Synthesis and Characterization of Chlorinated Thiophene Based Flavones

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Abstract

(E)-3 -(3- (2,5-dichlorothiophen-3-yl) -1- (2,3-dimethylphenyl) -1H-pyrazol-4-yl) -1-(2-*hydroxyphenyl)prop-2-en-1-ones were synthesized by Claisen-Schmidt condensation reaction between 3-(2,5-dichlorothiophen-3-yl)-1-(2,3-dimethylphenyl)-1H-pyrazole-4-carbaldehyde and substituted 2-hydroxy acetophenones. 2-(3-(2,5-Dichlorothiophen-3-yl)-1-(2,3-dimethylphenyl)-1H-pyrazol-4-yl)-4H-chromen-4-ones were synthesized by oxidative cyclization of corresponding chalcones using DMSO/I_2.The structures of newly synthesized compounds were confirmed by some spectral analysis methods like, IR, NMR and Mass.*

Keywords: Chlorinated thiophene, oxidative cyclization,Claisen-Schmidt condensation.

Introduction

Thiophene is a five membered heteroaromatic compound with sulfur as a heteroatom. Thiophene and its derivatives exist in petroleum or coal. Thiophene moiety is found in certain natural products. It is also incorporated in several pharmacologically active compounds. The compounds containing thiophene moiety are reported to have antiproliferative [1], antibacterial [2], anticonvulsant [3] and antiprotozoal [4].

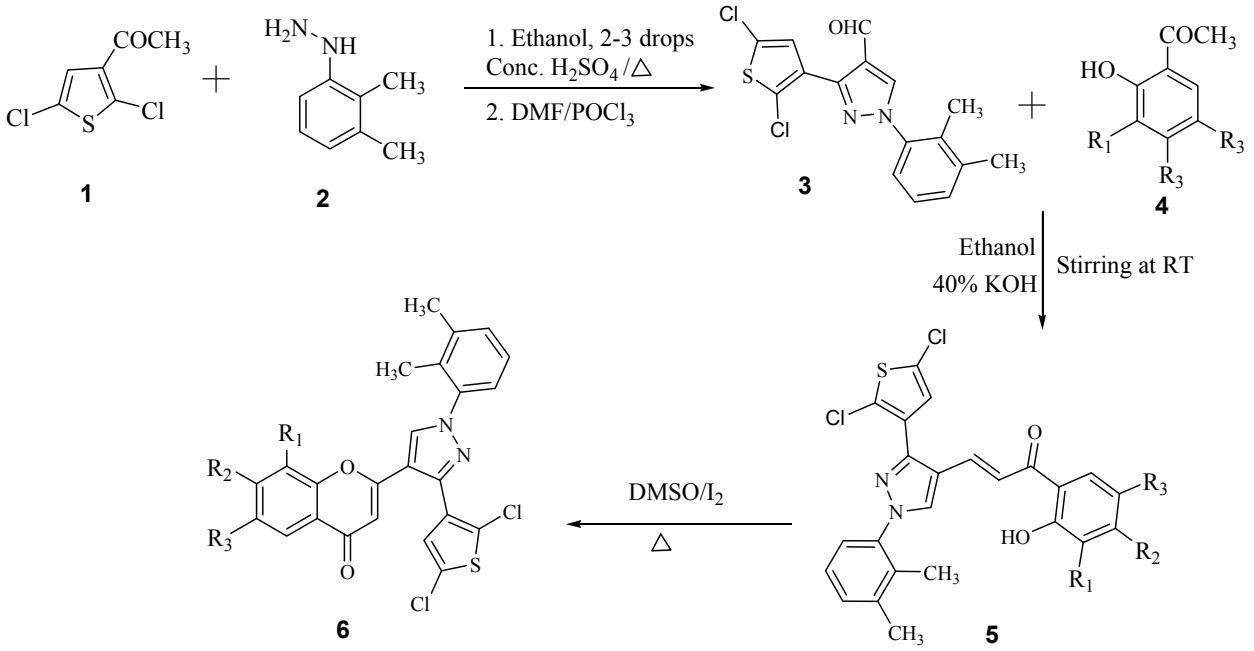
Chalcones are organic compounds possessing an enone moiety between two aromatic or heteroaromatic rings. These are the building blocks for the synthesis of various heterocyclic compounds like flavones, hydroxyl flavones, aurones and pyrazolines. Some chalcones are natural products found in various plant species around the world.Chalcones possess pharmacological activities like anticancer [5], anticancer [6] and antioxidant [6].

Flavones are group of naturally occurring oxygen containing heterocyclic compounds. They found in cereals and herbs. Flavones possess the activities such as antioxidant [7], antibacterial [8], antifungal [9] and antiviral [9].

Considering the biological importance of thiophene based heterocyclic compounds and in continuation of our work it was planned to synthesize chalcones and flavones containing chlorinated thiophene moiety.

Experimental

Melting points were recorded in open capillaries in liquid paraffin bath and are uncorrected. IR spectra were recorded on Perkin-Elmer FTIR spectrophotometer.^{1}H NMR spectra were recorded on Bruker Avance 400 MHz NMR spectrometer in DMSO as a solvent and TMS as an internal standard. Peak values are shown in σ (ppm). Mass spectra were recorded on Finnigan mass spectrometer.



