

## Spectral Studies and Synthesis of 10-Substituted 6a, 7-Dihydro-6H-7-(2-Chlorophenyl) - 6-(4-Methoxyphenyl) - [1] Benzopyrano [3, 4-c] [1,5]- Benzothiazepines

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**Abstract.** 1,5- benzothiazepine nuclei has tremendous biological activities. The patent drug diltiazem having 1,5- benzothiazepine nuclei used in cardiac ailment. For the synthesis of substituted 1,5- benzothiazepines, equimolar proportion of 5-substituted-2-amino benzenethiols, the substituents being fluoro, Chloro, bromo, methyl, methoxy, and ethoxy were reacted with 2-(4-anisyl)-3-(2-chlorobenzylidene)chromanone in dry toluene containing piperidine or trifluoroacetic acid in catalytic amount to give respective 10-substituted 6a, 7-dihydro-6H-7-(2-chlorophenyl)- 6-(4-methoxyphenyl)- [1] benzopyrano [3,4-c][1,5]- benzothiazepines. The products were conveniently obtained by refluxing for 3 hours in good yield. The structural investigations are based on the result of micro analytical data of elements and spectroscopic studies based on IR, H1 NMR, and mass spectra.

**Keywords:** 2-Aminobenzenethiols, 1,5-benzothiazepine, benzylidenechromanone, biological activities.

### 1. Introduction

1,5-benzothiazepine nuclei has attracted attention towards medicinal chemistry. Due to its tremendous biological activities such as coronary vasodilator[1], anti HIV[2], Calcium channel blocker[3], antihypertensive[4], antifungal[5], antibacterial[6], anticancer[7]etc. The benzothiazepine nuclei as drugs have been patented such as diltiazem[8]. Due to various biological activities of 1,5-benzothiazepine, great efforts have been made to synthesise 1,5-benzothiazepine derivatives.

Incorporation of substituents in fused benzene ring and in fused heterocyclic ring enhances biological activities[9,10,11]. It has been observed that incorporation of chlorine in benzothiazepine nuclei enhances anti-bacterial activities.

### 2. Result and discussion

The synthesis of 10-substituted 6a, 7-dihydro-6H-7-(2-chlorophenyl)- 6-(4-methoxyphenyl)- [1] benzopyrano [3,4-c][1,5]- benzothiazepines was carried in two steps-

#### 2.1 Step-I

2-chlorobenzaldehyde [1] is reacted with 4-methoxy flavanone [2] to give 3-(2-chlorobenzylidene) flavanone[3].

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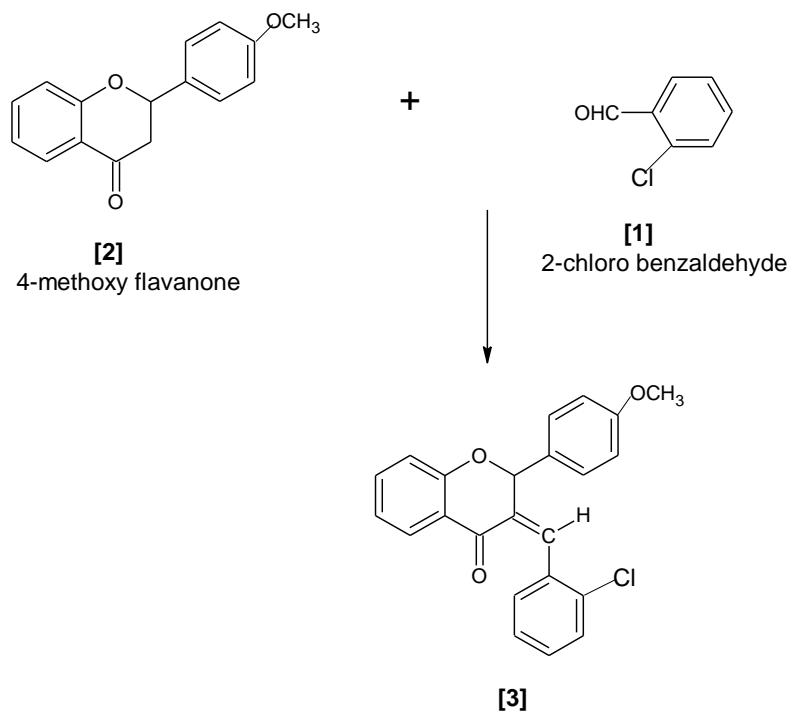


Fig.1: 3-(2-chlorobenzylidene)flavanone

## 2.2 Step II

In this step equimolar quantities of 3-(2-chlorobenzylidene) flavanone and 5-substituted-2-aminothiophenols were refluxed for about 6 hours in dry toluene containing trifluoroacetic acid as catalyst. The product [5] was obtained in good yield.

