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The Photoinduced Removal of Nitro Groups from Steroidal 6-Membered α,α′-Dinitro Cyclic Ketones[1)]

Hiroshi SUGINOME* and Yoshitaka KUROKAWA
Organic Synthesis Division, Department of Chemical Process Engineering,
Faculty of Engineering, Hokkaido University, Sapporo 060
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2,4-Dinitro-5α- and 5β-cholestan-3-ones were prepared by dinitration of the parent 3-ones by a modified standard method. Spectroscopy indicated that in ethanol these α,α′-dinitro ketones exist in their enol forms. Photolysis of these dinitro ketones in ethanol gave diosphenols arising from the removal of their two nitro groups. On the basis of the results of the irradiation of hypothesized intermediate obtained by synthesis, we suggest the path likely to lead to the removal of the nitro groups.

In our previous paper,[2)] we reported the results of the photoreaction of several steroidal 6-membered cyclic α-nitro ketones in ethanol. The investigation disclosed that steroidal 6-membered cyclic α-nitro ketones, which exist in ethanol in their enol form, give the corresponding α-hydroxyimino ketones arising from a hydrogen abstraction by the excited nitro group and the corresponding α-diketone arising from the nitro-nitrite rearrangement, while irradiation of 6-membered cyclic α-nitro ketones, which exist in ethanol in their keto forms, gave the corresponding α-hydroxyimino ketones without any accompanying formation of the corresponding α-diketones. An anomalous formation of 5α-cholestane-2,3-dione was found when 2-nitro-5α-cholestan-3-one, which in ethanol exists exclusively in its enol form was photolyzed. We then suggested the probable paths for the formation of all these products in the photolysis.

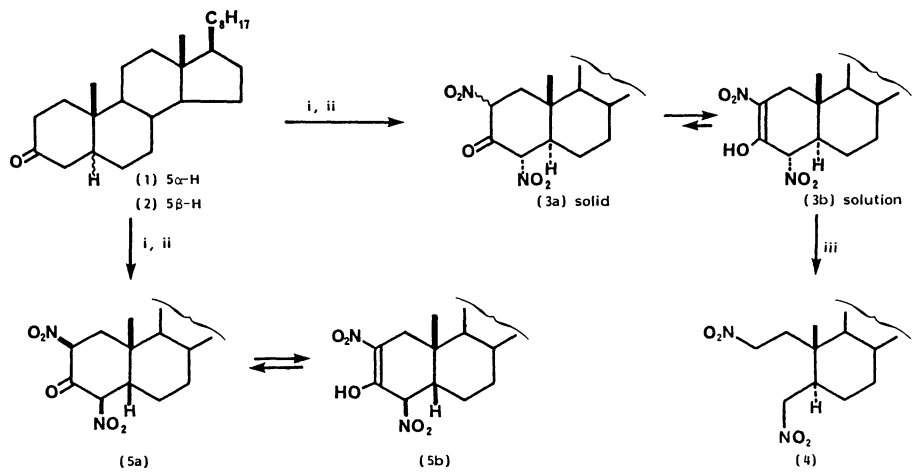
In this paper, we wish to report the results of the photoreaction of two steroidal 6-membered cyclic α,α′-dinitro ketones, 2,4-dinitro-5α-cholestan-3-one (**3**) and its 5β-epimer (**5**).

Preparation of the α,α′-Dinitro Ketones 3 and 5. The α,α′-dinitro ketones **3** and **5** chosen for the present study were prepared by α,α′-dinitration of 5α-and 5β-cholestan-3-one (**1** and **2**) with alkyl nitrate and potassium *t*-butoxide in *t*-butyl alcohol.[3)]

We found that the potassium salts of 2,4-dinitro-5α-cholestan-3-one (**3**) and 2,4-dinitro-5β-cholestan-3-one (**5**) readily gave the corresponding α,α′-dinitro ketones **3** and **5** with no accompanying formation of α,ω-secosteroids when the *dried* potassium salts dissolved in glacial acetic acid were poured into a large volume of iced water instead of being treated with HCl in a diethyl ether suspension.[3)] On the other hand, we found that the above treatment of the potassium salts contaminated with water led to the formation of α,ω-dinitro secosteroids[3-5)] (e.g., **4**).

We also found that the α,α′-dinitro ketone **3** is readily hydrolysed to α,ω-dinitro alkanes when **3** is heated in acetic acid-water under reflux for 3 h, is passed through a silica-gel column,[4)] or is subjected to preparative TLC on silica gel.

