BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 41 468—475 (1968)

Photolysis of Nitrite Esters bearing Nitrogen on the β-Carbon

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(Received October 2, 1967)

The results of photolysis of a number of nitrite esters derived from jervine, in which the respective β-carbon of nitrite group bears nitrogen, are described. It has been found that in these nitrites when a nitrogen on β-carbon was in the amide group, the irradiation caused the cleavage of α, β-single bond to the nitrite group. The reaction is exemplified by photolysis of 3*O*, *N*-diacetyl-22, 27-imino-11-oxojerva-5, 13(17)-diene-3β, 23β-diol 23-nitrite ester (Ic) to afford an aldehyde II. When a nitrogen on β-carbon of nitrite was tertiary (*e.g.*, XIb), however, no photoinduced fission of carbon-carbon bond in these nitrites was observed and the starting alcohol recovered unchanged. These results coupled with others, *e.g.*, the result of photolysis of 3*O*-acetyl-*N*-benzoyl-22, 27-imino-11-oxojerva-5, 12-diene-3β, 23β-diol 23-nitrite ester (IIIf) indicate the selective cleavage of acyl-nitrogen bond followed by acidic hydrolysis to an aldehyde during chromatography, as shown in the scheme V to VIII. It is noted that this reaction is contrasted with the reported results with regard to photolysis of nitrites bearing oxygen in place of nitrogen.

The study of the photolysis of organic nitrites has received considerable attention over the past 7 years largely because of its synthetic utility.2) Alkoxy radicals generated from nitrites were found to react in a variety of ways, depending on detailed structures around the nitrite group.

Our interest in this photochemical transformation is primarily a synthetic one and in this communication we describe some observations on a new mode of transformation.

22, 27-Imino-11-oxojerva-5, 13(17)-diene-3β, 23β-diol (Ia)3)which was prepared by Birch reduction of jervine4) was partially acetylated to yield the corresponding 30, *N*-diacetyl derivative (Ib) in 48% yield. The evidence for the introduction of an acetyl group at 3β-hydroxyl of Ia was provided by steric considerations and the disappearance of a band at 1050 cm^{-1} in its infrared pectrum which is characteristic of a Δ^5-3β-hydroxyl group.5) This was converted on treatment with nitrosyl chloride in pyridine6) into the corresponding nitrite (Ic). This was unstable7) and was readily hydrolyzed to regenerate the alcohol Ib. This nitrite in benzene was immediately photolysed (150 W high pressure mercury arc lamp) under the conditions commonly used for the Barton reaction.8) After about one hour no nitrite remained unchanged as indicated by a specific color test.9) The

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1) Photoinduced Transformations. IV. Part of this work has been briefly reported. H. Suginome, M. Murakami and T. Masamune, *Chem. Commun.*, 343 (1966). Part III. H. Suginome, T. Tsuneno and T. Masamune, *Tetrahedron Letters*, **1967**, 4605.

2) For reviews see A. L. Nussbaum and C. H. Robinson, *Tetrahedron*, **17**, 35 (1962) and M. Akhtar in "Advances in Photochemistry," Vol. II, ed. by W. A. Noyes, G. S. Hammond and J. N. Pitts, Jr., Interscience Publishers, New York, N. Y. (1964), p. 263.

3) The configurations at C-22 and C-23 of jervine have recently been revised. J. W. Scott, L. J. Durham, H. A. P. deJongh, U. Burckhardt and W. S. Johnson, *Tetrahedron Letters*, **1967**, 2381. In this paper, a series of compounds derived from jervine will be formulated on the basis of this revised formula.

4) T. Masamune, M. Takasugi, M. Gohda, H. Suzuki, S. Kawahara and T. Irie, *J. Org. Chem.*, **29**, 2282 (1964).

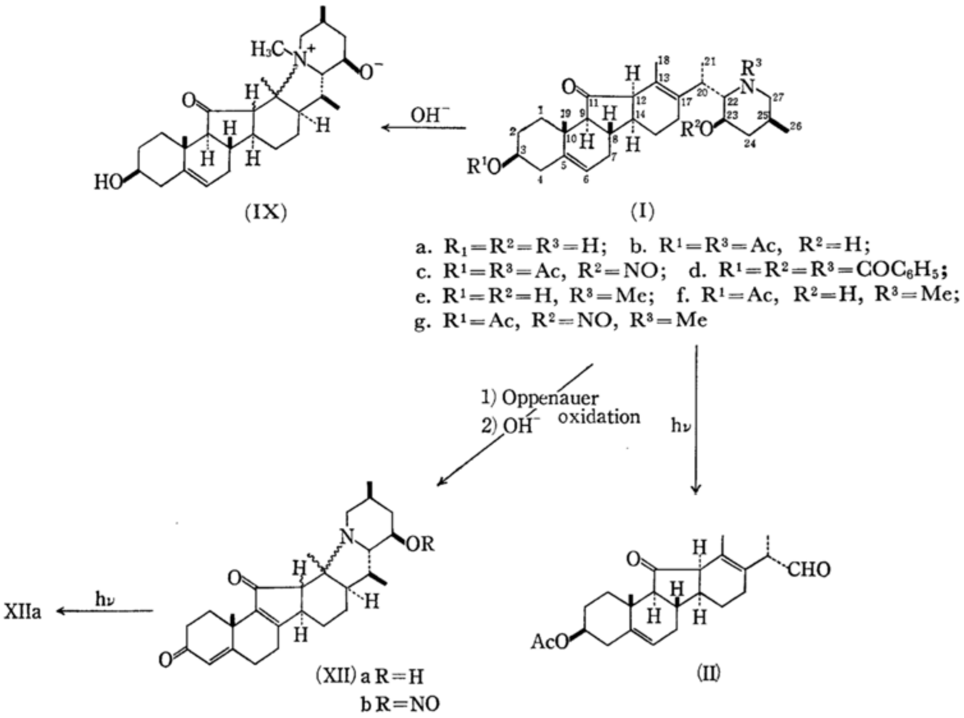
5) T. Masamune, Y. Mori, M. Takasugi and A. Murai, *Tetrahedron Letters*, **1964**, 913.

