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Abstract

Full Text

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SYNTHESIS AND TRANSFORMATIONS
OF cis- AND trans-1-ETHYNYL-1-DECALOLS

We have studied the condensation of cis- and trans-α-decalones with acetylene, with the aim of using the acetylenic alcohols thereby obtained for introducing into the decalin nucleus dioxoacetone, glycerol, and dioxocarboxylic side chains characteristic of corticoid hormones, by methods developed in our laboratory (^{1}).

The condensation of trans-α-decalone I with acetylene was carried out in the presence of powdered caustic potash under pressure (^{2}) and in a solution of liquid ammonia in the presence of sodium (^{3}). In the latter case a mixture of isomeric trans-1-ethynyl-1-decalols was obtained, from which, by freezing at $-70°$ and chromatography of the residue on aluminum oxide, it was possible to isolate the epimeric trans-1-ethynyl-1-decalols II and III in a ratio of $1:2$. (The yields in percent are indicated under the arrows; the constants (m.p., b.p., n_D^{20}, d_4^{20}) of the compounds obtained are given under the formulas.)

$$\mathrm{I} \quad \xrightarrow[90\%]{\mathrm{CH{\equiv}CH,\ Na/NH_3}} \quad \begin{array}{l} \mathrm{II}\quad \text{m.p. } 54\text{–}55° \\ \mathrm{III}\quad \text{b.p. } 86\text{–}87°/1\ \text{mm} \\ n_D^{20}\ 1.5044, \quad d_4^{20}\ 1.0041 \end{array}$$

As is known, cis-α-decalone under the influence of acids and alkalis readily isomerizes into trans-α-decalone (^{4}, ^{5}); therefore it seemed unlikely that cis-1-ethynyl-1-decalols could be obtained under the strongly alkaline conditions of acetylene synthesis by the Favorskii method. However, when the reaction of cis-α-decalone IV with sodium acetylide in a solution of liquid ammonia was carried out, cis-1-ethynyl-1-decalol V was obtained in an overall yield of 60%.

$$\mathrm{IV} \quad \xrightarrow[60\%]{\mathrm{CH{\equiv}CH,\ Na/NH_3}} \quad \mathrm{V}\quad \text{m.p. } 55\text{–}56°$$

Only about 10% of cis-α-decalone IV underwent isomerization in this process and was isolated in the form of trans-α-decalone I. It turned out that the condensation reaction with acetylene successfully competed with the isomerization reaction, which proceeds through the stage of enolization:

$\mathrm{IV} \rightarrow \rightarrow \mathrm{I}$

The fact that trans-α-decalone, and not trans-acetylenic alcohols, is isolated from the reaction mixture excludes an enol mechanism for the acetylenic synthesis and once again confirms the correctness of the organometallic mechanism of this reaction (2). The stereoselective course of the acetylenic synthesis in the case of cis-α-decalone, with formation of only one cis-1-ethynyl-1-decalol V, is in agreement with the results of the previously described addition reactions to the carbonyl group of cis-α-decalone (6).

At the present time it is generally accepted that the conformation of cis- and trans-decalins is determined by the combination of two cyclohexane rings in the chair form (7), in which there are two geometrically nonequivalent types of bonds between carbon atoms and substituents, occupying equatorial (e) or axial (a) positions (8).

From the literature data it is known that esterification of compounds with an axial position of the hydroxyl groups, and hydrolysis of the corresponding esters, are sterically more hindered in comparison with the reactions of compounds with equatorially situated oxy groups. The acid phthalates obtained from trans-α- and trans-β-decalols (9,10) with an equatorial arrangement of the alcohol groups are saponified, respectively, 19 and 7 times faster than the esters of epimeric decalols with axially oriented hydroxyl groups.

By acetylation with acetic anhydride (11), the 1-ethynyl-1-decalols II, III and V gave, in high yields, the corresponding acetates VI, VII and VIII,

VI $T_{\text{b.p.}}$ 106–108°/2 mm, VII $T_{\text{m.p.}}$ 79–80° VIII $T_{\text{m.p.}}$ 65–67°
n_D^{20} 1.4940, d_4^{20} 1.0344

where it was found that acetylenic alcohol III and its derivatives form acetyl derivatives more readily than the epimeric alcohol II. By analogy with trans-α-decalol it may be assumed that the hydroxyl group in alcohol III is in the equatorial position, and in the more difficultly acetylated isomer II—in the axial position:

II III

From cis-1-ethynyl-1-decalol V and its derivatives, their acetates were obtained very readily under mild conditions. Taking into account the general asymmetry of the cis-decalin molecule, it may be supposed that one of the isomers of the cis-acetylenic alcohols (with an axial hydroxyl) should have been esterified with extreme difficulty. Therefore, the ease with which alcohol V and its

derivatives form acetates, indicates, in all probability, an equatorial arrangement of the hydroxyl group in these compounds.