The IR spectrum of α,α′-dinitro-5α-cholestan-3-one (**3**) in Nujol indicated that in the mull it exists in a keto form **3a**. Its ^{1}H NMR spectrum in $CDCl_3$, however, exhibited two doublets at δ 2.32 and 2.78 (J=16.6 Hz) and a doublet at δ 5.08 (J=11.2 Hz) assignable to the C-1 methylene and the 4β-H of the enol form, 2,4α-dinitro-5α-cholest-2-en-3-ol (**3b**). The IR spectrum of



i) $CH_3CH_2CH_2ONO_2$-$(CH_3)_3COK$ ii) CH_3COOH iii) CH_3COOH-H_2O-reflux or SiO_2-H_3O^+

Scheme 1.

the solution ($CHCl_3$) and the UV spectra (hexane or ethanol) also indicated that in the solution it exists entirely in the enol form **3b**.

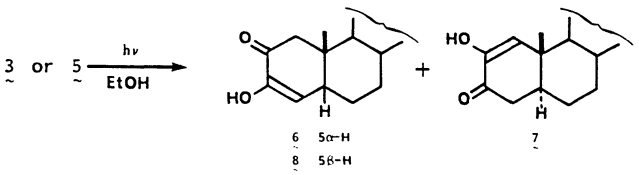
In contrast to the behavior of α,α'-dinitro-5α-cholestan-3-one (**3**), the IR spectrum of the 5β-epimer **5** in Nujol indicated that in the mull its keto and enol forms are in equilibrium. ^{1}H NMR spectrum of **5** in $CDCl_3$ exhibited a series of signals assignable both to the keto form, 2β,4β-dinitro-5β-cholestan-3-one (**5a**) and to the enol form, 2,4β-dinitro-5β-cholest-2-en-3-ol (**5b**). The ratio of the signal areas indicated that the ratio of the two forms was approximately 1 to 1 in $CDCl_3$ (see Experimental).

Photochemistry of α,α'-Dinitro-5α- and 5β-cholestan-3-ones (3 and 5). The photolysis of the two nitro ketones **3** and **5** was carried out in ethanol and in *t*-butyl alcohol under the conditions established for 6-membered cyclic α-nitro ketones reported in our previous paper.[2]

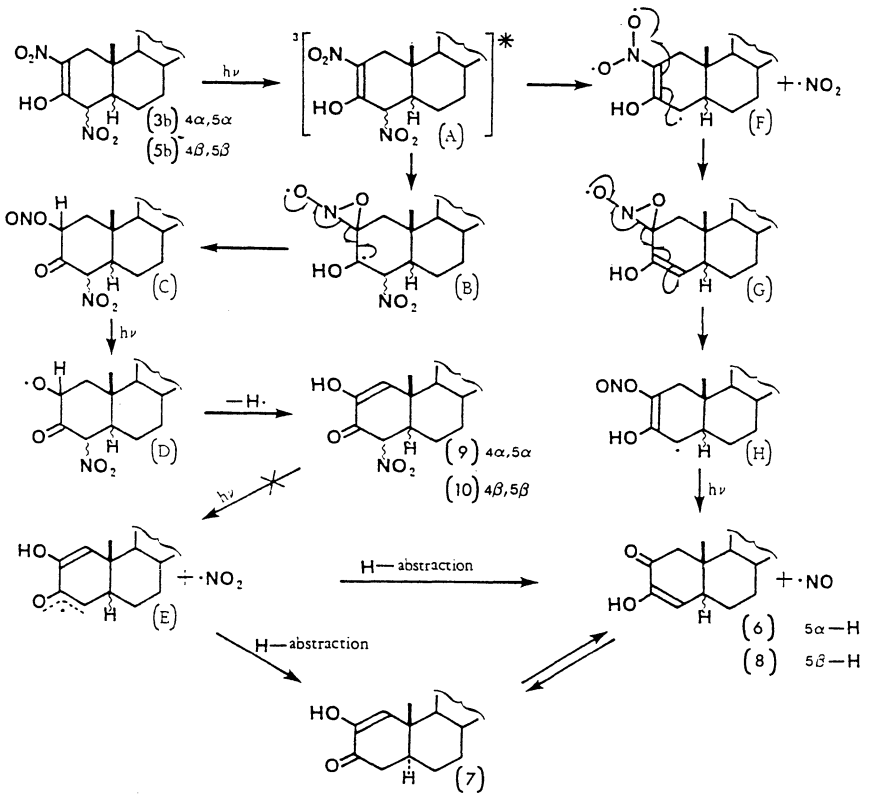
Photolysis of 2,4α-dinitro-5α-cholest-2-en-3-ol (**3b**) in ethanol with a Hanovia 450-W high-pressure mercury arc through a Pyrex filter in an atmosphere of nitrogen gave a product mixture from which a mixture of diosphenols, 3-hydroxy-5α-cholest-3-en-2-one **6** and its isomer **7**[2] was obtained in a 55% yield. Its purification by means of preparative TLC gave a 1 : 1 crystalline mixture of **6** and **7**. Essentially the same results were obtained when the photolysis was carried out in a less hydrogen-donating protic solvent, *t*-butyl alcohol.

