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Synthesis of 1,2,4-trihalophenothiazin-3-ones and Their Conversion into (1,4)-Benzothiazino-(2,3-b)-Phenothiazines

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1,2,4-Trihalophenothiazin-3-ones were prepared by condensing 2-amino benzenthiols with chloranil/bromanil in 1 : 1 molar ratio. Compounds were further condensed with the same or different 2-aminobenzenthiol which afforded (1,4)-benzothiazino-(2,3-b)-phenothiazines.

INTRODUCTION

Phenothiazinone and phenoxazine derivatives containing aminoquinone system have been studied for biological and pharmaceutical activities and to obtain useful pigments[1–3]. Triphenodithiazines form an important class of compounds among the dyes of thiazine series[4]. Dyes of this series are useful for dying cotton, cellulose materials, rubber, paper and plastics in various shades[5–8]. In continuation of our interest in the synthesis and usages of these compounds, we wish to report the synthesis of some new phenothiazinone (III) and (1,4)-benzothiazino-(2,3-b)phenothiazine derivatives (V).

RESULTS AND DISCUSSION

In the present work 1,2,4-trihalophenothiazin-3-ones (III) were prepared by the reaction of substituted 2-aminobenzenthiols (I) and chloranil/bromanil (II). The compound (III) was further condensed with same or different 2-aminobenzenthiol (IV) which afforded symmetrical substituted (1,4)-benzothiazino-(2,3-b)-phenothiazines (Vi, j) and unsymmetrical (1,4)-benzothiazino-(2,3-b) phenothiazines (V a–h, Scheme 1). Symmetrical triphenodithiazines (V i, j) were also prepared by an alternative single-step procedure. In this method chloranil/bromanil was condensed with substituted 2-aminobenzenthiol in a molar ratio of 1:2 (Scheme II). The products prepared by single-step method were identical (TLC, IR and mixed melting point) with those obtained by two-step reaction. Unsymmetrical substituted triphenodiathiazines (V a–h) were also synthesised using another route (Scheme III). In this procedure substituted 2-aminobenzenthiols (IV) were condensed with chloranil/bromanil (II) to get substituted 1,2,4-trihalophenothiazin-3-ones (III) which on further condensation with (I) provided compounds (V). The products (V) prepared by alternative route (Scheme III) were identical with those prepared by Scheme I.

IR spectra: 1,2,4-Trihalophenothiazin-3-ones exhibit strong band in the

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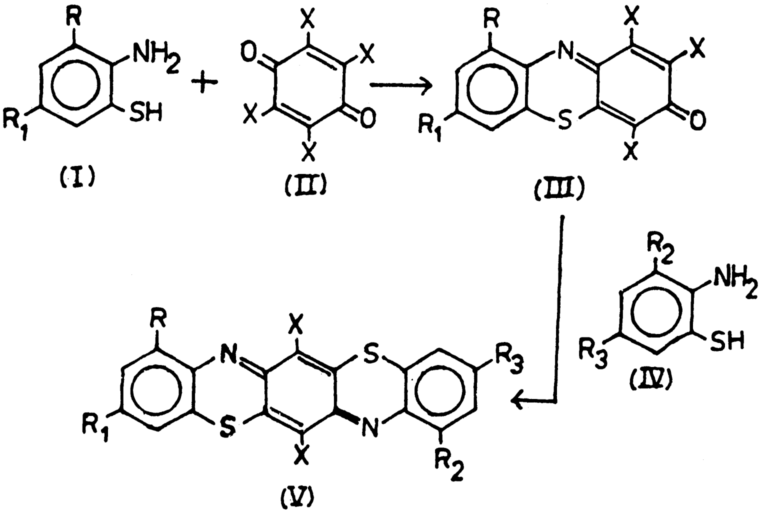
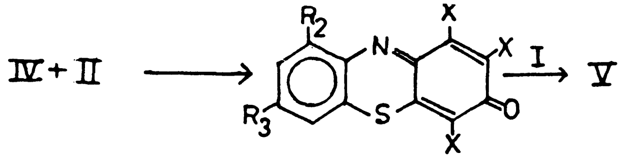


Scheme I

$$\mathrm{I} + \mathrm{II} \longrightarrow \mathrm{V} \qquad (R_2 = R,\ R_3 = R_1)$$

Scheme II



Scheme III

region 1675–1620 cm^{-1} due to C═C stretching vibration. In chloro derivatives bands in the region 765– 745 cm^{-1} are due to (C—Cl) stretching vibrations. Two sharp peaks (1560–1535 cm^{-1} and 1341–1310 cm^{-1}) are obtained in nitro derivatives due to symmetric and unsymmetric vibration of NO_2 group. The bands in the region 1600–1200 cm^{-1} can be assigned to (C—C) and (C—N) ring vibrations. Similarly 1,4-benzothiazeno-(2,3'-b)-phenothiazines show a number of sharp and medium peaks in the region 1200–1625 cm^{-1} which can be assigned to (C—C) and (C—N) ring vibration and two sharp bands in the regions 1565–1520 cm^{-1} and 1360–1315 cm^{-1} are due to NO_2 groups.

