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Synthesis and Spectroscopic Studies of Bis-γ Pyrones

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Abstract: The Baker-Venkataramn transformation using NaOH in dimethylsulphoxide (DMSO) 77 have been employed for the coversions of ester (o-aroyloxy/ heteroaroyloxyacetophenones) into the corresponding bis β-diketones. A novel class of 2, 8-bis(aryl/heteroaryl) pyrano [3, 2-γ] chromene-4, 6-diones have been synthesized. Bis-β diketones obtained undergoes cyclisation to achieve 2, 8-bis(aryl/heteroaryl) pyrano [3, 2-γ] chromene-4, 6-diones with impressive yields. Reaction mechanism for their formation have been elucidated. 4, 6- Diacetylresorcinol was obtained by the acylation of resorcinol. The structures of these compounds were confirmed by IR, NMR and Mass spectral studies.

Keywords: 4, 6-Diacetyl resorcinol, Bis β-diketones, Pyrones, Spectral analysis.

I. Introduction

γ-Pyrone based natural products constitute a large class of biologically active compounds. The first isolation of the structurally rather simple γ-pyrone poppy acid from Papaver somniferum by F. W. Sertürner in γ-pyrone natural products were isolated. Most of these were derived from marine organisms in which they seem to play an important role as allomones or defense compounds [1-2] Chromones and their derivatives of different oxidation level are well known naturally occurring oxygen-containing heterocyclic compounds which perform important biological functions. They possess important biological activities, such as anti-tumor, anti-hepatotoxic, antioxidant, anti-inflammatory, anti-spasmolytic, oestrogenic and antibacterial activities [3-7] 2-Styrylchromones are one of the scarcest classes of natural chromones. Chromones [8] exhibit important biological as well as pharmacological activities [9]. Flavonoids [10] are the chromones that are also most abundantly in nature. Some chromones are also reported as anti-HIV agents. Khellin [11] Fig. 1 and 2, 4-thiazolidenedione [12] Fig. 2 are the chromones that are used as antispasmodic agent, in the treatment of anginapectoris and antidiabetic agent that improve peripheral insulin resistance in type-II diabetic patients respectively.

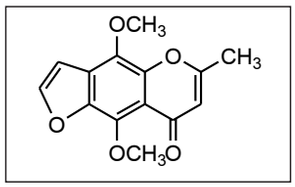


Fig. 1

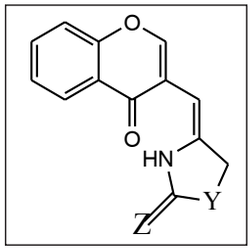


Fig. 2

The results indicate that compounds having dimethyl-aminomethyl in the 3-position are most active. Substitution in the benzene ring caused improvement in activity only in the case of 6-hydroxy and 6- or 7-alkoxy groups. Compound [13] was about as effective as Fuadin against *Schistosoma mansoni* when introduced intraperitoneally into infected ma number of alkylaminomethylchromanones Fig. 3 were synthesized and tested against *Endamoeba histolytica* and *Schistosoma mansoni* [14].

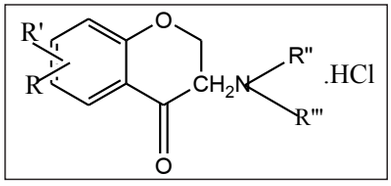


Fig. 3

The structure of the antibiotic novobiocin (I) has been reported [15-16]. Alcoholic hydrochloric acid cleavage the glycosidic linkage in novobiocin forming the methyl glycoside of 3-O carbamylnoviose 1*z and the aglycon, novobiocic acid (II) Fig. 4 [17].

