Reaction of Aromatic *N*-Oxides with Dipolarophiles. XIII. Cycloaddition Behavior of Some Nitrones toward *N*-Phenylmaleimide and Conformation Isomers of the Cycloadducts

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In connection with the stereoselective *exo* cycloaddition in the 1,3-dipolar reaction of 3,5-lutidine *N*-oxide and *N*-arylmaleimides, the cycloaddition behavior of some nitrones toward *N*-phenylmaleimide was investigated. In the reaction of cyclic nitrones with *N*-phenylmaleimide, pairs of isomers were isolated in a crystalline state. The low-temperature nuclear magnetic resonance measurements of the adducts suggested that the compounds are conformational isomers with regard to the ring inversion brought about by the mobility of the lone pair on nitrogen. The observed reactivity and regiochemistry are discussed in terms of frontier molecular orbital considerations.

Keywords 1,3-dipolar cycloaddition; frontier molecular orbital; conformational isomer; regioisomer; reactivity; nitron; *N*-phenylmaleimide; phenyl vinyl sulfone

Introduction

Previously, we reported that in the 1,3-dipolar cycloaddition of 3,5-dimethylpyridine (3,5-lutidine) *N*-oxide with *N*-substituted maleimides,¹⁾ the *exo* adducts were exclusively produced as the primary products which readily isomerized to the thermodynamically more stable *endo* 1,5-sigmatropy products, and the cycloaddition behavior was interpreted in terms of unfavorable secondary-orbital interactions²⁾ between the frontier molecular orbitals (FMO)³⁾ of both addends. During the course of the investigation, an important question arose concerning the 1,3-dipolar cycloaddition reactivity, *i.e.*, why does only 3,5-dimethylpyridine *N*-oxide show reactivity toward *N*-substituted maleimides. We considered that the inertness of other types of pyridine *N*-oxides such as unsubstituted pyridine *N*-oxide or 3-methylpyridine (3-picoline) *N*-oxide might be attributable to their high degree of aromaticity and stabilization of the ground state by charge-transfer complex formation between the dipoles and dipolarophiles.⁴⁾

Chart 1

In order to establish the difference between aromatic *N*-oxides and simple nitrones in the cycloaddition behavior, we studied the cycloaddition of some nitrones (Ia—d) with *N*-phenylmaleimide (IIa) and phenyl vinyl sulfone (IIb). The cyclic nitrones (Ib—d) do not have any π -electron system other than the nitron π -electron system, the reactivity of which is hardly influenced by secondary non-bonding interactions or charge-transfer complexation to stabilize the transition state. This paper describes the results of these studies.

Results

Cycloaddition of Nitrones (Ia—d) with *N*-Phenylmaleimide (IIa) *N*, α -Diphenylnitron (Ia) readily reacted with IIa to give a mixture of 1 : 1 cycloadducts assignable to *endo* and *exo* cycloadducts (IIIa).

Chart 2

In the reaction, the *endo* isomer was produced predominantly. The stereochemistry of the cycloadducts was determined from the dihedral angle relationship⁵⁾ between H_3-H_{3a} and $H_{3a}-H_{6a}$ based on the fact that the two phenyl groups of Ia lie in a *trans* configuration.⁶⁾

The cycloadditions of 2,4,4-trimethyloxazoline *N*-oxide (Ib) and 2-ethyl-4,4-dimethyloxazoline *N*-oxide (Ic) to IIa were carried out without isolation of Ib, c (*in situ* cycloaddition) because of high sensitivity to air.

