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Steroids. V.[1] Photolyses of Steroidal Oxime Acetates

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Photolyses of the oxime acetates (**1**) and (**7**) are examined, indicating that photomethanolyses of the C=N and NO-Ac groups to the CO and NOH groups, respectively, occur comparably as primary reaction.

A number of examples of the photo-Beckmann rearrangement of oximes have been recorded in the literatures[3] and the reaction mechanism was investigated. In the interests of the photo-Beckmann rearrangement of oxime ester, we examined photolyses of steroidal oxime acetates.

Photolysis of 6-acetoximino-3β-acetoxy-5α-cholestane (**1**) in methanol for 40 hours gave the two nitrogen-free compounds: *seco*-ester (**2**) (24%) and ketone (**3**) (5%) and two nitrogen-containing compounds: oxime (**4**) (15%) and lactam (**5**) (11%). The *seco*-ester (**2**) shows bands at 1728 and 1720 cm^{-1} (OAc and CO_2Me) in the infrared (IR) spectrum ($CHCl_3$) and signals at δ 3.63 (s, CO_2Me) and 2.50 (d, J 4 Hz, $2\times H$) in addition to signals due to the 3-H and 3-OAc group in the nuclear magnetic resonance (NMR) spectrum. Its mass fragments over m/e 290 are recorded in Table I. The peak at m/e 321 is particularly characteristic. The *seco*-ester (**2**) is now considered to be methyl 3β-acetoxy-5,6-secocholestan-6-oate on the basis of its spectral data and elemental analysis. Its structure was proved by its hydrolysis with the Claisen's alkali to 3β-hydroxy-5,6-secocholestan-6-oic acid (**6**).[4,5] The ketone (**3**) and oxime (**4**) were identified as 3β-acetoxy-5α-cholestan-6-one[6] and its oxime,[7] respectively. The lactam (**5**) shows band due to the lactam carbonyl group at 1670 cm^{-1} in the IR spectrum (CCl_4). Its NMR spectrum exhibits a single proton doublet at δ 5.72 (J 5 Hz) and a single proton sextet at δ 3.42 (J 10, 5, and 5 Hz). Addition of deuterium oxide extinguished the former signal and turned the latter into a quartet (J 10 and 5 Hz), suggesting the presence of the CH_2CHNH function. Its structure was identified with an authentic sample of 3β-acetoxy-6-aza-B-homo-5α-cholestan-7-one.[8] Cookson, *et al.*[4] and Quinkert, *et al.*[5] reported that photolysis of **3** in water or dioxane afforded **6**. In our case, also, it seems likely that the formation of **2** proceeded from **3** which originally resulted from **1** by photo-methanolysis. Since it is known that 6-hydroximino-5α-cholestane normally undergoes photo-Beckmann rearrangement,[3b] a main formation pathway of **5** is able to consider to proceed from **4** *via* photo-Beckmann rearrangement, although the direct pathway from **1** might not be negligible. Hence, it seems likely to consider that photo-methanolyses of the C=N and NO–Ac groups to the CO and NOH groups, respectively, occur comparably as primary photolysis of **1**.

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[2] Location: *Minato-ku, Tokyo 108, Japan.*

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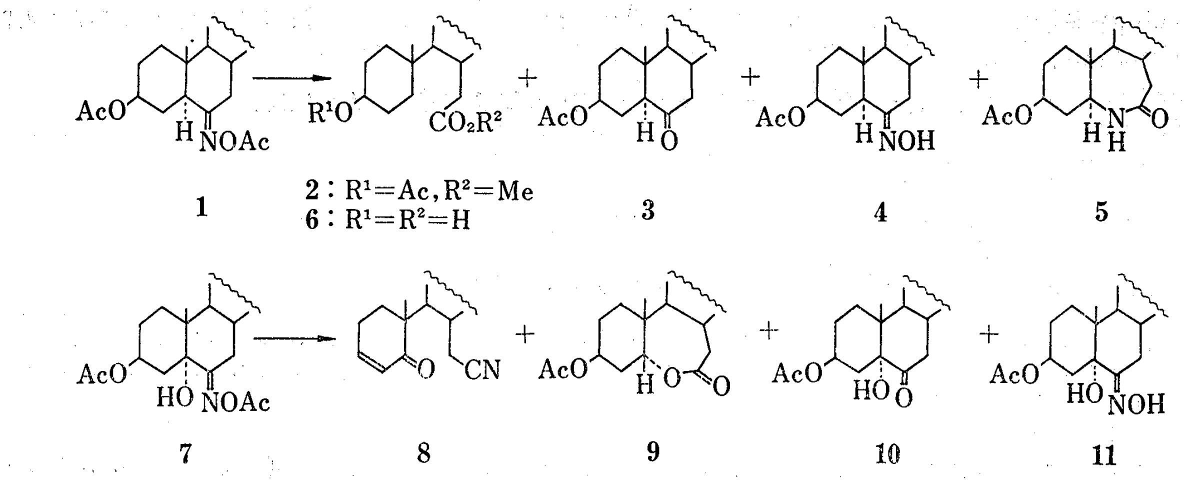


