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THE PREPARATION OF SOME 10-ACYLPHENOTHIAZINE-5-OXIDES

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Continuing our investigation on the preparation and oxidation of phenothiazine derivatives^{1, 2} in this paper we report the preparation of some unknown 10-arylophenothiazine-5-oxides.

A series of methods are presented in the literature for the preparation of phenothiazine-5-oxide derivatives³⁻¹⁵.

In our work the preparation of 10-(2-furoyl) phenothiazine-5-oxide, 10-(3-nitrobenzoyl) phenothiazine-5-oxide, 10-(4-brombenzoyl) phenothiazine-5-oxide, 10-(1-naphtoyl) phenothiazine-5-oxide and 10-(2-naphtoyl) phenothiazine-5-oxide, was achieved by the oxidation of the corresponding 10-arylophenothiazine with lead tetracetate. The reaction was carried out in glacial acetic and at room temperature with constant shaking for 6 hrs. Equimolar quantities of 10-arylophenothiazines and of lead tetracetate were used.

The prepared 10-arylophenothiazine-5-oxides were characterized by elemental analysis and by subsequent hydrolysis to phenothiazine-5-oxide.

The 10-arylophenothiazines were prepared by acylation of phenothiazine with the corresponding acid chloride.

Experimental

Melting points are uncorrected.

10-(1-Naphtoyl)phenothiazine.

To a solution of 4,98 g (0,025 mole) phenothiazine in 100 ml dry benzene 5 ml of 1-naphtoylchloride was added. The reaction mixture was refluxed for 3 hrs. The main part of benzene was then distilled off and petroleum ether was added to the residue. The separated precipitate was filtered off, washed with petroleum ether and dried. 7,5 g (84,94%) 10-(1-naphtoyl)phenothiazine of crude product was obtained. After four rec-

rysstallzations from ethanol-water, yellowish crystals, m.p. 170° were obtained.

Anal. $C_{23}H_{15}NOS$ (353,42) calc'd: C 78,15% H 4,28%
found: C 78,10% H 4,30%

10-(2-Naphtoyl)phenothiazine

This compound was obtained in the same maner as above by acylation of phenothiazine with 2-naphtoylchloride. A quantitative yield of crude 10-(2-naphtoyl)phenothiazine was obtained. After four recrystallizations from aceticacid-water, colorless, crystals, m.p. 185 were obtained.

Anal. $C_{23}H_{15}NOS$ (353,42) calc'd: C 78,15% H 4,28%
found: C 77,92% H 4,34%

10-(2-Furoyl)phenothiazine, 10-(3-nitrobenzoyl)phenothiazine and 10-(4-brombenzoyl)phenothiazine were prepared anologously by acylation of phenothiazine with the corresponding acid chloride².

10-(2-Furoyl)phenothiazine-5-oxide.

To a solution of 3 g (0,01 mole) 10-(2-furoyl)phenothiazine in 60 ml glacial acetic acid, 4,44 g (0,01 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 ethilenglycol 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 and dried. 2,8 g (90,6%) 10-(2-furoyl)phenothiazine-5-oxide as crude product was obtained. After five recrystallizations from acetone-water, pale pink crystals, m.p. 205—207° were obtained.

Anal. $C_{17}HNO_3S$ (309,35) calc'd: C 66,01% H 3,59% N 4,3%
found: C 65,83% H 3,57% N 4,35%

10-(1-Naphtoyl)phenothiazine-5-oxide

As in the method described above from 1,7 g (0,005 mole) of 10-(1-naphtoyl)phenothiazine and 2,22 g (0,005 mole) of lead tetraacetate dissolved in 60 ml glacial acetic acid, 1,7 g (95,6%) of crude 10-(1-naphtoyl)phenothiazine-5-oxide were obtained. After four recrystallizations from ethanol, pale pink crystals, m.p. 202° were obtained.

Anal. $C_{23}H_{15}NO_2S$ (369,42) calc'd: C 74,86% H 4,10%
found: C 74,90% H 3,98%

10-(2-Naphtoyl)phenothiazine-5-oxide

10-(2-naphtoyl)phenothiazine 1,7 g (0,005 mole) and 2,22 g (0,005 mole) of lead tetraacetate dissolved in 60 ml glacial acid were treated as in

oxidation described above. 1,5 g (90,5%) of crude product was obtained. After four recrystallizations from ethanol, pale pink crystals, m.p. 225° were obtained.

