

## ION RADICALS. I.

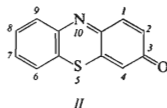
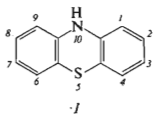
## PHENOTHIAZINIC CATION-RADICALS

M.RĂILEANU<sup>a</sup>, I.RADULIAN<sup>a</sup>, O.DULIU<sup>b</sup> and S.RADU<sup>a</sup><sup>a</sup> Department of Organic Chemistry, University of Craiova,<sup>b</sup> Department of Atomic Physics, University of Bucharest, Rumania

Received December 21st, 1970

By treating some derivatives of phenothiazine (*I*) and phenothiazine-3-one (*II*) with 65% and 96% sulphuric acid, a series of new cation-radicals have been obtained, as detected by ESR spectroscopy. It has been found that the ion-radicals so formed are stable in both weak and strong acid solutions.

During the last years, numerous papers dealing with the formation of the free radicals or the ion radicals of the phenothiazine series have been published. Some of these papers showed that action of sulphuric acid on phenothiazine (*I*) (ref.<sup>1</sup>), thionine<sup>1</sup>, octachlorophenothiazine<sup>2</sup>, phenothiazine-3-one (*II*) (ref.<sup>3</sup>) and phenothiazine 5-oxide<sup>3</sup> (*III*) leads to formation of ion-radicals. These have been studied especially by ESR and absorption spectroscopy. In view of the great interest shown in the last decade for the study of phenothiazinic radicals, we made an attempt to prepare some new ion radicals of this class. In the present paper the formation of new cation-radicals, accomplished by the action of sulphuric acid on some derivatives of phenothiazine (*I*) and phenothiazine-3-one (*II*), has been studied by ESR spectroscopy.



## EXPERIMENTAL

**Measurements.** The ESR spectra were recorded with the JEOL spectrometer, Model JES-ME-3-X operating in the X band with 100 KHz modulation. The samples were dissolved in 65 or 96% sulphuric acid at room temperature, except the dinitro derivative *VI* which was dissolved in hot 65% sulphuric acid.

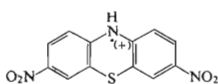
## Compounds Used

Most of the compounds studied were prepared according to literature: 3,7-dinitrophenothiazine (*IV*) (ref.<sup>4</sup>); phenothiazine 5-oxide (*III*) (ref.<sup>5</sup>); 3-nitro- (*V*) (ref.<sup>6</sup>), 3,7-dinitro- (*VI*) (ref.<sup>6</sup>), 1,3,7,9-tetranitro- (*VII*) (ref.<sup>7</sup>) phenothiazine 5-oxides; phenothiazine 5,5-dioxide (*VIII*) (ref.<sup>4</sup>); 3-nitro- (*IX*) (ref.<sup>4</sup>), 3,7-dinitro- (*X*) (ref.<sup>4</sup>), 3,7-dibromo- (*XI*) (ref.<sup>8</sup>), 1,3,7,9-tetranitro- (*XII*) (ref.<sup>4</sup>) phenothiazine 5,5-dioxides; phenothiazin-3-one (*II*) (ref.<sup>9</sup>), 7-chloro- (*XIII*) (ref.<sup>10</sup>), 4-nitro- (*XIV*) (ref.<sup>11</sup>), 2,4-dichloro- (*XVI*) (ref.<sup>12</sup>), 1,7,9-trichloro- (*XVII*) (ref.<sup>10</sup>) phenothiazin-3-ones.

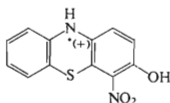
4-Iodophenothiazin-3-one (*XV*). Iodine (2.55 g) was added to a solution of mercuric oxide (2.1 g) in boiling acetic acid (300 ml). The mixture was stirred without heating till complete dissolution of iodine, filtered, and the hot filtrate (containing acetyl hypiodide<sup>13</sup>) was added to the ketone *II* (2.13 g). The solution was stirred for 16 hours without heating. Then a solution of sodium thiosulphate (0.50 g) in water (100 g) was added, the deposited precipitate was filtered, washed with water and recrystallized from methanol; yield 45%, m.p. 216–217°C. For C<sub>12</sub>H<sub>6</sub>INOS (339.2) calculated: 42.51% C, 1.76% H, 4.13% N; found: 42.69% C, 1.69% H, 4.05% N.

## RESULTS AND DISCUSSION

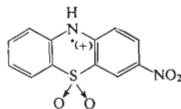
Sulphuric acid readily forms ion-radicals at room temperature from compounds *III*–*VI*, *IX*, *XIII*, *XIV*, *XVI*, and *XVII*. Phenothiazin-3-one (*II*) and the 4-iodo derivative *XV* do not give cation-radicals by treatment with 96% sulphuric acid, but these species are generated by the action of 65% sulphuric acid, similarly as are ion-radicals from compounds *III*, *V* and *VI* (these can be obtained also by the use of 70% perchloric acid). The phenothiazine derivatives *VII*, *X*, *XI* and *XII* do not form ion-radicals with 65 and 96% sulphuric acid and that either at room temperature or at 100°C.



