallization of product using ethanol was then performed.



Scheme 2 Synthesis of chalcones.

2.1.1 Synthesis of *(E)*-1-(5-methylfuran-2-yl)-3-phenylprop-2-en-1-one (1a)

The product chalcone form as light yellow solid (0.82 g, 76.98 %); R_f =0.82 in Hex:EtOAc (4:2); m.p. : 105.3-107.8°C; ATR-FTIR (cm^{-1}): 3117.7 (C-H aromatic), 1601.81 and 1446.55 (C=C aromatic), 1657.58 (conjugated C=O), 1574.32 (olefinic C=C), 1071.53 (C-O); ^{1}H NMR (CDCl3, 300 MHz), δ: δ 2.48 (3H, s, H-5a), δ 6.23 (1H, dd, *J*= 0.9 and 3.3 Hz,Ar- H), δ 7.27 (1H, d, *J*= 1.8, Ar-H), δ 7.37 (4H, m, Ar-H or H-α), δ 7.63 (2H,m, Ar-H or H-α) and δ 7.84 (1H, d, *J*= 15.8, H-β)

2.1.2 Synthesis of *(E)*-3-(4-bromophenyl)-1-(5-methylfuran-2-yl)prop-2-en-1-one (1b)

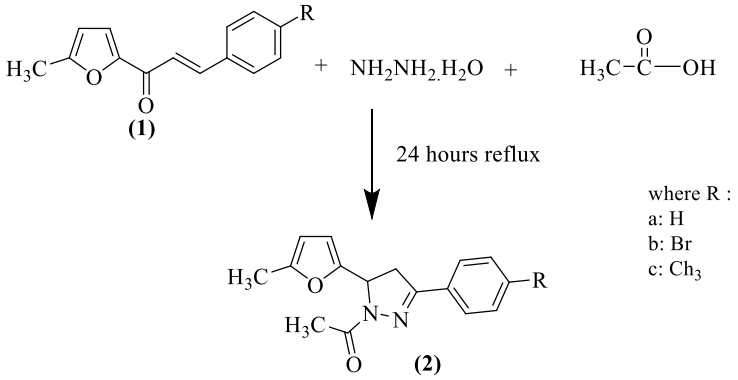
The product chalcone form as light yellow solid (0.56 g, 38.55 %); R_f =0.87 in Hex:EtOAc (4:2); m.p. : 154.6-157.2°C; ATR-FTIR (cm^{-1}): 3105.8 (C-H aromatic), 1601.48 and 1485.70 (C=C aromatic), 1649.52 (conjugated C=O and olefinic C=C), 1063.84 (C-O), 3073 (C-H sp^2), 2917.7 (C-H sp^3), 663.44 (C-Br); ^{1}H NMR ($CDCl_3$, 300 MHz), δ: δ 2.46 (3H, s, H-5a), δ 7.35 (1H, d, *J*= 15.8 Hz, H-α), δ 7.76 (1H, d, *J*= 15.8 Hz, H-β), δ 6.23 (1H, dd, *J*= 0.9 and 3.3 Hz, Ar-H), δ 7.27 (1H, d, *J*= 1.8 Hz, Ar-H) and δ 7.76 (4H, m, H-2', H-3', H-5'and H-6').

2.1.3 Synthesis of *(E)*-1-(5-methylfuran-2-yl)-3-(*p*-tolyl)prop-2-en-1-one (1c)

The product chalcone form as bright yellow solid (0.75 g, 66.33 %);R_f =0.33 in Hex:EtOAc (4:1); m.p.: 93.2-94.0 °C, ATR-FTIR (cm^{-1}): 3120.7 (C-H aromatic), 2840.0 (C-H sp^3),1593.58 and 1421.90 (C=C aromatic), 1647.84 (conjugated C=O and olefinic C=C), 1066.37 (C-O); ^{1}H NMR ($CDCl_3$, 300 MHz), δ: δ 2.45 (3H, s, Ar-H), δ 3.86 (3H, s, Ar-H), δ 7.80 (1H, d, *J*= 15.9 Hz, H-β), δ 6.21 (1H, dd, *J*= 0.9 and 3.3 Hz, Ar-H), δ 6.92 (2H, dd, *J*= 1.8 and 6.9 Hz, Ar-H), δ 7.24 (2H, m, Ar-H or H-α) and δ 7.60 (2H, dd, *J*=1.8 and 6.9 Hz, Ar-H).