Anal. $C_{23}H_{15}NO_2S$ (369,42) calc'd: C 74,86% H 4,10%
found: C 74,96% H 3,92%

10-(3-Nitrobenzoyl)phenothiazine-5-oxide

In the same way as described above by the oxidation of 1,74 g (0,005 mole) of 10-(3-nitrobenzoyl)phenothiazine with 2,22 g (0,005 mole) of lead tetraacetate dissolved in 60 ml glacial acetic acid, 1,7 g (90,9%) of crude product was obtained. After recrystallization from ethanol-water pale yellow crystals, m.p. 205 were obtained.

Anal. $C_{19}H_{12}N_2O_4S$ (364,39) calc'd: C 62,62% H 3,33% N 7,69%
found: C 62,40% H 2,91% N 7,96%

10-(4-Brombenzoyl)phenothiazine-5-oxide

As above by the oxidation of 1,9 g (0,005 mole) of 10-(4-brombenzoyl)phenothiazine with 2,22 g (0,005 mole) lead tetraacetate dissolved in 60 ml glacial acetic acid, 1,9 (90,4%) of crude product was obtained. After recrystallization from ethanol-water crystals m.p. 225 were obtained.

Anal. $C_{19}H_{12}NO_2BrS$ (398,30) calc'd: C 57,92% H 3,04% N 3,52%
found: C 57,79% H 3,14% N 3,68%

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ИЗВОД

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СИНТЕЗА НА НЕКОИ 10-АРОИЛФЕНОТИАЗИН-5-ОКСИДИ

При оксидацијата на соодветни 10-ароилфенотиазински деривати со помош на оловен тетрацетат во ледена оцетна киселина и при собна температура се добиени: 10-(2-фуроил)фенотиазин-5-оксид, 10-(3-нитробензоил)фенотиазин-5-оксид, 10-(4-бромбензоил)фенотиазин-5-оксид, 10-(1-нафтоил)фенотиазин-5-оксид, и 10-(2-нафтоил)фенотиазин-5-оксид.

Исто така е опишано и добивањето на 10-(1-нафтоил)фенотиазин и 10-(2-нафтоил)фенотиазин.

REFERENCES

1. B. D. Podolešov, Croat. Chem. Acta 40/1968/201
2. B. D. Podolešov, and L. G. Kamčeva Annuaire de la Faculte des Sciences de L' Universite de Skopje sec. A./1969/91.
3. E. De B. Barnertt and S. Smiles, J. Chem. Soc. 97/1910/188
4. H. J. Bernstein and L. R. Rothstein, J. Am. Chem. Soc. 66/1944/1886
5. F. Kehrmann and Zybs, Ber. 52B/1919/ 130
6. D. Simov and St. Fakirov, Godišnic na Sofijskija Univ. Him. Fak .56/1961/62/111.
7. H. Gilman and R. D. Nelson, J. Am. Chem. Soc. 75/1953/5422.
8. R. D. Nelson, Iowa State Coll. J. Sci. 27/1953/ 229.
9. Smith Kline French Laboratories Neth.Appl 6.600.046 /1966/;, C.A. 66,2578g
10. H. Gilman aud D. A. Shirley, J. Am. Chem.Soc. 66 /1944/ 888
11. Yoshitomi Drug Manufg. Co.Ltd. Japan, Pat. 13.930 /60/; C.A. 55 14486h
12. C. Bodea and J. Silberg, Acad. R. P. Romine, Filiala Cluj, Studii Cercetari Chem. 14/1963/ 317.
13. N. L. Smith, J. Org. Chem. 16 /1951/ 415.
14. Sugita, Jitsuo, Tsujino, Youichi, Nipon Kagaku Zasshi 89 /1968/ 309 C. A. 69,67304v
15. Tsujino, Youichi, Tetrahedron Lett. 38 /1968/ 4111 C. A. 69,96623d.