

Photoinduced Transformations. Part 33.¹ Mechanism of Photoinduced Rearrangement of a (22*S*,25*S*)-*N*-Acetylveratr-13(17)-enine-11β-yl Nitrite, a Fused Cyclopentyl Nitrite, to a Nitrone²

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In order to define the pathway of photoinduced rearrangement of (22*S*,25*S*)-*N*-acetylveratr-13(17)-enine-3β,11β,23β-triol 3,23-diacetate 11-nitrite (1) to the six-membered ring nitrone (2), studies were made of the results of irradiation with monochromatic light and the solvent dependence of the reaction; the assumed intermediates were isolated and their reactions investigated at both 77 K and room temperature, and quantum yields were measured. On the basis of the results, together with those of cross-over experiments with ¹⁵N-labelled species previously reported, pathways from the nitrite to the nitrone are discussed.

We have previously³ reported the formation of a cyclic nitrone *via* photoinduced rearrangement of a steroidal cyclopentyl nitrite and some unusual reactions of this nitrone with acylating agents. We have briefly described investigations aimed at clarifying the pathway of the rearrangement,² and now give details of these studies (those of the cross-over experiments^{2b} were provided in Part 32¹).

RESULTS AND DISCUSSION

Photorearrangement Pathways.—Probable photo-rearrangement pathways¹⁻³ are shown in Scheme 1. They involve the following successive steps: (a) a homolysis of the O-NO bond to give nitric oxide and the corresponding 11β-alkoxyl radical (A); (b) β-cleavage of the 11β-alkoxyl radical at the 11,12-bond to afford an allyl radical (B); (c) combination of NO and the allyl

radical to afford a nitroso-aldehyde(s) [(C) and/or (C')]; (d) thermal or photochemical cyclization of the nitroso-aldehyde or the isomeric hydroxyimino-aldehyde (3) to afford the nitrone (2).

For the present studies we used (22*S*,25*S*)-*N*-acetyl-5α-veratr-13(17)-enine-3β,11β,23β-triol 2,23-diacetate 11-nitrite (1).¹

Intermediacy of the Nitroso-aldehyde.—The intermediacy of a nitroso-aldehyde in nitrite photolysis has been assumed in the well known transformation of a steroidal 17-nitrite into a hydroxamic acid by Barton and his colleagues.⁴

The assumed short-lived nitroso-aldehyde intermediate in our case could be trapped by low temperature photolysis. The nitrite (1) was irradiated in EPA (diethyl ether-isopentane-ethanol) matrix at a concentration of 4 × 10⁻⁴M or 7 × 10⁻³M and at 77 K through a

¹ Part 32, H. Suginome, T. Mizuguchi, and T. Masamune, *J.C.S. Perkin I*, 1976, 2365.

² Preliminary accounts, H. Suginome, T. Mizuguchi, and T. Masamune, (a) *J.C.S. Chem. Comm.*, 1972, 376; (b) *Tetrahedron Letters*, 1971, 4723.

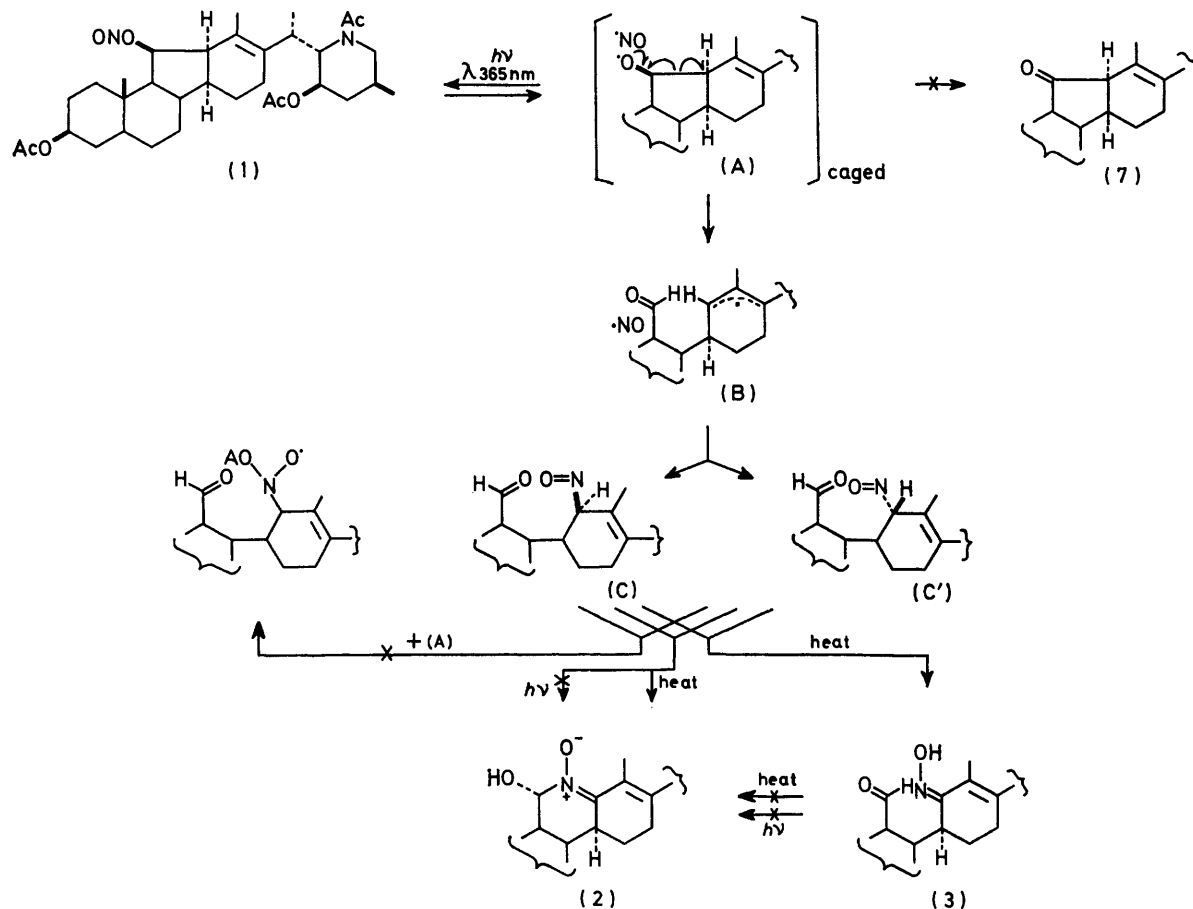
³ H. Suginome, N. Sato, and T. Masamune, *Tetrahedron Letters*, 1969, 3353; *Tetrahedron*, 1971, 27, 4863.