2.2 Synthesis of Pyrazoline Derivatives

Chalcones obtained from condensation reaction were refluxed for 24 hours with hydrazine hydrate (0.05 mL) and glacial acetic acid (10 mL). After the completion of reaction, the mixture was poured into crushed ice and stirred for 20 min. Then, the mixture was kept in the fridge overnight until the precipitate formed. The precipitate form was filtered and washed with distilled water. Later, in stage three, the compounds obtained were characterized by using ATR-FTIR, and ^{1}H NMR.



Scheme 3 Synthesis route of pyrazoline derivatives **(**2a, 2b and 2c).

2.2.1 Synthesis of 1-(5-(5-methylfuran-2-yl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (2a)

The pyrazoline derivatives (2a) obtain as white solid (0.11 g, 40.29%); m.p.: 129.0-130.0°C; R_f = 0.61 in *n*-Hex:EtOAc (7:3). ATR-FTIR (cm^{-1}): 3084.9 (C-H aromatic), 1580.18 and 1494.02 (C=C aromatic), 1641.04 (C=O and C=N), 1035.61 (C-O),1325.91 (C-N), 3037.0 (C-H sp^2), 2935.6 (C-H sp^3); ^{1}H NMR ($CDCl_3$, 300 MHz), δ: δ 2.43 (6H, s, H-5'a and H-1), δ 5.54 (1H, dd, *J*= 4.2 and 11.9 Hz, H-x), δ 3.02 (1H, dd, *J*= 4.5 and 17.4 Hz, H-a), δ 3.63 (1H, dd, J= 11.7 and 17.4 Hz, H-b), δ 6.11 (1H, dd, *J*= 0.9 and 3.3 Hz,H-3'), δ 6.61 (1H, d, *J*= 3.3, H-4') and δ 7.24 (5H, m, H-2'', H-3'', H-4'', H-5'' and H-6'').

2.2.2 Synthesis of 1-(3-(4-bromophenyl)-5-(5-methylfuran-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (2b)

The pyrarazoline derivatives was obtained as white solid (0.18 g, 51.60%); R_f = 0.72 in *n*-Hex:EtOAc (7:3); m.p. : 142.9-144.8 °C; ATR-FTIR (cm^{-1}): 3105.8 (C-H aromatic), 1575.68 and 1477.80 (C=C aromatic), 1647.64 (C=O and C=N), 1028.71 (C-O), 2956.5 (C-H sp^2), 2929.6 (C-H sp^3), 1324.17 (C-N), 663.44 (C-Br); ^{1}H NMR ($CDCl_3$, 300 MHz), δ: δ 2.43 (6H,s, H-5'a and H-1), δ 5.54 (1H, dd, *J*= 4.2 and 11.9 Hz, H-x), δ 3.02 (1H, dd, *J*= 4.5 and 17.4 Hz, H-a), δ 3.63 (1H, dd, J= 11.7 and 17.4 Hz, H-b), δ 6.11 (1H, dd, *J*= 0.9 and 3.3 Hz,H-3'), δ 6.61 (1H, d, *J*= 3.3, H-4') and δ 7.24 (5H, m, H-2'',H-3'',H-4'',H-5'' and H-6'').

2.2.3 Synthesis of 1-(5-(5-methylfuran-2-yl)-3-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (2c)

The pyrarazoline derivatives was obtained as white solid (0.15 g, 52.84%); m.p.: 114.7- 116.7°C; R_f = 0.46 in *n*-Hex:EtOAc (7:3); ATR-FTIR (cm^{-1}): 3081.9 (C-H aromatic), 1610.97 and 1436.23 (C=C aromatic), 1637.95 (C=O and C=N), 1035.02 (C-O), 1249.40 (C-N), 2956.5 (C-H sp^2), 2932.6 (C-H sp^3)x; ^{1}H NMR ($CDCl_3$, 300 MHz), δ: δ 2.41 (6H,s, H-5'a and H-1), δ 3.78 (3H, s, H-4''a), δ 5.49 (1H, dd, *J*= 4.5 and 11.7 Hz, H-x), δ 3.01 (1H, dd, *J*= 4.2 and 17.7 Hz, H-a), δ 3.60 (1H, dd, *J*= 11.7 and 17.7 Hz, H-b), δ 6.11 (1H, dd, *J*= 0.9 and 3.3 Hz, H-3'), δ 6.61 (1H, d, *J*= 3.3, H-4'), δ 6.83 (2H, d, *J*= 8.7, H-3'' and H-5'') and δ 7.15 (2H, d, *J*= 8.7, H-2'' and H-6'').