XVIII



XIX



XX

The ESR signals of all the cation-radicals formed in sulphuric acid solutions are very similar in shape, being formed of four lines in an approximate intensity ratio 1 : 2 : 2 : 1. These signals result from the interaction of the impair electron spin with the nitrogen nucleus and the proton<sup>14</sup> in position 10. An ESR signal of the same form has also been observed in the case of the cation-radical obtained from 2,2',4,4',6,6'-hexamethoxydiphenylamine<sup>15</sup>, being also caused by the interaction of the odd electron with the approximately equivalent nuclei of the N—H bond. The ESR signal given by the radical-cation XVIII obtained from the 3,7-dinitro derivative *IV* is shown in Fig. 1. On comparing the ESR spectra of the ion-radicals studied, we have observed that the signal of the radical-cation XIX, obtained from the 4-nitro deriva-

tive XIV, is markedly asymmetric (Fig. 2). When phenthiazine 5,5-dioxide (VIII) was treated with 96% sulphuric acid, the ESR signal consisted of only three lines, which could not be interpreted. It seems likely that this signal results from the superposition of two signals belonging to two different radical-ion species formed in the solution.

The solutions of the radical-ions obtained in 65 and 96% sulphuric acid give ESR signal practically of the same intensity even after 5 days. The aqueous acetic acid solution in which the radical-cation of 3-hydroxyphenothiazine was formed through one-electron reduction of phenothiazine-3-one (II) with sodium thiosulphate, gives very intense ESR signal even after 21 days. The radical-cations formed on heating compounds II, III and V with concentrated aqueous solution of oxalic acid or acetic acid are stable even at 100°C. These experiments show that in an acidic medium the cation-radicals formed are quite stable.

The formation of the cation-radicals from 3,7-dinitrophenothiazine (IV) and 3-nitrophenothiazine 5,5-dioxide (IX) shows that 96% sulphuric acid can bring about one-electron oxidation of some phenothiazine derivatives. It seems likely that these transformations proceed by identical mechanism as the oxidation of phenothiazine by 96% sulphuric acid<sup>3</sup>. It is worthy to note that in 3-nitrophenothiazine 5,5-dioxide (IX) the sulphur atom is in the highest oxidation state, so that the extraction of one electron by sulphuric acid from the nitrogen atom in position 10 is quite evident. The total oxidation reaction of compound IX by sulphuric acid can be thus described by equation (A).



The oxidation of phenothiazine (I) to the corresponding cation-radical can also be effected by 70% perchloric acid at 100°C. The fact that compounds X–XII do not form the corresponding ion-radicals on treating with 96% sulphuric acid may be a consequence of a blocking of the unshared electrons of the nitrogen atom in position 10 by the electronegative substituents attached to the ring, which makes their engagement in oxidation reaction more difficult, if not impossible.



FIG. 1

The ESR Signal Given by the Radical-Cation XVIII

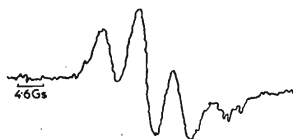
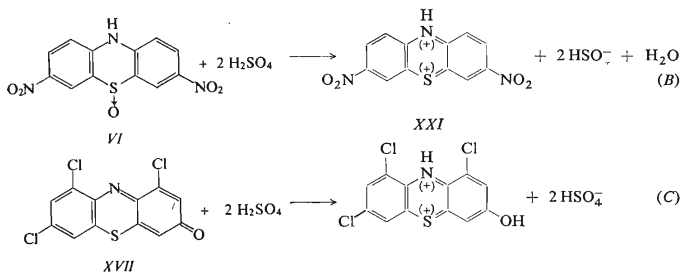


FIG. 2

The ESR Signal Given by the Radical-Cation XIX

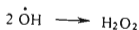
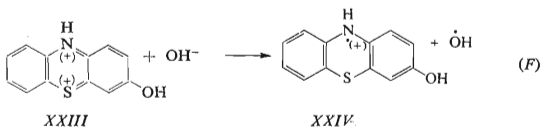
When compared with compounds *IV* and *IX*, the phenothiazine 5-oxides and the phenothiazin-3-ones form the cation-radicals with sulphuric acid by different mechanism. Shine and Mach<sup>3</sup> have assumed that phenothiazine 5-oxide (*III*) and phenothiazine-3-one (*II*) form cation-radicals by a process which involves an intermediate formation of  $\text{>S}^{(+)}\text{-OH}$  bond, which is then homolytically cleaved. Indeed, both compounds, being bases, can form phenothiazinium salts with sulphuric acid, as suggested by the authors. However, since the formation of the cation-radicals proceeds in a polar medium, we believe that not the homolytic, but the heterolytic cleavage of the formed  $\text{>S}^{(+)}\text{-OH}$  bond is taking place here. The authors have further assumed that the presence of water is quite requisite. By contrast with this assumption we have found that only in case of compounds *II* and *XV* it is necessary to use an aqueous sulphuric acid to generate corresponding cation-radicals. The sulphoxides *III*, *V* and *VI* and the phenothiazinones *XIII*, *XIV*, *XVI* and *XVII* form cation-radicals with 96% sulphuric acid already immediately after mixing. Therefore, a re-examination of the mechanism suggested by Shine and Mach<sup>3</sup> seems necessary. We believe that the possibility to form ion radicals from phenothiazine 5-oxides and phenothiazinones in 96% sulphuric acid indicate that these compounds, owing to their basic character, form first phenothiazinium sulphates (Eq. (B) and (C)), the