⁴ C. H. Robinson, O. Gnoj, A. Mitchell, E. P. Oliveto, and D. H. R. Barton, *Tetrahedron*, 1965, 21, 743.

Pyrex filter. The reaction was followed spectrophotometrically in the region 250–800 nm. Immediately after irradiation had begun the colour of the solid matrix became green, gradually changing to blue. The spectral changes are shown in Figures 3 and 4. Two species absorbing at 693 and at 323 nm were formed; after 3 min the amount of the latter had reached a maximum, and then the amount of the former increased at the expense of the latter. The intensity and the

interaction between the nitroso-group and the formyl group in the matrix at liquid nitrogen temperature, or to quenching of the reaction. When the matrix was brought to room temperature in the dark, the presence of the nitrone was shown both by the characteristic absorption maximum at 286 nm and by t.l.c.

The present result contrasts with the reported photochemical transformation of borneol nitrite into a cyclic hydroxamic acid: a 25% yield of an intermediate



SCHEME 1

position of the absorption maximum of the former species exactly corresponded to those expected for the $n_N \rightarrow \pi^*$ band of a C-nitroso-compound,⁵ and the species responsible was considered to be the intermediate nitroso-aldehyde [(C) and/or (C')], which was too unstable to survive at room temperature. The nitroso-aldehyde in the matrix was stable to further irradiation at 77 K. Reported molar absorptivities of C-nitroso-compounds at room temperature are in the range 14–30;⁶ on the basis of a value of 23 for the C-nitroso-aldehyde (C) and/or (C'), its yield from the nitrite in the matrix at 77 K was 100%. The resistance to cyclization of the C-nitroso-aldehyde under these conditions could be due to an inability to arrive at an appropriate geometry for

nitroso-aldehyde was produced by u.v. irradiation at room temperature, and this intermediate was said to be thermally stable.⁷

Pathway to the Nitrone from the Nitroso-aldehyde.—With regard to the formation of the nitrone from the nitroso-aldehyde (C) and/or (C') we envisaged at least four possible modes (Scheme 1): (a) thermal isomerization of the nitroso-aldehyde(s) into a hydroxyimino-aldehyde followed by intramolecular nucleophilic attack of the ambident hydroxyimino-group on the formyl carbon atom (mechanism A); (b) the same as (a) but

⁶ E. S. Stern and C. J. Timmons, 'Electronic Absorption Spectroscopy in Organic Chemistry,' Arnold, London, 1960, p. 960.

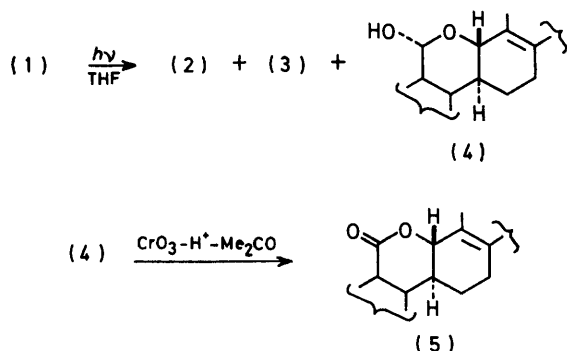
⁷ P. Kabasakalian and E. R. Townley, *J. Org. Chem.*, 1962, 27, 3562.

⁵ L. E. Orgel, *J. Chem. Soc.*, 1953, 1276; J. Mason, *ibid.*, 1957, 3904.

with excitation of the formyl group and/or the $\alpha\beta$ -unsaturated hydroxyimino-group (mechanism A^*); (c) direct cyclization of the ground state nitroso-aldehyde (mechanism B); (d) direct cyclization of the excited nitroso-aldehyde with excitation of the C -nitroso-group and/or the formyl group (mechanism B^*).

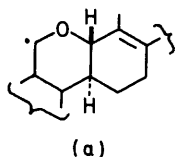
When the photoreaction of the nitrite (1) was conducted in dry tetrahydrofuran (THF), the major product was not the nitrone (2) but the hydroxyimino-compound (3) (66%); a small amount (15%) of the nitrone (2) was obtained, along with a third compound (4), m.p. 162–164 °C, which was the most polar. Compound (3) decomposed gradually at room temperature. Its electron impact mass spectrum (m/e 586) proved that it was an isomer of the nitrite (1). The i.r. spectrum (CHCl_3) showed bands at 3 200–3 600 (H-bonded OH) 2 748 (CHO), 1 725 (OAc), and 1 632 cm^{-1} (NAC). The u.v. spectrum exhibited maxima at 238 (ϵ 5 030) and 292 nm (2 200) in ethanol. The n.m.r. spectrum revealed signals at τ 0.45 (d, J 4.2 Hz, $\text{CH}\cdot\text{CHO}$), 7.91, 7.95, and 7.97 (each 3 H, s, NAc and 2 OAc), 8.42 and 9.06 (each 3 H, br, s, 18- and 19-H), 4.94 (1 H, br, s, 23-H), 5.30 (2 H, m, 3 α - and 22 β -H), 6.69 (2 H, br, s, 27-H), and 6.93 (1 H, m, 20 β -H). These spectral data, together with considerations related to the reaction pathway, were best reconciled with the hydroxyimino-aldehyde structure (3), our suggested intermediate in pathway A .

The presence of the hydroxyimino-group was further supported by the mass spectrum: m/e 570 ($M^+ - 16$) and 569 ($M - 17$); $M^+ - 16$ peaks are characteristic of alicyclic ketone oximes.⁸ A colour test for oximes⁹ gave a positive result.



