

OXIDATION OF PHENOTHIAZINE AND RELATED COMPOUNDS BY IODINE
IN DIMETHYLSULFOXIDE SOLUTION (I)

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It is well known that phenothiazine (Ia) forms charge transfer complex with various electron acceptors. Foster (2) has suggested that ionization to the cation radical (IIa) by single electron transfer occurs on mixing Ia with certain strong electron acceptors such as 2,3-dicyano-p-benzoquinone. In the present study, it was found that iodine, a moderate electron acceptor, in dimethylsulfoxide (DMSO) was good enough to cause the oxidation of Ia and its analogues to a radical species at room temperature.

Thus, a solution of Ia (1-mole) in DMSO was added dropwise to a solution of iodine (4-mole) in the same solvent at 30° under stirring. The addition took 30 minutes and the reaction mixture was stirred for an additional 10 minutes. After working up in a usual manner, there were obtained 3,10'-biphenothiazine (IIIa, 64%) (3), phenothiazone-3 (IV, 5%) and iodophenothiazone-3 (V, 9%). It is to be noted that 1,10'-biphenothiazine can not be detected in the thin layer chromatograms of the products.

The e.s.r. spectrum of the reaction mixture observed by a flow method was shown in FIG. 1. This spectrum has four large groups with intensity ratio of approximately 1:2:2:1, which is assigned to the cation radical (IIa) (4). The addition of water resulted in the increase of IV.

Accordingly, the formation of IIIa and IV from Ia can be formulated as shown in Chart 1.

Oxidation of phenoxazine (Ib) and phenoselenazine (Ic) by the same method as above gave similar results; IIIb (54%) and IIIc (65%) were obtained, respectively (5).

A remarkable result compared with that of DMSO-Ac₂O oxidation of these analogues (5) is a lack of the formation of 1,10'-dimer from Ia or Ib. It might be attributed to the difference of the reactivity between cation radical II and neutral radical VI; 1-position of II may be more sterically hindered by a proton at 10-position or solvated DMSO molecules than that of VI.

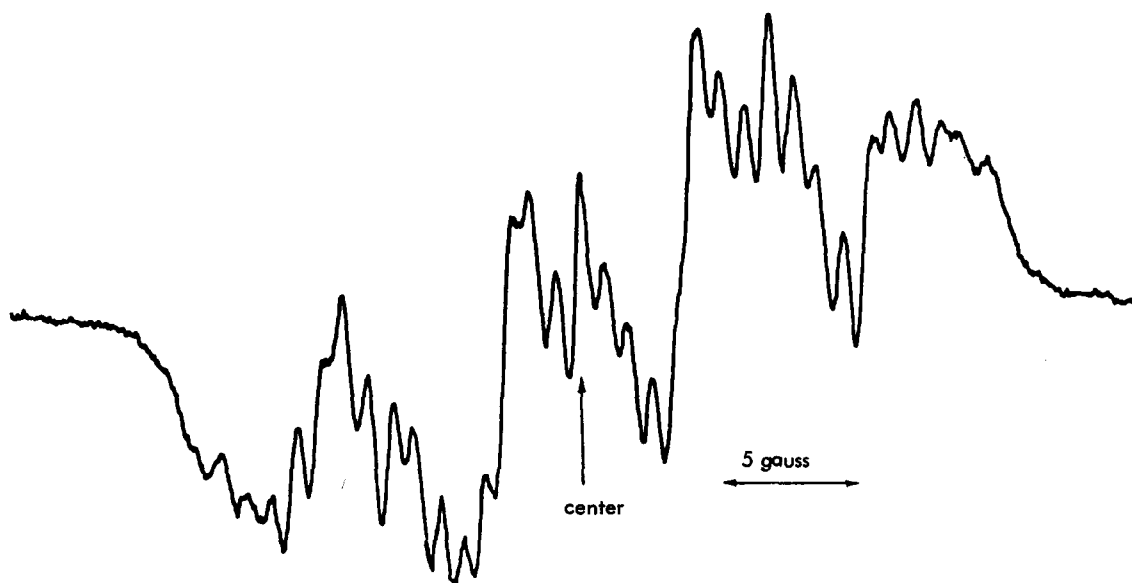


FIG. 1. The e.s.r. spectrum of Ia in DMSO solution of iodine observed by a flow method at room temperature.

