

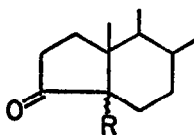
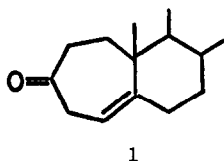
THE ROLE OF α -CLEAVAGE IN THE PHOTOCHEMISTRY OF A-HOMO-4A-CHOLESTENE-3-ONE
 STRUCTURE REVISION OF PHOTOPRODUCTS

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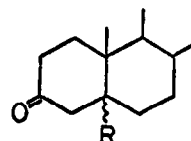
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Postulates for the mechanism of the singlet 1,3-acyl shift of β,γ -unsaturated ketones have ranged from concerted processes¹ to stepwise reactions involving either intimate radical pairs² or biradicals³ obtained from initial α -cleavage. Although there are examples of stereospecific 1,3-acyl migrations,² numerous β,γ -unsaturated ketones decarbonylate,⁴ form unsaturated aldehydes,^{2,3b,5} and undergo other radical-type processes.⁶ In order to study the chemistry of biradicals obtained by α -cleavage of β,γ -unsaturated ketones, we elected to examine the photochemistry of three compounds (1-3) which on α -cleavage could yield the same biradical. Fischer and Zeeh⁷ had examined the photochemistry of the A-homocholestenone 1 and reported that on direct irradiation 1 yielded a minor (MN) and major (MJ) photoproduct which they assigned (incorrectly, see below) as 2 and 3 respectively.



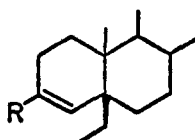
2, R = 5 β -vinyl
 3, R = 5 α -vinyl
 4, R = 5 α -ethyl
 5, R = 5 β -ethyl



7a, R = α -Me
 b, R = β -Me
 c, R = β -Et

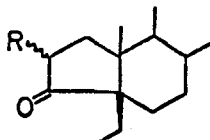
Since Fischer and Zeeh's structure assignments for 2 and 3 conflict with two interpretations (see below) of the observed photochemistry, a more rigorous structure determination was desirable. This was achieved by an unambiguous synthesis of 5 β -ethyl-A-norcholestanone (5). The 1,4-addition of lithium diethylcopper to Δ^4 -cholesten-3-one (6) yielded 5 β -ethylcholestan-3-one (7c) whose stereochemistry was assigned by the method of synthesis⁸ and a comparison of CD/ORD spectra (Table 1). The intermediate enolate from 6 and lithium diethylcopper was trapped with diethyl phosphochloridate⁸ yielding the enol phosphate 8. Reduction of 8 with lithium/ethyl amine in the presence of t-butanol⁸ yielded 9 which was ozonized

and oxidized to the diacid. 5 β -Ethyl-A-norcholestan-3-one (5) was prepared by esterification of the diacid followed by Dieckmann condensation to 10 (potassium t-butoxide/t-butanol), hydrolysis (HCl/HOAc) and decarboxylation. A comparison of 5 with dihydro-MJ showed them to be identical and quite different from the dihydro-MN. Therefore, the structure of MJ is 2 and MN is 3, reversing the previous assignment by Fischer and Zeeh.⁷