The product (4) was inferred to be a lactol from its spectral data and those of the product (5) of Jones oxidation. The electron impact mass spectrum of

* The lactol (4) is most probably formed *via* a pyranyl radical such as (a) (see H. Sugimoto, A. Furusaki, K. Kato, and T. Matsumoto, *Tetrahedron Letters*, 1975, 2757).



compound (4) showed, apart from the usual fragment peaks due to the piperidine ring at m/e 198, 156 (base peak), and 114, peaks at m/e 555 ($M^+ - \text{H}_2\text{O}$) and 357 (loss of piperidine from m/e 555). The u.v. spectrum (solvent methanol) showed only an intense maximum at 206 nm (ϵ 14 600) due to olefinic chromophores. The i.r. spectrum showed a series of intense bands at 3 536, 1 727, 1 642, and 1 027 cm^{-1} due to OH, OAc, NAc, and ether systems. The n.m.r. spectrum showed signals τ 9.15 (3 H), 8.26 (3 H), 7.97 (6 H), and 7.94 (3 H) (all s, 19-H, 18-H, OAc, and NAc), 5.92 (1 H, br, s, $W_{1/2}$ 9.0 Hz), 5.19 (1 H, d, J 10.5 Hz, 22 β -H, superimposed on broad 3 α -H signal at τ 5.29), and 4.92 (br, s, 23 α -H, superimposed on another one-proton signal). The one-proton signals at τ 5.92 and 4.92 were ascribed to the 12 β -H and the 11 β -H of the lactol structure, by comparison with the spectral data of the oxidation product (5).

The structure of compound (5) was deduced as follows. The electron impact mass spectrum showed M^+ at m/e 571 and a distinct peak at m/e 373 (2.3%, loss of piperidine), and suggested that the secondary alcohol group of the product (4) had been oxidized to yield a δ -lactone. In the i.r. spectrum no hydroxy-band was present and, beside the bands due to OAc (1 737 cm^{-1}) and NAc (1 644 cm^{-1}), a new shoulder was present at 1 751 cm^{-1} , assignable to the δ -lactone group. The n.m.r. spectrum showed signals at τ 8.95 (3 H), 8.17 (3 H), 7.98 (6 H), and 7.95 (3 H) (all s, 19-H, 18-H, OAc, and NAc), 5.68 (br, s, $W_{1/2}$ 9.0 Hz, 12 β -H), 5.21 (d, J 11.4 Hz, 22 β -H, superimposed on the broad 3 α -H signal at τ 5.30) and 4.97 (br, s, 23 α -H).

The hydroxy-group of the lactol (4) should be α -oriented on the basis of a comparison of 19-H chemical shifts of the lactol (4) and the lactone (5). By analogy with 11-oxo-steroids, a downfield shift of the 19-H signal in transforming the lactone (5) into the epimer of the lactol (4) with β -OH is expected. The upfield shift (0.2 p.p.m.) observed proves the α -hydroxy-configuration.

The configuration of the 12-H of the lactol (4) is not assigned conclusively, but the β -configuration is preferred on the basis of the width of the n.m.r. signal.*

We wished to discover whether the hydroxyimino-aldehyde (3) was transformed into the nitrone (2) by irradiation under the experimental conditions under which the nitrone (2) was obtained, or by thermal treatment in toluene. However neither irradiation in toluene through Pyrex nor thermal treatment in toluene afforded the nitrone (2); in each case most of the hydroxyimino-aldehyde (3) was recovered. This result ruled out mechanisms A and A^* , which involve the hydroxyimino-aldehyde (3) as an intermediate.

Effect of Solvents on Photolysis of the Nitrite (1).— Since the solvent had been found to exert a marked effect

* H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Mass Spectrometry of Organic Compounds,' Holden-Day, San Francisco, 1967, p. 372.

⁹ F. Feigl and V. Anger, trans. R. E. Oesper, 'Spot Tests in Organic Analysis,' Elsevier, Amsterdam, 1966, p. 286.

on the reaction product, we further studied the photolysis of the nitrite (1) in a number of protic and aprotic solvents. In each experiment the substrate (500 mg) was dissolved in the solvent (23 ml) and the solution was irradiated in a Pyrex vessel with 100 W high-pressure mercury arc under nitrogen until the starting nitrite had disappeared (usually *ca.* 4 h, although the reaction in acetic acid was complete within a slightly shorter time). The products were separated by preparative t.l.c. The results are shown in the Table, and indicate that (a) the

Yields of the products of photolysis of the nitrite (1) in various solvents

| Solvent | Yield (%) | | |
|-------------------------------|--------------------------|--|--------------------|
| | Nitrone (2) ^b | Hydroxyimino-aldehyde (3) ^c | 11 β -Ol (6) |
| THF ^a | 15 | 66 | 0 |
| Et ₂ O | 32 | 43 | 0 |
| Dioxan | 41 | 32 | 0 |
| MeOH ^d | 50 | 0 | 0 |
| AcOH | 61 | 0 | 14 |
| Penta-1,3-diene | 12 | 41 | 0 |
| CCl ₄ ^e | 63 | 0 | 0 |
| PhMe | 62 | 0 | 0 |

^a Another crystalline product (4) more polar than (2) or (3) (R_F 0) was obtained in poor yield (see text and Experimental section). ^b Based on the amounts of crystalline nitrone obtained from the initial separation by preparative t.l.c. followed by one recrystallization from ether. ^c Based on the amounts of the hydroxyimino-aldehyde (3) extracted in preparative t.l.c. ^d At least three minor, unidentified products less polar than the nitrone were formed. ^e An amorphous compound (*ca.* 8%), less polar than the hydroxyimino-aldehyde (3), which exhibited an aldehydic proton n.m.r. signal at τ 0.46 and might be an isomeric hydroxyimino-aldehyde, was obtained.

nitrone (2) is produced in both protic and aprotic solvents with Pyrex-filtered light; (b) a significant quantity of the hydroxyimino-aldehyde (3) (32–66%) is formed together with the nitrone (2) in ethereal solvents and in penta-1,3-diene; (c) the nitrone (3) is produced even in acetic acid, but in this case the parent 11 β -ol (6) is also formed in significant quantity; and (d) photolysis in toluene affords the nitrone as the sole product.

