SYNTHESIS OF 6,9-EPITHIOTACHYSTEROL<sub>3</sub> AND RELATED COMPOUNDS

Jacek W. Morzycki

Department of Chemistry, University of Warsaw,
Pasteura 1, 02093 Warszawa, Poland

Abstract — The synthesis of 6,9-epithiotachysterol<sub>3</sub> acetate and some other E-thiophene-des-A-steroids is described.

6,9-Epithiotachysterol<sub>3</sub> seems to be an interesting precursor of vitamin D<sub>3</sub> relatives. Its synthesis from the readily available ketone 1<sup>1</sup> is reported. The ozonolysis of C(9)-C(10) double bond<sup>2</sup> 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.<sup>3</sup> The reaction afforded compound 3α [δ 6.53 (s, 7-H); λ<sub>max</sub> 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 3β did not lead to the desired 19-methyl group migration and olefin 4α was obtained. An alternative approach to 6,9-epithiotachysterol<sub>3</sub> synthesis was the retropinacolic rearrangement of an appropriate derivative of 10-hydroxy compound 5α. The NaBH₄ reduction of 3α resulted in the formation of a single epimer of alcohol 5α in almost quantitative yield. The 10α configuration was deduced from 1H-NMR spectrum [α broad (w/2 = 15 Hz) multiplet of 10β-H at δ 3.66] and confirmed by chemical means. The reaction of 10-tosylate 5β 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 Δ<sup>1(10)</sup>-olefin 4b (about 5%). The products of rearrangement were 6,9-epithiotachysterol<sub>3</sub> acetate 7 [25%, δ 1.88 (bs, 19-H), λ<sub>max</sub> 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<sub>max</sub> 347 nm]. The elimination of 3β-substituent is less extensive at lower reaction temperature. The studies on desulfurization of 7 and its potential application in the synthesis of vitamin D<sub>3</sub> metabolites are under way.
ACKNOWLEDGEMENTS

The author sincerely thanks Professor D. H. H. Barton and Professor W. J. Rodewald for helpful discussions. Financial support from the Polish Academy of Sciences is gratefully acknowledged.

REFERENCES


Received, 3rd February, 1986