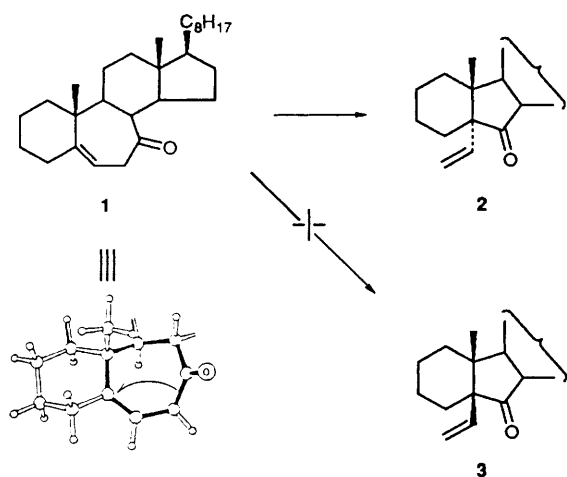


Photoinduced Molecular Transformations. Part 126.¹ Photo-Double Ring Contraction of 4 α -Homo-5 α -cholest-3-en-1-one,[†] a Steroidal β,γ -Unsaturated Cyclic Ketone, involving Photochemical 1,3-Acyl Migration

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Both direct and sensitized irradiation of 4 α -homo-5 α -cholest-3-en-1-one in *tert*-butyl alcohol with Pyrex-filtered light resulted in a photorearrangement to 1 α -vinyl-3,4-bisnor-5 α ,10 α -cholestane *via* a photochemical 1,3-acyl shift, followed by a photochemical loss of carbon monoxide from the resulting 2 α -vinyl-4-nor-5 α -cholestan-1-one.

In a previous paper,² we reported that the stereochemistry of products derived from photochemical 1,3-acyl shifts³ of some steroidal β,γ -unsaturated cyclic ketones depends upon the conformation of the ground state of the starting unsaturated ketones. For example, the direct irradiation of 7 α -homocholest-5-en-7 α -one **1** in *tert*-butyl alcohol with Pyrex-filtered light resulted in a conformation-specific photorearrangement to 5-vinyl-7-nor-5 α -cholestan-6-one **2**; only this product arose from an excited singlet state of the β,γ -unsaturated ketone and none of its 5 β -epimer **3** was formed (see Scheme 1).²

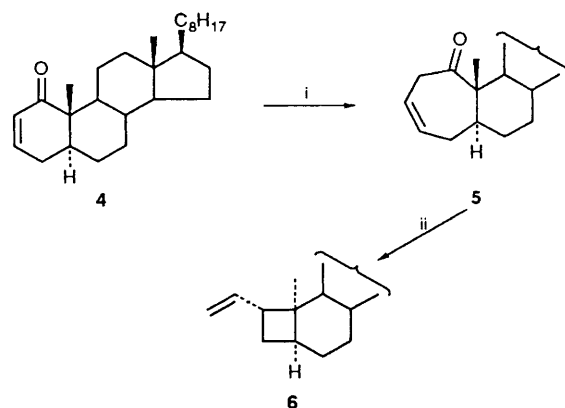


Scheme 1

In order to further confirm the validity of this conformational dependence of the stereochemistry of photochemical 1,3-acyl shifts of the β,γ -unsaturated cyclic ketone, we synthesized 4 α -homo-5 α -cholest-3-en-1-one **5** and investigated the stereochemistry of its photochemical 1,3-acyl shift. We found that the photolysis of the β,γ -enone **5** gave a 3,4-bisnorsteroid **6**, arising from a double ring contraction involving a photochemical 1,3-acyl shift.

Results and Discussion

Synthesis of 4 α -Homo-5 α -cholest-3-en-1-one 5.—The β,γ -unsaturated ketone **5** was prepared by a ring expansion of 5 α -cholest-2-en-1-one **4**. Thus, treatment of 5 α -cholest-2-en-1-one **4**⁴ with diazomethane in the presence of aluminium chloride^{5,6} in benzene–diethyl ether for 1 h gave 4 α -homo-5 α -cholest-3-en-1-one **5** in an 11% yield.



