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Synthesis, Spectral Studies and Anti-Inflammatory Activity of 2-Acetyl Thiophene

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Abstract: Some new chalcones have been synthesized by the condensation of 2-acetyl thiophene with various aromatic aldehydes in 40% alkali. The synthesized compounds were identified by spectral data and screened for anti-inflammatory activity. Some of these compounds showed moderate to considerable anti-inflammatory activity.

Keywords: Chalcone, Synthesis, Anti-inflammatory activity.

Introduction

Chalcones display interesting biological activities, including antimalarial[1], anti-inflammatory[2], cytotoxic[3,4], anticancer[5,6] and antimicrobial activities[7,8]. In the present study, some new chalcones **(1-8)** have been synthesized by the reaction of 2-acetyl thiophene with different aromatic aldehydes. The structures of the various synthesized compounds are assigned on the basis of elemental analyses, IR and ^{1}H NMR spectral data. These compounds were also screened for their anti-inflammatory activity.

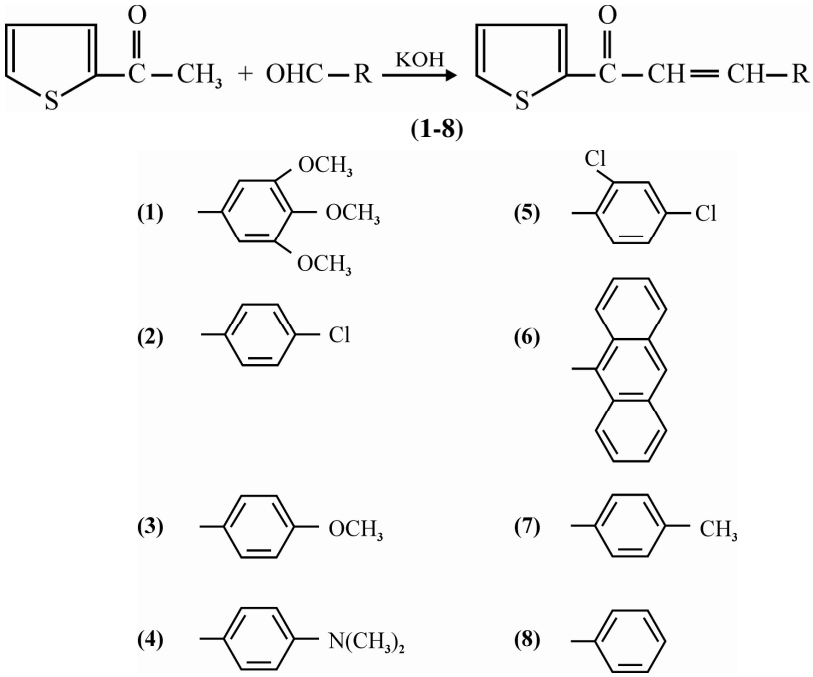
Experimental

Melting points were determined on a capillary melting point apparatus and are uncorrected. ^{1}H NMR spectra was recorded in the indicated solvent on Bruker WM 400 MHz spectrometer with TMS as internal standard. Infrared spectra were recorded in KBr on Perkin-Elmer AC-1 spectrophotometer. Microanalyses were performed on Carlo Erba EA-1108 element analyzer and were within the ±0.5% of the theoretical values. Column chromatography was performed on silica gel (Merck, 60-120 mesh).

*General procedure for the preparation of chalcones (**1-8**)*

A mixture of 2-acetyl thiophene (0.01 mol) and appropriate aldehyde (0.01 mol) was stirred in ethanol (30 mL) and then an aqueous solution of KOH (40%, 15 mL) was added to it.

The mixture was kept overnight at room temperature and then it was poured in to crushed ice and acidified with HC1. The solid separated was filtered and crystallized from ethanol (Scheme 1). The characterizations data of these compounds are described in Tables 1 & 2.



Scheme 1. Synthesis of some new chalcones of 2-acetyl thiophene (**1-8**).

