# 6,6-DIMETHYL-6,11-DIHYDRO(1)BENZOTHIOPYRANO(4,3-b)INDOLES: NOVEL POLYCYCLIC HETEROAROMATIC COMPOUNDS

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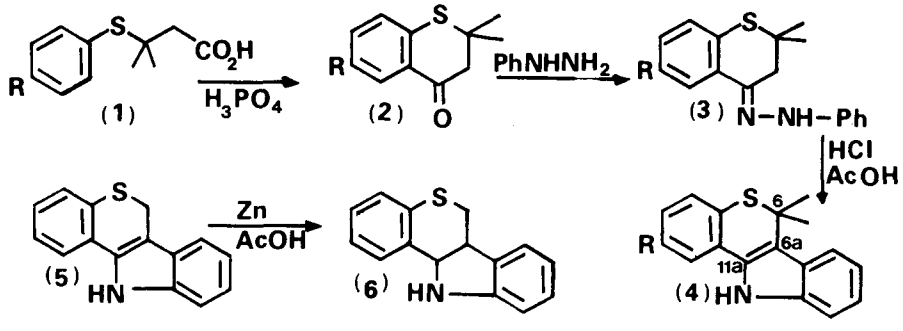
In the course of our studies on polycyclic heteroaromatics we have investigated the synthesis of benzothiopheno[3,2-c]quinolines and the structurally related benzopyrano[4,3-b]indoles to determine their chemical reactivities and also to test their activities as mutagens carcinogens and further as antitumour substances (Kawase 1979). In the present work the synthesis of 6,6-dimethyl derivatives of 6,11-dihydro[1]benzothiopyrano[4,3-b]indoles was investigated to determine the effect of the 6,6-dimethyl group on the antineoplastic and antifungal activity of these compounds as a new class of heterocyclic pseudoazulene (Buu-Hoi 1972).

The synthetic route is outlined in Scheme 1. 4-Methylthiophenol was treated with 3,3-dimethylacrylic acid and hydrogen bromide to give 3-methyl-3-phenylthiobutanoic acid (1a) in 62% yield. Cyclization of this acid with polyphosphoric acid at 80°C afforded the 2,2,6-trimethyl-1-thiochroman-4-one (2a) in 55% yield {m.p. 60°C, $M^+$206.1, δ1.35 (2 x $CH_3$) 2.80 ($-CH_2-$)}(Kurth 1977). The phenylhydrazone (3a) was formed by treatment of the thiochroman-4-one (2a) with phenylhydrazine {for (3a) $M^+$296.2, νC=N 1600 $cm^{-1}$ δ1.25 (2 x $CH_3$) 2.21 (6-$CH_3$) 7.90 (N-H)}. Fischer indolization (as described by Mann, 1949) of the hydrazone (3a) was carried out directly in acetic acid/HCl to afford the hitherto unreported product 2,6,6-trimethyl-6,11-dihydro[1]benzothiopyrano[4,3-b]indole (4a) in 50% yield. {$M^+$279.0906, accurate mass for $C_{18}H_{17}NS$, m.p. 190-192°, δ8.25 (N-H),1.82(2 x $CH_3$), 2.32 (2-$CH_3$), ν N-H 3400 $cm^{-1}$}. 6,6-Dimethyl-6,11-dihydro [1]benzothiopyrano[4,3-b]indoles (4b) and (4c) were similarly prepared. The unsubstituted 6,11-dihydrobenzothiopyrano[4,3-b]indole (5) prepared by Fischer indolization of 1-thiochroman-4-one phenylhydrazone was easily reduced by treatment with zinc/acetic acid/HCl to yield the novel tetrahydrobenzothiopyrano [4,3-b]indole (6) in 18% yield {νC=C, 1610, N-H, 3500 $cm^{-1}$, δ2.80 - 3.82 (m, CH-$CH_2$-S) 4.38 (d, J 11 Hz, H-11a) 6.50 - 7.85 (m, aromatic H)}.

The novel polycyclic heteroaromatic compounds prepared above are structurally related to the pseudoazulenes, important mutagens, carcinogens and antitumour substances and should be of interest for their biological properties.




Scheme 1: (a) R=Me, (b) R=H, (c) R=Br, (d) R=Cl.

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