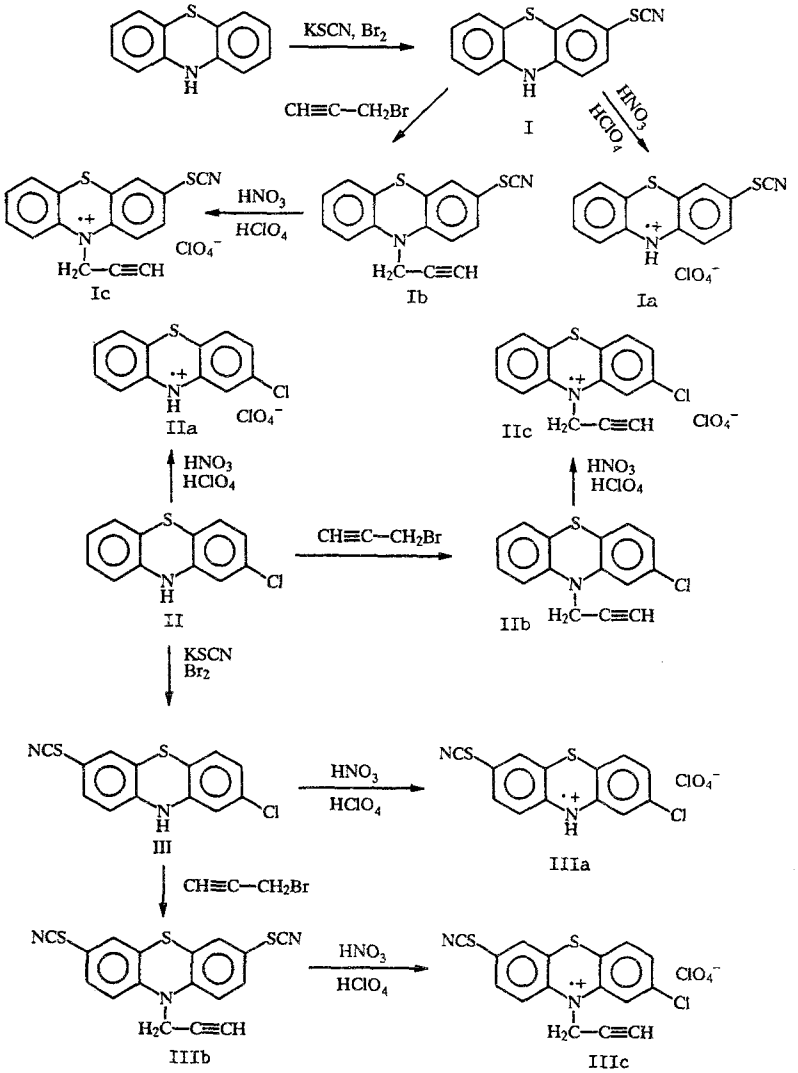
Chemistry of Heterocyclic Compounds, Vol. 29, No. 10, 1993

SYNTHESIS AND PROPERTIES OF CERTAIN n-PROPARGYLPHENOTHIAZINES AND THEIR CATION RADICALS

E. P. Konovalova, O. B. Tomilin, V. N. Yuzhalkin, and É. P. Sanaeva

N-Propargyl derivatives of 3-thiocyanato-, 2-chloro-, and 7-thiocyanato-2-chlorophenothiazines have been synthesized. Their capability for one-electron oxidation, forming cation radicals, has been investigated. EPR spectra of cation radicals obtained by different methods have been examined.

With the aim of searching for new model compounds that are capable of solid-phase topochemical polymerization to form high-spin polyconjugated structures [1, 2], we have synthesized N-propargyl-3-thiocyanatophenothiazine (Ib), N-propargyl-2-chlorophenothiazine (IIb), N-propargyl-7-thiocyanato-2-chlorophenothiazine (IIIb), and the corresponding cation radicals (Ic-IIIc), through the reaction scheme that is shown below.



N. P. Ogarev Mordovian State University, Saransk 430000. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1422-1425, October, 1993. Original article submitted October 18, 1993.