Similar photolysis of an equilibrium mixture of 2β,4β-dinitro-5β-cholestan-3-one (**5a**) and 2,4β-dinitro-5β-cholest-2-en-3-ol (**5b**) gave a product in a 48% yield. Spectroscopy confirmed that the structure of the crystalline produt **8** was 3-hydroxy-5β-cholest-3-en-2-one (**8**). The diosphenol has been prepared by Sandmeier and Tamm only as a mixture of diosphenol **8** and 2-hydroxy-5β-cholest-1-en-3-one.[6]

The photochemistry of cyclic α,α'-dinitro ketones has never previously been reported.[7,8] Our present experiments show that the photolysis of α,α'-dinitro ketones in alcohol results in the efficient removal of the two nitro groups to give the corresponding α-diketones. Two probable paths leading to the α-diketones are outlined in Scheme 3. Thus, the first probable path would involve the removal of the 2-nitro group from an excited nitro ketone **A** through the species B, C, and D through a nitro nitrite rearrangement[8,9] to give 4-nitro-2,3-diketone **9** as in the case of the 6-membered cyclic α-nitro ketones reported in our previous paper.[2] A photoinduced homolysis of the C–N bond of 4-nitro-2,3-diketone **9** followed by the



Scheme 2.



Scheme 3.

hydrogen abstraction from the solvent might then give the α-diketones **6**, **7**, and **8**.

A second possible path, on the other hand, would involve an initial homolysis of the C-N bond[10] of the 4-nitro group to give a nitrite radical **H** through an oxaziridine **G**. The homolysis of the C-N bond is considered to be especially facile since the generated species **F** is a stabilized allylic radical. In order to distinguish these two paths, we prepared 2-hydroxy-4α-nitro-5α-cholest-1-en-3-one **9** and carried out its photolysis.

Thus, nitration of 5α-cholestane-2,3-dione with butyl nitrate and potassium *t*-butoxide in THF gave mononitro-5α-cholestane-2,3-dione **9** in a 30% yield. The IR, NMR, and mass spectra confirmed that the structure was the desired 2-hydroxy-4α-nitro-5α-cholest-1-en-3-one (**9**). The IR spectra exhibited two bands at 1695 and 1648 cm^{-1} assignable to the α,β-unsaturated carbonyl group and a strong band at 1560 cm^{-1} due to the unconjugated nitro group. The ^1H NMR spectrum exhibited a singlet (1H) at δ 6.60 assignable to the proton attached to the C-1 and a doublet at δ 5.29 with J=13.55 Hz assignable to the 4β-proton.

We found that nitro ketone **9** is recovered unchanged when it is subjected to photolysis in ethanol for 3 h under the same conditions established for the photolysis of α,α′-dinitro ketone **3**. The result excludes the first path involving the intermediates **C** and **D** in the formation of α-diketones **6**, **7**, and **8**. The α-diketones are therefore very likely to be formed through intermediates **F**, **G**, and **H**, whose formations are triggered by the homolysis of the C_4-NO_2 bond.

Experimental

For the instruments used and the general procedure see Ref. 2.