Scheme 2 Reagents and conditions: i, CH₂N₂–AlCl₃–benzene–diethyl ether; ii, *hν* > 300 nm, Bu'OH

Direct Irradiation of 4 α -Homo-5 α -cholest-3-en-1-one 5 in *tert*-Butyl Alcohol (Scheme 2).—The UV spectrum of the β,γ -unsaturated ketone **5** in ethanol exhibited an absorption maximum at 290 nm (ϵ 66) assignable to the $n \rightarrow \pi^*$ transition. Photolysis of the ketone **4** in *tert*-butyl alcohol using a 450 W high-pressure Hg arc through a Pyrex filter in an atmosphere of nitrogen gave a major product **6** in 37% yield. Its molecular formula was established as C₂₈H₄₆O by means of high-resolution mass spectrometry. The IR spectrum showed an absence of any carbonyl absorption, but exhibited a series of bands assignable to a vinyl group at 1638, 995 and 909 cm⁻¹. The ¹H NMR spectrum included a series of signals attributable to a vinyl group (see Experimental section for details). These spectral results in conjunction with the probable products which may arise from 1,2- and 1,3-acyl shifts suggested that the product was 1-vinyl-3,4-bisnor-5 α -cholestane **6** derived from a photochemical 1,3-acyl shift followed by photochemical decarbonylation. The *cis* disposition of the 1-vinyl group and the 10-methyl group was established on the basis of the following results from nuclear Overhauser enhancement (NOE) measurements. Thus, irradiation of a signal at δ 0.86 due to the 10-Me caused an enhancement of the areas of the signals at δ 1.92 (2 α -H in the methylene envelope). Irradiation of a signal at δ 2.52 (1 β -H) caused an enhancement of the areas of the signals at δ 5.83 (1'-H_A) and at δ 1.90 (2 β -H in the methylene envelope). Of the two structures (1 α -vinyl-3,4-bisnor-5 α , 10 α -cholestane **6** and 1 β -vinyl-3,4-bisnor-5 α -cholestane **7**) which are consistent with these spectral results, the former was assigned for product **6** based on a consideration of the genesis of its formation (*vide infra*).

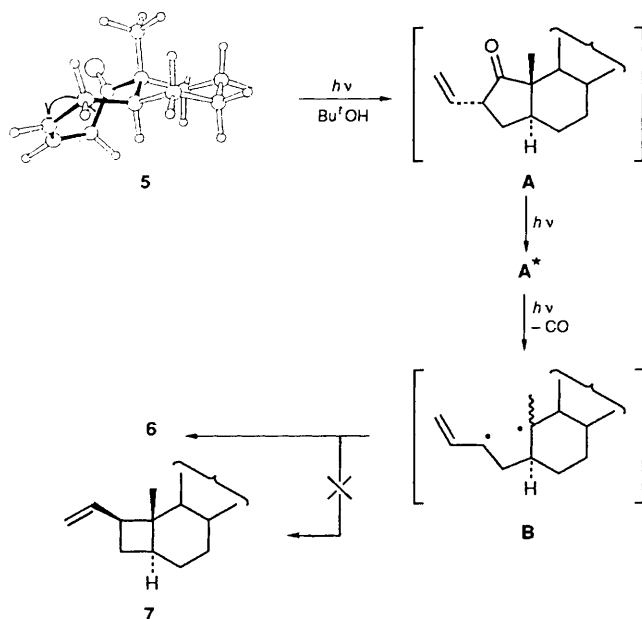
Sensitized Irradiation of 4 α -Homo-5 α -cholest-3-en-1-one 5.—

[†] Nomenclature according to 1989 I.U.P.A.C. recommendations: *Pure Appl. Chem.*, 1989, **61**, 1783.

