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Synthesis of Some New Fluorinated Phenothiazines

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Chlorohydroquinone, 2,3-dichloro-9,10-dihydro-9,10-*o*-benzeno-1,4-anthraquinone and 2,3-dichloro-1,4-naphthoquinone undergo condensation with zinc salt of 2-amino-4-fluorobenzenethiol to give 2-fluoro-phenothiazin-7-ol, 6-chloro-8,13-dihydro-8,13-*o*-benzeno-naphtho-2-fluoro-(2,3-a)-phenothiazin-7(H) ones, 6-chloro-10-fluoro-5H-benzo-[a]-phenothiazin-5-one and 6-chloro-10-fluoro- 12H-benzo-[a]-phenothiazin-5-ol.

INTRODUCTION

Only a few fluorophenothiazines have been reported in the literature[1, 2], although a great amount of work has been done in various phenothiazines[3–7], During the last few years a growing number of useful applications of fluorinated organic compounds[8, 9] has increased the desirability of the preparation of fluorinated compounds and therefore the fluorophenothiazines were selected for the present investigation. In continuation of our work[10–12] we have synthesized new 2-fluorophenothiazin-7-ol, 6-chloro-8,13-dihydro-8,13-*o*-benzeno naphtho-2-fluoro-(2,3-a)-phenothiazin-7(H)-one, 6-chloro-10-fluoro-5H-benzo-[a]-phenothiazin-5-one and 6-chloro-10-fluoro-12H-benzo-[a]-phenothiazin-5-ol.

EXPERIMENTAL

The preparation of 2-fluorophenothiazin-7-ol **(III)** (Scheme-1) was initiated with the condensation of zinc salt of 2-amino-4-fluorobenzenethiol **(I)**[13, 14] and 2-chlorohydroquinone **(II)** by the method of Nodiff *et al.*[15] 2,3-Dichloro-9-10 dihydro-9,10-*o*-benzeno-1,4-anthraquinone **(IV)** underwent condensation with zinc salt of 2-amino-4-fluorobenzenethiol **(I)**[16] to give **(V)** in 95% ethanol. Further, 6-chloro-10-fluoro-5H-benzo-[a]-phenothiazin-5-one **(VII)** is prepared by reacting 2,3-dichloro-1,4-naphthoquinone **(VI)** with zinc salt of 2-amino-4-fluorobenzenethiol **(I)** in ethanol. The compound number **(VII)** on reduction with sodium hydrosulphite[17] in acetone gave 6-chloro-10-fluoro-12H-benzo-[a]-phenothiazin-5-ol **(VIII)**. The compounds synthesised are characterised by spectral and analytical data.

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(I)
(II)
(III)
(IV)
(V)
(VI)
(VII)
(VIII)
Na OH
Et OH, O_2
95% Ethanol
1:1 Molar Ratio
Ethanol
Reflux
Sodium Hydrosulphite
Acetone
(I) +
(I) +

Scheme - 1

2-Fluorophenothiazin-7-ol (III): A mixture of 8.238 g (0.026 mole) of compound **(I)** and 7.514 g (0.052 mole) of compound **(II)**, 100 mL of ethanol and 2.1 g of sodium hydroxide in 5 mL of water was heated under reflux for 45 min during the reaction oxygen was passed through the solution. After that the hot solution was filtered and the filtrate was poured into 1 litre of ice-cold water containing 9.0 g of sodium dithionate. It was then extracted with ether and the solvent layer was dried over anhydrous magnesium sulphate. The ether was evaporated under reduced pressure and the unreacted compound **(II)** was removed by distillation at 125–130°C (0.05 mm).

The solid thus obtained was crystallized from benzene, yield 45%; m.p. 84°C, IR (KBr): 3355s (> NH), 3275s (—OH), 1610s, 1430m, 1130s (C—F), 920m, 830m, 645s (C—S—C) cm^{-1}. Mass (M^+): 233 (m/e), Analysis: Found: C, 61.84; H, 3.49; N, 6.06; S, 13.68%. $C_{12}H_8FNOS$ requires: C, 61.80; H, 3.43; N, 6.00; S, 13.73%.

6-Chloro-8,13-dihydro-8,13-*o*-benzenonaphtho-2-fluoro-[2,3-a]-phenothi azin-7(H)-ones (V): A mixture of compounds **(IV)** (0.005 mole) and **(I)** (0.0025 mole) in 95% ethanol (10 mL) was stirred for 1 h at room temperature and then refluxed for 80 min. The solution was cooled, filtered and washed well with water, 10% aq. HCl, water and finally with dilute ethanol. It is recrystallized from benzene. Yield 65%; m.p. 155°C, IR (KBr): 3110w, 1620m (C=O), 1580s, 1560m, 1380m, 1125s (C—F), 840m, 820m, 760m, 730w, 640s (C—S—C) cm^{-1}. Mass (M^+): 441.5 (m/e), Analysis: Found: C, 70.61; H, 3.01; N, 3.14; S, 7.29%. $C_{26}H_{13}ClFNOS$ requires: C, 70.66; H, 2.94; N, 3.17; S, 7.25%.

