SOME TRANSFORMATIONS OF cis-3-METHOXY-18-NOR-
1,3,5(10),9(11)-ESTRATETRAENE-15,17-DIONE

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We have shown previously [1] that the condensation of 4-cyclopentone-1,3-dione with 1,2-dihydro-7-methoxy-
4-vinyl-1,2-dihydronaphthalene gives a good yield of the adduct (I), which has a steroid skeleton. It was of interest to study the
possibility of the selective removal of its 15-keto group with the object of passing to systems allied to estrone. One
possible way for the achievement of this object could be the reduction of the corresponding enol ether with lithium
aluminum hydride, as described for the case of bicyclic β-diketones [2] and (±)-3-hydroxy-14-iso-18-norandrost-
9(11)-enedione [3]. However, it is necessary to take account of the fact that, on account of the lack of sym-
metry in the adduct (I), its treatment with diazomethane should lead to the formation of a mixture of isomeric enol
ethers, whose structures require special proof.

We showed that in the action of diazomethane on the adduct (I) a mixture of adducts is indeed formed, and by
the fractional crystallization of this we succeeded in isolating the individual enol ethers (II) and (III). It could be
supposed that the isomer (III) of m. p. 167-168°, formed in the predominant amount and containing according to the
ultraviolet spectrum [4] a 9(11) double bond, has the structure (III), corresponding to enolization at the least screened
keto group, as observed previously for some steroid β-diketones [5]. For this product we studied the Grignard reac-
tion with CH₃MgI, and with the aid of this we succeeded in confirming its structure.

The reaction of the enol ether (III) with methylmagnesium iodide is fairly complex, and as the only crystalline
product we succeeded in isolating an unsaturated monoketone whose ultraviolet spectrum contains absorption bands
at 260 and 282 mμ; this shows that it contains a conjugated carbonyl group and a 8(9) double bond, which could
arise as a result of the isomerization of the original 9(11) double bond in the treatment of the reaction products under
acidic conditions [6]. Under the conditions of acid isomerization this ketone does not change, and scarcely any hy-
drogenation occurs over a palladium catalyst. However, in hydrogenation in alcoholic solution over platinum it ab-
sorbs one molecular proportion of hydrogen and gives a product which according to its infrared spectrum does not
contain a carbonyl group. These results enable us to conclude that the original unsaturated ketone probably has the
structure (IV), which corresponds most satisfactorily with the experimental data. On this basis we may suppose that
the product of the hydrogenation of (IV) in alcohol has the structure (V). (See the structure at the top of the next page.)

In the hydrogenation of the unsaturated ketone (IV) over a platinum catalyst in acetic acid, a more complex
transformation occurred, and a product of composition C₁₉H₁₅O which did not contain a carbonyl group was obtained.
The ultraviolet spectrum of this compound showed intense absorption at 280 mμ, characteristic for substituted me-
thoxybiphenyls [7]. All this provides grounds for the view that the product formed under these hydrogenation con-
ditions has the structure (VI) and is probably formed by the aromatization of the intermediate alcohol (V). In cor-
respondence with this structure (VI) is readily dehydrogenated when heated with selenium and gives a crystalline
substance of m. p. 97-98°, which corresponds to known 7-methoxy-1'-methyl-1,2-cyclopentenophenanthrene [16,17-
dihydro-3-methoxy-15-methyl-15H-cyclopenta[a]phenanthrene] (VII). Hence, when account is taken of data in
the literature on 1,2-addition in the case of enols of cyclic β-diketones [3], all the above-described transformations
confirm the structures of the isomeric enol ethers which we isolated.

EXPERIMENTAL

Preparation of the Enol Ethers (II) and (III). Etherate diazomethane was added to a suspension of 2 g of (I)
(λmax 259 mμ, ε 39400) in ether, and the resulting solution was left overnight. Ether was driven off, and we ob-
tained 1.9 g of a crystalline substance of m. p. 113-120°, which was dissolved in 20 ml of hot methanol. The solution was left overnight, and the mixture of crystals obtained consisted of two different crystalline forms—large rhombs (II) and plates (III). These were separated by hand and recrystallized from absolute methanol. We obtained: 1) 0.15 g of the isomer (II), m. p. 158-160°, λ max 241 mμ, ε 19900, λ2 max 267 mμ, ε 14200, λ3 max 292.5 mμ, ε 4550 (shoulder). Found: C 76.75; 76.20; H 6.91; 6.82%. C19H20O3. Calculated: C 77.0; H 6.80%; and 2) 0.28 g of the isomer (III), which after crystallization from absolute methanol had m. p. 167-168°, λ max 243 mμ, ε 21100, λ2 max 266 mμ, ε 15700, λ3 max 292.5 mμ, ε 4150 (shoulder).* In thin-layer chromatography on unbound alumina in 1:1 benzene-ethyl acetate the enol ether (II) had Rf 0.712, whereas the enol ether (III) had Rf 0.585, which can be made the basis of their preparative separation.

Reaction of the Enol Ether (III) with Methylmagnesium Iodide. A solution of 300 mg of the enol ether (III) in 10 ml of tetrahydrofuran was added with stirring and cooling with ice to a Grignard reagent prepared from 0.48 g of magnesium and 2.8 g of methyl iodide. The reaction mixture was heated for 1 h at the boiling point of ether and was then treated with 5% hydrochloric acid. From the ether layer we isolated 300 mg of an oil, which was heated at 170-180° in a vacuum with 0.5 g of KHSO4. The cooled mixture was extracted with ether, the extract was washed with sodium carbonate solution, ether was driven off, and the residue (230 mg) was treated with boiling methanol. Methanol was driven off, and we isolated 120 mg of a light-yellow oil, which was applied to a column containing 10 g of alumina. The product obtained by elution with 60 ml of petroleum ether was a mobile yellow oil (30 mg), which was not investigated further. By further elution with a 1:1 mixture of benzene and petroleum ether we isolated 80 mg of the unsaturated ketone (IV), which after crystallization from absolute methanol had m. p. 116-117°; yield 28%. Ultraviolet spectrum (in alcohol): λ max 260 mμ, ε 15300, λ2 max 282 mμ, ε 16500, λ3 (in CHCl3) 1699; 1609 cm⁻¹. Found: C 81.18; 81.50; H 7.16; 7.03%. C19H20O2. Calculated: C 81.39; H 7.19%. In the reaction of the enol ether (II) with the Grignard reagent no individual crystalline product could be isolated.

Reaction was carried out similarly with 3 g of the mixture of enol ethers (II) and (III) of m. p. 113-130°, and we obtained 2.5 g of a semisolid oil, which was chromatographed as described above on a column containing 200 g