Chemical Conversion of Uridine into 4-Thiouridine *via* the 4-(1,2,4-Triazol-1-yl)pyrimidin-2(1*H*)-one Intermediate

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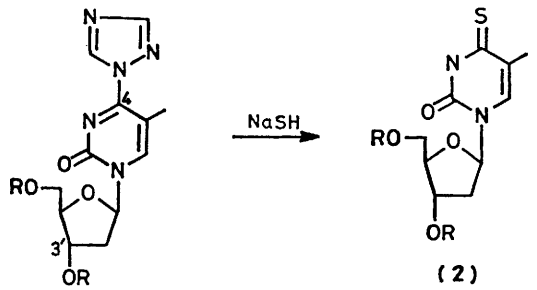
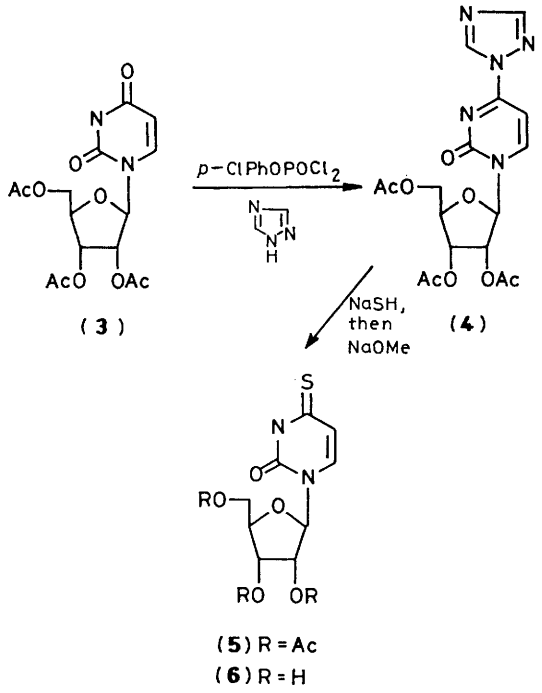
In an aqueous solution of sodium hydrosulphide at room temperature, 4-(1,2,4-triazol-1-yl)-1-(2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosyl)pyrimidin-2(1*H*)-one, prepared from uridine, is converted into the 4-thiopyrimidin-2(1*H*)-one derivative which can be deacetylated to yield 4-thiouridine.

4-Thiouridine (**6**), the modified nucleoside in many transfer RNAs,[1] was first synthesized by Fox *et al.*, *via* direct thiation of protected uridine with phosphorus pentasulphide.[2] Another approach involving chlorination, methoxylation, and thiation has also been used for this purpose.[3] However, elevated temperatures are generally required for these preparations.

In this communication the conversion of uridine into 4-thiouridine at room temperature is described. In a model study, the triazolyl compound (**1**), prepared from thymidine with 1,2,4-triazole and *p*-chlorophenyl phosphodichloridate,[4,5] was treated with sodium hydrosulphide in acetone–water (3:1, v/v) for 20 min. The protected 4-thiothymidine (**2**) was obtained (85% yield). Subsequent u.v. (λ_{max} 334 nm), ^{1}H



(**1**) R = $SiMe_2Bu^t$ (**2**)



n.m.r. (disappearance of triazolyl protons), and elemental analysis of (**2**) confirmed the designated structure.[2]

For the preparation of 4-thiouridine, 2′,3′,5′-tri-*O*-acetyluridine (**3**) was treated with 1,2,4-triazole (3.0 mol. equiv.) and *p*-chlorophenyl phosphodichloridate (1.5 mol. equiv.) in pyridine for 48 h to give the triazolyl derivative (**4**), m.p. 173—175 °C (77% yield).[4,5] Subsequent treatment of (**4**) with sodium hydrosulphide in acetone–water for 15 min yielded 2′,3′,5′-tri-*O*-acetyl-4-thiouridine (**5**) in 85% yield. Deacetylation of (**5**) by sodium methoxide readily gave 4-thiouridine (**6**) (89%)[2] (identical t.l.c., u.v., and ^{1}H n.m.r. spectra to those of an authentic sample).

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