6-Chloro-10-fluoro-5H-benzo-[a]-phenothiazin-5-one (VII): A mixture of compounds **(I)** (0.025 mole) and **(VI)** (0.056 mole) in dry ethanol (100 mL) was stirred for 1 h and heated under reflux for 4 h. On cooling, a dark red solid precipitated, which was filtered, washed with HCl (4%) and cold water, dried and recrystallized from benzene. Yield 68%; m.p. 180°C, IR (KBr): 1660s (C=O), 1600s, 1440m, 1123s (C—F), 865m, 850s, 760m, 725w, 645w cm^{-1}. Mass (M^+): 315.5 (m/e), Analysis: Found: C, 60.89; H, 2.26; N, 4.47; S, 10.09%. $C_{16}H_7ClFNOS$ requires: C, 60.85; H, 2.21; N, 4.43; S, 10.14%.

6-Chloro-10-fluoro-12H-benzo-[a]-phenothiazin-5-ol (VIII): A mixture of compounds **(VII)** (0.005 mole), sodium hydrosulphite (2 g), water (5 mL) and acetone (50 mL) was heated under reflux for 1.5 h. The mixture that turned colourless was allowed to cool and poured into a solution of sodium hydrosulphite (5 g) in ice-cold water (1 litre). The solid thus obtained was extracted with ether, washed with water and dried over sodium sulphate. After evaporating the solvent under reduced pressure it is recrystallized from petroleum-ether-benzene mixture. Yield 70%; m.p. 300°C, IR (KBr): 3400s (> NH), 3220b (—OH), 1435w, 1600m, 1125s (C—F), 870s, 850m, 750m, 720m, 640m (C—S—C) cm^{-1}. Mass (M^+): 317.5 (m/e). Analysis: Found: C, 60.45; H, 2.80; N, 4.37; S, 10.12%. $C_{16}H_9ClFNOS$ requires: C, 60.47; H, 2.83; N, 4.40; S, 10.07%.

REFERENCES

1. N.L. Smith, *J. Org. Chem.*, **15**, 1125 (1950).
2. A. Roe, H.V. Montgomery and W.A. Vernell, *J. Org. Chem.*, **21**, 28 (1956).
3. M. Terdic and C. Bodea, *Rev. Roum. Chim.*, **13**, 833 (1968).
4. E.A. Nodiff, K. Tanabe, F. Schnierle, S. Morosawa and T.W. Hoffman, K. Takeda and A.A. Manian, *J. Heterocyclic Chem.*, **7**, 203 (1970).
5. E.A. Nodiff, H.L. Sharma, T. Khono, F. Schnierle, M. Mori and A.A. Manian, *J. Heterocyclic Chem.*, **8**, 321 (1971).
6. R.L. Mittal and S.K. Jain, *J. Chem. Soc. (C)*, 1875 (1971).
7. S.K. Jain and R.L. Mittal, *Indian J. Chem.*, **12**, 780 (1974).
8. C.M. Murphy, H. Ravner and N.L. Smith, *Ind. Eng. Chem.*, **42**, 2479 (1950).
9. R. Duschinsky, E. Pleven and C. Heidelberger, *J. Am. Chem. Soc.*, **79**, 4559 (1957).
10. S.B. Tambi, M. Anand, V. Taneja, C.L. Gupta and R.L. Gupta, *J. Heterocyclic Chem.*, **20**, 803 (1983).
11. V. Taneja, C.L. Gupta and R.L. Mittal, *Chemistry and Industry*, 187 (1984).
12. R.L. Mittal, P. Taneja, V. Khatri and L. Prakash, *Revue Roumaine Chimie*, **33**, 463 (1988).
13. P.C. Taunk and R.L. Mittal, *Monatsch. Chem.*, **102**, 760 (1971).
14. N. Steiger, U.S. Patent, 2,454,260 (Nov. 16, 1948); *Chem. Abstr.*, **43**, 1438b (1949).
15. E.A. Nodiff and M. Hausman, *J. Org. Chem.*, **31**, 625 (1966)
16. R.L. Mittal, V. Taneja, C.L. Gupta and S.B. Gupta, *Revue Roumaine Chimie*, **30**, 757 (1985).
17. R.L. Mittal, C.L. Gupta, V. Taneja and S.B. Gupta, *Indian J. Chem.*, **24B**, 551 (1985).

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