Chart 3

Interestingly, pairs of crystals were isolated in all cases. The crystals showed different melting points and depression of the mixed melting points. More interesting is the spectroscopic behavior of the cycloadducts. For example, the infrared (IR) spectra of the crystals (IIIc and III'c) isolated from Ic and IIa showed different spectral patterns. The carbonyl groups absorbed at 1720 and 1728 cm^{-1} respectively. On the other hand, the proton nuclear magnetic resonance ($^1\text{H-NMR}$) spectra of both crystals showed similar spectral patterns. These facts suggested that the crystals should not be assigned as the *endo* and *exo* isomers. The *endo* nature of the cycloadduct was established on the basis of inspection of the nuclear Overhauser effect (NOE)

difference spectra obtained by irradiation of the protons of the C_{5a} -alkyl group. In the case of IIIc (III'c), significant NOE was observed between CH_3-CH_2 and $C_{5b}-H$.

The cycloadducts have an interesting molecular structure, which involves three types of five-membered ring (A, B and C rings) holding four hetero atoms. Of the rings, the succinimide moiety (C ring) is planar and not flexible. The A and B rings involve bonds linked to the N-O bond. Such bonds are known to have higher torsional barriers and heterocycles involving such bonds are less flexible than the corresponding homocyclic system.⁷⁾ The lone-pair on sp^3 nitrogen (N_2) moves sparingly from the *syn* to the *anti* position and *vice versa* with regard to the C_{5a} -alkyl group by nitrogen inversion.⁸⁾

Chart 4

In the conformation with the *cis* ring juncture, there appears to be an interaction between the lone pair and C_{5a} -alkyl group, whereas, in the case of *trans* ring juncture, there is an interaction between the lone pair and the succinimide ring. Another type of interaction may be steric repulsion between the rings, wherein the conformation with the *cis* ring juncture may suffer from repulsive interaction between the A and C rings as compared with the conformation with the *trans* ring juncture. This may be consistent with the fact that compound IIIc exhibited the imido carbonyl absorption at 1728 cm^{-1} , which is 8 cm^{-1} higher than that of III'c.

Compounds IIIb (IIIc) and III'b (III'c) are considered to be conformational isomers⁸⁾ having little energetic preference and frozen in a crystalline state in which crystal packing forces may be operative. To confirm this assumption, the NMR spectra of IIIb and IIIc were measured at a low temperature (-40°C). At that temperature, overlapped signals of two isomeric compounds were observed in each case. In the case of IIIb, a set of $C_{8a}-H$ ($O-CH-CO$) methine protons in the ^1H -NMR spectrum indicated the population (IIIb : III'b) to be *ca.* 2 : 3.

Fig. 1. The 400 MHz ^1H -NMR Signals of the C_4 -H, C_{5b} -H and C_{8a} -H Protons of IIIb at 27°C and -40°C

Müller and Eschenmoser reported that *N*-methoxy-3,3-dimethoxycarbonyl-5-cyano-1,2-oxazolidines are stable enough to be isolated as *cis* and *trans* invertomers (crystalline diastereomer), in which the torsion barriers are higher in bonds linking two heteroatoms, and rates of inversion at tetrahedral nitrogen are significantly reduced.^{8a)}

Next, we chose 2-methyl-3,4,5,6-tetrahydropyridine *N*-oxide (Id) as a model compound which is structurally similar to 3,5-lutidine *N*-oxide. The nitron Id showed high reactivity toward *N*-phenylmaleimide (IIa), giving the cycloadduct IIIId as a sole product. The stereochemistry of IIIId was tentatively assigned as *endo* on the basis of the similarity of the ^1H -NMR spectral data to those of IVd described below (the chemical shift of C_{6a} -Me is nearly identical with that of *endo* IVd depicted in Chart 6). In the reaction, we could not isolate neither the *exo* isomer (A) nor the invertomer arising from the nitrogen inversion described above.

Chart 5

Cycloadditions of Ia—d with Phenyl Vinyl Sulfone (IIb)

Phenyl vinyl sulfone (IIb) has been an important synthon for carbon skeletal construction and can be used in the Diels–Alder reaction as a chemical equivalent of ethylene.⁹⁾ In the light of its high reactivity, we investigated the cycloaddition behavior of phenyl vinyl sulfone toward various pyridine *N*-oxides. Contrary to our expectation, no reaction occurred and decomposition of the starting material was observed under severe reaction conditions.

