

The Photochemical Reaction of Some Ketoximes and Their Derivatives

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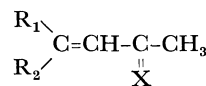
The photochemical reaction of mesityl oxide oxime was investigated. In protic solvents, the reaction *via* oxaziridine proceeded, while in aprotic solvents, *syn-anti* isomerization was the main reaction pattern. A cyclobutanol formation, which is a new type of reaction in the oxime system, was observed. The photochemical reactions on some other ketoximes and their derivatives were also investigated.

Recently several workers have investigated the photochemistry of oximes and their derivatives. The reactions can be classified into four types; (1) *syn-anti* isomerization,¹⁾ (2) photo-Beckmann rearrangement,²⁾ (3) nitrile formation,³⁾ and (4) ketone formation.⁴⁾ deMayo^{2a,5)} proposed a mechanism *via* the oxaziridine formed for the polar state of oxime for the photo-induced conversion of benzaldehyde oxime into benzamide with an intramolecular oxygen migration. The reaction scheme through the intermediacy of the oxaziridine for the photo-Beckmann rearrangement and ketone formation from oximes has been confirmed in an indirect way by Mukai *et al.*^{2d,6)} These authors have also discussed possible states of excited states in the photochemistry of some α,β -unsaturated ketoximes.

We investigated photochemical reactions on several ketoximes and their *O*-methyl ethers, thus disclosing several new results.

Results

When mesityl oxide oxime (**1a**, a mixture of *anti*⁷⁾ 78% and *syn* 22%) containing 5% of isomesityl oxide oxime (**2a**) was irradiated with Pyrex-filtered light in methanol, mesityl oxide (**1b**), isomesityl oxide (**2b**), a cyclobutanol, **3**, and two amides, **4** and **5**, were obtained. Product identification was carried out spectroscopically with samples collected by preparative gas chromatography. The yields of the products were obtained by gas-chromatographic analysis; they are plotted against irradiation time in Fig. 1. It was confirmed that the irradiated reaction mixture was stable upon further standing under the present reac-

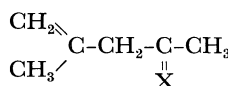


1 a: $R_1=R_2=CH_3$, $X=N-OH$

b: $R_1=R_2=CH_3$, $X=O$

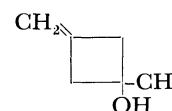
c: $R_1=Ph$, $R_2=H$, $X=N-OH$

d: $R_1=Ph$, $R_2=H$, $X=N-OCH_3$

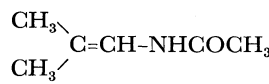


2 a: $X=N-OH$

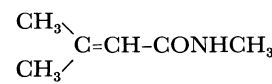
b: $X=O$



3



4



5

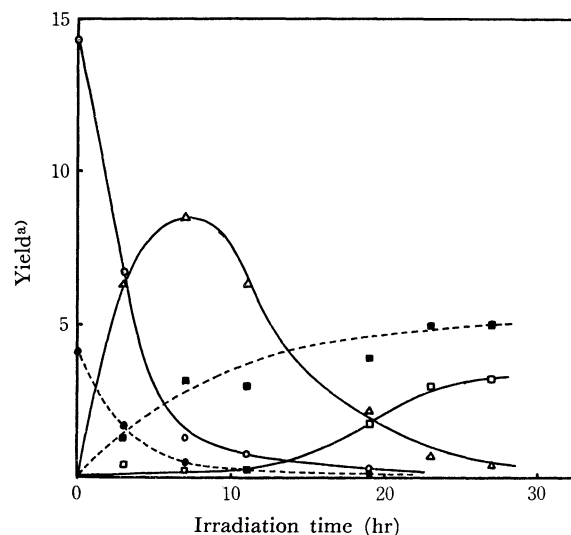


Fig. 1. Conversion of oximes and yields of products as a function of irradiation time.

—○— *anti*-**1a** —□— **3** —●— *syn*-**1a**

—■— **4+5** —△— **1b**

a) Figures refer to the relative area under each peak on the gas chromatogram, that of isomesityl oxide oxime (**2a**) being assigned an arbitrary value of 1.

tion conditions, but without the light. Since **2a** is supposed to be stable to the Pyrex-filtered light, in view of the lack of reactivity of the saturated ketoximes (such as cyclohexanone oxime) to this light source, the **2a** present in the starting material as a contaminant was used as the internal reference in the analysis by gas chromatography. It was found that the products and product distribution obtained from the photolysis

1) G. Ciamician and P. Silber, *Ber.*, **36**, 4268 (1903).