Although this solvent dependence of the reaction is not entirely understood, the possibility that toluene might function as a sensitizer for excitation of the C-NO group is excluded on the basis of the results of photolysis with monochromatic light (see following section).

Photolysis of the Nitrite (1) with Monochromatic Light and Quantum Yield Measurements.—Of the remaining two probable modes of reaction, *i.e.* thermal and photochemical cyclization of the short-lived nitroso-aldehyde (mechanisms *B* and *B**), the cyclization involving a formyl group and an excited C-NO group (*B**) has pre-empted, though it led to a cyclic hydroxamic acid.⁷

If the nitrone (2) is formed directly from the nitroso-aldehyde we may readily ascertain whether this process is thermal or photochemical by photolysis of the nitrite (1) with monochromatic light which is only able to excite the O-NO of the nitrite, not the C-NO group or the CHO

group of the assumed intermediate [(C) and/or (C')]. The O-NO group generally shows a characteristic absorption structured band at *ca.* 370 nm due to the $n \rightarrow \pi^*$ transition.¹⁰ Stronger absorption at shorter wavelength was observed for gaseous methyl nitrite and was ascribed to an intramolecular charge-transfer band.¹¹ The absorption of the O-NO group of the nitrite (1) in methanol is shown in Figure 1. We first examined the

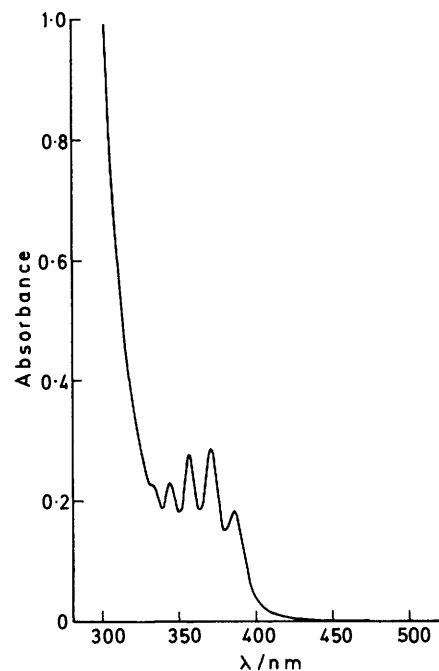


FIGURE 1 U.v. absorption of the nitrite (1) ($3.4 \times 10^{-3}M$) in methanol

photolysis in methanol with monochromatic light of various wavelengths, *i.e.* 230, 257, 285, 311, 338, and 365 ± 7.5 nm, generated by a JASCO CRM-FA grating spectroirradiator equipped with a 2 kW xenon arc. The quantum yield of the decomposition of the nitrite (1) was found to be 0.7 with 365 ± 7.5 nm light. (Quantum yields of photodecomposition with 338 ± 7.5 , 311 ± 7.5 , 257 ± 7.5 , and 230 ± 7.5 nm light were 0.6, 0.5, 0.6, 0.6, and 0.5, respectively.)

In Figure 2 the change of the u.v. spectrum of a methanolic solution of the nitrite (1) when irradiated with 365 ± 7.5 nm light is shown. Gradual appearance of the maximum at 286 nm, due to the nitrone (2), is observed. As described previously, by-product formation was minimal in methanol and the nitroso-intermediate seemed to be transformed into the nitrone nearly quantitatively in this solvent. We were able to estimate an approximate quantum yield of the formation of the nitrone in methanol, by following the formation of the nitrone spectroscopically; the value obtained was 0.3 with irradiation at 365 ± 7.5 nm. Since this light is able to excite neither the formyl group nor the nitroso-

¹⁰ J. G. Calvert and J. N. Pitts, jun., 'Photochemistry,' Wiley, New York, 1967, p. 450.

¹¹ M. Tanaka, J. Tanaka, and S. Nagakura, *Bull. Chem. Soc. Japan*, 1966, **39**, 766.

group of the hypothetical intermediate, mechanism B^* is excluded and the cyclization to the nitrone is shown to be a thermal reaction.

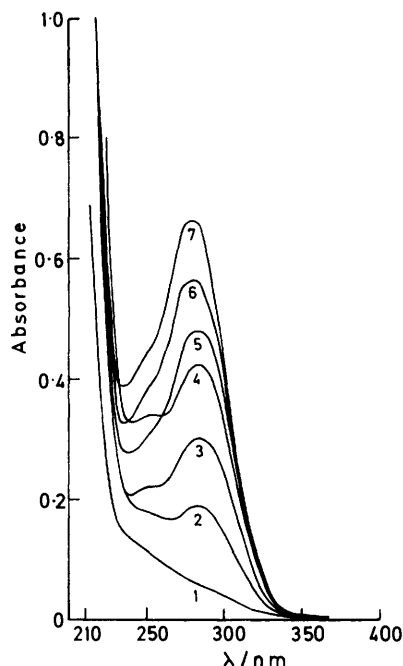


FIGURE 2 Increase in the absorption maximum at 286 nm of a solution of the nitrite (1) ($2.0 \times 10^{-2}M$) in methanol on irradiation with monochromatic light (365 ± 7.5 nm) after 1, 2 min; 2, 3 min; 4, 6 min

Moreover, the quantum yield measurements exclude the formation of the nitroso-aldehyde *via* a chain reaction.¹ This conclusion is supported by the observation that the nitroso-aldehyde formed at low temperature in EPA matrix is transformed into the nitrone when brought to room temperature.