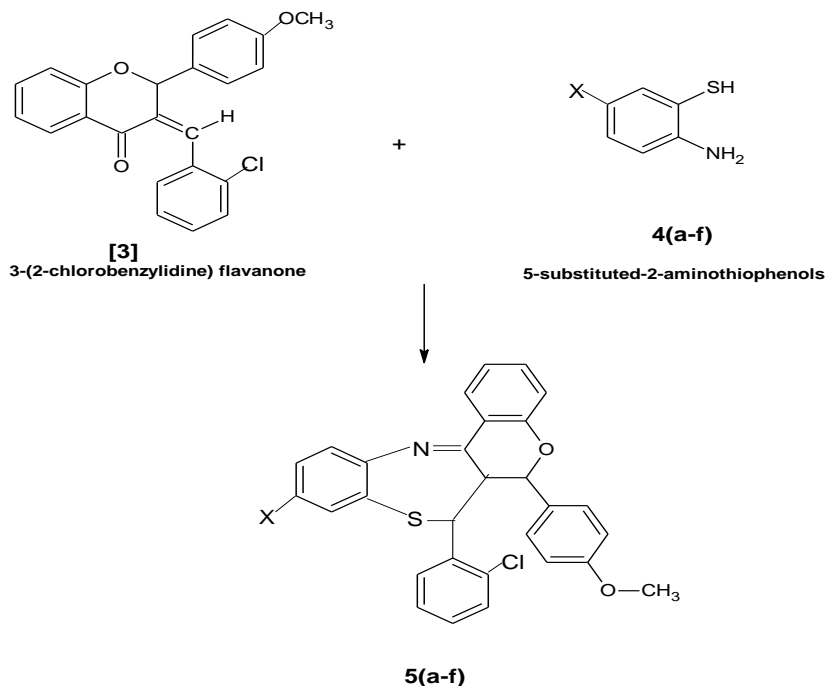


Fig.2: 10-substituted 6a, 7-dihydro-6H-7-(2-chlorophenyl)- 6-(4-methoxyphenyl)- [1] benzopyrano [3,4-c][1,5]- benzothiazepines

Compd	5a	5b	5c	5d	5e	5f
X	F	Cl	Br	CH <sub>3</sub>	OCH <sub>3</sub>	OC <sub>2</sub> H <sub>5</sub>

## 3. Spectral analysis

The IR spectra of all the 6 compounds showed strong absorption in the region 1615-1606  $\text{cm}^{-1}$  which indicates the presence of C=N. Absence of absorption peak around 1680 and 3400-3100  $\text{cm}^{-1}$  indicates that both precursors have reacted to give the target compound.

In  $^1\text{H-NMR}$  spectra of 5a-5f, the double doublet at  $\delta=3.70$  ( $J_1=12.3\text{Hz}$ ,  $J_2=1.1\text{Hz}$ ) may be assigned to  $\text{C}_{6a}$ -H. A doublet at  $\delta=4.98$  ( $J=12.2$ ) may be assigned to  $\text{C}_7$ -H. The multiplet at  $\delta=6.04$ -8.26 may be assigned to 15 aromatic protons. Appearance of singlet at 3.87 may be assigned to 3 protons of  $\text{OCH}_3$  group. In compound 5f a quartet at 3.76 and a triplet at 1.36 may be assigned to protons of  $\text{OC}_2\text{H}_5$  group.

The mass spectra of compounds (5a-f) showed  $\text{M}^+$  peak and  $[\text{M}+2]$  peak. The  $[\text{M}+2]$  peak was found to be about 1/3 of  $\text{M}^+$  peak which indicates the presence of chlorine.