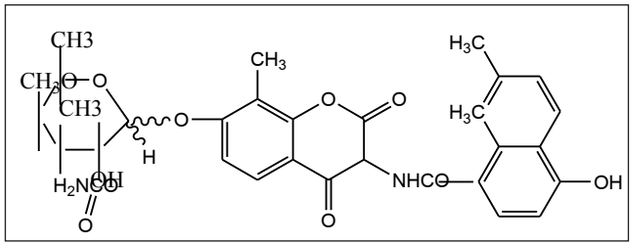
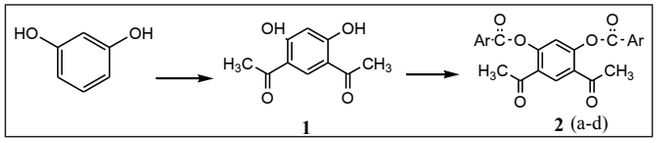


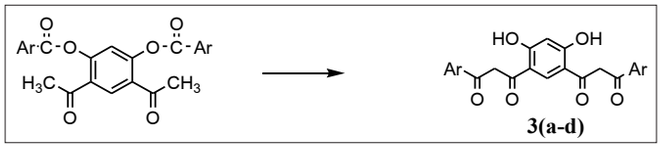
Fig. 4

II. Scheme

1. 1, 3-Diaroyloxy/heteroaroyloxy-4, 6-diacetophenones *2(a-d)*



2. 3', 3–(4, 6-dihydroxy-1,3-phenyl) bis (1-aryl/heteroaryl propane-1, 3diones)



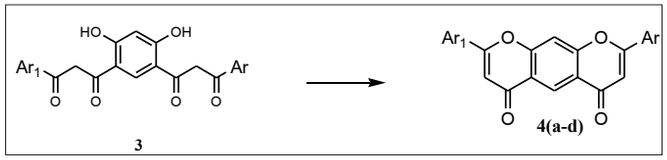
Ar = Ar_1 (a) C_6H_5

(b) 4-$CH_3C_6H_4$

(c) 4-$OCH_3C_6H_4$

(d) 4-CLC_6H_4

3. 2, 8-bis(aryl/heteroaryl) pyrano [3,2-γ] chromene-4, 6-diones *4(a-d)*



Ar = Ar_1 (a) C_6H_5

(b) 4-$CH_3C_6H_4$

(c) 4-$OCH_3C_6H_4$

(d) 4-CLC_6H_4

III. Present Work

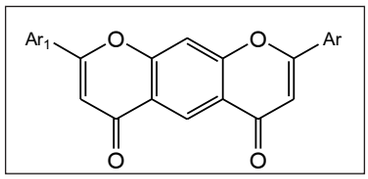
In the present wok, glacial acetic acid-sulphuric acid (Bakervenkatraman method) have been employed for the cyclisation of β-diketones 3, 3'-(4, 6-dihydroxy-1, 3-phenyl) bis (1-aryl/heteroaryl propane-1, 3 diones) to the corresponding chromones.

Glacial acetic acid sulphuric acid were the chemicals used.

IV. Experimental Methods

1. *4, 6-Diacetylresorcinol (Resdiacetophenones)*: Resorcinol (20.0 g, 0.181 mole) was dissolves in (42.65 g, 0.4178 mole) of acetic anhydride (63.16 g, 0.4644 mole) of $ZnCl_2$ was added and the mixture was heated. After 3 hours of the mixture at 150° to 160 °C, 4, 6-diacetylresorcinol crystallized out. After cooling, 25 g of water was added for hydrolyzing the remaining acetic anhydride, then 40 g of methanol was added and, for growing crystals, the resulting mixture was heated under reflux for 30 minutes, then cooled and subjected to solid–liquid separation. The solid was washed with 168 g of methanol and then dried where by 26.03 g (0.1340 mole) of 4, 6-diacetylresorcinol was obtained. The yield was 73.8% on the resorcinol basis.
2. *1,3-Dibenzoloxy-4,6-diacetophenone*: 4,6-Diacetylresorcinol (resdiacetophenones) (0.1 mole) and dry pyridine (10 ml), Benzoyl chloride (0.2 mole) was added slowly maintining the temperature below 20 °C. The reaction mixture was kept overnight and poured on a mixture of ice and HCl. Generally a solid compound separated which was washed with water and dilute NaOH solution and crystallized from ethanol. The yield is 70% m.p- 90 °C. The other 1, 3-Diaroyloxy/heteroaroyloxy-4, 6-diacetophenone were *2a-d* prepared by adopting the same procedure. The physical and analytical data of the compounds 2a-d are given in Table I.
3. *3, 3'-(4, 6-dihydroxy-1, 3-phenyl) bis (1-methoxyphenyl propane-1,3dione)*: 1,3-Dibenzoyloxy-4,6-diacetophenones (0.005 moles) was dissolved in 4ml of DMSO. To that solution powdered NaOH (2 g) was added with vigorous stirring for about five minutes. The stirring was continued for about 5 min further. The reaction mixture was then cooled and poured on cold water. The pale yellow solid product obtained was washed with water dried and crystallized from alcohol. The yield 67% and m.p 121 °C.
4. *2, 8-bis (4-methoxyphenyl) pyrano [3, 2-γ] chromene-4, 6-dione 4c*: (Ar =Ar_1=4-$OCH_3C_6H_5$). The mixture of 3'-(4, 6-dihydroxy-1, 3- phenyl) bis (4-methoxyphenyl propane-1, 3dione) (3-6 g, 0.015 mole) in glacial acetic acid (20 ml) and H_2SO_4 were heated in a water bath for one hour with occasional stirring and poured over crushed ice. It was cooled and filtered washed with water and dried at 50 °C. It is crystallised from petroleum ether yield. The yield is 75% and m.p 135 °C.

