Formation of *trans*-Fused [2*s* + 2*a*] Adducts in the Photocycloaddition of a Dienone to an Electron Deficient Olefin

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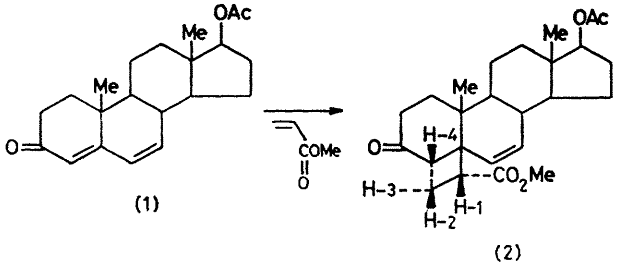
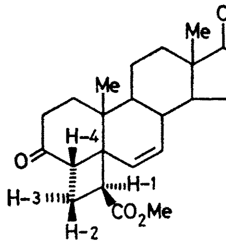
Summary The photocycloaddition of a linear steroidal dienone to the electron deficient olefin, methyl acrylate, furnishes the *trans*-fused cyclobutane adducts, together with the *cis*-fused adduct; the breakdown in the stereospecificity of this cycloaddition as a function of increasing olefin ionization potential is in agreement with theoretical predictions.

RECENTLY Epiotis and Shaik have calculated the potential energy surface for triplet $\pi\pi^*$ cycloadditions and concluded that if the enone and olefin were a good donor–acceptor pair then non-Woodward–Hoffman addition, *i.e.* [2*s*+2*a*], would occur to yield *trans*-fused cyclobutanes.[1] As the enone and olefin became poorer donor–acceptor pairs, they predicted formation of a diradical which would merge into exclusively [2*s*+2*s*] cycloaddition when the olefin and enone became good donor–donor or acceptor pairs. Previous results have indicated that a simple steroidal-4-en-3-one formed mixtures of *cis*- and *trans*-adducts with electron rich olefins,[2] partly owing to near accidental degeneracy of the $n\pi^*$ and $\pi\pi^*$ triplet states in the chromophore.[3] In distinct contrast to the enone, the photocycloaddition of a linear 4,6-dien-3-one to olefins of varying electron richness, from ethylene to 1,1-diethoxyethylene, yielded only regio- and stereo-specific *trans*-fused cyclobutanes.[4] This may be attributed, in part, to the large gap (*ca.* 25 kcal mol)$^{-1}$† between the $n\pi^*$ and $\pi\pi^*$ triplets, so that reaction occurs exclusively through the low lying $\pi\pi^*$ state. We here present our results on the photocycloaddition of 17β-hydroxyandrosta-4,6-dien-3-one acetate (**1**), (Δ^6-testosterone acetate), to the electron deficient olefin methyl acrylate, which indicate that *trans*-adducts are the major products. Our results also confirm the theoretical predictions[1] about the breakdown of stereospecific addition upon going from electron rich to electron poor olefins, which is the direct opposite of what would be expected using a tetramethylene as an intermediate.

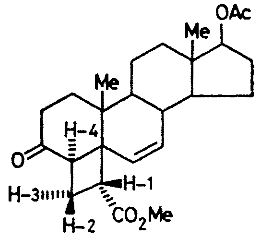


(1) (2)

When the dienone (**1**) was irradiated, under argon, in the presence of distilled methyl acrylate, with a 450 W mercury lamp (Pyrex filter), a rapid reaction occurred to generate a number of adducts. The major adduct (**2**),‡ m.p. 179—181·5 °C, was isolated by crystallization from ethyl acetate after removal of solvent, and was identified as a *trans*-fused cyclobutane on the basis of its physical data and subsequent chemical transformations. A *trans*-fusion was indicated by, *inter alia*, its i.r. carbonyl frequency (1730 cm^{-1}) as well as its strongly positive chiroptical effects. A combination of europium induced shifts, double resonance, and INDOR allowed the determination of the four proton cyclobutane system and the assignment of the methoxycarbonyl group as indicated. The stereochemistry of this group is indicated by the similarity of the coupling constants of H-1 and H-4 with those of H-2 and H-3. The configurations of *trans*- and *cis*-fused [2+2] steroid adducts have been determined by a combination of n.m.r. and chiroptical effects.[2b,5] Chromatography on silica and fractional crystallization yielded the *trans*-fused epimer (**3**),‡ m.p. 134—136 °C, in low yield. The difference in coupling constants of H-1 and H-4 with H-2 and H-3 is noteworthy. Both *trans*-epimers are fairly labile on chromatography, both being converted into the same *cis*-4β,5β-isomer (**4**),‡ m.p. 120—124 °C. The same compound was obtained from



