The Effects of Lewis Acid on the 1,3-Dipolar Cycloaddition Reaction of *C*-Arylaldonitrones with Alkenes

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The regio- and stereoselectivity of the 1,3-dipolar cycloaddition reactions of *C*-aryl-*N*-alkylaldonitrones (1a—e) with some alkenes were found to be affected significantly by the addition of Lewis acid. The rate of the reaction was also affected by adding the Lewis acid. In the reactions using allyl alcohol as a dipolarophile an addition of Lewis acid caused a remarkable acceleration of the reaction and a great change in the stereoselectivity. In the reactions using ethyl acrylate as a dipolarophile the regioselectivity was reversed whether the reaction was performed in the presence or the absence of Lewis acid; *i.e.* isoxazolidine-5-carboxylates were obtained mainly in the absence of Lewis acid although isoxazolidine-4-carboxylates were obtained mainly in the presence of Lewis acid. When the reaction of *C*,*N*-diarylaldonitrones (1k, 1m, 1n) with ethyl acrylate was carried out in the presence of Lewis acid, the cleavage of the N–O bond of the cycloadducts giving γ-aminoalcohols was also observed besides a reverse phenomenon of regioselectivity.

Key words cycloaddition; nitrone; Lewis acid; regioselectivity; stereoselectivity

1,3-Dipolar cycloaddition reaction has been known to be one of useful methods for the synthesis of five-membered heterocycles.[1—3] Some five-membered heterocyclic rings found in the structure of natural products has been built up directly by the reaction.[3,4] Though several dipoles other than nitrones have been used for the synthesis of natural products, nitrones have been found to have wide applications.[4] Some functional groups found in the structure of natural products have been known to be prepared all at once by ring-opening reaction of the cycloadducts.[5—21]

The structure and stereochemistry of the cycloadducts depend largely on electronic nature of dipole and dipolarophile because 1,3-dipolar cycloaddition reaction is one of representative concerted reactions.[1—3] Total synthesis of natural product has been effectively achieved by using 1,3-dipolar cycloaddition that shows high selectivity in stereo-, regio-, and diastereoselectivity. Some Diels–Alder reactions have been known to be speeded up and to proceed stereo- and regioselectively by adding Lewis acid.[22—24] On the other hand, another situation occurs in 1,3-dipolar cycloaddition reaction because 1,3-dipoles show zwitter ionic character. Most 1,3-dipoles have been known to react with Lewis acid to give stable ionic salts and, consequently, any cycloaddition reaction was not observed. On the other hand, a few 1,3-dipoles have been known to react with Lewis acid to give unstable ionic salts that exhibit 1,3-dipolar nature and undergo high selective cycloaddition reaction with dipolarophiles.[25—41] Some 1,3-dipolar cycloaddition reactions of nitrones and alkenes have been known to be speeded up and to proceed stereo- and regioselectively by introducing Lewis acid (see Chart 1[31] and 2[36]). The Lewis acid can complexed with both the nitrone and the dipolarophile in the reaction shown in Chart 1.[31] Two transition states shown in the Chart may be regarded as significant. Diastereoselectivity of the reaction has been well explained on the basis of the difference of steric hindrance in the two transition states. The benzoyl group of *C*-benzoylnitrone has an influence on the regioselectivity of the cycloaddition reaction shown in Chart 2.[36]

In these examples shown above, Lewis acid can also interact with several functional groups other than oxygen atom of nitrone group. In this study, we investigated some effects of Lewis acids on the reaction of nitrone that substituted with two hydrocarbon groups (inert group to Lewis acid) with dipolarophile that substituted with one functional group (active group to Lewis acid). Concretely, *C*,*N*-diaryl- and *N*-alkyl-*C*-arylaldonitrones were chosen for the substrate. *C*-Alkylaldonitrones were not chosen because of the thermoinstability. Results from the *C*,*N*-diaryllnitrones were quite different from those from *C*-aryl-*N*-alkylnitrones by appearance, though the exact nature of the two reactions is the same.

Results and Discussions

1,3-Dipolar Cycloaddition Reaction of *N*-Alkyl-*C*-arylnitrones with Dipolarophiles in the Absence of Lewis Acid The reaction of *N*-benzyl-*C*-phenylnitrone (**1a**) with a variety of mono- and 1,1-disubstituted alkenes (**2A**—**P**) was carried out under various conditions and the results ware

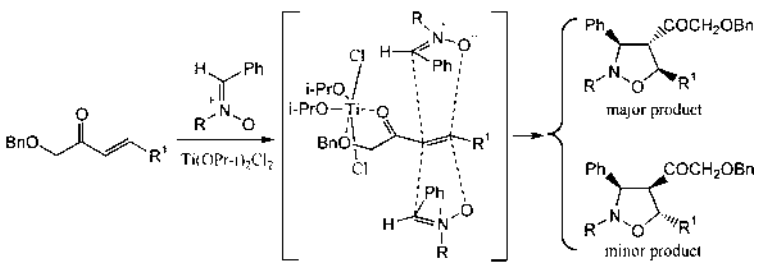

Chart 1. Titanium Catalyzed Nitrone–Alkene Cycloaddition[31]

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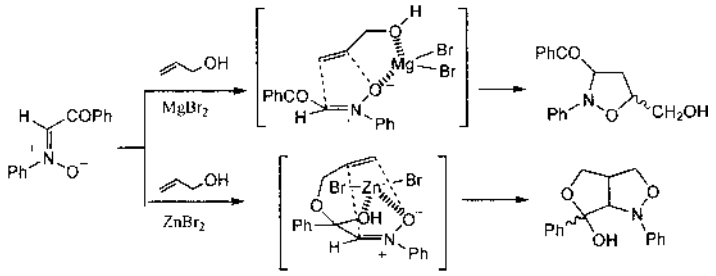


Chart 2. Lewis Acid Catalyzed Cycloaddition of *C*-Benzoylnitrone and Allyl Alcohol[36)]

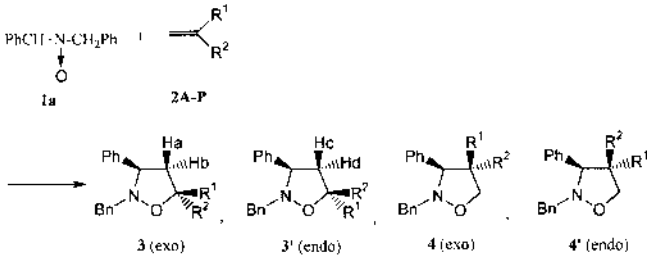


Chart 3. 1,3-Dipolar Cycloaddition Reaction of Nitrone (**1a**) with Dipolarophiles (**2A**—**P**)

Table 1. 1,3-Dipolar Cycloaddition Reaction of **1a** with Dipolarophiles (**2**)

Run No.	Dipolarophile[a)]			Reaction conditions			Recovery of **1a**	Total yields of adducts	Ratio of adducts **3** : **3′** : **4** : **4′**
	2	R^1	R^2	Solvent[b)]	Time	Additive[c)]			
1	**2A**	CO_2Et	H	Benzene	7 h	None	0%	97%	10 : 72 : 4 : 14
2	**2A**	CO_2Et	H	Benzene	24 h	$MgBr_2 \cdot Et_2O$	10%	74%	6 : 14 : 43 : 37
3	**2A**	CO_2Et	H	Benzene	16 h	$MgBr_2 \cdot Et_2O$	20%	78%	10 : 14 : 49 : 27
4	**2A**	CO_2Et	H	Benzene	16 h	$MgBr_2 \cdot Et_2O$	14%	85%	9 : 33 : 39 : 19
5	**2A**	CO_2Et	H	Benzene	22 h	$ZnBr_2$	46%	47%	8 : 21 : 54 : 17
6	**2A**	CO_2Et	H	Benzene	22 h	$ZnCl_2$	50%	47%	6 : 27 : 50 : 17
7	**2A**	CO_2Et	H	Benzene	48 h	$TiCl_4$	25%	21%	0 : 41 : 35 : 24
8	**2A**	CO_2Et	H	Benzene	48 h	$BF_3 \cdot Et_2O$	64%	15%	0 : 15 : 65 : 20
9	**2B**	CN	H	Benzene	8 h	None	0%	94%	30 : 34 : 6 : 30
10	**2B**	CN	H	Benzene	24 h	$MgBr_2 \cdot Et_2O$	61%	32%	28 : 25 : 15 : 32
11	**2C**	Ph	H	Benzene	30 h	None	0%	96%	76 : 24
12	**2D**	OBu	H	Neat	36 h	None	0%	94%	63 : 37
13	**2E**	OAc	H	Toluene	34 h	None	18%	60%	62 : 38
14	**2F**	CH_2Br	H	Toluene	45 h	None	20%	75%	70 : 30
15	**2G**	CH_2OH	H	Toluene	32 h	None	0%	95%	62 : 38
16	**2G**	CH_2OH	H	Toluene	2 h	$MgBr_2 \cdot Et_2O$	0%	62%	22 : 78
17	**2G**	CH_2OH	H	Benzene	12 h	$MgBr_2 \cdot Et_2O$	0%	79%	24 : 76
18	**2G**	CH_2OH	H	CCl_4	18 h	$MgBr_2 \cdot Et_2O$	0%	97%	23 : 77
19	**2G**	CH_2OH	H	Toluene	24 h	$ZnBr_2$	30%	68%	36 : 64
20	**2H**	CH_2OAc	H	Toluene	40 h	None	0%	98%	66 : 34
21	**2I**	$CH(OH)C_3H_7$	H	Toluene	32 h	None	10%	50%	60 : 40
22	**2J**	$C(OH)(CH_3)_2$	H	Toluene	60 h	None	25%	50%	60 : 40
23	**2K**	CH_2O Allyl	H	Toluene	27 h	None	0%	98%	66 : 34
24	**2L**	CH_2SCH_3	H	Toluene	24 h	None	25%	65%	75 : 25
25	**2M**	C_6H_{13}	H	Toluene	96 h	None	53%	30%	73 : 27
26	**2N**	CH_3	CO_2Et	Benzene	20 h	None	0%	99%	65 : 35
27	**2N**	CH_3	CO_2Et	Benzene	24 h	$MgBr_2 \cdot Et_2O$	68%	31%	52 : 48
28	**2P**	CH_3	CN	Benzene	22 h	None	0%	99%	70 : 30

a) Ten-fold excess of dipolarophile was used. *b*) All reactions except for run No. 12 were carried out at the refluxing temperature of the solvent. Reaction shown in run No. 12 was carried out at the boiling temperature of the dipolarophile (94 °C). *c*) All reactions using Lewis acid were carried out under nitrogen atmosphere. An equimolar amount of Lewis acid and nitrone was used in all cases except for runs No. 3 and 4. In runs No. 3 and 4, the Lewis acid was used twice and 0.3, respectively, as much as nitrone.

summarized in Chart 3 and Table 1. All four possible cycloadducts (**3**, **3′**, **4**, **4′**), two regioisomers and the two stereoisomers, were obtained from the reactions using electron-deficient alkenes such as ethyl acrylates (**2A**) and acrylonitrile (**2B**). On the other hand, an exclusive formation of one regioisomer, 5-substituted isoxazolidines, was observed in reactions using the other types of alkenes (**2C**—**P**) as a dipolarophile. Any reaction was not observed in the treatment of **1a** with isopropenyl acetate (**2Q**) and methyl isopropenyl ether (**2R**) at the temperature below 110 °C.

The structure of the cycloadducts was established as below. *C*-Aryl-*N*-methylnitrone has been known to react with styrene or the other monosubstituted alkenes to give 5-substituted isoxazolidines regioselectively[43,51] (see Chart 4[51]). The structures of major and minor products of the reaction have been known to be *cis*- and *trans*-3,5-disubstituted isoxazolidines (**3** and **3′**), respectively, on the basis of the analyses of the ^{1}H-NMR spectra[51]: though, in *cis*-isomer, the magnetic environment of one proton (Ha) at 4-position of the isoxazolidines is quite different from that of the other proton (Hb) at the same position of the ring, those of the corresponding two protons (Hc, Hd) of *trans*-isomer resemble each other. In other words, the difference in the chemical shift of the two protons (Ha, Hb) in *cis*-isomer (**3**) is larger than those in *trans*-isomer (**3′**). The major formation of *cis*-isomer (**3**) can be explained as a result of sterically unhindered *exo* attack of the two substrates in the transition state of the reaction (see Chart 5).

The chemical shifts of methylene protons (Ha, Hb, Hc, Hd) at 4-position of *exo* and *endo* cycloadducts of **1a** and alkenes (**2A**—**G**) were shown in Table 2 along with the value of the differences (Hb−Ha, Hd−Hc) between the chemical shifts. Determination of the stereochemistry of the cycloadducts (**3**, **3′**) could be easily made by the comparison of the differences between the chemical shifts of the methylene protons at the ring of the two isomers. The structures of *cis*- and *trans*-3,4-disubstituted isoxazolidines (**4**, **4′**) were also established on the basis of the analyses of the ^{1}H-NMR spectra. Regioisomers (**4**, **4′**) are easily distinguishable from the other regioisomers (**3**, **3′**) by comparison the coupling patterns of the ring protons of them. Determination of the stereochemistry of the cycloadducts (**4aA**, **4′aA**) could be easily made from the chemical shifts of the ethyl group in the ester group at 4-position of isoxazolidine ring. The ester group of the cycloadduct (**4aA**) is in *cis* relationship with neighboring phenyl group and, consequently, the former group suffers a

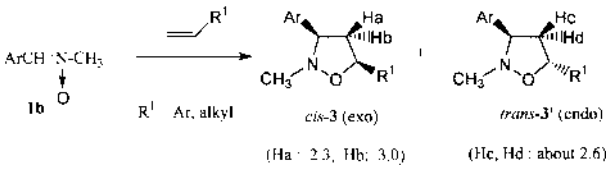


Chart 4. Authorized Structures of Nitrone–Alkene Cycloadducts

Chemical shifts of the ring protons (Ha−Hd) were shown in the parentheses at δ unit.[51]

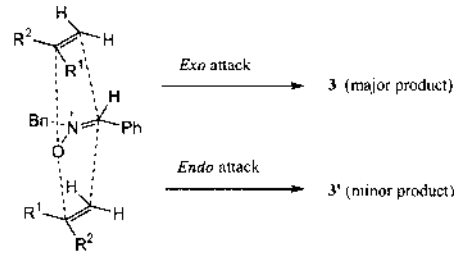
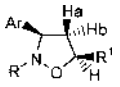
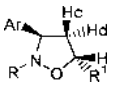


Chart 5. Two Possible Alkene's Approaches to Nitrone (**1a**); (bulkiness of R^1 and R^2: $R^1 > R^2$)

Table 2. Chemical Shifts of Ring Protons (Ha–Hd) of 2,3,5-Trisubstituted Isoxazolidine **3** and **3′**

