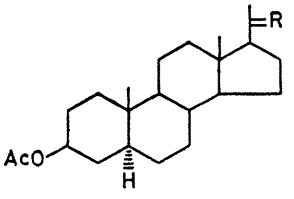
Rapid, Efficient Regeneration of Steroidal Ketones from Thioacetals by Periodic Acid

By JAMES CAIRNS and ROBERT T LOGAN*

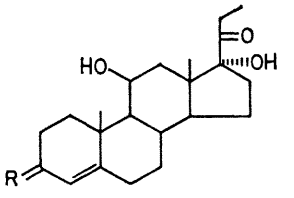
(*Scientific Development Group, Organon Laboratories Limited, Newhouse, Lanarkshire* ML1 5SH, *Scotland*)

Summary Periodic acid smoothly regenerates a variety of steroidal ketones from their thioacetals at room temperature in common solvents and generally in high yield

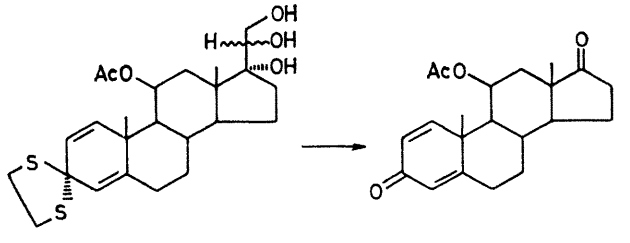
THE emergence of methods for the efficient formation and removal of thioacetals[1] has led to rapid progress in the chemistry of sulphur compounds as masked carbonyl derivatives In particular, the regeneration of ketones from thioacetals has received much attention, hydrolysis *via* mercury salts, oxidation at the sulphur atoms, or alkylation to a sulphide being most frequently employed [1,2] Major advantages of oxidative methods are avoidance of the use of toxic mercury compounds, and the much more rapid cleavage compared with alkylative methods



(1), R = -SCH$_2$CH$_2$S-
(2), R = O

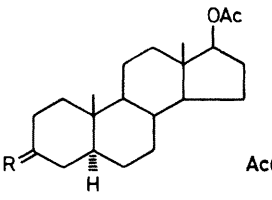


(3), R = -SCH$_2$CH$_2$S-
(4), R = O

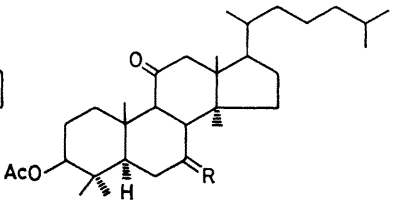


(5) (6)

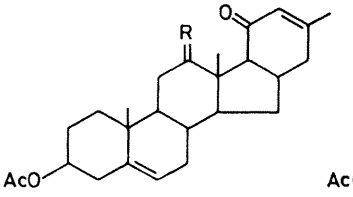
We report that periodic acid is a useful additional oxidising agent for the rapid, efficient regeneration of ketones from thioacetals In a typical procedure, the thioacetal (1 part) was dissolved in a suitable solvent (see Table) (30 parts) and treated at 22 °C with periodic acid (0 25 parts) dissolved in the minimum volume of water The course of the reaction was followed by t l c Excess of reagent and iodine were removed by the addition of sodium hydrogen sulphite solution The product was isolated by addition of water (60 parts) followed by filtration, or extraction



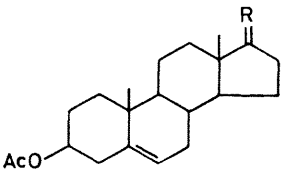
(7), R = -SCH$_2$CH$_2$S-
(8), R = O



(9), R = -SCH$_2$CH$_2$S-
(10), R = O



(11), R = -SCH$_2$CH$_2$S-
(12), R = O



(13), R = -SCH$_2$CH$_2$S-
(14), R = O

The results obtained for a number of representative thioacetals† are summarised in the Table In most cases conversion into the ketone was almost quantitative, since in only two examples, (**9**) and (**13**), were significant amounts of by-products formed

Since sodium periodate has been used for the conversion of a sulphide into a monosulphoxide prior to dehydrosulphenylation,[3] and the easy acid-catalysed hydrolysis of dithioacetal *S*-oxides has been described,[4] we support the view[5] that this cleavage proceeds *via* the monosulphoxide which is readily hydrolysed in the acidic medium A

TABLE

Thioacetal	Solvent[a]	Temp /°C	Time/min	Product	Purity (%, by g l c)
(**1**)	CH_2Cl_2–MeOH(2 : 1)	22	5	(**2**)	97
(**3**)	EtOH	70[b]	2	(**4**)	98
(**5**)[c]	THF–H_2O (5 . 1)	22	2[d]	(**6**)	98
(**7**)	CH_2Cl_2–MeOH (1 : 1)	22	20	(**8**)	98 5
(**9**)	CH_2Cl_2–MeOH(1 : 1)	22	20	(**10**)	85
(**11**)	DMF	22	2	(**12**)	98
(**13**)	CH_2Cl_2–MeOH (1 : 1)	22	40	(**14**)	75

[a] THF = tetrahydrofuran, DMF = dimethylformamide [b] Elevated temperature required to solubilise the thioacetal [c] Mixture of 20-isomers, not characterised [d] Time to remove thioacetal, side-chain cleavage took 1 h One part by weight of periodic acid was used in this reaction

† Unless otherwise specified, satisfactory analytical and spectroscopic data were obtained for all thioacetals and ketones

second product of the cleavage reaction appears to be an insoluble polymeric disulphide $(SCH_2CH_2S)n$, m.p. 133—135 °C, purified by Soxhlet extraction into, and crystallisation from, chloroform.

We thank Mr. T. Clarkson for technical assistance and Dr. W. McMeekin and his staff for analytical services.

(*Received*, 20*th June* 1980; *Com.* 670.)

[1] B.-T. Grabel and D. Seebach, *Synthesis*, 1977, 357, and references quoted therein.
[2] D. H. R Barton and W. D. Ollis, 'Comprehensive Organic Chemistry,' Pergamon, Oxford, 1979, Vol. 3, p. 71, and references quoted therein.
[3] B. M. Trost and T. N. Salzmann, *J. Am. Chem. Soc.*, 1973, **95**, 6840; H. J. Reich and J. M. Renga, *J. Chem. Soc., Chem. Commun.*, 1974, 135.
[4] K. Ogura and G. Tsuchihashi, *Tetrahedron Lett.*, 1971, 3151.
[5] M. Hojo and R. Masuda, *Synthesis*, 1976, 678.