Tetrahedron Letters No. 30, pp 3027 - 3030, 1972. Pergamon Press. Printed in Great Britain.

# STEROIDAL PHOTOCHEMISTRY

# THE PHOTOCYCLOADDITION OF A 3-KETO-4,6-DIENE TO BUTADIENE

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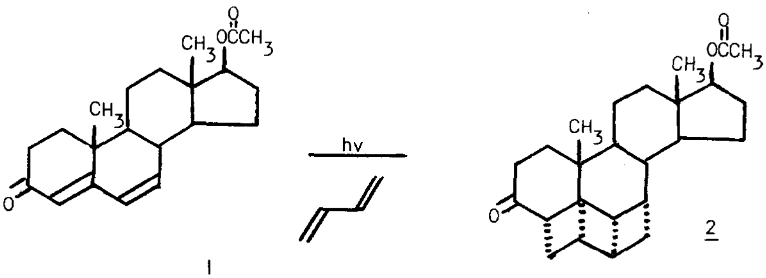
(Received in USA 30 May 1972; received in UK for publication 19 June 1972)

Recently we reported on the cycloaddition of a steroidal enone to various olefins and determined that, like the simpler cyclohexenones, both cis and trans isomers were formed, and that the reaction proceeded from the triplet state.[1] On the other hand, the cycloaddition of a steroidal 3-keto-4,6-diene generated only the trans-fused cyclobutane, and could not be quenched by butadiene.[2] The purpose of this communication is to indicate the novel chemistry of the steroidal dienone-butadiene adducts.

A solution of 6-dehydrotestosterone acetate (1), 10 g. in 300 ml of ethyl acetate was irradiated through a pyrex filter with a 450 W medium pressure mercury arc while passing a slow stream of butadiene through the solution. After 8 hours, starting material had all been consumed, and tlc indicated the formation of two major and two minor products which were separated by chromatography on silica. The first compound eluted 2, (mp 181-2°) (25%), analyzed correctly for an adduct of 1 and butadiene and possessed a parent molecular ion at m/e = 382 in the mass spectrum. The ir showed the 17-acetate at 1740 $cm^{-1}$ and an unconjugated cyclohexanone at 1715 $cm^{-1}$, and only $n \to \pi^*$ absorption in the uv. The angular methyl groups resonated at 0.82δ and 1.08δ. However, the most spectacular observation was the complete absence of any olefinic resonances, indicating that both steroidal double bonds had added across both diene double bonds to form three fused cyclobutane rings. The stereochemistry of 2 was determined to be 4α,5α,6α,7α by ORD/CD, which showed a positive Cotton effect with a molecular amplitude of a= +26, and a positive CD curve. A similar molecular amplitude was found for the 4α,5α-ethylene adduct of 3-keto-4-ene steroids.[1,3] Compound 2 could be saponified with sodium methoxide in methanol and acetylated to regenerate 2.

The second compound eluted, 3, (mp 223-5°), was the major product (50%), and was identified as the *trans*-fused 4α,5β-{4 + 2} Diels-Alder adduct on the basis of the following observations.[4] The cyclohexanone carbonyl appears at 1720 cm$^{-1}$ and 3 has only $n\rightarrow\pi^*$ uv absorption. The nmr shows a two proton multiplet (5.59-5.82δ) overlapping a sharp two proton singlet at 5.64δ. These two sets of protons are not separated in $C_6D_6$ or at 100 MHz. Additionally, the 4β-proton appears as a quartet at 2.38δ and the angular methyl groups at 0.81δ and 0.91δ. The ORD/CD showed a positive Cotton effect with a molecular amplitude of a= +95 and a positive CD curve. Sodium methoxide in methanol and subsequent reacetylation gave the 4β,5β-{4 + 2} epimer 4, mp 127-29°. The cyclohexanone carbonyl appeared at 1720 cm$^{-1}$ and the nmr showed a four proton multiplet at 5.60δ for the olefinic protons and the angular methyls as a six proton singlet at 0.87δ. Again, neither $C_6D_6$ nor running at 100 MHz resolved the olefinic multiplets. The ORD/CD demonstrated the 4β,5β-stereochemistry with a strong negative Cotton effect with a molecular amplitude of a= -213, and a negative CD curve.

