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Notes on the Formations of Oxaziridines by the Irradiation and Benzoylation of (22*S*, 25*S*)-*N*-Acetyl-11a-aza-c-homo-5α-veratra-11a,13(17)-diene-3β,11β,23β-triol 11a-Oxide, a Fused 6-Membered-ring Nitrone[1]

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The irradiation of the title nitrone (**5**) with monochromatic light afforded a single isomeric oxaziridine (**6**), which reverted to the original nitrone (**5**) thermally at room temperature. The title nitrone was also converted into another oxaziridine (**8**) by treatment with benzoic anhydride.

In our previous paper,[1] we proposed a pathway for the formation of the title nitrone (**5**) *via* the photorearrangement of a (22*S*, 25*S*)-veratr-13(17)-enine-11β-yl nitrite (**2**) on the basis of several pieces of experimental evidence.

We wish to report here on the transformations of the nitrone (**5**) into a single isomeric oxaziridine (**6**) by irradiation with monochromatic light (285 nm) and on a reaction toward acylating reagents which led to a product (**8**) with an oxaziridine ring.

Results

Photochemical Oxaziridine Formation.[2] The photochemical behavior of the nitrone (**5**) in ethanol toward Pyrex-filtered light was parallel to the nitrone we previously reported.[3] Thus, thenitrone (**5**) in ethanol was transformed into a single, less polar substance on 3 h irradiation with the Pyrex-filtered light generated by 100-W high-pressure Hg arc lamp. The less polar substance should be an oxaziridine (**6**), since it reverted to the starting nitrone when refluxed in acetone for *ca.* 1 h and it oxidized the iodide ion to iodine. The configuration of the oxaziridine ring could not be assigned since it was thermally unstable, even at room temperature. However, the α-configuration is more probable on the basis of the concideration of the relative stalility.

The quantitative transformation of the nitrone (**5**) into the corresponding oxaziridine (**6**) with monochromatic light and the quantitative thermal regeneration of the nitrone (**5**) from the oxaziridine (**6**) at room temperature were confirmed spectroscopically. Thus, a methanolic solution of the nitrone (**5**) (5.8×10^{-5} M) was irradiated with monochromatic light (285 nm) at room temperature. The nitrone (**5**) was completely transformed into the oxaziridine (**6**) by irradiation for 2 min, as was indicated by the vanishing of the absorption maximum at 285 nm of the nitrone (**5**) (Fig. 1). When the irradiated solution was set aside at room temperature in the dark, the oxaziridine gradually reverted to the nitrone, and after 18 h the oxaziridine (**6**) was quantitatively transformed into the nitrone (**5**)[2] as was indicated by the gradual appearance of the absorption maximum at 285 nm in the solution (Fig. 2).

The quantum yields of the oxaziridine formation in methanol and in isopropyl alcohol with monochromatic light (285 nm) were found to be 0.17 and 0.10 respectively. The formation of the oxaziridine was also observed in ethanol, *t*-butyl alcohol, dioxane, tetrahydrofuran, and cyclohexane. The nitrone (**5**) was equally transformed into the oxaziridine in methanol containing triplet quenchers, piperylene, or oxygen. The quantum yields of the oxaziridine formation were found to be 0.16 and 0.19 respectively. These facts indicated that the oxaziridine was formed from the singlet-excited nitrone.[4]

