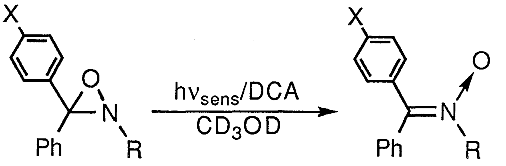
Stereoselective Ring Opening of Geometrically Constrained Oxaziridines by Photosensitized Electron Transfer

Yasunori Iwano, Yasuhiko Kawamura,* and Tokunaru Horie
Department of Chemical Science and Technology, Faculty of Engineering,
The University of Tokushima, Minamijosanjima-cho, Tokushima 770

(Received August 25, 1994)

Stereoselective isomerizations of geometrically constrained oxaziridines **1** to the corresponding nitrones **2** could be induced by 9,10-dicyanoanthracene-photosensitized electron transfer.

The nitrone photocyclization to oxaziridine proceeds by a disrotatory stereospecific manner. That reverse thermal process of oxaziridine to the nitrone, however, results in a mixture of the E and Z isomers of the nitrone because of the two possible conrotatory motions of the C-O bond cleavage.[1] Moreover, experimental studies[2] on the thermal ring opening of oxaziridine revealed that the reaction showed a more complicated feature. For example, although the 2-t-butylmonoaryloxaziridines gave the corresponding nitrones quantitatively, the 3,3-diaryl substituted ones gave diaryl ketone oximes by concerted elimination of isobutene from the oxaziridines.[3] Under the present circumstances, little information about the ring opening of oxaziridines is available and the putative stereochemical course still has been uncertain.[4] Here, we wish to report the stereoselective ring opening of the sterically constrained oxaziridines such as 3,3-diaryloxaziridines (**1b**-**1f**) to the corresponding arylnitrones under the 9,10-dicyanoanthracene (DCA)-sensitized electron-transfer photoreaction conditions.[5]



E-1 Z-2

(X = H, Cl, CF_3, and OMe; R = t-Bu and i-Pr)

Photosensitized electron-transfer (PET) reaction of **1a** (X=H, R=t-Bu) in MeCN gave the corresponding **2a** in 61% (based on a reacted **1a**) yield with 51% conversion of **1a** along with the minor products, benzophenone **3a** (15%) and N-t-butylbenzanilide **4a** (3%) (Table 1). In contrast, the direct photoreaction of **1a** gave **3a** and the thermal reaction of **1a** gave benzophenone oxime exclusively as reported earlier.[2] Only the PET reaction enabled the ring opening of **1a**. To enhance the reactivity of **1a** and to suppress undesirable paths to **3a** and **4a**, choice of MeOH as solvent gave a favorable result. Furthermore, to clarify the stereochemical course of the reaction, oxaziridines with two different aryl groups at the 3-position (**1b**-**1f**) were prepared in a usual way and each E and Z isomer was subjected to the reaction in MeOH. Results are summarized in Table 1.[6] Intriguing features of the reactions are: 1) Oxaziridines having 2-t-butyl group isomerized to the corresponding **2** with 71-99% stereoselectivity and E-oxaziridines gave Z-nitrones predominantly and vice versa. 2) Reaction efficiency of the isomerization was higher in **1** with 3-(p-methoxyphenyl) group than the others. 3) Reactions of **1e** with less bulkier isopropyl group at the 2-position gave divergent results and **1f** no longer reacted.[7]

Fluorescence of DCA was quenched effectively by all substrates except for **1f** with the lower limit of diffusion-controlled rate (k_q). The values also are correlated with the negative free energies for the single electron transfer (ΔG) calculated by the Rehm-Weller equation (Table 1).[8] The reaction was retarded in benzene-d_6 and that in the presence of easier

Table 1. Stereoselective isomerization of 3,3-diaryloxaziridines **1** to nitrones **2**[a]

Compd.	X	R	Irrad. time / h	Conv.[b]/ %	Yield / %[b] (Z-2 / E-2)	k_qx10^{-9} [c]/ $M^{-1}s^{-1}$	E^{ox} [d]/ V vs. SCE	ΔG [e]/ kJ mol^{-1}
1a	H	t-Bu	6	51	61	0.85	1.82	-22.1
E-1b	Cl	t-Bu	6	48	81(74/26)	0.49	1.92	-12.5
Z-1b	Cl	t-Bu	6	44	86(19/81)	0.71	2.02	-2.84
E-1c	CF_3	t-Bu	10	43	58[g](81/19)	0.60	2.16	+10.7
Z-1c	CF_3	t-Bu	10	41	59[g](29/71)	0.45	2.11	+5.84
Z-1d	MeO	t-Bu	2	91	99(8/92)	7.44	1.60	-43.3
E-1e	MeO	i-Pr	5	7	71 (80/20)	7.63	1.72	-31.8
1e[f]	MeO	i-Pr	2	64	97(1/99)	5.86	1.72	-31.8
E-1f	Cl	i-Pr	10	0	-	-	-	-
Z-1f	Cl	i-Pr	10	0	-	-	-	-

[a] [1] = 1.6 x 10^{-2} mol dm^{-3}, [DCA] = 1.0 x 10^{-4} mol dm^{-3}. In CD_3OD under Ar atmosphere except for the reaction of **1a** which was reacted in MeCN. [b] Determined by NMR spectroscopy. Cyclododecane was used as internal standard. [c] Fluorescence quenching rate constant of the singlet excited DCA with **1** in MeOH. [d] Measured in dry MeCN under Ar atmosphere at room temperature. Supporting electrolyte was $Et_4N^+ClO_4^-$. [e] Calculated according to the Rehm-Weller equation.[8] [f] Z-E mixtures (86/14) were used. [g] Benzophenone derivative was formed as a major byproduct and unidentified compounds were contained a little.