6) R. H. Pickard and H. Hunter, *J. Chem. Soc.*, **1923**, 434.

7) All nitrites described in this paper were found to be very unstable to moisture and this seems to be general for nitrites substituted by nitrogen on the β-carbon of nitrite group. Similar instability has recently been reported on the nitrites substituted by oxygen in place of nitrogen. A. L. Nussbaum, R. Wayne, E. Yuan, O. Zagneetko Sarre and E. P. Oliveto, *J. Am. Chem. Soc.*, **87**, 2451 (1965).

8) D. H. R. Barton, J. M. Beaton, K. E. Geller and M. M. Pechet, *J. Am. Chem. Soc.*, **82**, 2640 (1960); **83**, 4076 (1961).

9) F. Feigl, "Spot Tests in Organic Analysis," Elsevier Publ. Co., New York, N. Y. (1960), p. 178.



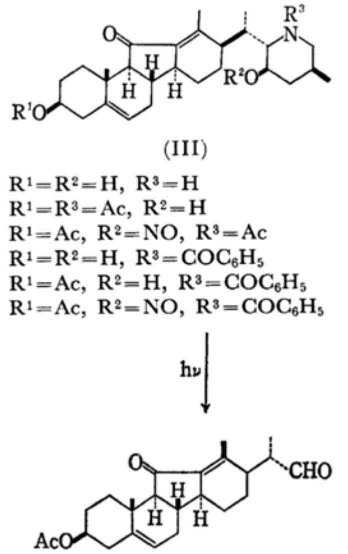
(IX) (I)

a. $R_1=R^2=R^3=H$; b. $R^1=R^3=Ac$, $R^2=H$;
c. $R^1=R^3=Ac$, $R^2=NO$; d. $R^1=R^2=R^3=COC_6H_5$;
e. $R^1=R^2=H$, $R^3=Me$; f. $R^1=Ac$, $R^2=H$, $R^3=Me$;
g. $R^1=Ac$, $R^2=NO$, $R^3=Me$

(XII) a R=H
b R=NO

(II)

examination of the product by TLC showed this to be rather a complex mixture, and this was then subjected to chromatographic separation on the column of silicic acid. The least polar fraction which was eluted with a mixed solvent of benzene and ether crystallized on evaporation of the solvent, and had mp 150—152°C, after purification. A structure II could be assigned to this substance on the following basis. Elemental analysis and mass spectrometry (M^+ 384) indicated a molecular formula $C_{24}H_{32}O_4$, corresponding to the loss of nitrogen moiety in Ib. In the NMR spectrum of the compound Ib, signals due to *N*-acetyl, *O*-acetyl, 18- and 19-methyl groups appeared as singlets at τ 8.00,[*1] τ 8.03,[*1] τ 8.15 and τ 9.03, respectively, and those due to 21- and 26-methyl groups as a coincident broad doublet centered at τ 8.83 ($J=6.6$). However, the NMR spectrum of II retained only three singlets at τ 7.99, τ 8.16 and τ 9.05, which are attributable to *O*-acetyl, 18- and 19-methyl groups, respectively. A doublet in II was exactly a half of that of the corresponding doublet of Ib, indicating that either the 21-methyl or the 26-methyl had been removed from the starting diacetyl derivative Ib. Moreover, the NMR spectrum of II showed the presence of an aldehydic proton as a doublet centered at τ 0.56 ($J=4.2$). The IR spectrum of the product also showed the presence of typical aldehyde bands[10] at 2697, 2799 and 1740 cm^{-1} (shoulder) and a notable feature of this IR spectrum was the absence of a band due to an *N*-acetyl group. Only the structure II reasonably accommodates all the spectral data and the molecular formula mentioned above.



(III)

a. $R^1=R^2=H$, $R^3=H$
b. $R^1=R^3=Ac$, $R^2=H$
c. $R^1=Ac$, $R^2=NO$, $R^3=Ac$
d. $R^1=R^2=H$, $R^3=COC_6H_5$
e. $R^1=Ac$, $R^2=H$, $R^3=COC_6H_5$
f. $R^1=Ac$, $R^2=NO$, $R^3=COC_6H_5$

(IV)

In a similar manner, the isomeric 3*O*, *N*-diacetyl derivative IIIb was prepared by partial

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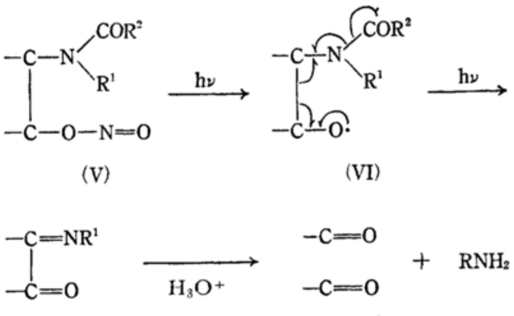
[*1] These two signals are assigned to *N*- and *O*-acetyl groups but which is *O*-acetyl or *N*-acetyl was not determined.