The photolysis of the enone **5** in the presence of either benzophenone or Michler's ketone in *tert*-butyl alcohol similarly gave the steroidal cyclobutane **6** in 21 and 20% yields. An examination of the products indicated that no product due to a photochemical 1,2-acyl shift was formed in this sensitized photolysis. The sensitized photolysis of the enone **5** in acetone gave only an intractable mixture of products.

Probable Path leading to the Steroidal Cyclobutane 6.—The formation of a cyclobutane ring, such as that in product **6**, in the photolysis of β,γ -unsaturated steroidal ketone is unprecedented.

Scheme 3 outlines the probable genesis of product **6**. Thus, a



Scheme 3

photochemical 1,3-acyl shift first forms A/B *trans*-5 α -cholestan-1-one **A**. In our previous paper,² we reported that the stereochemistry of the products of a 1,3-acyl shift in photo-rearrangements of β,γ -unsaturated enones depends upon the conformation of the ground state of the starting β,γ -unsaturated steroidal ketones; the ratio of the stereoisomers of the products was found to depend on the ground-state population of the conformers of the starting unsaturated ketones. In a previous paper² we also showed that the predominant conformation of the β,γ -enone **5** obtained by means of empirical force-field calculations is a boat conformation (91.76%), as shown by an ORTEP drawing in Scheme 3. The conformation-specific photochemical 1,3-acyl shift should, therefore, first give 1- α -vinyl-A/B *trans*-5 α -cholestan-1-one **A** (see Scheme 3).

A subsequent photochemical decarbonylation^{7,8,9} generates a biradical **B**, the cyclization of which gives a more stable A/B *cis*-fused bisnorsteroid **6** rather than an A/B *trans* isomer **7**. We were unable to isolate the intermediate **A** arising from a conformation-specific 1,3-acyl shift. Photochemical decarbonylation in this system should thus be especially facile, since the formation of the biradical is assisted by the vinyl group and the carbon substituted by three alkyl groups.

Experimental

M.p.s were determined using a Yanagimoto micro m.p. apparatus. IR spectra were determined for Nujol mulls with a JASCO IR 810 infrared spectrophotometer. ¹H NMR spectra

were determined in CDCl₃ (SiMe₄ as internal reference) with a JEOL ES-400 spectrometer operating at 400 MHz. *J* Values are in Hz. High- and low-resolution mass spectra were recorded with a JEOL JMS-DX 303 mass spectrometer at the Faculty of Pharmaceutical Sciences of this university. PLC was carried out on Merck silica gel 60 PF₂₅₄ (Art. 7749). The photolysis was carried out in a Pyrex tube with a 450-W high-pressure Hg arc lamp (Ushio).

5 α -Cholest-2-en-1-one 4⁴.—This α,β -unsaturated ketone was prepared according to a reported procedure; m.p. 70–74 °C (acetone) [lit.,^{4a} m.p. 69–70 °C (methanol); lit.,^{4b} m.p. 58–60 °C (dichloromethane–methanol)].

Synthesis of 4 α -Homo-5 α -cholest-3-en-1-one 5.—To a cooled, stirred solution (an ice-salt bath) of 5 α -cholest-2-en-1-one **4** in benzene–diethyl ether (1:1) a solution of diazomethane [prepared from nitrosomethylurea (1.5 g) in diethyl ether–40% aq. potassium hydroxide (8 ml) and dried over potassium hydroxide pellets]¹⁰ was added dropwise; powdered aluminium chloride (25 mg) in five portions was also added during the course of 50 min. The mixture was stirred for an additional 10 min at 0–5 °C according to the published procedure for a similar ring-enlargement reaction.^{5,6} The solvent was then removed under reduced pressure to give a residue (1.211 g) which was subjected to column chromatography on silica gel (25 g, Merck No. 7734, 30:1 hexane–ethyl acetate). The first fraction was the starting enone (350 mg). The second fraction was a crystalline 4 α -homo-5 α -cholest-3-en-1-one **5**, which was recrystallized from ethanol to give a pure material (95 mg, 11.3% based on a consumed starting material), m.p. 102–103 °C (Found: C, 84.2; H, 11.65. C₂₈H₄₆O requires C, 84.35; H, 11.63%); $\nu_{\max}/\text{cm}^{-1}$ 1705 (CO) and 1652 (C=C); λ_{\max} (ethanol)/nm 290 (ϵ 66); δ 0.64 (3 H, s, 18-H), 0.86 (6 H, d, *J* 6.6, 27-H and 28-H), 0.88 (3 H, d, *J* 6.2, 21-H), 2.12–2.13 (2 H, m, 4 α -H), 2.68 (1 H, dd, *J* 13.1 and 8.3, 2 β -H), 3.76 (1 H, ddd, *J* 13.1, 2.5 and 1.8, 2 α -H), 5.52–5.65 (2 H, m, 3 H and 4-H); *m/z* 398 (M⁺, 0.9), 383 [(M – Me)⁺, 1.4], 370 [(M – CO)⁺, 44.7], 355 [(M – Me – CO)⁺, 12.4] and 316 [(M – C₅H₆O)⁺, 100%].

