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ACID-CATALYZED REARRANGEMENTS OF CYCLOBUTANONES
IV - A NOVEL TOTAL SYNTHESIS OF A STEROID

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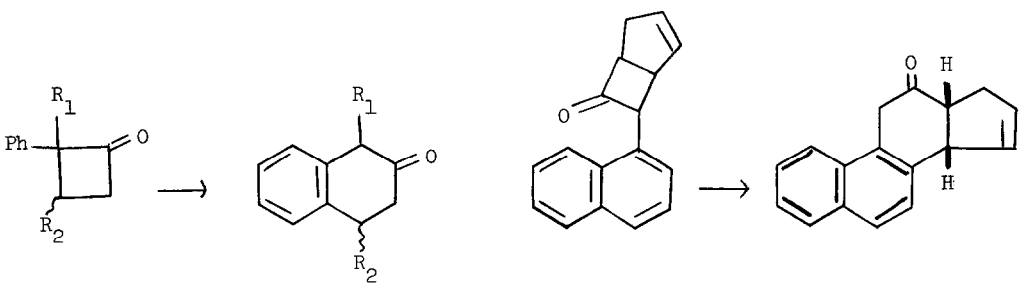
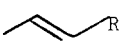
Our recent findings that α-phenylcyclobutanones with a stabilizing group at C-3 (i.e. 1) undergo acid-catalyzed cyclizations to β-tetralones (2)[1] prompted us to investigate the possible extension of such reactions to the syntheses of polycyclic systems such as

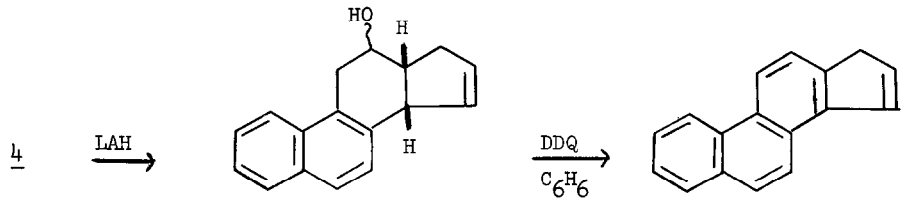


1 2 3 4

R_1 = H, Ph
R_2 = OR,  , Ph

steroids. Cyclobutanone 3 (m.p. 114-115°) was obtained from cycloaddition of 1-naphthylketene to 1,3-cyclopentadiene. The regiospecificity of cycloaddition of ketenes to 1,3-cyclopentadiene is well established[2-4]; however the stereochemistry of the naphthyl group with respect to the ring junction has not been unequivocally defined, although there is evidence that when the two ketene substituents differ in steric bulk the larger one tends to assume the more hindered position in the product.[5,6]

Treatment of 3 with catalytic amounts of trifluoroacetic acid in refluxing chloroform produced an isomeric compound (in 70% yield) to which we assign the steroid structure 4 (m.p. 84-85°; ν c=o 1715 cm^{-1}; m/e = 234). Proof for the steroid backbone was obtained by its conversion to 17-H-cyclopenta[a]phenanthrene (6) via the alcohol 5 in 90% overall yield.



4 5 6

Hydrocarbon 6 was identical in all respects with an authentic sample[7]. The stereochemistry of the ring junction in 4 was assigned based on the nmr coupling constant for the bridgehead protons (J = 4 Hz). Furthermore investigations of thermodynamic stabilities of hydroindanones point to the greater stabilization of the cis form[8].

The rearrangement of 3 to 4 represents a simple route to 12, 13 and 14 functionalized (steroid numbering system) steroids and cyclopenta[a]phenanthrenes, a number of which exhibit carcinogenic properties.[7] We are currently investigating the possibility of extending these reactions towards the total synthesis of estrogenic substances.

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   We would like to thank Dr. Coombs for providing an authentic sample and a uv spectrum of 6.
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