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Synthesis and Pharmacological Activity of Some Phenoxy Chalcones

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Some new phenoxy chalcones were prepared by condensing different aromatic aldehydes with phenoxy acetophenones. All the synthesized compounds were confirmed by ^{1}H NMR and MASS spectral studies and were screened for their antiinflammatory activity. Some of the synthesized compounds show potent antiinflammatory activity.

Key Words: Phenoxy acetophenones, Aromatic aldehyde, Phenoxy acetophenone, Antiinflammatory activity.

INTRODUCTION

Chalcones a class of naturally occurring pigments, have a broad spectrum of biological activities such as antiinflammatory[1], antibacterial[2,3], antifungal[4], anthelmintic[5] and antitumor[6] activities. In view of the above mentioned facts, we intend to synthesize some substituted 4'-phenoxy chalocones and screen them for antiinflammatory activity.

EXPERIMENTAL

The structures of all these compounds were established by ^{1}H NMR and mass spectral studies. Melting points were determined in capillaries in liquid paraffin and are uncorrected. ^{1}H NMR spectra were recorded on Bruker DRX (300 MHz, FT NMR) spectrometer using TMS as an internal standard (δ ppm) and mass spectra on Jeol 5x102/DA-6000 mass spectrometer.

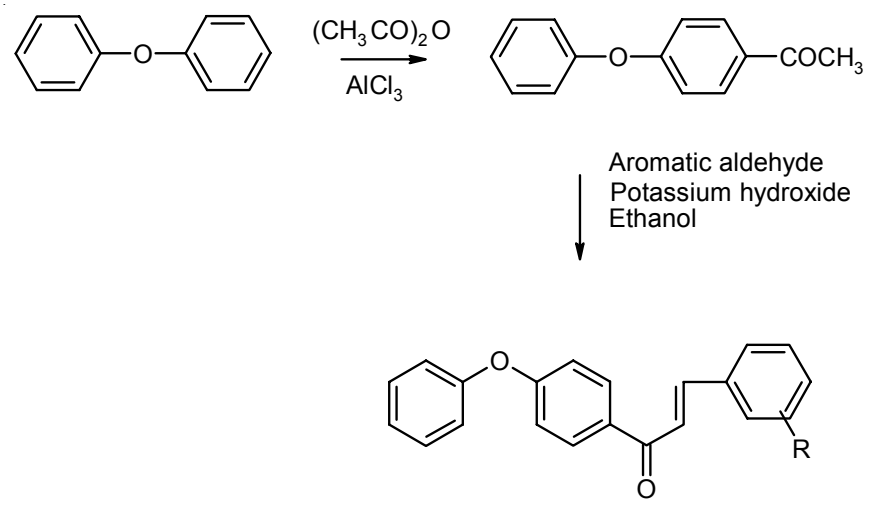
Synthesis of phenoxy acetophenone (I): To a cooled mixture of biphenyl ether (0.33 mol, 55 mL) and aluminium chloride (18.8 g) in carbon disulphide (87.5 mL), acetic anhydride (12 mL) was added and refluxed for 2 h. After 2 h, the reaction mixture was cooled to room temperature and poured into a mixture of crushed ice and conc. HCl. It was then extracted with diethyl ether. After removing the ether, the residue was recrystallized

in ethanol. Yield: 78.72 %; m.p.: 48-50°C; IR (KBr, cm^{-1}): 1680 ν(C=O), 1230 ν(C-O-C), 1580, 740, 680; ^{1}H NMR ($CDCl_3$): δ 2.56 (s, 3H, -$COCH_3$), 6.98~7.39 (m, 9H, aromatic protons); MS: m/z 212 (M^+), 197, 141, 115, 77.

General synthesis of substituted 4'-phenoxy chalcones (Ia-d): To a stirred solution of potassium hydroxide (3 g) in water (3 mL) and ethanol (50 mL) mixture, 4'-phenoxy acetophenone (0.03 mol, 6.37 g) and aromatic aldehyde (0.01 mol) were added. The reaction mixture was stirred vigorously for 3 h and then poured into crushed ice, a solid mass separates out. The product was filtered, washed with cold water (50 mL) and recrystallized from methanol (Table-1) (**Scheme-I**).