Further Considerations of the Reaction Pathways and the Mode of Cyclization of the Nitroso-aldehyde.—Recent studies^{12,13} by a different approach firmly established that the primary process in the photodecomposition of an excited alkyl nitrite is bond scission to form an alkoxy radical and nitric oxide. The quantum yield of this process has been measured both in solution and in the gaseous state and has been reported to be 0.76¹⁴ in the case of octyl nitrite in hexane with light of wavelength greater than 300 nm, unity¹⁵ in the case of the vapour-phase photolysis of *t*-butyl nitrite with light of wavelength of 253.7 nm, and 0.36¹⁶ in the case of the vapour-phase photolysis of isopropyl nitrite with light of wavelength 366 nm. It was suggested that photo-

† The unimportance of this primary process in nitrosomethane formation was proved by McMillan *et al.*¹⁸

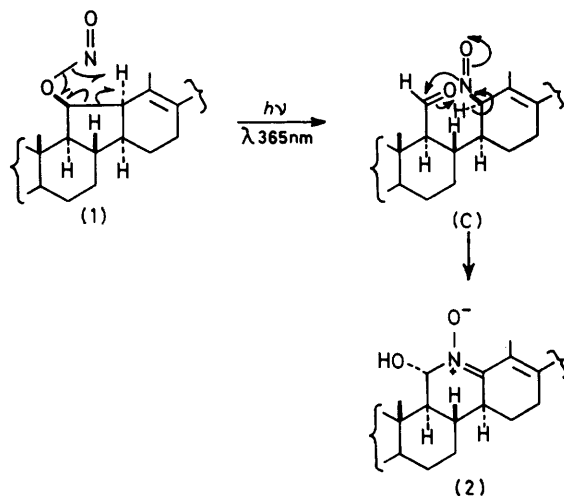
¹² (a) A. L. Nussbaum and C. H. Robinson, *Tetrahedron*, 1962, **17**, 35; (b) M. Akhtar, *Adv. Photochem.*, 1964, **2**, 263; (c) R. O. Kan, 'Organic Photochemistry,' McGraw-Hill, New York, 1966, p. 233; (d) R. H. Hesse, *Adv. Free Radical Chem.*, 1969, **3**, 83.

¹³ J. A. Gray and D. W. G. Style, *Trans. Faraday Soc.*, 1952, **48**, 1137; P. L. Hanst and J. G. Calvert, *J. Phys. Chem.*, 1959, **63**, 2071.

lysis in the vapour phase of some simple nitrites, *i.e.* *t*-butyl nitrite and isopropyl nitrite, with light of 253.7 nm to some extent generated vibrationally excited alkoxy radicals.^{15,16}

In spite of the foregoing evidence, it was still not conclusively proved that the nitroso-aldehyde(s) was really formed *via* intermediates (A) and (B). We may visualize another mode of the formation (Scheme 2) which explains the stereochemical outcome of the reaction. In this mechanism, migration of NO from oxygen to C-12 is concerted with cleavage of the 11,12-bond; thus intramolecular migration of NO from the O-NO group to C-12 occurs, to afford an aldehyde with a β -oriented nitroso-group. This process is similar to that proposed¹⁷ for the formation of nitrosomethane and acetone in the photolysis of *t*-butyl nitrite.† Intramolecular migration of the 12 α -hydrogen atom to the formyl carbonyl group from the α -side in concert with C-N bond formation would then lead to the observed nitrone with the 11 α -hydroxy-group.

This hypothetical mechanism was thought attractive^{2a} since it seemed to account for the facts that (a) only a single nitrone, with an α -oriented 11-hydroxy-group, was produced; (b) none of the product in which NO had combined with the C-17 end of the allyl radical (B) was obtained; and (c) the nitrone was formed even in carefully dried aprotic solvents.^{2a} The prior formation of the nitroso-aldehyde intermediate (C) with a β -oriented nitroso-group by migration of the NO group as in Scheme 2 is a necessary step, since it is unlikely that only



SCHEME 2

a single nitroso-aldehyde with a β -nitroso-group is formed by the combination of nitric oxide with a

¹⁴ P. Kabasakalian and E. R. Townley, *J. Amer. Chem. Soc.*, 1962, **84**, 2711.

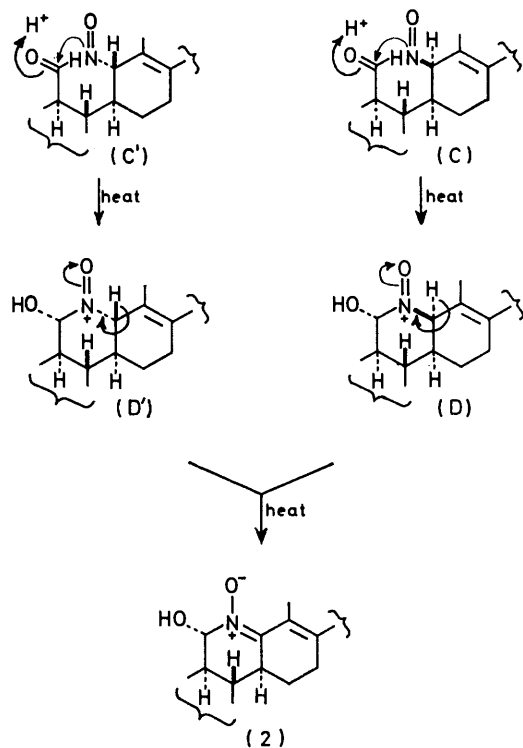
¹⁵ G. R. McMillan, *J. Amer. Chem. Soc.*, 1962, **84**, 4007.

¹⁶ B. E. Ludwig and G. R. McMillan, *J. Amer. Chem. Soc.*, 1969, **91**, 1085.

¹⁷ C. S. Coe and T. F. Doumani, *J. Amer. Chem. Soc.*, 1948, **70**, 1516.

¹⁸ G. R. McMillan, J. G. Calvert, and S. S. Thomas, *J. Phys. Chem.*, 1964, **68**, 116.

stabilized allyl radical (B) (Scheme 1) formed by β -scission of an 11β -alkoxy radical. However, cross-over experiments with labelled and unlabelled nitrites¹ showed complete scrambling of nitric oxide in the rearrangement, thus ruling out the mode of cyclization depicted in Scheme 2. Of several other possibilities we prefer a mode which involves: (a) electrophilic attack of the formyl carbon atom on the nitroso-nitrogen atom to afford an oxoammonium ion [(D) and/or (D')]; and (b) loss of the C-12 hydrogen atom of the oxoammonium ion(s)¹⁹ to afford the single nitrone (2) with an 11α -hydroxy-group, as shown in Scheme 3.*



SCHEME 3

This rationalization does not require the exclusive formation of the 12β -nitroso-aldehyde as the intermediate. Since in a nitrone with an 11β -OH the hydroxy-group and the 10-methyl group are in a quasi-1,3-diaxial relationship, the corresponding 11α -ol would be expected to be more stable, and to be formed preferentially by cyclization of the nitroso-aldehyde. One difficulty in interpreting the cyclization in this way is the question of the source of the proton taken up by the formyl oxygen when the photolysis is performed in

* The C-NO group is normally considered to function as an electrophilic species; a number of electrophilic reactions of C-nitroso-compounds are known.²⁰

¹⁹ Cf. C. F. J. A. Cella, J. A. Kelly, and E. F. Kenahan, *Tetrahedron Letters*, 1975, 2869.

