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"SYNTHETIC STUDY OF 3-HALO-2-(2'-FURYL)-6- CHLORO-8-SUBSTITUTED-CHROMONES AND 2-(2'-FUROYL)-5-CHLORO-7-SUBSTITUTED COUMARAN-3-ONE"

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ABSRACT

1-(2'-Furyl)-3-(2"-hydroxy-5"-chloro-3"-substituted phenyl)-1,3-propanedione(Ia-c) reacts with sulphuryl chloride in dioxane to give 3-chloro-2-(2'-furyl)-6-chloro substituted chromone (IIa-c). (Ia-c) reacts with Br_2 in dioxane to yield 3-bromo-2-(2'-furyl)-6-chloro-8-substituted chromone (IId-f). Similarly, (Ia-c) also reacts with ICl in dioxane to yield 3-iodo-2-(2'-furyl)-6-chloro-8-substituted chromone (IIg-i). (IIa-c) (IId-f) (IIg-i) reacts with ethanolic sodium hydroxide gave 2-(2'-furoyl)-5-chloro-7-substituted coumaran-3-one (IIIa-c). The structures of the newly synthesized compounds were confirmed on the basis of chemical, *elemental analyses and spectral data.

Keywords Flavones, chromones, coumaran-3-one.

INTRODUCTION

Earlier reports[1-4] revel that 3-chloroflavones are synthesized by reacting flavones with either thionyl chloride or sulphuryl chloride. The major defects in this method are the prolong refluxing and formation of side products. Bromoflavones[5] have been prepared by the bromination of 2-hydroxy dibenzoylmethane with dioxane-dibromide complex in DMF solvent and subsequent cyclization. 3-bromoflavaones from flavaones were prepared by reacting Br_2 in acetic acid the presence of catalytic amount of mercuric acetate[6]. 3-Haloflavones were obtained [7] from 2-hydroxy dibenzoylmethane. 3-chloroflavones were synthesized by reacting 2-hydroxydibenzoylmethane with sulphurylchloride in dioxane[8]. 3-Bromochromones and 3-chlorochromones have been prepared by reacting 1-(2'-furyl)-3-(2-hydroxyphenyl)-1, 3-propanedione with dioxane-dibromide complex[9] and sulphuryl chloride in dioxane[8]. The compounds

that contain the chromone skeleton (4*H*-benzopyran-4-one) (flavones and chromones) are widely spread in nature, and they are part of the flavonoid family[9]. These compounds have been reported to exhibit multiple biological properties, for example antibacterial, antifungal[10,11], anticancer[9], antioxidant[12], and anti-HIV[13].

3-Bromoflavone on treatment with hot ethanolic NaOH gave 2-benzoyl coumaran-3-one [14,15]. 3-Bromo-2-styryl chromones were converted into coumaran-3-ones with alkali[8]. 3-Chloroflavones converted into coumarone-3-ones[8] by the action of hot ethanolic alkali. 3-Haloflavone on treatment with ethanolic alkali gave 2-benzoyl coumaran-3-one[6, 7]. 3-Chlorochromones and 3-bromochromones were γconverted into 2-(2'-furoyl) - coumaran-3-one[9] by reacting with hot ethanolic NaOH.

Literature survey indicated that the synthesis of 3-chloro chromones, 3-bromochromones and 3-iodo chromones have not been reported from 1-(2'furyl)-3-(2"-hydroxy-3"-substituted-5"-chlorophenyl)-1, 3-bromoflavones. This prompted us to synthesize 3-halo chromones. Also literature survey indicates that 3-chloro-7-substituted-2-(2'-furoyl) coumarone-3-ones were not prepared. Hence it was thought to prepare these compounds. The starting material 1, 3-propanediones were prepared by known methods[15].

EXPERIMENTAL

The melting points of all the products were determined in open capillary tubes and are uncorrected. IR spectra (cm^{-1}) were recorded using KBr on Shimadzu FT-IR 400 PC Spectrometer, ^1H NMR spectra ($CDCl_3$) were recorded on Brucker-Avance II-400 NMR Spectrometer using TMS as internal standard (chemical shift in δ ppm).