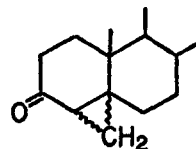
8, R = (EtO)₂P(O)-

9, R = H



10, R = CO₂Me

5, R = H



11a, 4 α , 5 α -methano

b, 4 β , 5 β -methano

Photolysis of 3 in t-butanol yielded 2 as demonstrated by isolation and spectroscopic comparison. No other photoproduct was observed by glpc conditions in which >2% of 1 would have been observed. The quantum yield for the formation of 2 from 3 was approximately one-third that of 2 and 3 from 1. These results, in conjunction with the absence of detectable quantities of 1 in the irradiation of 3, suggest that the reaction simply involves α -cleavage and recombination rather than the sequence 3 + 1 \rightarrow 2. However, 2 was photostable under conditions in which 90% of 3 is converted to 2. Irradiation of 2 and 3 in acetone lead in each case to the formation of 11a and 11b respectively.⁹ The stereospecificity of the observed oxa-di- Π -methane rearrangement and the failure to observe 2 (or 3) in the acetone sensitized irradiation of 3 (or 2) proves that triplet photoepimerization (α -cleavage) does not occur. These results indicate (1) that the conversion of 3 \rightarrow 2 in t-butanol is a singlet reaction¹⁰ and (2) that either 2 and 3 do not intersystem cross, or the oxa-di- Π -methane rearrangements are far less efficient than the epimerization of 3.

The conversion of 3 \rightarrow 2 must involve α -cleavage and recombination of the resulting biradical. However, 2 did not isomerize to either 3 or 1 and thus was remarkably photostable. (See eq. 1.) Three postulates can be advanced to explain these results. First,



Table 1. CD and ORD Data

Comp'd.	CD, θ , nm [ORD, ϕ nm]	Comp'd.	CD, θ , nm
7a	[+4000 (370) ^{a,d}]	4	- 4,200° (295) ^{b,d}
7b	- 950° (290) ^e	5	+ 2,620° (305) ^e
7c	- 1,075° (290) ^e	12a	+ 6,310° (305) ^{c,e}
2	+10,000° (300) ^e	12c	+ 2,177° (305) ^{c,e}
3	-13,400° (300) ^{b,d}		

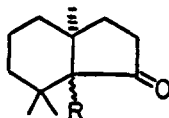
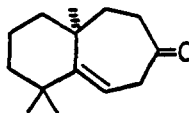
^aW. Nagata, S. Hirai, H. Itazaki and K. Taketa, *Justus Liebigs Ann. Chem.* **641**, 184 (1961).

^bRef. 7. ^cA generous sample of 12 was supplied by Dr. G. Shaffer. ^d95% EtOH as solvent.

^eMeOH as solvent.

the nature of the A-B ring fusion in these A-nor steroids could markedly affect the rate of α -cleavage. Yang has suggested¹³ that relief of steric strain at the transition state increases the rate of α -cleavage in trans-8-methyl-1-hydrindanone relative to the cis isomer. Second, the ring closure of biradical intermediates may be stereoelectronically controlled. For example, Yang¹³ has examined the stereochemistry of ring closure of biradicals derived from saturated bicyclic ketones and concluded that these intermediates exhibit a preference for axial ring closure. Third, the mode of ring closure may instead reflect some conformational preference of the intermediate biradicals. The failure of either 2 or 3 to yield 1 may be due to the much greater ease of formation of a five membered ring relative to a seven-membered one.

The observation of the photolability of 3 compared to 2 can be used to assign the stereochemistry of the photoproduct (12a or 12b) obtained from the photolysis of 13 by G. W. Shaffer.¹⁴ Shaffer reported that this photoproduct was fairly stable when irradiated in isopropanol yielding 5-10% of a compound whose retention time was identical to 13. These results strongly suggest that the stereochemistry at the ring junction is cis, i.e. 12a. This conclusion is also supported by a comparison of the c.d. spectrum of 12a and

12a, R = α -vinylb, R = β -vinylc, R = α -ethyl

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12c with those of 2-5, (Table 1).

In addition to the structure revision of the photoproducts, we have found (1) the first example of singlet photoepimerization of a β,γ -unsaturated ketone; (2) that the singlet α -cleavage and recombination is a highly stereoselective process; (3) the absence of triplet α -cleavage for 2 and 3; and (4) support for formation of 2 from 1 via either a concerted path or intimate radical pair but not via a long lived biradical.

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- (10) The multiplicity from which photoepimerization occurs in this work differs from that of Chambers and Marples¹¹ who noted triplet (but not singlet) epimerization for a steroid β,γ -unsaturated ketone. However Schaffner et al.^{1b,12} have also failed to observe triplet α -cleavage in two cases under conditions where α -cleavage would have been observable.
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