3. RESULTS AND DISCUSSION

3.1. Synthesis of Chalcones

3.1.1 Synthesis of *(E)*-1-(5-methylfuran-2-yl)-3-phenylprop-2-en-1-one (1a)

The synthesis of *(E)*-1-(5-methylfuran-2-yl)-3-phenylprop-2-en-1-one (1a) was achieved by Claisen-Schmidt condensation. The reaction was carried out between aldehyde which was benzaldehyde and ketone 2-acetyl-5-methylfuran in the presence of base, sodium hydroxide (NaOH) in ethanol. The product formed was light yellow solid (0.82 g, 76.98 %) with the melting point of 105.3-107.8 °C.

The reaction begins with the formation of enolate ion from ketone via proton abstraction at the α-carbon by a hydroxide ion. Nucleophilic attack at the carbonyl carbon of the aldehyde by enolate ion followed by addition of proton from a water molecule gave a β-hydroxyketone. Dehydration occur to eliminate a water molecule produced the desired chalcone.

The IR spectrum of compound (1a) exhibit C-H aromatic stretch at 3117.7 cm^{-1}. The presence of carbonyl group was observed at 1657.58 cm^{-1}. The absorption bond of the carbonyl group was less than the expected value attributed due to the presence of C=C group. Moreover, the conjugation of benzene ring reduced the frequency as the delocalization of pi electrons has reduced the electron density of the carbonyl double bond. The spectrum displayed the absorption band for C=C olefinic (1574.32 cm^{-1}) and C-O (1071.53 cm^{-1}). Besides, the presence of C=C aromatic stretch were observed at 1601.81 and 1446.55 cm^{-1}.

The ^{1}H NMR spectrum showed a singlet peak at δ 2.48 (3H) due to the presence of methyl group at position 5. The double of double peak appeared at δ 6.23 (1H, *J*= 0.9 and 3.3 Hz) and doublet peak at δ 7.27 (1H, *J*= 1.8 Hz) corresponding for H-4 and H-3 respectively. The multiple peak appear at δ 7.37-7.63 indicates the proton of aromatic benzene. The existence of H-β can be proved by doublet peak at δ 7.84 with *J*= 15.8 Hz and H-α which is overlapping with Ar-H at δ 7.37 which gives multiplet peak.

3.1.2 Synthesis of *(E)*-3-(4-bromophenyl)-1-(5-methylfuran-2-yl)prop-2-en-1-one (1b)

The synthesis of *(E)*-3-(4-bromophenyl)-1-(5-methylfuran-2-yl)prop-2-en-1-one (1b) was achieved by Claisen-Schmidt condensation. The reaction was carried out between aldehyde which was 4-bromobenzaldehyde and ketone 2-acetyl-5-methylfuran in the presence of base, sodium hydroxide (NaOH) in ethanol. The product formed was light yellow solid (0.56 g, 38.55 %) with the melting point of 154.6-157.2°C.

The IR spectrum showed the presence of C-H sp^2 and C-H sp^3 at 2917.7 cm^{-1} and 3073 cm^{-1}respectively. Besides, the absorption band at 3105.8 cm^{-1} indicate the presence of C-H aromatic. The carbonyl group (C=O) and olefinic C=C can be observed at the absorption band 1649.52 cm^{-1}. The peak at 1063.84 cm^{-1} was assigned to the C-O stretching and C=C aromatic can be observed at 1601.48 cm^{-1} and 1485.70 cm^{-1}. Lastly, the presence of C-Br was display at 663.44 cm^{-1}.

The ^{1}H NMR spectrum for compound (1b) showed a singlet peak at δ 2.46 (3H) that was assigned to the methyl group at position 5. The existence of H-α and H-β was proved by the presence of doublet peak at δ 7.35 (1H, *J*= 15.8 Hz) and δ 7.76 (1H, *J*= 15.8 Hz) respectively. The doublet of doublet peak at δ 6.23 (1H, *J*= 0.9 and 3.3 Hz) and doublet peak at δ 7.27 (1H, *J*= 1.8) contributed to the H-4 and H-3 respectively. The remaining proton signal were from the Ar-H at δ 7.76 (4H) with multiplet peak.