(3)



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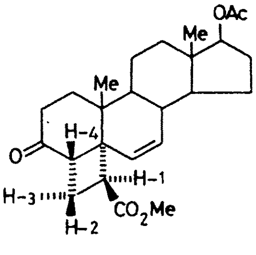

(5)

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† 4·184 J = 1 kcal.

‡ All new compounds gave satisfactory microanalytic and spectral data. N.m.r. data for compounds (**2**)—(**5**) were as follows: (**2**) δ 3·15 (H-1), 2·57 (H-2), 2·04 (H-3), and 3·44 (H-4), $J_{1,2}$ 10·8, $J_{1,3}$ 7·2, $J_{2,3}$ −11·0, $J_{2,4}$ 10·0, and $J_{3,4}$ 7·5 Hz; (**3**) δ 2·73 (H-1), *ca.* 2·5 (H-2), 2·30 (H-3), and 3·86 (H-4), $J_{1,2}$ 2, $J_{1,3}$ 6·5, $J_{2,3}$ −11, $J_{2,4}$ 9·5, and $J_{3,4}$ 8 Hz; (**4**) δ 3·33 (H-1), *ca.* 2·3 (H-2), 2·82 (H-3), and 2·54 (H-4), $J_{1,2}$ 9, $J_{1,3}$ 9, $J_{2,3}$ −11, $J_{2,4}$ 3, and $J_{3,4}$ 11 Hz; (**5**) δ 3·63 (H-1), 2·95 (H-2), *ca.* 1·5 (H-3), and 2·65 (H-4), $J_{1,2}$ 10·5, $J_{1,3}$ 8, $J_{2,3}$ −12, $J_{2,4}$ 10·5 and $J_{3,4}$ 3 Hz.

both (**2**) and (**3**) by saponification and epimerization with potassium methoxide in anhydrous methanol, followed by reacetylation. The epimer thus obtained has the methoxycarbonyl group in the stereochemically less encumbered position.

The other final major product was obtained from chromatography in admixture with the *trans*-cyclobutane (**2**). Hydrolysis of the 17β-acetate group allowed chromatographic separation yielding the 17β-hydroxy compound, m.p. 171—178 °C, which reformed the original compound (**5**),‡ m.p. 198—202 °C, after reacetylation with acetic anhydride in pyridine. Compound (**5**) was determined to be a *cis*-fused 4α,5α-cyclobutane by its stability to base and a positive Cotton effect in the O.R.D. ($a = +25$). The shielded position of the 10-methyl group at δ 0·75 indicated that the methoxycarbonyl cyclobutane had forced the A-ring into the boat conformation. Determination of the coupling constants for the cyclobutane protons allowed the placement of the ester group in the less sterically congested position indicated. No evidence was obtained for the occurrence of the epimer of compound (**5**).

Since these adducts are not stable to g.l.c., quenching studies, using the low energy quencher 3,3,4,4-tetramethyldiazetidine 1,2-dioxide,[6] were based on the relative rates of disappearance of the starting dienone (**1**) using its strong u.v. absorbance. Under these conditions the cycloaddition was strongly quenched, indicating a triplet reaction, and, based on other results,[7] a $\pi\pi^*$ state with an energy of *ca.* 50 kcal mol^{-1}.†

These experiments have shown that not only can the $\pi\pi^*$ triplet state lead to *trans*-fused cyclobutanes with electron deficient olefins, but that the breakdown in stereospecific addition, going from [$2s+2a$] to a mixture of [$2s+2a$] and [$2s+2s$] as a function of increasing ionization potential of the olefin, is in accordance with Epiotis and Shaik's theoretical predictions.[1]

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