1

2 : R^1=Ac, R^2=Me
6 : R^1=R^2=H

3

4

5

7

8

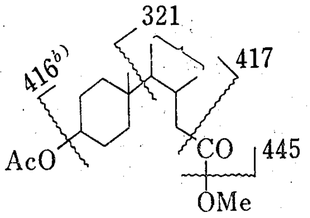
9

10

11

Chart 1

TABLE I. Mass Fragments over *m/e* 290 of the *seco*-Ester (2)[a]



m/e	Formula	*m/e*	Formuls
476 (2)[c]	$C_{30}H_{52}O_4$ (M)	401 (5)	M–($CH_3CO_2H+CH_3$)
445 (4)	M–CH_3O	342 (41)	M–($CH_3CO_2H+CH_3+CO_2CH_3$)
417 (5)	M–CO_2CH_3	321 (100)	M–$C_9H_{15}O_2$
416 (6)	M–CH_3CO_2H	290 (16)	M–($C_9H_{15}O_2+CH_3O$)

a) 75 eV, 130°
b) This is accompanied by a rearrangement of a hydrogen atom.
c) relative intensity (%)

Photolysis of 6-acetoximino-3*β*-acetoxycholestan-5*α*-ol (**7**) in methanol for 72 hours gave the keto nitrile (**8**) (4%), the two nitrogen-free compounds: lactone (**9**) (11%) and ketone (**10**) (6%), and a mixture containing the oxime (**11**). The keto nitrile (**8**) shows bands at 2240 (CN) and 1676 cm^{-1} (CO) in the IR spectrum (CCl_4) and two doublet signals due to the vinyl protons at δ 6.80 and 6.00 in the NMR spectrum. Its structure was identified as 6-cyano-5,6-secocholest-3-en-5-one[9] by comparison of the IR and NMR spectra. Since on standing in methanol at room temperature for 72 hours **7** exhibited the formation of **8** very positively on thin-layer chromatography (TLC),[10] **8** might not be formed by irradiation and may be precluded from photo-products. The lactone (**9**) exhibits band due to the lactone carbonyl group at 1710 cm^{-1} in the IR spectrum (nujol) and signal due to the C$\underline{H}$OCO at δ 4.33 (t, *J* 4 Hz) in addition to signal due to the C$\underline{H}$OAc at δ 5.00 (bs, W_H 24 Hz), revealing the likely presence of the *ε*-lactone ring B in its molecule. Its structure was identified with an authentic sample of 3*β*-acetoxy-5*α*-hydroxy-5,6-secocholestan-6-oic lactone.[4] The ketone (**10**), which was established as 3*β*-acetoxy-5*α*-hydroxy-cholestan-6-one,[11] is known to convert into **9** by irradiation.[4] Accordingly, in this case, it seems appropriate to consider that **10**, which resulted from **7** by photo-methanolysis, was photolyzed to give **9**. The oxime (**11**) was identified as

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[9] M. Onda and K. Takeuchi, *Chem. Parm. Bull.* (Tokyo),**21**, 1287 (1973),
[10] Silica gel plate (0.25 mm), benzene.
[11] R.G. Schultz, *J. Org. Chem.*, **24**, 1955 (1959).

3β-acetoxy-6-hydroximinocholestan-5α-ol[12] by comparison of the IR spectrum, TLC, and gas chromatography (GLC). Thus, photolysis of **7** is also considered to proceed in a similar manner to that of **1**. This fact is of interest, because, as we previously reported,[9] **7** was found to undergo smoothly an abnormal Beckmann rearrangement to give **8** in almost quantitative yield by reflux in methanol or alumina.

