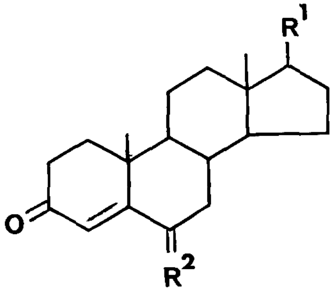
Tetrahedron Letters,Vol.22,No.51,pp 5127-5128,1981 0040-4039/81/515127-02$02.00/0
Printed in Great Britain

OXIDATION WITH SODIUM PEROXIDE
DIRECT INTRODUCTION OF A γ CARBONYL GROUP INTO α,β UNSATURATED KETOSTEROIDS

Herbert L. Holland, * Ulrich Daum and Elly Riemland
Department of Chemistry, Brock University
St. Catharines, Ontario, Canada L2S 3A1

Aqueous sodium peroxide oxidises the conjugated Δ^4-3-ketosteroids **1a**-**1d** to the corresponding Δ^4-3,6-diones in good yield. Saturated carbonyl and alcohol groups are not affected by the reaction.

General synthetic methodology for the introduction of a γ carbonyl group into α,β unsaturated ketones is not well developed; in the steroid field, this conversion has been previously carried out via chromic oxidation of 5,6-epoxy-3-alcohols.[1] As part of a re-investigation of the epoxidation of Δ^4-3-ketosteroids, we have found that treatment of **1a**-**1d** with aqueous sodium peroxide leads directly to the corresponding 6-ketones **2a**-**2d** in high yield (Table 1). The products were identified by comparison with authentic samples.



1a, R^1 = O, $R^2 = H_2$
1b, R^1 = β-OH, $R^2 = H_2$
1c, R^1 = β-$COCH_3$, $R^2 = H_2$
1d, R^1 = β-C_8H_{17}, $R^2 = H_2$
2a, $R^1 = R^2 = O$
2b, R^1 = β-OH, R^2 = O
2c, R^1 = β-$COCH_3$, R^2 = O
2d, R^1 = β-C_8H_{17}, R^2 = O

Table 1. Conversion of Δ^4-3-ketosteroids to Δ^4-3,6-diones with sodium peroxide

starting material	product	% conversion	% yield (isolated)
1a	**2a**	72	55
1b	**2b**	70	43
1c	**2c**	85	63
1d	**2d**	75	56

In addition to recovered starting material and product, minor traces (<1%) of another (unidentified) product have been detected in this reaction during optimum conversions, obtained by the procedure described below. Alteration of reaction temperature, time, or reactant ratios led to lower conversion or significant overoxidation to other products.

The saturated ketone groups of **1a** and **1c** and of 5α-cholestan-3-one (in a separate experiment), were not affected by the reaction. In addition, the dienones androsta-1,4-diene-3-one-17β-ol and androsta-4,6-diene-3-one-17β-ol were recovered unchanged. The use of lithium peroxide in place of sodium peroxide leads only to the formation of 4,5-epoxy-3-ketones (α:β ratio 1:1) in low yield. The following evidence suggests that the sodium peroxide oxidation is not a simple base catalysed autoxidation; parallel reactions using sodium hydroxide and oxygen lead to a complex mixture of oxidation products, and, as noted by others,[2] base catalysed autoxidation of Δ^4-3-ketosteroids gives principally (in low yield), 3-keto-$\Delta^{4,6}$-diene-4-ols. Further experiments to investigate the synthetic limitations and mechanism of the sodium peroxide reaction are in progress.

Experimental Procedure

Water (10 mL) was added drop-wise over a 2 h period to a stirred mixture of progesterone (**1c**, 1g) and sodium peroxide (4 g) in ethanol (50 mL). The mixture was then acidified (dil. HCl) and extracted with chloroform. The extract was washed and evaporated. The product was isolated by chromatography on silica gel and characterised by tlc and spectral comparison with an authentic sample.

1. J. R. Hanson and T. D. Organ, J. Chem. Soc. (C) 2473 (1970).

2. B. Camerino, B. Patelli and R. Sciaky, Tet. Letters, 554 (1961); Gazz. Chim. Ital. 92, 676, 693 (1962).

(Received in USA 12 August 1981)