To establish the cycloaddition reactivity to 1,3-dipoles, the cycloaddition behavior toward the nitrones Ia—d was investigated. These nitrones (Ia—d) readily reacted with IIb to afford the corresponding cycloadducts (IVa—d).

In the reaction of IIb with Ia, four stereoisomers (regioisomers and their *endo/exo* isomers) are possible. In the ^1H -NMR spectrum of IVa, the C_3 -H proton signal was observed as a doublet ($J=4.8\text{ Hz}$) indicating that the PhSO_2 group is attached to the vicinal carbon of C_3 -Ph and the product is an *endo* cycloadduct.

The cycloaddition of IIb with Ib and Ic were carried out without isolation of the dipoles. The cycloadducts were very sensitive to moisture and readily underwent ring cleavage by water to give the 2-aminoethanol derivative (IVb and IVc). The ready ring cleavage might be brought about by release of strain due to dipole–dipole interaction between the sulfonyl function and ring hetero atoms.

The six-membered nitron Id readily added to IIb to give the cycloadduct (IVd). The configuration of the PhSO_2 group was determined by an NOE experiment involving irradiation of the methyl group (C_{6a}). The NOE was

observed between C₇-H and C_{6a}-Me, suggesting the *endo* adduct.

Cycloaddition Behavior of Quinoline *N*-Oxide (Ie) toward *N*-Phenylmaleimide (IIa) 1,3-Dipolar cycloadditions of quinoline *N*-oxide (Ie) with various dipolarophiles have been well investigated and its cycloaddition behavior was clarified from both synthetic and theoretical viewpoints.¹⁰⁾

It has been suggested that the degree of aromaticity of heterocycles is not altered by *N*-oxidation and the aromaticities of the *N*-oxides are parallel with those of their parent molecules, because the unshared electron pair of the nitrogen does not participate in the aromaticity.¹¹⁾ The values of the resonance energies per π -electron (REPE) of heterocycles correlate well with other criteria of aromaticity. The REPE value of quinoline is smaller than that of pyridine.¹²⁾ On the other hand, it can be expected that fusion of a conjugated system (benzene ring) to pyridine *N*-oxide will increase the cycloaddition reactivity as a consequence of the reduced separation between the highest occupied molecular orbital (HOMO) (which is raised) and lowest unoccupied molecular orbital (LUMO) (which is lowered).

Based on this background, we carried out the cycloaddition of Ie with IIa. As a result, Ie did not show any cycloaddition reactivity toward IIa. When a solution of Ie was mixed with a solution of IIa, the solution became light yellow-green. The color did not discharge upon heating above 60 °C and remained during the reaction period. The visible spectrum of a mixture of Ie and IIa in sulfolane solution showed the absorption maximum at 430 nm, suggesting that the charge-transfer complexes may exist only in solution in equilibrium with their components.

Discussion

As hitherto mentioned, aliphatic nitrones used in this

study showed high reactivity toward both acyclic and cyclic dipolarophiles and gave mainly *endo* cycloadducts. This is in sharp contrast to the result in the case of aromatic *N*-oxides.

In order to understand this discrepancy, modified neglect of diatomic overlap (MNDO)¹³⁾ calculations were performed and the stabilization energies due to FMO interactions were evaluated according to the perturbation theory.¹⁴⁾ For simplicity, the calculations were performed on model compounds, e.g. pyridine *N*-oxide (If), *N*, α -dimethylnitrone (Ig) and unsubstituted maleimide (Iic). The calculated orbital energy levels and coefficients are listed in Table I.

As described in the previous paper,¹⁾ the reaction of pyridine *N*-oxides with *N*-substituted maleimides falls into the category of a "normal type" reaction in Sustmann's classification¹⁵⁾ for cycloadditions wherein the dominant interaction is the one between the HOMO of the 1,3-dipole and the LUMO of the dipolarophile.