2) a) J. H. Amin and P. de Mayo, *Tetrahedron Lett.*, **1963**, 1585. b) R. T. Taylor, M. Douek, and G. Just, *ibid.*, **1966**, 4143. c) G. Just and L. S. Ng, *Can. J. Chem.*, **46**, 3381 (1968). d) T. Oine and T. Mukai, *Tetrahedron Lett.*, **1969**, 157. e) H. Sugimoto and H. Takahashi, *ibid.*, **1970**, 5119. f) H. Izawa, P. de Mayo, and T. Tabata, *Can. J. Chem.*, **47**, 51 (1969). g) B. L. Fox and H. M. Rosenberg, *Chem. Commun.*, **1969**, 1115.

3) a) T. Sato and H. Obase, *Tetrahedron Lett.*, **1967**, 1633. b) G. Just and C. Pace-Asciak, *Tetrahedron*, **22**, 1069 (1966). c) A. Slojiljković and R. Tasovac, *Tetrahedron Lett.*, **1970**, 1405.

4) J.-P. Vermès and R. Beugelmans, *ibid.*, **1969**, 2091.

5) P. de Mayo, "Solvay Institute 13th Chemistry Conference, Reactivity of Photoexcited Organic Molecule," Interscience Publishers, New York, N. Y. (1967), p. 320.

6) T. Oine and T. Mukai, Abstracts of papers presented at the 3rd ICHG, Sendai, August, 1971, p. 145.

7) The prefix *anti* implies that the oxime hydroxyl group and the C-C double bond are on the other side of the C-N double bond.

TABLE 1. PHOTOLYSIS OF KETOXIMES AND THEIR DERIVATIVES

Oximes	Solvent		Irr. time (hr)	Filter	Method ^{a)} of work-up	Product ^{b)} (relative ratio)
1a 1.3 g	MeOH	130 ml	c)	Pyrex	A	c)
1a 0.054 g	MeOH AcOH	6 ml 0.07 ml	20	Pyrex	A	1b (22), 3 (1), 4 (77)
1a 0.02 g	Ether	4 ml	106	Pyrex	A	<i>anti</i> - 1a (53), <i>syn</i> - 1a (28), 1b (8), 4 and 5 (4), 13^{d)} (2), 14^{e)} (5)
1a 0.6 g	<i>n</i> -Hexane	60 ml	72	Pyrex	A	<i>anti</i> - 1a (39), <i>syn</i> - 1a (19), 1b (21), 3 (3), 4 (6), 5 (14)
1c 1 g	Ether	100 ml	22	Pyrex	B	<i>trans-anti</i> - 1c (70) <i>cis-anti</i> - 1c (30)
1d 0.1 g	MeOH	10 ml	8	Pyrex	B	<i>trans-anti</i> - 1d (68) <i>cis-anti</i> - 1d (32)
8 0.9 g	MeOH	100 ml	7	none	C	7
9 1 g	MeOH AcOH	100 ml 2 ml	18	none	D	Camphor, 10 , 11

a) A: The solvent was removed through a column under an ordinary pressure, and the residue was analyzed by gas chromatography. B: The solvent was removed *in vacuo* and the residue was analyzed by gas chromatography. C: The solvent was removed *in vacuo*, the residue was distilled under a reduced pressure, and the distillate was analyzed by gas chromatography. D: The solvent was removed *in vacuo*, the residue was diluted with ether and washed with an aqueous sodium bicarbonate solution, the ether was removed, and the residue was fractionated on an alumina column with chloroform.

