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CONVERSION OF THE ALLYLIC AND HOMOALLYLIC STEROIDAL ALCOHOLS TO THE CORRESPONDING SATURATED KETONES BY MEANS OF THE ACTIVATED Ra/Ni

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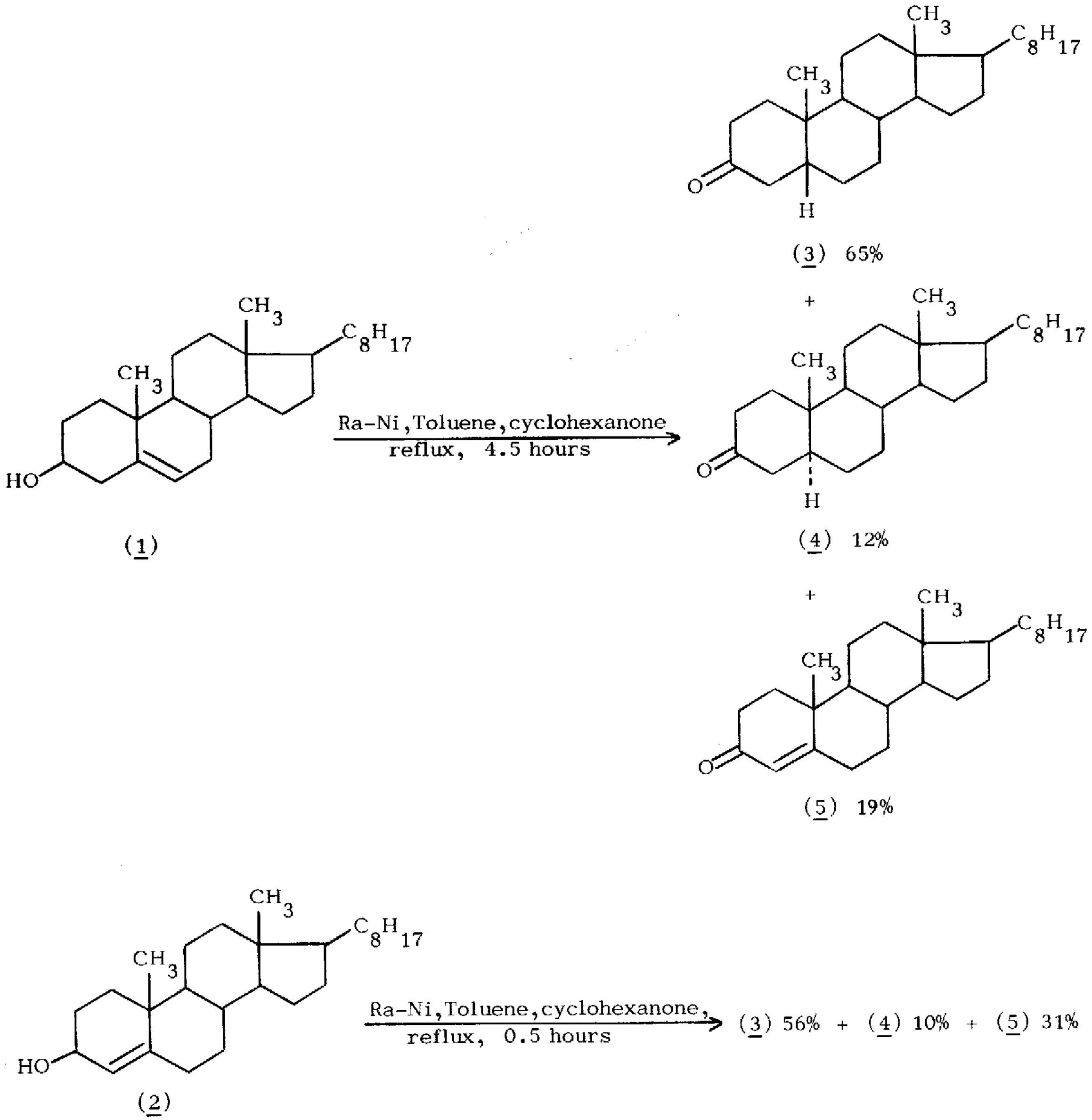
Summary: Conversion of the allylic and homoallylic alcohols (1) and (2) to the corresponding saturated ketones (3) and (4), by means of the activated Ra/Ni, in the presence of cyclohexanone, was achieved stereospecificially and high yields.

