

SYNTHESIS OF 7-SUBSTITUTED 4H-1,4-BENZOTHAZINES

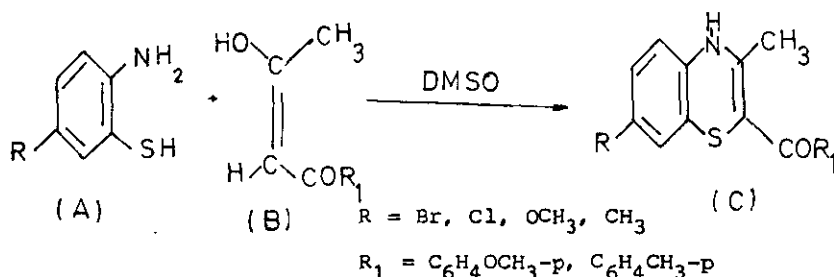
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Abstract - One step synthesis is reported for 7-substituted 4H-1,4-benzothiazines involving the condensation of 5-substituted 2-aminobenzenethiols with p-methoxy- and p-methylbenzoylacetone in DMSO which causes oxidative cyclisation.

4H-1,4-benzothiazines form an interesting series of medicinally important heterocycles¹⁻⁴ and we have recently reported the synthesis of 5-substituted 4H-1,4-benzothiazines⁵. In continuation of our work it has been considered worthwhile to extend studies on synthesis of 7-substituted 4H-1,4-benzothiazines.

In this communication we are reporting the synthesis of 7-substituted 4H-1,4-benzothiazines (C). The title compounds have been synthesized by oxidative cyclisation of 5-substituted 2-aminobenzenethiols (A) with β -diketones (B) (p-methoxy- and p-methylbenzoylacetone) in DMSO. The formation of 7-substituted 4H-1,4-benzothiazines is represented in Scheme I. 5-substituted 2-aminobenzenethiols (A) have been prepared by the alkaline hydrolysis of 6-substituted 2-aminobenzothiazoles^{5,6}.



Scheme - I

EXPERIMENTAL

All the melting points are uncorrected. The purity of synthesized compounds was tested by thin-layer chromatography. The ir spectra of all these 7-substituted 4H-1,4-benzothiazines invariably showed an NH-absorption in the region 3200-

3340 cm^{-1} and carbonyl group absorption in the region 1600-1615 cm^{-1} . The absorption bands in the region 1335-1395 cm^{-1} are attributed to C-CH₃ ring vibrations. The nmr spectra of all these compounds exhibit a broad signal at τ 1.0-1.43 due to NH proton and the multiplets in the region τ 2.95-3.70 due to aromatic ring protons. Resonance signals in the region τ 7.8-7.9 show the presence of a CH₃ group in the allylic form at position 3 i.e. a C=C-CH₃ linkage. A singlet in the region τ 6.02-6.30 is observed in benzothiazines (C-1, C-2, C-3, C-4, C-7) due to O-CH₃ groups.

The mass spectrum shows molecular ion peaks in accordance with their molecular weights.

Synthesis of 5-substituted 2-aminobenzenethiols (A).— 5-substituted 2-aminobenzenethiols required in the synthesis of 7-substituted 4H-1,4-benzothiazines have been prepared following the details reported elsewhere⁵.

2-amino-5-bromobenzenethiol, mp 113°C (lit., mp 113-115°C⁸)

2-amino-5-chlorobenzenethiol, mp 110°C (lit., mp 110°C⁸)

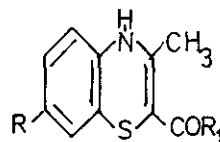
2-amino-5-methoxybenzenethiol, mp 105°C (lit., mp 103-105°C⁸)

2-amino-5-methylbenzenethiol, mp 90°C (lit., mp 90°C⁷)

Synthesis of 7-substituted 4H-1,4-benzothiazines (C, 1-8).— To a stirred suspension of β -diketones (B; 0.01 mol) (p-methoxy- and p-methylbenzoylacetone) in DMSO (5 ml) was added (A; 0.01 mol) 5-substituted 2-aminobenzenethiol and refluxed for 1 h. The reaction mixture was cooled down to room temperature and filtered, washed with a small quantity of methanol and recrystallised from methanol to get pure compounds. Physical data of 7-substituted 4H-1,4-benzothiazines are summarised in Table-1.

Table 1

Physical data of 7-substituted 4H-1,4-benzothiazines(C,1-8)



Compd. No.	R	Compound R ₁	Mp °C	Colour	Yield %	Molecular Formula	% Found			% Calcd.		
							C	H	N	C	H	N
C-1	CH ₃	C ₆ H ₄ OCH ₃ p	155	Red	75	C ₁₈ H ₁₇ O ₂ NS	69.20	5.43	4.52	69.45	5.46	4.50
C-2	Cl	C ₆ H ₄ OCH ₃ p	187	Blood red	70	C ₁₇ H ₁₄ O ₂ NSCl	61.29	4.24	4.23	61.53	4.22	4.22
C-3	OCH ₃	C ₆ H ₄ OCH ₃ p	170	Dark red	65	C ₁₈ H ₁₇ O ₃ NS	66.25	5.21	4.26	66.05	5.19	4.28
C-4	Br	C ₆ H ₄ OCH ₃ p	195	Red	68	C ₁₇ H ₁₄ O ₂ NSBr	54.38	3.74	3.70	54.25	3.72	3.72
C-5	CH ₃	C ₆ H ₄ CH ₃ p	181	Dark red	65	C ₁₈ H ₁₇ ONS	73.50	5.78	4.76	73.22	5.76	4.74
C-6	Cl	C ₆ H ₄ CH ₃ p	190	Red	70	C ₁₇ H ₁₄ ONSCl	64.28	4.45	4.41	64.65	4.43	4.43
C-7	OCH ₃	C ₆ H ₄ CH ₃ p	177	Dark red	68.5	C ₁₈ H ₁₇ O ₂ NS	69.00	5.43	4.48	69.45	5.46	4.50
C-8	Br	C ₆ H ₄ CH ₃ p	122	Red	73	C ₁₇ H ₁₄ ONSCl	56.75	3.86	3.90	56.66	3.88	3.88

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