

STEROIDS CCCVII. ⁽¹⁾
PHOTOCHEMICAL CYCLOADDUCTS. PART II. ⁽²⁾ ADDITION OF
1-ACETOXYBUT-1-EN-3-ONE TO 3 β -ACETOXPREGNA-5,16-DIEN-20-ONE.

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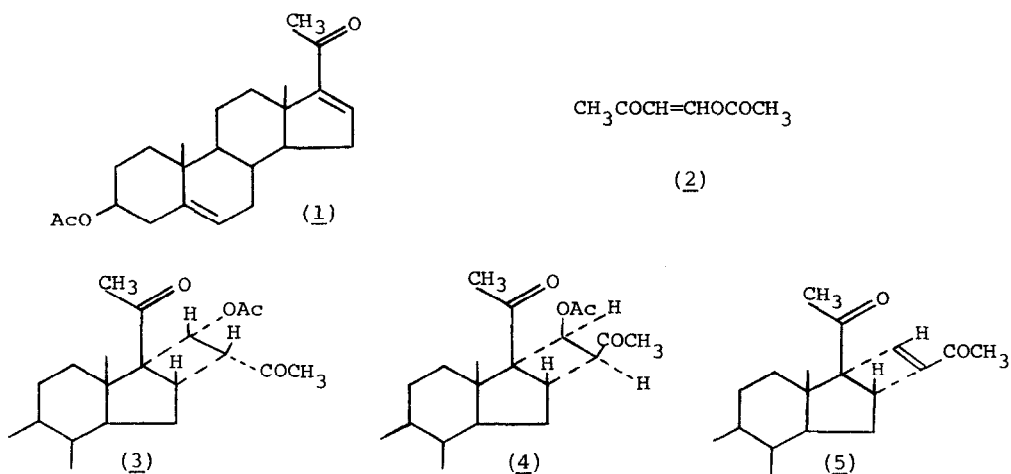
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Although examples of the photochemical dimerization of α,β -unsaturated ketones to yield substituted cyclobutanes are well documented, ⁽⁵⁾ the photochemical cycloaddition of two different α,β -unsaturated ketones has not been reported. We now wish to describe an example of the latter reaction which, in contrast to the orientation observed in the dimerization process, gives only cyclobutanes having the anti-orientation of the ketone functions. ⁽⁶⁾

Irradiation of a benzene solution of 3 β -acetoxypregna-5,16-dien-20-one ⁽¹⁾ containing a sixfold excess of 1-acetoxybut-1-en-3-one ⁽²⁾ with a 70 watt Hanau Q81 high pressure mercury lamp at 20° for 4 hr. followed by purification by preparative t.l.c. led to the isolation of two crystalline cyclobutane adducts ⁽³⁾ (43%) [m.p. 228-231°; $[\alpha]_D^{CHCl_3}$ -80°. Found: C, 71.66; H, 8.47; O, 19.92] and ⁽⁴⁾ (18%) [m.p. 184-186°; $[\alpha]_D^{CHCl_3}$ -41°. Found: C, 71.68; H, 8.22; O, 19.90], the acetylcyclobutene ⁽⁵⁾ (8%) [m.p. 173-176°; $[\alpha]_D^{CHCl_3}$ -17°; λ_{max}^{EtOH} 254, 294 m μ (log ϵ 3.8, 3.0); n.m.r. ⁽⁸⁾ (60 M.c.) 0.73 (18-H), 1.03 (19-H), 2.01 (3-acetoxy-H), 2.20 (21-H), 2.23 (16'-acetyl-H), 5.40 (multiplet, 6-H) and 6.73 p.p.m. (doublet, $J=1$ c.p.s. 17'-H). Found: C, 76.13; H, 8.64; O, 15.41] and recovered starting material ⁽¹⁾ (9%).

The cyclobutanes ⁽³⁾ and ⁽⁴⁾ are formulated as cis fused adducts by analogy with previous work. ^(2,5b,9) The α orientation of the cyclobutane ring is assigned on the basis of the 18-H resonance singlets (60 M.c.) at 0.62 and 0.60 p.p.m. exhibited by ⁽³⁾ and ⁽⁴⁾ respectively. ^(2,8) The lowest field cyclobutyl proton ($H-C-OCOCH_3$) in the 100 megacycle n.m.r. spectra of ⁽³⁾ and

(4) appears as a doublet at 5.40 and 5.72 p.p.m. respectively, $J = 6$ c.p.s., which collapses to a singlet upon irradiation at the resonance frequency of its neighboring proton (\underline{H} -C-COCH₃). The resonance pattern of the latter proton in these spectra is a triplet (2.62 p.p.m.) for (3) and a quartet (3.21 p.p.m.) for (4) due to vicinal coupling with two protons. Decoupling at the resonance frequency of the cyclobutyl proton \underline{H} -C-OCOCH₃ collapsed each multiplet to a doublet. This shows that the acetyl and acetoxy cyclobutyl substituents are located at the 16' and 17' positions respectively; consequently, adducts (3) and (4) differ only in the stereochemistry of these substituents.



