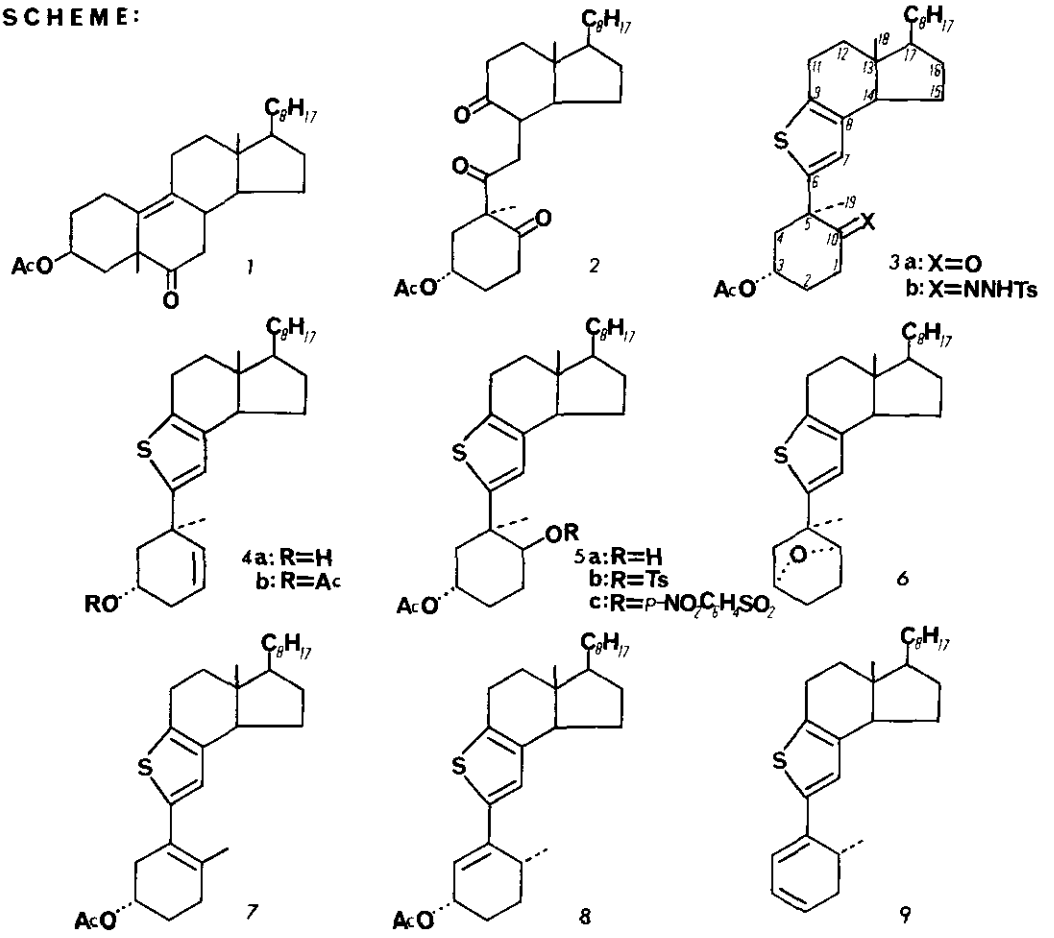
# SYNTHESIS OF 6,9-EPITHIOTACHYSTEROL$_3$ AND RELATED COMPOUNDS

Jacek W. Morzycki
Department of Chemistry, University of Warsaw,
Pasteura 1, 02093 Warszawa, Poland

Abstract — *The synthesis of 6,9-epithiotachysteryl$_3$ acetate 7 and some other B-thiophene-des-A-steroids is described.*

6,9-Epithiotachysterol$_3$ seems to be an interesting precursor of vitamin D$_3$ relatives. Its synthesis from the readily available ketone 1[1] is reported. The ozonolysis of $C_{(9)}$-$C_{(10)}$ double bond[2] 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 [$\delta$ 6.53 (s, 7-H); $\lambda_{max}$ 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-epithiotachysterol$_3$ synthesis was the retropinacolic rearrangement of an appropriate derivative of 10-hydroxy compound 5a. The $NaBH_4$ reduction of 3a resulted in the formation of a single epimer of alcohol 5a in almost quantitative yield. The 10S configuration was deduced from $^1$H-NMR spectrum [a broad (w/2 = 15 Hz) multiplet of 10$\beta$ -H at $\delta$ 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-epithiotachysteryl$_3$ acetate 7 [25%, $\delta$ 1.88 (bs, 19-H), $\lambda_{max}$ 294 nm], its double bond isomer 8 [$\delta$ 6.27 (4-H), the ratio of both isomers 2 : 1] and the highly conjugated compound 9 [40%, $\delta$ 6.19, 5.98, 5.70 (d, m and m, 4-H, 3-H and 2-H), $\lambda_{max}$ 347 nm]. The elimination of 3$\beta$-substituent is less extensive at lower reaction temperature. The studies on desulfurization[4] of 7 and its potential application in the synthesis of vitamin D$_3$ metabolites are under way.

**SCHEME:**




ACKNOWLEDGEMENTS

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

REFERENCES

1. W. H. Szczepek, Acta Chim. Hung.,in press; P. Kočovsly and V. Černy, Coll. Czech. Chem. Comm., 42, 2415 (1977).
2. J. W. Morzycki, J. Jurek, and W. J. Rodewald, Tetrahedron Letters, 26, 4243 (1985); R. J. Gell, P. S. Littlewood, B. A. Marpless, and B. Lythgoe, J. Chem. Soc., 4914 (1964).
3. Comprehensive Organic Chemistry, vol. 4 (edited by P. G. Sammes), Pergamon Press, Oxford, 1979, p. 829.
4. P. J. Owens and C. H. Amberg, Can. J. Chem., 40, 941 (1962).

Received, 3rd February, 1986