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THE APPARENT CONJUGATE REDUCTION OF SOME α-BENZYLTHIO AND α-BENZYLSULFONYL SUBSTITUTED α,β-UNSATURATED CYCLOHEXENONES*

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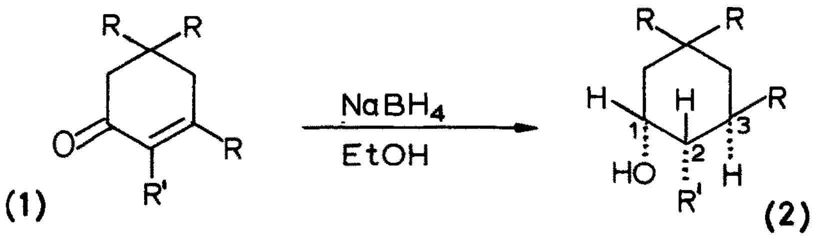
The metal hydride reduction of α,β-unsaturated carbonyl compounds to allylic alcohols has frequently been reported to proceed with concomitant saturation of the double bond[1]. In particular cycloalkenones seem to be sensitive to this mode of reaction[2]. β-Alkyl substituents have been shown to suppress the double bond saturation and some isolated examples of reduction of α-alkyl substituted enones reveal that double bond saturation is almost completely prevented[3]. Although the hydride delivery in the $LiAlH_4$ reduction of 3-phenylallyl alcohols has been demonstrated to be intramolecular[4], this process is considered unlikely for the $NaBH_4$ reduction of cyclohexenones on basis of the observation that the corresponding allylic alcohols, once formed, are not reduced by $NaBH_4$. In these cases the reaction is explained as a 1,4-addition of the metal hydride followed by a slower reduction of the initially formed enolate.

We have observed that the α-benzylthio substituted enones <u>1a-c</u>[6] are reduced stereospecifically with sodium borohydride in ethanol at r.t. to the saturated alcohols <u>2a-c</u>, respectively.



a) R = H ; R' = benzylthio
b) R = H ; R' = m-methoxybenzylthio
c) R =CH_3; R' = m-methoxybenzylthio

Although the formation of 2a-c can be explained on basis of 1,4-addition followed by reduction of the resulting enolate, we prefer to regard this reaction as a 1,2-addition to the carbonyl function, followed by an intramolecular hydride transfer from the formed alkoxy borohydride to the vinyl ether system (fig. 1). The intramolecular hydride transfer is possibly facilitated in the present case by activation of the alkoxy borohydride moiety through participation of the sulfide acting as a Lewis base. Our preference is based on the fact that reactions of sodium borohydride with excess of 1c lead to mixtures of the starting material and the alcohol 2c in ratios corresponding to the consumption of 1 mole of $NaBH_4$/mole of enone. The relative configuration of 2c (the only detectable reaction product) is a direct logical consequence of the suggested reaction mechanism.