Preparation of 2ξ,4α-Dinitro-5α-cholestan-3-one (3). Freshly sublimed potassium *t*-butoxide (4.0 g) was dissolved by heating in dry *t*-butyl alcohol (68 ml) in a nitrogen atmosphere. The solution was cooled to 19 °C and 5α-cholestan-3-one (**1**) (2.0 g) was dissolved in it. To the solution propyl nitrate (4 ml) was added over the course of 10 min and the solution was stirred for 20 h at 18—20 °C, after which the solution was poured into iced water. The separated potassium salt of dinitrocholestane was filtered off and dried. The yield of potassium salt was 2.468 g. The potassium salt was dissolved in glacial acetic acid and the solution was poured into iced water. The separated crystals of 2,3-dinitro-5α-cholestan-3-one (**3**) (2.3 g) were collected by filtration and recrystallized from ethyl alcohol. Mp 199—201 °C. IR (Nujol) 1737 (C=O) and 1558 cm^{-1} (NO_2); IR ($CHCl_3$) 1642 (C=C) and 1562 (4α-NO_2) and 1530 (br, 2-NO_2); (Found: C, 67.90; H, 9.37; N, 5.70%; Calcd for $C_{27}H_{44}N_2O_5$: C, 67.90; H, 9.31; N, 5.88%); UV (hexane), λ_{max} 308.5 nm (ε; 5790); (ethanol), 353 nm (ε; 8570); (ethanol and 1 equiv mol of sodium ethoxide), 345.5 nm (ε; 12170); ^1H NMR ($CDCl_3$), δ=0.67 (3H, s, 18-H), 0.87 (3H, s, 19-H), 2.32 (1H, d, J=16.60 Hz, 1-H), 2.78 (1H, d, J=16.60 Hz, 1-H), and 5.08 (1H, d, J=11.23 Hz, 4β-H); MS m/z (rel intensity) 476 (M^+, 87.8%), 430 (M^+-NO_2, 13.3), 322 (73.8), 321 (91.4), 69 (86.8), 57 (96.4), 55 (97.2), and 43 (100).

2,4-Dinitro-2,3-seco-*A*-nor-5α-cholestane (4). 2,4-Dinitro-5α-cholestan-3-one (**3a**) (50 mg) dissolved in glacial acetic acid (17 ml) and water (6 ml) was heated under reflux for 3 h. After the addition of hot water, the solution was extracted with dichloromethane three times. The combined solution was washed with water several times and dried over anhydrous sodium sulfate. The usual work-up gave a dinitro compound (63 mg), mp 165—169 °C. (lit,[5] 169—172 °C). UV, λ_{max} (EtOH) 277 nm (ε; 64); MS m/z (rel intensity) 450 (M^+, 23.8), 433 (M^+-NO_2, 9.8), 420 (19.8), 402 (15.5), 329 (18.3), and 55 (100%).

Preparation of 2,4-Dinitro-5β-cholestan-3-one (5a). Freshly sublimed potassium *t*-butoxide (3.0 g) was dissolved by heating in dry *t*-butyl alcohol (50 ml) in a nitrogen atmosphere. The solution was cooled to 20 °C and 5β-cholestan-3-one (**2**) (1.5 g) was added. To the solution, propyl nitrate (2 ml) was then added over a period of 10 min. More propyl nitrate (1 ml) was added after 30 min and the solution was stirred for 15 h at 16—20 °C. The solution was poured into iced water, and the mixture was made acidic (pH 3) with acetic acid. The orange colored precipitates were collected by filtration. The dried precipitates (2.0 g) were dissolved in glacial acetic acid (150 ml) and iced water (300 ml) was added to the solution. The colorless solid (1.83 g) was collected by filtration and dried. The dinitro ketone **5a** was recrystallized from ethanol to give crystals (698 mg, 37.2%), mp 177—179 °C. (Found: C, 68.03; H, 9.31; N, 5.85%. Calcd for $C_{27}H_{44}N_2O_5$: C, 68.03; H, 9.31; N, 5.88%); UV (EtOH) 353 nm (ε; 1060); IR (Nujol) 1751 (C=O) and 1655 (C=C) and 1548 (NO_2); ^1H NMR; the keto form, δ=0.66 (s, 18-H), 1.19 (s, 19-H), 5.33 (dd, J=12.4 and 5.12 Hz, 2α-H), and 5.58 (d, J=10.25 Hz, 4α-H), the enol form, 0.69 (s, 18-H), 1.26 (s, 19-H), 2.31 (d, J=17.09 Hz, 1-H), 3.08 (d, J=17.09 Hz, 1-H), and 5.71 (d, J=12.7 Hz, 4α-H); MS m/z (rel intensity) 476 (M^+, 18.7), 430 (M^+-NO_2, 31.9), 412 (19.5), 383 (36.4), 57 (100), and 55 (99.0%).

Photolysis of 2ξ,4α-Dinitro-5α-cholestan-3-one (3). (a) In Ethanol. α,α′-Dinitro ketone **3**, (300 mg, 0.63 mmol) in absolute ethanol (450 ml) was irradiated for 3 h with a Hanovia 450-W high-pressure mercury arc through a Pyrex filter in an atmosphere of dry nitrogen. Removal of the solvent under reduced pressure gave an oily residue (325 mg) which was subjected to preparative TLC with dichloromethane to give a mixture of diosphenols **6** and **7** (139 mg, 55.2%). This mixture was again purified by means of preparative TLC to give diosphenols (59 mg, 23.5%). This was recrystallized from methanol-water to give crystals of a 1 : 1 mixture of **6** and **7** (32 mg, 12%), mp 119—155 °C.

