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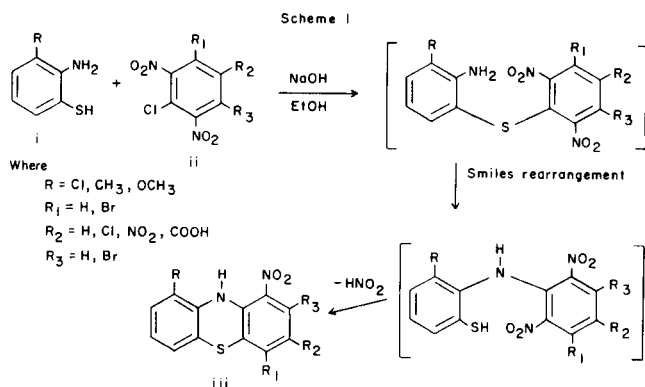
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Synthesis of the title compounds by the Smiles rearrangement has been reported. 1-Nitrophenothiazines have been prepared by the reaction of 2-amino-3-chloro/methyl/methoxythiophenol with substituted *o*-halonitrobenzenes in ethanolic sodium hydroxide, in which Smiles rearrangement occurs *in situ*. 1-chloro/methyl-7-substituted phenothiazines have been prepared by Smiles rearrangement of 3-chloro/methyl-2-formamido-2'-nitro-4'-substituted diphenyl sulphides. The latter were prepared by the formylation of the diphenyl sulphides obtained by the condensation of 2-amino-3-chloro/methylthiophenols with substituted *o*-halogenonitrobenzenes in ethanolic sodium acetate. Spectral studies are also included.

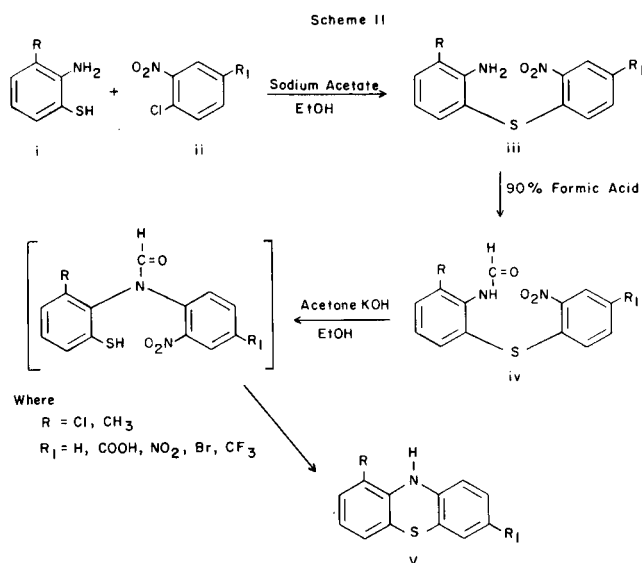
J. Heterocyclic Chem., **21**, 893 (1984).

New phenothiazine drugs are constantly being synthesized and tested clinically. Keeping in view the significant applications of phenothiazines in medicine [2-10] and in industry [11-14], it is considered worthwhile to extend studies on phenothiazines.

Synthesis of hitherto unknown phenothiazines has been reported. 1-Nitrophenothiazines have been prepared by the condensation of 2-amino-3-chloro/methoxy/methylthiophenol with appropriately substituted *o*-halonitrobenzenes in ethanolic sodium hydroxide where a Smiles rearrangement occurs *in situ* (Scheme 1). 1-Chloro/methyl-7-substituted phenothiazines were synthesized by a Smiles rearrangement of 3-chloro/methyl-2-formamide-2'-nitro-4'-substituted diphenyl sulphides in alcoholic potassium hydroxide. The formyl derivatives were prepared by the formylation of resultant diphenyl sulphides obtained by the condensation of 2-amino-3-chloro/methylthiophenol with substituted *o*-halonitrobenzenes in ethanolic sodium acetate (Scheme 2).



The thiols required to synthesize the title compounds were prepared by the method reported by us elsewhere [15,16].



EXPERIMENTAL

All the melting points are uncorrected and purity of the samples is checked by thin-layer chromatographic technique in various non-aqueous solvent systems. Analytical data are satisfactory. The ir spectra were scanned on a Perkin-Elmer model 577 infrared spectrometer. Mass spectra were scanned on Jeol JMS D-300 mass spectrometer at 70 eV and 100 μ A ionization potential.

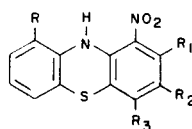
Preparation of Substituted 1-Nitrophenothiazines.

To a stirred suspension of 2-amino-3-chloro/methyl/methoxythiophenol (0.12 mole) and reactive *o*-halonitrobenzene (0.01 mole) in ethanol (20 ml), alcoholic solution of sodium hydroxide (0.01 mole) was added and contents were refluxed for four hours. The contents were cooled, filtered and washed with water. Crystallization from methanol/acetone afforded the desired products. The physical data are tabulated in Table 1.