As seen in Table I, the HOMO energy levels of both 1,3-dipoles are very similar to each other. The stabilization energies (ΔE) of the dominant interactions assuming approach of addends in parallel planes separated at 3.0 Å are

TABLE I. MNDO Calculation Data for Pyridine *N*-Oxide (If), *N*, α -Dimethyl Nitrone (Ig) and Maleimide (Iic)

Calcd values		If	Ig	Iic
LUMO (eV), Pz		-0.474	0.152	-1.156
Coefficients	O	-0.393	-0.424	
	N	0.529	0.596	
	C	-0.287	-0.625	[0.549]
HOMO ^{a)} (eV), Pz		-8.769	-8.890	-11.351
Coefficients	O	-0.646	-0.688	
	N	0.226	0.231	
	C	0.379	0.657	[0.657]
Bond length (Bond order)		N=C 1.411 (1.163)	1.348 (1.523)	
Net charges	O	-0.421	-0.438	
	N	0.263	0.200	
	C	-0.080	-0.172	-0.07

a) The electron density of the orbitals, HOMO (-11.32 eV) and NHOMO (-11.17 eV), localized on N and O, respectively.

Fig. 2. FMO Interactions of Pyridine *N*-Oxide (If) and *N*, α -Dimethyl Nitrone (Ig) with Maleimide (Iic)

simply expressed as follows:

$$\Delta E[\text{If}(\text{HOMO}) - \text{Ic}(\text{LUMO})] = 2(0.646 \cdot C \cdot \beta_{\text{co}} + 0.379 \cdot C \cdot \beta_{\text{cc}})^2 / (-7.613) = -0.052 \text{ eV}$$

$$\Delta E[\text{Ig}(\text{HOMO}) - \text{Ic}(\text{LUMO})] = 2(0.688 \cdot C \cdot \beta_{\text{co}} + 0.657 \cdot C \cdot \beta_{\text{cc}})^2 / (-7.734) = -0.106 \text{ eV}$$

where the denominator is the energy separation between the dipole HOMO and the dipolarophile LUMO, C is the LUMO coefficient of Ic and β_{co} and β_{cc} are resonance integrals at 3.0 Å for C–O (0.55 eV) and C–C (1.20 eV), respectively.¹⁶⁾

The calculation indicates that the stabilization energy for the reaction of Ig is about twice as much as that for If, indicating that nitrones inherently show high cycloaddition reactivity toward dipolarophiles. The low reactivity of aromatic N -oxide is considered to be brought about by decrease of the FMO electron density on the $\text{>C=N} \rightarrow \text{O}$ system delocalized into the pyridine nucleus.

The detailed perturbation calculation data for both interactions are summarized in Table II.

An important controlling factor which must be taken into consideration for the cycloaddition reactivity is degree of aromaticity.¹⁷⁾ However, quantitative prediction can not be done by an FMO consideration. The degree of stabilization of the $\text{>C=N} \rightarrow \text{O}$ system of If by aromatic-ring resonance seems to reflect the C=N bond length of the MNDO optimized structure. The C=N bond length of If (1.411 Å, bond order 1.163) is considerably longer than that for Ig (1.348 Å, bond order 1.523) (see Table I).

As regards the reactivity of quinoline N -oxide (Ie), the resonance energy of Ie is considered to be essentially the same as that of If. In Ie, the fusion of the benzene ring to If compresses the HOMO–LUMO energy gap. Such a situation is more favorable for charge-transfer complex formation than in the case of If; in other words, it is unfavorable for cycloaddition because of stabilization of the ground state.⁴⁾ In the reaction of Ie and IIa, the perturbation interaction energy could not overcome the stabilization energy of the ground state. Thus, the cycloaddition behavior of aromatic N -oxides can be rationalized in terms of counterbalancing aromatic and electronic factors.^{4b)}

TABLE II. Calculated Reactivity of Maleimide (Iic) toward Pyridine N -Oxide (If) and N,α -Dimethyl Nitron (Ig) Based on the Perturbation Equation^{a)}