10) S. Pinchas, *Anal. Chem.*, **27**, 2 (1955).

acetylation of *N*-acetyl-22, 27-imino-11-oxojerva-5, 12-diene-3β, 23β-diol[11] (IIIa) in good yield. The nitrite was again unstable and was immediately photolyzed in benzene. Examination of the product by thin layer chromatography showed that the composition of the product was noticeably simpler than that from the photolysis of Ic. Column chromatography with silicic acid enabled us to isolate a single compound IV as the least polar material in 13% yield.

The compound, which was analyzed for a formula $C_{24}H_{32}O_4$, melted at 192—194°C and had the bands at 1699 cm^{-1} (α, β-unsaturated C=O), 1727 cm^{-1} (*O*-acetyl), 1628 cm^{-1} (conjugated C=C) and 2700 and 1727 cm^{-1} (aldehyde) in its infrared spectrum. The NMR spectrum of this clearly indicated the compound to be an aldehyde. It showed signals corresponding to C-19 methyl at τ 8.93, C-21 methyl at τ 9.12 (doublet, J=6.6), *O*-acetyl at τ 7.97 and C-18 methyl at τ 7.85. A signal due to aldehydic proton appeared at τ 0.18 as doublet (J=1.4 cps). From these results it is clear that the compound is correctly formulated as IV.

The course of this reaction apparently involves the formation of imino-intermediates VII followed by acid hydrolysis during separation by chromatography on silicic acid. The following sequence V-VIII may be proposed for this photochemical fragmentation.



In the scheme shown the photochemical excitation of the system V generates an alkoxyl radical VI which collapses in a variety of ways to afford stable species, one being a process to lead to VII in which the acyl-nitrogen linkage would most probably be cleaved. In order to confirm this fission of acyl-nitrogen bond, we attempted to examine the photolysis of the nitrite Ig in which the nitrogen has a methyl group in place of an acetyl substituent. Although Birch reduction of *N*-methyl jervine[12] gave rise to a well-defined compound Ie having mp 185.5—189°C, the selective acetylation for the C-3 hydroxyl group to afford If proved to be difficult, owing to the facile migration of the 13(17) double bond to the α, β-position of 11-carbonyl, as shown by the appearance of the absorption at 1626 cm^{-1} in the crude product from acetylation, and subsequent interaction between the α, β-unsaturated double bond and the basic nitrogen to afford partly the cyclic product during acetylation procedure. Actually, the compound Ie was very easily convertible into a compound with base which is formulated as a zwitterion IX from its spectral and analytical data and by analogy of the reaction.[4,13] In the infrared spectrum the compound IX showed the bands at 1734 cm^{-1} and 3440 and 3630 cm^{-1} due to a five-membered ring ketone and a hydroxyl stretching vibration, respectively. Treatment of IX in acetic acid with aqueous potassium iodide afforded the highly crystalline hydriodide.

Furthermore, in the NMR spectrum of the starting compound Ie, three singlets due to *N*-methyl, C-19 methyl and C-18 methyl appeared at τ 7.76, τ 9.06 and τ 8.09. But all these peaks in the compound IX shifted to τ 7.84, τ 8.97 and τ 8.26, respectively.

The synthesis of the compound of type If was equally unsuccessful in isomeric 22, 27-imino-11-oxojerva-8, 13(17)-diene series in which a double bond is located at the 8-position instead of the 5-position in If and in this cyclopentenone system there seemed some possibility of affording the compound of type If. 5α, 6-Dihydroisojervine was oxidized selectively at 3-position to yield the corresponding 3-ketone X.[4] However, attempted *N*-methylation with methyl iodide and potassium hydroxide led exclusively to a weak tertiary base XIa as experienced in the analogous compounds.[4,13] The structure XIa was evident from its IR and the NMR spectra.

We then considered the use of nitrite of the hexacyclic base XIa or XIIa, in which the β-carbon of the nitrite group has a tertiary nitrogen, to obtain more insight into the process from V to VIII. As already cited, the formation of this type of compound was first observed by Wintersteiner and Moor.[13] Birch reduction product Ia of jervine was submitted to Oppenauer oxidation to yield the corresponding Δ^4, 3-ketone. Crude Δ^4, 3-ketone gave rise to a tertiary base XIIa which was treated with nitrosyl chloride in pyridine in the usual manner. After work-up as usual, an unstable nitrite, mp 143—146°C, XIIb was obtained in excellent yield. This was immediately photolyzed in dry benzene without further purification. The photolyzed product consisted solely of the starting alcohol XIIa and no other noticeable products were produced as revealed by thin-layer

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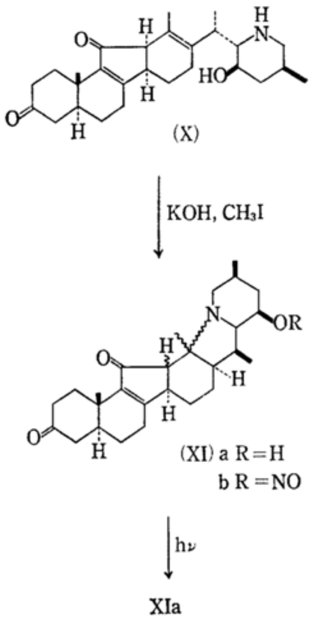
11) T. Masamune, K. Orito and A. Murai, This Bulletin, **39**, 2503 (1966).

12) K. Saito, H. Suginome and M. Takaoka, This Bulletin, **11**, 172 (1936).

13) O. Wintersteiner and M. Moor, *J. Am. Chem. Soc.*, **75**, 4938 (1953).

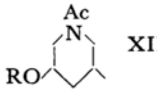


chromatography. The hexacyclic base XIa described above was also converted into the corresponding nitrite XIb and the nitrite was photolyzed. This likewise gave the original alcohol XIa exclusively.