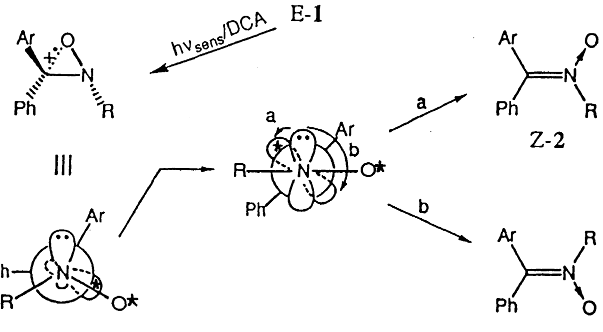
Table 2. Solvent effect on the photosensitized electron transfer reactions of the nitrone **2b**[a]

Compd.	Solvent	Irrad. time / h	Yield / %[b] **2b** (Z/E)	**1b** (Z/E)
E-**2b**	CD$_3$OD	10	77 (18/82)	9 (81/19)
Z-**2b**			73 (77/23)	9 (21/79)
E-**2b**	CD3CN	1	92 (64/36)	3[c]
Z-**2b**			89 (62/38)	3[c]

[a] [**2b**] = 1.6 x 10^{-2} mol dm^{-3}, [DCA] = 1.0 x 10^{-4} mol dm^{-3} in each solution under Ar atmosphere. [b] Determined by NMR spectroscopy using cyclododecane as internal standard. [c] Stereoselectivity was not determined.

oxidizable compound, 1,2,4,5-tetramethoxybenzene[9] also was retarded. These results suggest that the single electron transfer (SET) is most likely to be the reaction process as well as the fluorescence quenching mechanism for the singlet excited DCA. Actually, oxaziridine **1f** with higher oxidation potential (>2.2 V vs. SCE) no longer quenched the fluorescence of DCA and this is compatible with no isomerization of **1f**.

To gain information about the reason for the occurrence of stereoselectivity, PET reactions of **2b** were studied additionally (Table 2). In CD3OD, stereomutation of **2b** was as low as ca. 20% even after the 10-h irradiation. Concurrently, the ring closure to **1b** somewhat proceeded in again stereoselective manner. In contrast, the reaction in CD3CN also was studied but the results were of no importance from the standpoint of the stereoselective isomerizations of **1** and **2**. Moreover, although the epimerization of **1** at a nitrogen atom at the 2-position was examined, it did not occur at all.



Scheme 1.

The reaction mechanism and stereochemical outcome are considered based on the above observations as follows (Scheme 1): Since stereomutations in **2** were a minor process in the reaction conditions, occurrence of the stereoselective isomerization of **1** was ascribable to the structural properties inherent to **1**. That is, after the initial SET from the aryl group, the subsequent electron redistribution of the C-O bonding electrons occurs. It seems probable that either ensuing cation or radical at the benzylic position takes the sp^2 hybridization as a lower energy structure similar to a usual carbocation and a carbon radical. Concomitantly, rehybridization of the nitrogen at the 2-position in **1** will occur as proposed in the thermal isomerization of the analogous oxaziridines.[2] Relieving the steric hindrance between the 2-t-butyl group and that cofacial aryl group at the 3-position should be advantageous to such rehybridizations. Then to attain the maximum overlap between lone pair electrons of the nitrogen and the p-orbital on the benzylic position, the least motion (a) of the electron lobes occurred and afforded the nitrone cation radical as observed predominant stereoselectivity.

The reactivities of E-**1e** and Z-**1e** showed a clear contrast. Base on the MO calculations of them,[10] HOMO energy of E-**1e** is slightly higher than that of Z-**1e**; thus suggesting that the initial one-electron transfer is easier in E-**1e** with the singlet excited DCA. The results in the product study, however, are conflicting. Although the detailed results will be reported in the subsequent paper, the ring opening of E- and Z-2-t-butyl-3-(p-chlorophenyl)-3-methyloxaziridine proceeded smoothly (conv. 62 and 22%, respectively at 2h) and this followed the above proposed scheme. The result suggests that the steric interference between one of the 3-aryl groups and the 2-i-propyl group in Z-**1e** is not solely a driving force for easier occurrence of the reaction. At present, the reason for this peculiarity only observed in E-**1e** and Z-**1e** is inexplicable and the clear explanation is awaiting for a further work.

This work was supported by Grant-in-Aid for Scientific Research No. 04640506 from the Ministry of Education, Science and Culture.

References and Notes

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5 Photoreactions were performed with a 400 W high-pressure mercury lamp through a glass filter (≥400 nm) under anaerobic conditions.
6 Stereochemistries of **1** and **2** were determined by the signal broadening of one of the aryl groups in **1** examined by the NOE experiment and the shift reagent experiments for **2**, respectively.
7 When 2,6,9,10-tetracyanoanthracene was employed as a photosensitizer in the reaction of E-**1f**, Z-**2f** was formed stereospecifically in 39% yield at the 39% conversion of E-**1f** after the 2-h irradiation and E-**2f** was formed from Z-**1f** also stereospecifically in 38% yield at the 38% conversion after the same irradiation period.
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9 Half-wave oxidation potential is reported as +0.81 V vs. SCE: C. K. Mann and K. K. Barnes, "Electro-chemical Reactions in Nonaqueous Systems," Marcel Dekker, New York (1970), p. 252.
10 Computer calculations were carried out using the CAChe-MOPAC program (Release 6.1) available from Sony-Tektronix, Co. Semiempirical PM3 SCF-MO calculations were executed to search an energy-optimized structure and Frontier electrophilic density was calculated. The results showed that the electrons were most highly located on the aryl group positioned as E against the N-alkyl group: J. J. P. Stewart, *QCPE Bull.*, **9**, 10 (1989).