

PHOTOCHEMISTRY OF 17-NITROSTEROIDS

Syed H. Imam and Brian A. Marples*

Department of Chemistry, The University of Technology, Loughborough.

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The solution photochemistry of nitro-compounds has attracted considerable recent attention¹ and inter- and intra-molecular hydrogen abstraction processes have been of particular interest. In continuation of our studies in the functionalisation of unactivated carbon atoms in steroids,² we have explored some aspects of the potential of the nitro-group in this context. We report here some of our preliminary results on the photochemical behaviour of 3 β -acetoxy-17 β -nitro-5 α -androstane (4).³

The nitro-compound (4) was prepared from the oxime (2)⁴ by the method of Patchett and co-workers.⁵ The photolyses were carried out with a 125W medium pressure Hg lamp in water cooled quartz apparatus and in an atmosphere of nitrogen. The photoreactions were markedly solvent dependent and the major products were, in ether, 3 β -acetoxy-5 α -androstane (5)⁶ (18%), in iso-propanol, the hydroxylamine (6) (35%), and in ethanol/NaOEt (4 moles), the hydroxamic acid (8) (30%) and the 17,18-cyclosteroid (9)⁷ (8%).

The 17-denitro-compound (5), was isolated by preparative t.l.c., and presumably arises via C-N bond cleavage and abstraction of H from the solvent or steroid.

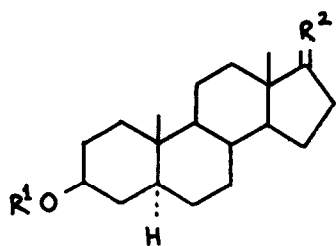
The hydroxylamine (6) which was also isolated by preparative t.l.c. was converted to a solid by trituration with a small amount of methanol. Full characterisation was not possible owing to its relative instability. However, the ¹H n.m.r. spectrum of the hydroxylamine (6) in CDCl₃ showed a characteristic⁸ two proton multiplet (τ 5.3, N-H and N-OH) which was readily removed by shaking with D₂O, and a one proton triplet (τ 6.95, 17-H). As expected,⁸ the N-H and N-OH signals were separated (τ 5.4 and 3.1) in DMSO-d₆. The mass spectrum of the hydroxylamine (6) showed a

low intensity molecular ion (m/e 349) and a base peak at m/e 332.2588 corresponding to $[M-OH]^+$ (calculated for $C_{21}H_{34}NO_2$ 332.2589). The hydroxylamine (6) formed a hydrochloride and reduction of the oxime (2) with diborane⁹ gave the hydroxyhydroxylamine (7) which had similar spectroscopic data to those of its acetate (6). Decomposition of the hydroxylamine (6) in ethanol/NaOEt in the absence of oxygen gave the oxime (3) (50%) and a number of minor unidentified products. While base-catalysed dismutation of benzyl- and aryl-hydroxylamines has previously been reported,⁹ we are unaware of similar processes in alkylhydroxylamines, and the absence of significant quantities of the expected 17-amino-compound as a co-product casts some doubt on the mechanism of the decomposition reaction. Also, while photoreductions of aromatic nitro-compounds in isopropanol have been reported¹ no similar processes appear to be known for aliphatic nitro-compounds.

The crude reaction mixture obtained from the ethanol/NaOEt photolysis by evaporation was extracted with chloroform to yield a neutral fraction which on t.l.c. gave the 17,18-cyclosteroid (9).⁷ An aqueous solution of the chloroform-insoluble residue was adjusted to pH6 and extracted with chloroform to give the crude hydroxamic acid (8) which was crystallised from methanol. Spectroscopic data are in accord with structure (8); in particular the i.r. spectrum exhibits a typical carbonyl band^{11,12} at 1615 cm^{-1} . Further confirmatory evidence for the structure of the hydroxamic acid (8) was provided by its conversion by Zn/AcOH reduction and acetylation to the lactam (10)⁴ ($\nu_{\text{max.}}\ 1650\text{ cm}^{-1}$) which was also obtained by Beckmann rearrangement of the oxime (2).