Table I: Characterisation Data of Compounds 5a-f

Compound NO.	R	M.P. $^{\circ}\text{C}$	Rf	Yield %	Molecular Formula (Mol. Wt.)	Elemental Analysis % Found (Calcd)		
						C	H	O
5a	F	121-123	0.74	58	$\text{C}_{29}\text{H}_{21}\text{NO}_2\text{SClF}$ (501.5)	69.72 (69.39)	4.34 (4.18)	6.57 (6.38)
5b	Cl	110-111	0.72	64	$\text{C}_{29}\text{H}_{21}\text{NO}_2\text{SCl}_2$ (518)	67.29 (67.18)	4.40 (4.05)	6.29 (6.17)
5c	Br	123-125	0.78	68	$\text{C}_{29}\text{H}_{21}\text{NO}_2\text{SClBr}$ (562.5)	61.98 (61.86)	4.02 (3.73)	5.78 (5.68)
5d	$\text{CH}_3$	110-111	0.70	45	$\text{C}_{30}\text{H}_{24}\text{NO}_2\text{ClS}$ (497.5)	72.57 (72.36)	4.95 (4.82)	6.58 (6.43)
5e	$\text{OCH}_3$	108-110	0.68	59	$\text{C}_{30}\text{H}_{24}\text{NO}_3\text{ClS}$ (513.5)	70.67 (70.10)	4.93 (4.67)	9.47 (9.34)
5f	$\text{OC}_2\text{H}_5$	114-115	0.69	64	$\text{C}_{31}\text{H}_{26}\text{NO}_3\text{ClS}$ (527.5)	70.94 (70.52)	5.06 (4.92)	9.34 (9.10)

Table II: Characteristic Data of Compounds 5a-f

Compd.	$^1\text{HNMR}$ ( $\delta$ , ppm)					
	$\text{C}_{10}$ -XH	$\text{C}_6$ -H	$\text{C}_{6a}$ -H	$\text{C}_7$ -H	Aromatic Protons	$\text{C}_{4'}$ - $\text{OCH}_3$ -H
5a	--	4.90(d, $J=1.1$ )	3.67(dd, $J_1=12.2$ , $J_2=1.2$ )	4.96	6.01 - 8.29	3.87
5b	-	4.91(d, $J=1.1$ )	3.68(dd, $J_1=12.1$ , $J_2=1.1$ )	4.97	6.24 - 8.23	3.86
5c	-	4.89(d, $J=1.0$ )	3.65(dd, $J_1=12.1$ , $J_2=1.0$ )	4.96	6.13 - 8.21	3.86
5d	2.32(s, 3H)	4.91(d, $J=1.0$ )	3.66(dd, $J_1=12.1$ , $J_2=1.1$ )	4.97	6.15 - 8.20	3.87
5e	3.82(s, 3H)	4.90(d, $J=1.2$ )	3.69(dd, $J_1=12.2$ , $J_2=1.2$ )	4.97	6.11 - 8.23	3.88
5f	3.76(q, 2H) 1.36(t, 3H)	4.90(d, $J=1.1$ )	3.68(dd, $J_1=12.1$ , $J_2=1.2$ )	4.96	6.15 - 8.20	3.87

## 4. Experimental Section

All the melting points were determined in open capillary tubes and were uncorrected. The purity of the compounds was checked by TLC on silica gel G coated glass plates using benzene –methanol-ammonia (7:2:1) as solvent system. The IR spectra were recorded on potassium bromide pellets using Perkin-Elmer RX1 FT IR spectrometer (range:4000-450  $\text{cm}^{-1}$ ). The  $^1\text{H}$  –NMR spectra were recorded on DRX-300 MHz Bruker, Switzerland NMR using  $\text{CDCl}_3$  as solvent. The mass spectra were recorded on JMS-T100LC, Accu TOF (DARTMS) mass spectrometer

4.1 10-fluoro- 6a, 7-dihydro-6H-7-(2-chlorophenyl)- 6-(4-methoxyphenyl)- [1] benzopyrano [3,4-c][1,5]-benzothiazepine(5a)-

2-amino-5-fluoro benzenethiol (0.14gm, 0.001mol) and 2-(4-anisyl)-3-(2-chlorobenzylidene) (0.37gm, 0.001mol) were dissolved in dry toluene (15ml) separately and mixed. Trifluoroacetic acid (1ml) was added as catalyst and refluxed for 3 hours. The mixture was cooled and excess toluene was removed under reduced pressure to obtain light yellow solid. The crude solid was crystallized with methanol. Purity was checked by TLC and spectra were recorded of 10-fluoro- 6a, 7-dihydro-6H-7-(2-chlorophenyl)- 6-(4-methoxyphenyl)- [1] benzopyrano [3,4-c][1,5]- benzothiazepine.[5a, m.p. 120-22°C,yield 0.29gm]

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