1. Synthesis of 3-chloro-2-(2'-furyl)-6-chlorochromone (IIa)

To a solution of 1-(2'-furyl)-3-(2"-hydroxy-5"-chlorophenyl)-1, 3-propanedione (Ia) (0.01 mole) in dioxane (20 ml), sulphurylchloride (0.8

ml) was added. The reaction mixture was refluxed for one hour, cooled, diluted with water. The crude product obtained was crystallized from ethanol to get (IIa) in 65% yield, m. p. 111^{0}C.

It gave negative test with neutral $FeCl_3$ solution showing the absence of phenolic –OH group and indicating cyclisation.

IR(KBr) **:** 1630 (C=O); 1610,1580 (C=C); 1385 (γ-pyrone ring); 870,850 (2'-furyl ring);

760-635 cm^{-1} (C-Cl) .

PMR ($CDCl_3$) **:** 6.78-8.06 δ (m, 6H, Ar-H and heteroatomic H)

From spectral data, the compound (IIa) was assigned the structure as 3-chloro-2-(2'-furyl)-6-chlorochromone. Other compounds were synthesized in the same manner and reported in Table 1.

2. Synthesis of 3-Bromo-2-(2'furyl)-6-chlorochromone (IId)

To a solution of 1-(2'-furyl)-3-(2"-hydroxy-5"-chlorophenyl)-1, 3-propanedione (Ia) (0.01 mole) in dioxane (20 ml), 0.5 ml liquid bromine was added with constant stirring for a period of half hour. After one hour, reaction mixture was diluted with water. The crude product obtained was crystallized from ethanol to get (IId) in 55% yield, m.p.138^{0}C.

It gave negative test with neutral $FeCl_3$ solution showing the absence of phenolic –OH group and indicating cyclisation.

IR(KBr) **:**1640 (C=O); 1610,1580 (C=C); 1340 (γ-pyrone ring); 880,850 (2'-furyl ring);

760 (C-Cl) and 635 cm^{-1} (C-Br)

PMR ($CDCl_3$) **:**6.50-8.12 δ (m, 6H, Ar-H and heteroatomic H)

From spectral data, the compound (IId) was assigned the structure as 3-bromo-2-(2'-furyl)-6-chlorochromone. Other compounds were synthesized in the same manner and reported in Table 1.

3. Synthesis of 3-iodo-2-(2'furyl)-6-chlorochromone (IIg)

To a solution of 1-(2'-furyl)-3-(2"-hydroxy-5"-chlorophenyl)-1, 3-propanedione (Ia) (0.01 mole) in dioxane (20 ml), a solution of ICL (1 ml, 16.25% w/v in acetic acid) was added. The mixture was boiled for 15 minutes. After one hour, mixture was diluted with cold water and extracted with ether. Evaporating ether extract, solid obtained was crystallized from ethanol to get (IIg) in 54% yield, m.p. 172^{0}C.

It gave negative test with neutral $FeCl_3$ solution showing the absence of phenolic –OH group and indicating cyclisation.

IR(KBr) :1660 (C=O); 1610,1595 (C=C); 1340 (γ-pyrone ring); 885,860 (2'-furyl ring);

750 (C-Cl) and 500 cm^{-1} (C-I)

PMR ($CDCl_3$) :6.65-8.21 δ (m, 6H, Ar-H and heteroatomic H)

From spectral data, the compound (IIg) was assigned the structure as 3-iodo-2-(2'-furyl)-6-chlorochromone. Other compounds were synthesized in the same manner and reported in Table 1.

4. Synthesis of 2-(2'-furoyl)-5-chloro-7-substituted coumaran-3-one (IIIa)

To a solution of 3-chloro-2-(2'-furyl)-6-chlorochromone (Ia) (1.0 g) in ethanol (20 ml) was added aqueous sodium hydroxide (10 ml, 20%). The mixture was refluxed for three hours. The product was isolated by acidification with HCl (50%) and crystallized from ethanol to get compound (IIIa), yield 65%, m.p. 117-118^{0}C.