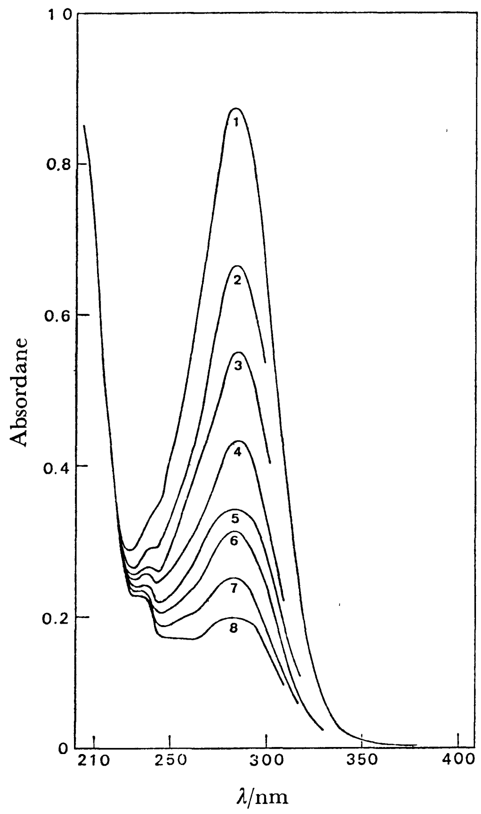


Fig. 1. Decline in the UV spectrum of **5** on irradiation with 285 nm light in 5.8×10^{-5} M methanol.
1: before irradiation, 2: 5 s irradiation, 3: 10 s, 4: 15 s, 5: 20 s, 6: 25 s, 7: 30 s, 8: 35 s.

The Reaction of the Nitrone (5) with Acylating Reagent. The treatment of this nitrone (**5**) with benzoic anhydride and pyridine at room temperature afforded a mixture of products from which only the major product, **8** (mp 194—195 °C) was obtained in a pure form. The results of the elemental analysis and the mass spectrum were consistent with a molecular formula of $C_{40}H_{54}O_8$-

N_2. The oxaziridine structure was assigned to this compound on the basis of the IR and NMR spectra in a manner entirely analogous to the product in the benzoylation of the nitrone we previously reported.[3)] The assignments of the NMR signals are described in the table. As in the previous case,[2)] the N-Ac protons were considerably shielded and appeared near the signal due to the 19-H. The signal due to the N-Ac was further confirmed by a comparison of ^{1}H NMR spectra between the product **8** and the deuterium-labeled compound **9**.

The partial $[^2H]_3$ acetylation of (22*S*,25*S*)-5α-veratr-13(17)-enine-3β,11β,23β-triol (**1**) afforded a deuterium-labeled derivative (**3**). Its subsequent nitrosation afforded (22*S*,25*S*)-*N*-$[^2H]_3$acetyl-5α-veratr-13(17)-enne-3β,11β,23β-triol 3,23-di-$[^2H]_3$ acetate 11-nitrite (**4**). The nitrite (**4**) in carbon tetrachloride was photolyzed by a procedure analogous to that used in the case of the **2** nitrite to afford the nitrone(**7**)in a 28% yield. The treatment of it with benzoic anhydride and pyridine under the same conditions as were used for the **5** nitrone afforded a mixture of products. Its recrystallization from ether afforded an oxaziridine (**9**). The ^{1}H NMR spectrum of compound **9** indicated the presence of all the signals found in the spectrum of compound **8** with the exceptions of two sharp signals at τ 8.02 and at τ 8.86 due to the OAc and NAc of the product (**8**).

Therefore, the singlet at τ 8.86 in the spectrum of the product (**8**) was assigned to that of NAc. This considerable shielding of NAc protons, found in the spectrum of the product (**8**), was attributable to an anisotropy by the newly introduced phenyl ring. The assignments of the rest of the signals of the product (**8**) are shown in the table. There was a clear doublet at τ 3.32 (J= 9.6) ascribable to the 11β-H on the newly formed oxaziridine ring. An inspection of the Dreiding model of compound **8** in conjunction with the considerable shielding of the *N*-acetyl protons by the benzene ring in the ^{1}H NMR spectrum suggested that the configura-

