SINGLE STEP SYNTHESIS OF 3-METHYL-5/7-SUBSTITUTED 4H-1,4-BENZOTHIAZINES

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ABSTRACT

The present work deals with one-pot synthesis of substituted 4H-1,4-benzothiazines via condensation and oxidative cyclization of 2-aminobenzenethiols with 3,4-dichloro benzoyl acetone (β-diketone) in dimethyl sulfoxide. The structure of all the synthesized compounds has been assigned by elemental and spectral studies.

INTRODUCTION

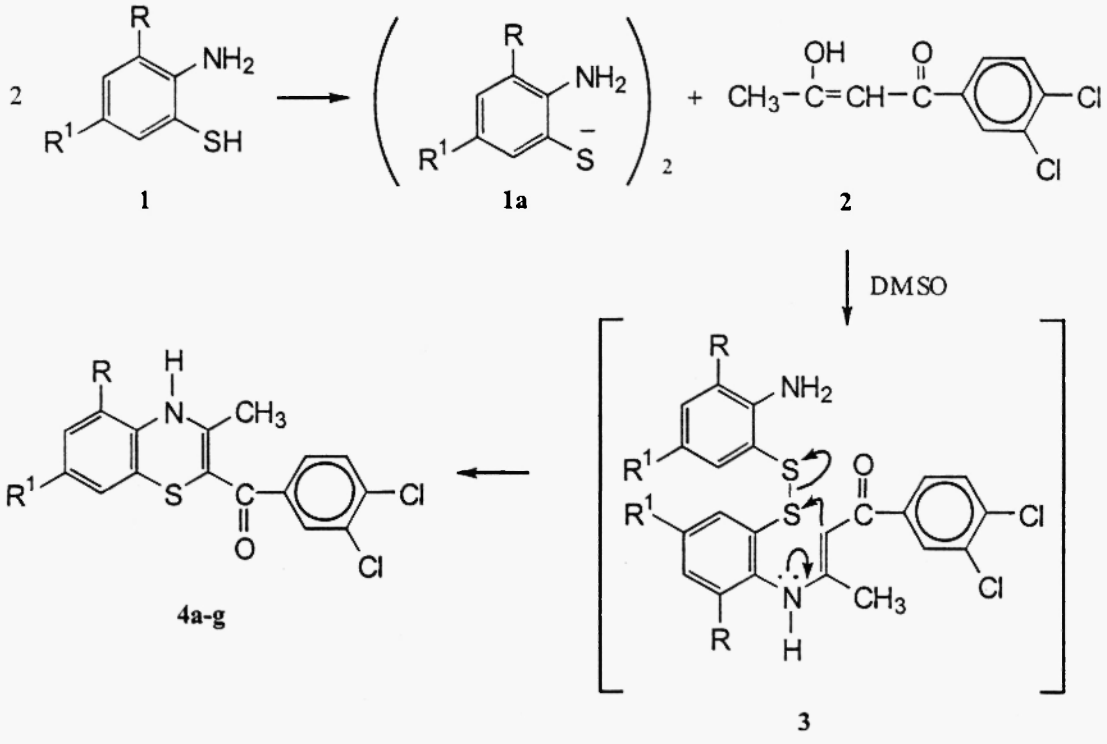
Phenothiazines contain a fold along nitrogen-sulphur axis which is considered to be one of the structural specificities to impart biological activites to phenothiazines. Similarly 4H-1,4-benzothiazines contain a fold along nitro-sulphur axis, hence these are anticipated to possess a wide spectrum of biological activities similar to that of phenothiazines. It is considered worthwhile to synthesize hithertro unknown benzothiazines.

RESULTS AND DISCUSSION

3-Methyl-5/7-substituted-4H-1,4-benzothiazines have been synthesized by a single step reaction via condensation and oxidative cyclization of 2-aminobenzenethiols**1** with 3,4-dichlorobenzoylacetone**2** in dimethyl sulfoxide. It is believed that enamino-ketone**3** (3-5) is formed as intermediate. Under the above experimental conditions 2-aminobenzenethiols**1** are readely oxidized to bis-(2-aminophenyl) disulphide**1a** (6,7) which cyclize to 4H-1,4-benzothiazines**4** by scission of sulphur-sulphur bond (2) due to high reactivity of α-position of enamino ketone system**3** towards neucleophilic attack (Scheme-1)