Distance (Å)	FMO interaction Dipolarophile—1,3-Dipole		Stabilization energy ΔE (eV)
	Iic	If	
3.0	HOMO	LUMO	−0.0249
	LUMO	HOMO	−0.0520
		Total	−0.0769
1.5	HOMO	LUMO	−1.81
	LUMO	HOMO	−4.10
		Total	−5.91
	Iic	Ig	
3.0	HOMO	LUMO	−0.0725
	LUMO	HOMO	−0.106
		Total	−0.179
1.5	HOMO	LUMO	−4.05
	LUMO	HOMO	−6.93
		Total	−10.98

a) The FMO interactions of the 3rd term were calculated.

Fig. 3. FMO Interaction of N,α -Diphenyl Nitron (Ia) with Phenyl Vinyl Sulfone (Iib), Showing the Predominant Regioisomer

The observed regiochemistry of the reaction of I with phenyl vinyl sulfone (Iib) follows the principle of maximum overlap¹⁴⁾ of FMO theory as exemplified in Fig. 3.

Experimental

All melting points are uncorrected. ^1H -NMR spectra were taken with Hitachi R-600 and JEOL GX-400 spectrometers for ca. 10% (w/v) solution with tetramethylsilane (TMS) as an internal standard; chemical shifts are expressed in δ values. IR spectra were recorded on a JASCO IR-G infrared spectrophotometer equipped with a grating. Visible absorption spectra were taken with a Hitachi 150-20 spectrometer. Mass spectra (MS) were taken with a JEOL JMS-01SG double-focussing spectrometer operating at an ionization potential of 75 eV. High performance liquid chromatographic analyses (HPLC) were performed on a JASCO FAMILIC 100N chromatograph equipped with a ultraviolet detector and a column of Fine Pak SIL C12. Flash chromatography was carried out with Merck Silica gel 60.

Molecular orbital calculations were performed on a FACOM M-360 computer at the Computer Center of Kumamoto University.

Materials N -Phenylmaleimide (IIa), phenyl vinyl sulfone (Iib),⁹⁾ N,α -diphenylnitron (Ia),¹⁸⁾ 2,4,4-trimethyl-oxazoline N -oxide (Ib),¹⁹⁾ 2-ethyl-4,4-dimethyl-oxazoline N -oxide (Ic),¹⁹⁾ 2-methyl-3,4,5,6-tetrahydropyridine N -oxide (Id)²⁰⁾ and quinoline N -oxide (Ie)¹⁰⁾ were prepared according to the established methods.

Cycloaddition of N,α -Diphenyl Nitron (Ia) with N -Phenylmaleimide (IIa) A solution of Ia (0.5 g, 2.54 mmol) and IIa (0.44 g, 2.54 mmol) in toluene was heated at 80 °C for 1.5 h. After cooling in a refrigerator for 2 h, the precipitates were filtered off by suction. The crystals were purified by recrystallization from CH_2Cl_2 –petroleum ether to give colorless needles in 97% yield. After recrystallization, the filtrate was diluted with petroleum ether to give small colorless needles.

exo Adduct (IIIa): mp 201–202 °C. IR (KBr): 1726 (C=O) cm^{-1} . ^1H -NMR (in CDCl_3) δ : 4.0 (1H, dd, J =7.8, 9.0 Hz, >CH-C=O), 4.95 (1H, d, J =9.0 Hz, >CH-O-), 5.27 (1H, d, J =7.8 Hz, >CH-Ph), 7.5–7.0 (15H, m, Ph). MS m/z : 370 (M^+). Anal. Calcd for $\text{C}_{23}\text{H}_{16}\text{N}_2\text{O}_3$: C, 74.54; H, 4.90; N, 7.56. Found: C, 74.26; H, 4.78; N, 7.56.

endo Adduct (IIIa'): mp 150–151 °C. IR (KBr): 1714 (C=O) cm^{-1} . ^1H -NMR (in CDCl_3) δ : 4.0 (1H, dd, J =7.6, 1.0 Hz, >CH-C=O), 5.10 (1H, d, J =7.6 Hz, >CH-O-), 5.70 (1H, d, J =1.0 Hz, >CH-Ph), 6.6 (2H, m, Ph), 6.9–7.6 (13H, m, Ph). MS m/z : 370 (M^+).