3.1.3 Synthesis of *(E)*-1-(5-methylfuran-2-yl)-3-(*p*-tolyl)prop-2-en-1-one (1c)

The synthesis of *(E)*-1-(5-methylfuran-2-yl)-3-(*p*-tolyl)prop-2-en-1-one (1c) was achieved by Claisen-Schmidt condensation. The reaction was carried out between aldehyde which was 4-methylbenzaldehyde and ketone 2-acetyl-5-methylfuran in the presence of base, sodium hydroxide (NaOH) in ethanol. The product formed was bright yellow solid (0.75 g, 66.33 %) with the melting point of 93.2-94.0 °C.

The IR spectrum showed the presence of C-H sp^3 2840 cm^{-1}. The absorption band at 3120.7 cm^{-1} indicate the presence of C-H aromatic. The carbonyl group (C=O) and olefinic C=C can be observed at the absorption band 1647.84 cm^{-1}. Besides, the peak at 1066.37 cm^{-1} was assigned to the C-O stretching and C=C aromatic can be observed at 1593.58 cm^{-1} and 1421.90 cm^{-1}.

The ^{1}H NMR spectrum for compound **(1c)** showed a singlet peak at δ 2.45 (3H) that was assigned to the methyl group at position 5. Another singlet peak at δ 3.86 (3H) indicate the methyl group at aromatic ring. The existence of H-β was proved by the presence of doublet peak at δ 7.80 (1H, *J*= 15.8 Hz). The doublet of doublet peak at δ 6.21 (1H, *J*= 0.9 and 3.3 Hz) contributed to the H-4 as the same *J* value were obtained for all chalcone.

3.2 Synthesis of pyrazoline derivatives

3.2.1 Synthesis of 1-(5-(5-methylfuran-2-yl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (2a)

Compound (2a) was synthesized by condensation reaction of chalcone (1a) and hydrazine hydrate in the presence of acid catalyst such as acetic acid. The step involved addition of hydrazine, protonation of –OH group and elimination of H_2O afford the final product (2a). Compound (2a) obtained as white solid (0.11 g, 40.29%).

The IR spectrum of compound (2a) obtained shows the presence of C-H sp^2 at 3037.0 cm^{-1} and a C-H sp^3 at 2935.6 cm^{-1}. The absorption band at 1641.04 cm^{-1} was attributed to the acetyl C=O and C=N functional group. The C-H aromatic gave rise to the absorption band at 3084.9 cm^{-1} and the presence of aromatic C=C functional group can be observed at 1580.18 and 1494.02 cm^{-1}. In addition, the C-N absorption band at 1325.91 cm^{-1} proved the formation of pyrazoline ring. Lastly, the C-O absorption at 1035.61 cm^{-1} confirmed the existence of the furan moiety.

The ^{1}H NMR spectrum of compound (2a) showed singlet peak for furan –CH_3 at δ 2.43 (3H) which overlapped with the –CH_3 acetyl group from the pyrazoline ring also with singlet peak (3H) at δ 2.43. The presence of pyrazoline ring was proven by the doublet of doublet peaks at δ 5.54 (1H, dd, *J*= 4.2 and 11.7 Hz, H-x), δ 3.023 (1H, dd, *J*= 4.5 and 17.4 Hz, H-a) and δ 3.63 (1H, dd, *J*= 11.7 and 17.4 Hz, H-b). In addition, doublet of doublet peaks at δ 6.11 (1H, *J*= 0.9 and 3.3 Hz) indicate the presence of H-3' and doublet peak at δ 6.61 (1H, *J*= 3.3) were assigned for H-4' of furan. Lastly, the remaining proton signal were showed for the Ar-H at δ 7.24 (5H) with doublet peak.

3.2.2 Synthesis of 1-(3-(4-bromophenyl)-5-(5-methylfuran-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (2b)

Compound (2b) was synthesized by condensation reaction of chalcone (1b) and hydrazine hydrate in the presence of acid catalyst such as acetic acid. The pyrazoline obtained as white solid (0.18 g, 51.60%).