Raney-Ni shows a versatile hydrogenative and dehydrogenative catalytical properties and because of that, this reagent has been widely used on the laboratory and industrial scale. Hydrogenative-dehydrogenative properties of this particular reagent has been usually investigated on different appropriate substrates and under various experimental conditions [1]. For these reasons we were prompted to investigate utility of activated Ra/Ni in order to achieve migration of hydrogen from one part of molecule to another unsaturated part thereof, in selected substrates, under controlled experimental conditions.

In a present paper we wish to report a new application of Ra/Ni. It was found that allylic and homoallylic steroidal alcohols can be transformed, in one-pot reaction, into corresponding saturated ketones by using activated Ra/Ni as catalyst. This type of hydrogen transfer has been studied on the Δ^5-cholesten-3β-ol (1) and Δ^4-cholesten-3β-ol (2). Steroidal alcohols (1) and (2) react in presence of Ra/Ni in aprotic solvent and cyclohexanone, under nitrogen, affording both 5β-cholestan-3-one (3) and 5α-cholestan-3-one (4) as main reaction products[*]. In addition, Δ^4-cholesten-3-one (5) was also isolated. The reaction products were separated by cromatogra-



Scheme 1.

phy on the silica gel column and characterized by m.p.,$[\alpha]_D$, IR, NMR and elemental analysis (Scheme 1).

As can be seen from the scheme, under such experimental conditions, the first step in this transformation probably involves oxidative dehydrogenation of the allylic and homoallylic hydroxyl group, subsequent transfer of the hydrogens to the catalyst, followed by hydrogenation of olefinic double bond.

In order to prove this asumption, alcohol (1) was treated under the same experimental conditions, which means in the presence of activated Ra/Ni, but without cyclohexanone. Reaction was stopped due to the total consumption of alcohol (1). It was isolated 86% of (3) and (4) (in ratio 5:1), 6% of unsaturated ketone (5) and 6% of 5β-cholestan-3α-ol (NMR,$[\alpha]_D$, m.p.) by column chromatography on silica gel.

Comparing the yields in first reaction (Scheme 1, alcohol (1)) with second one (with the same alcohols), one can notice drastic decrease in percentage content of unsaturated ketone (5). This fact can be rationalized as a result of possible hydrogen transfer from carbon atom bearing hydroxylic group to the catalyst, and subsequently to unsaturated ketone (5). In other words, it could be inferred that in the first reaction (Scheme 1, alcohol (1)) the excess of cyclohexanone is responsible for decrease in the amount of saturated ketone (3) and (4), and increase in the amount of unsaturated ketone (5), because of the lack of hydrogen in the system. If the hydrogen transfer had occurred from Ra/Ni itself, than the amount of 5β-cholestan-3α-ol would have probably increased, on the expense of smaller amount of ketone (3) and (4).

By comparing reaction times (Scheme 1), one can see that hydrogen transfer from hydroxylic function to the olefinic bond is 9 times faster in allylic alcohol than in the homoallylic one. 5:1 Ratio of 5β- (3) to 5α- (4) saturated ketones, obtained in the reaction of alcohols (1), (2), and in experiment without cyclohexanone, indicates that Δ^4-cholesten-3-one (5) is an intermediate in the reaction in both type of unsaturated alcohols. Relatively high stereospecificity of this hydrogen transfer reaction, indicated that hydrogen migration from hydroxylic group to the olefinic bond is probably a concerted process.

It is convenient that this dehydrogenation-hydrogenation reaction, induced by Ra/Ni, can be achieved in one-pot operation and under mild and simple experimental conditions.

Further investigation on the generality of Ra/Ni induced hydrogen transfer reactions, and stereochemical and mechanistical aspects of the reactions this type, are under way.

REFERENCES AND NOTES

1. J. S. Pizey, Raney Nickel, in Synthetic Reagents, Vol. II, p. 175, 186-187, 286-287, Ellis Horwood Ltd and Wiley, 1974.

[*] In a typical experiment, 3 g of activated Ra/Ni (previosly washed with acetone) and 50 ml of toluene were placed in the flask and nitrogen was passed with vigorous stirring. The suspension was heated to b.p. of toluene in order to remove acetone and traces of water. After that alcohol (1) 1 g and 0,6 ml of cyclohexanone were added to warm reaction mixture. Then, reaction mixture was refluxed under nitrogen, and after 4,5 hours the starting alcohol (1) was completely consumed (rate of reaction was followed by TLC). From the mixture 0,658 g (65%) of 5β-cholestan-3-one (3), 0,126 g (12%) 5α-cholestan-3-one (4) and 0,190 g (19%) of Δ^4-cholesten-3-one (5) were isolated by chromatography on silica gel (0.063-0,2 mm). For all compounds correct m.p., IR, NMR and elemental analysis were obtained.

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