Preparation of 2-Amino-3-chloro/methyl-2'-nitro-4'-substituted Diaryl Sulphide.

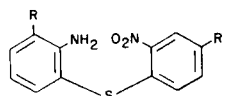
To a refluxing solution of 2-amino-3-chloro/methylbenzenethiol (0.012 mole) in ethanol (20 ml), ethanolic solutions of sodium hydroxide (0.01 mole) and *o*-halonitrobenzene (0.01 mole in 10 ml ethanol) were added

Table 1
Physical Data of Substituted 1-Nitrophenothiazines



	R	Compounds			Yield (%)	Mp (°C)	Molecular Formula	Analysis % Found/(Calcd.)		
		R ₁	R ₂	R ₃				C	H	N
a	OCH ₃	H	COOH	H	67.5	184	C ₁₄ H ₁₀ N ₂ SO ₅	53.24 (52.83)	3.17 (3.14)	8.87 (8.80)
b	OCH ₃	H	NO ₂	H	69.5	220	C ₁₃ H ₉ N ₃ SO ₅	48.40 (48.90)	2.84 (2.82)	13.25 (13.16)
c	OCH ₃	H	Cl	H	66.5	210	C ₁₃ H ₉ ClN ₂ SO ₃	50.86 (50.56)	2.89 (2.91)	9.14 (9.07)
d	OCH ₃	Br	H	Br	72.0	235	C ₁₃ H ₈ Br ₂ N ₂ SO ₃	36.31 (36.11)	1.86 (1.85)	6.52 (6.48)
e	CH ₃	H	COOH	H	63.5	225	C ₁₄ H ₁₀ N ₂ SO ₄	55.23 (55.63)	3.33 (3.31)	9.31 (9.27)
f	Cl	H	COOH	H	62.8	217	C ₁₃ H ₇ ClN ₂ SO ₄	48.01 (48.37)	2.16 (2.17)	8.76 (8.68)

Table 2
Physical Data of Substituted 2-Amino-2'-nitrodiphenyl Sulphides



	Compounds		Yield (%)	Mp (°C)	Molecular Formula	Analysis % Found/(Calcd.)		
	R	R ₁				C	H	N
a	Cl	H	85.0	93	C ₁₂ H ₉ ClN ₂ SO ₂	51.28 (51.33)	3.23 (3.20)	9.96 (9.98)
b	Cl	COOH	79.0	89	C ₁₃ H ₉ ClN ₂ SO ₄	48.10 (48.07)	2.75 (2.77)	8.69 (8.62)
c	Cl	NO ₂	82.0	84	C ₁₂ H ₈ ClN ₃ SO ₄	44.19 (44.23)	2.47 (2.45)	13.01 (12.90)
d	CH ₃	H	74.5	123	C ₁₃ H ₁₂ N ₂ SO ₂	60.10 (60.00)	4.60 (4.61)	10.74 (10.77)
e	CH ₃	CF ₃	67.0	118	C ₁₄ H ₁₁ F ₃ N ₂ SO ₂	51.28 (51.21)	3.33 (3.35)	8.57 (8.53)
f	CH ₃	Br	72.5	113	C ₁₃ H ₁₁ BrN ₂ SO ₂	46.11 (46.02)	3.23 (3.24)	8.29 (8.26)

and refluxed for four hours. The resultant solution was concentrated, cooled and kept overnight in an ice chamber and the solid which separated out was filtered and washed. Crystallization from methanol afforded the desired products. The physical data are tabulated in Table 2.

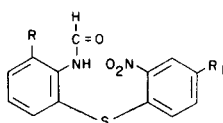
Preparation of 3-Chloro/methyl-2-formamido-2'-nitro-4'-substituted Diaryl Sulphide.

The diaryl sulphide (0.01 mole) in 90% formic acid (20 ml) was refluxed for four hours. The contents of the reaction flask were then poured into crushed ice. The solid which separated was collected, washed and crystallized from methanol. The physical data are tabulated in Table 3.

Preparation of 1-Chloro/methyl-7-substituted Phenothiazines.

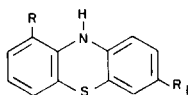
To the solution of formyl derivatives (0.01 mole) in acetone (15 ml), an alcoholic solution of potassium hydroxide (0.2 g in 5 ml of ethanol) was added. The colour of the solution darkened immediately on addition of the alkaline alcoholic solution. The contents were heated for half an hour. To this refluxing solution, again an alcoholic solution of potassium hydroxide (0.2 g in 5 ml of ethanol) was added and refluxing was continued for two hours. The contents were then cooled and poured into crushed ice. The solid which separated out was collected, washed with cold water and 30% ethanol. Crystallization from methanol/benzene afforded the desired phenothiazines. The physical data are summarized in Table 4.