Experimental

Melting points were determined on a micro hot-stage and are uncorrected. IR spectra were recorded on a JASCO IR-G spectrometer. NMR spectra were measured on a Varian T-60 spectrometer for deuteriochloroform solution. Mass spectra were determined on a JEOL JMS-01S spectrometer. GLC was carried out with a Shimadzu GC-3AF. A glass column of 200 cm × 4 mm was packed with 1.5% SE-30 on Shimalite W (80—100 meshes). The operating conditions were as follows: sensitivity, 1000; range, 0.8. Identification was carried out by mixed mp and comparison of IR and NMR spectra. Irradiation was carried out with a 40 W low pressure mercury lamp under nitrogen at room temperature until starting material disappeared on TLC.

Preparations of Oxime Acetates——The corresponding oximes were acetylated with acetic anhydride in the presence of pyridine at room temperature. a) 6-Acetoximino-3β-acetoxy-5α-cholestane (1),[13] needles of mp 130—131° (from *n*-hexane). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1765 (NOAc), 1730 (3β-OAc), and 1635 (C=N). NMR: δ 4.67 (bs, W_H 24 Hz, 3α-H), 3.39 (q, *J* 12 and 4 Hz, 7β-H), 2.18 (s, NOAc), 2.03 (s, 3β-OAc), and 0.93 (s, 10β-Me). *Anal.* Calcd. for $C_{31}H_{51}O_4N$: C, 74.21; H, 10.25; N, 2.79. Found: C, 74.06; H, 10.18; N, 2.90. b) 6-Acetoximino-3β-acetoxycholestan-5α-ol (7), needles of mp 148—149° (from *n*-hexane). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3450 (OH), 1765 (NOAc), 1740 (3β-OAc), and 1640 (C=N). NMR: δ 5.04 (bs, W_H 24 Hz, 3α-H), 3.07 (q, *J* 12 and 4 Hz, 7β-H), 2.18 (s, 5α-OAc), 2.06 (s, 3β-OAc), and 0.91 (s, 10β-Me). *Anal.* Calcd. for $C_{31}H_{51}O_5N$: C, 71.92; H, 9.93; N, 2.71. Found: C, 72.01; H, 9.93; N, 2.75.

Photolysis of 6-Acetoximino-3β-acetoxy-5α-cholestane (1)——A solution of the oxime acetate (**1**) (470 mg) in methanol (100 ml) was irradiated for 40 hr. After evaporation of solvent *in vacuo*, the oily residue (470 mg) was chromatographed on silica gel (50 g). The first fraction, eluted with benzene, gave methyl 3β-acetoxy-5,6-secocholestan-6-oate (**2**) (107 mg, 24%) as an oil. NMR: δ 4.65 (bs, W_H 24 Hz, 3α-H), 3.63 (s, 7-CO_2Me), 2.50 (d, *J* 4 Hz, 7-H_2), 2.00 (s, 3β-OAc), and 0.97 (s, 10β-Me). Mass Spectrum Calcd. for $C_{30}H_{52}O_4$: M, 476.3865. Found: M$^+$, 476.3839. A solution of the *seco*-ester (**2**) (36 mg) in methanol (1 ml) with the Claisen's alkali (0.6 ml) was refluxed for 5 hr. The usual work-up gave 3β-hydroxy-5,6-secocholestan-6-oic acid (**6**) (29 mg) as needles, mp 195—197° (from *n*-hexane). Mass Spectrum Calcd. for $C_{27}H_{48}O_3$–H_2O: M, 402.3497. Found: M$^+$–H_2O, 402.3495. The second fraction, eluted with benzene–chloroform (1:1), gave an oil (88 mg). After preparative TLC on silica gel plates (0.75 mm) using chloroform as solvent, the zone with *Rf* 0.65 was collected and eluted with chloroform, giving 3β-acetoxy-5α-cholestan-6-one (**3**) (21 mg, 5%) as needles, mp 131—133° (from *n*-hexane). The third fraction gave 3β-acetoxy-6-hydroximino-5α-cholestane (**4**) (65 mg, 15%) as plates, mp 206—208° (from methanol). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3400 (OH), 1735 (OAc), and 1650 (C=N). NMR: δ 4.67 (bs, W_H 24 Hz, 3α-H), 3.34 (q, *J* 12 and 4 Hz, 7β-H), 2.03 (s, 3β-OAc), and 0.92 (s, 10β-Me). *Anal.* Calcd. for $C_{29}H_{49}O_3N$: C, 75.76; H, 10.74; N, 3.05. Found: C, 75.71; H, 10.78; N, 3.01. The fourth fraction afforded a solid (103 mg). The same preparative TLC as above (*Rf* 0.3) gave 3β-acetoxy-6-aza-B-homo-5α-cholestan-7-one (**5**) (50 mg, 11%) as plates, mp 222—223° (from acetonitrile). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3200 (NH), 1735 (OAc), and 1670 (NCO). NMR: δ 5.72 (d, *J* 5 Hz, NH), 4.67 (bs, W_H 24 Hz, 3α-H), 3.42 (sext, *J* 10, 5, and 5 Hz, 5α-H), 2.30 (d, *J* 5 Hz, 7-H_2), 2.03 (s, 3β-OAc), and 0.93 (s, 10β-Me). *Anal.* Calcd. for $C_{29}H_{49}O_3N$: C, 75.76; H, 10.74; N, 3.05. Found: C, 75.81; H, 10.68; N, 3.03.