b) Identification was carried out on pure samples obtained by preparative gas chromatography, except for samples marked with an asterisk, which contained the isomer indicated in the parentheses. **1b**, **2b**, **7**, **10**, and camphor: the retention times as shown by gas chromatography and the IR spectra were identical with those of the authentic samples. **3**: MS: *m/e* 98 (P). The IR and NMR spectra showed peaks identical with the reported values.¹³⁾ **4**: MS: *m/e* 113 (P). IR (CCl₄): 3300 (s), 1660 (vs) and 1505 cm⁻¹ (vs). NMR (CCl₄): δ 1.67 (s, 6H), 2.07 (s, 3H), 6.56 (d, *J*=12 Hz, 1H) and 8.65 (bs, 1H). **5*** (containing **4**): NMR (CDCl₃): δ 1.80 (s, 3H), 2.10 (s, 3H), 2.73 (d, *J*=5 Hz, 3H), 5.47 (bs, 1H) and 5.82 (bs, 1H). *cis*-*anti*-**1c*** (containing *trans*-*anti*-**1c**): NMR (CDCl₃): δ 1.73 (s, 3H), 6.10 and 6.40 (AB type q, *J*=12 Hz, 2H), 6.85 (m, 5H) and 7.73 (bs, 1H). *cis*-*anti*-**1d**: IR (neat): 1054 (s), 895 (s), 775 (m) and 695 cm⁻¹ (m). NMR (CDCl₃): δ 1.76 (s, 3H), 3.82 (s, 3H), 6.25 and 6.54 (AB type q, *J*=12 Hz, 2H) and 7.15 (s, 5H). **11**: mp 133–136°C. IR (CHCl₃): 3400 (w) and 1660 cm⁻¹ (vs). Found: C, 71.91; H, 10.55; N, 8.29%. Calcd for C₁₀H₁₇NO: C, 71.81; H, 10.25; N, 8.38%.

c) See Fig. 1.

d) Isobutyl methyl ketone.

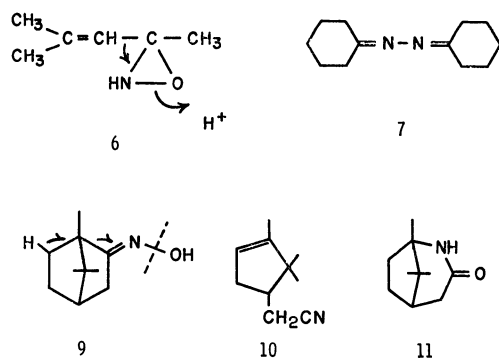
e) Unidentified.

of **1a** were greatly solvent-dependent. The results are summarized in Table 1. Evidently, *syn*-*anti* isomerization became the major reaction pattern in non-polar solvents, while only one amide, **4**, was obtained selectively in an acidic solvent. Compounds **1c**, **1d**, **8**, and **9** were also irradiated under the conditions specified in Table 1. The structure **11** was assigned to the product from **9** in view of the results of the elemental analysis, the amide carbonyl band in the IR spectrum at 1660 cm⁻¹, and the absence of an olefinic proton signal in the NMR spectrum. The

melting point (133–136°C) of this compound was lower than that of the reported value (156–160°C)⁹⁾ for **11**, but the possibility of the alternative structure of α-camphidone was excluded in view of the still higher melting point of α-camphidone (230–232°C).

Discussion

Oxime Disappearance. Figure 1 shows that the amount of mesityl oxide (**1b**) increases to reach a maximum and then decreases during the last stages of the reaction. As it has already been pointed out,⁹⁾ and has been confirmed in the present study, that **1b** is stable to the Pyrex-filtered light under various conditions, the decrease in the amount of **1b** upon prolonged irradiation can be explained by assuming that the curve is actually a plot of the amount of a photolabile intermediate from which the ketone is formed during the work-up of the reaction mixture. In view of the previous proposals, oxaziridine, **6**, is the most probable



8) M. Nakazaki and K. Naemura, This Bulletin, **37**, 532 (1964).

9) N. C. Yang and M. J. Jorgensen, *Tetrahedron Lett.*, **1964**, 1203.

candidate for the intermediate; this is consistent with the proposed scheme that the oxaziridine intermediate is formed in the initial step of the irradiation of oxime.

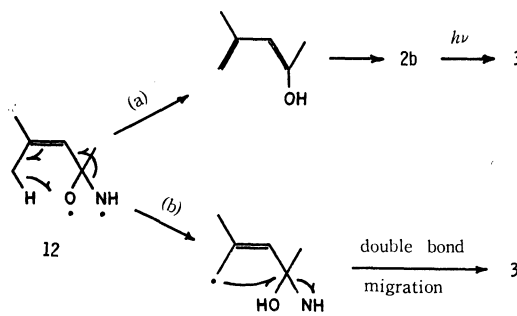
The formation of these products (**1b**, **2b**, **3–5**), which can be assumed to be secondary products from **6**, was greatly depressed when the photolysis was carried out in ether; the *syn-anti* isomerization became a major reaction pattern, instead (Table 1). Similarly, the amide formation from benzylideneacetone oxime (**1c**) upon the irradiation in methanol^{2d} was replaced by an exclusive *cis-trans* isomerization when the irradiation was carried out in ether. Benzylideneacetone oxime *O*-methyl ether (**1d**) also underwent only *cis-trans* isomerization, even in methanol. These findings definitely support the argument by de Mayo⁵) that an ionic dissociation of oxime hydrogen might be a necessary step in the formation of an oxaziridine intermediate. In a similar sense, the formation of 6-hexanelactam and hexanamide from cyclohexanone oxime upon irradiation (quartz) in methanol^{2b}) was greatly retarded, and an azine, **7**, became the main product upon the irradiation (quartz) of cyclohexanone oxime *O*-methyl ether (**8**) in methanol. Probably homolytic N–O bond fission, followed by dimerization, became dominant in this case. Both isomerizations (*cis-trans* and *syn-anti*) seemed to proceed through singlet states, because the reactions were not affected by the presence of piperylene in the range of quencher concentrations of 0.1–1M. **1a** indicates a weak $n-\pi^*$ band at 310 nm ($\pi-\pi^*$ at 235 nm) in the UV spectrum, while the $n-\pi^*$ bands of **1c** and **1d** are completely covered with strong $\pi-\pi^*$ bands at 284 nm. It seems reasonable to assume that the $\pi-\pi^*$ state induces a *cis-trans* isomerization, while the $n-\pi^*$ state induces a *syn-anti* isomerization.