Photolysis of 4 α -Homo-5 α -cholest-3-en-1-one 5.—A solution of the enone **5** (104 mg) in *tert*-butyl alcohol (30 ml) in a Pyrex tube was irradiated with a 450-W high-pressure Hg arc under an atmosphere of nitrogen for 17 h according to a previously reported method.² The solvent was removed under reduced pressure to give an oily product (109 mg) which was subjected to PLC (silica gel–hexane) to afford three fractions. The most mobile fraction [24 mg, 23% (37% based on the consumed enone)] was an oily 1 α -vinyl-3,4-bisnor-5 $\alpha,10\alpha$ -cholestane **6** (Found: M⁺, 370.3624. C₂₈H₄₆O requires *M*, 370.3599); $\nu_{\max}/\text{cm}^{-1}$ 1638, 995 and 909 (CH=CH₂); δ 0.63 (3 H, s, 18-H), 0.86 (6 H, d, *J* 6.6, 27-H and 28-H), 0.87 (3 H, s, 19-H), 0.89 (3 H, d, *J* 6.3, 21-H), 2.52 (1 H, ddd, *J* 9.3, 7.9 and 6.4, 1 β -H), 4.91 (1 H, ddd, *J* 17.1, 2.4 and 1.4, 2'-H_c), 4.94 (1 H, ddd, *J* 10.5, 2.4 and 1.0, 2'-H_b) and 5.83 (1 H, ddd, *J* 17.1, 10.5 and 6.4, 1'-H_a); *m/z* 370 (M⁺, 39), 355 [(M – Me)⁺, 18], 316 [(M – C₄H₆)⁺, 100%] and 301 [(M – C₄H₆ – Me)⁺, 29].

The second fraction (4 mg) was an intractable mixture.

After these mobile fractions had been removed from the TLC plate, the plates were developed again with hexane–ethyl acetate (30:1) to give the 3rd and 4th fractions. The more mobile 3rd fraction (3 mg) was an intractable oily product and the 4th fraction (35 mg) was the starting enone **5**.

Photolysis of 4 α -Homo-5 α -cholest-3-en-1-one 5 in the Presence of Benzophenone or Michler's Ketone.—A solution of the enone **5** (12 mg, 0.03 mmol) and benzophenone (0.4 mg, 0.002 mmol) in dry *tert*-butyl alcohol (5 ml) in a Pyrex vessel was irradiated

for 10 h with a 100-W high-pressure mercury arc in a nitrogen atmosphere. Evaporation of the solvent gave a residue which was subjected to PLC (benzene) to give two major and four minor fractions. The more mobile fraction (1.9 mg, 17%, 21% based on the consumed enone) was a cyclobutane derivative **6**. The less mobile fraction (2.3 mg, 19%) was the starting material.

Similar photolysis of the enone **5** in the presence of Michler's ketone instead of benzophenone as a sensitizer for 10 h gave the bisnorsteroid **6** in 16% yield (20% based on the consumed enone) and recovered enone **5** in 20% yield.

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