Substituent			Compound							
			 *cis*-**3**, ppm				 *trans*-**3′**, ppm			
Ar	R	R^1	No.	Ha	Hb	Δ(Hb−Ha)	No.	Hc	Hd	Δ(Hd−Hc)
Ph	Bn	CO_2Et	**3aA**	2.65 (ddd)	2.99 (ddd)	0.34	**3′aA**	2.71 (dt)	2.78 (ddd)	0.07
Ph	Bn	CN	**3aB**	2.62 (ddd)	3.08 (ddd)	0.46	**3′aB**	2.79 (dt)	2.99 (ddd)	0.20
Ph	Bn	Ph	**3aC**	2.43 (dt)	3.15 (dt)	0.72	**3′aC**	2.60 (ddd)	2.75 (dt)	0.15
Ph	Bn	OBu	**3aD**	2.31 (ddd)	2.89 (ddd)	0.58	**3′aD**	2.46 (ddd)	2.64 (ddd)	0.18
Ph	Bn	OAc	**3aE**	2.41 (ddd)	3.04 (ddd)	0.63	**3′aE**	2.63 (dd)	2.63 (dd)	0.00
Ph	Bn	CH_2Br	**3aF**	2.23 (dt)	2.92 (dt)	0.69	**3′aF**	2.51 (dt)	2.57 (ddd)	0.06
Ph	Bn	CH_2OH	**3aG**	2.25 (dt)	2.79 (dt)	0.54	**3′aG**	2.37 (dt)	2.55 (ddd)	0.18
Ph	CH_3	CH_2OH	**3bG**	2.26 (ddd)	2.75 (ddd)	0.49	**3′bG**	2.37 (dt)	2.50 (ddd)	0.13
o-Tol	Bn	CH_2OH	**3cG**	2.04 (ddd)	2.80 (dt)	0.76	**3′bG**	2.18—2.33 (m)	2.55 (ddd)	0.29
2-Naphthyl	Bn	CH_2OH	**3dG**	2.36 (ddd)	2.82 (dt)	0.46	**3′cG**	2.43—2.53 (m)	2.55—2.65 (m)	0.12
o-Anisyl	Bn	CH_2OH	**3eG**	2.06 (ddd)	2.80 (dt)	0.74	**3′dG**	2.51—2.60 (m, 2H)		<0.1
2-Pyridyl	Bn	CH_2OH	**3gG**	2.36—2.48 (m)	2.85(dt)	0.43	**3′fG**	2.46—2.78 (m, 2H)		*ca.* 0.15
6-Me-2-pyridyl	CH_3	CH_2OH	**3hG**	2.50—2.53 (m)	2.83 (dt)	0.32	**3′gG**	2.50—2.70 (m, 2H)		*ca.* 0.1
2-Quinolyl	CH_3	CH_2OH	**3iG**	2.40—2.60 (m)	2.91 (dt)	0.41	**3′hG**	2.63—2.75 (m, 2H)		<0.1
2-Furyl	CH_3	CH_2OH	**3jG**	*a)*	*a)*	*a)*	**3′iG**	2.34—2.50 (m)	2.53—2.64 (m)	0.17
Ph	Bn	CH_2OAc	**3aH**	2.00—2.10 (m)	2.83 (dt)	0.78	**3′aH**	2.41 (t)	2.41 (t)	0.00
Ph	Bn	CH(OH)Pr	**3aI**	2.23 (ddd)	2.79 (dt)	0.56	**3′aI**	2.36 (dt)	2.45—2.53 (m)	0.13
Ph	Bn	$C(OH)Me_2$	**3aJ**	2.23 (dt)	2.56—2.65 (m)	0.38	**3′aJ**	2.56 (ddd)	2.67 (dt)	0.11
Ph	Bn	CH_2O-Allyl	**3aK**	2.16 (ddd)	2.78 (dt)	0.74	**3′aK**	2.38 (dt)	2.51 (ddd))	0.13
Ph	Bn	CH_2SCH_3	**3aL**	2.16 (ddd)	2.88 (dt)	0.72	**3′aL**	2.45—2.50 (m, 2H)		<0.1
Ph	Bn	C_6H_{13}-*n*	**3aM**	2.04 (ddd)	2.78 (dt)	0.79	**3′aM**	2.18 (ddd)	2.36 (dt)	0.18
Ph	Ph	CO_2Et	**3kA**	2.71 (dt)	3.06 (dt)	0.35	**3′kA**	2.69 (ddd)	2.95 (ddd)	0.26
Ph	Tol-*p*	CO_2Et	**3mA**	2.67 (dt)	3.04 (dt)	0.37	**3′mA**	2.71 (ddd)	2.91 (ddd)	0.20
Ph	Cl-Ph	CO_2Et	**3nA**	2.71 (dt)	3.07 (dt)	0.36	**3′nA**	2.69 (dt)	2.94 (ddd)	0.25

a) This compound was not obtained.

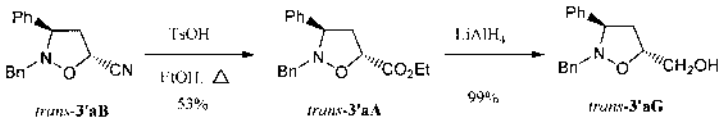


Chart 6. Functional Group Transformations for Structure Elucidation of the Cycloadducts (**3′aA**, **3′aB**, **3′aG**)

shielding effect of the latter group. The methylene protons of the ester group of **4aA** appears at δ 3.70 ppm though those of **4′aA** at δ 4.26 ppm. Major product from the reaction of *N*-methylnitrone (**1b**) with ethyl acrylate (**2A**) has been reported to be not **3′A** but **3A**.[49] The result differs from our one. Therefore, a reduction was carried out to the major product with a view to obtaining definite information on the structure. Our elucidation was found to be correct from the evidence that the spectra of the reduction product were fully consistent with those of *cis*-2-benzyl-5-(hydroxymethyl)-3-phenylisoxazolidine (**3′aG**) that obtained form the reaction of **1a** with allyl alcohol (**2G**) (see Chart 6).

The structures of cycloadducts (**3aB**, **3′aB**, **4aB**, **4′aB**) from acrylonitrile (**2B**) were deduced from the comparison of their ^{1}H-NMR spectra with those of **3aA**, **3′aA**, **4aA**, and **4′aA**, respectively. To make sure of the structures of cycloadducts from acrylonitrile a functional group transformation of cyano group into ester group was also done. The structure of cycloadducts (**3aN**, **3′aN**) from ethyl methacrylate (**2N**) was decided tentatively by considering the cycloaddition reaction mechanistically as shown below.

The formation of four cycloadducts, *i.e.*, two regioisomers and two stereoisomers, may be supposed for the 1,3-dipolar cycloaddition reaction of nitrone (**1a**) with monosubstituted alkenes or 1,1-unsymmetrically disubstituted alkenes. Though one regioisomer, 5-monosubstituted or 5,5-unsymmetrically disubstituted isoxazolidine (**3aC**—**3aP**, **3′aC**—**3′aP**), was formed exclusively in many reactions (runs No. 11—15, 20—26, 28) summarized in Table 1, a formation of a small amount of the other regioisomer, 4-substituted isoxazolidine (**4aA**, **4′aA**, **4aB**, **4′aB**), was also observed in the reaction with electron-deficient alkenes such as acrylate (**2A**) and acrylonitrile (**2B**) (runs No. 1, 9). These results are consistent with previous studies on 1,3-dipolar cycloaddition reaction of nitrone.[1—3,42—50]

The formation and the ratio of two stereoisomers can be explained on the basis of both electronic and steric factors as follows. Aldonitrones such as **1a** have been known to be stable in *Z*-configuration.[1—3,42—50,52] Monosubstituted alkenes such as **2C**—**M** have been known to have relatively high HOMO and to undergo exclusively a dipole-LUMO/dipolarophile-HOMO controlled reaction with the *Z*-aldonitrone (**1a**) (see Chart 7).[1—3] Though the reaction proceeds with high regioselectivity, the stereoselectivity of the reaction was poor one. Transition states leading to two stereoisomers are shown in Chart 5. Steric repulsion between substituents in the *exo* transition state that leading to *cis*-3,5-disubstituted isoxazolidine (**3**) is smaller than those in *endo* transition state that leading to *trans*-one (**3′**). Consequently, **3** was formed exclusively (see runs No. 11—15, 20—26, 28).

A dipole-HOMO/dipolarophile-LUMO controlled reaction also occurs beside a dipole-LUMO/dipolarophile-HOMO controlled reaction in cases using **2A** and **2B** because the energy level of LUMO of these alkenes is very low in comparison with that of **2C**—**2M**. The former reaction leads 4-substituted isoxazolidines (**4aA**, **4′aA**) and the latter one leads 5-substituted isoxazolidines (**3aA**, **3′aA**) (see Chart 7). Taking into account of steric factor shown in Chart 5, **3aA** may be supposed to be formed mainly. But the *endo*-adduct (**3′aA**) was generated in an amount larger than *exo*-adducts (**3aA**). This result can be explained as a result of secondary orbital interaction between the ester group with the nitrogen atom of nitrone group (see run No. 1 in Table 1).

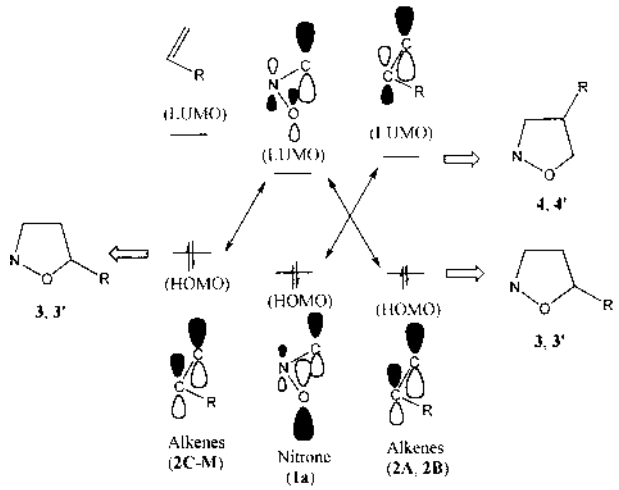


Chart 7. Interaction Scheme of Nitrone (**1a**) with Alkenes (**2A**—**M**)

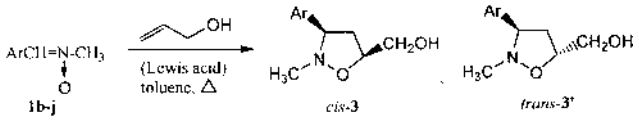


Chart 8. Reaction of *N*-Methylnitrone (**1b**—**j**) with Allyl Alcohol (**2G**)

The results of the reaction of **1a** with ethyl methacrylate (**2N**) can be explained as follows. LUMO of methacrylate (**2N**) is higher than that of acrylate (**2A**) and, consequently, a dipole-HOMO/dipolarophile-LUMO controlled reaction hardly occurs. Thus, **4N** and **4′N** were not obtained from the reaction. In the *exo* transition state of Chart 5, more bulky substituent (methyl group) occupies *exo* position and ester group occupies endo position in which the secondary orbital interaction shown above acts effectively. In the *endo* transition state, two unfavored situations cooperate. Thus, the amount of *exo*-adducts (**3aN**) exceeded that of *endo* adducts (**3′aN**).

The order of the reactivity of various alkenes towards nitrone (**1a**) could be estimated from the Table 1 to be **2A**, **2B** (electron-deficient monosubstituted alkenes)>**2N**, **2P** (electron-deficient 1,1-disubstituted alkenes)>**2C** (alkene substituted with conjugative group)>**2D** (electron-rich alkenes substituted with powerful electron-donating group)>**2E** (electron-rich alkenes substituted with weak electron-donat-

Table 3. 1,3-Dipolar Cycloaddition Reaction of **1b**—**i** with Allyl Alcohol (**2G**)[a,b]

Run No.	Nitrone		Reaction conditions		Recovery of **1a**	Total yields of adducts	Ratio of adducts *cis*-**3** : *trans*-**3′**
	1	Ar	Time	Additive[c]			
29	**1b**	Ph	24 h	None	14%	84%	60 : 40
30	**1b**	Ph	3 h	$MgBr_2 \cdot Et_2O$	0%	62%	22 : 78
31	**1c**	*o*-Tol	21 h	None	0%	50%	63 : 37
32	**1c**	*o*-Tol	6 h	$MgBr_2 \cdot Et_2O$	0%	65%	20 : 80
33	**1d**	2-Naphthyl	24 h	None	0%	50%	55 : 45
34	**1d**	2-Naphthyl	5 h	$MgBr_2 \cdot Et_2O$	0%	50%	25 : 75
35	**1e**	*o*-Anisyl	22 h	None	0%	70%	67 : 33
36	**1e**	*o*-Anisyl	5 h	$MgBr_2 \cdot Et_2O$	0%	70%	28 : 72
37	**1f**	Mesityl	42 h	None	85%	0%	—:—
38	**1f**	Mesityl	2 h	$MgBr_2 \cdot Et_2O$	95%	0%	—:—
39	**1g**	2-Pyridyl	24 h	None	0%	60%	60 : 40
40	**1g**	2-Pyridyl	2 h	$MgBr_2 \cdot Et_2O$	0%	80%	100 : 0
41	**1g**	2-Pyridyl	24 h	$ZnCl_2$	40%	35%	100 : 0
42	**1g**	2-Pyridyl	42 h	$ZnBr_2$	0%	65%	85 : 15
43	**1g**	2-Pyridyl	10 h	$Ti[OC_3H_7\text{-}i]_4$	0%	80%	60 : 40
44	**1h**	6-Methyl-2-pyridyl	21 h	None	0%	70%	50 : 50
45	**1h**	6-Methyl-2-pyridyl	2 h	$MgBr_2 \cdot Et_2O$	0%	50%	60 : 40[d]
46	**1h**	6-Methyl-2-pyridyl	8 h	$MgBr_2 \cdot Et_2O$	0%	60%	100 : 0[d]
47	**1i**	2-Quinolyl	8 h	None	0%	20%	50 : 50
48	**1i**	2-Quinolyl	32 h	$MgBr_2 \cdot Et_2O$	10%	0%	—:—
49	**1j**	2-Furyl	40 h	None	0%	55%	0 : 100
50	**1j**	2-Furyl	2 h	$MgBr_2 \cdot Et_2O$	0%	40%	0 : 100

a) All reactions were carried out in toluene at the refluxing temperature. *b*) Ten-fold excess of allyl alcohol was used. *c*) All reactions using Lewis acid were carried out under nitrogen atmosphere. An equimolar amounts of Lewis acid and nitrone was used in all catalyzed reactions. *d*) *Trans*-isomer (**3′hG**) was found to be suffered succeeding complex reactions and disappeared upon long heationg under the conditions.

ing group)>**2F**—**M** (unactivated alkenes)≫**2Q**, **2R** (electron-rich 1,1-disubstituted alkenes). It was found from this result that nitrone (**1a**) shows the representative reactivity known as Sustmann type II.

Many reactions of allyl alcohol (**2G**) with a variety of *N*-methylnitrones (**1b**—**j**), of which carbon atom was substituted with a variety of aryl groups, were also carried out. The results were summarized in Chart 6 and Table 3. The results similar to that from **1a** were obtained in all cases except for two nitrones (**1f**, **1j**). In the case of *C*-mesitylnitrone (**1f**) the nitrone was recovered unchanged and this result can be explained as a result of the steric effect of the bulky mesityl group, *i.e.*, the coplanarity of mesityl group and nitrone group was broken by the steric hindrance and, consequently, the reactivity of the nitrone (**1f**) was reduced remarkably. In the case of *C*-(2-furyl)nitrone (**1j**) an exclusive formation of *trans*-3-(2-furyl)-5-(hydroxymethyl)-isoxazolidine (**3′jG**) was observed. At present we could not find a reasonable explanation for this result.

1,3-Dipolar Cycloaddition Reaction of *N*-Alkyl-*C*-arylnitrones with Dipolarophiles in the Presence of Lewis Acid The reaction of *C*-aryl-*N*-alkylnitrone (**1a**—**j**) with alkenes (**2A**—**P**) was also carried out in the presence of a variety of Lewis acid under various conditions. In reactions using allyl alcohol (**2G**) or ethyl acrylate (**2A**) as a dipolarophile some remarkable changes were observed and the results were summarized in Table 1 and 3. As a result of employing some different types of Lewis acid as the catalyst it was found that magnesium bromide etherate was the most effective catalyst to cause a dramatic change (see runs No. 2, 5—8, 16, 19). The minimum amount of the catalyst needed to cause the dramatic change was found to be an equimolar amount with nitrone (see runs No. 2—4).

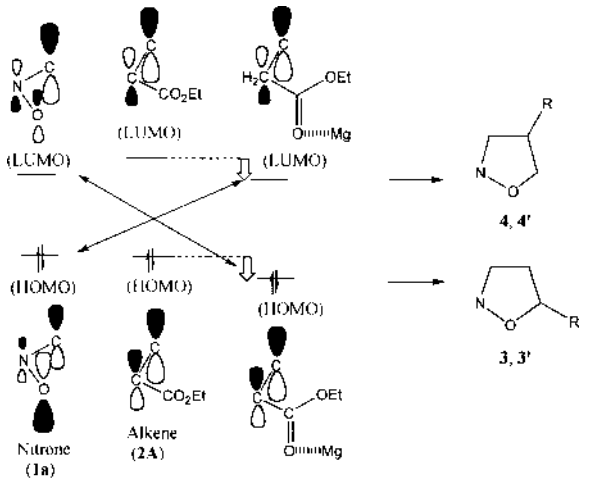


Chart 9. Interaction Scheme of Nitrone (**1**) with Acrylate (**2A**) in the Presence of $MgBr_2$

Comparing the result from the Lewis acid catalyzed reaction of **1a** and ethyl acrylate (**2A**) with that of uncatalyzed reaction, two obvious changes were observed (see runs No. 1, 2). One is a retardation of the reaction by adding Lewis acid and the other is a remarkable change in both the stereoselectivity and the regioselectivity. Isoxazoline-4-carboxylates (**4**, **4′**) were always the main product in the Lewis acid catalyzed reactions. The serious retardation of the reaction was observed in cases using Lewis acid other than magnesium bromide. The retardation of the reaction can be explained as follows. Stable salt, which shows no reactivity toward **2A**, was formed from nitrone (**1a**) and magnesium bromide at once. The stable salt is in equiliblium with **1a** and free liberated Lewis acid but the equiliblium constant is so small that the

cycloadducts were formed gradually. The major formation of isoxazolidine-4-carboxylates in the Lewis acid catalyzed reactions can be explained as a result of nitrone-HOMO/dipolarophile-LUMO interaction (see Chart 9). Though the interaction is small in the absence of Lewis acid, it is significant in the presence of Lewis acid because a chelation of Lewis acid with carbonyl oxygen atom of acrylate occurs and, consequently, an energy level of the LUMO lowered considerably.