Table 1. Physical data of compounds (**1-8**).

Compound	M.F.	M.P, °C	Yield, %	Elemental analyses, %					
				C		H		N	
				Found	Calcd	Found	Calcd	Found	Calcd
1	$C_{16}H_{16}O_4S$	135	95	43.00	43.20	43.10	43.20	10.50	10.80
2	$C_{13}H_9SCl$	110	96	52.24	52.00	35.94	36.00	9.36	9.00
3	$C_{14}H_{12}O_2S$	70	86	48.55	48.20	41.57	41.30	7.12	6.83
4	$C_{15}H_{15}OSN$	100	83	45.44	45.45	45.68	45.45	3.42	3.03
5	$C_{13}H_8OSCl_2$	95	92	51.62	52.00	32.06	32.00	3.92	4.00
6	$C_{21}H_{16}OS$	140	80	54.90	53.84	41.11	41.02	2.59	2.56
7	$C_{14}H_{12}OS$	105	89	50.06	50.00	42.76	42.85	3.61	3.51
8	$C_{13}H_{10}OS$	90	87	52.09	52.00	40.11	40.00	4.06	4.00

Anti-inflammatory activity

Synthesized compounds (**1–8**) were tested for their anti-inflammatory activity. Male albino rats weighing between 200-250 g were used for the experiment. Carragenan induced paw oedema method described by Singh and Ghosh[9] was followed for the acute anti-inflammatory model and the results are presented in Table 3.

Table 2. Spectral data of the compounds (**1-8**).

Compound.	IR (KBr, cm^{-1})	^1H NMR ($CDCl_3$, ppm)
1	3330 (–OH). 720(–C=O), 1650 (–CH=CH), 1175 ($–OCH_3$), 650(C–S).	7.69(1H, d, J= 16Hz, –CO–CH=), 7.89 (1H, d, J= 16Hz, =CH–Ar), 3.90-3.95 (9H, s, 3X–OCH_3), 7.20 (1H, m, C–4^1–H), 7.28 (2H, d, C–2^1–H, C–5^1–H), 7.78 (2H, s, C–2–H, C–6–H).
2	1725 (–C=O), 1640(–CH=CH), 850 (C–CL), 650 (C–S)	7.70 (1H, d, J=16Hz, –CO–CH=), 7.88 (1H, d, J=16Hz, =CH–Ar), 7.80 (1H, d, J=9Hz, C–5^1–H), 7.58 (2H, d, C–3–H, C–5–H), 7.40 (2H, d, C–2–H, –C–6–H), 7.38 (1H, d, J=16Hz, C–3–H), 7.20 (1H, m, C-4^1-H).
3	1720 (–C=O), 1648 (–CH=CH), 1170 ($–OCH_3$), 666 (C–S)	6.94 (1H, d, J = 16Hz, – CO –CH=), 7.61 (1H, d, J = 16Hz = CH – Ar), 7.86 (2H, d, C–3^1–H, –C–5^1–H), 7.68 (2H, d, C–3–H, –C–5–H), 7.18 (1H, m, C–4^1–H), 6.92 (2H, d, –C–2–H, –C–6–H).
4	1730 (–C=0), 1638 (–CH=CH), 1180($N(CH_3)_2$), 676 (C–S)	6.70 (1H, d, J = 16Hz , –CO–CH=), 7.55 (1H, d, J=16Hz, =CH–Ar), 3.05 (1H, s, $N(CH_3)_2$), 7.86 (2H, d, C–5^1–H, C–3^1–H), 7.82 (2H, d, C–3–H, C–5–H), 7.63 (2H, d, C–2–H, C–6–H), 7.17 (1H, m, C–4^1–H).
5	1735 (–C=O), 1636 (–CH=CH), 855 (C–Cl), 686 (C–S)	7.31 (1H, d, J=16Hz, –CO–CH=), 7.87 (1H, d, J=16Hz, =CH–Ar) 7.71 (1H, d, J=8Hz, –C–5–H), 7.69 (1H, d, J=9Hz, –C–3^1–H), 7.67 (1H, d, –C–6–H), 7.48 (1H, s, –C–3–H), 7.20 (1H, m, –C–4^1–H).
6	1710 (–C=0), 1655 (–CH=CH), 645 (C–S)	7.44 (1H, d, J= 16Hz, –CO–CH=), 7.74 (1H, d, J= 16Hz, =CH–Ar) 8.83 (1H, d, J=9Hz, C–5^1–H), 8.09 (1H, m, C–4^1–H), 8.06 (1H, d, J=9Hz, C–3^1–H), 7.18-7.79 (10H, m, Ar–H).
7	1732(–C=O), 1645 (–CH=CH), 652 (C–S)	7.39(1H, d, J=16Hz , –CO–CH=), 7.56 (1H, d, J=16Hz, =CH–Ar), 7.88 (1H, d, J=9Hz, –C–5^1–H), 7.68 (2H, d, –C–2–H, –C–6–H), 7.58 (1H, d, J=8Hz, –C–3^1–H), 7.23 (2H, d, –C–3–H, –C–5–H), 7.19 (1H, m, –C–4^1–H).
8	1700 (–C=0), 1650 (–CH=CH), 650 (C–S)	7.69 (1H, d, J=16Hz , –CO–CH=), 7.84 (1H, d, J=16Hz =CH–Ar), 7.19 (1H, m, C–4–H), 7.87 (1H, d, J=9Hz, C–5^1–H), 7.44 (1H, m, C–4^1–H), 7.42 (1H, d, J=9Hz, C–3^1–H,), 7.40(2H, d, C–3–H, C–5–H), 7.64 (2H, m, C–2–H, C–6–H).

