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Synthesis of Some New Bischromones from Bischalcones

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ABSTRACT

Some novel Di (6/8-chloro-8/6-Chromonyl) Methyl ethers i.e**.** Bischromones –I & II were synthesized by oxidative cyclisation of Di (5'-chloro-4'/2'-hydroxy-3'-chalconyl) methyl ethers i.e. Bischalcones- I & II and screened for antifungal activity.

Key words: Synthesis, Bischromones and Bischalcones

INTRODUCTION

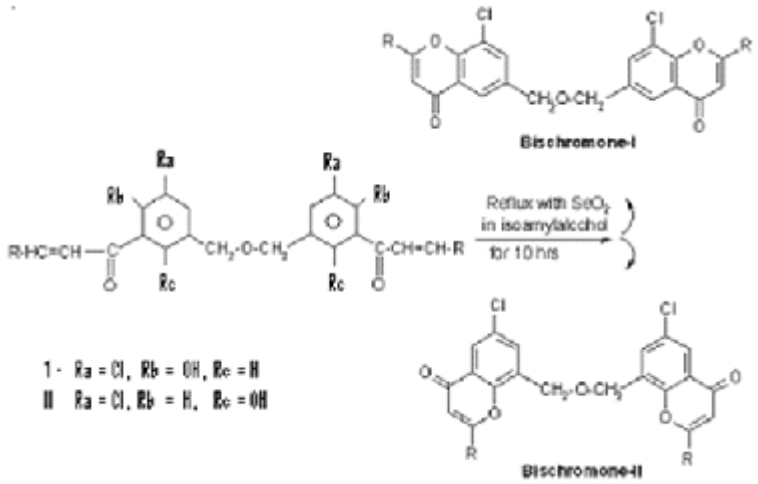
The Bischromones are used primarily in treating allergic asthma, exercise-induced asthma, sometimes in intrinsic asthma and also in the studies of various allergic lung diseases[1]. Chromolyn sodium (Intal) is used principally in the treatment of bronchial asthma[2]. It is the only biscromone drug now licensed by the Food & Drug Administration[3]. It is available as a powder and in capsule form. The Disodiumchromoglycate (DSCG/ INTAL) and related compounds there of, including generally bischromones as anti allergenic, anti-PACVIS (Pathological cardiovascular ischemic state) agents[4], and in the treatment of Bronchial asthma in children[5]. It also have an effect on the release of bistamine & degranulation of rat mast cells[6-7]. The Disodiumchromoglycate (DSCG) related compounds shows inhibition of homologous passive cutaneous anaphylaxis (PCA)[7]. Lomudal inhibits the bronchospam induced by the antigen & inhibits least partially the post exercise fall in FEV in children and adults[9]. A khelin like 7,7'-Glycerol bridged bischromone found anti anaphylacetic antivit[10].

Use of bischromones in studies of various allergic lung diseases has provided researchers with valuable information about the body's immune mechanisms. Therefore it was thought worthwhile to synthesize some new bischromones from bischalcones.

General Method

A mixture of Bischalcones-I/II (0.01 mole) and selenium oxide (0.08 mole) in isoamyl alcohol (50 ml) was refluxed for 10-12 hours. The reaction mixture was cooled and filtered to remove black precipitate of selenium formed during the reaction. Isoamyl alcohol from the filterate was removed by steam distillation and non-volatile residue thus obtained was extracted with hot benzene. Benzene

layer was washed with aqueous $NaHCO_3$ (10%) and then by distilled water to remove any acidic and water soluble impurities. The benzene was removed by evaporation and residue was crystallized from proper solvent (Scheme 1).



