Formation of Ketones from Alkyl Nitrites in the Solid State

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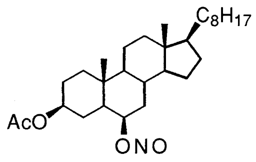
Alkyl nitrites selectively afforded the corresponding ketones upon photoirradiation in the solid state. It was suggested by the X-ray crystallographic analysis that the cavity in crystal and the initial conformation of the nitroso group had an influence on the yield of the ketones.

The reactions of organic molecules in crystal lattice have been of increasing interest in recent years, since quite unique selectivity of reactions could be achieved due to crystalline environment.[1] Although a number of successful results were reported up to the present, the kind of reaction is still limited, and the development of a new solid-state reaction is a matter of importance. Alkyl nitrites are known to afford an alkoxy radical and nitric oxide upon photoirradiation in solution.[2] This reaction has been mainly applied to the activation of an alkyl group, and known as the Barton reaction:[3] The resulting alkoxy radical abstracts a hydrogen from an axial methyl carbon, and an oxime group is introduced to the carbon by the reaction of the carbon radical with nitric oxide, followed by hydrogen transfer. However, the photoreaction of alkyl nitrites in the solid state has not been thoroughly investigated up to the present. During the course of our study on the solid state organic chemistry, we recently found that alkyl nitrites showed a characteristic photoreactivity in crystal. Here, we report the photoreaction of alkyl nitrites in the solid state.



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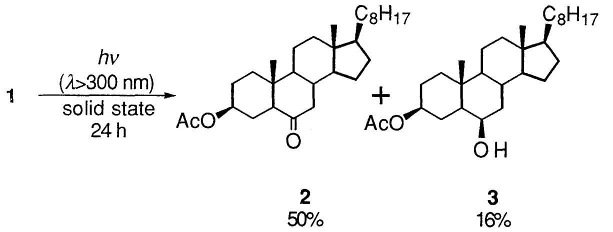
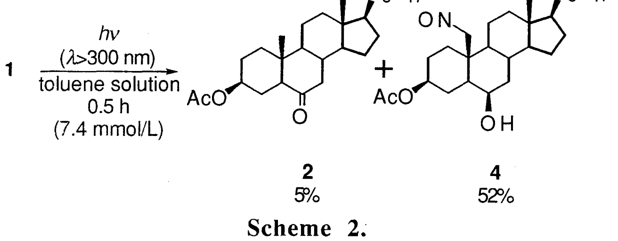


Scheme 1.

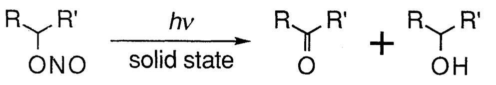


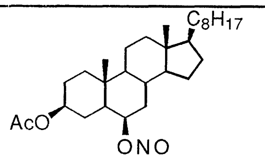
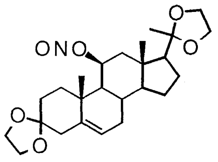
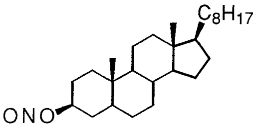
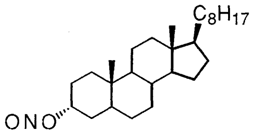
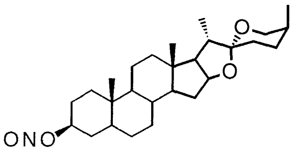
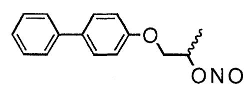
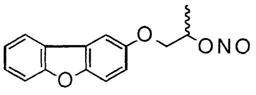
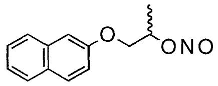
Scheme 2.

Nitrites were prepared by the reaction of the corresponding alcohols with nitrosyl chloride in the presence of pyridine, as described in the literature.[3] When, 6β-nitroso-oxy-5α-cholestan-3β-yl acetate (**1**) was irradiated by a 500-W super-high-pressure mercury lamp for 24 h through a cut-off filter (λ>300 nm) in the solid state, ketone **2** and alcohol **3** were obtained in 50% and 16% yields, respectively (Scheme 1). On the other hand, when a toluene solution of **1** was irradiated for 0.5 h by the same light source, the Barton-type hydrogen-abstracted product **4**[4] was obtained as a major photoproduct (52%) with a trace amount of **2** (5%), as reported in the literature (Scheme 2).[5] Since ketones were obtained generally in low yields by the photoreaction of alkyl nitrites in solution,[6] these results awoke our interests. We then applied the solid-state reaction to various kinds of alkyl nitrites derived from steroids and those from acyclic alcohols (Table 1) in order to study the generality of this solid-state reaction. As a result, in the cases of nitrites derived from steroids, the corresponding ketones were obtained as major photoproducts in moderate yields upon irradiation in the solid state (entries 1–5).[7,8] On the other hand, nitrites prepared from acyclic alcohols afforded the corresponding ketones with less selectivity (entries 6–8), although the reactions smoothly proceeded.

