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NOTES

A Single Step Synthesis of Substituted 3,7-dimethyl-5-nitro-4H-1,4-benzothiazines

PURNIMA ADWANI, NEHA MATHUR, VANDANA GUPTA and K.G. OJHA*
Department of Chemistry
S.D. Government College, Beawar-305 901, India

In this communication, the authors report the synthesis of substituted 3,7-dimethyl-5-nitro-4H-1,4-benzothiazines.

Similar to phenothiazines, 1,4-benzothiazines also possess a wide spectrum of pharmacological activities[1]. Drugs containing nitro group find a very important place in the field of medicine. Nitro goup containing drugs are of interest in the sense that the biological activity changes for nitro group compounds depending on the moiety to which nitro group is attached[2].

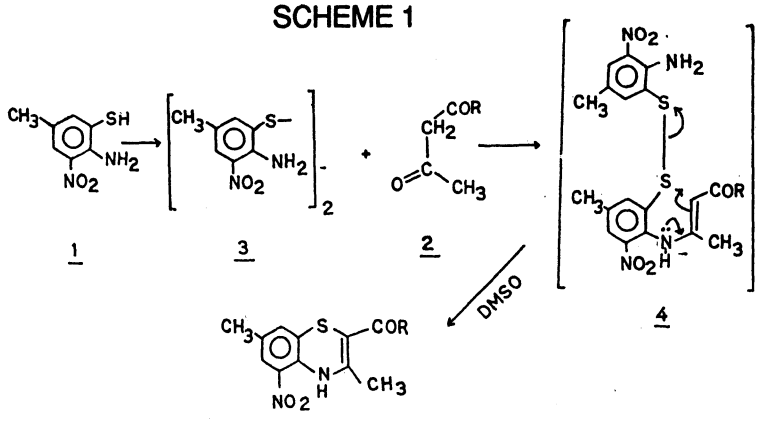
In continuation to our research programmes concerning development of heterocyclic pharmaceuticals, it is considered worthwhile to synthesize 4H-1,4-bezothiazine derivatives with nitro group substituted in the benzene ring. In this communication we are reporting the synthesis of substituted 3,7-dimethyl-5-nitro-4H-1,4-benzothiazines (**5**).

Their synthesis involves the condensation and subsequent oxidative cyclization of substituted benzenethiol (**1**) with active methylene compounds (**2**) in dimethyl sulphoxide (scheme I). 2-Amino-5-methyl-3-nitrobenzenethiol was prepared by thiocyanogenation[3] of 4-methyl-2-nitroaniline using cupric chloride and potassium thiocyanate. (m.pt. 127°C, yield 65%; structure confirmed by IR, NMR and mass spectral data).

Under the experimental conditions *o*-aminobenzenethiols (**1**) exist as disulphides (**3**)[1] and the reaction is believed to proceed via the formation of an intermediate enamino-ketone (**4**). Because of high nucleophilic reactivity of α-position of the enamino-ketone system, the formation of 4H-1,4-benzothiazines may be considered to be intramolecular nucleophilic attack in intermediate enamino-ketone followed by oxidative cyclization.

All the m.pts. are uncorrected. The purity of the synthesised compounds was checked by TLC and characterized by their elemental analyses and spectral studies.

SCHEME 1



1 3 2 4 5

Preparation of 4H-1,4-benzothiazines (5a–h)

Substituted 2-aminobenzenethiol (**1**, 0.01 mol) was added to the stirred suspension of active methylene compound (**2**, 0.01 mol) in DMSO (5 ml) and the resulting mixture was refluxed for 30 minutes. The reaction mixture was cooled to room temperature and solid substance separated was filtered, dried and crystallized from CH_3OH. The physical and analytical data are given in Table 1.

TABLE 1
PHYSICAL DATA OF SUBSTITUTED 1, 4-BENZOTHIAZINES.

Compound **5**	R	M.pt. °C	Yield %	Molecular Formula	N%* Found (Calcd.)
a	*m*-CH_3O-C_6H_4	169	49	$C_{18}H_{16}N_2SO_4$	7.85 (7.86)
b	*p*-CH_3O-C_6H_4	173	52	$C_{18}H_{16}N_2SO_4$	7.81 (7.86)
c	*p*-CH_3-C_6H_4	157	59	$C_{18}H_{16}N_2SO_3$	8.21 (8.23)
d	*p*-Cl-C_6H_4	171	53	$C_{17}H_{13}N_2SO_3Cl$	7.72 (7.76)
e	C_6H_5	166	51	$C_{17}H_{11}N_2SO_3$	8.65 (8.66)
f	OC_2H_5	151	61	$C_{13}H_{14}N_2SO_4$	9.49 (9.52)
g	OCH_3	142	58	$C_{12}H_{12}N_2SO_4$	10.01 (10.00)
h	CH_3	132	63	$C_{12}H_{12}N_2SO_3$	10.57 (10.60)

*All the compounds gave satisfactory C and H analyses.

IR [cm^{-1}]; 3220–3380 (NH), 1520–1575 (NO_2 sym), 1300–1350 (NO_2 asym), 1020–1030 (C–O–C sym), 1260–1275 (C–O–C asym) 1580–1620 (CO), PMR (δ); 8.40–9.41 (s, NH), 6.32–7.68 (H, arom), 3.80–4.12 (s, OCH_3 at C-3).

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