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# ANSA-STEROIDS

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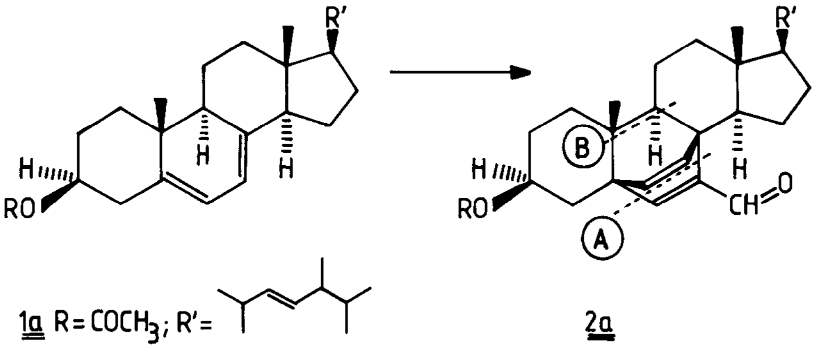
Abstract: The backbone of steroids is broken by a cycloaddition-retro-reaction sequence of propargylic aldehyde to generate a 14-membered ansa compound.

In connection with experiments aiming at the use of ergosterol as chiral, configuration directing butadiene which may later be disconnected in the well documented retro-Diels-Alder reaction[1] we studied the cycloaddition of ergosterol acetate **1a** to propargylic aldehyde, to notice that the expected α,ß-unsaturated aldehyde **2a** was only formed in refluxing dichloro-methane with Tungsten-hexachloride[2] as Lewis acid catalyst (regioselectivity see below). If the starting materials or compound **2a** are just heated in toluene the high yield formation of the aromatic aldehyde **3a** is observed (85%). Obviously the retro-reaction does not split off the acetylenic aldehyde (line Ⓐ) but the backbone of the steroid is broken (line Ⓑ) and the unsaturated ansa compound **3a** is formed in a very clean reaction. This is among other things indicated by the broad singulet of one aromatic proton at 7.75 δ and a narrow AB quartet for two protons at 7.40 δ. Additionally one of the methyl signals is broadened and shifted to 1.25 δ. Most characteristic however, is the unusual appearance of the corresponding olefinic proton signal at 3.5 δ which is due to its dipping into the π-system of the aromatic ring.

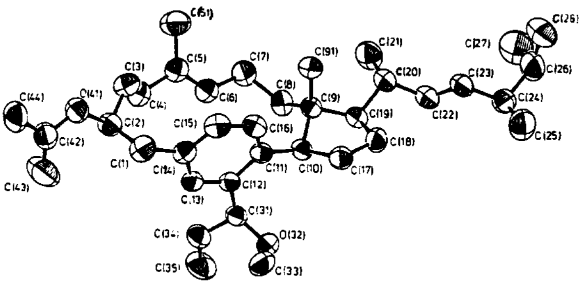


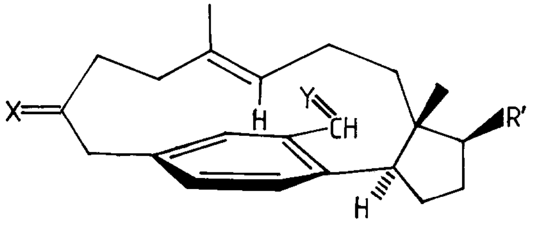
**1a** $R = COCH_3$; R'=
**1b** $R = COC_6H_5$; $R' = OCOC_6H_5$

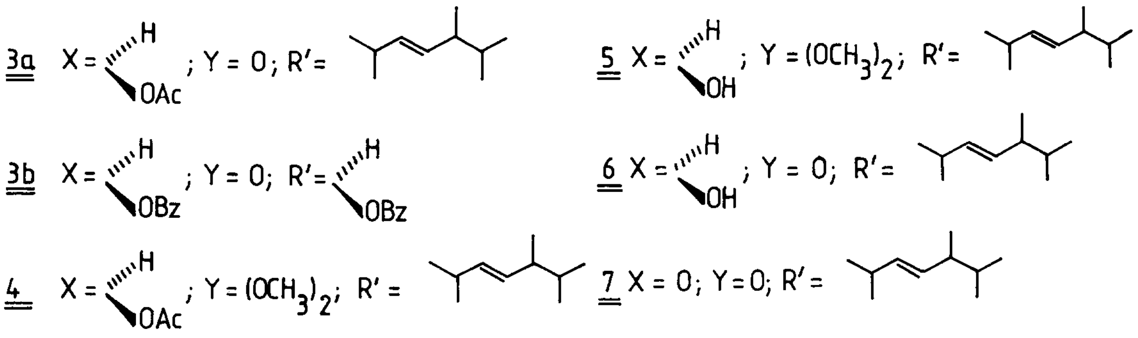
**2a**
**2b**

As NMR data did not convincingly differentiate between the two possible regioisomers the constitution, configuration, and conformation of these compounds was secured by an X-ray structure determination[3] of the easily accessible (leave at room temperature in methanol with a trace of PTA) crystalline dimethyl acetal **4** (see plot).

A number of obvious derivatives as for instance the hydroxy-acetal 5, the hydroxy-aldehyde 6, and the keto-aldehyde 7 were prepared in high yield using standard techniques and application of this cycloaddition, again followed by a backbone fragmentation, to the more simple steroid 1b[4] was achieved easily.







This is to our knowledge the first retro-reaction which fragments the whole hydrophenanthrene system of a steroid, leading to a cyclopentane derivative. There is only one AB-ring splitting retro-Diels-Alder process in the literature.[5] Obvious ring transformations like ozonisation (ring opening) and Baeyer-Villiger oxidation (makrolide formation) are being studied and will be included in a full paper.

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## REFERENCES

[1] H.H.Inhoffen, Liebigs Ann.Chem. 508, 81 (1934).

[2] R.K.Haynes, Aust.J.Chem. 31, 121 (1978).

[3] The X-structure determination was done at the GBF Stöckheim and details will be published in a furthcoming full paper.

[4] The authors thank Dr.H.Laurent, Schering AG, Berlin/Bergkamen for generously providing this compound.

[5] P.Yates and F.M.Walliser, Canad.J.Chem. 1976, 3508.

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