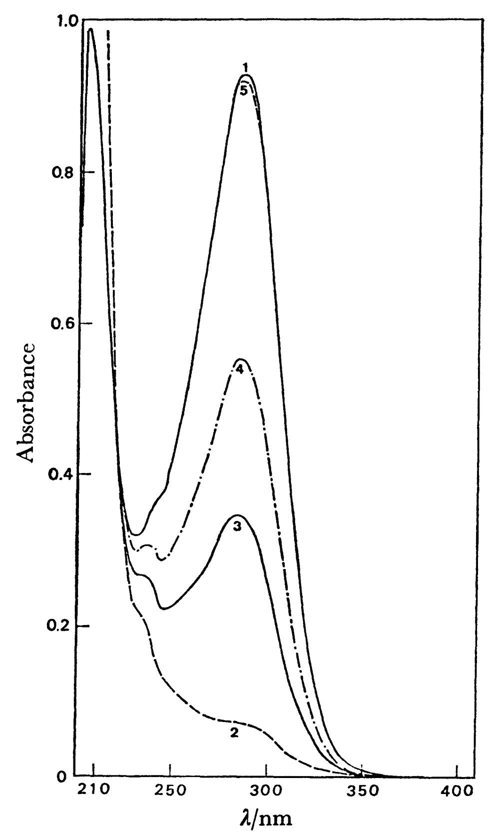


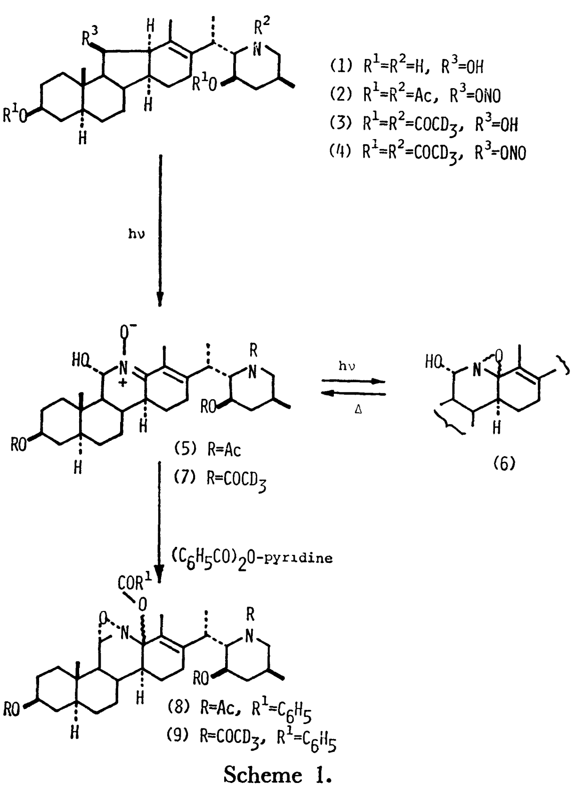
Fig. 2. Increase in the absorption maximum at 285 nm of the solution of **6** in 6.5×10^{-5} M methanol at room temperature.
1: the UV spectrum of **5** before irradiation, 2: after 2 min irradiation, 3: the UV spectrum of the solution when the solution irradiated for 2 min (the solution A) was set aside for 30 min in the dark at room temperature, 4: the UV spectrum of the solution A after 80 min in the dark, 5: the solution A after 18 h in the dark at room temperature.

TABLE. CHEMICAL SHIFTS (τ values) AND COUPLING CONSTANTS (Hz)

Compound	Chemical shifts											
	3-αH	11-αH	12-αH	18-H	19-H	20β-H	21-H	22-βH	23-αH	26-H	27-H	N-Ac, OAc
4	5.35 br	5.85 (q)	7.35 (s)	8.27 (s)	9.03 (s)	6.85 (q)	8.86 (d)	5.21 (d)	4.89 (bs)	8.86 (d)		—
7	*ca.* 5.34	*ca.* 5.34	—	7.09 (s)	9.09 (s)	6.84 (q)	8.87 (q)	5.22 (d)	4.97 (bs)	8.87 (d)	6.64 (bs)	—
8	5.34 br	3.32 (d) (11-βH)	—	8.13 (s)	9.08 (s)	a	8.89 or 9.01 (d)	5.22 (d)	4.98 (bs)	8.89 or 9.01 (d)		8.86 (s) (NAc) 8.02 (s) (OAc)
9	5.34 br	3.32 (d) (11-βH)	—	8.14 (s)	9.09 (s)	a	8.89 or 9.01 (d)	5.22 (d)	4.98 (bs)	8.89 or 9.01 (d)		—

Compound	Coupling constants							
	11-αH, 12-αH	11-αH, (11-βH) 9-αH	12-αH, 14-αH	20-αH, 21-H	20-βH, 22-βH	22-βH, 23-βH	25-αH, 26-H	Other signals and the coupling constants
4	5.3	2.7	9.8	6.6	10.5	1.5	6.6	
7	—	a	—	6.6	10.5	1.5	6.6	
8	—	11-βH, 9-αH 9.6	—	6.6 or 6.0	10.5	1.5	6.6 or 6.0	1.8—2.7 (m) benzoyl H
9	—	11-βH, 9-αH 9.6	—	6.6 or 6.0	10.5	1.5	6.6 or 6.0	1.8—2.7 (m) benzoyl H

a) Unassignable.