Amide Formation. We found that the amide formation is also subject to a solvent effect. In contrast with the formation of two amides, **4** and **5**, upon the irradiation of **1a** in methanol, only one amide, **4**, was obtained upon the photolysis of **1a** in methanol containing acetic acid. Evidently a selective migration of the olefinic group occurs in methanol-acetic acid, while both alkyl and olefinic migrations occur non-selectively in methanol. We interpret the present result in terms of the difference in degree of protonation to the intermediate oxaziridine. That is, in an acidic solvent, protonation to an excited state of the oxaziridine would be effective, and this would induce a heterolytic N–O bond fission, as is shown in **6**, giving rise to a selective migration of the olefinic group; this seems likely in view of the preferential migratory aptitude of the olefinic group over the alkyl group in the reaction involving electron-deficient nitrogen.¹⁰) However, in methanol, the proton-donating power of the solvent is weak and homolytic N–O bond fission in the excited oxaziridine would become dominant, thus inducing a non-selective migration of olefinic and alkyl groups. In contrast with the results obtained above, an exclusive migration of olefinic group in methanol has been reported in the styryl ketone oxime system;^{2d})

this result was also confirmed with **1c** in the present study. These results seem reasonable because, in this system, the phenyl group would effectively stabilize the transition state for the olefinic-group migration, thus favoring the heterolytic N–O bond fission even in a non-acidic solvent.

We also observed that the acidic solvent greatly favors the Beckmann-type rearrangement. Previously we investigated the photolysis of camphor oxime (**9**) in methanol and obtained Beckmann-fragmentation products (for instance, **10**) as well as camphor.^{3a}) It is probable that the Beckmann-fragmentation products arise through a homolytic cleavage of the N–O bond, as is shown in **9**, while camphor arises from the oxaziridine intermediate, which, because of the thermal unstability due to the ring strain, decomposes into camphor before it can be subject to a photochemical reaction. On the contrary, a lactam, **11**, was the product when the irradiation was carried out in an acidic solvent. Probably the Beckmann-type rearrangement became preferable because of the protonation of the excited state of the oxaziridine intermediate. The same type of reaction has been reported with the adamantanone oxime system.¹¹)

Cyclobutanol Formation. Although the γ -hydrogen abstraction in excited carbonyl compounds is a well-known type-II reaction, mesityl oxide is photostable under the conditions examined so far.⁹) This lack of reactivity has been attributed to the assumption that the lowest state is the $\pi-\pi^*$ triplet, which exhibits substantially reduced reactivity in intramolecular hydrogen abstraction.¹²) Therefore, it is notable that a cyclobutanol, **3**, which is an expected but not realized product from mesityl oxide, was obtained from the oxime.



As the possible routes for the formation of **3**, we propose mechanisms (a) and (b) from a radical derived from oxaziridine (**12**). A scheme through an intermediacy of **12** was deduced from the fact that the formation of **3** was accompanied by the formation of two amides, **4** and **5**. When the irradiation was carried out in an acidic medium, where the possibility of a heterolytic cleavage of the N–O bond has been speculated about (*vide supra*), the formation of **3** was negligible (<1%). We consider that the mechanism (a),

11) T. Sasaki, S. Eguchi, and T. Toru, *Chem. Commun.*, **1970**, 1239.