TABLE-1
PHYSICAL CHARACTERISTICS OF THE SYNTHESIZED COMPOUNDS

Compound	R	m.p. (ºC)	Yield (%)
Ia	H	80-82	77.46
Ib	4-Methoxy	60-64	74.36
Ic	3,4-Dimethoxy	106-108	76.47
Id	3,4-Methylene dioxy	126-128	74.06



Scheme-I

Spectral data

4'-Phenoxy chalcone (1a): ^{1}H NMR ($CDCl_3$): δ 8.04 (d, 2H, phenoxy substituted phenyl protons), 7.82 (d, 1H, alkenyl β-proton), 7.52 (d, 1H, alkenyl α-proton), 7.2 ~ 7.04 (m, 12H, aromatic protons); MS: m/z 300 (M^+), 272, 207, 197, 154, 103, 77.

1b: ^{1}H NMR ($CDCl_3$): δ 7.77 (d, 1H, alkenyl β-proton), 7.55(d, 2H, phenoxy substituted phenyl protons), 7.39 ~ 7.02 (m, 10H, aromatic protons and α-proton), 6.88 (d, 2H, phenyl protons ortho to methoxy group), 3.78 (s, 3H, methoxy); MS : m/z 330 (M^+), 237, 197, 170, 154, 77.

1c: ^{1}H NMR ($CDCl_3$): δ 8.03~7.09 (m, 13H, aromatic protons and alkenyl protons), 6.88 (d, 1H, phenyl proton ortho to methoxy group), 3.78 (s, 3H, methoxy); MS: m/z 360 (M^+), 346, 330, 267, 212, 197, 157, 77.

1d: ^{1}H NMR ($CDCl_3$): δ 8.01~7.14 (m, 13H, aromatic protons and alkenyl protons), 6.85 (d, 1H, phenyl proton ortho to methylene dioxy group), 6.01 (s, 2H, methylene dioxy group); MS: m/z 344 (M^+), 316, 251, 199, 77.

Antiinflammatory activity: All the synthesized compounds were screened for antiinflammatory activity by carrageenan induced rat paw edema method[7] in Albino rats at a dose of 20 mg/kg. The test compounds were made into homogeneous suspension with distilled water, 1 % CMC and were administered orally. The percentage inhibition was noted at the end of 3 h of administration of carrageenan. Carrageenan induced paw edema method of the test compounds was compared with known standard compound (Indomethacin). Among the synthesized compounds, **Ic** and **Id** showed significant antiinflammatory activity.

RESULTS AND DISCUSSION

All the synthesized compounds were characterized by ^{1}H NMR and mass spectral data. In ^{1}H NMR of compounds the characteristic alkenyl protons merges with the aromatic region only in 4'-unsubstituted phenoxy chalcones, they show at δ 7.52 and δ 7.82. Further, the methoxy protons and methylene dioxy protons appear at δ 3.78 and δ 6.01, respectively. By analyzing the mass spectra it was found that the molecular ion peaks were strong probably due to the rigid ring structure. Among the synthesized compounds, **Ic** and **Id** were found to be potent than the other compounds. Compound **Ic** and **Id** show 37.11 and 50.60 % inhibition, respectively after 3 h when compared with standard drug indomethacin, which show 70.43 % inhibition (Table-2).

TABLE-2
ANTIINFLAMMATORY ACTIVITY OF THE
SYNTHESIZED COMPOUNDS

Compound	Dose (mg/kg)	% Inhibition of edema at 3 h
I	20	15.90
Ia	20	21.10
Ib	20	31.40
Ic	20	37.11*
Id	20	50.60*
Std. (Indomethacin)	10	70.43*

*$p < 0.01$ and $n = 6$, where n = number of rats used in each group.

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