(Figure: structural diagram showing conformational decalin framework with labels H(a), H(e), (a)HO, (a): CH C)

In carrying out comparative experiments on the rate of hydration of the acetylenic alcohols II, III, and V in aqueous methanol in the presence of mercuric sulfate, it was found that trans-1-ethynyl-1-decalol III, already at 20°, is completely hydrated within 10 hours, forming trans-1-acetyl-1-decalol IX. Hydration of the acetylenic alcohol II was accomplished under the same conditions only as the result of 10 hours' boiling at 65°, with formation of trans-1-acetyl-1-decalol X. At 20° the acetylenic alcohol II does not undergo hydration and is recovered completely.

$$\text{III} \quad \xrightarrow[\text{80\%}]{\text{hydration, 10 hr, 20°}} \quad \begin{array}{l} \text{IX } T_{\text{bp}}\ 80\text{–}82°/1\text{ mm}, \\ n_D^{20}\ 1.4898,\ d_4^{20}\ 1.0337 \end{array}$$

$$\text{II} \quad \xrightarrow[\text{63\%}]{\text{hydration, 10 hr, 65°}} \quad \begin{array}{l} \text{X } T_{\text{bp}}\ 106\text{–}107°/2\text{ mm}, \\ n_D^{20}\ 1.4970,\ d_4^{20}\ 1.0502 \end{array}$$

The isomeric acetates VI and VII behave similarly on hydration. Trans-1-acetyl-1-decalol IX readily forms both the semicarbazone and the 2,4-dinitrophenylhydrazone, whereas from trans-1-acetyl-1-decalol X only the semicarbazone was obtained, and with great difficulty; this indicates shielding of the acetyl group in this compound.

Hydration of cis-1-ethynyl-1-decalol V likewise could not be effected at 20°; however, as little as one hour’ s boiling at 65° proved sufficient for obtaining cis-1-acetyl-1-decalol XI, which with difficulty gives only the semicarbazone and does not form a 2,4-dinitrophenylhydrazone.

$$\text{V} \quad \xrightarrow[\text{71\%}]{\text{hydration, 1 hr, 65°}} \quad \text{XI } T_{\text{mp}}\ 36\text{–}37°$$

These data show that the carbon chain in compounds V and XI is also appreciably shielded by the neighboring cyclohexane ring. Earlier (12), a sharp difference was also observed in the rate of hydration of 9-methyl-1-ethynyl-6-ketodecalols with opposite configuration of the substituents at C_1.

By oxidation with sodium hypobromite, the acetyldecalols IX, X, and XI were

the corresponding stereoisomeric 1-oxydecalincarboxylic acids XII, XIII, and XIV were obtained:

$$\begin{array}{ccccc}
\text{IX} & \xrightarrow[89\%]{\text{NaOBr}} & \text{XII, m.p. } 149\text{–}150^\circ & \xrightarrow[95\%]{\mathrm{CH_3COCl}} & \text{XV, m.p. } 164\text{–}165^\circ \\
\mathrm{COCH_3,\ OH} & & \mathrm{COOH,\ OH} & & \mathrm{COOH,\ OCOCH_3} \\
 & & & & \\
\text{X} & \xrightarrow[54\%]{\text{NaOBr}} & \text{XIII, m.p. } 115\text{–}116^\circ & & \text{XVI} \\
\mathrm{COCH_3,\ OH} & & \mathrm{COOH,\ OH} & & \mathrm{COOH,\ OCOCH_3} \\
 & & & & \\
\text{XI} & \xrightarrow[75\%]{\text{NaOBr}} & \text{XIV, m.p. } 134\text{–}136^\circ & \xrightarrow[75\%]{\mathrm{CH_3COCl}} & \text{XVII, m.p. } 141\text{–}142^\circ \\
\mathrm{COCH_3,\ OH} & & \mathrm{COOH,\ OH} & & \mathrm{COOH,\ OCOCH_3}
\end{array}$$

The lower yield of acid XIII in this case is probably explained by the greater steric hindrance of the carbon chain, noted above, in trans-1-ethynyl-1-decalol II and in the acetyl-1-decalol X obtained from it.

On acetylation of the oxydecalincarboxylic acids under mild conditions (boiling with acetyl chloride in ether[13]), only acetates XV and XVII were isolated, whereas acid XIII was recovered unchanged from the reaction, and acetate XVI could not be obtained under these conditions.

Having established the ease of acetylation of the hydroxyl group in the acetylenic alcohols III and V, and also in the oxydecalincarboxylic acids XII and XIV, we assigned to them an equatorial position of the hydroxyl, in contrast to trans-1-ethynyl-1-decalol II, in which the hydroxyl is apparently oriented axially.

From consideration of the data on the rate of hydration of the isomeric ethynyldecalols II, III, and V, on the ability of the hydration products to give derivatives at the carbonyl group, and on the ease of oxidation of acetyldecalols IX, X, and XI with sodium hypobromite, it becomes evident that in compounds with an axial arrangement of the hydroxyl groups (II, X, XIII) the side chain undergoes the greatest steric hindrance, whereas in compounds with an equatorially oriented oxy group (III, IX, XII) the side chain is least sterically hindered; this, in all probability, is connected with a different degree of shielding of it by the rings.

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