An Improved Synthesis of 13-*epi*-Steroids

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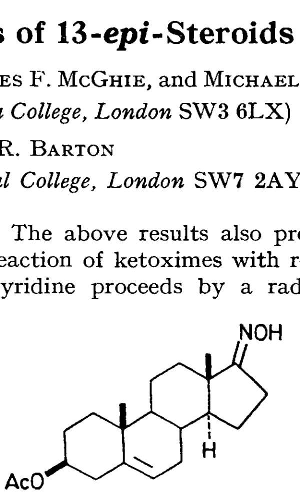
Summary Treatment of oximes of 17-keto steroids with refluxing acetic anhydride and pyridine, and acid hydrolysis of the resulting enamides, constitutes an efficient route to 13-*epi*-17-keto-steroids; this observation is evidence that the former reaction proceeds by a free-radical pathway.

We have recently described two general methods whereby ketoximes may be converted into enamides in excellent yield.[1] In one procedure the oxime is reduced in the presence of acetic anhydride by chromous or titanous acetate. In this way 3β-acetoxyandrost-5-en-17-one oxime[2] (I) afforded the expected and known[3] enamide (II), m.p. 229—232°, $[\alpha]_D - 15°$ (in EtOH). Alternatively, the oxime is subjected to prolonged treatment with refluxing acetic anhydride and pyridine. Using this method the oxime (I) gave a mixture of two products. By chromatography on silica gel an enimide (III; R = Ac), m.p. 118—121°, $[\alpha]_D -99°$ (in $CHCl_3$), and an enamide (III; R = H),† m.p. 160—163°, $[\alpha]_D -102°$ (in $CHCl_3$) were isolated. Chromatography on alumina[1] gave the enamide as the sole product (85%).

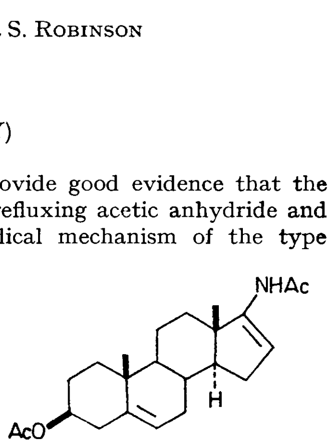
The formulation of these products as 13-*epi*-steroids followed from a comparison of their optical rotations and other spectroscopic data with those of the normal enamide (II). Confirmation was obtained by acid hydrolysis[1] of (III; R = H) to the 13-*epi*-ketone (IV), which was identical in all respects to an authentic sample.[4]

In addition to the experimental advantages normally associated with a thermal as opposed to the previous photochemical procedure,[5,6] the present method gives superior yields.

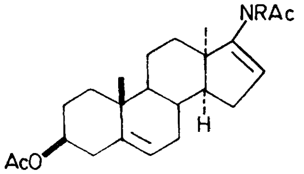
The above results also provide good evidence that the reaction of ketoximes with refluxing acetic anhydride and pyridine proceeds by a radical mechanism of the type



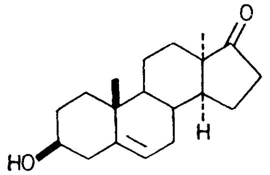
(I)



(II)



(III)



(IV)

postulated in our original publication.[1] Ring opening and reclosure *via* a carbonium ion species is not a feasible alternative under these (basic) reaction conditions.

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† These two products were apparently in equilibrium under the reaction conditions. Satisfactory analytical and spectroscopic data were obtained for all new compounds reported herein.

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