Scheme 1.

tion of compound **8** at the C-13 position was β. However, this assignment is not conclusive.

Although we obtained the oxaziridine (**8**) as the major product, we were unsuccessful in isolating a compound with a pyridine nucleus corresponding to the compound which was isolated previously.[2] This probably shows that the compound with the pyridine nucleus was formed only in a poor yield in this benzoylation. This difference from the previous case demonstrate that a balance of two competitive processes leading to oxaziridine and to a compound with a pyridine nucleus depends upon a rather slight modification of the substrate structure.

Experimental

For the instruments used and the general procedures, see Part 30.[5]

The Formation of the Oxaziridine (6) on the Irradiation of the Nitrone (5) in Ethanol and the Thermal Treatment of the Oxaziridine (6).

The nitrone (**5**) (53 mg) in ethanol (73 ml) was irradiated through Pyrex with a 100-W high-pressure Hg arc lamp under nitrogen. The progress of the reaction was monitored by TLC (Solvent: acetone/chloroform 1/3). After 3.5 h, the nitrone disappeared and was transformed into a less polar substance which appeared as a single spot on the TLC. After the removal of the solvent at 22 °C, the residue developed a yellow color on the addition of a KI–acetic acid solution. This residue was dissolved in 10 ml of acetone and they refluxed for 1 h 10 min. An examination by TLC of this solution showed that nearly all the oxaziridine had reverted to the starting nitrone. The acetone was then evaporated and the residue was recrystallized from isopropyl ether to yield crystals (29 mg) which were identical with the starting nitrone.

The Transformation of the Nitrone (5) into the Oxaziridine (6) in Methanol on Irradiation with 285 nm Light. *Quantum-yield Measurements*: Solutions of the nitrone (**5**) containing 1,3-pentadiene or oxygen were prepared by dissolving 0.16 mg of the nitrone in 5 ml of methanol containing *ca.* 0.2 g of 1,3-pentadiene and 0.21 mg of the nitrone in 5 ml of methanol saturated with oxygen.

The solutions for the quantum-yield measurements were prepared by dissolving 0.17 mg of the nitrone (**5**) in 5 ml of methanol and 0.19 mg of **5** in 5 ml of isopropyl alcohol. Each 4 ml portion of the solutions in silica cells (10×10×45 mm) was placed in a chamber of the Jasco CRM-FA grating spectro-irradiator. The solutions were then irradiated with a 285 nm light. Figure 1 shows the decline in the intensity of the absorption maximum of compound **5** at 285 nm in methanol.

The quantum yields of the transformation of the nitrone (**5**) into the oxaziridine (**6**) were measured as in the case of the disappearance of the nitrite.[1] The decreases in the absorbance at 285 nm of the UV spectrum of the solutions upon the irradiation for 5 s in the case of methanol and for 20 s in the case of isopropyl alcohol were found to be 0.2 and 0.47.

Since the molar absorptivity at 285 nm in the UV spectrum of the **5** nitrone was known to be 15800, and since the output of the Xe arc lamp at 285 nm was 0.6×10^5 erg/cm^2, s, the quantum yield of the decomposition of the nitrone in methanol was calculated to be 0.18.

In the same manner, the quantum yield of the decomposition of the nitrone in isopropyl alcohol was calculated to be 0.10.