The X-ray powder diffraction patterns of the samples before and after irradiation showed that the present reaction was a crystal-to-crystal transformation. Therefore, the photoreaction of the nitrites in the solid state is considered to proceed under the influence of the crystal lattices. The mechanism of the ketone formation in the solid state remains unclear at present. However, it is proposed that a "cage-radical" or concerted mechanism must be operated in solution; the ketone formation in solution occurs at the early stage before the transfer of a hydrogen atom to the alkoxy radical produced.[5] Taking this mechanism into account, it is considered that the initial geometrical relationship between the nitroso group and the α-hydrogen of the nitrite in the crystal would affect the yield of the ketone obtained by the reaction in the solid state. The X-ray crystallographic analysis of **1**[9] (Figure 1) showed that the direction of the RO–NO bond is opposite to the axial methyl group of **1** (C20), indicating that this conformation is quite unfavorable for the abstraction of the hydrogen on C20 by the alkoxy radical generated by irradiation. In addition, H(6)–C(6)–O(1)–N(5) atoms of **1** are almost in the same plane with dihedral angle of 6.2° (Figure 1). On the basis of the concept of reaction cavity in crystal[10] this geometrical relationship seems to be quite favorable for the ketone formation via either the radical or concerted mechanism, since the minimum movement of the atoms is required for the formation of the ketone. In a similar manner, the high selectivity for the ketone formation from the other steroidal nitrites in the solid state could be explained, since it is supposed that the conformational relationship between the nitroso

Table 1. Photoreaction of Alkyl Nitrites in the Solid State



Entry	Nitrite	Irrad. time / h	Ketone / %	Alcohol / %
1		24^a	50	16
2		4.5^a	69	20
3		76^a	64	5
4		142^b	65	8
5		168^a	62	8
6		89^b	13	64
7		23^b	27	29
8		61^b	24	5

^{a}Irradiation was performed by a 500 W super-high-pressure mercury lamp at room temperature through a cut-off filter (λ>300 nm).
^{b}λ>250 nm.

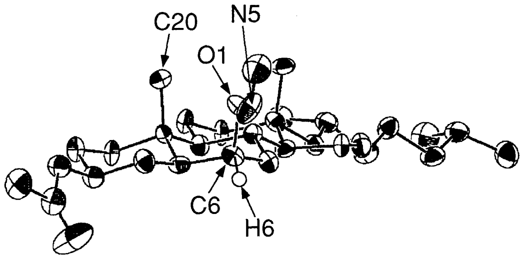


Figure 1. ORTEP drawing of **1**.

group and the α-hydrogen for these compounds is similar to that of **1**. On the other hand, in the cases of the nitrites prepared from acyclic alcohols in Table 1, the molecular-mechanic (MM) calculation[11] suggested that the H–C-O-N dihedral angles are almost 30° in these compounds. This result indicates that the nitroso-nitrogen is more apart from the α-hydrogen than those in the steroidal nitrites and that the larger movement of the atoms than that for **1** is required for the formation of the ketones; this unfavorable conformation of the nitrosyl group would result in low yields of the ketones.

In summary, photoirradiation of steroidal nitrites in the solid state mainly afforded the corresponding ketones, which were usually by-products in solution reaction. The selective formation of the ketones is considered to be attributed to the favorable conformation of the nitroso group, in addition to the effect of the reaction cavity in crystal.

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References and Notes

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7 In contrast, in benzene, the nitrite in entry 5, which did not undergo the Barton reaction, afforded a mixture of the corresponding alcohol and ketone in a ratio of 32:68 upon irradiation for 1.5 h.
8 As a result of the time-conversion analysis of the photoproducts, it was ascertained that the alcohol and ketone were directly produced from the corresponding nitrite upon irradiation.
9 Crystal data for **1** $C_{29}H_{49}NO_4$, M=475.70, monoclinic, space group $P2_1$, a=13.89(1) Å, b=7.663(5) Å, c=12.976(9) Å, β=100.50(6)°, V=1358(2) Å^3, Z=2, Dc=1.16 gcm^{-3}, R=0.082, reflections used=1771.
10 M. D. Cohen, *Angew. Chem., Int. Ed. Engl.*, **14**, 386 (1975); Y. Ohashi, A. Uchida, and A. Sekine, in "Reactivity in Molecular Crystals," ed by Y. Ohashi, Kodansha, Tokyo (1993) pp. 115–176.
11 PCMODEL was applied for the MM calculation.