These results demonstrate that in a photochemically excited system, ·O-C-C-N-alkyl, as that from XIb or XIIb, *N*-alkyl bonds are stable under the conditions of the Barton reaction and that acyl-nitrogen linkage is selectively cleaved in the scheme shown in V–VIII.

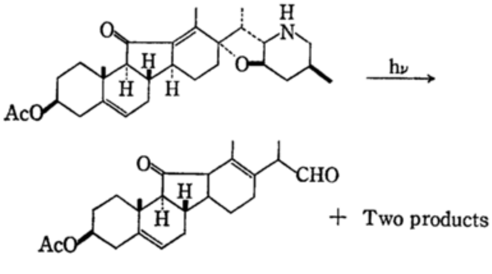
In order to probe further into the effect of *N*-substituents, *N*-benzoyl analogue of IIIc was newly synthesized. 22, 27-Imino-11-oxojerva-5, 13(17)-diene-3β, 23β-diol (Ia) was treated with benzoic anhydride to afford its crude tribenzoyl derivative Id. This was hydrolyzed to yield the corresponding *N*-benzoyl derivative IIId, mp 230.5—232.5°C. The *N*-benzoyl derivative IIId was submitted to partial acetylation to yield the corresponding 3*O*-acetate IIIe, mp 144.5—146°C. Conversion of this into the corresponding nitrite IIIf mp 206—208°C and the photolysis of the nitrite gave a mixture of the products. Column chromatography of the product afforded the aldehyde IV, which was identical with the specimen obtained from the photolysis of the nitrite IIIc, and also a small amount of benzoic acid. The nature of the reaction which leads to the formation of benzoic acid has not been fully understood. But this result supplements the evidence for the occurrence of acyl-nitrogen fission.

Moreover, we tried to confirm this acyl-nitrogen cleavage by studying some simpler system. *N*-Acetyl-3-hydroxy-5-methylpiperidine[14] XIIIa was converted into the corresponding unstable nitrite XIIIb. However, the photolysis of this nitrite gave rise to a complex mixture of amines which was characterized only by qualitative tests and we have not been successful in isolating any single amine.


XIIIa R=H
b R=NO

Although the cleavage reaction described here has obviously limited synthetic value, it may provide a useful synthetic route to certain aldehydes which are inaccessible by other procedures.[15]

It has been reported by Barton and coworkers[16] that in a number of nitrites vicinally substituted by an oxygen-bearing moiety, photolysis leads to an oxidative fission of carbon-carbon bond. In these cases the oxygen-bearing moieties could be carbonyl, hydroxyl-bearing tertiary carbon and ethyleneacetal groups. However, when the group was acetoxyl-bearing carbon, *i. e.*, the nitrite of 4-pregnene-3-one-17α, 20β-diol 20-acetate in which we have a system Ac–O–C–C–O–N=O, no carbon-carbon bond cleavage was observed and the starting alcohol was recovered unchanged. Moreover, several similar cases in the nitrite photolysis have been reported. For example, Kwok and Wolff[17] have reported that O-radical generated from the nitrite ester of 5α-androstane-2β, 3α, 17β-triol-3, 17-diacetate performed the normal Barton reaction. Moreover, Barton and his colleagues have reported[18] that the nitrite of 12α-hydroxy oleanolic acid acetate lactone was capable of achieving the normal Barton reaction. In these nitrites, ONO group is equally in the system



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[14] This compound was prepared by K. Orito in this laboratory through the catalytic hydrogenation of the corresponding aromatic amine, acetylation of the piperidine obtained and subsequent hydrolysis.

[15] R. W. Franck and W. S. Johnson, *Tetrahedron Letters,* **1963**, 545; R. W. Franck, G. P. Rizzi and W. S. Johnson, *Steroids,* **1964**, 464.

[16] A. L. Nussbaum, E. P. Yuan, C. H. Robinson, A. Mitchell, E. P. Oliveto, J. M. Beaton and D. H. R. Barton, *J. Org. Chem.,* **27**, 20 (1962).

[17] R. Kwok and M. E. Wolff, *ibid.,* **28**, 423 (1963).

[18] D. H. R. Barton, P. G. Sammes and M. Silva, *Tetrahedron,* Suppl. No. 7, 57 (1966).

AcO–C–C–ONO and no products from carbon-carbon bond cleavage were obtained.19)

The observed difference in the photolytic behavior between Ac–N–C–C–ONO system and Ac–O–C–C–ONO is of considerable interest. It may be noted that the difference in photolytic behavior between the two systems is parallel to the difference of the bond energy of O–C and N–C.

Nearly simultaneously with our preliminary publication1) Jeger and his colleagues published20) the results of the photolysis of *O*-acetyljervine which seem to be relevant to the problem discussed here. On irradiation with light of 253.7 mμ, *O*-acetyljervine gave a mixture of the products from which they isolated three compounds. One of these is an aldehyde which is, in all probability, identical with the aldehyde IV obtained by us during the photolysis of the nitrite IIIc.

It is to be noted that they have found *N, O*-diacetyljervine to be photochemically inert, since they postulated21) a similar process to ours for the formation of this aldehyde. As in the photolysis of *O*-acetyljervine different energy source and solvent (20 W, low pressure mercury arc lamp, 16 hr, dioxane) were employed, it would be difficult to assess this difference in the results.

Experimental

All melting points were determined on a Yanagimoto-type hot-stage and uncorrected. Unless stated otherwise, infrared spectra were determined in Nujol using an Nihonbunko DS-402G type spectrophotometer. NMR spectra were determined on a Japan electron optics 3H 60 high resolution NMR spectrometer in deuteriochloroform solution using tetramethylsilane as an internal reference. The course of reactions and the progress in column chromatography were followed by thin layer chromatography on Merck silica gel G.