Photolysis of 6-Acetoximino-3β-acetoxycholestan-5α-ol (7)——A solution of the oxime acetate (**7**) (1.05 g) in methanol (108 ml) was irradiated for 72 hr. After removal of solvent *in vacuo*, the oily residue (1.03 g) was chromatographed on silica gel (100 g). Elution with benzene–chloroform (85:15) gave an oil (344 mg). After preparative TLC on silica gel plates (1 mm) using chloroform-methanol (100:1) as solvent, the zone with *Rf* 0.65 was collected and eluted with chloroform, giving an oil (60 mg) whose re-chromatography on neutral alumina (grade III, 6 g) using benzene as solvent gave 6-cyano-5,6-secocholest-3-en-5-one (**8**) (37 mg, 4%). NMR: δ 6.80 (bd, *J* 8 Hz, 3-H), 6.00 (d, *J* 8 Hz, 4-H), 2.80 (q, *J* 16 and 4 Hz, 7-H_A), and 1.05 (s, 10β-Me). Mass Spectrum Calcd. for $C_{27}H_{43}ON$: M, 397.3345. Found: M$^+$, 397.3310. The fraction with *Rf* 0.45 gave 3β-acetoxy-5α-hydroxy-5,6-secocholestan-6-oic lactone (**9**) (105 mg, 11%) as needles, mp 230—232° (from *n*-hexane). IR ν_{max}^{Nujol} cm^{-1}: 1720 (3β-OAc) and 1710 (lactone carbonyl). NMR: δ 5.00 (bs, W_H 24 Hz, 3α-H), 4.33 (t, *J* 4 Hz, 5β-H), 2.97 (q, *J* 14 and 9 Hz, 7-H_A), 2.38 (q, *J* 14 and 2 Hz, 7-H_B), 2.00 (s, 3β-OAc), and 1.00 (s, 10β-Me). *Anal.* Calcd. for $C_{29}H_{48}O_4$: C, 75.61; H, 10.50. Found:

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[12] G. Drefahl and K. Ponsold, *Chem. Ber.*, 91, 271 (1958).

[13] Q.R. Peterson, *Proc. Indiana Acad. Sci.*, 73, 127 (1963) [*C.A.*, **62**, 11873 (1965)].

C, 75.48; H, 10.30. Mass Spectrum Calcd. for $C_{29}H_{48}O_4$: M, 460.3552. Found: M^+, 460.3552. The fraction with *Rf* 0.35 afforded 3β-acetoxy-5α-hydroxycholestan-6-one (**10**) (55 mg, 6%) as needles, mp 234—236° (from ether). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3410 (OH), 1735 (OAc), and 1710 (CO). NMR: δ 5.02 (bs, W_H 24 Hz, 3α-H), 1.98 (s, 3β-OAc), and 0.93 (s, 10β-Me). *Anal.* Calcd. for $C_{29}H_{48}O_4$: C, 75.61; H, 10.50. Found: C, 75.55; H, 10.45. The next elution with chloroform of silica gel column gave a semi-solid (58 mg), crystallization of which did not give pure compound. TLC on silica gel (chloroform–methanol 20: 1) showed a main spot with *Rf* 0.35 corresponding to 3β-acetoxy-6-hydroximinocholestan-5α-ol[11] and two faint spots. GLC: main peak, t_R 11.55 min. IR $\nu_{\max}^{\text{CHCl}_3}$ cm^{-1}: 3400 (OH), 1715 (3β–OAc), and 1640 (C=N).