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STEREOSPECIFICITY IN THE PHOTOISOMERIZATION OF STEROIDAL α-KETOLS TO LACTONES

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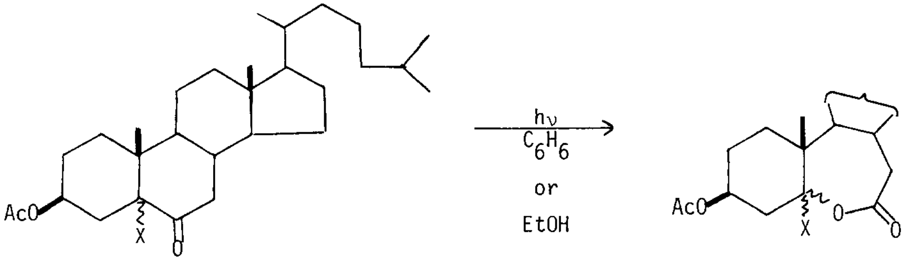
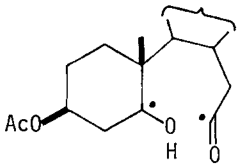
Abstract: The photoisomerization of 5-hydroxy-6-cholestanones to lactones involves ketene intermediates formed by migration of H-7α; its stereospecificity is independent of hydrogen bonding and is attributed to slowing of rotation about the C-9 - C-10 bond in the alkyl acyl diradicals that are the ketene precursors.

Cookson *et al.*[1] have reported that ultraviolet irradiation of the epimeric α-ketols 1 and 2 in benzene or ethanol results in their stereospecific isomerization to the lactones 3 and 4, respectively. These observations are of considerable interest in terms of the generally accepted mechanism for reactions of this kind, which involves the intermediacy of alkyl acyl diradicals and ketenes of types 5 and 6.[2] In these terms the stereospecificity of the reactions implies that the alkyl radical centre in 5 retains its configuration in the course of hydrogen transfer to give 6. We have investigated further the photochemistry of 1 and 2 and related compounds with the object of obtaining additional insights into this unusual stereospecificity.



1 X = α-OH
2 X = β-OH

3 X = β-H
4 X = α-H



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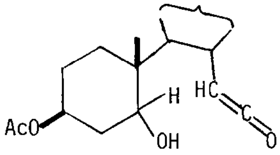

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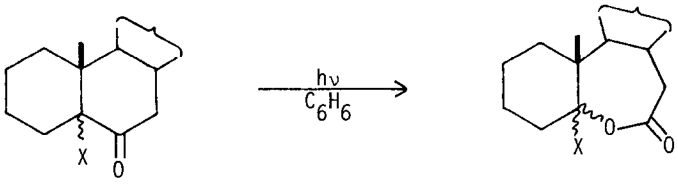
Repetition of the earlier photolyses of 1 and 2 and examination of the reaction products by high performance liquid chromatography confirmed the stereospecificity of the reactions. Photolysis of the epimeric α-ketols 7 and 8 in benzene was shown to lead stereospecifically to the lactones 9 and 10,[3] respectively, establishing that the 3-substituent in 1 and 2 plays no role in the stereospecificity of their photoisomerization reactions. Irradiation of 11, the O-methyl ether of 1, in ethanol also proceeded with complete stereoselectivity to give the ester 12,[4] the analogue of 3. This last result indicates that hydrogen-bonding in diradicals 5 derived from the α-ketols 1 and 2,[5] is not a crucial factor in the stereospecific photoisomerization of the latter.

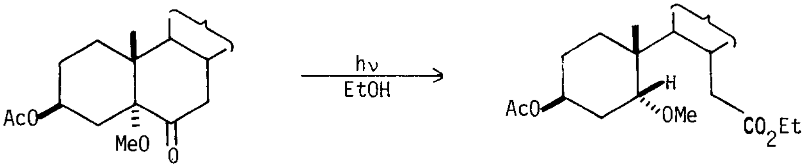


7 X = α-OH

8 X = β-OH

9 X = β-H

10 X = α-H



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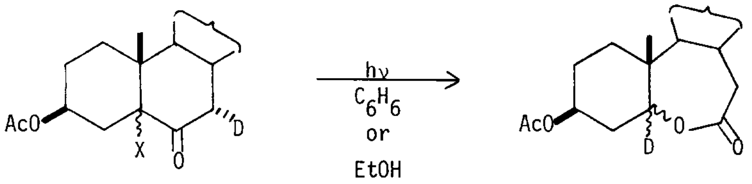
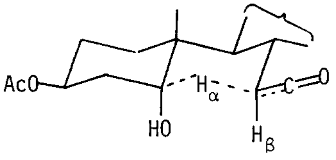
To explore the photoisomerization further the deuterium-labeled compounds 13 and 14[6] were irradiated in benzene and in ethanol. The products were 15 and 16, respectively, in either solvent; these results show that it is the 7α-hydrogen of 1 and 2 that is transferred in the conversion of 5 to 6. Similar stereoselective hydrogen transfer has been observed in the photolyses of carvonecamphor[7] and ent-3-ketobeyeran-17-oic acid.[8] These observations may suggest that the ketenes 6 are formed from the diradicals 5 via favoured transition states 17 and 18, wherein transfer of the original 7α-H of 1 and 2 to the alkyl radical centre of 5 occurs much more rapidly than does ring inversion of ring A in 5, which would result in loss of stereospecificity. Alternatively, if hydrogen transfer takes place faster than rotational equilibration to the favoured transition state, the stereospecific hydrogen transfer may simply reflect the initial motion of the carbonyl group upon α-cleavage.[9] It is also interesting that irradiation of the O-deuterio compounds 19 and 20 in benzene proceeds with some stereoselection to give 21 (7aβ-D; 7aα-D = 3:1) and 22 (7aβ-D; 7aα-D = 1:9), respectively.



13 X = α-OH
14 X = β-OH

15 X = β-D
16 X = α-D



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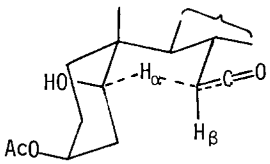

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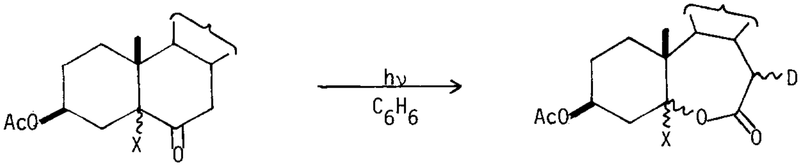
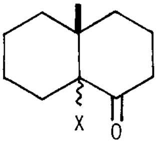


19 X = α-OD
20 X = β-OD

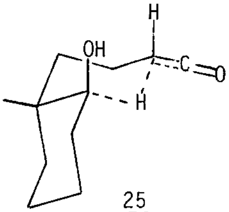
21 X = β-H
22 X = α-H

We have also found that the corresponding photoreactions of the bicyclic α-ketols 23 and 24 do not show the stereospecificity observed in the cases of 1 and 2. The lack of stereospecificity in the reactions of 23 and 24 suggests that the stereospecific reactions of 1 and 2 do not involve concerted formation of ketenes of type 6 from their excited states.[10] We propose that this difference between the steroidal and bicyclic ketols may have its origin in two factors. First, in the steroids, rings C and D slow rotation about the C-9 - C-10 bond, keeping H-7α in the vicinity of C-5 and thus favouring rapid hydrogen transfer without inversion of C-5. Second, in the cases of 23 and 24 a transition state of type 25 with the non-steroid *cis* conformation may be involved.



23 X = α-OH

24 X = β-OH



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