3*O*, *N*-Diacetyl-22, 27-imino-11-oxojerva-5, 13(17)-diene-3β, 23β-diol (Ib). 22, 27-Imino - 11 - oxojerva-5, 13(17)-diene-3β, 23β-diol4) (Ia) (4.038 g) and freshly distilled acetic anhydride (2.003 g) in dry pyridine (7.14 g) were set aside at room temperature. After 24 hr, a further amount of acetic anhydride (0.201 g) was added and the mixture was set aside for an additional 24 hr and heated for 10 min on a water bath. Benzene was added to the cooled solution and the solvents were evaporated by a rotatory evaporator. To the residue, there was added 10% aqueous sodium carbonate solution (20 m*l*) and the mixture was extracted with chloroform (60 m*l*, 40 m*l*, 40 m*l*, successively). The chloroform solution was washed with water (50 m*l*,) dried with sodium sulfate and evaporated. The residue was chromatographed on silicic acid (80 g, Mallinckrodt, 100 mesh) eluting with benzene-ether mixtures with increasing amounts of ether to give, successively, 3*O*, 23*O*, *N*-triacetyl derivative (295 mg), a mixture of tri- and diacetyl derivatives (331 mg), 3*O*, *N*-diacetyl derivative (2.3 g). The latter was recrystallized from ethyl acetate and *n*-hexane to yield Ib (2.07 g), mp 112—134°C. This was again purified from ether. mp 159—161°C. $[\alpha]_D^{18}$ +41.4° (*c* 2.4, methanol). IR: ν_{max} 1733 cm^{-1} (O–Ac and 11-C=O), 3400 cm^{-1} (broad, C23–OH), 1625 cm^{-1} (N–Ac), NMR: τ 9.03 (C–19 methyl), τ 8.15 (C–18 methyl), τ 8.03 and τ 8.00 (O– and N–Ac). Found: C, 72.51; H, 8.87; N, 2.48%. Calcd for $C_{31}H_{45}O_5N$: C, 72.76; H, 8.86; N, 2.74%.

3*O*, *N*-Diacetyl-22, 27-imino-11-oxojerva-5, 13(17)-diene-3β, 23β-diol 23-Nitrite (Ic). To 3*O*, *N*-diacetyl 22, 27 - imino -11- oxojerva-5, 13(17)-diene-3β, 23β-diol (Ib) (202 mg) in dry pyridine (0.95 g) there was added a mixture of nitrosyl chloride and pyridine at −30—−35°C until the solution persisted orange color. The solution was allowed to stand for 20 min at −17—−40°C and the reaction was then quenched with ice water. The resultant precipitates of the nitrite were filtered, washed with water and dried at room temperature under vacuum to afford 212 mg of crude nitrite Ic, mp 87—90°C (decomp.). This nitrite was unstable and was positive in the color reaction with diphenylamine-sulfuric acid.9) Owing to the presence of *N*-acetyl absorption, a double band due to N=O stretching frequency in the infrared spectrum was not clear. However, two bands (768 and 795 cm^{-1}), which are most probably due to N–O stretching,22) were descernible.

After a few hours a thin layer chromatogram of this nitrite showed the appearance of a spot of significant amount of the starting material. Therefore, this nitrite was immediately used in the next step without further purification.

Photolysis of the Nitrite Ester (Ic). The nitrite ester Ic (212 mg) in dry benzene (10 m*l*) at 15°C and under an atmosphere of dry nitrogen was irradiated with a 150-W high pressure mercury arc lamp for 67 min. After removal of a small amount of precipitation, the dark brown solution was concentrated to dryness and the residue was chromatographed on silicic acid (6 g) with benzene containing an increasing amount of ether. The least polar product (50 mg), eluted with benzene and ether, crystallized on evaporation of the solvent. This was washed with *n*-hexane and recrystallized from aqueous ethanol to yield aldehyde II (22 mg) mp 149.5—152°C. IR: ν_{max} 1731 cm^{-1} (O–Ac and 11-C=O) 2697 cm^{-1}, 2799 cm^{-1} and 1740 cm^{-1} (shoulder) (aldehyde) NMR: τ 9.05 (C-19 methyl) τ 8.16 (C-18 methyl) τ 8.83 (doublet, J=6.6) (C-21 methyl), τ 7.99 (O–acetate) and τ 0.56 (doublet, J=4.2) (aldehyde). Found: C, 75.47; H, 8.62%. Calcd for $C_{24}H_{32}O_4$: C, 74.97; H, 8.39%.

3*O*, *N*-Diacetyl-22, 27-imino - 11 - oxojerva - 5, 12-diene-3β, 23β-diol (IIIb). *N*-Acetyl-22, 27-imino-11-oxojerva-5, 12-diene-3β, 23β-diol (2.477 g) and acetic anhydride (0.576 g) in dry pyridine (2.19 g) were set aside for 22 hr at room temperature and then heated for 10 min on the water bath. To this solution there was added acetic anhydride (200 mg) and the solution was

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19) As Kwok and Wolff have quoted, there is naturally a possibility that both hydrogen abstraction and oxidative fission occurred competitively in their case and only the product of abstraction was isolated.

20) G. Bozzato, K. Schaffner and O. Jeger, *Chimia.*, **20**, 114 (1966).

21) G. Bozzato, Ph. D. Thesis, E. T. H. Zürich (1966). We are grateful to Professor O. Jeger for the correspondence and sending the thesis by Dr. G. Bozzato.

