1-ARYLSULPHONYL-3-*n*-BUTYL-2-METHYL-2-THIOPSEUDOUREAS

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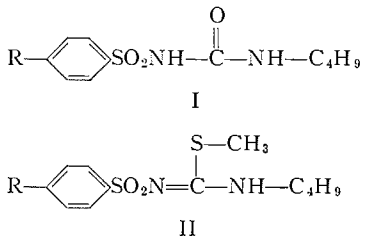
Compounds containing the thiopseudourea grouping have recently come under investigation in our laboratories (1). Since certain 1-arylsulphonyl-3-*n*-butylureas (I) have been shown to possess useful hypoglycemic activity, it was of interest to prepare some 1-arylsulphonyl-3-*n*-butyl-2-methyl-2-thiopseudoureas (II) for pharmacological screening. Cox (2) has reported the preparation of a series of 1-arylsulphonyl-2-methyl-2-thiopseudoureas which have shown some value as bacteriostatic agents.



(*a*) R = CH_3
(*b*) R = $NHCOCH_3$
(*c*) R = NH_2

The sulphonylthiopseudoureas were prepared by the condensation of the appropriate sulphonyl chlorides with 1-*n*-butyl-2-methyl-2-thiopseudourea. Acid hydrolysis of 1-(*p*-acetaminobenzenesulphonyl)-3-*n*-butyl-2-methyl-2-thiopseudourea (II*b*) gave the 1-(*p*-aminobenzenesulphonyl)-3-*n*-butyl-2-methyl-2-thiopseudourea (II*c*).

The sulphonylthiopseudoureas were administered orally to rabbits which had been fasted for 24 hours. None of the compounds tested showed a significant hypoglycemic action.

EXPERIMENTAL*

1-(p-Toluenesulphonyl)-3-n-butyl-2-methyl-2-thiopseudourea

Potassium carbonate (33 g., 0.24 mole) was suspended in 90 ml. of a 3:1 acetone–water solution cooled in an ice-water bath. A well-ground mixture of *p*-toluenesulphonylchloride (12.4 g., 0.065 mole) and 1-*n*-butyl-2-methyl-2-thiopseudourea hydroiodide† (19.9 g., 0.0725 mole) was slowly added with vigorous stirring. The addition was completed after 30 minutes and the stirring was continued at room temperature for another 3 hours. The reaction contents were then added to 250 ml. of water, causing the product to separate out, 17.8 g. (91% yield), m.p. 72°–77° C. Two recrystallizations from isopropanol gave 11.5 g., m.p. 85°–86° C. Calculated for $C_{13}H_{20}N_2S_2O_2$: C, 51.97; H, 6.71; N, 9.32; S, 21.35. Found: C, 52.25; H, 6.92; N, 9.19; S, 20.93.

1-(p-Acetaminobenzenesulphonyl)-3-n-butyl-2-methyl-2-thiopseudourea

This compound was prepared in the same manner as the preceding example. Potassium carbonate (66 g., 0.48 mole), *p*-acetaminobenzenesulphonyl chloride (30.3 g., 0.13 mole), and 1-*n*-butyl-2-methyl-2-thiopseudourea hydroiodide† (39.2 g., 0.143 mole) gave 44 g. of product with m.p. 129°–135° C. Two recrystallizations from isopropanol gave 21.8 g., m.p. 141°–142° C. Calculated for $C_{14}H_{21}N_3S_2O_2$: C, 48.96; H, 6.17; N, 12.24; S, 18.67. Found: C, 49.15; H, 6.02; N, 12.11; S, 18.51.

**All melting points are uncorrected.*
†The preparation of this compound is described by Kirsten and Smith (3).

1-(p-Aminobenzenesulphonyl)-3-n-butyl-2-methyl-2-thiopseudourea

1-(*p*-Acetaminobenzenesulphonyl)-3-*n*-butyl-2-methyl-2-thiopseudourea (15.5 g., 0.045 mole) was refluxed for 2 hours in a solution consisting of 67 ml. of 7% hydrochloric acid and 30 ml. of ethanol. After cooling and addition of a large amount of water, the solution was neutralized with ammonium hydroxide, causing the product to separate out, 12.8 g. (95% yield), m.p. 158°–159° C. One recrystallization from methanol did not raise the melting point. Calculated for $C_{12}H_{19}N_3S_2O_2$: C, 47.81; H, 6.35; N, 13.94; S, 21.28. Found: C, 48.35; H, 6.72; N, 14.06; S, 21.10.

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