²⁰ Cf. J. E. Baldwin, A. K. Qureshi, and B. Sklarz, *J. Chem. Soc. (C)*, 1969, 1073.

²¹ A. D. Allen, *J. Chem. Soc.*, 1954, 1969.

²² K. Nakamoto and R. E. Rundle, *J. Amer. Chem. Soc.*, 1956, 78, 1113.

aprotic solvents; protons removed from C-12 or protic impurities are possibilities. In agreement with this assumption, the Table shows that whereas the product of photolysis of the nitrite (1) in protic solvents is exclusively the nitrone (2), in aprotic solvents the nitrone is accompanied by a large quantity of the hydroxyimino-aldehyde (3). Perhaps in aprotic solvents the supply of protons to the carbonyl oxygen is not smooth enough, resulting in slower formation of the nitrone (2), and allowing formation of the by-product.

In agreement with this hypothesis, a high yield of the nitrone (2) was attained in the photolysis in acetic acid. However, a significant amount of the 11β -ol was also formed. Whether or not an excited species was involved in this hydrolysis is not certain, but the hydrolysis was probably an acid-catalysed ground state process.²¹ Dimerization^{22,23} of C-nitroso-compounds may perhaps be considered to be analogous to the present cyclization.

The present rearrangement shows several other features of interest. It is well known that C-nitroso-compounds²⁴ and nitrones²⁵ are excellent diamagnetic radical scavengers. Addition to C-nitroso-compounds and nitrones of reactive free radicals gives nitroxide radicals. Therefore, it seems unusual that even a trace of a product of a radical addition reaction between the intermediary nitroso-aldehyde (C) and/or (C') and the nitrone (2) was not formed in the present case. For example, the nitroso-aldehyde (C) and/or (C') might have been expected to react with the 11β -alkoxy radical to afford alkoxy alkyl nitroxides.²⁶ Although the precise reason is not clear, the low steady state concentration of radicals and the crowded environment at the reaction centres of both the intermediates and the nitrone presumably help to prohibit the formation of nitroxide radicals.

In the photolysis of simple secondary alkyl nitrites the possibility of the formation of the corresponding ketone *via* disproportionation between the alkoxy radical and nitric oxide [$R_2CHONO \rightarrow R_2CO + HNO$ (or NOH)] has been suggested.¹⁶ However, in the present reaction, it was confirmed that none of the corresponding 11-ketone (7) was formed.

EXPERIMENTAL

For instruments used and general procedures see *J.C.S. Perkin I*, 1976, 1297.

Photolysis of the Nitrile (1) in Various Solvents.—*Solvents.* Tetrahydrofuran (Wako, reagent grade) was dried with lithium aluminium hydride and distilled. Methanol (Wako,

²³ For a review see J. H. Boyer, in 'The Chemistry of Nitro and Nitroso Groups, Part 1,' ed. H. Feuer, Interscience, New York, 1969, p. 215.

²⁴ A. K. Hoffmann, A. M. Feldman, E. Gelblum, and W. G. Hodgson, *J. Amer. Chem. Soc.*, 1964, 86, 639; G. R. Chalfont, M. J. Perkins, and A. Horsfield, *J. Chem. Soc. (B)*, 1970, 401; M. J. Perkins, P. Ward, and A. Horsfield, *ibid.*, p. 395; S. Terabe and R. Konaka, *J. Amer. Chem. Soc.*, 1969, 91, 5669.

²⁵ E. G. Janzen, *Accounts Chem. Res.*, 1971, 4, 31.

²⁶ A. Mackor, T. A. J. W. Wajer, T. J. de Boer, and J. D. W. van Voorst, *Tetrahedron Letters*, 1967, 385; S. Shih, R. J. Pritchett, and J. M. Riveros, *ibid.*, 1968, 4897.

reagent grade) was dried by refluxing with calcium oxide and distilled. Penta-1,3-diene (Wako, reagent grade) was a mixture of *cis*- and *trans*-isomers and was dried first with sodium and then with lithium aluminium hydride and distilled. Dioxan (Wako, reagent grade) was dried with lithium aluminium hydride and distilled. Carbon tetrachloride (Wako, reagent grade) was dried (P_2O_5) and distilled. Glacial acetic acid (Wako, reagent grade) was treated with chromic oxide and distilled. Diethyl ether was dried with lithium aluminium hydride and distilled.

Photolysis. The procedures for photolysis and product isolation were essentially the same as in the case of the photolysis in toluene.¹ The amounts of the substrate and volumes of solvents were as follows: nitrite (200 mg) in tetrahydrofuran (9.2 ml); nitrite (500 mg) in diethyl ether (113 ml); nitrite (500 mg) in dioxan, methanol, acetic acid, penta-1,3-diene, or carbon tetrachloride (23 ml).