22) P. Tarte, *Bull. Soc. Chem. Belges*, **60**, 227 (1951).

again heated for 30 min. After addition of benzene, the solvent was removed and to the residue were added water (30 m*l*) and 10% aqueous sodium carbonate (20 m*l*) and this was extracted with chloroform (50 m*l*, 40 m*l* and 40 m*l*, successively). The chloroform layer was washed with water (70 m*l*) and dried over magnesium sulfate. After evaporation of the solvent, the residue (3.03 g) was chromatographed on silicic acid (49 g). Elution with a mixture of benzene-ether with an increasing amount of ether afforded 3*O*, 23*O*, *N*-triacetyl-22, 27-imino-11-oxojerva-5, 12-diene-3β-, 23β-diol (0.227 g), a mixture of di- and triacetyl derivatives (38 mg) 3*O*, *N*-diacetyl-22, 27-imino-11-oxojerva-5, 12-diene-3β, 23β-diol (IIIb) (1.31 g) and a mixture of di- and monoacetyl derivatives (0.805 g) successively. The diacetyl derivative was recrystallized from aqueous ethanol to yield pure IIIb (0.741 g) mp 217.5—220°C. IR: ν_{max} 1645 cm^{-1} (N–Ac), 1697 cm^{-1}(11-C=O), 1733 cm^{-1} (O–Ac) 3505 cm^{-1} (OH) NMR: τ 9.25 (J=6.0) (C-26 methyl) τ 8.95 (C-19 methyl), τ 8.73 (J=6.0) (C-21 methyl), τ 7.92 (C-18 methyl), τ 8.00 and τ 7.83 (N–Ac and O–Ac). Found: C, 72.95; H. 8.94; N, 2.84%. Calcd for $C_{31}H_{45}O_5N$: C, 72.76; H, 8.86; N, 2.74%.

3*O*, *N*-Diacetyl-22, 27-imino-11-oxojerva-5, 12-diene-3β, 23β-diol Nitrite (IIIc). Compound IIIb (201 mg) was dissolved in dry pyridine and treated with nitrosyl chloride-pyridine mixture at −30°C until the solution persisted greenish yellow color. This was set aside for 7 min and poured into ice water. The resultant precipitates were collected by filtration to yield nitrite IIIc, 261 mg, mp 212—214°C (decomp.). This was unstable, and, dried for 4 hr under vacuum, was used immediately for the next photolysis.

Photolysis of Nitrite Ester (IIIc). The nitrite ester IIIc (261 mg) in dry benzene (12 m*l*) at 14°C and under an atmosphere of dry nitrogen was irradiated with a 150-W high pressure mercury arc lamp (Daikakogyo HLVA type, Japan) for 2 hr and 10 min. The residue was chromatographed on silicic acid (7 g). The least polar product (23 mg), eluted with benzene, crystallized on evaporation of the solvent. This was recrystallized from aqueous ethanol (17 mg) mp 192—194°C.[23] IR: ν_{max} 1699 cm^{-1} (α, β-unsaturated C=O), 1727 cm^{-1} (O–Ac and aldehyde) 1628 cm^{-1} (C=C) 2700 cm^{-1} (aldehyde). NMR: τ 8.97 (C-19 methyl) τ 9.12 (C-21 methyl) (J=6.6) τ 7.97 (O–Ac) τ 7.85 (C-18 methyl), τ 0.18 (J=1.4 cps) (aldehyde). Found: C, 75.03; H, 8.31%. Calcd for $C_{24}H_{32}O_4$: C, 74.97; H, 8.39%.

The Preparation of XIa. 5α, 6-Dihydroisojervone[4] (X) (200 mg), potassium hydroxide (63 mg) and methyliodide (82 mg) in ethanol (8 m*l*) were heated at 72°C for 95 min in a sealed tube. After the removal of ethanol, the residue was extracted with chloroform (20 m*l*) and water (10 m*l*). The organic layer was washed and dried. After the removal of the chloroform, the residue was recrystallized from acetone to yield 42 mg of XIa, mp 235—236°C (decomp.). The residue gave a further 84 mg of XIa by the preparative T.L.C. NMR: C-19 and C-18 methyls, τ 8.71 and τ 8.76. IR: 1703 cm^{-1} (six membered ketone), 1685 and 1635 cm^{-1} (CO–C=C), 3470 cm^{-1} (OH) Found: C, 75.93; H, 9.10; N, 3.54%. Calcd for $C_{27}H_{39}O_3N$: C, 76.19; H, 9.24; N, 3.29%.

The Preparation and Photolysis of Nitrite (XIb). The alcohol XIa (84 mg) in pyridine (1 m*l*) was treated with nitrosyl chloride in pyridine at −25°C in the usual manner. The nitrite obtained softened at 90°C and melted at 160°C with decomposition (63 mg). IR: 1713 cm^{-1} (six membered ketone), 1695 and 1640 cm^{-1} (CO–C=C). The nitrite (63 mg) in benzene (13 m*l*) was photolyzed in the usual manner for 90 min. After the removal of the solvent, T. L. C. revealed that the product was solely the starting alcohol XIa.