(22S,25S)-N-[H^2]$_3$Acetyl-veratr-13(17)-enine-3β,11β,23β-triol 3,23-di-[^2H]$_3$-acetate (3). The triol (**1**) (620 ml) and acetic anhydride-d_6 (2.5 ml) in pyridine (6.2 ml) were stirred for 22 h at room temperature. After the addition of methanol (10 ml), the solvent was removed with added benzene under reduced pressure. The residue was dissolved in chloroform and the chloroform solution was washed with 2M-hydrochloric acid, a 5% aqueous sodium hydrogencarbonate solution, and water successively. After the removal of the chloroform, the amorphous residue (955 mg) was submitted to column chromatography (Mallinckrodt silicic acid; 100 mesh: eluent, benzene) to yield 462 mg of colorless crystals of the tri-[^{2}H]$_3$ acetyl derivative (**3**). The analytical specimen was obtained by recrystallization from ether. Mp 196—197°C. Found: C, 69.84, H and D, 10.80, N, 2.36%. Calcd for $C_{33}H_{42}D_9O_6N$: C, 69.92; H and D, 10.67; N, 2.47%. ν_{max} 1736 cm^{-1} (OCOCD$_3$), 1632 cm^{-1} (NCOCD$_3$), 3468 (OH), 1244, 1079 cm^{-1}. NMR; see Table. MS, *m/e* 568 (M+2, 0.2%), *m/e* 361 (0.5%), *m/e* 204 (54%), *m/e* 160 (100%), *m/e* 116 (16%).

Nitrosation of the 11β-ol (3). To a solution of the 11β-ol (**3**) (430 mg) in acetic acid (6 ml) at 60°C, there was added sodium nitrate (200 mg) within a period of 30 s. To the reaction mixture there was then added water (40 ml). The resultant precipitates of the nitrite were collected by filtration, washed with a 10% aqueous sodium hydrogencarbonate solution, washed with water, and dried *in vacuo*. Yield, 435 mg. NMR; see Table.

Photolysis of the Nitrite (4). The above nitrite (435 mg) in carbon tetrachloride (20 ml) was irradiated through Pyrex with a 100-W high-pressure Hg arc for 8.5 h under argon. A small amount of a solid which appeared on the wall of the vessel was dissolved in chloroform. The photolyzed solution and the chloroform solution were combined, and the solvent was removed. The residue was submitted to preparative TLC (solvent: acetone/benzene 1/5). The amorphous crude nitrone was recrystallized from ether to afford 120 mg of the nitrone (**7**). Mp 126—127 °C. Found: C, 66.30; H and D, 10.20; N, 4.52%. Calcd for $C_{33}H_{41}D_9O_7N_2$: C, 66.50; H and

D, 9.98; N, 4.73%. NMR; see Table.

Benzoylation of the Nitrone (5). The nitrone (**5**) (79 mg) and benzoic anhydride (100 mg) in pyridine (3.5 ml) were stirred for 24 h at room temperature. The reaction mixture was then poured into a mixture of ice and water (80 ml). The mixture was extracted with chloroform (20 ml × 2). The chloroform solution was washed successively with 2M-hydrochloric acid (20 ml), a 5% aqueous sodium hydrogencarbonate solution (20 ml), and water, and then dried (Na_2SO_4). The removal of the solvent afforded a residue (310 mg). This was submitted to preparative TLC (acetone/chloroform 1 : 3). Four fractions-A (142 mg), B (44 mg), C (17 mg), and D (17 mg) were obtained in the order of increasing polarity. The least polar fraction, A, was recovered benzoic anhydride. The B fraction was recrystallized from ether to yield 11 mg of the oxaziridine (**8**). Mp 194—195 °C. Found: C, 69.40, H, 7.55; H, 4.30%. Calcd for $C_{40}H_{54}O_8N_2$: C, 69.54; H, 7.88; N, 4.06%. UV $\lambda_{\max}^{\mathrm{EtOH}}$ 231 nm (ε; 11000). $\nu_{\max}$ ($CHCl_3$) 1720 cm^{-1} (OAc and $OCOC_6H_5$), 1629 cm^{-1} (NAc). NMR; see text.

Benzoylation of the Nitrone (7). The above nitrone (**7**) (90 mg) and benzoic anhydride (110 mg) in pyridine (3.5 ml) were stirred for 3 h. After the addition of 2 M hydrochloric acid (500 ml), the reaction mixture was extracted with chloroform (50 ml+40 ml+20 ml). The chloroform solution was washed successively with a 5% aqueous sodium hydrogencarbonate solution and water and then dried (Na_2SO_4). After the removal of the solvent, the residue was recrystallized from ether to yield 28 mg of the pure oxaziridine (**9**). Mp 243—244 °C (from acetone). Found: C, 68.40; H and D, 8.90; N, 3.80%. Calcd for $C_{40}H_{45}D_9O_8N$: C, 68.64; H and D, 9.07; N, 4.00%. NMR see Table.

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