Table 3
Physical Data of Substituted 2-Formamido-2'-Nitrodiphenyl Sulphides



Compounds	R	R ₁	Yield (%)	Mp (°C)	Molecular Formula	Analysis % Found/(Calcd.)		
						C	H	N
a	Cl	H	79.0	221	C ₁₃ H ₉ ClN ₂ SO ₃	50.45 (50.56)	2.92 (2.91)	9.13 (9.07)
b	Cl	COOH	73.5	216	C ₁₄ H ₉ ClN ₂ SO ₅	47.53 (47.65)	2.52 (2.53)	7.99 (7.93)
c	Cl	NO ₂	82.0	186	C ₁₃ H ₈ ClN ₃ SO ₅	43.29 (44.13)	2.27 (2.26)	11.83 (11.88)
d	CH ₃	H	76.5	189	C ₁₄ H ₁₂ N ₂ SO ₃	58.49 (58.33)	4.19 (4.16)	9.69 (9.72)
e	CH ₃	CF ₃	61.0	198	C ₁₅ H ₁₁ 1/2F ₃ N ₂ SO ₃	50.43 (50.56)	3.10 (3.08)	7.94 (7.86)
f	CH ₃	Br	69.5	185	C ₁₄ H ₁₁ BrN ₂ SO ₃	45.65 (45.78)	2.98 (2.99)	7.69 (7.63)

Table 4
Physical Data of 1-Chloro/methyl-7-substituted Phenothiazines



Compounds	R	R ₁	Yield (%)	Mp (°C)	Molecular Formula	Analysis % Found/(Calcd.)		
						C	H	N
a	Cl	H	73.0	110	C ₁₂ H ₈ ClNS ₃	61.33 (61.67)	3.44 (3.42)	6.02 (5.99)
b	Cl	COOH	69.5	195	C ₁₃ H ₈ ClNSO ₂	55.80 (56.21)	2.86 (2.88)	5.01 (5.04)
c	Cl	NO ₂	68.0	202-203	C ₁₂ H ₇ ClN ₂ SO ₃	51.22 (51.70)	2.53 (2.51)	9.96 (10.05)
d	CH ₃	H	63.0	181	C ₁₃ H ₁₁ NS	73.03 (73.24)	5.18 (5.16)	6.61 (6.57)
e	CH ₃	CF ₃	64.5	167	C ₁₄ H ₁₀ F ₃ NS	59.40 (59.78)	3.59 (3.56)	4.95 (4.98)
f	CH ₃	Br	71.5	214	C ₁₃ H ₁₀ BrNS	53.89 (53.42)	3.41 (3.42)	4.83 (4.79)

Infrared Spectra.

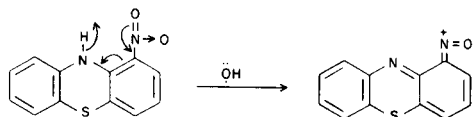
All the compounds were studied *via* infrared spectroscopy. Phenothiazines except 1-nitro, exhibited a sharp peak in the region 3395-3360 cm⁻¹ which is assigned to the NH stretching vibrations, but 1-nitrophenothiazines show a large shift in the secondary N-H vibrational frequency. This shifting to lower frequency suggests a six membered chelate through N-H...O-N bonding. All of the nitrophenothiazines exhibited two peaks of medium intensity in the region 1530-1565 cm⁻¹ and 1330-1365 cm⁻¹ due to asymmetric and symmetric valence vibrations of an aromatic nitro group. Phenothiazines having a methyl group exhibited two peaks corresponding to CH deformation vibrations in the region 1465-1445 cm⁻¹ and 1360-1395 cm⁻¹. Peaks corresponding to the chlorine atom are ob-

served in all chloro derivatives at 720-740 cm⁻¹. The carboxylic derivatives of phenothiazines exhibit a sharp peak in the region 1685-1695 cm⁻¹ due to the carbonyl groups. Peaks corresponding to the ether linkage have also been observed in phenothiazines having methoxy groups at position 9.

Mass Spectra.

Mass spectra of phenothiazines have their most abundant peak corresponding to the molecular ion. All the phenothiazines show exactly similar behaviour on electron impact fragmentation and nitrophenothiazines have exhibited the characteristics of an aromatic nitro group [17] in the fragmentation besides the other fragmentations caused by different sub-

stituents. Moieties $M^+ - 30$, $M^+ - 46$ and $M^+ - 47$ are observed with variable intensity in nitrophenothiazines and are ascribed to the loss of NO , NO_2 and HNO_2 , respectively. Some 1-nitrophenothiazines exhibited additional peak at $M^+ - 17$ which is assigned to the loss of the $\cdot\text{OH}$ radical by McLafferty rearrangement [18] as shown below.



Chloro/bromophenothiazines exhibited two molecular ion peaks due to isotropic [19] effects. Trifluoromethyl derivatives, exhibit a peak at $M^+ - 50$ which may be assigned to the loss of $\cdot\text{CF}_2$ moiety. Acidic derivatives show simultaneous loss of fragments having a mass of 17 and 28. These are assigned to the loss of OH and CO , respectively.

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