The Preparation of XIIa. (Experiments by N. Sato). 22, 27-Imino-11-oxojerva-5, 12-diene-3β, 23β-diol (Ia) (3.7 g) was dissolved in 500 m*l* of dry toluene and 150 m*l* of the solvent was removed by distillation. To this solution, there was added 40 m*l* of cyclohexanone and then 60 m*l* of the solvent was distilled to remove a trace of water. A solution of 3.7 g of aluminum isopropoxide in 19 m*l* of dry toluene was added. The reaction mixture was refluxed for 6.5 hr. On cooling, 10 m*l* of water was added to the solution and the precipitate was removed by filtration. To the filtrate there was added 2 N aqueous hydrochloric acid (50 m*l*) and the salt (3.0 g) formed was collected by filtration. The salt was dissolved in water (2.5 *l*) and the aqueous solution was extracted with ether. The aqueous solution was made up to pH 8.0 with 2 N aqueous ammonia, extracted with chloroform (total volume, 700 m*l*), washed with water and dried over sodium sulfate. After evaporation, 3.4 g of crude Δ^4, 3-ketone was obtained. This was purified by making the complex (2.0 g) with chloroform. The complex (1.0 g) was immediately submitted to cyclization with base to yield XIIa. The chloroform complex in 5% methanolic potassium hydroxide was refluxed for 1 hr. The resultant compound was extracted with ether. The ethereal solution was washed with water and dried over sodium sulfate. After evaporation of the solvent, the residue was recrystallized from ethanol to yield XIIa mp 222—224°C. IR: 1728 cm^{-1} (five membered ring ketone), 1655 and 1616 cm^{-1} (α, β-unsaturated ketone). UV λ_{max} 232 mμ (ε; 9800) (ethanol) NMR τ 8.81 and τ 8.70 (C-19 and C-18 methyls). Found: C, 76.31; H, 9.22; N, 3.41%. Calcd for $C_{29}H_{39}O_3$: C, 76.19; H, 9.24; N, 3.29%.

The Nitrite XIIb. Compound XIIa (200 mg) in pyridine (1 m*l*) was treated with nitrosyl chloride in pyridine at −30°C until dark green color persisted. The reaction mixture was poured into ice water. The resultant precipitate was collected by filtration and dried under vacuum. Mp 143—146°C (204 mg). T.L.C. gave only one spot. IR: 1730 cm^{-1} (five membered ketone), 1671 and 1638 cm^{-1} (α, β-unsaturated ketone) 1618 cm^{-1} (weak) 1660 cm^{-1} (shoulder), 795 and 802 cm^{-1} (doublet) and 675 cm^{-1} (–O–NO).

Photolysis of the Nitrite (XIIb). The nitrite (204 mg) in dry benzene (15 m*l*) was irradiated under an atmosphere of dry nitrogen at 14—16°C. After 68 min. no nitrite remained unchanged. The residue (233 mg) gave only one spot on T.L.C. This was dissolved in methanol. To the solution there was added ether and *n*-hexane to yield the crude alcohol XIIa. This was again recrystallized from acetone, mp 222—224°C.

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23) In our preliminary communication,[1] the melting point of this was described as mp 167—171°C.

***N*-Benzoyl-22, 27-imino-11-oxojerva-5, 12-diene-3β, 23β-diol (IIId).** 22, 27-Imino-11-oxojerva-5, 13-(17)diene-3β, 23β-diol (2.38 g) and benzoic anhydride (4.65 g) in dry pyridine (20 m*l*) were set aside overnight at room temperature. Then, the reaction mixture was further heated for 1 hr on a water bath. After the removal of pyridine under reduced pressure, there was added aqueous 5% sodium carbonate (80 m*l*). This was extracted with chloroform (100 m*l*, 50 m*l*, and 50 m*l*, successively).

The combined organic layer was washed with water (100 m*l*, twice) and dried over sodium sulfate. The residue (7.7 g) in 6% methanolic potassium hydroxide (50 m*l*) was refluxed for 1.5 hr under nitrogen atmosphere. After 30 min, solid appeared in the solution and methanol (20 m*l*) was added. The solution was further refluxed for 1 hr and cooled. The crystals that appeared were collected by filtration. A total amount of 2.32 g of crude benzoyl derivative IIIc was obtained. After purification from methanol, it melted at 230.5—232.5°C. $[\alpha]_D^{18}$ −8.2 (*c* 2.0, pyridine) IR: 1623 cm^{-1} (*N*-benzoyl), 1703 cm^{-1} (C=O). NMR: MeOH τ 6.49 C-18 methyl, τ 7.79 C-19 methyl, τ 8.93, phenyl proton, τ 2.62. Found: C, 75.74; H, 8.64; N, 2.29%. Calcd for $C_{33}H_{45}O_6N\frac{1}{2}MeOH$: C, 75.65; H, 8.65; H, 2.58%.

3*O*-Acetyl-*N*-benzoyl-22, 27-imino-11-oxojerva-5, 12-diene-3β, 23β-diol (IIIe). To *N*-benzoyl-22, 27-imino-11-oxojerva-5, 12-diene-3β, 23β-diol (1.01 g) in pyridine (20 m*l*) there was added acetic anhydride (2 m*l*) at −10°C. The reaction mixture was set aside for four days at −5°C. To the reaction mixture, methanol was added and the mixture was heated for 2 hr on a water bath. The solvent was removed and to the residue water was added and this was extracted with chloroform (50 m*l*, 50 m*l* and 30 m*l*).

The chloroform solution was washed and dried. After the removal of the solvent the residue was chromatographed on alumina (Merck, standard, 25 g). Elution with benzene containing an increasing amount of ether gave diacyl derivative (231 mg), the mixture of di- and mono-acetyl derivatives (110 mg) and desired 3*O*-acetyl derivative IIIe (680 mg, 62%). The mono-acetyl derivative was recrystallized from aqueous ethanol (644 mg) mp 144.5—146°C. $[\alpha]_D^{18}$ −67.7° (*c* 2.1, methanol). IR: 1629 cm^{-1} (Ph–C=O), 1705 cm^{-1} (C=C–C=O) and 1735 cm^{-1} (–O–COCH$_3$) 3400 cm^{-1} (broad, OH). Found: C, 72.89; H, 8.51; N, 2.28%. Calcd for $C_{36}H_{47}O_5N\cdot H_2O$: C, 73.06; H, 8.35; N, 2.37%. After purification from aqueous ethanol, diacetate had mp 233—235°C. IR: 1633 cm^{-1} (benzoyl), 1702 cm^{-1} (C=C–C=O) and 1739 cm^{-1} (–OCOCH$_3$). Found: C, 73.66; H, 8.06; N, 2.76%. Calcd for $C_{38}H_{49}O_6N$: C, 74.11; H, 8.02; N, 2.27%.