Comparing the result from the Lewis acid catalyzed reaction of **1a** and allyl alcohol (**2G**) with that of uncatalyzed reaction, two obvious changes were observed (see runs No. 15, 16). One is an acceleration of the reaction by adding the Lewis acid and the other is a remarkable change in the stereoselectivity. This result may be explained on the basis of the difference of the nitrone's configuration as follows. Though the stable configuration of nitrone (**1a**) has been known to be *Z*-form in the absence of Lewis acid, it may be *E*-form in the presence of Lewis acid. The formation of salts between nitrone (**1a**) and magnesium bromide is apparent by the separation from the benzene solution of sparing soluble precipitate, from which the nitrone (**1a**) was recovered quantitatively by the treatment with aqueous alkaline solution. The salt reacts gradually with allyl alcohol to give nitrone-magnesium-allyl alcohol complex, in which magnesium can be ragard as an atom that binds *E*-nitrone and allyl alcohol in the situation like *E-exo* transition state (see Chart 10).

Some derivatives of allyl alcohol, such as *O*-acylated allyl alcohol (**2H**), *O*-allylated allyl alcohol (**2K**), α-alkylated allyl alcohols (**2I**, **2J**), and allyl methyl sulfid (**2L**), were also examined. Though these dipolarophiles behave in a similar manner as allyl alcohol (**2G**) in the absence of Lewis acid, a quite different behavior was observed in the presence of Lewis acid. These dipolarophiles (**2H**—**L**) can not form the binded *exo* transition state because the steric hindrance around the oxygen atom and, consequently, no cycloadduct was formed. Both substrates were recovered in high yield from the reaction mixtures.

When the phenyl group at the carbon atom of nitrone (**1b**) was substituted for more bulky aromatic groups such as 2-tolyl, 2-naphthyl, and *o*-anisyl, the *E-exo* transition state shown in Chart 10 may become more favorable one than *Z-exo* transition state. But the introduction of these aryl groups has brought about no improvement in the stereoselectivity (compare run 30 with runs 32, 34, and 36 in Table 3). At present we could not find a reasonable explanation for this result.

When the phenyl group at the carbon atom of nitrone (**1b**) was substituted for heteroaromatic groups, those are capable of chelating with Lewis acid effectively, such as 2-pyridyl, 6-methyl-2-pyridyl, and 2-quinolyl groups, the *Z-exo* transition state shown in Chart 11 may become more favorable one than *E-exo* transition state.[37] In fact, the former two nitrones (**1g**, **1h**) gave *cis*-cycloadducts (**3gG**, **3hG**) exclusively. On the other hand, owing to the strongness of the chelation between 2-quinolyl group and Lewis acid, Lewis acid may be interacted only with nitrone (**1i**) to give stable salt and, consequently, any cycloaddition reaction with allyl alcohol may not be expected (see run 48). However, *trans*-cycloadduct (**3′jG**) was obtained from the catalyzed reaction, that took place more rapidly than analogous non-catalyzed reaction. It is obvious that Lewis acid acts in the rete-determining step of the reaction but we could not find a reasonable explanation for this result at present.

Reactions of nitrone **1a** with nine dipolarophiles other than acrylate, allyl alcohol and the some derivatives (**2A**, **2G**, **2H**—**K**) were also carried out in the presence of magnesium bromide. In cases of styrene (**2C**), allyl bromide (**2F**), allyl methyl sulfid (**2L**), 1-octene (**2M**), and methacrylonitrile (**2P**) both starting materials were recovered unchanged and this result may be ascribed mainly to the formation of stable salt between **1a** and magnesium bromide. In cases of electron rich alkenes such as butyl vinyl ether (**2D**) and vinyl acetate (**2E**) any cycloadducts were not obtained because the Lewis acid caused the polymerization of the alkenes in preference to cycloaddition with **1a**. In cases of acrylonitrile (**2B**) and ethyl methacrylate (**2N**), minor changes in the regio- and/or stereoselectivity were observed though the drastic retardation of the reaction rate was also observed.

The Effect of Lewis Acid on 1,3-Dipolar Cycloaddition Reaction of *C*,*N*-Diarylnitrones with Dipolarophiles The reaction of *C*-phenyl-*N*-arylnitrones (**1k**—**n**) with ethyl acrylate (**2A**) or ethyl methacrylate (**2N**) was carried out under several conditions and the results were summarized in Chart 12 and Table 4. In the absence of Lewis acid the formation of all or some of four possible cycloadducts (**3**, **3′**, **4**, **4′**) was

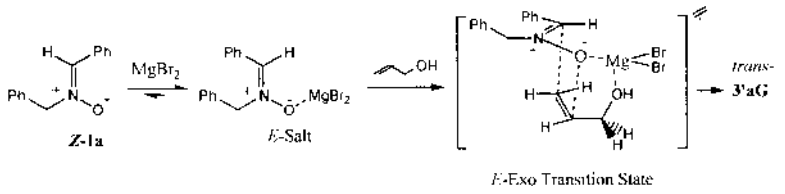


Chart 10. Binding Effect of Two Substrates (**1a** and **2G**) by Magnesium Atom

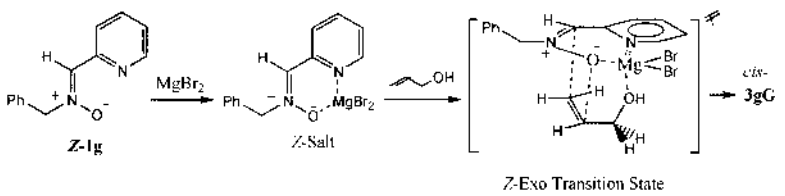


Chart 11. Binding Effect of Two Substrates (**1g** and **2G**) by Magnesium Atom

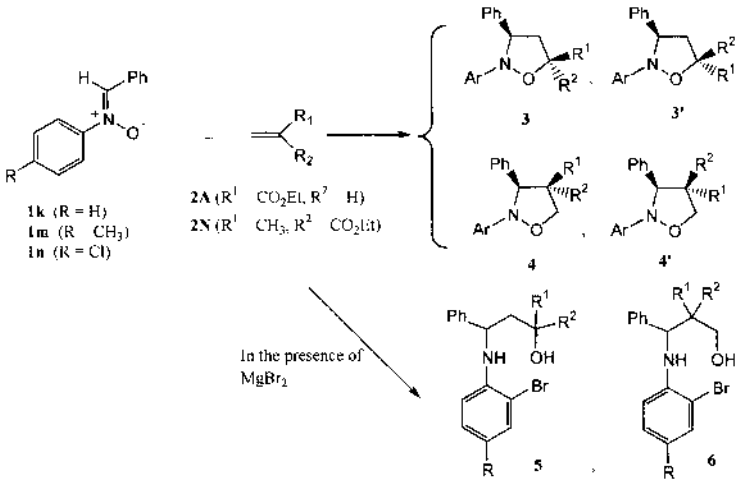


Chart 12. 1,3-Dipolar Cycloaddition Reaction of **1k**, **1m**, and **1n** with **2A** or **2N**

Table 4. 1,3-Dipolar Cycloaddition Reaction of **1k**, **1m**, and **1n** with **2A** or **2N**[a)]

Run No.	Nitrone		Alkene **2**	Reaction conditions[b)]			Total yields of adducts	Ratio of adducts	Ratio of 5- : 4-[c)]
	1	R		Solvent	Time	Additive		**3** : **3′** : **5** : **4** : **4′** : **6**	
51	**1k**	H	**2A**	$CHCl_3$	3 h	—	97%	26 : 44 : 0 : 14 : 16 : 0	70 : 30
52	**1k**	H	**2A**	$CHCl_3$	6 h	$MgBr_2 \cdot Et_2O$	60%	0 : 0 : 28 : 0 : 32 : 40	28 : 72
51	**1m**	CH_3	**2A**	Benzene	7 h	—	96%	25 : 41 : 0 : 13 : 21 : 0	66 : 34
51	**1m**	CH_3	**2A**	Benzene	18 h	$MgBr_2 \cdot Et_2O$	58%	0 : 0 : 21 : 0 : 0 : 79	21 : 79
52	**1n**	Cl	**2A**	$CHCl_3$	3 h	—	97%	22 : 42 : 0 : 12 : 24 : 0	64 : 36
51	**1n**	Cl	**2A**	Benzene	6 h	$MgBr_2 \cdot Et_2O$	63%	0 : 0 : 13 : 0 : 24 : 63	13 : 87
51	**1k**	H	**2N**	$CHCl_3$	3 h	—	100%	85 : 15 : 0 : 0 : 0 : 0	100 : 0
51	**1k**	H	**2N**	Benzene	24 h	$MgBr_2 \cdot Et_2O$	57%	0 : 0 : 88 : 12 : 0 : 0	88 : 12
52	**1m**	CH_3	**2N**	Benzene	3 h	—	97%	87 : 13 : 0 : 0 : 0 : 0	100 : 0
54	**1m**	CH_3	**2N**	Benzene	18 h	$MgBr_2 \cdot Et_2O$	60%	0 : 0 : 100 : 0 : 0 : 0	100 : 0
55	**1n**	Cl	**2N**	Benzene	9 h	—	100%	88 : 12 : 0 : 0 : 0 : 0	100 : 0
56	**1n**	Cl	**2N**	Benzene	20 h	$MgBr_2 \cdot Et_2O$	31%[d)]	0 : 0 : 100 : 0 : 0 : 0	100 : 0

a) Molar ratio of nitrone, alkene, and Lewis acid was 1 : 10 : 1. *b*) All reactions were carried out in the solvent at the refluxing temperature. *c*) Symbol (5-) shows 5-substituted isoxazolidine (**3**, **3′**) and it's derivatives (**5**). Symbol (4-) shows 4-substituted isoxazolidine (**4**, **4′**) and it's derivatives (**6**). *d*) Compound (**8nN**) was also obtained in 10% yield.

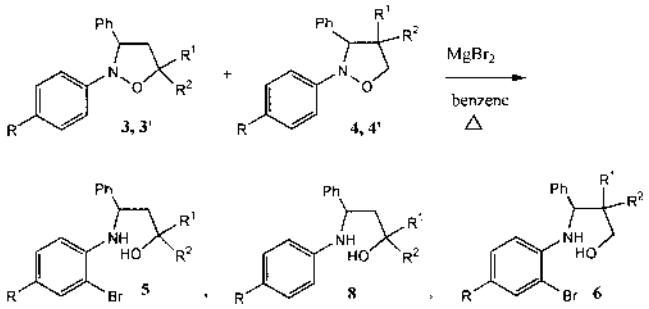


Chart 13. Reaction of 2-Arylisoxazolidines with $MgBr_2$

observed and the total yield of the cycloadducts went up to over 96%. This result resembles to that of the corresponding *N*-alkylnitrone (**1a**). However, the isolated yields of cycloadducts were poor in the similar reactions that carried out in the presence of magnesium bromide because the cycloadducts undergo further ring opening reaction under the reaction conditions. Products from these catalyzed reactions were not isoxazolidines (**3**, **3′**, **4**), but γ-aminoalcohols (**5**, **6**, **8**), a ring opening product of the isoxazolidines and its brominated one, and benzalaniline (**7**). The rate of consumption of *N*-arylnitrone (**1k**—**n**) was slower in the catalyzed reaction than in the non-catalyzed one.

The generation of γ-aminoalcohols (**5**, **6**, **8**) can be explained as a result of a ring-opening reaction of initial cycloadducts, 2,3-diarylisoxazolidines (**3**, **3′**, **4**, **4′**), because the former compounds were obtained effectively by the treatment of the latter compounds with magnesium bromide (see Chart 13 and Table 5).

The regioselectivity of the cycloaddition reaction could be deduced from the comparison of the total amount of isoxazolidine-5-carboxylates and the ring opening products (**3**, **3′**, **5**, **8**) with that of isoxazolidine-4-carboxylates and the ring opening products (**4**, **4′**, **6**) (see Table 4). In the reaction of nitrones (**1k**—**n**) with ethyl acrylate (**2A**), two opposite results in regioselectivity were obtained whether the reaction was carried out in the presence or the absence of Lewis acid. This result may be explained in a similar manner as described in the reaction of *N*-alkylnitrone (**1a**) with **2A**.

Similar reactions using ethyl methacrylate (**2N**) or styrene (**2C**) instead of **2A** were also carried out. Comparing the result from the Lewis acid catalyzed reaction of **1k** and ethyl acrylate (**2N**) with that of uncatalyzed reaction, a retardation of the reaction by adding Lewis acid was observed and γ-(2-

Table 5. Lewis Acid Catalyzed Ring Opening Reaction of Isoxazolidines **3**, **3′**, **4**, and **4′**[a)]

Run No.	Isoxazolidines: Substituents R	R^1	R^2	Ratio of (**3**+**3′**) : (**4**+**4′**)	Reaction time	Total yields of **5**, **8**, **4′**, **6**	Ratio of **5** : **8** : **4′**: **6**	Ratio of 5- : 4-[b)]
63	H	CO_2Et	H	70 : 30	3 h	89%	69 : 0 : 15 : 16	69 : 31
64	H	CH_3	CO_2Et	100 : 0	4 h	83%	100 : 0 : 0 : 0	100 : 0
65	CH_3	CO_2Et	H	66 : 34	6 h	85%	68 : 0 : 0 : 32	68 : 32
66	CH_3	CH_3	CO_2Et	100 : 0	10 h	66%	85 : 15 : 0 : 0	100 : 0
67	Cl	CO_2Et	H	64 : 36	3 h	70%	68 : 0 : 24 : 8	68 : 32
68	Cl	CH_3	CO_2Et	100 : 0	12 h	51%	67 : 33 : 0 : 0	100 : 0

a) A benzene solution of an equimolar mixture of isoxazolidines and the Lewis acid was heated to reflux. *b*) Symbol (5-) shows 5-substituted isoxazolidines (**3**, **3′**) and it's ring-opening derivatives (**5**, **8**). Symbol (4-) shows 4-substituted isoxazolidine (**4**, **4′**) and it's ring-opening derivative (**6**).

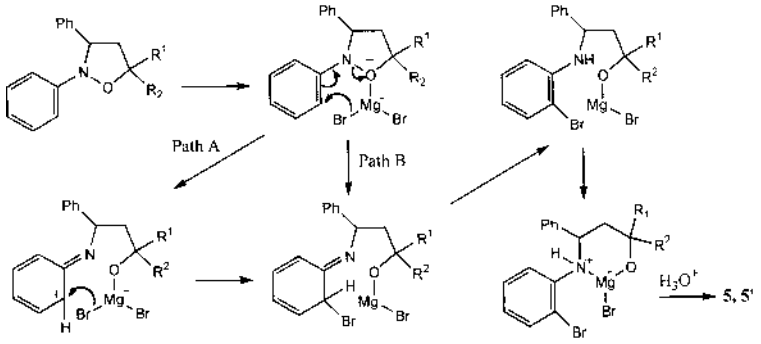


Chart 14. The Mechanism of the Ring-Opening Reaction by $MgBr_2$

bromoaryl)aminoalcohols (**5kN**, **5′kN**) were the only isolable compounds from the reaction mixtures. A remarkable change in both the stereoselectivity and the regioselectivity was not observed. Both cycloadducts and γ-aminoalcohols were not obtained from reaction of **1k**—**n** with styrene (**2C**) in the presence of Lewis acid.

Reaction Mechanism of the Ring Opening Reaction of Isoxazolidines Following reagents have been known so far to be effective for the reductive cleavage of N–O bond of isoxazolidine; $LiAlH_4$,[10,11,17)] Zn/AcOH,[14—16,21)] Raney nickel,[9)] H_2-Pd/carbon,[8,13,18,21)] H_2-$PdCl_2$,[12)] and H_2-$Pd(OH)_2$.[12,20)] Though our method described above contains a problem that aryl group at the nitrogen atom of the isoxazolidines suffers bromination, it may be simplest method for the cleavage of N–O bond of isoxazolidines.

The mechanism of the formation of γ-(2-bromoaryl)-aminoalcohols (**5**) from 2-arylisoxazolidines (**3**) may be explained as a result of a series of reactions *via* path A shown in Chart 14; *i.e.*, (i) chelation of magnesium bromide to the oxygen atom of 2,3-diphenylisoxazolidiens (**3**), (ii) heterolysis of the N–O bond to give carbocation, (iii) a nucleophilic addition of bromo anion to *ortho*-position of the 2-phenyl group in the isoxazolidine ring, (iv) a prototropy giving magnesium salt of γ-(2-bromoaryl)aminoalcohol, and (v) hydrolysis of the salt to free γ-(2-bromoaryl)aminoalcohol (**5**) in working up the reaction mixture with water. Though another more directive pathway (path B in the Chart 14) that consists of concerted bromination reaction may also be supposed, this could be ruled out by the following evidence. 3-(2-Bromophenyl)amino-1,3-diphenyl-1-propanol (**5kC**), *N*-(4-bromophenyl)-3-amino-1,3-diphenyl-1-propanol (**7kC**), and 3-(phenylamino)-1,3-di-phenyl-1-propanol (**8kC**) were obtained in 13, 28, and 10% yields, respectively, from the treatment of 2,3,5-triphenylisoxazolidines (**3kC**), prepared by the reaction of **1k** and styrene (**2C**) in the absence of Lewis acid, with magnesium bromide. The formation of the latter compound (**7kC**) can be explained only by stepwise bromination shown in path A.

