SYNTHESIS OF S-METHYL-6-PROPYL-2-THIOURACIL-^{35}S AND 6-PROPYLURACIL-2-^{14}C

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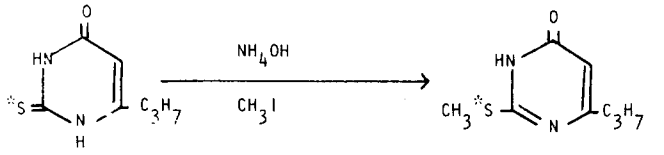
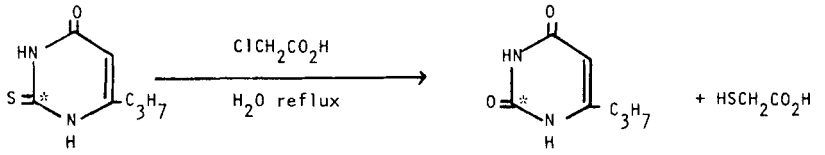
Two of the minor metabolites of the antithyroid drug 6-propyl-2-thiouracil (I) have been isolated from rat urine identified as S-methyl-6-propyl-2-thiouracil (II) and 6-propyluracil (III) [1]. The title compounds were synthesized for further biological studies *in vivo* and *in vitro*.

Compound II was prepared by methylation of 6-propyl-2-thiouracil-^{35}S (Ia) (Amersham-Searle Corp., Arlington Heights, Illinois) with methyl iodide (Fig. 1) according to the method described by Barret *et al.* [2] for the synthesis of S-methyl-2-thiouracil. Compound III was prepared by desulferation of 6-propylthiouracil-2-^{14}C (Ib) (New England Nuclear, Boston, Massachusetts) with chloroacetic acid by adoption of Wheeler and Liddle method [3] for the preparation of uracil from 2-thiouracil (Fig. 2).



Ia II

FIGURE 1



Ib FIGURE 2 III

EXPERIMENTAL

S-Methyl-6-propyl-2-thiouracil-^{35}S (II) - To a solution of 345 µg (2.03 µmoles) of 6-propyl-2-thiouracil-^{35}S in 3.5 ml of 0.5 N ammonium hydroxide, 7 ml of ethanol and 39.9 mg of methyl iodide were added. The mixture was heated at 68° for 10 min., then cooled. The solution was lyophilized and the desired product was purified by chromatography on Bio-Gel P-2 column (2 x 115 cm) and on preparative thin-layer plates of silica gel using benzene:isopropanol (60:10), and compared with an authentic unlabelled standard.

6-Propyluracil-2-^{14}C (III) - An aqueous solution of 1.02 mg of chloroacetic acid in 2 ml of water was mixed with 895 µg (5.26 µmoles) of 6-propylthiouracil-2-^{14}C and allowed to reflux for 2 hrs. The mixture was lyophilized and the desired product was purified by column chromatography on Bio-Gel P-2, and its purity was confirmed by tlc as compared with an authentic unlabelled standard.

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