TABLE I: CHARACTERIZATION DATA OF 2, 8-BIS (ARYL/HETROARYAL) PYRANO [3, 2-γ] CHROMENE-4, 6-DIONES 4a-d*



Compound	*Colour of $Fecl_3$*	*Ar = Ar_1*	*M. F*	*Yield %*	*M. P* (0ºC)*	*Found (Cald)*		
						C	*H*	*N*
4a	yellow	C_6H_5	$C_{24}H_{14}O_4$	81.98	130	78.64 (78.68)	4.80 (4.86)	-
4b	yellow	4-OCH_3C6H_5	$C_{26}H_{18}O_6$	70.42	135	73.15 (73.23)	4.14 (4.22	-
4c	yellow	4-$CLC6H_4$	$C_{24}H_{12}O_4C_{l2}$	68..96	145	66.10 (66.20)	2.60 (2.75)	-
4d	yellow	4-CH_3C6H_4	$C_{26}H_{18}O_4$	76.14	130	79.75 (79.78)	4.54 (4.56)	-

V. RESULT AND DISCUSSION

The products (entry 4a- 4d) were characterized based on their IR, ^{1}H NMR, Mass and elemental analysis. The mass spectra of these compounds displayed molecular ion peaks at appropriate m/z values. This synthetic strategy is more attractive than earlier methods due to easily recoverable and reusable catalyst, easy workup and higher yields of the product.

8-bis (4-methoxyphenyl) pyrano [3, 2-γ] chromene - 4, 6-dione 4c: IR(KBr)vmax= :

3413 cm^{-1}(C=Cpeak), 1610 cm^{-1} (C=O, 1685 cm^{-1} (aromatic CH_3C=O), 29281 cm^{-1} (aromatic stretching C-H); ^{1}H NMR (DMSO-d6, d,400 MHz) 7.42–8.18 (m, 14H, ArH), 3.55 (s, H, CH_2). Anal. Calcd. for $C_{26}H_{18}O_6M^+$): (395) C, 68.12; H, 4.08. Found: C, 68.10; H, 4.6, which gives characteristic peak at 12.72 which corresponds to enolic proton and at), δ 12.02 which is being due to phenolic proton adjacent to carbonyl group. It confirms the formation of -diketones.

VI. CONCLUSION

All the synthesized compounds were characterized by Melting point, Elemental analysis, IR and ^{1}H NMR. Analysis indicated by the symbols of the elements is very close to the theoretical values. Using a modified Baker–Venkataraman reaction we have synthesised a novel class of 4 novel class of 2, 8-bis(aryl/hetroaryal) pyrano [3, 2-γ] chromene-4, 6-diones 3-acyl-¥-pyrones. The present review represents a broad description for the methods used in the synthesis of chromones and the rigid bicyclic chromone fragment has been classified as a privileged structure in drug discovery, due to its use in a wide variety of pharmacologically active compounds such as anti-tumor, anti-hepatotoxic, antioxidant, anti-inflammatory, anti-spasmolytic, oestrogenic and antibacterial activitiy.

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