Cycloaddition of 2,4,4-Trimethyloxazoline N -Oxide (Ib) with N -Phenylmaleimide (IIa) A solution of triethyl orthoacetate (1.05 g, 6.6 mmol) and hydroxylamine hydrochloride (0.75 g, 5.4 mmol) in CH_2Cl_2 (6 ml) was

stirred at 25°C for 1 h. To the solution was added a mixture of IIa (0.93 g, 5.4 mmol) and triethylamine (7.5 ml), and the whole was refluxed for 4 h. After cooling, triethylamine hydrochloride was filtered off. The solvent was evaporated off *in vacuo* and the residue was chromatographed on silica gel (2 cm × 50 g) using CHCl₃-AcOEt (10:1) as an eluent to give III'b (IIIb) in 21% yield. The crystalline mass was recrystallized from CH₂Cl₂ to give colorless needles (III'b). The filtrate was diluted with petroleum ether followed by recrystallization to give colorless crystals (IIIb).

Crystalline III'b: mp 167.5–168.5°C. IR (KBr): 1714 (C=O) cm⁻¹. ¹H-NMR (in CDCl₃) δ: 1.34 (3H, s, C₃-Me), 1.46 (3H, s, C₃-Me), 1.68 (3H, s, C_{5a}-Me), 3.78 (1H, d, *J* = 7.7 Hz, C₄-H), 3.82 (1H, d, *J* = 8.1 Hz, C_{5b}-H), 3.85 (1H, d, *J* = 7.7 Hz, C₄-H), 5.03 (1H, d, *J* = 8.1 Hz, C_{8a}-H), 7.2–7.5 (5H, m, Ph). MS *m/z*: 302 (M⁺). Anal. Calcd for C₁₆H₁₈N₂O₄: C, 63.56; H, 6.00; N, 9.27. Found: C, 63.53; H, 5.99; N, 9.35.

Crystalline IIIb: mp 166–167°C. IR (KBr): 1716 (C=O) cm⁻¹. ¹H-NMR (in CDCl₃) δ: 1.34 (3H, s, C₃-Me), 1.46 (3H, s, C₃-Me), 1.68 (3H, s, C_{5a}-Me), 3.78 (1H, d, *J* = 7.7 Hz, C₄-H), 3.82 (1H, d, *J* = 7.7 Hz, C_{5b}-H), 3.85 (1H, d, *J* = 7.7 Hz, C₄-H), 5.03 (1H, d, *J* = 7.7 Hz, C_{8a}-H), 7.2–7.5 (5H, m, Ph). MS *m/z*: 302 (M⁺).

Cycloaddition of 2-Ethyl-4,4-dimethyloxazoline N-Oxide (Ic) with N-Phenylmaleimide (IIa) The cycloaddition of IIa and Ic, which was prepared from triethyl orthopropionate (1.17 g, 6.6 mmol) and hydroxylamine hydrochloride (0.75 g, 5.4 mmol), was carried out according to the procedure used for the reaction of Ib and IIa (29% yield). Recrystallization gave two kinds of crystals, mp 126–127°C (III'c) and 121–121.5°C (IIIc).

