

An 8,9-Seco-steroid by Reaction of an 8 β ,9 β -Epoxy-11-oxo-steroid with Methanolic Potassium Hydroxide

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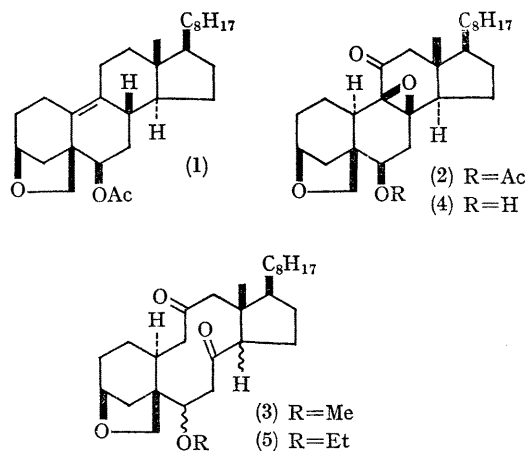
Summary Treatment of the 6 β -acetoxy-8 β ,9 β -epoxy-11-ketone (2) with methanolic potassium hydroxide solution gave the 8,9-seco-6 β -methoxy-8,11-diketone (3).

We have recently reported¹ the preparation of the epoxy-ketone (2), along with other products, by oxidation of the olefin (1) with chromic acid. Attempted hydrolysis of (2) with methanolic potassium hydroxide solution (1%) surprisingly gave the 8,9-seco-methoxy-diketone (3) (89%), m.p. 117.5–119.5° (aqueous methanol), and not the 6 β -hydroxy-compound (4).

The structure of (3) is based largely on mass and other spectral and analytical data. The mass spectrum (Table) shows the molecular formula is C₂₈H₄₆O₄ and the base peak arises from the loss of methanol. The ¹H n.m.r. (CDCl₃) spectrum shows important peaks at τ 5.27–5.5 (m, 2OCH), 6.63 (q, *J*_{AB} ca. 7.6 Hz., OCH₂), 6.06 (s, OMe), and 9.31 (s, 18-Me). The i.r. spectrum confirms the presence of the methoxy-group (2820 cm.⁻¹) and the carbonyl group (1720 cm.⁻¹), and the absence of a hydroxy-group.

We suggest that (3) is formed by the route shown (Scheme). The initial steps are hydrolysis of the 6 β -acetoxy-group and hydride reduction of the 11-keto-group.†

† Hydride reduction of the epoxy-group may take place directly.



Although hydride reduction of carbonyl groups with potassium alkoxide² is not unusual, such an efficient reduction as is apparent here would not be expected particularly under the conditions employed. Step (c) to (d) is a retro-aldol reaction and the final step (e) to (3)

TABLE

Base peak		Molecular ion		Rel. abund. (%)	Other ions		Metastable peaks	
<i>m/e</i>	Formula (calc. mass)	<i>m/e</i>	Formula (calc. mass)		<i>m/e</i>	Rel. abund. (%)	<i>m/e</i>	Transition
414·3137	C ₂₇ H ₄₂ O ₃ (414·3134)	446·3365	C ₂₈ H ₄₆ O ₄ (446·3396)	18	386	12	359·9	414 — 386
					356	5	328·3	386 — 356
					278	21		
					263	16		

(path *x*) involves Michael addition of methoxide to the Δ^6 -7-ketone. It is possible that a transannular Michael addition following attack of methoxide ion at C-11 (path *y*) could give the acetal (6). Since however the product is stable in aqueous methanolic sulphuric acid, we prefer the structure (3). In addition, loss of methanol from the molecular ion in the mass spectrum is more reasonable for (3) than for (6).³ Also, the ¹H n.m.r. spectrum of the compound shows a pronounced increase in signals in the region τ 6·8—7·8 which may be attributed in part to the protons at C-9 and C-12 in (3). The formation of the medium-ring compound (3) by retro-aldolisation is unusual. Previous work⁴ suggests a tetracyclic structure would be preferred.

Apart from the initial hydrolysis, all the steps outlined would be reversible. Compound (3) was treated with EtOD-NaOD (72 hr. at 60°) in the expectation that the methoxy-group would be replaced by an ethoxy-group and that up to a maximum of 7 hydrogen atoms (positions 7, 9, 11, and 14) would be replaced by deuterium atoms. Mass spectral analysis of the product showed ions at *m/e* 460, 461, 462, 464, and 465 corresponding to the \bar{d}_0 (7%), \bar{d}_1 (25%), \bar{d}_2 (10%), \bar{d}_4 (9%), and \bar{d}_5 (50%) species of (5).[†] The absence of any appreciable quantity of \bar{d}_6 and \bar{d}_7 species indicates that two of the hydrogen atoms of (3) are exchanged with difficulty. The configuration at C-6 and C-14 in (3) cannot be assigned at present with any certainty.

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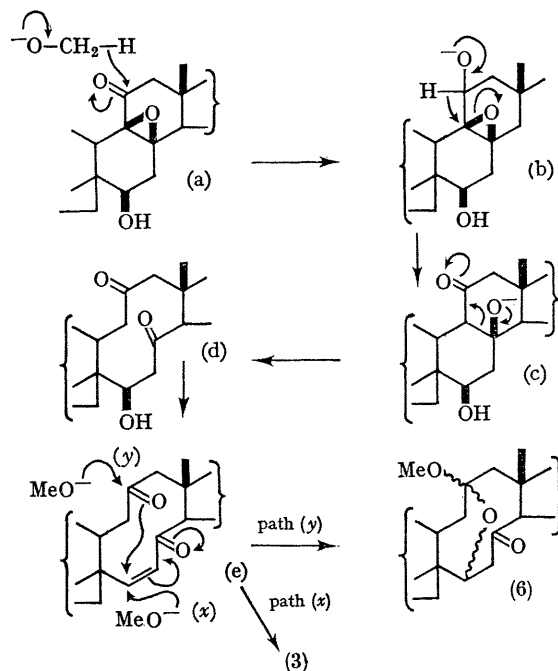
[†] These figures are approximate due to a high background. It is possible that small amounts of \bar{d}_3 , \bar{d}_6 , and \bar{d}_7 species are present.

¹ I. G. Guest, J. G. Ll. Jones, B. A. Marples, and (in part) M. J. Harrington, *J. Chem. Soc. (C)*, 1969.

² D. N. Kirk and A. Mudd, *J. Chem. Soc. (C)*, 1969, 804.

³ H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden Day, San Francisco, 1967, ch. 6.

⁴ (a) H. L. Slates and N. L. Wendler, *Experientia*, 1961, **17**, 161; (b) G. Sntzke and A. Nisar, *Annalen*, 1965, **683**, 159.



SCHEME

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