The IR spectrum of compound (2b) obtained shows the presence of C-H sp^2 at 2956.5 cm^{-1} and a C-H sp^3 at 2929.6 cm^{-1}. The absorption band at 1647.64 cm^{-1} was attributed to the acetyl C=O and C=N functional group. The C-H aromatic gave rise to the absorption band at 3105.8 cm^{-1} and the presence of aromatic C=C functional group can be observed at 1575.68 and 1477.80 cm^{-1}. In addition, the C-N absorption band at 1324.17 cm^{-1} proved the formation of pyrazoline ring. Lastly, the C-O absorption at 1028.71 cm^{-1} confirmed the existence of the furan moiety and absorption band at 663.44 cm^{-1} indicated the presence of C-Br at aromatic ring.

The ^{1}H NMR spectrum of compound (2b) showed singlet peak for furan –CH_3 at δ 2.41 (3H) which overlapped with the –CH_3 acetyl group from the pyrazoline ring also with singlet peak (3H) at δ 2.41. The presence of pyrazoline ring was proven by the doublet of doublet peaks at δ 5.48 (1H, dd, *J*= 4.5 and 12.0 Hz, H-x), δ 2.98 (1H, dd, *J*= 4.5 and 17.4 Hz, H-a) and δ 3.63 (1H, dd, *J*= 11.7 and 17.7 Hz, H-b). In addition, doublet of doublet peaks at δ 6.12 (1H, *J*= 0.9 and 3.3 Hz) indicate the presence of H-3' and doublet peak at δ 6.62 (1H, *J*= 3.3) were assigned for H-4' of furan. Lastly, the remaining proton signal were showed for the Ar-H at δ 7.09 (2H, d, *J*= 8.4, H-3'' and H-5'') and δ 7.43 (2H, d, *J*= 8.4, H-2'' and H-6'').

3.2.3 Synthesis of 1-(5-(5-methylfuran-2-yl)-3-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (2c)

Condensation of chalcone (1c) and hydrazine hydrate afford 1-(5-(5-methylfuran-2-yl)-3-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (2c) as white solid (0.15 g, 52.84 %).

The IR spectrum of pyrazoline derivative (2c) obtained shows the presence of the C-H sp^2 at 2956.5 cm^{-1} and a C-H sp^3 at 2932.6 cm^{-1}. The absorption band at 1637.95 cm^{-1} was attributed to the acetyl C=O and C=N functional group. The C-H aromatic gave rise to the absorption band at 3081.9 cm^{-1} and the presence of aromatic C=C functional group can be observed at 1610.97 and 1436.23 cm^{-1}. In addition, the C-N absorption band at 1249.40 cm^{-1} proved the formation of pyrazoline ring. Lastly, the C-O absorption at 1035.02 cm^{-1} confirmed the existence of the furan moiety.

The ^{1}H NMR spectrum of compound (2c) showed singlet peak for furan –CH_3 at δ 2.41 (3H) which overlapped with the –CH_3 acetyl group from the pyrazoline ring also with singlet peak (3H) at δ 2.41. Another singlet peak can be observerd at δ 3.78 (3H, s) which indicates the –CH_3 the para position of benzene ring. The presence of pyrazoline ring was proven by the doublet of doublet peaks at δ 5.49 (1H, dd, *J*= 4.5 and 11.7 Hz, H-x), δ 3.01 (1H, dd, *J*= 4.5

and 17.7 Hz, H-a) and δ 3.60 (1H, dd, *J*= 11.7 and 17.7 Hz, H-b). In addition, doublet of doublet peaks at δ 6.11 (1H, *J*= 0.9 and 3.3 Hz) indicate the presence of H-3' and doublet peak at δ 6.61 (1H, *J*= 3.3) were assigned for H-4' of furan. Lastly, the remaining proton signal were showed for the Ar-H at δ 6.83 (2H, d, *J*= 8.7, H-3'' and H-5'') and δ 7.15 (2H, d, *J*= 8.7, H-2'' and H-6'').