Properties of (IIIa)

1. Crystalline solid, m.p. 117-118^{0}C.
2. Compound gave brown colouration with neutral ethanolic $FeCl_3$ solution showing the presence of an enolic or phenolic group.
3. On shaking the compound (IIIa) with neutral solution of copper-acetate, an insoluble greenish yellow copper- comlex was obtained. This copper-complex gave back the former compound (IIa) on treatment with cold dilute sulphuric acid (the mix.m.p remained undepressed)

IR (KBr) : 3120(O-H stretching of enol); 1610 (C=O); 890,870 (2'-furyl) and 740 cm^{-1} (C-Cl).

PMR ($CDCl_3$) : 6.75-7.70 (m,6H, Ar-H and heteroatomic H) and 8.95 δ (br, 1H, -OH)

From the chemical properties, analytical results and spectral data of compound (IIIa), the structure assigned to it was 2-(2'-furoyl)-5-chloro-coumaran-3-one. The other compounds listed in table 2, were prepared by the similar method.

Sheme 1

Table 1. 3-Halo-2-(2'-furyl)-6-chloro-8-substituted chromones

Compound	R_1	R_2	M.P.^{0}C	Yield (%)	Molecular formula
IIa	H	Cl	111	65	$C_{13}H_6O_3Cl_2$
IIb	NO_2	Cl	112	50	$C_{13}H_5O_5NCl_2$
IIc	Br	Cl	116	58	$C_{13}H_5O_3BrCl_2$
IId	H	Br	138	53	$C_{13}H_6O_3ClBr$
IIe	NO_2	Br	124-125	50	$C_{13}H_5O_5NClBr$
IIf	Br	Br	119	52	$C_{13}H_5O_3ClBr_2$
IIg	H	I	172	54	$C_{13}H_6O_3ICl$
IIh	NO_2	I	123	50	$C_{13}H_5O_5NICl$
IIi	Br	I	184	50	$C_{13}H_5O_3IClBr$

*All the compounds (IIa-i) gave satisfactory results on elemental analysis.

Table 2. 2-(2'-Furoyl)-5-chloro-7-substituted coumaran-3-ones.

Compound	R	M.P.^{0}C	Yield (%)	Molecular formula
IIIa	H	118	65	$C_{13}H_7O_4Cl$
IIIb	NO_2	142	70	$C_{13}H_6O_6NCl$
IIIc	Br	136	72	$C_{13}H_6O_4ClBr$
IIId	H	118	62	$C_{13}H_7O_4Cl$
IIIe	NO_2	142	65	$C_{13}H_6O_6NCl$
IIIf	Br	136	68	$C_{13}H_6O_4ClBr$
IIIg	H	118	60	$C_{13}H_7O_4Cl$
IIIh	NO_2	142	62	$C_{13}H_6O_6NCl$
IIIi	Br	136	65	$C_{13}H_6O_4ClBr$

*All the compounds (IIIa-i) gave satisfactory results on elemental analysis.

RESULTS AND DISCUSSION

In present work, 2-(2'-furoyl)-5-chloro-7-substituted coumaran-3-one (IIIa-c) were prepared by the reaction of 3-iodo-2-(2'-furyl)-6-chloro-

8-substituted chromone (IIa-c) (IId-f) (IIg-i) with ethanolic sodium hydroxide.

Here starting material, 3-chloro-2-(2'-furyl)-6-chloro substituted chromone (IIa-c) and3-bromo-2-(2'-furyl)-6-chloro-8-substituted chromone (IId-f) were synthesized by1-(2'-furyl)-3-(2"-hydroxy-5"-chloro-3"-substituted phenyl)-1,3-propanedione(Ia-c) reacts with sulphuryl chloride in dioxane and also with Br2 in dioxane respectively.

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