 0009-3122/93/2910-1222$12.50

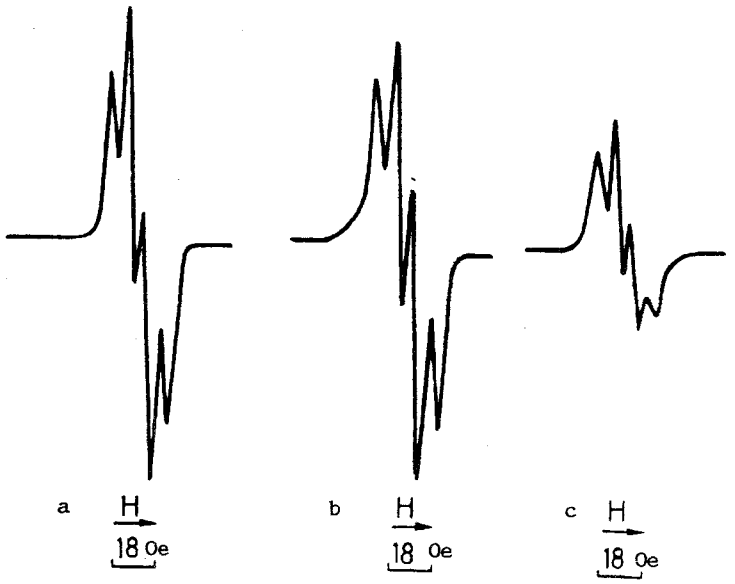


Fig. 1. EPR spectra: *a*) cation radical IIa in acetonitrile; *b*) cation radical obtained by oxidation of IIb by chloranil in acetonitrile; *c*) cation radical obtained by oxidation of IIIb by chloranil in acetonitrile.

The 3- and 7-thiocyanatophenothiazines were obtained by the action of potassium thiocyanate on phenothiazine and 2-chlorophenothiazine in the presence of bromine, in glacial acetic acid [3]. The propargyl group was introduced into position 10 of the phenothiazine ring under conditions of interfacial catalysis in the presence of triethylbenzylammonium chloride (TEBA) [4]. As the oxidizing agent we used a solution of nitric acid and perchloric acid, and also such one-electron oxidants as perhalogenated o-quinones. With the latter type of oxidizing agent, the reaction was performed by pouring together a solution of o-chloranil or o-bromanil with a solution of I-III or Ib-IIIb, in acetonitrile at room temperature. It was noted that the compounds without substituents at the nitrogen atom, i.e., compounds I-III, were very readily oxidized in comparison with Ib-IIIb; this is in agreement with data reported in [5]. The presence of a bulky substituent in position 10 of the phenothiazine ring compels the phenothiazine molecule to assume the H-extra configuration, in which the electron pair of the nitrogen is positioned between the planes of the benzene rings and is not conjugated to as great a degree with the π-system of the phenothiazine ring. Thereby, the nitrogen plays a smaller role in delocalization of electrons, and this leads to a lowering of the HOMO energy [5]. The products obtained in the oxidation, in both cases, were crystalline, dark-violet substances, readily soluble in THF, acetonitrile, and acetone, but insoluble in benzene and toluene.

The radical nature of compounds Ia-IIIa and Ic-IIIc was proved by means of EPR: The perchlorates that were obtained were paramagnetic in the solid state and in solution. For studying the EPR spectra of Ia-IIIa and Ic-IIIc, we prepared solutions in different solvents with concentrations of 7×10^{-3}, 3×10^{-3}, and 2×10^{-3} M (acetonitrile, chlorobenzene, THF). The type of solvent and the concentration did not have any influence on the character of the HFS of the EPR spectra; a lowering of the solution concentration resulted in lower intensities of the EPR signal, and at a concentration of 2×10^{-3} M no signal was registered. The HFS of the EPR spectra of samples Ia-IIIa and Ic-IIIc, obtained by either method, consisted of a quartet with a 1:2:2:1 intensity ratio; this can be explained by interaction of the unpaired electron with the nitrogen nucleus and with one proton. Here, $a_N \sim a_H \sim$ 7-8 Oe (Fig. 1).

This sort of character of the EPR spectra in the case of the cation radicals Ic-IIIc was somewhat unexpected. One of the possible reasons why only one proton of the methylene group is evident in the EPR spectrum may be a steric factor leading to nonequivalence of the protons of the CH_2 group ($a_{H1} >> a_{H2}$). Here, the propargyl group is located above the phenothiazine ring in the H-extra position. It should be noted that we had observed the same sort of picture in the EPR spectrum of N-ethylphenothiazinium perchlorate. At the same time, in the case of the cation radical of N-methylphenothiazine, we obtained an EPR spectrum consisting of a sextet with a 1:4:7:7:4:1 intensity ratio, indicating almost equal interaction of the unpaired electron with the nitrogen nucleus and three equivalent protons of the methyl group; this is in agreement with data reported in [6].

EXPERIMENTAL

The IR spectra were taken in a UR-20 instrument (in white mineral oil and in KBr tablets); the EPR spectra were taken in an ÉPA-2M instrument, using Mn^{2+} ions in the lattice of MgO as a standard. The course of the reactions and the purity of the products were monitored by means of TLC on Silufol UV-254 plates, development in UV light.

The elemental analyses of compounds IB, IIb, and IIIb for C, H, and N matched the calculated values.

3-Thiocyanatophenothiazine (I) and 7-thiocyanato-2-chlorophenothiazine (III) were synthesized by methods similar to those that had been described previously in [3].

Propargyl Bromide. To a mixture of 68.4 g (1.04 moles) of propargyl alcohol and 15 ml of pyridine, chilled to 0°C, 37 ml of freshly distilled PBr_3 was added dropwise with stirring; the temperature was held at 50-60°C, and then the reaction mixture was refluxed for 1 h. The propargyl bromide was distilled from the reaction mixture, collecting the 82-84°C fraction. The propargyl bromide product was dried over K_2CO_3 and redistilled. Yield 59%.