EXPERIMENTAL

Melting points of all the compounds were determined in open capillaries and are uncorrected. IR spectra were recorded on Perkin-Elmer model 781 in

KBr/nujol. The purity of the compounds was checked on thin layers of silica-gel in various nonaqueous solvent systems. Bromanil was prepared by the method described by Torry and Hunter[9]. Substituted 2-aminobenzenthiols were prepared by the method reported in literature[10–12].

Preparation of substituted 1,2,4-trihalophenothiazin-3-ones (III a–j)

To a suspension of chloranil/bromanil (II, 0.01 mol) in ethanol (20 mL) was added a solution of substituted 2-aminobenzenthiol (I, 0.01 mol) in ethanol (10 mL) and anhydrous sodium acetate (0.05 mol). The reaction mixture was refluxed for 6 h. After cooling to room temperature the solid separated was filtered, washed with water and finally with 30% ethanol. The products were recrystallised from benzene. Physical data are given in Table 1.

TABLE 1

PHYSICAL DATA OF 1,2,4-TRIHALOPHENOTHIAZIN-3-ONES (III, a–j)

S. No.	Compounds			m.p. (°C)	Yield %	Molecular formula	N* % Found (Calcd.)
	R	R_1	X				
a	H	H	Cl	104	61	$C_{12}H_4NSOCl_3$	4.40(4.42)
b	H	H	Br	137	55	$C_{12}H_4NSOBr_3$	3.08(3.11)
c	H	Cl	Cl	141	50	$C_{12}H_3NSOCl_4$	3.86(3.98)
d	H	Cl	Br	147	48	$C_{12}H_3NSOBr_3Cl$	2.85(2.88)
e	CH_3	NO_2	Cl	116	53	$C_{13}H_5N_2SO_3Cl_3$	7.42(7.45)
f	CH_3	NO_2	Br	171(d)	49	$C_{13}H_5N_2SO_3Br_3$	5.45(5.50)
g	NO_2	CH_3	Cl	110	55	$C_{13}H_5N_2SO_3Cl_3$	7.42(7.45)
h	NO_2	CH_3	Br	166	50	$C_{13}H_5N_2SO_3Br_3$	5.47(5.50)
i	OCH_3	NO_2	Cl	168	50	$C_{13}H_5N_2SO_4Cl_3$	7.14(7.15)
j	OCH_3	NO_2	Br	165	55	$C_{13}H_5N_2SO_4Br_3$	6.30(6.33)

*All the compounds gave the satisfactory C, H and S analyses.

Preparation of 1,4-Benzothiazino-(2,3-b)-phenothiazines (V a–j)

Method A: To a mixture of 1,2,4-trihalophenothiazin-3-ones (III 0.01 mol) and substituted 2-aminobenzenthiol (I, 0.01 mol in ethanol (20 mL) was added anhydrous sodium acetate (0.05 mol). The reaction mixture was refluxed for 6 h, cooled to room temperature and the solid separated out was filtered, washed with water followed by 30% ethanol and recrystallised from benzene. Physical data are given in Table 2.

Method B: To a stirred suspension of chloranil/bromanil (0.01 mol) and 2-aminobenzenthiol (0.02 mol) in ethanol (20 mL) was added anhydrous sodium acetate (0.01 mol). The mixture was refluxed for 6 h, cooled to room temperature and the solid separated out was filtered, washed with water followed by 30% ethanol and recrystallised from benzene. Physical data are given in Table 2.

TABLE 2
PHYSICAL DATA OF SOME SUBSTITUTED TRIPHENODITHIAZINES (V, a–j)

S. No.	Compounds					m.p. (°C)	Yield (%)	Molecular formula	N* % Found (Calcd.)
	R	R_1	R_2	R_3	X				
a	H	H	CH_3	NO_2	Cl	194	59	$C_{19}H_9N_3S_2O_2Cl_2$	9.39(9.41)
b	H	H	CH_3	NO_2	Br	199	57	$C_{19}H_9N_3S_2O_2Br_2$	7.82(7.85)
c	H	Cl	CH_3	NO_2	Cl	229	51	$C_{19}H_8N_3S_2O_2Cl_3$	8.72(8.74)
d	H	Cl	CH_3	NO_2	Br	240	54	$C_{19}H_8N_3S_2O_2Br_2Cl$	7.36(7.37)
e	CH_3	NO_2	CH_3	NO_2	Cl	183(d)	49	$C_{20}H_{10}N_4S_2O_4Cl_2$	11.06(11.08)
f	CH_3	NO_2	CH_3	NO_2	Br	213	55	$C_{20}H_{10}N_4S_2O_4Br_2$	9.40(9.42)
g	CH_3	NO_2	NO_2	CH_3	Cl	186(d)	48	$C_{20}H_{10}N_4S_2O_4Cl_2$	11.05(11.08)
h	CH_3	NO_2	NO_2	CH_3	Br	216	56	$C_{20}H_{10}N_4S_2O_4Br_2$	9.40(9.42)
i	CH_3	NO_2	OCH_3	NO_2	Cl	218	55	$C_{20}H_{10}N_4S_2O_5Cl_2$	10.72(10.74)
j	CH_3	NO_2	OCH_3	NO_2	Br	223	52	$C_{20}H_{10}N_4S_2O_5Br_2$	9.09(9.10)

*All the compounds gave the satisfactory C, H and S analysis.

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