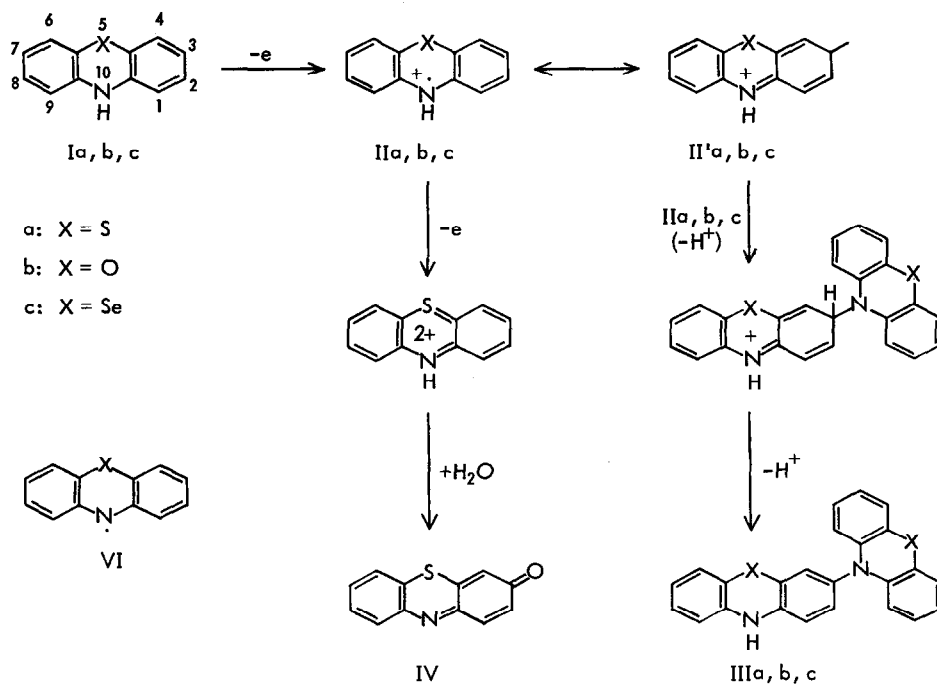


Chart 1

The oxidation of substituted phenothiazines with the same method as above was also carried out.

2-Chlorophenothiazine (VII) gave two isomeric dimers, VIII (mp 193–194°, 30%) and IX (mp 201–202°, 30%), which were isolated by preparative thin layer chromatography (silica gel, petroleum ether–ether = 2:1 v/v). Anal. Calcd. for $(C_{12}H_7ClNS)_2$: C, 61.92; H, 3.04; Cl, 15.24; N, 6.02; S, 13.78; mol wt, 465.5. Found: VIII: C, 61.16; H, 3.58; Cl, 15.07; N, 5.45; S, 13.71; mol wt, 471. IX: C, 61.71; H, 3.34; Cl, 15.05; N, 5.92; S, 13.82; mol wt, 502.

It was previously reported that oxidation of IIIa with concentrated sulfuric acid gives monocation (X) with a planar structure, which turns green in solutions (6). Under the same condition VIII resulted in a green colored solution, while IX did not. This difference can be explained by the incapability of IX to form a planar cation (X) due to steric hindrance. Consequently, VIII is assigned to be 8-chloro, and IX to be 2-chloro-dimer, respectively.

On the other hand, 3-substituted or 3,7-disubstituted phenothiazine gave different results; 3,7-dichlorophenothiazine (XII) yielded 7-chlorophenothiazone-3 (XIII, mp 251–252°, 60%) (7), and 3-methylphenothiazine (XIV) gave 3-formylphenothiazine (XV, yellow needles, mp 204–205°, 30%). Anal. Calcd.

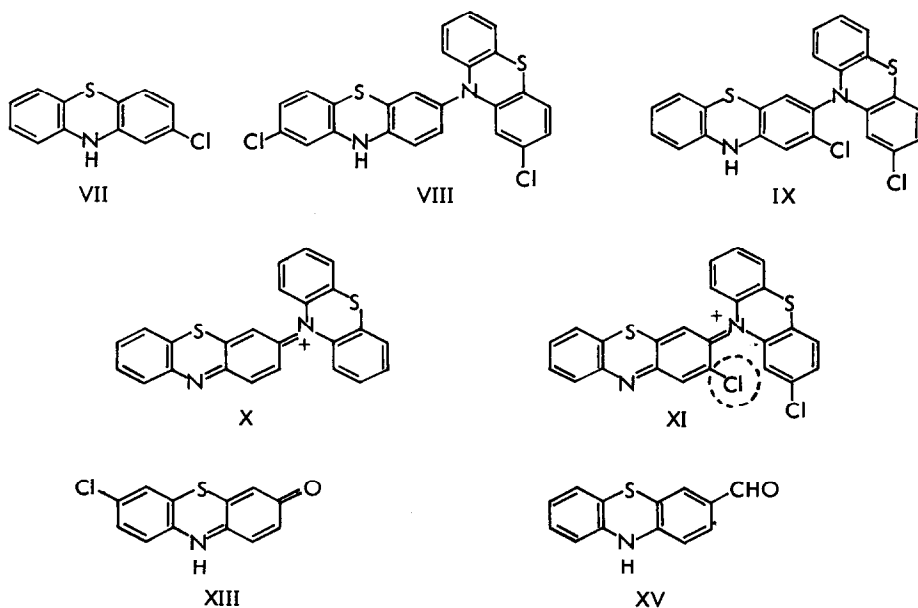


Chart 2

for $C_{13}H_9NOS$ (XV): C, 68.70; H, 3.99; N, 6.19; O, 7.09; S, 14.11; mol wt, 227.3. Found: C, 68.13; H, 4.07; N, 6.27; O, 7.16; S, 14.04; mol wt, 224. IR (nujol): 3300 cm^{-1} (N-H), 1660 cm^{-1} (C=O). NMR (DMSO): τ 0.35 (aldehyde proton).

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