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NOTE

Synthesis and Antibacterial Activity of Pyrimidine-2-Thione Derivatives

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Pyrimidine-2-thiones **(2a-m)** have been prepared by heating chalcone derivatives **(1a–m)** with thiourea in ethanolic potassium-hydroxide and reacted with chloroacetic acid and acetyl choride yielding the products **3–4.**

Thiazole compounds possess considerable fungicidal action[1–3]. The present work was carried out with the aim of preparing new heterocyclic compounds containing thiazolyl and pyrimidyl moieties for pharmacological studies. Thus compounds **(1a–m)** were reacted with thiourea in ethanolic potassium hydroxide affording the pyrimidine-2-thione derivatives **(2).** The IR spectra of **2** showed bands characteristic of NH, C=S and N—C=S functions.

Treatment of **2a–m** with chloroacetic acid in acetic acid/acetic anhydride in the presence of sodium acetate yielded 7-(2′-hydroxy-4′-methoxy-5′-bromo-phenyl) - 2 - acetyl-5 - substituted - 3 - oxo - 2,3,4,5 - tetrahydrothiazolone - (3-2-a)-pyrimidine **(3a–m).**

Treatment of **2a–m** with acetyl chloride yielded the acetylation product **(4a–m).**

Antibacterial Activity of Pyrimidine-2-Thione Derivatives

The antibacterial activity of synthesised compounds was determined against *Staphylococcus aureus* and *Escherichia coli* by paper disc method at a concentration of 50 mg/d. Antibacterial activity of synthesised compounds was compared with the known antibiotic cloxacillin.

Evaluation of bacterial activity reveals that all the compounds were less active against both the organisms.

The m.p.'s were recorded in open capillaries and are uncorrected. The IR spectra were recorded on a Perkin-Elmer-377 spectrophotometer and the PMR on a Varian Model EM-360L spectrophotometer. Satisfactory microanalyses were obtained.

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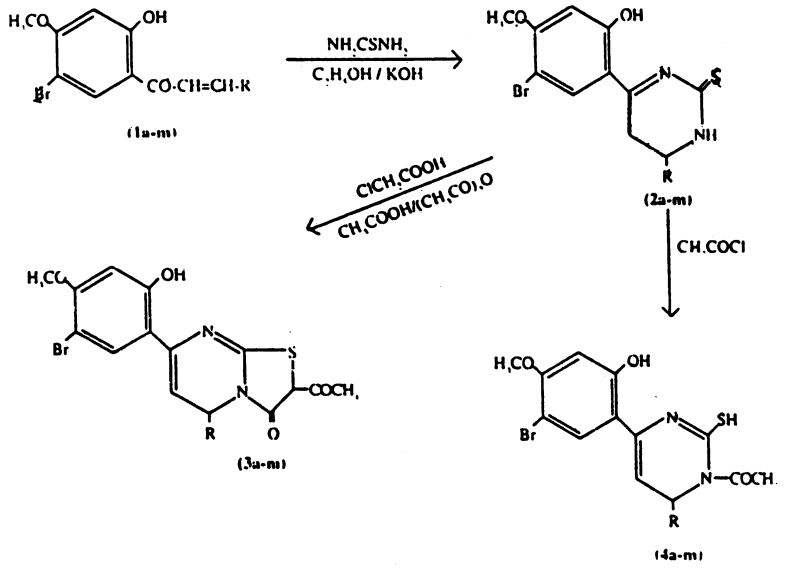

(a) R = —C_6H_5 (f) R = 2,4-$(Cl)_2C_6H_3$ (j) R = 3-$NH_2C_6H_4$
(b) R = 2-$OCH_3C_6H_4$ (g) R = 4-$CH_3C_6H_4$ (k) R = 4-$N(CH_3)_2C_6H_4$
(c) R = 2-ClC_6H_4 (h) R = 4-$C_3H_7C_6H_4$ (l) R = 4-OH-3-$OCH_3C_6H_3$
(d) R = 3-ClC_6H_4 (i) R = 3-$NO_2C_6H_4$ (m) R = 3,4-$(O)_2CH_2C_6H_3$
(e) R = 4-ClC_6H_4