Though similar reaction mechanism was reported on the reaction of *N*-arylisoxazolidine with hydrochloric acid,[53,54)] a quite different mechanism may be proposed for the ring-opening reaction from the evidence that the generation of a small amount of non-brominated γ-aminoalcohole (**8kC**, **8mN**) was observed.

It has been known that several reductants are effective for the reductive cleavage of the N–O bond of isoxazolidines. We described in this paper that Lewis acid is effective to give drastic changes in the stereoselectity and the regioselectivity in nitrone cycloaddition and also effective to give reductive cleavage of the N–O bond of the 2-phenylisoxazolidines reagent though the benzene ring of the 2-phenylisoxazolidines underwent halogenation reaction.

Experimental

^{1}H-NMR spectra (300 MHz) and ^{13}C-NMR spectra (75 MHz) were measured and expressed in ppm (δ) using residual $CHCl_3$ (δ: 7.26) and $CDCl_3$ (δ: 77.0), respectively, as the internal standards. Infrared spectra (IR) were recorded on a Nicolet Model 205 spectrophotometer. High resolution mass spectra (HRMS) (EI, unless otherwise stated) were taken for most of the key liquid products together with, or in place of, elemental analyses. Melting points were obtained on a Yanagimoto micro melting point determination apparatus and are uncorrected. Flush colum chromatography was performed using silica gel (Merck silica gel).

Materials *C*-Phenyl-*N*-benzylnitrone (**1a**) was prepared according to

the method described in the literature.[55,56]

Preparation of *C*-Aryl-*N*-methylnitrones (1b—f).[56—59] Typical Procedure: Preparation of *N*-Methyl-*C*-phenylnitrone (1b) To a chloroform solution (30 ml) of *N*-methylhydroxyl-amine hydrochloride (420 mg, 5.0 mmol) and benzaldehyde (530 mg, 5.0 mmol) was added triethylamine (750 ml, 7.5 mmol) and the mixture was stirred for 22 h at the room temperature. After an evaporation of the solvent by rotary evaporator, water was added to the white crystalline residue and extracted with benzene several times. The benzene solution was dried with anhydrous magnesium sulfate. Evaporation of the solvent by rotary evaporator gave colorless crystals, which was mixed well with cyclohexane and filtered to give *N*-methyl-*C*-phenylnitrone (**1b**) as colorless crystals in 78% yield (530 mg); mp. 73—75 °C (lit.[56] mp. 84 °C); ^{1}H-NMR: 3.89 (s, 3H), 7.36 (s, 1H), 7.40—7.43 (m, 3H), 8.19—8.22 (m, 2H).

***N*-Methyl-*C*-(2-tolyl)nitrone (1c)** In the same manner as described in the synthesis of **1b**, nitrone (**1c**) was obtained as a colorless oil in 98% yield; ^{1}H-NMR ($CDCl_3$) δ: 2.37 (s, 3H), 3.91 (s, 3H), 7.17—7.22 (m, 1H), 7.26—7.31 (m, 2H), 7.52 (s, 1H), 9.09—9.12 (m, 1H). *Anal.* Calcd for $C_9H_{11}NO$: C, 72.45; H, 7.43; N, 9.39. Found: C, 72.40; H, 7.28; N, 9.55.

***N*-Methyl-*C*-(2-naphthyl)nitrone (1d)** In the same manner as described in the synthesis of **1b**, nitrone (**1d**) was obtained as colorless crystals in 98% yield; mp. 107—109 °C (lit.[57] mp. 106—108 °C); ^{1}H-NMR ($CDCl_3$) δ: 3.49 (s, 3H), 7.51 (dd, 2H, J=2.4, 9.6 Hz), 7.51 (s, 1H), 7.80—7.83 (m, 1H), 7.84—7.90 (m, 2H), 7.91—7.95 (m, 1H), 9.20 (s, 1H).

***C*-(*o*-Anisyl)-*N*-methylnitrone (1e)** In the same manner as described in the synthesis of **1b**, nitrone (**1e**) was obtained as colorless crystals in 98% yield; mp. 65—68 °C; ^{1}H-NMR ($CDCl_3$) δ: 3.85 (s, 3H), 3.88 (s, 3H), 6.87 (d, 1H, J=8.4 Hz), 7.02 (t, 1H, J=7.5 Hz), 7.36 (t, 1H, J=7.8 Hz), 7.82 (s, 1H), 9.24 (d, 1H, J=7.8 Hz). *Anal.* Calcd for $C_9H_{11}NO_2$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.38; H, 6.66; N, 8.55.

***C*-Mesityl-*N*-methylnitrone (1f)** In the same manner as described in the synthesis of **1b**, nitrone (**1f**) was obtained as colorless crystals in 98% yield; mp. 65—68 °C; ^{1}H-NMR ($CDCl_3$) δ: 2.26 (s, 9H), 3.90 (s, 3H), 6.88 (s, 2H), 7.54 (s, 1H). *Anal.* Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.40; H, 8.77; N, 8.10.

***N*-Methyl-*C*-(2-pyridyl)nitrone (1g)** In the same manner as described in the synthesis of **1b**, nitrone (**1g**) was obtained as colorless crystals in 98% yield; mp. 45—48 °C; ^{1}H-NMR ($CDCl_3$) δ: 3.92 (s, 3H), 7.26—7.30 (m, 1H), 7.69 (s, 1H), 7.76 (t, 1H, J=7.8 Hz), 8.62 (d, 1H, J=4.8 Hz), 9.10 (d, 1H, J=8.1 Hz). *Anal.* Calcd for $C_7H_8N_2O$: C, 61.75; H, 5.92; N, 20.58. Found: C, 61.77; H, 5.90; N, 20.71.

***N*-Methyl-*C*-(6-methyl-2-pyridyl)nitrone (1h)** In the same manner as described in the synthesis of **1b**, nitrone (**1h**) was obtained as colorless crystals in 98% yield; mp. 44—46 °C; ^{1}H-NMR ($CDCl_3$) δ: 2.53 (s, 3H), 3.89 (s, 3H), 7.14 (d, 1H, J=7.8 Hz), 7.65 (s, 1H), 7.66 (t, 1H, J=7.8 Hz), 8.91 (d, 1H, J=7.8 Hz). *Anal.* Calcd for $C_8H_{10}N_2O$: C, 63.98; H, 6.71; N, 18.65. Found: C, 63.88; H, 6.59; N, 18.51.

***N*-Methyl-*C*-(2-quinolyl)nitrone (1i)** In the same manner as described in the synthesis of **1b**, nitrone (**1i**) was obtained as colorless crystals in 98% yield; mp. 98—100 °C; ^{1}H-NMR ($CDCl_3$) δ: 3.97 (s, 3H), 7.55 (t, 1H, J=7.5 Hz), 7.71 (t, 1H, J=7.5 Hz), 7.81 (d, 1H, J=8.4 Hz), 7.86 (s, 1H), 8.02 (d, 1H, J=8.4 Hz), 8.23 (d, 1H, J=8.7 Hz), 9.11 (d, 1H, J=8.7 Hz). *Anal.* Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05. Found: C, 71.10; H, 5.69; N, 14.90.

***C*-(2-Furyl)-*N*-methylnitrone (1j)** In the same manner as described in the synthesis of **1b**, nitrone (**1j**) was obtained as colorless crystals in 98% yield; mp. 80—82 °C (lit.[58,59] mp. 91—92 °C); ^{1}H-NMR ($CDCl_3$) δ: 3.83 (s, 3H), 6.55 (d, 1H, J=3.6 Hz), 7.47 (s, 1H), 7.53 (s, 1H), 7.75 (d, 1H, J=3.6 Hz).

Preparation of *C*,*N*-Diarylnitrones (1k—n).[56,60,61] Typical Procedure: Preparation of *C*,*N*-diphenylnitrone (1k) To a dispersion of zinc dust (31 g, 0.48 mol) in 50% aqueous ethanol (400 ml) was added nitrobenzene (25 g, 0.20 mol) with stirring. The reaction was initiated by the dropwise addition of a saturated aqueous solution of ammonium chloride (13 g, 0.24 mol). The temperature of the mixture rose to reflux by the addition of ammonium chloride (about 70 °C). When the temperature of the reaction mixture dropped to 50 °C, the basic zinc salts were filtered off by a glass funnel using a celite bed. Sodium chloride was added to the warm filtrate until the saturated solution was obtained. After cooling the mixture to room temperature, the mixture was further cooled in a freezer over a knight (at about −20 °C). Colorless crystals of phenylhydroxylamine was precipitated from the solution and obtained in 66% yield (13.0 g) by filtration: mp. 78—80 °C.

To an ethanol solution of phenylhydroxylamine (6.5 g, 66 mmol) was added benzaldehyde (7.0 g, 66 mmol) and the mixture was heated to reflux for 1 h. Yellowish crude crystals were obtained by evaporation of the solvent from the reaction mixture by a rotary evaporator, from which nitrone (**1k**) was obtained in 70% yield (9.1 g) as colorless crystals by filtration with cyclohexane; mp. 106—111 °C (lit.[56] mp. 112—114 °C); ^{1}H-NMR ($CDCl_3$) δ: 7.45—7.50 (m, 6H), 7.76—7.79 (m, 2H), 7.92 (s, 1H), 8.38—8.41 (m, 2H).

***C*-Phenyl-*N*-(*p*-tolyl)nitrone (1m)** In the same manner as described in the synthesis of **1k**, nitrone (**1m**) was obtained from *p*-nitrotoluene as colorless crystals in 45% total yield; mp. 122—125 °C (lit.[60,61] mp. 127—128 °C); ^{1}H-NMR ($CDCl_3$) δ: 2.40 (s, 3H), 7.25 (d, 2H, J=8.7 Hz), 7.43—7.48 (m, 3H), 7.65 (d, 2H, J=8.7 Hz), 7.89 (s, 1H), 8.36—8.40 (m, 2H).

***C*-Phenyl-*N*-(4-chlorophenyl)nitrone (1n)** In the same manner as described in the synthesis of **1k**, nitrone (**1n**) was obtained from *p*-chloronitrobenzene as colorless crystals in 40% total yield; mp. 171—174 °C (lit.[60] mp. 176—177 °C); ^{1}H-NMR ($CDCl_3$) δ: 7.44 (d, 2H, J=9.0 Hz), 7.45—7.49 (m, 3H), 7.73 (d, 2H, J=9.0 Hz), 7.89 (s, 1H), 8.36—8.39 (m, 2H).

Reaction of Nitrones with Dipolarophiles in the Absence of Lewis Acid. Typical Procedure: Reaction of 1a with Ethyl Acrylate (2A) A benzene solution (25 ml) of **1a** (1.06 g, 5.0 mmol) and ethyl acrylate (5.0 g, 50 mmol) was heated to reflux for 7 h. After an evapolation of the solvent and an excess amount of ethyl acrylate by rotary evapolator, colorless oily residue was passed through the column chromatography packed with silica gel to give *cis*- and *trans*-2-benzyl-5-(ethoxycarbonyl)-3-phenylisoxazolidines (**3aA**, **3′aA**) and *cis*- and *trans*-2-benzyl-4-(ethoxycarbonyl)-3-phenylisoxazolidines (**4aA**, **4′aA**) in 97% total yields (1.51 g). The ratio of the four isomers (**3aA**, **3′aA**, **4aA**, **4′aA**) was found to be 10 : 72 : 4 : 14, respectively, by the analysis of the ^{1}H-NMR spectra. Some of the four isomers were isolated by the chromatography though the yields were poor. Chloroform and the mixed solvent with ethanol were used for the eluent.

(3*R**,5*S**)-2-Benzyl-5-(ethoxycarbonyl)-3-phenylisoxazolidine (**3aA**): ^{1}H-NMR ($CDCl_3$) δ: 1.31 (t, 3H, J=7.2 Hz), 2.65 (ddd, 1H, J=4.8, 8.7, 12.6 Hz), 2.99 (ddd, 1H, J=7.8, 9.3, 12.6 Hz), 3.78 (d, 1H, J=13.8 Hz), 4.01 (d, 1H, J=13.8 Hz), 4.25 (q, 2H, J=7.2 Hz), 4.25 (dd, 1H, J=7.8, 8.7 Hz), 4.63 (dd, 1H, J=4.8, 9.3 Hz), 7.22—7.50 (m, 10H). HR-MS *m*/*z*; 311.1520 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

(3*R**,5*R**)-2-Benzyl-5-(ethoxycarbonyl)-3-phenylisoxazolidine (**3′aA**): ^{1}H-NMR ($CDCl_3$) δ: 1.31 (t, 3H, J=7.2 Hz), 2.71 (dt, 1H, J=8.7, 12.3 Hz), 2.78 (ddd, 1H, J=4.8, 7.2, 12.3 Hz), 3.96 (d, 1H, J=14.4 Hz), 4.03 (d, 1H, J=14.4 Hz), 4.05 (dd, 1H, J=7.2, 8.7 Hz), 4.24 (q, 2H, J=7.2 Hz), 4.66 (dd, 1H, J=4.8, 8.7 Hz), 7.22—7.50 (m, 10H). HR-MS *m*/*z*; 311.1524 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

(3*R**,4*R**)-2-Benzyl-4-(ethoxycarbonyl)-3-phenylisoxazolidine (**4aA**): ^{1}H-NMR ($CDCl_3$) δ: 0.78 (t, 3H, J=7.5 Hz), 3.57 (dd, 1H, J=6.9, 10.5 Hz), 3.70 (q, 2H, J=7.5 Hz), 3.74 (d, 1H, J=14.1 Hz), 4.01 (d, 1H, J=14.1 Hz), 4.12—4.26 (m, 3H), 7.22—7.50 (m, 10H). HR-MS *m*/*z*; 311.1515 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

(3*R**,4*S**)-2-Benzyl-4-(ethoxycarbonyl)-3-phenylisoxazolidine (**4′aA**): ^{1}H-NMR ($CDCl_3$) δ: 1.24 (t, 3H, J=7.2 Hz), 3.44 (dt, 1H, J=6.3, 7.8 Hz), 3.80 (d, 1H, J=13.8 Hz), 3.96 (d, 1H, J=13.8 Hz), 4.10 (d, 1H, J=7.8 Hz), 4.17 (dd, 1H, J=7.5, 14.1 Hz), 4.18 (dd, 1H, J=7.5, 14.1 Hz), 4.25 (q, 2H, J=7.2 Hz), 7.22—7.50 (m, 10H). HR-MS *m*/*z*; 311.1517 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

The following compounds were prepared in yields shown in Table 1 according to Typical Procedure.

(3*R**,5*S**)-2-Benzyl-5-cyano-3-phenylisoxazolidine (**3aB**): ^{1}H-NMR ($CDCl_3$) δ: 2.62 (ddd, 1H, J=3.6, 8.4, 12.9 Hz), 3.08 (dt, 1H, J=9.0, 12.9 Hz), 3.77 (dd, 1H, J=8.1, 9.0 Hz), 3.77 (d, 1H, J=15.3 Hz), 4.10 (d, 1H, J=15.3 Hz), 4.82 (dd, 1H, J=3.6, 9.0 Hz), 7.26—7.53 (m, 10H). HR-MS *m*/*z*; 264.1260 (Calcd for $C_{17}H_{16}N_2O$: 264.1263).

(3*R**,5*R**)-2-Benzyl-5-cyano-3-phenylisoxazolidine (**3′aB**): ^{1}H-NMR ($CDCl_3$) δ: 2.78 (dt, 1H, J=8.7, 12.9 Hz), 2.99 (ddd, 1H, J=4.2, 6.9, 12.9 Hz), 3.98 (d, 1H, J=13.8 Hz), 4.04 (d, 1H, J=13.8 Hz), 4.22 (dd, 1H, J=6.9, 8.7 Hz), 4.82 (dd, 1H, J=4.2, 8.7 Hz), 7.30—7.53 (m, 10H). HR-MS *m*/*z*; 264.1265 (Calcd for $C_{17}H_{16}N_2O$: 264.1263).

(3*R**,4*S**)-2-Benzyl-4-cyano-3-phenylisoxazolidine (**4aB**): ^{1}H-NMR ($CDCl_3$) δ: 3.68 (d, 1H, J=14.4 Hz), 3.73 (dt, 1H, J=7.2, 8.7 Hz), 3.95 (d, 1H, J=8.7 Hz), 4.05 (d, 1H, J=14.4 Hz), 4.17 (dd, 1H, J=7.2, 8.7 Hz), 4.36 (t, 1H, J=8.7 Hz), 7.30—7.53 (m, 10H). HR-MS *m*/*z*; 264.1270 (Calcd for $C_{17}H_{16}N_2O$: 264.1263).