Scheme 1:

EXPERIMENTAL

The purity of the compounds was checked by TLC. Melting points of the compounds were determined in open capillary tubes and are incorrected. The IR spectra were recorded on Perkin-Elmer IR Infra cord in KBr disc. ^{1}H-NMR spectra were recorded on a 300 MHz Brucker spectrometer using TMS as an internal standard. The titled compounds Bischromons-I & II i.e. Di (6/8- chloro-2-phenyl-8/6-Chromonyl) methyl ethers were synthesized by oxidative cyclisation of Bischalcones I & II i.e. Di (5'-chloro-4'/2'-hydroxy-3'-chalconyl) methyl ethers. These Bischalcones I & II on refluxing with SeO_2 in isoamyl alcohol for 10 hrs., afforded Bis- Chromones- I & II (Table-I & II)

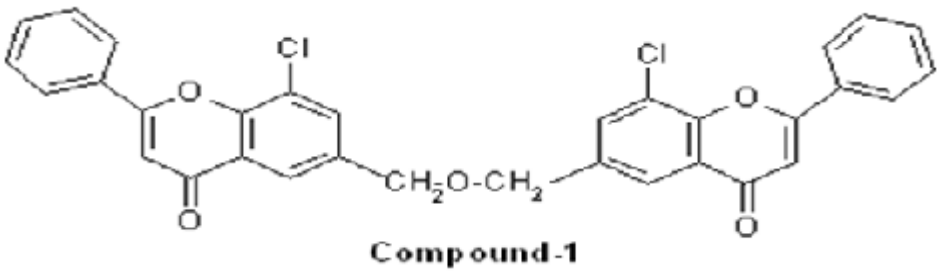
Discussion of IR & ^{1}H-NMR

The representative member [comp.-1(Bischromons-I, from Table-I)] have shown following spectral data.

IR (KBr): nmax cm^{-1}:1635 (C=O), 1364-1361 (Pyrone-oxide vibration), 1563-1538 (ethylenic bond), 1100-1080 (asymmetrical (C-O-C stretch)

^{1}H-NMR: ($CDCl_3$, 300 MHz), dppm : 8.22 [d,2H,Jm=2.6 Hz,(H-5)], 8.07 [m,4H (H-2',6')], 7.60 [d,2H,Jm=2.6Hz,(H-7)],7.50 [m,6H, (H-3',4',5'], 6.78 [s,2H,(H-3)] ,4.03 [s,4H, ($_2$HC-O-CH_2)]

Therefore the structure of comp.-1 is



Scheme 2:

Table 1: Di (8-chloro-6-Chromonyl) Methyl ethers i.e. Bischromones-I

S.No.	R.	m.p.(°C)	Yield (%)	Analysis found (Calcd) Chlorine
1.	Phenyl	251	50	12.67 (12.79)
2.	o-Chlorophenyl	162	65	22.42 (12.79)
3.	p-Chlorophenyl	242	65	22.58 (22.75)
4.	o-Methyl phenyl	233	70	12.48 (12.17)
5.	p-Methoxy phenyl	225	72	11.33 (12.09)
6.	o-Hydroxy phenyl	213	50	12.48 (12.09)
7.	m-Hydroxy phenyl	217	68	12.47 (12.09)
8.	p-Hydroxy phenyl	238	75	12.47 (12.09)
9.	α-Naphthyl	266	70	10.62 (10.83)

Table 1: Di (6-chloro-8-Chromonyl) Methyl ethers i.e. Bischromones-II

S.No.	R.	m.p.(°C)	Yield (%)	Analysis found (Calcd) Chlorine
1.	Phenyl	226	50	12.67 (12.79)
2.	o-Chlorophenyl	161	62	22.52 (22.75)
3.	p-Chlorophenyl	216	60	22.38 (22.75)
4.	o-Methyl phenyl	210	60	12.67 (12.17)
5.	p-Methoxy phenyl	246	70	11.32 (12.09)
6.	α -Naphthyl	261	75	10.62 (10.83)

Hence, the name of the compound is Di (8-chloro-2-phenyl-6-Chromonyl) Methyl ether.

Antifungal Activity

The antifungal screening of some of the representative compounds of the type I and II was carried out by dry weight method. In general they were found to be stimulatory against Penicillium Notatum at 100 ppm and 250 ppm concentrations.

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