Tetrahedron Letters No. 19, pp 1989 - 1990, 1972. Pergamon Press. Printed in Great Britain.

NOVEL CLEAVAGE OF ETHYLENETHIOKETALS TO CARBONYL COMPOUNDS WITH METHYL IODIDE

Hsin-Lan Wang Chang

The Squibb Institute for Medical Research
New Brunswick, New Jersey, 08903

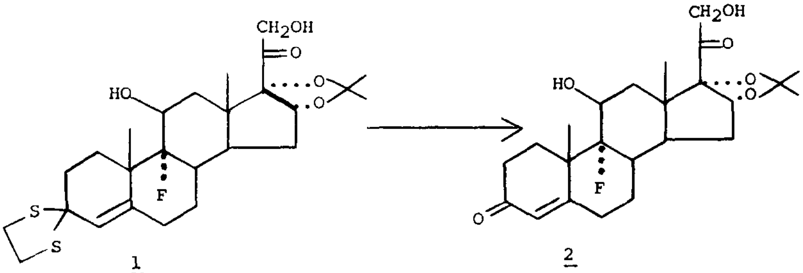
(Received in USA 1 March 1972; received in UK for publication 7 April 1972)

The importance of ethylenethioketals as carbonyl-protecting groups in steroid chemistry has been summarized.[1,2] Although ethylenethioketals, in general, are easily prepared, the difficulties associated with their cleavage and reformation of the parent ketones have restricted their use.

The methods employed for the cleavage of ethylenethioketals include: a) hydrolysis with mercuric chloride;[3] b) oxidation of the ethylenethioketal to the corresponding disulfone or disulfoxide, followed by alkaline hydrolysis;[4,5] c) hydrolysis with N-halosuccinimide in the presence of silver ion;[6] d) hydrolysis with trialkyloxonium tetrafluoroborate;[7] and e) hydrolysis with chloramine-T.[8]

In this communication, we wish to report a simple method of general applicability for the hydrolytic cleavage of ethylenethioketals, employing methyl iodide in aqueous alcoholic solutions. The following experimental procedure is typical of the method employed.

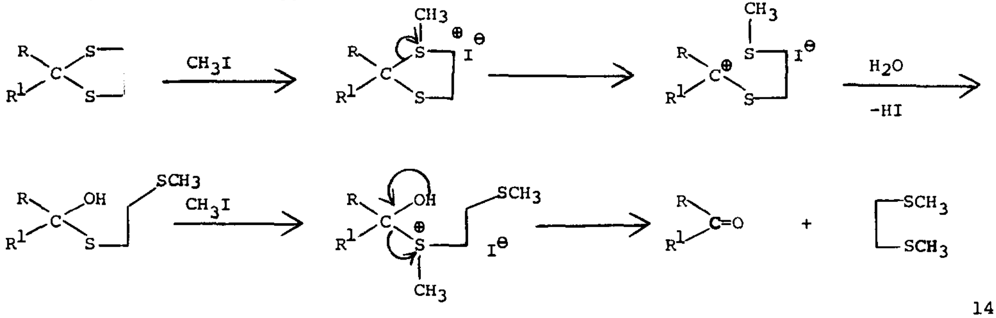
A solution of the 3-ethylenethioketal of 9-fluoro-11β,16α,17,21-tetrahydroxypregn-4-ene-3,20-dione 16,17-acetonide (1)[9] (1.32 g) and methyl iodide (2.96 ml) in 96% methanol (32 ml) was refluxed for 2-20 hr, and then evaporated. The residue was treated with water and extracted with ether. The ether extracts were washed first with sodium hydroxide solution, then with water, dried and evaporated to give the steroidal ketone (2)[10] in 60-83% yield.



1 2

Treatment of the ethylenedithiol adducts of benzaldehyde,[11] acetophenone,[12] and methylisobutylketone[13] under similar conditions gave the parent carbonyl compounds (yields based on the isolated crystalline 2,4-dinitrophenylhydrazone derivatives) in 67%, 74%, and 55%, respectively.

The following mechanism is suggested for this reaction:



The utility of this method for the cleavage of 1,3-dithianes and related compounds is apparent.[14,15]

ACKNOWLEDGMENTS: The author wishes to thank Drs. P. A. Diassi, S. D. Levine and B. R. Vogt for their help and encouragement in the course of this work.

REFERENCES

1. L.F. Fieser and M. Fieser, Steroids, Reinhold, New York, 1959, pp. 307-310.
2 C. Djerassi, Steroid Reactions, Holden-Day, Inc., San Francisco, 1963, pp. 22-30.
3. N. Pappas and H.R. Nace, J.Amer.Chem.Soc., 81, 4556 (1959).
4. S.J. Daum and R.L. Clarke, Tetrahedron Lett., 165 (1967).
5. P.R. Heaton, J.M. Midgley and W.B. Whalley, J.Chem.Soc.,Sect. D, 750 (1971).
6. E.J. Corey and E.W. Erickson, J.Org.Chem., 36, 3553 (1971).
7. I. Stahl, M. Hetschko and J. Gosselck, Tetrahedron Lett., 4077 (1971).
8. W.F. Huurdeman, H. Wynberg and D.W. Emerson, Tetrahedron Lett., 3449 (1971).
9. Phytogen Products, Belgian Patent #739940, October 7, 1969.
10. J. Fried, A. Borman, W.B. Kessler, P. Grabowich and E.F. Sabo, J.Amer.Chem.Soc., 80, 2338 (1958)
11. H. Fasbender, Chem.Ber., 20, 460 (1887).
12. E.E. Reid and A. Jelinek, J.Org.Chem., 15, 448 (1950).
13. C.N.R. Rao, R. Vanketaragharan and T.R. Kasturi, Can.J.Chem., 42, 36 (1964).
14. E.J. Corey and D. Seebach, Angew.Chem.Int.Ed.Engl., 77, 1075 (1965).
15. D. Seebach, Synthesis, 1, 17 (1969).