Crystalline III'c: mp 126–127°C. IR (KBr): 1720 (C=O) cm⁻¹. ¹H-NMR (in CDCl₃) δ: 1.09 (3H, t, *J* = 7.3 Hz, Me of Et), 1.31 (3H, s, C₃-Me), 1.44 (3H, s, C₃-Me), 1.90 and 2.15 (2H, multiplet due to restricted rotation about C_{5a}-CH₂-), 3.74 (1H, d, *J* = 8.1 Hz, C₄-H), 3.79 (1H, d, *J* = 8.1 Hz, C₄-H), 3.86 (1H, d, *J* = 7.7 Hz, C_{5b}-H), 5.00 (1H, d, *J* = 7.7 Hz, C_{8a}-H), 7.2–7.5 (5H, m, Ph). MS *m/z*: 316 (M⁺). Anal. Calcd for C₁₇H₂₀N₂O₄: C, 64.54; H, 6.37; N, 8.85. Found: C, 64.68; H, 6.54; N, 9.01.

Crystalline IIIc: mp 121–121.5°C. IR (KBr): 1728 (C=O) cm⁻¹. ¹H-NMR (in CDCl₃) δ: 1.10 (3H, t, *J* = 7.3 Hz, Me of Et), 1.31 (3H, s, C₃-Me), 1.44 (3H, s, C₃-Me), 1.90 and 2.15 (2H, multiplet due to restricted rotation about C_{5a}-CH₂-), 3.74 (1H, d, *J* = 8.1 Hz, C₄-H), 3.79 (1H, d, *J* = 8.1 Hz, C₄-H), 3.89 (1H, d, *J* = 7.7 Hz, C_{5b}-H), 4.99 (1H, d, *J* = 7.7 Hz, C_{8a}-H), 7.26–7.5 (5H, m, Ph). MS *m/z*: 302 (M⁺).

Cycloaddition of 2-Methyl-3,4,5,6-tetrahydropyridine N-Oxide (Id) with N-Phenylmaleimide (IIa) A solution of Id (0.26 g, 2.31 mmol) and IIa (0.45 g, 2.6 mmol) in toluene was heated at 80°C for 4 h. The solvent was evaporated off *in vacuo*. The residue was purified by flash chromatography on silica gel (2 cm × 20 g). The fraction eluted with CHCl₃-AcOEt (10:1) gave IIIId as colorless needles in 56% yield, mp 166.5–167.5°C (from CH₂Cl₂-petroleum ether). IR (KBr) 1700 cm⁻¹ (C=O). ¹H-NMR (in CDCl₃) δ: 1.20–1.92 (6H, m, CH₂CH₂CH₂), 1.38 (3H, s, C_{6a}-Me), 3.00 (1H, m, C₃-H), 3.22 (1H, d, *J* = 7.3 Hz, C_{6a}-H), 3.42 (1H, weakly split d, *J* = 14.6 Hz, C₃-H), 4.93 (1H, d, *J* = 7.3 Hz, C_{9a}-H), 7.26–7.49 (5H, m, Ph). MS *m/z*: 286. Anal. Calcd for C₁₆H₁₈N₂O₃: C, 67.12; H, 6.34; N, 9.78. Found: C, 67.12; H, 6.19; N, 9.70.

Cycloaddition of N,α-Diphenyl Nitroene (Ia) with Phenyl Vinyl Sulfone (IIb) A solution of Ia (0.34 g, 2.00 mmol) and IIb (0.39 g, 2.00 mmol) in dioxane (5 ml) was heated at 60°C for 7 h. After cooling, the solvent was evaporated off *in vacuo*. The precipitates were filtered off by suction and recrystallized from CH₂Cl₂-MeOH to give IVa as colorless prisms, mp 121–122°C in 79% yield. IR (KBr): 1300, 1150 (SO₂) cm⁻¹. ¹H-NMR (in CDCl₃) δ: 4.15, 4.35 (2H, m, -CH₂-O-), 4.51 (1H, weakly split dd, *J* = 4.8, 10 Hz, >CH-SO₂-), 4.95 (1H, d, *J* = 4.8 Hz, >CH-Ph), 7.13–7.83 (15H, m, 3Ph). MS *m/z*: 365 (M⁺). Anal. Calcd for C₂₁H₁₉NO₃S: C, 69.02; H, 5.24; N, 3.83. Found: C, 69.06; H, 5.17; N, 3.78.