SCHEME 1

Table: 1. Characterization data of synthesized compounds

Sr. No.	Compound	R_1	R_2	R_3	M.P. (^{0}C)	Yield (%)
1	5a	H	CH_3	Cl	158-159	65
2	5b	Cl	H	Cl	216-218	69
3	5c	CH_3	H	CH_3	217-219	52
4	5d	H	H	Cl	185-187	56
5	5e	H	H	F	180-182	58
6	5f	H	H	H	179-181	51
7	6a	H	CH_3	Cl	211-213	66
8	6b	Cl	H	Cl	255-257	70
9	6c	CH_3	H	CH_3	239-241	50
10	6d	H	H	Cl	224-226	61
11	6e	H	H	F	202-204	60
12	6f	H	H	H	199-201	58

General Procedure for the synthesis of chalcones

3-(2, 5-Dichlorothiophen-3-yl)-1-(2, 3-dimethylphenyl)-1*H*-pyrazole-4-carbaldehyde **3** (0.002 mol) was dissolved in 30 mL of ethanol with 2-hydroxyacetophenone **4** (0.002 mol) and 10 mL of 40% KOH was added in it. The reaction mixture was stirred at room temperature for 48 h. After completion of reaction the contents were poured into crushed ice and neutralized with acetic acid. The yellow solid thus obtained was filtered and crystallized from ethanol. Compounds synthesized by above method are listed in table 1.

(*E*)-1-(5-chloro-2-hydroxy-4-methylphenyl)-3-(3-(2,5-dichlorothiophen-3-yl)-1-(2,3-dimethylphenyl)-1*H*-pyrazol-4-yl)prop-2-en-1-one 5a:

FTIR (cm^{-1}): 3378 (-OH), 1658 (C=O), 1050 (Ar-Cl); ^{1}H NMR (400 MHz, DMSO d6, δ ppm): 2.10 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 7.23-8.28 (m, 8H, Ar-H and =CH), 8.99 (s, 1H, Pyrazole –H), 13.50 (s, 1H, OH); Mass m/z: 518 (M^+) with isotopic peaks .

(*E*)-1-(3,5-dichloro-2-hydroxyphenyl)-3-(3-(2,5-dichlorothiophen-3-yl)-1-(2,3-dimethylphenyl)-1*H*-pyrazol-4-yl)prop-2-en-1-one 5b:

FTIR (cm^{-1}): 3375 (-OH), 1660 (C=O), 1053 (Ar-Cl); ^{1}H NMR (400 MHz, DMSO d6, δ ppm): 2.15 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 5.1(s, 1H, -OH), 7.23-8.28 (m, 8H, Ar-H and =CH), 8.96 (s, 1H, Pyrazole –H), 13.54 (s, 1H, OH); Mass m/z: 538 (M^+) with isotopic peaks .

General Procedure for the synthesis of flavones

(*E*)-3-(3-(2,5-dichlorothiophen-3-yl)-1-(2,3-dimethylphenyl)-1H-pyrazol-4-yl)-1-(2-hydroxyphenyl)prop-2-en-1-ones **5** (0.001 mol) was dissolved in 15 mL of DMSO. To this reaction mixture, catalytic amount of iodine (50 mg) was added. Contents were heated at 140 ^oC for 2 h and kept overnight. To this reaction mixture 100 mL of cold water was added and the separated product was filtered and washed with dilute sodium thiosulphate solution (10%) for several times. Again it was washed with cold water and crystallized from alcohol to afford compound **6**. Compounds synthesized by above method are listed in table 1.

6-Chloro-2-(3-(2,5-dichlorothiophen-3-yl)-1-(2,3-dimethylphenyl)-1*H*-pyrazol-4-yl)-7-methyl-4H-chromen-4-one 6a:

FTIR (cm^{-1}): 3039 (Ar C-H) 1640 (C=O), 1045 (Ar-Cl); ^{1}H NMR (400 MHz, DMSO d6, δ ppm): 2.11 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 6.75 (s, 1H, chromone -H), 7.24-7.36 (m, 3H, Ar-H), 7.92-7.97 (m, 2H, Ar-H), 8.20 (s, 1H, thiophene -H), 8.85 (s, 1H, Pyrazole –H); Mass m/z: 516 (M^+) with isotopic peaks.

6,8-Dichloro-2-(3-(2,5-dichlorothiophen-3-yl)-1-(2,3-dimethylphenyl)-1H-pyrazol-4-yl)-4H-chromen-4-one 6b:

FTIR (cm^{-1}): 3041 (Ar C-H) 1643 (C=O), 1056 (Ar-Cl); ^{1}H NMR (400 MHz, DMSO d6, δ ppm): 2.15 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 6.78 (s, 1H, chromone -H), 7.27-7.40 (m, 3H, Ar-H), 7.98-8.17 (m, 2H, Ar-H), 8.25 (s, 1H, thiophene -H), 8.88 (s, 1H, Pyrazole –H); Mass m/z: 536 (M^+) with isotopic peaks.

Result and Discussion

The FTIR spectra of compound **5a** shows absorption band at band 1658 cm^{-1} frequency is due to presence of carbonyl group of chalcone. It also shows another absorption band at 3378 cm^{-1} because of hydroxyl group. The hydroxyl frequency is diminished when chalcone is converted into flavones. It indicates formation of Flavone ring. The stretching frequency appears at 1640 cm^{-1} corresponds to the carbonyl of flavone. The ^{1}H NMR peak of chromone proton is obtained at 6.75 δ indicates the formation of chromone ring and the disappearance of singlet at 13.50 δ of hydroxyl proton confirms the conversion of chalcone **5a** into flavone **6a**.

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