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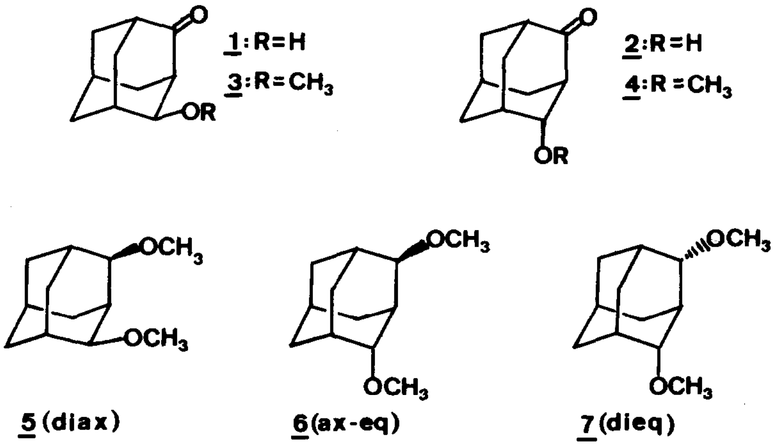
REARRANGEMENTS AND UNUSUAL REDUCTIONS WITH SODIUM HYDRIDE AND METHYL IODIDE

Helmut Duddeck*, H.-Thomas Feuerhelm and Günther Snatzke
Ruhr-Universität Bochum, Lehrstuhl für Strukturchemie, Postfach 102148,
D-4630 Bochum, FRG

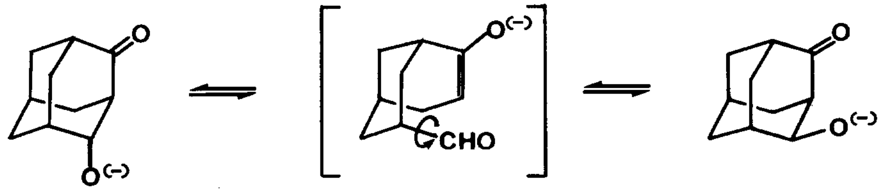
In the course of our ^{13}C NMR investigations of adamantane derivatives we wanted to prepare the 4-methoxyadamantanones 3 and 4[1]. To that end we refluxed the corresponding hydroxy compounds 1 and 2 with NaH in THF, and after cooling CH_3I was added and the reaction mixture stirred for one hour at room temperature[2].

Scheme 1 :



Surprisingly, both epimers 1 and 2 afforded 3 in 80% yield, the remaining 20% being the diaxial dimethoxyadamantane 5. Hydrolysis instead of reaction with CH_3I gave mixtures of the two epimeric hydroxyadamantanones 1 and 2 in ratios of about 3 : 1 to 7 : 1 regardless which epimer was used. This showed that the hydroxyadamantanones can be isomerized not only in acidic media[3] but also by base. We assume that they epimerize via an enolate-aldehyde-intermediate; rotation of the aldehyde group and re-cyclization gives the other isomer (Scheme 2). Apparently, the axial anion is methylated much more rapidly than the equatorial one so that only 3 is found according to the Curtin-Hammett-principle[4]. If, however, the carbonyl group in 2 is converted into the ethylene acetal, methylation of the equatorial hydroxy group can be carried out without epimerization. Then 4 is the only product after saponification.

Scheme 2:



As already mentioned, reduction is a side reaction under the conditions described above. Since only the diaxial isomer 5 was found we conclude that the axial epimer of Scheme 2 is reduced preferentially . Dimethoxyadamantane, however, is the only product isolated if CH_3I is added to the NaH-suspension together with 1 and 2, respectively, and the mixture is subsequently refluxed: Reaction of 1 afforded 5 only, whereas in the reaction with 2 we found 5 in 75% yield, the rest being a mixture of 6 and 7 which could not be separated properly from each other by g.c. Apparently, under these conditions the reduction becomes so fast that it competes with the epimerization.

When adamantanone was exposed to a mixture of NaH and CH_3I in refluxing THF we found the same reductive methylation to 2-methoxyadamantane in a yield of 75%, the rest being unreacted ketone. Obviously, the hydroxy group in 1 and 2 supports the reduction, but in principle their presence is not necessary. The reducing agent in this reaction is the NaH/CH_3I-complex since NaH alone did not afford any 2-adamantanol under analogous conditions.

Replacing NaH by another strong base like t-BuOK gave the same results for the epimerization/methylation-reaction, but reductive methylation could not be observed for any of the reactions described here.

Thus, the NaH/CH_3I-complex appears to represent a new reagent for the reductive methylation of non-enolizable ketones. This reaction must be different from several other NaH-reductions reported earlier[5]. Further investigations are in progress in this laboratory.

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