Table 3. Anti-inflammatory activity of the compounds (**1-8**).

Compound	% increase in paw thickness of various time intervals					
	0.5 h	01 h	2 h	3 h	4 h	6 h
Standard	20.26± 0.64	23.95± 0.66	58.02± 1.54	67.93± 1.65	97.09± 1.95	98.98± 1.98
Control	23.59± 1.35	22.69 ±1.71	56.46 ±1.28	72.02 ±1.86	86.43 ±4.03	87.66± 1.55
1	36.97± 0.78	46.54± 3.02*	56.95± 3.54**	65.22± 1.59	74.74± 1.73	87.66± 1.55
2	49.39± 2.97*	50.60± 2.51*	59.89± 0.96	74.90± 3.17*	82.42± 5.72***	94.43± 1.02
3	44.46± 2.20	69.62± 1.01	69.21± 2.58*	78.66± 4.77***	85.68± 4.31***	97.05± 4.32**
4	36.79± 2.54*	50.70± 3.77**	64.55± 3.28*	75.15± 3.21*	88.36± 3.31*	94.61± 1.95
5	36.26± 2.48*	50.43± 1.36	55.27± 1.44	78.19± 4.47***	82.24± 3.38**	89.23± 3.90**
6	43.91± 1.80	60.66± 2.92*	66.96± 4.39***	78.91± 4.79***	85.51± 4.41***	94.55± 2.04
7	18.64± 2.01	41.30± 4.07**	41.88± 0.09	67.63± 1.42	76.32± 3.89**	89.23± 3.89**
8						

Control: 1% sodium CMC gel, standard : aceclofenac standard and sample solution is 100 mg/ kg body weight, values are expressed as mean ±(n = 6) = 2.28, ** = 3.75, *** = 4.35.*
P < 0.05, P** < 0.01, P*** < 0.001 compared to control student t-test*

Results and Discussion

The screening results revealed that the compounds (**1-8**) exhibited moderate to considerable activity when compared with reference standard aceclofenac. The synthesized compounds showed anti-inflammatory activity in the range of 50-80% whereas standard drug showed 80-85% inhibition in paw edema. The results of anti-inflammatory activity indicated that compound **4** showed maximum anti-inflammatory activity.

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