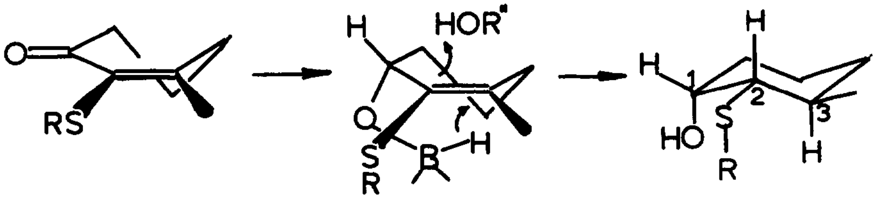
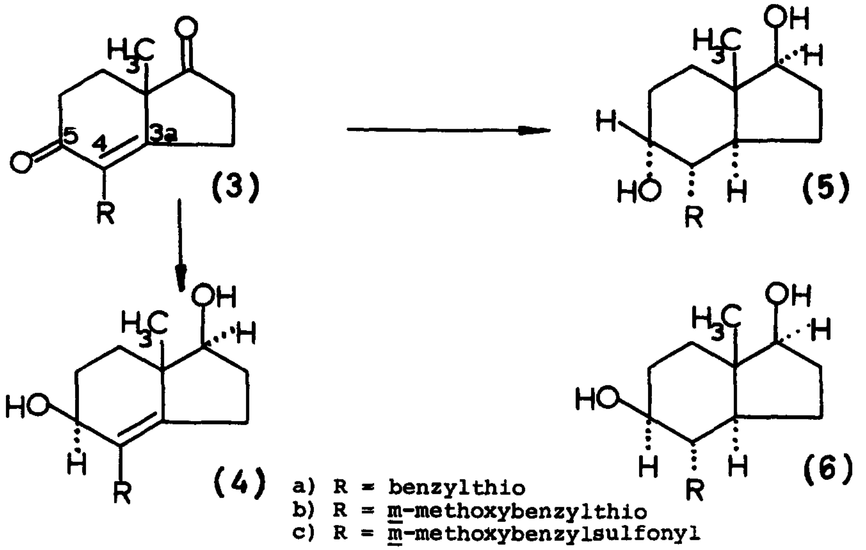


Fig. 1

The stereochemistry of 2c can be deduced from the 100 MHz NMR spectrum. The C2-hydrogen signal (2.30 ppm) shows splittings of 3 and 11 Hz. This proves that C2-H occupies an axial position and that it is flanked by one axial and one equatorial vicinal hydrogen. The C1-H (3.90 ppm) exhibits a $W_{1/2}$ of 7 Hz, clearly demonstrating its equatorial position.

The intramolecular course suggested for the above mentioned reduction is also supported by the reaction of the more rigid enones 3a[6] and 3b[6] with excess of $NaBH_4$ in ethanol to the alcohols 4a and b, respectively. Inspection of molecular models suggests that intramolecular transfer of hydride can not be accomplished without considerable strain, whereas no factors seem to be present to inhibit an attack from the α-side of the molecule on the vinyl ether in an intermolecular reaction.



a) R = benzylthio
b) R = m-methoxybenzylthio
c) R = m-methoxybenzylsulfonyl

The reduction of the benzylsulfonyl substituted system 3c[6] also takes place with concomitant saturation of the double bond and leads to a mixture of the alcohols 5c and 6c in a ratio of 9:1. It seems most likely that the latter reduction proceeds via two consecutive intermolecular 1,2-additions, since vinyl ethers are not commonly reduced under the reaction circumstances, whereas vinyl sulfones are, because of their enhanced electrofilicity. When ethyl acetate is used as a solvent the ratio of the isomers 5c and 6c changes to roughly 1:1. This reflects the known increased steric hindrance of the solvated hydride in hydroxylic solvents as compared to non-hydroxylic solvents, and it amplifies the impression of two consecutive reduction steps, since the reduction of the vinyl sulfone must have taken place during the destruction of the excess of borohydride in acidic medium.

The isomers 5c and 6c were separated by partial crystallisation. The stereochemistry follows from the NMR spectra.

5c : C4-H δ3.50 ($J_{3a,4}$ 12 Hz, $J_{4,5}$ 3 Hz); C5-H δ4.50, $W_{\frac{1}{2}}$ 7 Hz.

6c : C4-H δ3.44 ($J_{3a,4}$ 12 Hz, $J_{4,5}$ 11 Hz), C5-H δ4.55, $W_{\frac{1}{2}}$ 17 Hz.

It is worthy of note that both 5c and 6c possess a trans ring fusion. This reduction can thus be regarded as a new route to the difficultly accessible functionalised trans perhydroindane systems.

Footnotes and references:

* Taken in part from J.W. de Leeuw, doctoral thesis, Amsterdam 1970.

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5. Reference 1, p. 91.
6. The synthesis of this compound will be described elsewhere.