

SYNTHESIS OF 6,9-EPITHIOTACHYSTEROL₃ AND RELATED COMPOUNDS

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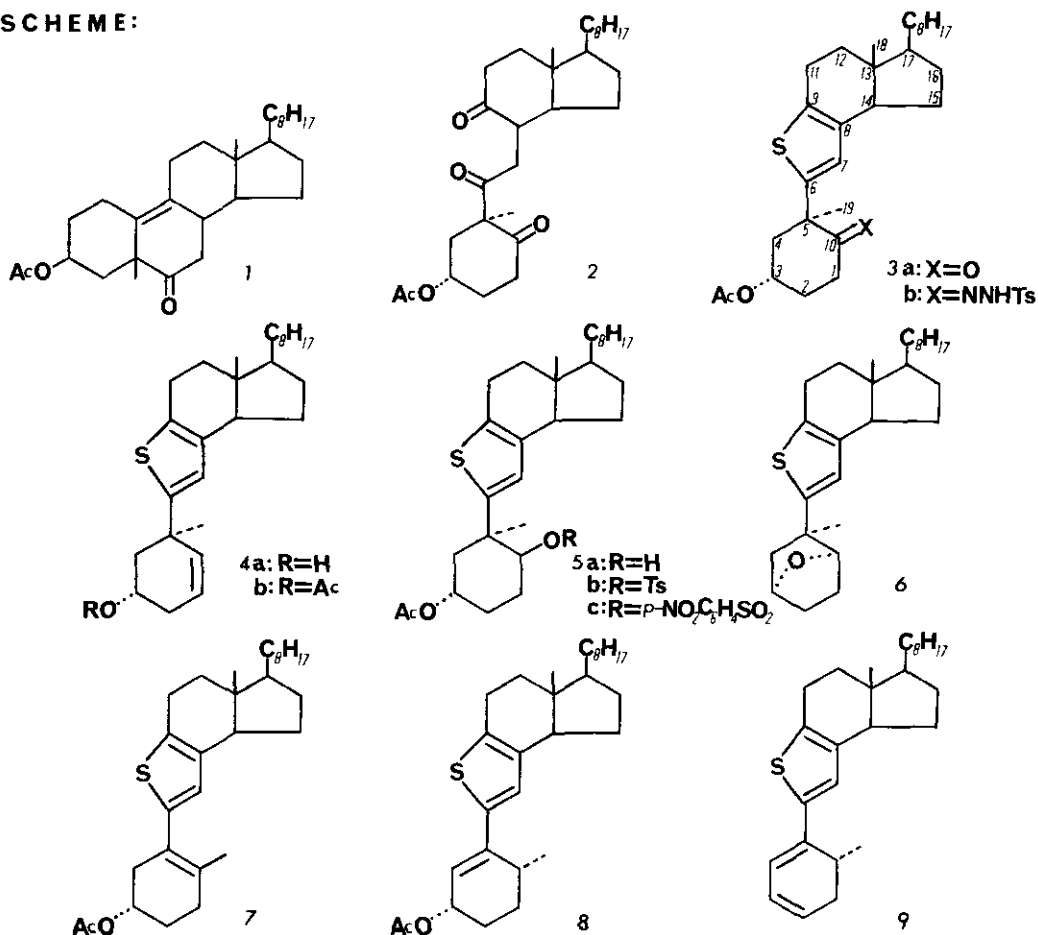
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Abstract — The synthesis of 6,9-epithiotachysterol₃ acetate 7 and some other B-thiophene-des-A-steroids is described.

6,9-Epithiotachysterol₃ seems to be an interesting precursor of vitamin D₃ relatives. Its synthesis from the readily available ketone 1¹ is reported. The ozonolysis of C₍₉₎-C₍₁₀₎ double bond² in 1 yielded B-seco compound 2. Triketone 2 contains a 1,4-dicarbonyl system which is known to give a thiophene derivative upon treatment with phosphorus pentasulfide.³ The reaction afforded compound 3a [δ 6.53 (s, 7-H); λ_{\max} 240 nm] in 70% yield. According to the synthetic plan 19-methyl group had to be moved from the quaternary position in 3 to its proper position at C-10. The Bamford - Stevens reaction of p-tosylhydrazone 3b did not lead to the desired 19-methyl group migration and olefin 4a was obtained. An alternative approach to 6,9-epithiotachysterol₃ synthesis was the retropinacolic rearrangement of an appropriate derivative of 10-hydroxy compound 5a. The NaBH₄ reduction of 3a resulted in the formation of a single epimer of alcohol 5a in almost quantitative yield. The 10S configuration was deduced from ¹H-NMR spectrum [a broad (w/2 = 15 Hz) multiplet of 10 β -H at δ 3.66] and confirmed by chemical means. The reaction of 10-tosylate 5b with KOH in diethylene glycol/diglyme at 120°C afforded ether 6 thus proving the trans relationship of substituents at C-3 and C-10. The solvolysis of 10-p-nitrobenzenesulfonate 5c in refluxing acetic acid in the presence of sodium acetate yielded mainly the rearranged products of elimination in addition to a small amount of $\Delta^{1(10)}$ -olefin 4b (about 5%). The products of rearrangement were 6,9-epithiotachysterol₃ acetate 7 [25%, δ 1.88 (bs, 19-H), λ_{\max} 294 nm], its double bond isomer 8 [δ 6.27 (4-H), the ratio of both isomers 2 : 1] and the highly conjugated compound 9 [40%, δ 6.19, 5.98, 5.70 (d, m and m, 4-H, 3-H and 2-H), λ_{\max} 347 nm]. The elimination of 3 β -substituent is less extensive at lower reaction temperature. The studies on desulfurization⁴ of 7 and its potential application in the synthesis of vitamin D₃ metabolites are under way.

SCHEME:



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