(3*R**,4*R**)-2-Benzyl-4-cyano-3-phenylisoxazolidine (**4′aB**): ^{1}H-NMR ($CDCl_3$) δ: 3.39 (dt, 1H, J=4.8, 8.1 Hz), 3.79 (d, 1H, J=14.1 Hz), 3.98 (d, 1H, J=8.1 Hz), 4.01 (d, 1H, J=14.1 Hz), 4.20—4.31 (m, 2H), 7.26—7.50 (m, 10H). HR-MS *m*/*z*; 264.1266 (Calcd for $C_{17}H_{16}N_2O$: 264.1263).

(3*R**,5*S**)-2-Benzyl-3,5-diphenylisoxazolidine (**3aC**): ^{1}H-NMR ($CDCl_3$)

δ: 2.43 (ddd, 1H, J=7.5, 9.3, 12.3 Hz), 3.15 (dt, 1H, J=7.2, 12.3 Hz), 3.92 (d, 1H, J=14.1 Hz), 4.09 (dd, 1H, J=7.2, 9.3 Hz), 4.11 (d, 1H, J=14.1 Hz), 5.27 (t, 1H, J=7.5 Hz), 7.22—7.54 (m, 15H). HR-MS *m/z*; 315.1629 (Calcd for $C_{22}H_{21}NO$: 315.1623).

(3*R**,5*R**)-2-Benzyl-3,5-diphenylisoxazolidine (**3′aC**): ^{1}H-NMR ($CDCl_3$) δ: 2.60 (ddd, 1H, J=6.3, 8.4, 12.6 Hz), 2.75 (dt, 1H, J=8.4, 12.6 Hz), 3.97—4.15 (m, 1H), 5.23—5.30 (m, 1H), 7.22—7.54 (m, 15H). HR-MS *m/z*; 315.1626 (Calcd for $C_{22}H_{21}NO$: 315.1623).

(3*R**,5*S**)-2-Benzyl-5-butoxy-3-phenylisoxazolidine (**3aD**): ^{1}H-NMR ($CDCl_3$) δ: 0.91 (t, 3H, J=7.2 Hz), 1.33—1.45 (m, 2H), 1.53—1.63 (m, 2H), 2.31 (ddd, 1H, J=3.0, 9.3, 12.9 Hz), 2.89 (ddd, 1H, J=6.3, 8.1, 12.9 Hz), 3.40 (dt, 1H, J=6.6, 9.6 Hz), 3.68 (d, 1H, J=14.7 Hz), 3.70 (dd, 1H, J=8.1, 9.3 Hz), 3.71 (dt, 1H, J=6.6, 9.6 Hz), 4.03 (d, 1H, J=14.7 Hz), 5.16 (dd, 1H, J=3.0, 6.3 Hz), 7.21—7.56 (m, 10H). HR-MS *m/z*; 311.1880 (Calcd for $C_{20}H_{25}NO_2$: 311.1885).

(3*R**,5*R**)-2-Benzyl-5-butoxy-3-phenylisoxazolidine (**3′aD**): ^{1}H-NMR ($CDCl_3$) δ: 0.97 (t, 3H, J=7.2 Hz), 1.40—1.48 (m, 2H), 1.58—1.67 (m, 2H), 2.46 (ddd, 1H, J=4.8, 10.2, 12.6 Hz), 2.64 (ddd, 1H, J=0.9, 6.6, 12.6 Hz), 3.43 (dt, 1H, J=6.9, 9.3 Hz), 3.82 (dt, 1H, J=6.9, 9.3 Hz), 4.09 (s, 2H), 4.32 (dd, 1H, J= 6.6, 10.2 Hz), 5.19 (d, 1H, J=4.8 Hz), 7.21—7.45 (m, 10H). HR-MS *m/z*; 311.1884 (Calcd for $C_{20}H_{25}NO_2$: 311.1885).

(3*R**,5*S**)-5-Acetoxy-2-benzyl-3-phenylisoxazolidine (**3aE**): ^{1}H-NMR ($CDCl_3$) δ: 2.11 (s, 3H), 2.41 (ddd, 1H, J=3.0, 9.3, 13.8 Hz), 3.04 (ddd, 1H, J=6.6, 8.1, 13.8 Hz), 3.80 (d, 1H, J=14.7 Hz), 3.80 (dd, 1H, J=8.1, 9.3 Hz), 4.08 (d, 1H, J=14.7 Hz), 6.36 (dd, 1H, J=3.0, 6.6 Hz), 7.22—7.57 (m, 10H). HR-MS *m/z*; 297.1364 (Calcd for $C_{18}H_{19}NO_3$: 297.1365).

(3*R**,5*R**)-5-Acetoxy-2-benzyl-3-phenylisoxazolidine (**3′aE**): ^{1}H-NMR ($CDCl_3$) δ: 2.08 (s, 3H), 2.63 (dd, 2H, J=3.0, 8.4 Hz), 4.02 (d, 1H, J=13.8 Hz), 4.15 (d, 1H, J=13.8 Hz), 4.25 (t, 1H, J=8.4 Hz), 6.39 (t, 1H, J=3.0 Hz), 7.24—7.51 (m, 10H). HR-MS *m/z*; 297.1372 (Calcd for $C_{18}H_{19}NO_3$: 297.1365).

(3*R**,5*S**)-2-Benzyl-5-(bromomethyl)-3-phenylisoxazolidine (**3aF**): mp. 74—76 °C; ^{1}H-NMR ($CDCl_3$) δ: 2.23 (ddd, 1H, J=5.4, 9.0, 12.6 Hz), 2.92 (dt, 1H, J=7.5, 12.6 Hz), 3.46 (dd, 1H, J=8.1, 9.6 Hz), 3.66 (dd, 1H, J=5.7, 9.6 Hz), 3.75 (d, 1H, J=14.7 Hz), 3.86 (dd, 1H, J=7.5, 9.0 Hz), 4.00 (d, 1H, J=14.7 Hz), 4.39—4.48 (m, 1H), 7.23—7.44 (m, 10H).

(3*R**,5*R**)-2-Benzyl-5-(bromomethyl)-3-phenylisoxazolidine (**3′aF**): Colorless oil; ^{1}H-NMR ($CDCl_3$) δ: 2.51 (dt, 1H, J=8.7, 12.6 Hz), 2.57 (ddd, 1H, J=5.1, 7.5, 12.6 Hz), 3.42 (dd, 1H, J=6.6, 10.2 Hz), 3.50 (dd, 1H, J=7.2, 10.2 Hz), 3.76 (d, 1H, J=14.4 Hz), 3.88 (dd, 1H, J=7.5, 8.7 Hz), 3.98 (d, 1H, J=14.4 Hz), 4.42—4.50 (m, 1H), 7.24—7.47 (m, 10H).

(3*R**,5*S**)-2-Benzyl-5-(hydroxymethyl)-3-phenylisoxazolidine (**3aG**): ^{1}H-NMR ($CDCl_3$) δ: 1.63 (br s, 1H), 2.25 (ddd, 1H, J=5.4, 9.3, 12.3 Hz), 2.79 (dt, 1H, J=8.1, 12.3 Hz), 3.66 (d, 1H, J=14.4 Hz), 3.74—3.83 (m, 3H), 3.99 (d, 1H, J=14.4 Hz), 4.30—4.39 (m, 1H), 7.24—7.48 (m, 10H). HR-MS *m/z*; 269.1621 (Calcd for $C_{17}H_{19}NO_2$: 269.1416).

(3*R**,5*R**)-2-Benzyl-5-(hydroxymethyl)-3-phenylisoxazolidine (**3′aG**): ^{1}H-NMR ($CDCl_3$) δ: 1.83 (brs, 1H), 2.37 (dt, 1H, J=8.7, 12.3 Hz), 2.55 (ddd, 1H, J=5.4, 7.8, 12.3 Hz), 3.56—3.82 (m, 3H), 3.70 (d, 1H, J=14.4 Hz), 3.98 (d, 1H, J=14.4 Hz), 4.03—4.39 (m, 1H), 7.24—7.48 (m, 10H). HR-MS *m/z*; 269.1622 (Calcd for $C_{17}H_{19}NO_2$: 269.1416).

(3*R**,5*S**)-5-(Acetoxymethyl)-2-benzyl-3-phenylisoxazolidine (**3aH**): ^{1}H-NMR ($CDCl_3$) δ: 2.00—2.10 (m, 1H), 2.02 (s, 3H), 2.83 (dt, 1H, J=8.1, 12.9 Hz), 3.77 (d, 1H, J=14.7 Hz), 3.83 (t, 1H, J=8.1 Hz), 4.00 (d, 1H, J=14.7 Hz), 4.11 (d, 1H, J=11.4 Hz), 4.53 (d, 1H, J=11.1 Hz), 4.38—4.47 (m, 1H), 7.17—7.45 (m, 10H). HR-MS *m/z*; 311.1518 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

(3*R**,5*R**)-5-(Acetoxymethyl)-2-benzyl-3-phenylisoxazolidine (**3′aH**): ^{1}H-NMR ($CDCl_3$) δ: 2.08 (s, 3H), 2.41 (t, 2H, J=8.1 Hz), 3.74 (d, 1H, J=14.4 Hz), 3.83 (t, 1H, J=8.1 Hz), 4.00 (d, 1H, J=14.7 Hz), 4.12 (d, 1H, J=11.1 Hz), 4.35 (d, 1H, J=11.1 Hz), 4.38—4.47 (m, 1H), 7.17—7.45 (m, 10H). HR-MS *m/z*; 311.1514 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

(3*R**,5*S**)-2-Benzyl-5-(1-hydroxybutyl)-3-phenylisoxazolidine (**3aI**): ^{1}H-NMR ($CDCl_3$) δ: 0.92 (t, 3H, J=7.2 Hz), 1.31—1.55 (m, 4H), 2.23 (ddd, 1H, J=5.4, 9.3, 12.6 Hz), 2.79 (dt, 1H, J=8.1, 12.6 Hz), 3.05 (d, 1H, J=4.5 Hz), 3.65 (d, 1H, J=14.4 Hz), 3.65—3.72 (m, 1H), 3.79 (dt, 1H, J=8.1, 9.3 Hz), 3.97 (d, 1H, J=14.4 Hz), 3.97—4.03 (m, 1H), 7.21—7.50 (m, 10H). HR-MS *m/z*; 311.1880 (Calcd for $C_{20}H_{25}NO_2$: 311.1885).

(3*R**,5*R**)-2-Benzyl-5-(1-hydroxybutyl)-3-phenylisoxazolidine (**3′aI-1**): Diastereomer A: ^{1}H-NMR ($CDCl_3$) δ: 0.92 (t, 3H, J=7.2 Hz), 1.34—1.56 (m, 4H), 1.90—2.05 (br s, 1H), 2.36 (dt, 1H, J=8.1, 12.3 Hz), 2.45 (m, 1H), 3.48—3.54 (m, 1H), 3.73 (d, 1H, J=14.1 Hz), 3.76—3.85 (m, 1H), 3.98 (d, 1H, J=14.1 Hz), 4.13 (dt, 1H, J=5.4, 8.1 Hz), 7.21—7.50 (m, 10H). HR-MS *m/z*; 311.1888 (Calcd for $C_{20}H_{25}NO_2$: 311.1885).

(3*R**,5*R**)-2-Benzyl-5-(1-hydroxybutyl)-3-phenylisoxazolidine (**3′aI-2**): Diastereomer B: ^{1}H-NMR ($CDCl_3$) δ: 0.92 (t, 3H, J=7.2 Hz), 1.20—1.60 (m, 4H), 2.50—2.68 (m, 2H), 3.56 (s, 1H), 3.63 (d, 1H, J=14.4 Hz), 3.79 (dd, 1H, J=8.1, 9.0 Hz), 3.95—4.04 (m, 2H), 3.99 (d, 1H, J=14.4 Hz), 4.16 (ddd, 1H, J=2.4, 6.0, 8.4 Hz), 7.21—7.50 (m, 10H). HR-MS *m/z*; 311.1889 (Calcd for $C_{20}H_{25}NO_2$: 311.1885).

(3*R**,5*S**)-2-Benzyl-5-(1-methyl-1-hydroxyethyl)-3-phenylisoxazolidine (**3aJ**): ^{1}H-NMR ($CDCl_3$) δ: 1.13 (s, 3H), 1.28 (s, 3H), 1.82—1.95 (br s, 1H), 2.23 (dt, 1H, J=8.4, 11.4 Hz), 2.56—2.65 (m, 1H), 3.73 (d, 1H, J=14.1 Hz), 3.70—3.80 (m, 1H), 4.03 (d, 1H, J=14.1 Hz), 4.03 (dd, 1H, J=8.4, 11.4 Hz), 7.21—7.50 (m, 10H). HR-MS *m/z*; 297.1731 (Calcd for $C_{19}H_{23}NO_2$: 297.1729).

(3*R**,5*R**)-2-Benzyl-5-(1-methyl-1-hydroxyethyl)-3-phenylisoxazolidine (**3′aJ**): ^{1}H-NMR ($CDCl_3$) δ: 1.10 (s, 3H), 1.19 (s, 3H), 2.56 (ddd, 1H, J=6.0, 9.9, 12.3 Hz), 2.67 (dt, 1H, J=7.8, 12.3 Hz), 3.37 (s, 1H), 3.62 (d, 1H, J=14.1 Hz), 3.79 (dd, 1H, J=7.8, 9.9 Hz), 3.95 (d, 1H, J=14.1 Hz), 3.93—3.98 (m, 1H), 7.24—7.48 (m, 10H). HR-MS *m/z*; 297.1733 (Calcd for $C_{19}H_{23}NO_2$: 297.1729).

(3*R**,5*S**)-5-(Allyloxymethyl)-2-benzyl-3-phenylisoxazolidine (**3aK**): ^{1}H-NMR ($CDCl_3$) δ: 2.04 (ddd, 1H, J=6.3, 9.0, 12.6 Hz), 2.78 (dt, 1H, J=7.8, 12.6 Hz), 3.47 (dd, 1H, J=4.5, 10.2 Hz), 3.71 (t, 1H, J=6.9 Hz), 3.77 (d, 1H, J=14.7 Hz), 3.92—4.07 (m, 3H), 3.98 (d, 1H, J=14.7 Hz), 4.35—4.44 (m, 1H), 5.11—5.33 (m, 2H), 5.79—5.98 (m, 1H), 7.20—7.50 (m, 10H). HR-MS *m/z*; 309.1725 (Calcd for $C_{20}H_{23}NO_2$: 309.1729).

(3*R**,5*R**)-5-(Allyloxymethyl)-2-benzyl-3-phenylisoxazolidine (**3′aK**): ^{1}H-NMR ($CDCl_3$) δ: 2.38 (dt, 1H, J=7.8, 12.3 Hz), 2.51 (ddd, 1H, J=5.4, 7.8, 12.3 Hz), 3.54 (d, 1H, J=4.5 Hz), 3.77 (d, 1H, J=14.7 Hz), 3.83 (d, 1H, J=8.1 Hz), 3.92—4.07 (m, 3H), 3.98 (d, 1H, J=14.7 Hz), 4.35—4.44 (m, 1H), 5.11—5.33 (m, 2H), 5.79—5.98 (m, 1H), 7.20—7.50 (m, 10H). HR-MS *m/z*; 309.1729 (Calcd for $C_{20}H_{23}NO_2$: 309.1729).

(3*R**,5*S**)-2-Benzyl-5-(methylthio)-3-phenylisoxazolidine (**3aL**): ^{1}H-NMR ($CDCl_3$) δ: 2.03 (s, 3H), 2.16 (ddd, 1H, J=6.0, 9.0, 12.6 Hz), 2.66 (dd, 1H, J=6.6, 13.5 Hz), 2.88 (dt, 1H, J=7.5, 12.6 Hz), 2.90 (dd, 1H, J=6.6, 13.5 Hz), 3.74 (d, 1H, J=14.4 Hz), 3.86 (dt, 1H, J=6.6, 13.5 Hz), 3.98 (d, 1H, J=14.1 Hz), 4.13 (dt, 1H, J=5.4, 8.1 Hz), 7.21—7.45 (m, 10H). HR-MS *m/z*; 299.1338 (Calcd for $C_{18}H_{21}NOS$: 299.1344).

(3*R**,5*R**)-2-Benzyl-5-(methylthio)-3-phenylisoxazolidine (**3′aL**): ^{1}H-NMR ($CDCl_3$) δ: 2.18 (s, 3H), 2.45—2.50 (m, 2H), 2.67 (dd, 1H, J=6.9, 13.8 Hz), 2.75 (dd, 1H, J=4.8, 14.4 Hz), 3.75 (d, 1H, J=14.1 Hz), 3.98 (dd, 1H, J=14.1 Hz), 4.35—4.49 (m, 2H), 7.20—7.50 (m, 10H). HR-MS *m/z*; 299.1343 (Calcd for $C_{18}H_{21}NOS$: 299.1344).

