SYNTHESIS OF SOME D-HOMO-18-NORESTRONE DERIVATIVES*

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As we have shown previously [1], in the condensation of 3,4-dihydro-6-methoxy-1-vinyl-naphthalene (I) with benzoquinone the adduct (II) is formed, and this is converted on reduction into the syn-cis diketone (III). The isomerization of the latter in an alkaline medium leads to the anti-trans diketone (IV).

\[
\begin{align*}
\text{CH}_3\text{O} & \quad \text{CH}_2\text{O} \\
\text{CH}_3 \quad \text{CH}_2\text{COOH} \\
\text{Zn} & \quad \text{OH}^- \\
\text{CH}_3\text{O} & \quad \text{CH}_2\text{O}
\end{align*}
\]

In the present work we investigated some reactions of the diketones (III) and (IV) with the object of obtaining 17α-derivatives of steroids, which might be of physiological interest.

For the diketone (IV) the ethynylation reaction proceeds the more selectively. When it reacts with lithium acetylide, 17αβ-ethynyl-17αα-hydroxy-3-methoxy-D-homo-18-norestra-1,3,5,9-tetraen-15 one (V) is formed in about 70% yield. The ethynylation of the ketone (III) proceeds less selectively, and the corresponding ketol (VI) was isolated in only 30% yield. In accordance with the observed selectivity both the diketones (III) and (IV) form only mono-2,4-dinitrophenylhydrazones, and the ketols (V) and (VI) do not form hydrazones.

\[
\begin{align*}
\text{CH}_3\text{O} & \quad \text{CH}_2\text{O} \\
\text{CH}_3 \quad \text{OH} \\
\text{(IV)} & \quad \text{(V)} & \quad \text{(VI)}
\end{align*}
\]

The structure of the ketol (V) was proved by its conversion into 1-ethyl-8-methoxychrysene (VII), which was obtained also by a confirmatory synthesis. Hydrogenation of the ketol (V) in presence of palladium on lead carbonate (Lindlar's catalyst) led to the ethylenic alcohol (VIII) and to the alcohol (IX). Reduction of the latter by the Kizhner-Wolff method gave the alcohol (X), which was converted into 1-ethyl-8-methoxychrysene (VII).

\[
\begin{align*}
\text{CH}_3\text{O} & \quad \text{CH}_2\text{O} \\
\text{OH} & \quad \text{OH} \\
\text{(V)} & \quad \text{(VIII)} & \quad \text{(IX)}
\end{align*}
\]

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The confirmatory synthesis of 1-ethyl-8-methoxychrysene (VII) was carried out by the method used by Robins and Walker [2] for the preparation of 8-methoxy-1-methylchrysene. The diketone (III) was converted into the monoketal (XI), which after reduction and hydrolysis gave the ketol (XII). The latter was converted by Grignard reaction with ethylmagnesium bromide into the diol (XIII). Further dehydration and dehydrogenation led to 1-ethyl-8-methoxychrysene (VII), which was found to be identical with the sample obtained as above.

The spatial configuration of the ethynyl and hydroxy groups in the ketol (V) was assumed tentatively on the basis of an examination of a molecular model of the diketone (IV), from which it is seen that the β-region is more accessible to attack than the α-region. The same conclusion is reached by Burtner and Gentry [3], who carried out the ethynylation of 3β-hydroxy-D-homo-18-norandrost-17α-ene, which is very similar to the diketone (IV) in spatial configuration. A model of the diketone (III) shows that attack from the β-region is again most favored; it is difficult to resolve beforehand the question of the choice between the carbon atoms C14 and C17α, i.e., of the position of the ethynyl group. An attempt to remove the 15-CO group in the ketol (V) by Clemmensen reduction led merely to the isomeric ketol (XIV) with a displaced double bond; the keto group, being considerably screened, remained untouched. We assign the CD-cis structure to the ketol (XIV) on the basis of considerations which we give below. The Kizhner reduction of the ketol (VIII) under the Huang-Minlon conditions was accompanied by demethylation and led to the diol (XV). Such demethylation in presence of alkaline agents has been noted in the literature. For example, on being heated with the sodium derivative of ethylene glycol in ethylene glycol, the dimethyl ether of diethylstilbestrol is converted into diethylstilbestrol [4].