In ethanol/NaOEt it is assumed that the nitro-compound (4) exists essentially as the anion and presumably the hydroxamic acid (8) is formed through the oxaziridine (11) (Scheme). Similar intermediates are proposed in the photolysis of nitrones,¹³ oximes,¹⁴ and the nitronic acids (12) and (13).¹⁵ While the rearrangement observed here appears to have analogies in the photochemistry of nitrones and oximes, it is quite a different reaction from those reported for the nitronic acids (12) and (13). Similar intermediates to (11) are proposed in the reactions of carbonyl compounds with benzenesulphonohydroxamic acid and base.¹¹ However, the ketone (1) failed to react under these conditions.

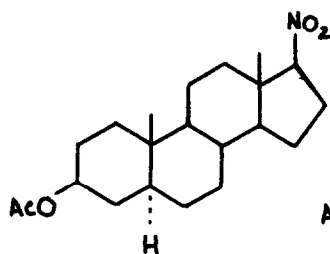
The formation of the 17,18-cyclosteroid (9) clearly involves a hydrogen abstraction from C(18). Owing to the low yield of this product we are uncertain whether it arises from the free nitro-compound (4) or its anion. Photolysis of the compound (4) in ethanol alone gives no hydroxamic acid and we have so far been unable to determine whether the 17,18-cyclosteroid (9) is a product. Final clarification of the precise mechanism is being sought.



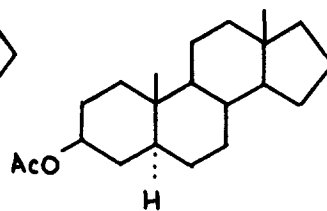
1 $R^1 = \text{Ac}, R^2 = \text{O}$

2 $R^1 = \text{Ac}, R^2 = \text{NOH}$

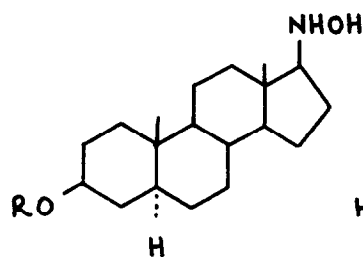
3 $R^1 = \text{H}, R^2 = \text{NOH}$



4

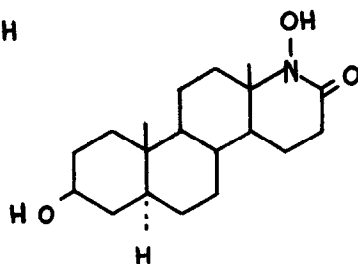


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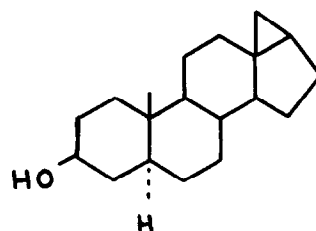


6 $R = \text{Ac}$

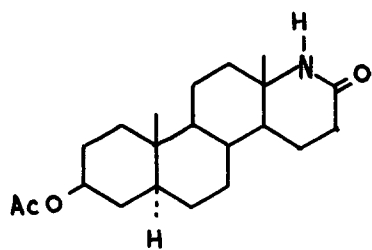
7 $R = \text{H}$



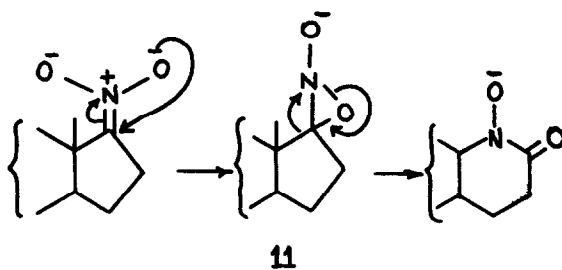
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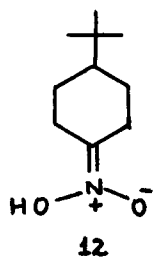
9



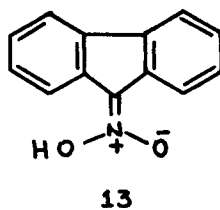
10



Scheme



12



13

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