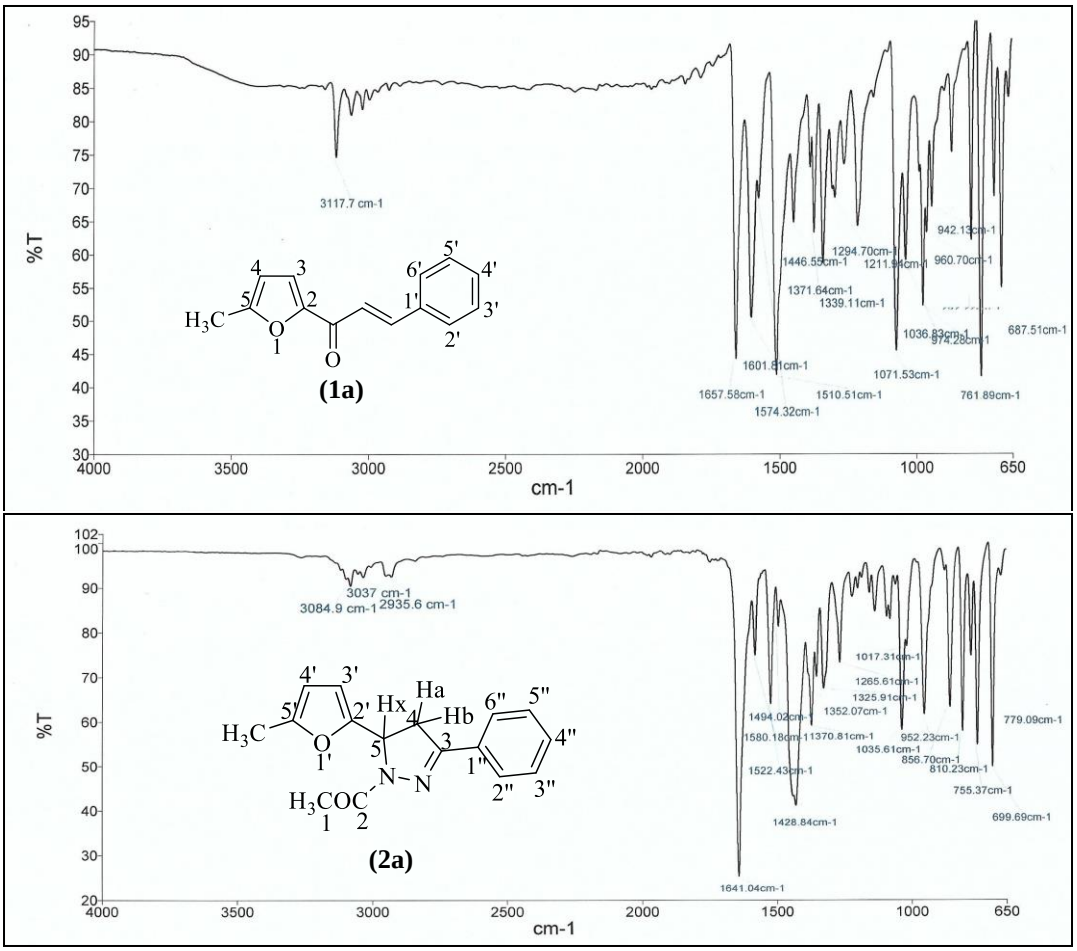


Figure 2 FTIR spectrum of chalcone 1a (top) and pyrazoline derivative 2a (bottom).

