THE OXIDATION OF 10-AROYLPHENOTHIAZINES WITH LEAD TETRAACETAT

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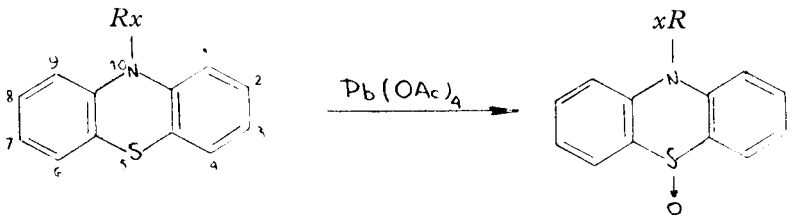
For the oxidation of the sulfide sulfur in 10-substituted derivatives of phenothiazine a variety of oxidizing agents have been used. To the best of our knowledge the oxidation reaction was accomplished with folowing reagents: potassium permanganate[1,2], sodium nitrite in acetic acid[4,3], nitric acid (sp. g. 1.42 and 1.50) in acetic acid [5—6], 30% hydrogen peroxide in ethanol [4, 5, 7, 9—11], 30% hydrogen peroxide in methanol in the presence of oxalic acid[12], 30% hydrogen peroxide in glacial acetic acid [5, 7, 8, 14—16], 30% hydrogen peroxide in dioxane[4], m-chloroperbenzoic acid in chloroform at 10°C[8], hypochlorous acid[15], alkylhydroperixides [13, 14], and chromium trioxide[17].

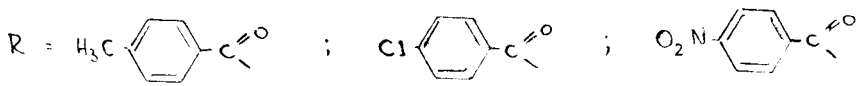
In an earlier paper[18] we presented the results of our work on the oxidation of some 10-acylphenothiazines with lead tetraacetate in 99% acetic acid. It was found that the sulfur of the phenothiazine nucleus undergoes oxidation which leads to the corresponding sulfoxides. It was also found that the oxidation is dependent on the nature of the acyl group attached to the phenothiazine nitrogen.

Continuing our investigation on the oxidation of the phenothiazine sulfur we now report the oxidation of some 10-aroylphenothiazines with lead tetraacetate.

As previously[18] the oxidation reaction was carried out in 99% acetic acid at room temperature with constant shaking for 6 hrs. using equimolar quantities of 10-aroylphenothiazines and lead tetraacetate. Under such conditions the oxidation of 10-p-toluoylphenothiazine, 10-p-chlorobenzoylphenothiazine and 10-p-nitrobenzoylphenothiazine has been attempted. It was found that all mentioned 10-aroylphenothiazines were oxidized to the corresponding sulfoxides.

The formation of 10-p-toluoylphenothiazine-5-oxide, 10-p-chlorobenzoylphenothiazine-5-oxide and 10-p-nitrobenzoylphenothiazine-5-oxide was confirmed by elemental analysis as well as by subsequent hydrolysis to phenothiazine-5-oxide. The formation of phenothiazine-5-oxide was confirmed by elemental analysis and also by the presence of a strong band at around 1065 cm^{-1} in the infrared spectrum[19].





As in the case of the oxidation of 10-acylphenothiazines[18] small quantities of red by-product were formed in the course of all oxidations.

The 10-aroylphenothiazines which were oxidized were prepared by acylation of phenothiazine with the corresponding acid chloride.

Further investigations on the oxidation of phenothiazine derivatives with lead tetraacetate are presently under way.

Experimental

Melting points are uncorected.

PREPARATION OF 10-AROYLPHENOTHIAZINES

10-*p*-*Toluoylphenothiazine*

To a solution of 9.96 g (0.05 mole) of dry phenothiazine in 100 ml dry benzene, 10 g of p-toluoylchloride was added. The reaction mixture was refluxed for 4 hrs. The main part of benzene was then distilled off and petroleum ether was added tonthe residue. The separated precipitate was filtered off, washed with petroleum ether and dried. After recrystallization from acetic acid-water 15 g (94%) of white needles, m.p. 198—200°, were obtained.

Anal. $C_{20}H_{15}NOS$ (317.42) calc'd.:C 75.67% H 4.80% N 4.41%
found.:C 75.60% H 4.57% N 4.65%

10-p-chlorobenzoylphenothiazine and 10-p-nitrobenzoylphenothiazine were prepared analogously by acylation of phenothiazine with exess of p-chlorobenzoylchloride and p-nitrobenzoylchloride respectively.

10-*p*-*Chlorobenzoylphenothiazine*

This compound was obtained quantitatively in form of white needles, m.p. 170—171°, by recrystallization from acetic acid—water.