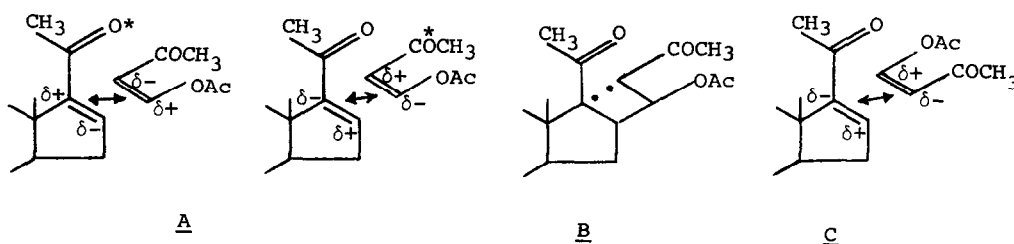
A tentative assignment of stereochemistry of the 16' and 17' substituents is based on the following spectral and chemical data. The 17'-H doublet in the 100 megacycle spectrum of the predominant adduct (3) shows additional fine splitting, $J = 1.5$ c.p.s., which is attributed to 1,3-cis coupling with the 16 β -proton (confirmed by double resonance measurements).⁽¹⁰⁾ Since $J_{16\beta,16'} = J_{16',17'} = 6$ c.p.s., the 16 β ,16' and 17' cyclobutane protons are assigned the all-cis arrangement as depicted in (3). In the case of the second adduct (4), the 17' proton does not show long-range coupling with the 16 β -proton and since $J_{16\beta,16'}$ and $J_{16',17'}$ are unequal, 9 and 6 c.p.s. respectively, it is inferred that the 16 β and 16' protons are trans related whereas the 16' and 17' protons are cis (see 4).^(11,12)

Prolonged treatment of (3) in methanol/chloroform containing dimethylaniline (10 days at 20°) eliminated acetic acid and afforded in 50% yield an unsaturated ketone identical in all respects with the third photolysis product. This establishes the structure of the latter as the 16'-acetylcyclobutene (5).⁽¹³⁾

The adduct (4) was unaffected by dimethylaniline at 20° while at elevated temperatures it gave a complex mixture of products. The behavior of (3) and (4) in the presence of dimethylaniline is consistent with the assigned stereochemistry, the altered reactivity of the latter adduct being attributed to the inaccessibility of the 16' proton to abstraction by base.

Adducts (3) and (4) are derived formally from cis (2), whereas the starting 1-acetoxybut-1-en-3-one contains ca. 90% of the trans isomer.⁽¹⁴⁾ Since irradiation of synthetic (2) leads to a mixture of cis and trans enones containing 30% of the former isomer, it is likely that the more reactive cis isomer is formed by photochemical isomerization of (2) prior to cycloaddition.

The high degree of orientational specificity observed in this cycloaddition suggests that (3) and (4) are derived from a precisely aligned complex of the reactants.⁽¹⁵⁾



Mechanistically, syn adducts are predicted from an oriented π complex of an $n \rightarrow \pi^*$ excited enone and a ground state enone (path A)⁽¹⁶⁾ or on the basis of the most stable radical intermediates (path B). In the present instance, we propose that the observed anti-orientation of (3) and (4) is the result of a polar ground state complex of the reactants (path C),⁽¹⁷⁾ which undergoes photo excitation followed by concerted bond formation. Work is in progress to clarify the mechanistic aspects of this reaction.

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12. This interpretation does not take into account the electronegativity effect of the 16' and 17' substituents on the cyclobutane proton coupling constants. Consequently, the assignment of stereochemistry to (4) cannot be made with certainty on the basis of J values alone. For a discussion of effect of electronegativity on J see P. Laszlo and P. Schleyer, J. Am. Chem. Soc., 85, 2709 (1963) and K. L. Williamson, ibid., 85, 516 (1963).
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16. This mechanism correctly predicts the orientation observed in the cycloaddition of enones to simple electron releasing olefins but probably "cannot be extended to the photodimerization of enones".⁽¹⁵⁾
17. It is interesting to note that a methanol solution of (1) and (2) exhibits an absorption maximum at 280 m μ . This may be due to a complex of the reactants since individual solutions of (1) and (2) at the same concentration are devoid of absorption at that wavelength.