SYNTHESIS OF 6-[(4-CHROMON-3-YL-BENZOPYRANO[4,3-b] PYRIDIN-2-YL)]-2H-[1,4]-BENZOXAZIN-3(4H)-ONES

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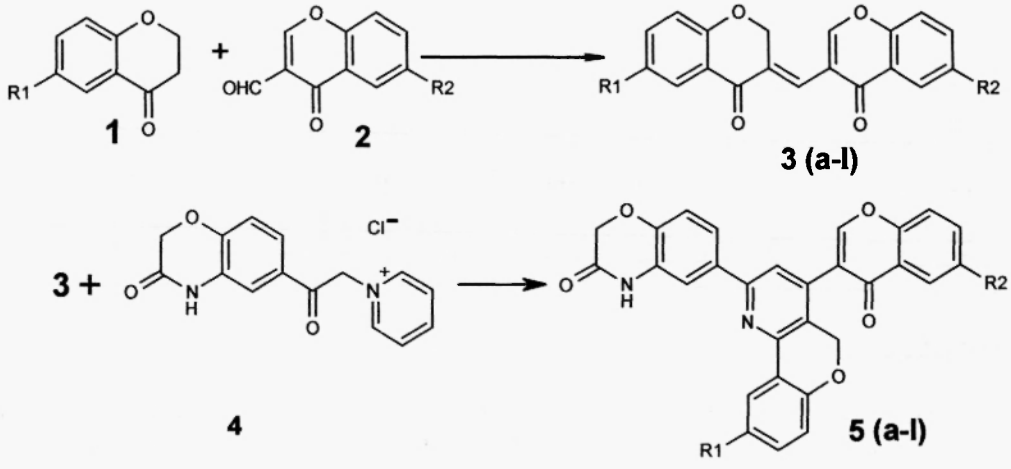
Abstract:

A series of new 6-[(4-chromon-3-yl-benzopyrano[4,3-b]pyridin-2-yl)]-2H-1,4-benzoxazin-3(4H)-ones (5a-l) have been prepared.

Introduction:

A variety of heterocyclic substituted benzoxazinones have been reported to possess interesting biological activities. For example 6-tetrahydrophthalimido benzoxazinone is a herbicide[1]. α-Adrenoceptor activities have been associated with imidazolylaminobenzoxazinones[2]. Several imidazolylmethyl[3] and thiazolyl benzoxazinones[4] exhibited significant antifungal and antiinflammatory activities. Bemoradan[5] is a pyridazinylbenzoxazinone derivative, which exhibited hypotensive, blood platelet aggregation inhibition, positive chronotropic and ionotropic activities. Furthermore, benzopyranopyridines[6] and chromones[7] are compounds of considerable interest because of their pharmacological properties. In view of this, and in continuation of our work on chromone based heterocycles[8] it was considered of interest to synthesize the title compounds in which all the three pharmacophores are present.



1,2,3,5 R_1 = H, CH_3, Cl, F and R_2=H, CH_3, F

SCHEME – 1

Results and Discussion

The required starting materials, benzopyranomethynylbenzopyranones(**3**a-l) were prepared according to the method reported earlier[9]. Thus reaction of chromanones(**1**a-d) with appropriately substituted 3-formylchromones(**2**a-c) in refluxing ethanol in presence of triethylamine gave **3**a-l in good yields. The other starting material 3-oxo-2H-[1,4]-benzoxazin-3,4-dihydro-6-acetylpyridinium chloride (4) was prepared by reaction of 6-chloroacetyl-2H-[1,4]-benzoxazinone[4] with pyridine at 100°C. Reaction of compound **4** with various benzopyranomethynylbenzopyranones(**3**a-l) in the presence of ammonium acetate in acetic acid under Krohnke's condition[10] gave the title 6-(chromonyl benzopyranopyridinyl)-benzoxazinones(**5**a-l) (Scheme–1) in good yields as crystalline solids. The compounds are homogeneous on TLC. The IR spectrum showed characteristic peaks at 1705 and 1645 cm^{-1} for lactam carbonyl and pyrone carbonyl. ^1H NMR spectrum showed two singlets at δ 4.6 and δ 5.2 for $-OCH_2$ of pyrone and $-OCH_2$ of benzoxazine ring respectively.

All the compounds reported in the present work (Table-1), were characterized by their IR, NMR and Mass spectra and supported by elemental analysis.

TABLE 1- PHYSICAL DATA OF 6(CHROMONYL BENZOPYRANOPYRIDINYL)-[1,4]BENZOXAZINONES-5a-l

Compound	R_1	R_2	Yield %	mp
5a	H	H	63	>300°
5b	H	CH_3	57	>300°
5c	H	F	58	>300°
5d	CH_3	H	61	>300°
5e	CH_3	CH_3	45	>300°
5f	CH_3	F	67	>300°
5g	Cl	H	62	>300°
5h	Cl	CH_3	51	>300°
5i	Cl	F	65	>300°
5j	F	H	60	>300°
5k	F	CH_3	47	>300°
5l	F	F	56	>300°

Experimental

Melting points were carried out in an open capillary and are uncorrected. NMR spectra were recorded on 200 Mz spectrophotometer and chemical shift values are expressed in δ (ppm).

General procedure for preparation of 3-(4-0xo-4H-1-benzopyrano-3-methynyl)-2,3-dihydro-4H-1-benzopyran-4-ones (3a-l)

A mixture of 3-formylbenzopyran-4-one (**2**, 0.1 mole) and 4H-1-benzopyran-4-one (**1**, 0.15 mole) in ethanol (100 ml) and triethylamine (50 ml) was refluxed for 3 hrs. The reaction was followed by TLC. At the end of the reaction it was cooled and the solid was filtered washed and recrystallized with ethanol to give pure **3** in 67-80% yields.

General procedure for preparation of (3-0xo-2H[1,4]-benzoxazin-6-yl)acetyl pyridiniumchloride (4)

A mixture 6-chloroacetylbenzoxazinone (**2**, 2.5 g, 0.1 mole), pyridine (100 ml) and toluene (100 ml) was refluxed for 1 hr. The separated solid was filtered and washed with toluene to give pure **4** as white crystalline solid (27.4 g, 90%, mp>300°C).

6-[(4-Chromon-3-yl)-benzopyrano[4,3-b]pyridin-2-yl]-2H-[1,4]-benzoxazin-3(4H)-one (5a)

A mixture of **4** (3.04 g, 0.01 mole), **3a**(3.0 gm, 0.01 mole) and ammonium acetate(4.62 gm, 0.06 mole) in glacial acetic acid(30 ml) was refluxed under stirring for 2 hrs. The separated solid was filtered, washed with water, ethanol, dried and recrystallized from DMSO to give pure **5a**(3.0 g, 63%) mp>300°C IR: 1705, 1645 cm^{-1}; NMR(DMSO-d_6): δ 4.6(s, 2H, OCH_2), 5.2(s, 2H, OCH_2), 6.9-8.0(m, 12H, ArH), 8.5(s, 1H, chromone H), 10.6(s, 1H, NH). Mass m/z at (M^+) 474. Anal. Caled for $C_{29}H_{18}N_2O_5$: C, 73.41; H, 3.79; N, 5.90. Found: C, 73.37; H, 3.82; N, 5.92

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