Cycloaddition of 2,4,4-Trimethyloxazoline N-Oxide (Ib) with Phenyl Vinyl Sulfone (IIb) A solution of triethyl orthoacetate (1.05 g, 6.6 mmol) and hydroxylamine hydrochloride (0.75 g, 5.4 mmol) in CH₂Cl₂ (6 ml) was stirred at 25°C for 1 h. To the solution was added a mixture of IIb (1.11 g, 6.6 mmol) and triethylamine (7.5 ml, 5.4 mmol), and the whole was refluxed for 10 h. After cooling, triethylamine hydrochloride was filtered off. The solvent was evaporated off *in vacuo* and the residue was chromatographed on silica gel (2.5 cm × 60 g) using C₆H₆-AcOEt (1:8) as an eluent to give a yellow oil (IVb) in 8.8% yield. IR (film): 3400 (OH), 1715 (C=O) cm⁻¹. ¹H-NMR (in CDCl₃, 60 MHz) δ: 1.05 (6H, s, 2Me), 2.12 (3H, s, CO-Me), 3.0–3.6 (4H, m, O-CH₂CH-SO₂ and OH), 4.05 (2H, s, HO-CH₂), 7.5–8.15 (5H, m, Ph). MS *m/z*: 315 (M⁺).

Cycloaddition of 2-Ethyl-4,4-dimethyloxazoline N-Oxide (Ic) with Phenyl Vinyl Sulfone (IIb) The reaction IIb with Ic, which was prepared from

triethyl orthopropionate (1.17 g, 6.6 mmol) and hydroxylamine hydrochloride (0.75 g, 5.4 mmol), was carried out according to the procedure used for the reaction of Ib with IIb. The product (IVc) was isolated as a yellow oil in 14% yield. IR (film): 3400 (OH), 1710 (C=O) cm⁻¹. ¹H-NMR (in CDCl₃, 60 MHz) δ: 1.25 (6H, s, 2Me), 1.40 (3H, t, *J* = 7.5 Hz, Me of Et), 2.6 (2H, q, *J* = 7.5 Hz, methylene of Et), 3.1–3.8 (4H, m, O-CH₂CH-SO₂ and OH), 4.25 (2H, s, HO-CH₂), 7.70–8.40 (5H, m, Ph). MS *m/z*: 329 (M⁺).

Cycloaddition of 2-Methyl-3,4,5,6-tetrahydropyridine N-Oxide (Id) with Phenyl Vinyl Sulfone (IIb) A solution of Id (0.31 g, 2.7 mmol) and IIb (0.5 g, 2.8 mmol) in toluene was heated at 80°C for 4 h. The solvent was evaporated off *in vacuo*. The residue was purified by flash chromatography on silica gel (2 cm × 20 g). The fraction eluted with CHCl₃-AcOEt (1:3) gave IVd as colorless needles: mp 115.5–116.5°C (from ether-petroleum ether) in 45% yield. IR (KBr): 1300, 1100 (SO₂) cm⁻¹. ¹H-NMR (in CDCl₃) δ: 1.25–2.36 (6H, m, CH₂CH₂CH₂), 1.41 (3H, s, Me), 2.97 and 3.32 (2H, m, N-CH₂), 3.75 (1H, dd, *J* = 10, 7.3 Hz, -CH₂-O-), 3.85 (1H, dd, *J* = 10, 7.3 Hz, -CH₂-O-), 4.28 (1H, dd, *J* = 7.3, 7.3 Hz, >CH-SO₂-), 7.56–7.88 (5H, m, Ph). MS *m/z*: 281 (M⁺). Anal. Calcd for C₁₄H₁₉NO₃S: C, 59.76; H, 6.81; N, 4.98. Found: C, 60.10; H, 6.99; N, 4.79.

Acknowledgment The authors are grateful to Eisai Co., Ltd., for financial support of this work. The authors also wish to express their thanks to the members of the Analytical Department of this Faculty for microanalyses and spectral measurements.

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