Azoalkenes as Intermediates in the Formation of Osazones from Steroid α-Halogeno-ketones

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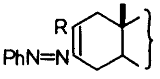
THE recent Communication by Caglioti and his coworkers[1] on the formation of cyclohexan-1,2-dione phenylosazone from 2-acetoxycyclohexanone, with 1-phenylazocyclohexene as intermediate, prompts us to report our findings in this field.

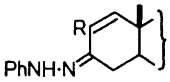
Following the observation that the so-called[2,3] phenylhydrazone of $3\beta,5\alpha$-dihydroxycholestan-6-one was in fact 6-phenylazocholest-5-en-3β-ol[4] and that the latter compound could be prepared[4] from other 5α- and 5β-substituted cholestan-6-ones, we attempted to extend this elimination reaction to 2-substituted cholestan-3-ones and phenylhydrazine. The reaction of 2,4-dinitrophenylhydrazine with steroid α-bromo-ketones has been previously studied.[5–7]

Reaction of 2α-bromocholestan-3-one with phenylhydrazine in boiling ethanol containing acetic acid gave an almost immediate precipitate of the orange-yellow 3-phenylazocholest-2-ene (I)[8] m.p. 178—179°, $[\alpha]_D + 94°$. This substance was distinct from the colourless phenylhydrazone (III) of cholest-1-en-3-one, m.p. 205° $[\alpha]_D +89°$. This contrasts with 2,4-dinitrophenylhydrazine reaction[5,6] where the product formed from 2α-bromocholestan-3-one was the dinitrophenylhydrazone of cholest-1-en-3-one. The ene-azo-compound was not isomerised to the hydrazone (III) on treatment with either hot alcoholic acid or base.

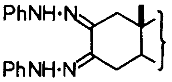
Treatment of 2,2-dibromocholestan-3-one with phenylhydrazine under the same conditions as above gave 2-bromo-3-phenylazocholest-2-ene (II) m.p. 164—165°, $[\alpha]_D + 103°$. Recrystallisation from acetone containing a trace of acid caused an immediate isomerisation to the almost colourless phenylhydrazone (IV) of 2-bromocholest-1-en-3-one m.p. 180—182° (dec.) $[\alpha]_D + 57°$ also obtained from phenylhydrazine and the parent ketone.



(I) R=H
(II) R=Br



(III) R=H
(IV) R=Br



(V)

Further treatment of either compounds (I) or (II) with phenylhydrazine in ethanolic acetic acid gave the phenylosazone of cholestan-2,3-dione, (V) m.p. approx. 206—209° (dec.) $[\alpha]_D + 132°$, in good yield. Under the conditions employed no intermediate phenylhydrazino-phenylhydrazone (*cf.*, ref. 1) was isolable. Nevertheless this demonstrates that azo-enes are intermediates in the formation of osazones from α-halogeno-ketones, and extends the findings of Caglioti.

The phenylhydrazone (IV) of 2-bromocholest-1-en-3-one was also obtained from the reaction of phenylhydrazine with 1α,2β-dibromocholestan-3-one, implying that elimination from this compound occurs from the ene-hydrazine form of the initially-formed phenylhydrazone. Similar αβ-unsaturated hydrazones have been isolated from 2-deoxy-sugar derivatives:[9,10] their formation again presumably occurring *via* the ene-hydrazine form of the initially formed hydrazones. Another reaction relevant to the present study is that of phenylhydrazine with *aldehydo*-D-glucose penta-acetate to give D-*arabino*-3,4,5,6-tetra-acetoxy-1-phenylazo-*trans*-hex-1-ene.[1]

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[8] All new compounds were crystalline and gave satisfactory analyses and spectra. All rotations are for chloroform solutions.

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