The IR spectra of all the synthesized 3-methyl-5/7-substetuted-4H-1,4-benzothiazines exhibit a single peak in the region 3400-3440 cm^{-1} due to N-H stretching vibrations. The sharp band in the region 1590-1600 cm^{-1} appears due to C=O stretching vibrations. The compounds 4a-g exhibit absorption bands between 1320-1450 cm^{-1} due to C-H deformation vibrations of CH_3 group at C_3. In compoundd 4b,d,e bands appearing in the regions 1210-1240 cm^{-1} and 1085-1095 cm^{-1} are attributed to C-O-C asymmetric

and symmetric stretching vibrations respectively. Compounds 4a-g exhibit a single peak in region 700-800 cm^{-1} due to C-Cl stretching vibrations.



Scheme-1

R/R^1 - CH_3/H, OC_2H/H, H/CH_3, H/OC_2H_5, H/OCH_3, H/Cl, CH_3/CH_3

The NMR spectra of all the compounds 4a-g exhibit a single peak in the region δ 8.05-9.41 due to NH proton. The multiplets observed in the region δ 6.25-8.07 are due to aromatic protons. The singlet observed in the region δ 2.02-2.34 in the compounds **4a-g** is assigned to CH_3 protons at C_3. Compounds **4a** and **4c** exhibit a single peak at δ 1.33 and δ 1.45 due to CH_3 protons at C_5 and C_7 respectively. Compounds **4b** and **4d** exhibit quartet in the regions δ 3.93-4.34 and 3.77-3.99 due to CH_2 protons at C_5 and C_7 respectively and the same compounds show triplet in the region δ 1.07-1.58 and δ 1.20-1.42 due to CH_3 protons at C_5 & C_7 respectively. Compound **4e** exhibits a singlet at δ 4.4 due to OCH_3 protons at C_7 and compound **4g** exhibits two singlets at δ 1.87 and δ 1.236 due to CH_3 protons at C_5 and C_7 respectively.

EXPERIMENTAL

All the melting points are uncorrected. The purity of synthesized compounds has been checked by thin layer chromatography. Elemental analysis and spectral studies are used for characterization of compounds. IR spectra are recorded on niclet-magna IR spectrophotometer model 550 using KBr disc. NMR spectra are recorded on 90 MHz Jeol. FX 90Q FT NMR using TMS as internal standard in DMSO-d_6.

Synthesis of substituted 4H-1,4-benzothiazines

To the stirred suspension of 3,4-dichlorobenzoyl acetone (**2**; 0.01 M) in dimethyl sulfoxide (5 ml) was added-2-aminobenzenethiols (**1**; 0.01 M) and the resulting mixture was refluxed for 30-40 minutes. The reaction mixture was concentrated and cooled down to room temperature and filtered. The product obtained was washed with petroleum ether and crystallized from methanol. The physical and analytical data of 4H-1,4-benzothiazines are given in Table 1.

Table 1 : Physical and analytical data of 4H-1,4-benzothiazines (4a-g)

Compounds	R	R^1	M.P	Yield %	Molecular formula	Found/Cald % C	H	N
a	CH_3	H	60	55.6	$C_{17}H_{13}NSOCl_2$	58.62 (58.28)	3.72 (3.71)	3.98 (4.00)
b	OC_2H_5	H	70	53.37	$C_{18}H_{15}NSO_2Cl_2$	56.67 (56.84)	3.92 (3.94)	3.70 (3.68)
c	H	CH_3	56	63.54	$C_{17}H_{13}NSOCl_2$	58.73 (52.28)	3.73 (3.71)	4.01 (4.00)
d	H	OC_2H_5	52	62.62	$C_{18}H_{15}NSO_2Cl_2$	56.82 (56.84)	3.92 (3.94)	3.65 (3.68)
e	H	OCH_3	84	59.29	$C_{17}H_{13}NSO_2Cl_2$	55.53 (55.73)	3.56 (3.55)	3.83 (3.82)
f	H	Cl	74	58.44	$C_{16}H_{10}NSOCl_3$	51.63 (51.82)	2.70 (2.69)	3.76 (3.77)
g	CH_3	CH_3	92	63.05	$C_{18}H_{15}NSOCl_2$	59.71 (59.34)	4.09 (4.12)	3.86 (3.84)

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