Continued elution gave the 6α,7α-Diels-Alder adduct 5, mp 133-5° ($MeOH/H_2O$), in 5% yield. That butadiene had been added across the 6,7-double bond was indicated by the enone absorption in the ir at 1675 cm$^{-1}$ and 1610 cm$^{-1}$ and an uv absorption at 244 nm (ε 12,500). The angular methyl groups resonated at 0.87δ and 1.23δ, and the cyclohexene protons appeared as a narrow two proton multiplet at 5.60δ ($\Delta W_{1/2}$=4Hz). The olefinic proton of the enone appeared as a doublet (J = 1Hz) due to allylic coupling with the axial 6β-hydrogen. Saponification and reacetylation regenerated 5. The saponification experiment, together with the allylic coupling in the nmr indicates that the adduct has the 6α,7α-configuration and is not *trans*-fused. The isomeric 6β,7β-isomer 6, mp 225-6° (ethyl acetate) (5%), was eluted directly after 5. Compound 6 shows only the enone grouping in the ir at 1670 cm$^{-1}$ and 1610 cm$^{-1}$, and has λmax at 245 nm (ε 16,000) in the uv. The angular methyl groups resonate at 0.83δ and 1.33δ, while the cyclohexene olefinic protons resonate as a two proton multiplet at 5.62δ with a sharp singlet at 5.81δ for the enone proton at C-4. The nmr in perdeuteriobenzene further resolves the olefinic protons with the cyclohexene hydrogens as a two proton multiplet at 5.55δ and the enone hydrogen as a sharp singlet at 5.81δ. The absence of allylic coupling demonstrates the presence of an equatorial 6α-hydrogen.



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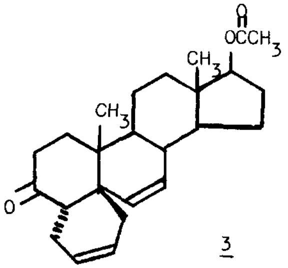

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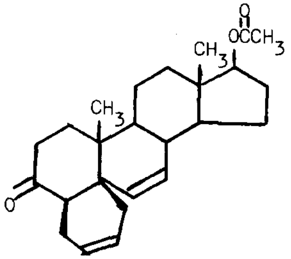

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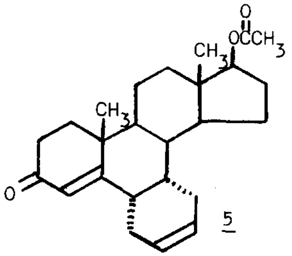

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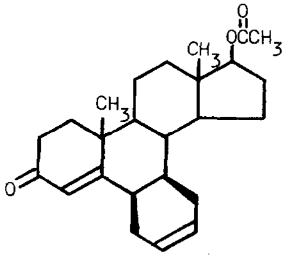

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The result of the photocycloaddition of the dienone to butadiene are unique and interesting for several reasons. The photochemistry of dienones has usually been concerned with molecular rearrangements and little is known of the cycloaddition reactions.[5] The isolation of 2 and the determination of the all cis-stereochemistry indicates that the initial addition is not likely to involve formation of the vinyl-4α,5β-cyclobutane, analagous to the {2 + 2} cycloaddition reactions of 1 with olefins, followed by either a second photochemical {2 + 2} cycloaddition or a thermal dimerization from a vibrationally excited ground state. Since 2 has all cis-stereochemistry, the interesting possibility arises that the cycloaddition may be a concerted photochemical {2 + 2 + 2 + 2} addition, which is suprafacially allowed with an even number of components.[6] The only literature analogy to the formation of 2 is the isolation in very low yield of a cyclobutanoxetane from the cycloaddition of dichloromaleimide to dimethylbutadiene.[7] Additionally, the isolation of the trans-Diels-Alder adduct 3 is unique, since there are only a few photo-Diels-Alder reactions known, and these are cis-additions.[8] Since 3 is a trans-photo Diels-Alder adduct, it is possible that the reaction is concerted.[9] Cantrell has shown that triplet enones can form cis-{2 + 2}-cyclo-adducts when irradiated in neat dienes.[10] Experiments are currently underway to determine the scope and mechanism of the photocycloaddition of dienones to dienes.

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