(3*R**,5*R**)-2-Benzyl-5-(methylthio)-3-phenylisoxazolidine (**3aM**): ^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, 3H, J=6.9 Hz), 1.23—1.40 (m, 8H), 1.45—1.60 (m, 1H), 1.73—1.86 (m, 1H), 1.99 (ddd, 1H, J=7.2, 8.7, 12.0 Hz), 2.78 (dt, 1H, J=7.2, 12.0 Hz), 3.84 (d, 1H, J=14.1 Hz), 3.94 (d, 1H, J=11.7 Hz), 3.99 (d, 1H, J=14.1 Hz), 4.16—4.26 (m, 1H), 7.20—7.50 (m, 10H). HR-MS *m/z*; 323.2244 (Calcd for $C_{22}H_{29}NO$: 323.2249).

(3*R**,5*S**)-2-Benzyl-5-(methylthio)-3-phenylisoxazolidine (**3′aM**): ^{1}H-NMR ($CDCl_3$) δ: 0.88 (t, 3H, J=6.9 Hz), 1.23—1.40 (m, 8H), 1.45—1.60 (m, 1H), 1.73—1.86 (m, 1H), 2.18 (ddd, 1H, J=6.3, 8.4, 12.0 Hz), 2.36 (dt, 1 H, J=8.1, 12.3 Hz), 3.74 (d, 1H, J=14.1 Hz), 3.88 (d, 1H, J=11.1 Hz), 3.99 (d, 1H, J=14.1 Hz), 4.16—4.26 (m, 1H), 7.20—7.50 (m, 10H). HR-MS *m/z*; 323.2239 (Calcd for $C_{22}H_{29}NO$: 323.2249).

Ethyl (3*R**,5*R**)-2-Benzyl-5-methy-3-phenylisoxazolidin-5-carboxylate (**3aN**): ^{1}H-NMR ($CDCl_3$) δ: 1.33 (t, 3H, J=7.2 Hz), 1.59 (s, 3H), 2.32 (dd, 1H, J=9,6, 12.6 Hz), 3.10 (dd, 1H, J=6.9, 12.6 Hz), 3.97 (s, 2H), 4.06 (dd, 1H, J=6.9, 9.6 Hz), 4.25 (q, 2H, J=7.2 Hz), 7.20—7.45 (m, 10H). HR-MS *m/z*; 325.1678 (Calcd for $C_{20}H_{23}NO_3$: 325.1678).

Ethyl (3*R**,5*S**)-2-Benzyl-5-methy-3-phenylisoxazolidin-5-carboxylate (**3′aN**): ^{1}H-NMR ($CDCl_3$) δ: 1.31 (t, 3H, J=7.2 Hz), 1.54 (s, 3H), 2.49 (dd, 1H, J=8.4, 12.6 Hz), 3.03 (dd, 1H, J=8.4, 12.6 Hz), 3.76 (d, 1H, J=15.3 Hz), 3.81 (t, 1H, J=8.4 Hz), 3.99 (d, 1H, J=15.3 Hz), 4.24 (q, 2H, J=7.2 Hz), 7.20—7.45 (m, 10H). HR-MS *m/z*; 325.1684 (Calcd for $C_{20}H_{23}NO_3$: 325.1678).

(3*R**,5*R**)-2-Benzyl-5-cyano-5-methyl-3-phenylisoxazolidine (**3aP**): ^{1}H-NMR ($CDCl_3$) δ: 1.70 (s, 3H), 2.50 (dd, 1H, J=9.0, 12.6 Hz), 3.13 (dd, 1H, J=6.3, 12.6 Hz), 4.06 (d, 1H, J=13.8 Hz), 4.14 (d, 1H, J=13.9 Hz), 4.42 (dd, 1H, J=6.3, 9.3 Hz), 7.26—7.44 (m, 10H). HR-MS *m/z*; 278.1417 (Calcd for $C_{18}H_{18}N_2O$: 278.1419).

(3*R**,5*S**)-2-Benzyl-5-cyano-5-methyl-3-phenylisoxazolidine (**3′aP**): ^{1}H-NMR ($CDCl_3$) δ: 1.69 (s, 3H), 2.67 (dd, 1H, J=9.0, 12.9 Hz), 2.83 (dd, 1H, J=8.4, 12.9 Hz), 3.77 (d, 1H, J=15.3 Hz), 3.83 (t, 1H, J=8.7 Hz), 4.06 (d, 1H, J=15.3 Hz), 7.25—7.56 (m, 10H). HR-MS *m/z*; 278.1422 (Calcd for $C_{18}H_{18}N_2O$: 278.1419).

Reaction of 1b with Ethyl Acrylate (2A) A benzene solution (25 ml) of **1b** (270 mg, 2.0 mmol) and ethyl acrylate (2.0 g, 20 mmol) was heated to reflux for 3 h. After an evapolation of the solvent and an excess amount of ethyl acrylate by rotary evapolator, colorless oily residue was passed through the column chromatography packed with silica gel to give *cis*- and *trans*-5-(ethoxycarbonyl)-2-methyl-3-phenylisoxazolidines (**3bA**, **3′bA**) and *cis*- and *trans*-4-(ethoxycarbonyl)-2-methyl-3-phenylisoxazolidines (**4bA**, **4′bA**) in 95% total yields (447 mg). The ratio of the four isomers (**3aA**, **3′aA**, **4aA**, **4′aA**) was found to be 21 : 58 : 9 : 12, respectively, by the analysis of the ^{1}H-NMR spectra. Some of the four isomers were isolated by the chromatography though the yields were poor. Chloroform and the mixed solvent with ethanol were used for the eluent.

(3*R**,5*S**)-5-(Ethoxycarbonyl)-2-methyl-3-phenylisoxazolidine (**3bA**): ^{1}H-NMR ($CDCl_3$) δ: 1.31 (t, 3H, *J*=7.2 Hz), 2.58—2.68 (m, 1H), 2.96 (ddd, 1H, *J*=7.2, 9.3, 12.9 Hz), 2.61 (s, 3H), 3.75—3.86 (m, 1H), 4.26 (q, 2H, *J*=7.2 Hz), 4.62 (dd, 1H, *J*=5.7, 9.3 Hz), 7.27—7.42 (m, 5H). HR-MS *m/z*; 235.1204 (Calcd for $C_{13}H_{17}NO_3$: 235.1208).

(3*R**,5*R**)-5-(Ethoxycarbonyl)-2-methyl-3-phenylisoxazolidine (**3′bA**): ^{1}H-NMR ($CDCl_3$) δ: 1.31 (t, 3H, *J*=7.2 Hz), 2.62—2.79 (m, 2H), 2.69 (s, 3H), 3.65—3.74 (m, 1H), 4.25 (q, 2H, *J*=7.2 Hz), 4.68 (dd, 1H, *J*=5.4, 9.9 Hz), 7.26—7.41 (m, 5H). HR-MS *m/z*; 235.1215 (Calcd for $C_{13}H_{17}NO_3$: 235.1208).

(3*R**,4*R**)-4-(Ethoxycarbonyl)-2-methyl-3-phenylisoxazolidine (**4bA**): ^{1}H-NMR ($CDCl_3$) δ: 0.75 (t, 3H, *J*=7.2 Hz), 2.65 (s, 3H), 3.56 (dd, 1H, *J*=6.9, 10.5 Hz), 3.70 (q, 2H, *J*=7.2 Hz), 4.12—4.25 (m, 3H), 7.22—7.50 (m, 5H). HR-MS *m/z*; 235.1211 (Calcd for $C_{13}H_{17}NO_3$: 235.1208).

(3*R**,4*S**)-4-(Ethoxycarbonyl)-2-methyl-3-phenylisoxazolidine (**4′bA**): ^{1}H-NMR ($CDCl_3$) δ: 1.22 (t, 3H, *J*=7.2 Hz), 2.64 (s, 3H), 3.44 (dt, 1H, *J*=6.3, 7.8 Hz), 4.10 (d, 1H, *J*=7.8 Hz), 4.12—4.24 (m, 2H). 4.25 (q, 2H, *J*=7.2 Hz), 7.22—7.50 (m, 5H). HR-MS *m/z*; 235.1217 (Calcd for $C_{13}H_{17}NO_3$: 235.1208).

Reaction of *C*-Aryl-*N*-methylnitrone (1b—j) with Allyl Alcohol (2G) in the Absence of Lewis Acid These reactions were carried out according to the method described in the reaction of **1a** with **2A** except for using toluene as the solvent. Yields and the ratio of *cis*- and *trans*-3-aryl-5-(hydroxymethyl)-2-methylisoxazolidines (**3**, **3′**) were summarized in Table 3. ^{1}H-NMR spectral data of the isoxazolidines were as follows.

(3*R**,5*S**)-5-(Hydroxymethyl)-2-methyl-3-phenylisoxazolidine (**3bG**): ^{1}H-NMR ($CDCl_3$) δ: 1.63 (br s, 1H), 2.25 (ddd, 1H, *J*=5.4, 9.3, 12.3 Hz), 2.61 (s, 3H), 2.79 (dt, 1H, *J*=8.1, 12.3 Hz), 3.74—3.83 (m, 3H), 4.30—4.39 (m, 1H), 7.24—7.48 (m, 5H). HR-MS *m/z*; 193.1105 (Calcd for $C_{11}H_{15}NO_2$: 193.1103).

(3*R**,5*R**)-5-(Hydroxymethyl)-2-methyl-3-phenylisoxazolidine (**3′bG**): ^{1}H-NMR ($CDCl_3$) δ: 1.83 (br s, 1H), 2.37 (dt, 1H, *J*=8.7, 12.3 Hz), 2.55 (ddd, 1H, *J*=5.4, 7.8, 12.3 Hz), 2.61 (s, 3H), 3.56—3.82 (m, 3H), 4.03—4.39 (m, 1H), 7.24—7.48 (m, 5H). HR-MS *m/z*; 193.1109 (Calcd for $C_{11}H_{15}NO_2$: 193.1103).

(3*R**,5*S**)-5-(Hydroxymethyl)-2-methyl-3-(2-methylphenyl)isoxazolidine (**3cG**): ^{1}H-NMR ($CDCl_3$) δ: 2.04 (ddd, 1H, *J*=5.4, 9.6, 12.6 Hz), 2.20 (br s, 1H), 2.35 (s, 3H), 2.61 (s, 3H), 2.80 (dt, 1H, *J*=8.1, 12.3 Hz), 3.62 (dd, 1H, *J*=4.8, 12.0 Hz), 3.68—3.78 (m, 1H), 3.84 (dd, 1H, *J*=3.0, 12.0 Hz), 4.30—4.40 (m, 1H), 7.12—7.24 (m, 3H), 7.47—7.51 (m, 1H). HR-MS *m/z*; 207.1258 (Calcd for $C_{12}H_{17}NO_2$: 207.1259).

(3*R**,5*R**)-5-(Hydroxymethyl)-2-methyl-3-(2-methylphenyl)isoxazolidine (**3′cG**): ^{1}H-NMR ($CDCl_3$) δ: 2.18—2.33 (m, 1H), 2.20 (br s, 1H), 2.35 (s, 3H), 2.55 (ddd, 1H, *J*=6.0, 8.1, 12.0 Hz), 2.61 (s, 3H), 3.62 (dd, 1H, *J*=4.8, 12.0 Hz), 3.68—3.78 (m, 1H), 3.84 (dd, 1H, *J*=3.0, 12.0 Hz), 4.30—4.40 (m, 1H), 7.12—7.24 (m, 3H), 7.47—7.51 (m, 1H). HR-MS *m/z*; 207.1266 (Calcd for $C_{12}H_{17}NO_2$: 207.1259).

(3*R**,5*S**)-5-(Hydroxymethyl)-2-methyl-3-(2-naphthyl)isoxazolidine (**3dG**): ^{1}H-NMR ($CDCl_3$) δ: 1.95 (br s, 1H), 2.36 (ddd, 1H, *J*=5.7, 9.6, 12.6 Hz), 2.61 (s, 3H), 2.82 (dt, 1H, *J*=8.1, 12.6 Hz), 3.60—3.70 (m, 2H), 3.84—3.92 (m, 1H), 7.46—7.54 (m, 3H), 7.80—7.86 (m, 4H). HR-MS *m/z*; 243.1256 (Calcd for $C_{15}H_{17}NO_2$: 243.1259).

(3*R**,5*R**)-5-(Hydroxymethyl)-2-methyl-3-(2-naphthyl)isoxazolidine (**3′dG**): ^{1}H-NMR ($CDCl_3$) δ: 1.95 (br s, 1H), 2.43—2.53 (m, 1H), 2.55—2.65 (m, 1H), 2.61 (s, 3H), 3.60—3.70 (m, 2H), 3.84—3.92 (m, 1H), 7.46—7.54 (m, 3H), 7.80—7.86 (m, 4H). HR-MS *m/z*; 243.1258 (Calcd for $C_{15}H_{17}NO_2$: 243.1259).

(3*R**,5*S**)-5-(Hydroxymethyl)-3-(2-methoxyphenyl)-2-methylisoxazolidine (**3eG**): ^{1}H-NMR ($CDCl_3$) δ: 2.06 (ddd, 1H, *J*=5.7, 9.0, 12.3 Hz), 2.20 (br s, 1H), 2.61 (s, 3H), 2.80 (dt, 1H, *J*=8.1, 12.3 Hz), 3.60—3.70 (m, 1H), 3.80—3.85 (m, 1H), 3.82 (s, 3H), 3.91—4.06 (m, 1H), 4.26—4.35 (m, 1H), 6.86 (d, 1H, *J*=7.8 Hz), 6.95 (t, 1H, *J*=7.5 Hz), 7.23 (t, 1H, *J*=7.5 Hz), 7.45 (d, 1H, *J*=7.5 Hz). HR-MS *m/z*; 223.1208 (Calcd for $C_{12}H_{17}NO_3$: 223.1208).

(3*R**,5*R**)-5-(Hydroxymethyl)-3-(2-methoxyphenyl)-2-methylisoxazolidine (**3′eG**): ^{1}H-NMR ($CDCl_3$) δ: 2.20 (br s, 1H), 2.51—2.60 (m, 2H), 2.61 (s, 3H), 3.60—3.70 (m, 1H), 3.80—3.85 (m, 1H), 3.82 (s, 3H), 3.91—4.06 (m, 1H), 4.26—4.35 (m, 1H), 6.86 (d, 1H, *J*=7.8 Hz), 6.95 (t, 1H, *J*=7.5 Hz), 7.23 (t, 1H, *J*=7.5 Hz), 7.45 (d, 1H, *J*=7.5 Hz). HR-MS *m/z*; 223.1202 (Calcd for $C_{12}H_{17}NO_3$: 223.1208).

(3*R**,5*S**)-5-(Hydroxymethyl)-2-methy-3-(2-pyridyl)isoxazolidine (**3gG**): ^{1}H-NMR ($CDCl_3$) δ: 2.36—2.48 (m, 1H), 2.59 (s, 3H), 2.85 (dt, 1H, *J*=8.7, 12.6 Hz), 3.60—3.75 (m, 2H), 3.75—3.91 (m, 2H), 4.31—4.39 (m, 1H), 7.11 (t, 1H, *J*=6.0 Hz), 7.38 (d, 1H, *J*=7.8 Hz), 7.59 (t, 1H, *J*=7.8 Hz), 8.44 (d, 1H, *J*=5.1 Hz). HR-MS *m/z*; 194.1064 (Calcd for $C_{10}H_{14}N_2O_2$: 194.1055).

(3*R**,5*R**)-5-(Hydroxymethyl)-2-methy-3-(2-pyridyl)isoxazolidine (**3′gG**): ^{1}H-NMR ($CDCl_3$) δ: 2.46—2.61 (m, 2H), 2.60 (br s, 1H), 2.65 (s, 3H), 3.62 (dd, 1H, *J*=4.8, 12.0 Hz), 3.81 (dd, 2H, *J*=2.7, 12.0 Hz), 4.30—4.38 (m, 1H), 7.19 (t, 1H, *J*=6.0 Hz), 7.45 (d, 1H, *J*=7.8 Hz), 7.67 (t, 1H, *J*=7.8 Hz), 8.54 (d, 1H, *J*=4.8 Hz). HR-MS *m/z*; 194.1064 (Calcd for $C_{10}H_{14}N_2O_2$: 194.1055).

(3*R**,5*S**)-5-(Hydroxymethyl)-2-methy-3-(6-methyl-2-pyridyl)isoxazolidine (**3hG**): ^{1}H-NMR ($CDCl_3$) δ: 2.50—2.53 (m, 1H), 2.52 (s, 3H), 2.67 (s, 3H), 2.83 (dt, 1H, *J*=8.7, 12.6 Hz), 3.72 (dd, 1H, *J*=4.2, 12.0 Hz), 3.80—3.96 (m, 3H), 4.40—4.50 (m, 1H), 7.04 (d, 1H, *J*=7.8 Hz), 7.18 (d, 1H, *J*=7.8 Hz), 7.54 (t, 1H, *J*=7.8 Hz). HR-MS *m/z*; 208.1217 (Calcd for $C_{11}H_{16}N_2O_2$: 208.1212).

