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NOTE

Synthesis and Bio-assay of Some 3-(2*H*-1,4-Benzothiazin-3-yl)-2-methylchromones

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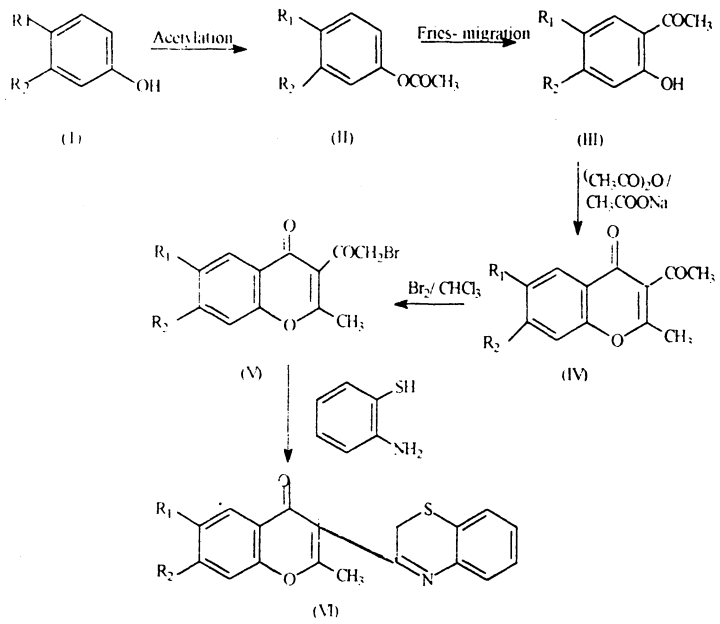
Some 3-(2*H*-1,4-Benzothiazin-3-yl)-2-methylchromones have been synthesized. Their structural assignments are made on the basis of elemental analysis and spectral characteristics. Tested compounds did not show any significant activity.

Key Words: 3-(2*H*-1,4-Benzothiazin-3-yl)-2-methylchromones, CNS-activity, Diuretic activity.

Synthesis and bio-assay of some heterocyclically substituted chromones has been reported by the author in earlier communications[1–9]. In continuation of these studies and keeping in view the medicinal activities of chromones like khellin and dimefline[10–12] as well as benzothiazines[13, 14], organic compounds containing these moieties have been synthesized according to reaction sequence presented in **Scheme-1**.



Scheme-1

Melting points were recorded in open capillaries and are uncorrected. Purity of the compounds was checked on TLC-plates coated with silica gel. IR-spectra were recorded on IR-20 spectrophotometer in nujol mull. 90 MHz PMR-spectra were scanned on Perkin-Elmer R-32 instrument using TMS as internal standard.

Synthesis of 3-(2*H*-1,4-benzothiazin-3-yl)-2-methylchromones

General procedure: An ethanolic solution of **Va–Vc** (10 mmol) and 2-aminothiophenol (10 mmol) was refluxed on a water-bath for 1 h. The solid so obtained was filtered and kept in liquid ammonia overnight. The residual solid was filtered, washed with water, dried and recrystallized from a suitable solvent. Characterization data for **VIa–VIc** are given in Tables 1 and 2.

TABLE-1
CHARACTERIZATION DATA OF 3-(2*H*-1,4-BENZOTHIAZIN-3-YL)-2-METHYLCHROMONES (**VIa–VIc**)

S.No.	Compound No.	R^1	R^2	m.p. (°C)	Yield (%)	Solvent for crystallization
1.	**VIa**	Cl	H	220–221	60	DMF
2.	**VIb**	CH_3	H	196–200	60	DMF
3.	**VIc**	Cl	CH_3	246	70	DMF

TABLE-2
ELEMENTAL ANALYSIS OF 3-(2*H*-1,4-BENZOTHIAZIN-3-YL)-2-METHYLCHROMONES (**VIa–VIc**)

Compd. No.	m.f.	Analysis (%)					
		C		H		N	
		Found	Calcd.	Found	Calcd.	Found	Calcd.
VIa	$C_{18}H_{12}NO_2SCl$	63.8	63.3	3.7	3.5	4.0	4.1
VIb	$C_{19}H_{15}NO_2S$	71.1	71.1	5.1	4.7	4.8	4.4
VIc	$C_{19}H_{14}NO_2SCl$	64.5	64.1	4.2	3.9	3.5	3.9

PMR (TFA) of Vb in δ: 2.67 [3H, s, C6-CH_3 (chromone)], 3.10 [3H, s, C2-CH_3 (chromone)], 4.35 [2H, s, C2-CH_2 (benzothiazine)], 7.55–7.77 [5H, m, C8-H (chromone) and C5-H , C6-H , C7-H and C8-H (benzothiazine)], 7.95 [1H, dd, C7-H (chromone), J = 9.0 and 2.5 Hz, *o*- and *m*-coupling, respectively], 8.28 [1H, d, C5-H (chromone), J = 2.5 Hz, *m*-coupling].

PMR (TFA) of Vc in δ 2.50 [6H, s, C7-CH_3 and C2-CH_3 (chromone)], 3.93 [2H, s, C2-CH_2 (benzothiazine)], 7.13 [1H, s, C8-H (chromone)], 7.47 [4H, m, C5-H, C6-H, C7-H and C8-H (benzothiazine)] , 7.86 [1H, s, C5-H (chromone)].

Structures assigned to these compounds are based upon elemental analysis (Table-1) and spectral characteristics. Though IR spectra of these compounds exhibited a strong band in the region 1630–1620 cm^{-1} (C-O str., chromones), they were not of much use as they did not afford any direct evidence of the presence

of benzothiazine moiety. However, IR confirmed condensation of 3-bromoacetyl chromone with 2-aminothiophenol, as it was devoid of the peaks at 1690 cm^{-1} (C—O str. $-COCH_2Br$ moiety of chromone) and peaks in the region 3300–3500 cm^{-1} (—NH_2 and —SH groups).

The structural details of the title compounds became apparent by a careful analysis of PMR-spectrum (TFA) of **VIa** (a typical compound of the series). Its spectrum showed signals at δ 3.05 [3H, s, C2-CH_3 (chromone)], 4.30 [2H, s, —CH_2 (benzothiazine)], 7.50–7.90 [5H, m, C8-H (chromone) and C5-H , C6-H, C7-H and C8-H (benzothiazine)], 8.00 [1H, dd, C7-H (chromone), J = 9.0 and 2.5 Hz, *o*- and $_m$-coupling, respectively] and last signal at δ 8.30 [1H, d, C5-H (chromone), J = 2.5 H , *m*-coupling].

There was exclusive formation of **VI** in comparison to literature report that 3-substituted-2*H*-1,4-benzothiazines are tautomeric with 3-substituted-4H-1,4-benzothiazines in the ratio 80 : 20[15]. This view is supported by PMR-spectra which shows —CH_2 protons of 2*H*-1,4-benzothiazines as well as IR-spectra which is devoid of the —NH stretching vibrations.

Biological Screening

Compound **VIa** was screened for ALD_{50} , CNS and anti-inflammatory activities. It did not show any significant activity; therefore, other compounds were not tested. However, these compounds were non-toxic (ALD_{50} > 1000).

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