12) P. J. Wagner, *Accounts Chem. Res.*, **4**, 168 (1971). Experiments questioning this assumption has been reported: R. A. Schneider and J. Meinwald, *J. Amer. Chem. Soc.*, **89**, 2023 (1967).

10) T. Sato, H. Wakatsuka, and K. Amano, *Tetrahedron*, **27**, 5381 (1971).

which involves isomesityl oxide (**2b**) as an intermediate, is preferable to (b) in view of the long induction period for the formation of **3** as compared with the formation of amides (Fig. 1). Isomesityl oxide was actually identified in the reaction mixture, but its quantitative analysis was unsuccessful because the peak on the gas chromatography overlapped with that of an unidentifiable component. The photochemical transformation of isomesityl oxide into cyclobutanol, **3**, has been established.¹³ The reaction corresponding to the well-known type-II reaction in carbonyl compounds is a new type of reaction in the oxime system.

Experimental

The IR spectra were measured on a Hitachi EPI-G3 spectrometer, while the NMR spectra were obtained on a JEOL MH-60 (60 MHz) spectrometer, using TMS as the internal reference. The mass spectra were determined on a Hitachi RMS-4 mass spectrometer, using an ionization energy of 70 eV.

Mesityl Oxide Oximes. The material prepared by the method reported by Harries¹⁴ was a mixture of *anti* (66%), *syn* (21%), and isomesityl oxide oxime (13%), as judged from the results of gas-chromatographic and NMR-spectroscopic analysis. Isomesityl oxide oxime and a mixture of *anti* and *syn* were isolated in preparative gas chromatography. The mixture of *anti* and *syn* isomers: IR (CCl₄): 3370 (s), 1670 (m) and 968 cm⁻¹ (s). NMR (CCl₄): δ 1.76—2.15 (m), 5.65 (m) for the olefinic proton of the *anti*-

isomer,¹⁵ 6.03 (m) for the olefinic proton of the *syn*-isomer and 9.67 (bs). Isomesityl oxide oxime: IR (CCl₄): 3250 (s), 1655 (m), 945 (m) and 896 cm⁻¹ (s). NMR (CCl₄): δ 1.70 (s, 3H), 1.82 (s, 3H), 2.90 (s, 2H), 4.93 (s, 2H) and 8.63 (bs, 1H).

The material was further fractionated, and a mixture of *anti* (75%), *syn* (20%), and isomesityl oxide oxime (5%) was used for the photoreaction.

trans-anti-Benzylideneacetone Oxime O-Methyl Ether (1d). Into a solution of *trans-anti*-benzylideneacetone oxime (16 g, mp 116°C, lit,¹⁶ mp 113—115°C) in anhydrous benzene (50 ml), we added sodium amide (4 g) at 30°C. The mixture was stirred for 15—16 hr, and then the solid was collected on a glass filter. The material was washed with benzene and dried *in vacuo*. The solid was suspended in ether (50 ml), methyl iodide (43 g) was added, and the mixture was refluxed for 20 hr under a slight pressure (with a mercury seal). The mixture was then filtered from a solid, the solvent was removed, and the residue was distilled. Bp 110—115°C/2—3 mmHg. IR (neat): 1053 (s), 965 (m), 750 (m) and 690 cm⁻¹ (m). NMR (CCl₄): δ 1.96 (s, 3H), 3.88 (s, 3H), 6.67 (s, 2H) and 7.18 (m, 5H).

Camphor Oxime. Mp 117.5°C. (lit,¹⁷ mp 117.5—118°C).

Cyclohexanone Oxime O-Methyl Ether. Bp 50—51°C/10 mmHg. (lit,¹⁸ bp 50°C/12 mmHg.)

Photolysis. The irradiation was carried out with a Riko high-pressure UVL-100P ultraviolet mercury lamp. The results are summarized in Table I.

16) B. Unterhalt, *Arch. Pharm.*, **299**, 274 (1966). Cf. S. Goszetyński and W. Zielinski, *Zeszyty Nauk. Politech. Slask., Chem.*, No. **24**, 239 (1964); *Chem. Abstr.*, **63**, 11298 (1965).

17) Beilsteins Handbuch der Organischen Chemie. Vol. VII, Verlag von Julius Springer, Berlin, p. 112 (1925).

18) L. G. Donaruma, *J. Org. Chem.*, **22**, 1024 (1957).

13) N. C. Yang and D-M. Thap, *Tetrahedron Lett.*, **1965**, 3671.

14) C. Harries, *Ann. Chem.*, **330**, 192 (1904).

15) G. Slomp and W. J. Wechter, *Chem. Ind.*, **1962**, 41.