(b) In *t*-Butyl Alcohol. α,α′-Dinitro ketone **3** (300 mg) in dry *t*-butyl alcohol (350 ml) was similarly irradiated for 3 h. A similar work-up of the solution gave a mixture of diosphenols **6** and **7** (89 mg, 34.3%). This mixture was recrystallized from methanol to give crystals at a 1 : 1 mixture of **6** and **7** (26 mg, mp 129—155 °C).

Photolysis of 2,4-Dinitro-5β-cholestan-3-one (5). α,α′-Dinitro ketone **5**, (300 mg, 0.63 mmol) in absolute ethanol (400 ml) was irradiated for 6 h with a Hanovia 450-W high-pressure mercury arc through a Pyrex filter in an atmosphere of dry nitrogen. Removal of the solvent under a reduced pressure gave an oily residue (341 mg) which was subjected

to preparative TLC with dichloromethane to give diosphenol **8** (124 mg, 47.8%). This was recrystallized from diethyl ether–methanol to yield the specimens for analysis (74 mg), mp 157—162 °C. (Found: C, 80.94; H, 11.07%. Calcd for $C_{27}H_{44}O_2$: C, 81.00; H, 11.29%); IR (Nujol) 3528 and 2438 (OH), 1666 cm^{-1} (C=O); ^1H NMR (270 MHz) δ=0.64 (3H, s, 18-H), 1.11 (3H, s, 19-H), 2.23 (1H, d, J=16.6 Hz, 1β-H), 2.71 (1H, d, J=16.6 Hz, 1α-H), 5.75 (1H, d, J=2.93 Hz, 4-H) and 5.81 (1H, s, OH); MS, m/z (rel intensity) 400 (M^+, 100), 385 [$(M-Me)^+$, 7.9], 314 (38.9), 287 (37.7), 274 (18.3), 269 (18.3), 220 (15.4), 159 (25.0), 137 (43.5), 95 (42.1), 81 (38.0), 69 (36.8), 55 (47.7), and 43 (45.4).

Synthesis of 2-Hydroxy-4α-nitro-5α-cholest-1-en-3-one (9). To a solution of potassium *t*-butoxide (0.42 g) in THF (10 ml) at −40 °C, a solution of 5α-cholestane-2,3-dione[5] (0.5 g) in THF (10 ml) was added dropwise. To this solution, propyl nitrate (0.38 ml) was added and the temperature of the solution was then neutralized with glacial acetic acid and poured into iced water. The aqueous solution was extracted with diethyl ether. The organic layer was washed with water and dried over anhydrous Na_2SO_4. Evaporation of the solvent left a product (599 mg) which was recrystallized from methanol to give 4α-nitro-2-hydroxy-5α-cholest-1-en-3-one (**9**) (165 mg, 30 %), mp 157—161 °C. The specimen for analysis was obtained by recrystallization from methanol. Mp 159—161 °C. IR (Nujol) 3404 (OH), 1695 (C=O), 1648 (C=C), and 1560 cm^{-1} (NO_2); ^1H NMR (270 MHz) δ=0.69 (3H, s, 18-H), 1.13 (3H, s, 19-H), 5.29 (1H, d, J=13.55 Hz, 4β-H) and 6.60 (1H, s, 1-H); MS m/z (rel intensity) 445 (M^+, 9.8), 429 [$(M-O)^+$, 8.6], 415 [$(M-NO)^+$, 31.6], 398 [$(M-NO_2H)^+$, 100], 387 (27.9), and 137 (80%); UV (EtOH) λ_{max} 270 nm (ε; 7850); (Found; C, 72.46; H, 9.77; N, 2.90%. Calcd for $C_{27}H_{43}NO_4$; C, 72.77; H, 9.73; N, 3.14%).

Attempted Photolysis of 2-Hydroxy-4β-nitro-5α-cholest-1-en-3-one (9). Nitro enone **9** (50 mg) in absolute ethanol (50 ml) was irradiated through a Pyrex-filter in an atmosphere of nitrogen with a Hanovia 450-W Hg arc for 2 h. Removal of the ethanol gave an oil (47 mg). Examination of this oil by preparative TLC and ^1H NMR indicated that it was virtually the pure recovered starting material; this was confirmed by spectroscopy after purification.

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