General method for the preparation of 4-(2′-hydroxy-4′-methoxy-5′-bromophenyl)-6-Substituted phenyl-1,2,5,6-tetrahydropyrimidine-2-thione. (2a–m)

A mixture of 2′-hydroxy-4′-methoxy-5′-bromochalcones (0.01 mol), thiourea (0.01 mol) and potassium hydroxide (1.0 g) in ethanol (30 mL) was refluxed on water bath at 70–80°C for 3 h. Then the reaction mixture was left for overnight. The solid separated was dried and crystallized from ethanol. m.p. (°C): **2a** 79, **2b** 148, **2c** 112, **2d** 108, **2e** 118, **2f** 134, **2g** 85, **2h** 97, **2i** 166, **2j** 158, **2k** 147, **2l** 82, **2m** 134; IR (KBr) (cm^{-1}): 1600 ν(C=N), 1160 ν(C=S), 3170 ν(N—H); PMR (DMSO-d_6): δ 2.6 (—CH—, pyrimidine ring), 2.27 (SH), 4.05 (—OCH_3), 5.74 (C=CH), 6.51 (—OH), 8.1 (NH) 7.3–8.0 (Ar—H).

General method for the preparation of 7-(2′-hydroxy-4′-methoxy-5′-bromophenyl)-2-acetyl-5-substituted-3-oxo-2,3,4,5-tetrahydrothiazolo-(3,2-a)-pyrimidine (3a–m)

A mixture of 4-(2′-hydroxy-4′-methoxy-5′-bromophenyl)-6-substituted phenyl-1,2,5,6-tetrahydro-pyrimidine-2-thione (0.005 mol), 0.5 g of chloroacetic acid and 2.0 g of fused sodium acetate in 5.0 mL of acetic acid and 2.0 mL of acetic anhydride was refluxed on a water bath at 80–90°C for 3 h and left overnight at room temperature. The reaction mixture was poured into water and the solid obtained was filtered and crystallised from light petroleum ether.

m.p. (°C): **3a** 78, **3b** 108, **3c** 105, **3d** 112, **3e** 86, **3f** 118, **3g** 94, **3h** 83, **3i** 158, **3j** 138, **3k** 142, **3l** 68, **3m** 119; IR (KBr) (cm^{-1}): 1650 ν(C=O), 3060 ν($COCH_3$); PMR (DMSO-d_6): δ 2.5 (—$COCH_3$), 5.4 (methin proton), 5.8 (—CH=C), 6.8–7.3 (Ar—H).

General method for the preparation of 6-(2′-hydroxy-4′-methoxy-5′-bromophenyl)-3-acetyl-4-substituted phenyl-3,4-dihydropyrimidine-2-thiol (4a–m)

A mixture of 4-(2′-hydroxy-4′-methoxy-5′-bromophenyl)-6-substituted phenyl-1,2,5,6-tetrahydro-pyrimidine-2-thione (1.0 g), and acetylchoride (8.0 mL) was heated under reflux for 2 h; excess of acetylchloride was evaporated and the oil obtained was treated with light petrol and the solid obtained was crystallized from benzene. m.p. (°C): **4a** 74, **4b** 115, **4c** 106, **4d** 114, **4e** 82, **4f** 108, **4g** 84, **4h** 124, **4i** 156, **4j** 148, **4k** 128, **4l** 58, **4m** 124; IR (KBr) (cm^{-1}): 3040 ν(—$COCH_3$), 1670 ν(C=O); PMR (DMSO-d_6): δ 2.38–2.4 (CH_3), 3.15–3.17 ($COCH_3$), 6.68–6.7 (OH), 7.0–7.05 (SH) and 7.3–8.0 (Ar—H).

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