N-Propargyl-3-thiocyanatophenothiazine (Ib, $C_{16}H_{10}N_2S_2$). To a mixture of 1.02 g (0.004 mole) of the phenothiazine I in 50 ml of benzene, 0.8 ml of DMSO, and 1 ml of a 50% aqueous NaOH solution, TEBA (on the tip of a scalpel) was added; then a mixture of 0.7 ml (0.008 mole) of propargyl bromide and 0.8 ml of DMSO was added dropwise with stirring at 37-39°C, and the stirring was continued for 6 h. When the reaction was completed (TLC in 4:1.5 hexane–ethyl acetate system), water was added to the reaction mixture in a 1:1 ratio; the organic layer was separated, washed with water to neutral reaction, and dried with magnesium sulfate, after which the solvent was removed. The residue was passed through a layer of aluminum oxide (30 cm), eluting with a 10:1 hexane–acetone system, after which the solvent was removed. Product mp 75-77°C. IR spectrum: 2170 cm^{-1} (SCN). Yield 40%.

N-Propargyl-2-chlorophenothiazine (IIb, $C_{15}H_{10}ClNS$). To a mixture of 3.36 g (0.014 mole) of the phenothiazine II in 34 ml of benzene, 2.1 ml of DMSO, and 4.5 ml of a 50% aqueous NaOH solution, TEBA (on the tip of a scalpel) was added; then a mixture of 3.47 ml (0.028 mole) of propargyl bromide and 2.1 ml of DMSO was added dropwise with stirring at 37-39°C. Stirring of the reaction mixture was continued for 6 h. The course of the reaction was monitored chromatographically on Silufol UV-254 plates in a 4:1.5 hexane–ethyl acetate system, development in UV light. At the completion of the reaction, water was added to the reaction mixture in a 1:1 ratio; the organic layer was separated, washed with water to neutral reaction, and dried over magnesium sulfate; then the solvent was driven off. The residue was passed through a layer of aluminum oxide (30 cm), eluting with a 5:1 hexane–benzene system; the solvent was removed. Product mp 110-111°C. IR spectrum 840 cm^{-1}. Yield 45%.

N-Propargyl-7-thiocyanato-2-chlorophenothiazine (IIIb, $C_{16}H_9ClN_2S_2$). To a mixture of 1.4 g (0.004 mole) of III in 50 ml of benzene, 0.8 ml of DMSO, and 1 ml of a 50% aqueous NaOH solution, TEBA (on the tip of a scalpel) was added. Then a mixture of 0.7 ml (0.008 mole) of propargyl bromide with 0.8 ml of DMSO was added from a dropping funnel while stirring the reaction mixture at 37-39°C. Stirring was continued for 6 h. The course of the reaction was monitored chromatographically on Silufol UV-254 plates in a 4:1.5 hexane–ethyl acetate system, development in UV light. Upon completion of the reaction, water was added to the reaction mixture in a 1:1 ratio; the organic phase was separated, washed with water to neutral reaction, and dried over magnesium sulfate; then the solvent was removed. The residue was passed through an aluminum oxide layer (30 cm), eluting with a 10:1 hexane–acetone system, after which the solvent was removed. Product mp 87-88°C. IR spectrum: 2172 cm^{-1} (SCN). Yield 32%.

Phenothiazinium (Ia-IIIa) and N-Propargylphenothiazinium (Ic-IIIc) Perchlorates. 0.001 mole of the phenothiazine derivative (I-III, Ib-IIIb) was suspended in 7 ml of 57% $HClO_4$; the mixture was chilled to 0°C, and 0.3 ml of concentrated HNO_3 (d = 1.36) was added while stirring. The stirring was continued for 30 min, after which the mixture was left at room temperature for 20 min; then water was added until a crystalline residue was completely precipitated. The crystals were filtered off, dried, washed on the filter with hexane, and redried.

The N-methylphenothiazinium and N-ethylphenothiazinium perchlorates were obtained by analogous procedures.

REFERENCES

1. V. M. Misin and M. I. Cherkashin, Usp. Khim., **34**, 956 (1985).
2. A. L. Buchachenko, Usp. Khim., **59**, 529 (1990).

3. A. A. Shtyrlina, D. Kh. Yakhmukhametova, K. M. Enikeev, I. É. Ismaev, and I. A. Nuretdinov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 10, 2361 (1983).
4. L. A. Remizova, T. A. Shustrova, and I. A. Favorskaya, Zh. Org. Khim., **22**, 992 (1986).
5. D. Simov, L. Kamenov, and St. Stoyanov, Khim. Geterotsikl. Soedin., No. 4, 497 (1973).
6. C. Lagercrantz, Acta Chem. Scand., No. 15, 1545 (1961).