$\text{HSO}_4^-$  anion of which subsequently undergoes an one-electron oxidation by the protonated phenothiazinium cations, affording peroxidisulphuric acid and the corresponding cation-radicals (Eq. (D) and (E)). In aqueous sulphuric acid, the phenothiazinium sulphates formed are partially transformed to the phenothiazinium hydroxides in which the protonated cation also oxidizes the  $\text{OH}^-$  ion. (Equations (F) and (G)); the protonated 3-hydroxyphenothiazinium cation (*XXIII*) does not oxidize the  $\text{HSO}_4^-$  ion which is weaker nucleophile.

The radical-cation *XXIV* is generated from compound *II* also in aqueous acetic or aqueous oxalic acid at 100°C. This reaction does not proceed, however, in glacial

acetic acid. These results show that the corresponding phenothiazinium salts are converted by water into 3-hydroxyphenothiazinium hydroxide, which then generates the radical cation *XXIV* according to Equation (F).



The cations derived from compounds *V*, *VI*, *XIII*, *XIV*, and *XVII* contain electronegative groups which bring about a decrease of the electron density on the ring, while the hydroxyl group in 3-hydroxyphenothiazinium cation exerts the opposite effect. For this reason the phenothiazinium cations containing electronegative groups are stronger oxidizing agents than the cation *XXIII*. Because of low electronegativity of iodine, the 3-hydroxy-4-iodophenothiazinium cation does not oxidize the  $\text{HSO}_4^-$  ion. The sulphoxide *VII* is a very weak base and therefore, it does not form the corresponding phenothiazinium sulphate with sulphuric acid. Furthermore, it is not oxidized by this reagent, since the unshared electron pair on the nitrogen is strongly blocked by the four nitro groups.

The coupling constants determined experimentally have values of 6.90 G for the phenothiazinium radical-cation, 6.55 G for the 3-nitro-substituted cation, and 6.25 G for the 3,7-dinitro cation. The diminution of the value of the coupling constant with increasing number of the nitro groups may be taken as evidence in favour of the assumption that electronegative groups stabilize the radical-cations by aiding in the delocalization of the unpaired electron of the nitrogen atom of the ring.

#### REFERENCES

1. Tuck L. D., Schieser D. W.: *J. Phys. Chem.* **66**, 937 (1962).
2. Bodea C., Silberg I.: *Rev. Roumaine Chim.* **9**, 9 (1964).
3. Shine H. J., Mach E. E.: *J. Org. Chem.* **30**, 2130 (1965).
4. Bodea C., Răileanu M.: *Studii și Cercetări Chim. Acad. R.P. Romania Fil. Cluj*, **3-4**, 303 (1957).
5. Bodea C., Răileanu M.: *Studii și Cercetări Chim. Acad. R.P. Romania Fil. Cluj*, **1**, 129 (1960).

6. Răileanu M., Turcu A.: *Rev. Roumaine Chim.* *11*, 1423 (1966).
7. Turcu A., Răileanu M.: *Rev. Roumaine Chim.* *14*, 1579 (1969).
8. Bodea C., Răileanu M.: *Ž. Obšč. Chim.* *33*, 1131 (1960).
9. Bodea C., Răileanu M.: *Studii și Cercetări Chim. Acad. R.P. Romania Fil. Cluj 2*, 325 (1960).
10. Bodea C., Răileanu M.: *Ann. Chem.* *614*, 171 (1958).
11. Bodea C., Terdic M., Broser E.: *Ann. Chem.* *715*, 122 (1968).
12. Terdic M., Bodea C.: *Rev. Roumaine Chim.* *13*, 1241 (1968).
13. Chen E. M., Keefer R. M., Andrews L. J.: *J. Chem. Soc.* *89*, 428 (1967).
14. Billon J. P., Cauquis G., Combrisson J.: *J. Chim. Phys.* *3*, 374 (1964).
15. Pobedimskij D. G., Buchačenko A. L., Neuman M. B.: *Ž. Fiz. Chim.* *42*, 1436 (1968).