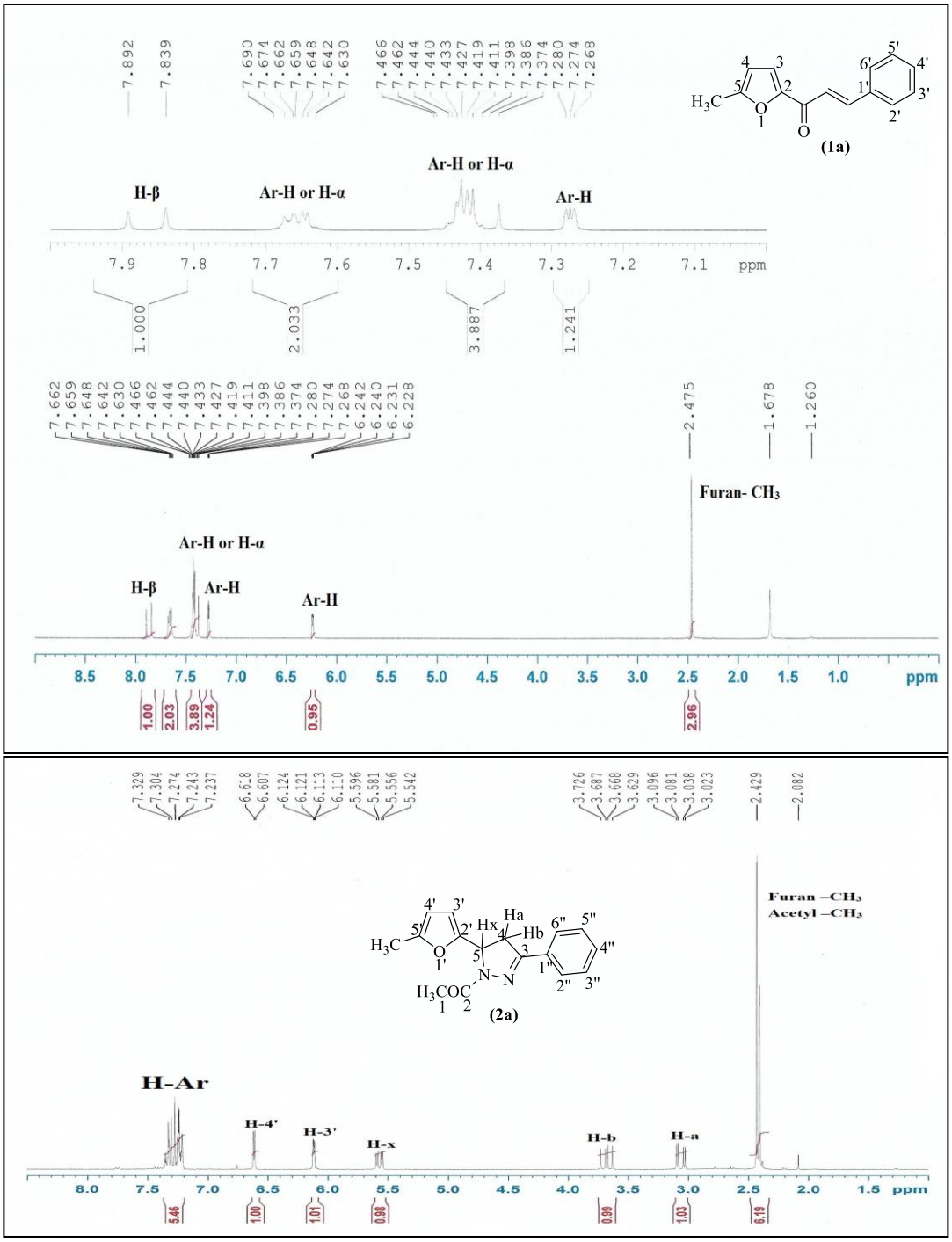


Figure 3 ^{1}H-NMR spectrum of chalcone 1a (top) and pyrazoline derivatives 2a (bottom).

4. CONCLUSION

Three furan-based heterocyclic chalcones were successfully synthesized *via* Claisen Schmidt condensation reaction with NaOH as the basic catalyst. Chalcones *(E)*-1-(5-methylfuran-2-yl)-3-phenylprop-2-en-1-one (1a), *(E)*-3-(4-bromophenyl)-1-(5-methylfuran-2-yl)prop-2-en-1-one (1b) and *(E)*-1-(5-methylfuran-2-yl)-3-(*p*-tolyl)prop-2-en-1-one (1c) were products of 2-acetyl-5-methylfuran and benzaldehyde (a), 4-bromobenzaldeyde (b), and 4-methylbenzaldehyde (c) respectively. Their *N*-acetylated pyrazoline derivatives were synthesized from the reaction of the heterocyclic chalcones with hydrazine hydrate in glacial acetic acid *via* the formation of a hydrazine intermediate to give 1-(5-(5-methylfuran-2-yl)-3-phenyl-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (2a), 1-(3-(4-bromophenyl)-5-(5-methylfuran-2-yl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (2b) and 1-(5-(5-methylfuran-2-yl)-3-(*p*-tolyl)-4,5-dihydro-1*H*-pyrazol-1-yl)ethan-1-one (2c). All the six compounds were obtained with a moderate yield and their molecular structures were confirmed using ATR-FTIR and NMR analyses.

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