(3*R**,5*R**)-5-(Hydroxymethyl)-2-methy-3-(6-methyl-2-pyridyl)isoxazolidine (**3′hG**): ^{1}H-NMR ($CDCl_3$) δ: 2.50—2.70 (m, 2H), 2.51 (s, 3H), 2.64 (s, 3H), 3.61 (dd, 1H, *J*=5.1, 12.0 Hz), 3.77 (dd, 1H, *J*=3.0, 12.0 Hz), 3.81—3.94 (m, 2H), 4.30—4.38 (m, 1H), 7.02 (d, 1H, *J*=7.8 Hz), 7.24 (d, 1H, *J*=7.8 Hz), 7.54 (t, 1H, *J*=7.8 Hz). HR-MS *m/z*; 208.1216 (Calcd for $C_{11}H_{16}N_2O_2$: 208.1212).

(3*R**,5*S**)-5-(Hydroxymethyl)-2-methy-3-(2-quinolyl)isoxazolidine (**3iG**): ^{1}H-NMR ($CDCl_3$) δ: 2.40—2.60 (m, 1H), 2.60 (br s, 1H), 2.69 (s, 3H), 2.91 (dt, 1H, *J*=8.4, 12.6 Hz), 3.76 (dd, 1H, *J*=5.1, 11.4 Hz), 3.83 (dd, 1H, *J*=3.0, 12 Hz), 4.05—4.17 (m, 1H), 4.44—4.54 (m, 1H), 7.52 (t, 1H, *J*=8.1 Hz), 7.64 (d, 1H, *J*=8.7 Hz), 7.70 (t, 1H, *J*=8.4 Hz), 7.79 (d, 1H, *J*=8.1 Hz), 8.07 (d, 1H, *J*=8.4 Hz), 8.16 (d, 1H, *J*=8.7 Hz). HR-MS *m/z*; 244.1214 (Calcd for $C_{14}H_{16}N_2O_2$: 244.1212).

(3*R**,5*R**)-5-(Hydroxymethyl)-2-methy-3-(2-quinolyl)isoxazolidine (**3′iG**): ^{1}H-NMR ($CDCl_3$) δ: 2.60 (br s, 1H), 2.63—2.75 (m, 2H), 2.69 (s, 3H), 3.67 (dd, 1H, *J*=5.1, 12.0 Hz), 3.83 (dd, 1H, *J*=3.0, 12.0 Hz), 3.95—4.05 (m, 1H), 4.37—4.44 (m, 1H), 7.52 (t, 1H, *J*=8.1 Hz), 7.64 (d, 1H, *J*=8.7 Hz), 7.70 (t, 1H, *J*=8.4 Hz), 7.79 (d, 1H, *J*=8.1 Hz), 8.07 (d, 1H, *J*=8.4 Hz), 8.16 (d, 1H, *J*=8.7 Hz). HR-MS *m/z*; 244.1218 (Calcd for $C_{14}H_{16}N_2O_2$: 244.1212).

(3*R**,5*R**)-3-(2-Furyl)-5-(hydroxymethyl)-2-methylisoxazolidine (**3′jG**): ^{1}H-NMR ($CDCl_3$) δ: 2.34—2.50 (m, 1H), 2.53—2.64 (m, 1H), 2.65 (s, 3H), 2.82 (br s, 1H), 3.59 (dd, 2H, *J*=4.5, 12.0 Hz), 3.78 (dd, 1H, *J*=3.0, 12.0 Hz), 4.30—4.45 (m, 1H), 6.27 (d, 1H, *J*=3.0 Hz), 6.31 (dd, 1H, *J*=1.8, 3.0 Hz), 7.37 (d, 1H, *J*=1.8 Hz). HR-MS *m/z*; 183.0899 (Calcd for $C_9H_{13}NO_3$: 183.0895).

Transformation of 3aA, 3′aA, 4aA, and 4′aA into 3′aG, 3aG, 4′aG, and 4aG To a suspension of lithium alminium hydride (110 mg, 2.9 mmol) in dry tetrahydrofuran (THF) (15 ml) was added a dry-THF solution (5 ml) of a mixture of **3aA**, **3′aA**, **4aA**, and **4′aA** (290 mg, 0.93 mmol; 10 : 72 : 4 : 14 mixture, respectively) at room temperature under an atmosphere of nitrogen and, then, the mixture was heated to reflux for 2 h with stirring. The reaction mixture was cooled down well and poured carefully into separatory funnel containing ice-water (50 ml). Saturated aqueous solution (20 ml) of potassium carbonate and chloroform (40 ml) were also added to the cooled mixture, which was shaken well. Emulsion thus formed was filtered through a glass funnel, fitted with Celite bed, and then the bed was washed well with chloroform. The chloroform layer was dried with anhydrous magnesium sulfate, from which the solvent was evaporated to give a mixture of **3aG**, **3′aG**, **4aG**, and **4′aG** (10 : 70 : 5 : 15 mixture, respectively) in 99% total yield (248 mg).

Alcoholysis of Nitrile (3′aN) An ethanol solution (10 ml) of **3′aN** (300 mg, 1.14 mmol) and *p*-toluenesulfonic acid monohydrate (300 mg, 1.58 mmol) was heated to 120 °C in a sealed tube and maintained at the temperature for 15 h with stirring. Evapolation of the solvent from the reaction mixture gave crystalline mass, which was dissolved in water and, then, extracted with chloroform several times. The combined toluene solution was dried with anhydrous magnesium sulfate, from which the solvent was evapolated by rotary evapolator. Viscous yellowish oily residue was passed

through the column chromatography packed with silica gel to give ester (**3′aA**) in 165 mg (53%) yield. Chloroform and the mixed solvent with ethanol were used for the eluent.

Reactions of *N*-Alkylnitrones (1a—j) with Alkenes (2A—P) in the Presence of Lewis Acids. Typical Procedure To a toluene solution (25 ml) of **1a** (211 mg, 1.0 mmol) and allyl alcohol (580 mg, 10 mmol) was added magnesium bromide etherate (260 mg, 1.0 mmol), and the mixture was heated to reflux for 2 h under nitrogen atmosphere with vigorous stirring. After cooling, water was added and extracted with toluene several times. The combined toluene solution was dried with anhydrous magnesium sulfate, from which the solvent and an excess amount of acrylate were evapolated by rotary evapolator. Viscous colorless oily residue was passed through the column chromatography packed with silica gel using a mixed solvent of chloroform and methanol (25 : 1) to give *cis*- and *trans*-2-benzyl-5-(hydroxymethyl)-3-phenylisoxazolidines (**3aG**, **3′aG**) in 14% (38 mg) and 48% (129 mg) yields, respectively.

Results of the other reactions were summarized in Tables 1 and 3.

Reactions of *C*-Phenyl-*N*-arylnitrones (1k—n) with 2A or 2N in the Absence of Lewis Acids These reactions were carried out according to the Typical Procedure described in the reaction of **1a** with **2A**. Reaction conditions and yields of products were shown in Table 4. ^{1}H-NMR spectral data of the isoxazolidines were as follows;

Ethyl (3*R**,5*S**)-2,3-Diphenylisoxazolidin-5-carboxylate (**3kA**): ^{1}H-NMR ($CDCl_3$) δ: 1.25 (t, 3H, J=7.2 Hz), 2.71 (dt, 1H, J=6.3, 12.6 Hz), 3.06 (dt, 1H, J=8.4, 12.6 Hz), 4.21 (q, 2H, J=7.2 Hz), 4.68 (dd, 1H, J=6.3, 8.4 Hz), 4.78 (dd, 1H, J=6.3, 8.4 Hz), 6.95—7.51 (m, 10H). HR-MS *m/z*; 297.1366 (Calcd for $C_{18}H_{19}NO_3$: 297.1365).

Ethyl (3*R**,5*R**)-2,3-Diphenylisoxazolidin-5-carboxylate (**3′kA**): ^{1}H-NMR ($CDCl_3$) δ: 1.23 (t, 3H, J=7.2 Hz), 2.69 (ddd, 1H, J=6.6, 7.8, 12.6 Hz), 2.95 (ddd, 1H, J=5.7, 7.2, 12.6 Hz), 4.19 (q, 2H, J=7.2 Hz), 4.72—4.79 (m, 2H), 6.92—7.56 (m, 10H). HR-MS *m/z*; 297.1369 (Calcd for $C_{18}H_{19}NO_3$: 297.1365).

Ethyl (3*R**,4*R**)-2,3-Diphenylisoxazolidin-4-carboxylate (**4kA**): ^{1}H-NMR ($CDCl_3$) δ: 0.91 (t, 3H, J=6.9 Hz), 3.65—3.82 (m, 1H), 3.76 (q, 2H, J=6.9 Hz), 4.33 (t, 1H, J=8.1 Hz), 4.56 (t, 1H, J=7.8 Hz), 5.01 (d, 1H, J=9.0 Hz), 6.92—7.56 (m, 10H). HR-MS *m/z*; 297.1360 (Calcd for $C_{18}H_{19}NO_3$: 297.1365).

Ethyl (3*R**,4*S**)-2,3-Diphenylisoxazolidin-4-carboxylate (**4′kA**): ^{1}H-NMR ($CDCl_3$) δ: 1.20 (t, 3H, J=7.2 Hz), 3.55 (ddd, 1H, J=5.7, 6.9, 7.8 Hz), 4.13 (q, 2H, J=7.2 Hz), 4.32 (dd, 1H, J=6.9, 8.4 Hz), 4.37 (dd, 1H, J=7.8, 8.4 Hz), 5.01 (d, 1H, J=5.7 Hz), 6.92—7.56 (m, 10H). HR-MS *m/z*; 297.1366 (Calcd for $C_{18}H_{19}NO_3$: 297.1365).

Ethyl (3*R**,5*S**)-2-(4-Methylphenyl)-3-phenylisoxazolidin-5-carboxylate (**3mA**): ^{1}H-NMR ($CDCl_3$) δ: 1.24 (t, 3H, J=7.2 Hz), 2.26 (s, 3H), 2.67 (dt, 1H, J=6.3, 12.6 Hz), 3.04 (dt, 1H, J=8.4, 12.6 Hz), 4.19 (q, 2H, J=7.2 Hz), 4.60 (dd, 1H, J=6.3, 8.4 Hz), 4.78 (dd, 1H, J=6.3, 8.4 Hz), 6.88—7.54 (m, 9H). HR-MS *m/z*; 311.1522 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

Ethyl (3*R**,5*R**)-2-(4-Methylphenyl)-3-phenylisoxazolidin-5-carboxylate (**3′mA**): ^{1}H-NMR ($CDCl_3$) δ: 1.26 (t, 3H, J=7.2 Hz), 2.25 (s, 3H), 2.71 (ddd, 1H, J=6.9, 7.5, 12.6 Hz), 2.91 (ddd, 1H, J=5.7, 7.2, 12.6 Hz), 4.20 (q, 2H, J=7.2 Hz), 4.67 (t, 1H, J=7.2 Hz), 4.75 (dd, 1H, J=5.7, 7.5 Hz), 6.88—7.54 (m, 9H). HR-MS *m/z*; 311.1510 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

Ethyl (3*R**,4*R**)-2-(4-Methylphenyl)-3-phenylisoxazolidin-4-carboxylate (**4mA**): ^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, 3H, J=7.2 Hz), 2.73 (s, 3H), 3.62—3.81 (m, 1H), 3.75 (q, 2H, J=7.2 Hz), 4.34 (t, 1H, J=8.1 Hz), 4.54 (t, 1H, J=7.8 Hz), 4.95 (d, 1H, J=9.0 Hz), 6.88—7.54 (m, 9H). HR-MS *m/z*; 311.1523 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

Ethyl (3*R**,4*S**)-2-(4-Methylphenyl)-3-phenylisoxazolidin-4-carboxylate (**4′mA**): ^{1}H-NMR ($CDCl_3$) δ: 1.20 (t, 3H, J=7.2 Hz), 2.27 (s, 3H), 3.54 (ddd, 1H, J=6.0, 6.6, 8.1 Hz), 4.12 (q, 2H, J=7.2 Hz), 4.32 (dd, 1H, J=6.9, 8.4 Hz), 4.37 (dd, 1H, J=7.8, 8.4 Hz), 4.93 (d, 1H, J=5.7 Hz), 6.88—7.54 (m, 9H). HR-MS *m/z*; 311.1523 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

Ethyl (3*R**,5*S**)-2-(4-Chlorophenyl)-3-phenylisoxazolidin-5-carboxylate (**3nA**): ^{1}H-NMR ($CDCl_3$) δ: 1.26 (t, 3H, J=7.2 Hz), 2.71 (dt, 1H, J=6.3, 12.6 Hz), 3.07 (dt, 1H, J=8.4, 12.6 Hz), 4.18 (q, 2H, J=7.2 Hz), 4.56 (dd, 1H, J=6.3, 8.4 Hz), 4.76 (dd, 1H, J=6.3, 8.4 Hz), 6.89—7.53 (m, 9H). HR-MS *m/z*; 331.0970 (Calcd for $C_{18}H_{18}NO_3Cl$: 331.0975).

Ethyl (3*R**,5*R**)-2-(4-Chlorophenyl)-3-phenylisoxazolidin-5-carboxylate (**3′nA**): ^{1}H-NMR ($CDCl_3$) δ: 1.24 (t, 3H, J=7.2 Hz), 2.69 (dt, 1H, J=7.2, 12.6 Hz), 2.94 (ddd, 1H, J=5.4, 7.2, 12.6 Hz), 4.22 (q, 2H, J=7.2 Hz), 4.67 (t, 1H, J=7.2 Hz), 4.76 (dd, 1H, J=5.4, 7.2 Hz), 6.89—7.53 (m, 9H). HR-MS *m/z*; 331.0968 (Calcd for $C_{18}H_{18}NO_3Cl$: 331.0975).

Ethyl (3*R**,4*R**)-2-(4-Chlorophenyl)-3-phenylisoxazolidin-4-carboxylate (**4nA**): ^{1}H-NMR ($CDCl_3$) δ: 0.90 (t, 3H, J=7.2 Hz), 3.61—3.80 (m, 1H), 3.77 (q, 2H, J=7.2 Hz), 4.30 (t, 1H, J=8.4 Hz), 4.56 (t, 1H, J=8.1 Hz), 4.91 (d, 1H, J=8.7 Hz), 6.89—7.53 (m, 9H). HR-MS *m/z*; 331.0972 (Calcd for $C_{18}H_{18}NO_3Cl$: 331.0975).

Ethyl (3*R**,4*S**)-2-(4-Chlorophenyl)-3-phenylisoxazolidin-4-carboxylate (**4′nA**): ^{1}H-NMR ($CDCl_3$) δ: 1.21 (t, 3H, J=7.2 Hz), 3.55 (ddd, 1H, J=5.7, 6.6, 7.8 Hz), 4.19 (q, 2H, J=7.2 Hz), 4.31 (dd, 1H, J=6.9, 8.4 Hz), 4.38 (t, 1H, J=8.1 Hz), 4.93 (d, 1H, J=6.0 Hz), 6.90 (d, 2H, J=9.0 Hz), 7.17 (d, 2H, J=9.0 Hz), 7.25—7.43 (m, 3H), 7.48—7.54 (m, 2H). HR-MS *m/z*; 331.0976 (Calcd for $C_{18}H_{18}NO_3Cl$: 331.0975).

Ethyl (3*R**,5*R**)-5-Methyl-2,3-diphenylisoxazolidin-5-carboxylate (**3kN**): ^{1}H-NMR ($CDCl_3$) δ: 1.09 (t, 3H, J=7.2 Hz), 1.65 (s, 3H), 2.35 (dd, 1H, J=9.0, 12.9 Hz), 3.35 (dd, 1H, J=7.2, 12.6 Hz), 4.02 (q, 2H, J=7.2 Hz), 4.77 (dd, 1H, J=7.2, 9.0 Hz), 6.84—7.49 (m, 10H). HR-MS *m/z*; 311.1524 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

Ethyl (3*R**,5*S**)5-Methyl-2,3-diphenylisoxazolidin-5-carboxylate (**3′kN**): ^{1}H-NMR ($CDCl_3$) δ: 1.27 (s, 3H), 1.61 (s, 3H), 2.68 (dd, 1H, J=9.0, 12.9 Hz), 3.04 (dd, 1H, J=6.6, 12.9 Hz), 4.22 (q, 2H, J=7.2 Hz), 4.48 (dd, 1H, J=6.6, 9.0 Hz), 6.84—7.49 (m, 10H). HR-MS *m/z*; 311.1528 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

Ethyl (3*R**,5*R**)-5-Methyl-2-(4-methylphenyl)-3-phenylisoxazolidin-5-carboxylate (**3mN**): ^{1}H-NMR ($CDCl_3$) δ: 1.31 (t, 3H, J=7.2 Hz), 1.63 (s, 3H), 2.33 (dd, 1H, J=9.0, 12.3 Hz), 2.41 (s, 3H), 3.31 (dd, 1H, J=6.9, 12.3 Hz), 4.05 (q, 2H, J=7.2 Hz), 4.70 (dd, 1H, J=7.2, 9.0 Hz), 6.85—7.48 (m, 9H). HR-MS *m/z*; 325.1684 (Calcd for $C_{20}H_{23}NO_3$: 325.1678).