(a) *In tetrahydrofuran.* The solution was irradiated for 2 h 20 min under argon. T.l.c. of an amorphous residue (291 mg) from the photolysis revealed the formation of a major product less polar than the nitrone together with a small amount of the nitrone (solvent acetone-chloroform, 1:4) and a small quantity of a polar product (R_F 0). This mixture was subjected to preparative t.l.c. (solvent acetone-chloroform, 1:4). Recrystallization of the crude nitrone fraction (47 mg) from ether afforded 30 mg of nitrone. All attempts to obtain the less polar amorphous fraction (131 mg) in crystalline state failed. However, the i.r., mass., and u.v. spectra were consistent with the hydroxyimino-aldehyde structure (see main text). A colour test⁹ for the oxime group gave a positive result, and a test for an aldehyde group with fuchsin-sulphurous acid afforded a violet colour. A small amount of the most polar product (R_F 0) was crystallized from acetone to yield the third product (4), m.p. 162–164°; for n.m.r. and i.r. data see main text; *m/e* 555 (0.6%), 537 (0.8), 357 (1.1), 339 (3.2), 318 (3.9), 198 (88.9), 156 (100), and 114 (23.0).

Jones oxidation of the lactol (4). To the lactol (4) (20 mg) in acetone (2.5 ml) were added a few drops of Jones reagent. The mixture was stirred for 30 min, then the excess of reagent was decomposed with aqueous 5% sodium hydrogen sulphite and the solution was extracted with ether. The ethereal solution was worked up and the product was recrystallized from ether to yield the lactone (5); for n.m.r. and i.r. data see main text; *m/e* 571 (0.6%, M^+), 373 (2.3), 318 (9.6), 198 (73.7), 156 (100), and 114 (22.6).

(b) *In diethyl ether.* The solution was irradiated for 5 h under argon. Crystals of the nitrone (2) which appeared on the wall of the vessel were dissolved in chloroform. The solvent was removed, the residue was extracted with chloroform, and the extract was washed with water, dried (Na_2SO_4), and evaporated. The residue (655 mg) was subjected to preparative t.l.c. The most polar fraction (R_F 0) afforded a residue (188 mg). This was recrystallized from ether to yield the nitrone (161 mg). The second most polar fraction (225 mg) was the hydroxyimino-aldehyde (3). Three very minor fractions less polar than the hydroxyimino-aldehyde (3) were obtained but these were not identified.

(c) *In dioxan.* The solution was irradiated for 4 h under nitrogen. The solvent was removed and the residue (707 mg) subjected to preparative t.l.c. (solvent acetone-benzene, 1:5). Of the three fractions, that of intermediate polarity (160 mg) was a hydroxyimino-aldehyde, obtained as a colourless amorphous solid. The most polar fraction

(245 mg) was recrystallized from ether to afford the nitrone (2) (205 mg).

In methanol. The solution was irradiated for 4 h under nitrogen. The solvent was removed and the residue (758 mg) subjected to preparative t.l.c. (solvent acetone-chloroform, 1:2). Recrystallization of the second least polar fraction (350 mg) from acetone-ether afforded the nitrone (148 mg). The least polar fraction (11 mg) gave three spots on t.l.c. This was again subjected to preparative t.l.c. (acetone-benzene, 1:6), but no well-defined product was obtained.

In glacial acetic acid. The solution was irradiated for 3 h 20 min under argon, poured into water, and extracted with chloroform. The extract was washed with 10% sodium carbonate solution and water, dried (Na_2SO_4), and evaporated. The residue was subjected to preparative t.l.c. (solvent acetone-benzene 1:5). The least polar fraction (84 mg) was recrystallized from ether to yield the 11 β -ol (71 mg). The most polar fraction (R_F 0) (358 mg) was recrystallized from ether to afford the nitrone (307 mg).

In penta-1,3-diene. The solution was irradiated for 4 h under nitrogen. When the photolysis was complete, crystals of the nitrone (2) appeared on the wall of the vessel. These were dissolved by addition of chloroform. The solvent was removed and the residue dissolved in chloroform. The solution was washed with water, dried (Na_2SO_4), and evaporated, and the residue (742 mg) was subjected to preparative t.l.c. (solvent acetone-benzene, 1:5) to afford the crude hydroxyimino-aldehyde (240 mg) and the crude nitrone (115 mg) (60 mg after recrystallization from ether).

In carbon tetrachloride. The solution was irradiated for 4 h under argon. When the photolysis was complete, crystals of the nitrone (2) appeared on the wall of the vessel. These were dissolved in chloroform and the solution was evaporated. The residue was dissolved in chloroform and the solution washed with water, dried (Na_2SO_4), and evaporated. The residue (639 mg) was subjected to preparative t.l.c. (solvent acetone-benzene, 1:5). Of the two fractions obtained, the less polar (42 mg) was amorphous and its n.m.r. spectrum was not identical with that of the hydroxyimino-aldehyde (3). Although lack of the material prevented further investigation, this could have been a geometrical isomer of the hydroxyimino-aldehyde (3). A more polar fraction (365 mg) was recrystallized from ether to afford the nitrone (2) (314 mg).

Attempted Thermal and Photochemical Cyclization of the Hydroxyimino-aldehyde (3) to the Nitrone (2).—The crude oxime (3) (100 mg) in dry toluene (4.6 ml) was set aside at room temperature for 38 h. T.l.c. revealed the absence of the nitrone (2). Part of the solution was heated at ca. 100 °C for 20 min and then refluxed for 1 h. However, no nitrone was formed (t.l.c.). Another part of the solution was irradiated with Pyrex-filtered light under nitrogen for 90 min. T.l.c. again showed that no nitrone (2) was formed.

Matrix Isolation of the Intermediate in the Photoinduced Nitrone Formation.—(a) The matrix was prepared by dissolving the nitrite (1) (32 mg) in EPA (1:1:2 v/v; 8 ml) ($6.7 \times 10^{-3}M$) and freezing the solution with liquid nitrogen, and was degassed three times by subjecting it to a freeze-thaw cycle. The matrix was irradiated through a Pyrex filter with a 250 W super-high-pressure mercury arc (USHIO UI 50IC). The changes in absorption spectrum (Figures 3 and 4) were noted at appropriate time intervals by transferring the matrix to a Cary u.v. spectrometer.