The Nitrite (IIIf). 3*O*-Acetyl-*N*-benzoyl-22, 27-imino-11-oxojerva-5, 12-diene-3β, 23β-diol (336 mg) in dry pyridine (4 m*l*) was treated with nitrosyl chloride-pyridine mixture at −40°C until the solution persisted blue color. This was set aside for 22 min and poured into ice water (500 m*l*). The resultant precipitates of the nitrite were collected by filtration, washed with water and dried at room temperature under vacuum (344 mg), mp 206—208°C (decomp.). This nitrite was positive for the nitrite color reaction with diphenylamine-sulfuric acid and was unstable.

Photolysis of the Nitrite Ester. The nitrite ester (334 mg) above in dry benzene (18 m*l*) at room temperature and under an atmosphere of dry nitrogen was irradiated with a 150 W high pressure mercury arc lamp for 85 min. After this period the color reaction disclosed complete disappearance of the nitrite. After removal of the solvent under reduced pressure, the oily residue was chromatographed on silicic acid (10 g). Elution with benzene and then benzene containing ether (0.5 vol%) gave 38 mg of the least polar fraction (A). Then, the column was eluted with ethyl acetate-methanol mixture. Eluate (B) (287 mg) was obtained. Tritulation of (A) above with ether gave 42 mg of the residue. This was dissolved in ether (20 m*l*) and extracted with 5% aqueous sodium hydrogen carbonate (1.5 m*l*) and water (3 m*l*). Ethereal layer was washed with water and dried over sodium sulfate. Removal of ether yielded 17 mg of the residue (C). Aqueous layer was acidified to pH 1 with 1 N hydrochloric acid and extracted with ether. From this ethereal solution, benzoic acid (2 mg) was obtained. Preparative thin layer chromatography of the eluate (B) afforded 39 mg of aldehyde as the least polar fraction. Recrystallization of this from aqueous ethanol afforded the aldehyde IV, 15 mg, mp 189—192°C. IR and NMR spectra of this aldehyde were completely superimposable with that obtained from IIIc.

***N*-Methyl-22, 27-imino-11-oxojerva-5, 13(17)-diene-3β, 23β-diol (Ie).** To a solution of liquid ammonia (300 m*l*) containing lithium (474 mg) there was added *N*-methyljervine[12] (3.92 g) in tetrahydrofuran (70 m*l*). A further amount of tetrahydrofuran (30 m*l*) was added while stirring. The mixture was stirred for 35 min and the blue color of the reaction mixture disappeared after this period. A further amount of lithium (30 mg) was added. Ammonium chloride (5 g) was added and the resulting colorless solution was kept at room temperature to remove ammonia and then tetrahydrofuran was removed under reduced pressure. To the residue there was added water (100 m*l*) and this was extracted with chloroform (four times, the total volume 450 m*l*). The chloroform layer was washed with water (150 m*l*), dried and evaporated. The residue was recrystallized from methanol. Crude Ie (2.59 g) was obtained in three crops. This was further recrystallized from methanol. Mp 185.5—189°C $[\alpha]_D^{18}$ +30.8° (*c* 2.5, pyridine). IR: 3400 cm^{-1}(OH), 1731 cm^{-1} (five membered C=O). NMR: τ 7.76 (N–Me), τ 8.09 (C-18 methyl) τ 9.06 (C-19 methyl). Found: C, 76.07; H, 9.87; N, 3.13%. Calcd for $C_{28}H_{43}NO_3$: C, 76.15; H, 9.81; N, 3.17%.

The Preparation of the Compound (IX). The compound Ie (292 mg) in methanol (10 m*l*) and 5% methanolic potassium hydroxide (2 m*l*) was refluxed for 2 hr under an atmosphere of dry nitrogen. To the reaction mixture methanol (10 m*l*) and 5% methanolic potassium hydroxide (2 m*l*) were again added and this was refluxed for 1 hr. After the removal of methanol, the residue was washed with water (30 m*l*) and dried (237 mg). This was recrystallized from methanol (156 mg). Mp 275—302°C (decomp.). IR: 3400 cm^{-1} (OH), 1731 cm^{-1} (five membered ketone). NMR: τ 7.84 (N–Me) τ 8.26 (C-18 methyl) τ 8.95 (C-19 methyl). Found: C, 75.95; H, 9.92; N, 3.01%. Calcd for $C_{28}H_{43}O_3N$: C, 76.15; H, 9.81; N, 3.17%.

The hydriodide was obtained as follows: the zwitterion IX (126 mg) in acetic acid (0.3 m*l*) was admixed with aqueous potassium iodide (20%, 0.4 m*l*). The highly crystalline hydriodide deposited immediately. This was collected by filtration and recrystallized from ethanol to yield colorless needles, (73 mg) mp 300°C. Found: C, 59.19; H, 7.89; N, 2.43%. Calcd for $C_{28}H_{44}O_3NI$: C, 59.04; H, 7.79; N, 2.46%.

The authors are grateful to Mr. S. Shimokawa for the measurements of NMR spectra and to the staff of the laboratory for microanalyses, the Faculty of Pharmaceutical Science of Hokkaido University, for the elemental analyses.