Anal. $C_{19}H_{12}ClNOS$ (337.81) calc'd.:C 67.55% H 3.58% N 4.14%
found.:C 67.33% H 3.70% N 4.35%

10-*p*-*Nitrobenzoylphenothiazine*

p-Nitrobenzoylphenothiazine was obtained in form of white needles, m.p. 220° by recrystallization from acetic acid-water. The yield was quantitative.

Anal. $C_{19}H_{12}N_2O_3S$ (348.37) calc'd.:C 65.50% H 3.47% N 8.03%
found.:C 65.23% H 3.70% N 8.30%

OXIDATION OF 10-AROYLPHENOTHIAZINES

10-*p*-*Toluoylphenothiazine*-5-*oxide*

To a solution of 1.58 g (0.005 mole) of 10-p-toluoylphenothiazine in 70 ml 99% acetic acid, 2.22 g (0.005 mole) of powdered lead tetraacetate was added. The reaction mixture was shaken at room temperature for 6 hrs. To the red-colored reaction mixture a few drops of ethileneglycol were then added, to remove any traces of unreacted lead tetraacetate. The main part of acetic acid was evaporated under reduced pressure and the residue was poured into water. The separated precipitate was filtered off, washed with water und dried. After recrystallization from ethanolwater shiny pale pink crystals, m.p. 180° were obtained. The yield was 1.4 g (84.3%).

Anal. $C_{20}H_{15}N_2OS$ (333.39) calc'd.:C 72.04% H 4.53% N 4.20%
found.:C 71.85% H 4.48% N 4.36%

10-*p*-*Chlorobenzoylphenothiazine*-5-*oxide*

10-p-chlorobenzoylphenothiazine 1.69 g (0.005 mole) and 2.22 g (0.005 mole) of lead tetraacetate dissolved in 60 ml 99% acetic acid were treated as in the oxidation described above. After recrystallization from ethanol-water 1.6 g (90.3%) of colorless crystals, m.p. 225° were obtained.

Anal. $C_{19}H_{12}ClNO_2S$ (353.81) calc'd.:C 64.77% H 3.42% N 3.96%
found.:C 64.51% H 3.18% N 4.16%

10-*p*-*Nitrobenzoylphenothiazine*-5-*oxide*

As in the method described above, from 1.74 g (0.005 mole) of 10-p-nitrobenzoylphenothiazine and 2.22 g (0.005 mole) of lead tetraacetate dissolved in 70 ml 99% acetic acid, 1.7 g (93.4%) of 10-p-nitrobenzoylphenothiazine-5-oxide were obtained in the form of pale pink crystals, m.p. 245°, from ethanol.

Anal. $C_{19}H_{12}N_2O_4S$ (364.37) calc'd.:C 62.62% H 3.33% N 7.69%
found.:C 62.49% H 3.25% N 7.80%

HYDROLYSIS OF 10-P-TOLUOYLPHENOTHIAZINE-5-OXIDE

A solution of 1.66 g (0.005 mole) of 10-p-toluoylphenothiazine-5-oxide in 30 ml of ethanol and 5 ml of 10% sodium hydroxide was refluxed for 20 minutes. From the brown-colored solution the main part of ethanol was then distilled and the separated crystals were filtered off. After two recrystallizations from ethanol 0.55 g (51.4%) of phenothiazine-5-oxide were obtained in the form of colorless platelets, m.p. 258° dec. The mixed melting point with authentic specimen of phenothiazine-5-oxide was undepressed. The IR spectrum showed a strong band at around 1065 cm^{-1}.

The IR spectrum was run as Nujol mull on a Perkin Elmer Model 521 Infrared spectrophotometer.

Anal. $C_{12}H_9NOS$ (215.87) calc'd.:C 66.96% H 4.21% N 6.05%
found.:C 66.71% H 4.49% N 6.24 %

10-p-Chlorobenzoylphenothiazine-5-oxide and 10-p-nitrobenzoylphenothiazine-5-oxide were hydrolyzed by similar procedure to give phenothiazine-5-oxide.

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ИЗВОД

ОКСИДАЦИЈА НА 10-АРОИЛФЕНОТИАЗИНСКИ ДЕРИВАТИ СО ОЛОВЕН ТЕТРААЦЕТАТ

Б. Д. Подолешов

Изнесени се резултатите добиени при оксидацијата на 10-*p*-толуоилфенотиазин, 10-*p*-хлорбензоилфенотиазин и 10-*p*-нитробензоилфенотиазин со помош на оловен тетраацетат во 99% оцетна киселина и при собна температура.

Утврдено е дека наведените фенотиазински деривати се оксидираат до соодветните сулфоксиди: 10-*p*-толуоилфенотиазин-5-оксид, 10-*p*-хлорбензоилфенотиазин-5-оксид и 10-*p*-нитробензоилфенотиазин-5-оксид.

Исто така дадена е и синтезата на 10-*p*-толуилфенотиазин, 10-*p*-хлорбензоилфенотиазин и 10-*p*-нитробензоилфенотиазин. Овие соединенија се добиени со ацилација на фенотиазин со соодветни киселински хлориди во бензол.

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