After 1 h the matrix had become blue, and further irradiation did not cause any change of the blue colour. The

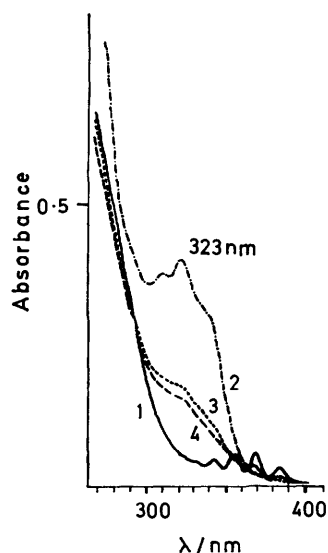


FIGURE 3 Variation of the u.v. spectrum of the nitrite (1) on irradiation with Pyrex-filtered light in EPA matrix ($4 \times 10^{-4} \text{M}$) at 77 K: 1, start; 2, after 10 min; 3, 20 min; 4, 30 min

ratio of the absorbance at 693 nm after 1 h irradiation to the absorbance at 386 nm due to the nitrite in the matrix before irradiation was 9.5:21. Since the molar absorptivity at

solution revealed the formation of the nitrone, together with a small amount of a less polar substance.

(b) A preparative scale experiment was also carried out. The matrix in a Pyrex vessel was prepared as above from the nitrite (100 mg) in EPA (1:1:1 v/v; 9 ml), irradiated for 1.5 h, and brought to room temperature. The blue colour was retained for *ca.* 1.5 min and then vanished. The solvent was removed and the residue was subjected to preparative t.l.c. (acetone-benzene 2:5) to afford the crude nitrone (57 mg). Recrystallization from ether gave 39 mg (39%) of crystalline nitrone (2).

Photolysis of the Nitrite (1) with Monochromatic Light.—The two solutions for the quantum yield measurements were made by dissolving the nitrite (1) (310 mg) in methanol (40 ml) (solution A) and nitrite (1) (200 mg) in methanol (20 ml) (solution B). Samples (4 ml) of these solutions in silica cells ($10 \times 10 \times 45 \text{ mm}$) were placed in the chamber of a JASCO CRM-FA grating spectroirradiator equipped with a 2 kW xenon arc. Solution A was irradiated at six different wavelengths at room temperature (230, 257, 285, 311, 338, and 365 nm).

The decrease in the absorbance at 386 nm after irradiation for 2 min with $365 \pm 7.5 \text{ nm}$ light was 0.15. Since the molar absorptivity at 386 nm (O—O band) of the nitrite (1) is 52 and the output of the xenon arc at 365 nm was $1.15 \times 10^8 \text{ erg cm}^{-2}$, the quantum yield of the decomposition of the nitrite is 0.7.

The quantum yield of the formation of the nitrone (2) with $365 \pm 7.5 \text{ nm}$ light was obtained as follows. Solution B was irradiated as in the case of solution A. The change in the u.v. spectrum of the solution was measured at

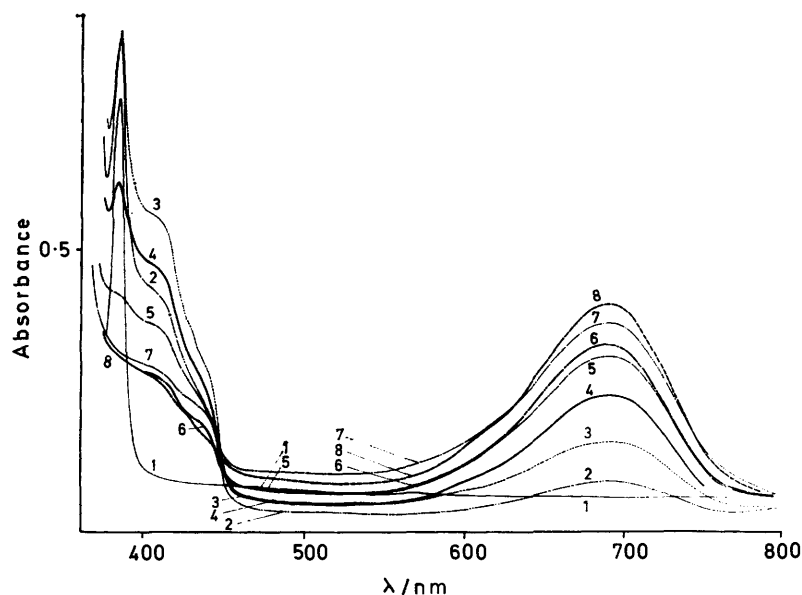


FIGURE 4 Variation of the u.v. spectrum of the nitrite (1) on irradiation with Pyrex-filtered light in EPA matrix ($7 \times 10^{-4} \text{M}$) at 77 K: 1, start; 2, after 1 min; 3, 3 min; 4, 4 min; 5, 10 min; 6, 20 min; 7, 35 min; 8, 60 min

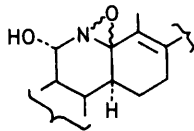
386 nm of the nitrite is 52, if we were to assume that the molar absorptivity of the nitroso-aldehyde is 24, extent of nitrite transformation into the nitroso-compound would be 100%.

When the matrix was brought to room temperature the blue colour remained for *ca.* 30 s and then vanished. T.l.c. (solvent acetone-benzene 1:5) of the residue from this EPA

intervals by pipetting out a sample (0.1 ml), diluting it with methanol (to 10 ml) and measuring the u.v. spectrum. Figure 2 shows the u.v. absorption due to the nitrone at various time intervals. The increase of absorbance at 286 nm was plotted against the output of the lamp (measured with a JASCO RMI light integrator). This plot was linear between 4 and 7 min after commencement of irradiation.

The increase of the absorbance at 286 nm in the diluted solution within this 3 min interval was 0.48.* Thus, the quantity of the nitrone formed during 3 min in 4 ml of

* The nitrone in methanol is slowly transformed into the oxaziridine (b) by irradiation with 365 ± 7.5 nm light. Thus when a methanolic solution of the nitrone ($6.5 \times 10^{-5}M$) was irradiated, the decrease of absorbance at 285 nm after 4 and 40 min irradiation was found to be 0.075 and 0.455, respectively. However, this reaction would have a negligible effect on the quantum yield measurement.



(b)

the solution was 1.2×10^{-5} mol. The output of the lamp to the cell (40×10 mm) in 3 min measured by the light integrator was 13.4 W. On the basis of these data the quantum yield was calculated to be 0.3.

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