Ethyl (3*R**,5*S**)-5-Methyl-2-(4-methylphenyl)-3-phenylisoxazolidin-5-carboxylate (**3′mN**): ^{1}H-NMR ($CDCl_3$) δ: 1.30 (t, 3H, J=7.2 Hz), 1.60 (s, 3H), 2.22 (s, 3H), 2.65 (dd, 1H, J=9.0, 12.6 Hz), 3.03 (dd, 1H, J=6.9, 12.6 Hz), 4.21 (q, 2H, J=7.2 Hz), 4.40 (dd, 1H, J=6.6, 9.0 Hz), 6.85—7.48 (m, 9H). HR-MS *m/z*; 325.1685 (Calcd for $C_{20}H_{23}NO_3$: 325.1678).

Ethyl (3*R**,5*R**)-2-(4-Chlorophenyl)-5-methyl-3-phenylisoxazolidin-5-carboxylate (**3nN**): ^{1}H-NMR ($CDCl_3$) δ: 1.14 (t, 3H, J=7.2 Hz), 1.64 (s, 3H), 2.34 (dd, 1H, J=9.1, 12.3 Hz), 3.33 (dd, 1H, J=7.2, 12.3 Hz), 4.04 (q, 2H, J=7.2 Hz), 4.69 (dd, 1H, J=7.2, 9.6 Hz), 6.84—7.46 (m, 9H). HR-MS *m/z*; 345.1140 (Calcd for $C_{19}H_{20}NO_3Cl$: 345.1132).

Ethyl (3*R**,5*S**)-2-(4-Chlorophenyl)-5-methyl-3-phenylisoxazolidin-5-carboxylate (**3′nN**): ^{1}H-NMR ($CDCl_3$) δ: 1.29 (t, 3H, J=7.2 Hz), 1.60 (s, 3H), 2.67 (dd, 1H, J=9.0, 12.6 Hz), 3.03 (dd, 1H, J=6.9, 12.6 Hz), 4.21 (q, 2H, J=7.2 Hz), 4.41 (dd, 1H, J=6.6, 9.0 Hz), 6.84—7.46 (m, 9H). HR-MS *m/z*; 345.1144 (Calcd for $C_{19}H_{20}NO_3Cl$: 345.1132).

Reactions of *C*-Phenyl-*N*-arylnitrones (1k—n) with 2A or 2N in the Presence of Lewis Acids. Typical Procedure To a chloroform solution (25 ml) of **1k** (211 mg, 1.0 mmol) and ethyl acrylate (1.0 g, 10 mmol) was added magnesium bromide etherate (260 mg, 1.0 mmol), and the mixture was heated to reflux for 6 h under nitrogen atmosphere with vigorous stirring. After cooling, water was added and extracted with chloroform several times. The combined chloroform solution was dried with anhydrous magnesium sulfate, from which the solvent and an excess amount of acrylate were evapolated by rotary evapolator. Viscous yellow oily residue was passed through the column chromatography packed with silica gel using a mixed solvent of chloroform and ethanol to give a pair of diastereomer of ethyl 4-(2-bromophenylamino)-2-hydroxybutanoate (**5kA**), a pair of diastereomer of ethyl 3-(2-bromophenylamino)-2-(hydroxymethyl)-3-phenylpropanoate (**6kA**), and **4′kA** in 17% (64 mg), 46% (174 mg), and 19% (56 mg) yields, respectively.

Ethyl 4-(2-Bromophenylamino)-2-hydroxy-4-phenylbutanoate (**5kA**: Diastereomer A): ^{1}H-NMR ($CDCl_3$) δ: 1.26 (t, 3H, J=7.2 Hz), 2.06—2.35 (m, 2H), 4.19 (q, 2H, J=7.2 Hz), 4.60 (dd, 1H, J=6.0, 8.1 Hz), 4.74—4.80 (m, 1H), 6.39 (d, 1H, J=8.7 Hz), 6.46—6.52 (m, 1H), 7.12—7.42 (m, 7H). HR-MS *m/z*; 377.0633 (Calcd for $C_{18}H_{20}NO_3Br$: 377.0627).

Ethyl 4-(2-Bromophenylamino)-2-hydroxy-4-phenylbutanoate (**5kA**: Diastereomer B): ^{1}H-NMR ($CDCl_3$) δ: 1.27 (t, 3H, J=7.2 Hz), 2.06—2.35 (m, 2H), 4.19 (q, 2H, J=7.2 Hz), 4.66 (dd, 1H, J=3.9, 8.1 Hz), 4.74—4.80 (m, 1H), 6.40 (d, 1H, J=8.7 Hz), 6.46—6.52 (m, 1H), 7.12—7.42 (m, 7H). HR-MS *m/z*; 377.0630 (Calcd for $C_{18}H_{20}NO_3Br$: 377.0627).

Ethyl 3-(2-Bromophenylamino)-2-(hydroxymethyl)-3-phenylpropanoate (**6kA**: Diastereomer A): ^{1}H-NMR ($CDCl_3$) δ: 1.21 (t, 3H, J=7.2 Hz), 2.95—3.05 (m, 1H), 3.74—3.85 (m, 2H), 3.81—4.22 (m, 2H), 4.12 (q, 2H, J=7.2 Hz), 4.87 (d, 1H, J=7.2 Hz), 6.41—7.41 (m, 9H). HR-MS *m/z*; 377.0622 (Calcd for $C_{18}H_{20}NO_3Br$: 377.0627).

Ethyl 3-(2-Bromophenylamino)-2-(hydroxymethyl)-3-phenylpropanoate (**6kA**: Diastereomer B): ^{1}H-NMR ($CDCl_3$) δ: 1.16 (t, 3H, J=7.2 Hz), 2.95—3.05 (m, 1H), 3.74—3.85 (m, 1H), 3.81—4.22 (m, 2H), 4.16 (q, 2H, J=7.2 Hz), 4.82 (d, 1H, J=6.9 Hz), 6.41—7.41 (m, 9H). HR-MS *m/z*; 377.0625 (Calcd for $C_{18}H_{20}NO_3Br$: 377.0627).

Similarly, the following γ-aminoalcohols were obtained in yields shown in Table 4 from the reaction of **1k**—**m** with **2A** or **2N**.

Ethyl 4-(2-Bromo-4-methylphenylamino)-2-hydroxy-4-phenylbutanoate (**5mA**: Diastereomer A): ^{1}H-NMR ($CDCl_3$) δ: 1.27 (t, 3H, J=7.2 Hz), 2.15 (s, 3H), 2.12—2.35 (m, 2H), 4.13 (dd, 1H, J=7.2, 12.0 Hz), 4.19 (q, 2H, J=7.2 Hz), 4.71—4.76 (m, 1H), 6.39 (d, 1H, J=8.1 Hz), 6.79 (d, 1H, J=8.1 Hz), 7.20—7.37 (m, 6H). HR-MS *m/z*; 391.0780 (Calcd for $C_{19}H_{22}NO_3Br$: 391.0783).

Ethyl 4-(2-Bromo-4-methylphenylamino)-2-hydroxy-4-phenylbutanoate (**5mA**: Diastereomer B): ^{1}H-NMR ($CDCl_3$) δ: 1.27 (t, 3H, J=7.2 Hz), 2.15 (s, 3H), 2.12—2.35 (m, 2H), 4.19 (q, 2H, J=7.2 Hz), 4.32 (dd, 1H, J=3.0, 9.0 Hz), 4.71—4.76 (m, 1H), 6.34 (d, 1H, J=8.1 Hz), 6.79 (d, 1H, J=8.1 Hz), 7.20—7.37 (m, 6H). HR-MS *m/z*; 391.0791 (Calcd for $C_{19}H_{22}NO_3Br$: 391.0783).

Ethyl 3-(2-Bromo-4-methylphenylamino)-2-(hydroxymethyl)-3-phenylpropanoate (**6mA**: Diastereomer A): ^{1}H-NMR ($CDCl_3$) δ: 1.22 (t, 3H, J=7.2 Hz), 2.14 (s, 3H), 2.92—3.02 (m, 1H), 3.74—3.85 (m, 2H), 4.14 (q, 2H, J=7.2 Hz), 4.81—4.86 (m, 1H), 6.34 (d, 1H, J=8.1 Hz), 6.79 (d, 1H, J=8.1 Hz), 7.22—7.33 (m, 6H). HR-MS *m/z*; 391.0795 (Calcd for $C_{19}H_{22}NO_3Br$: 391.0783).

Ethyl 3-(2-Bromo-4-methylphenylamino)-2-(hydroxymethyl)-3-phenylpropanoate (**6mA**: Diastereomer B): ^{1}H-NMR ($CDCl_3$) δ: 1.16 (t, 3H, J=7.2 Hz), 2.14 (s, 3H), 2.92—3.02 (m, 1H), 3.74—3.85 (m, 1H), 3.96 (dd, 1H, J=3.6, 12.0 Hz), 4.16 (q, 2H, J=7.2 Hz), 5.12 (d, 1H, J=3.9 Hz), 6.31 (d, 1H, J=7.8 Hz), 6.78 (d, 1H, J=8.1 Hz), 7.22—7.33 (m, 6H). HR-MS *m/z*; 391.0789 (Calcd for $C_{19}H_{22}NO_3Br$: 391.0783).

Ethyl 4-(2-Bromo-4-chlorophenylamino)-2-hydroxy-4-phenylbutanoate (**5nA**: Diastereomer A): ^{1}H-NMR ($CDCl_3$) δ: 1.27 (t, 3H, J=7.2 Hz), 2.19 (ddd, 1H, J=3.9, 9.3, 14.4 Hz), 2.31 (ddd, 1H, J=3.0, 8.1, 14.4 Hz), 3.00 (br s, 1H), 4.19 (q, 2H, J=7.2 Hz), 4.24—4.33 (m, 1H), 4.73 (dd, 1H, J=3.9, 8.1 Hz), 5.60 (br s, 1H), 6.30 (d, 1H, J=8.7 Hz), 6.94 (dd, 1H, J=2.4, 8.7 Hz), 7.20—7.36 (m, 5H), 7.39 (d, 1H, J=2.4 Hz). HR-MS *m/z*; 411.0240 (Calcd for $C_{18}H_{19}NO_3BrCl$: 411.0237).

Ethyl 4-Methyl-2,3-diphenylisoxazolidin-4-carboxylate (**4kN**): ^{1}H-NMR ($CDCl_3$) δ: 1.03 (s, 3H), 1.24 (t, 3H, J=6.9 Hz), 3.93 (d, 1H, J=8.4 Hz), 4.16 (q, 2H, J=7.2 Hz), 6.80—7.50 (m, 10H). HR-MS *m/z*; 311.1518 (Calcd for $C_{19}H_{21}NO_3$: 311.1521).

Ethyl 4-(2-Bromophenylamino)-2-hydroxy-2-methyl-4-phenylbutanoate (**5kN**: Diastereomer A): mp. 126—128 °C (from ethanol); ^{1}H-NMR ($CDCl_3$) δ: 1.23 (t, 3H, J=7.2 Hz), 1.45 (s, 3H), 2.23 (dd, 1H, J=9.0, 14.4 Hz), 2.33 (dd, 1H, J=4.8, 14.4 Hz), 3.72 (br s, 1H), 4.06 (q, 1H, J=7.2 Hz), 4.11 (q, 1H, J=7.2 Hz), 4.43 (dd, 1H, J=4.8, 9.0 Hz), 5.50 (br s, 1H), 6.32 (dd, 1H, J=1.5, 8.1 Hz), 6.49 (dt, 1H, J=1.5, 7.5 Hz), 6.95 (ddd, 1H, J=1.5, 7.5, 8.1 Hz), 7.20—7.31 (m, 5H), 7.38 (dd, 1H, J=1.5, 7.5 Hz). IR (KBr) cm^{-1}: 3486, 3323, 1730. HR-MS *m/z*; 391.0780 (Calcd for $C_{19}H_{22}NO_3Br$: 391.0783). *Anal.* Calcd for $C_{19}H_{22}NO_3Br$: C, 57.53; H, 5.74; N, 3.63. Found: C, 57.35; H, 5.88; N, 3.86.

Ethyl 4-(2-Bromo-4-methylphenylamino)-2-hydroxy-2-methyl-4-phenylbutanoate (**5mN**: Diastereomer A): ^{1}H-NMR ($CDCl_3$) δ: 1.24 (t, 3H, J=7.2 Hz), 1.45 (s, 3H), 2.18 (s, 3H), 2.21 (dd, 1H, J=9.3, 14.7 Hz), 2.32 (dd, 1H, J=4.5, 14.7 Hz), 4.02—4.17 (m, 2H), 4.41 (dd, 1H, J=4.5, 9.3 Hz), 6.26 (d, 1H, J=8.1 Hz), 6.76 (d, 1H, J=8.1 Hz), 7.19—7.31 (m, 6H). HR-MS *m/z*; 405.0935 (Calcd for $C_{20}H_{24}NO_3Br$: 405.0940).

Ethyl 4-(2-Bromo-4-chlorophenylamino)-2-hydroxy-2-methyl-4-phenylbutanoate (**5nN**: Diastereomer A): ^{1}H-NMR ($CDCl_3$) δ: 1.24 (t, 3H, J=7.2 Hz), 1.44 (s, 3H), 2.22 (dd, 1H, J=9.3, 14.7 Hz), 2.32 (ddd, 1H, J=0.6, 4.5, 14.7 Hz), 3.63 (s, 1H), 4.00—4.20 (m, 2H), 4.32—4.40 (m, 1H), 5.63 (d, 1H, J=4.2 Hz), 6.20 (d, 1H, J=8.7 Hz), 6.90 (dd, 1H, J=2.4, 8.7 Hz), 7.20—7.35 (m, 5H), 7.38 (d, 1H, J=2.4 Hz). HR-MS *m/z*; 425.0388 (Calcd for $C_{19}H_{21}NO_3BrCl$: 425.0393).

Ethyl 4-(4-Chlorohenylamino)-2-hydroxy-2-methyl-4-phenylbutanoate (**8nN**): ^{1}H-NMR ($CDCl_3$) δ: 1.26 (t, 3H, J=7.2 Hz), 1.43 (s, 3H), 2.09—2.37 (m, 2H), 4.00—4.20 (m, 2H), 4.29 (dd, 1H, J=4.2, 9.6 Hz), 6.39 (d, 2H, J=8.7 Hz), 6.99 (d, 2H, J=8.7 Hz), 7.20—7.40 (m, 5H). HR-MS *m/z*; 347.1281 (Calcd for $C_{19}H_{22}NO_3Cl$: 347.1288).

Treatment of 2-Arylisoxazolidines with Lewis Acid. Typical Procedure To a benzene solution (25 ml) of a mixture of **3kA**, **3′ka**, **4kA**, and **4′kA** (288 mg, 1.0 mmol; 26 : 44 : 14 : 16 mixture, respectively), was added magnesium bromide etherate (260 mg, 1.0 mmol), and the mixture was heated to reflux for 3 h under nitrogen atmosphere with vigorous stirring. After cooling, water was added and extracted with chloroform several times. The combined organic solution was dried with anhydrous magnesium sulfate, from which the solvents were evapolated by rotary evapolator. Viscous yellow oily residue was passed through the column chromatography packed with silica gel using a mixed solvent of chloroform and ethanol to give butanoates (**5kA**), propanoates (**6kA**) and **4′kA** in 61% (224 mg), 14% (51 mg), and 13% (37 mg) yields, respectively.

Similarly, ethyl 2-hydroxy-2-methyl-4-(4-methylphenylamino)-4-phenylbutanoate (**8mN**) was obtained from **3mN**.

Ethyl 2-Hydroxy-2-methyl-4-(4-methylphenylamino)-4-phenylbutanoate (**8mN**): ^{1}H-NMR ($CDCl_3$) δ: 1.28 (t, 3H, J=7.2 Hz), 1.45 (s, 3H), 2.14 (dd, 1H, J=9.6, 14.7 Hz), 2.18 (s, 3H), 2.30 (dd, 1H, J=3.9, 14.7 Hz), 4.13 (q, 1H, J=7.2 Hz), 4.16 (q, 1H J=7.2 Hz), 4.37 (dd, 1H, J=3.9, 9.6 Hz), 6.45 (d, 2H, J=8.4 Hz), 6.89 (d, 2H, J=8.4 Hz), 7.19—7.31 (m, 5H). HR-MS *m/z*; 327.1832 (Calcd for $C_{20}H_{25}NO_3$: 327.1834).

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