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Highly *lk*-Selective Asymmetric Nitrile Oxide Cycloadditions to a C_2-Symmetric 1,3-Diacryloyl-2,2-dimethylimidazolidine and 4-Chiral 3-Acryloyl-2,2-dialkyloxazolidines

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Abstract: 1,3-Dipolar cycloadditions of benzonitrile oxide to the acrylamides derived from a C_2-symmetric 2,2-dimethylimidazolidine and 4-chiral 2,2-dialkyloxazolidines show high *lk*-diastereoselectivities. Easy separation of the major *lk*-isomers from the minor *ul*-diastereomers is followed by reductive removal of the chiral auxiliaries to produce optically pure 2-isoxazoline-5-methanols. Absolute diastereoselectivities were recorded in the nitrile oxide cycloadditions of 3-acryloyl-2,2-dialkyl-4-(diphenylmethyl)oxazolidines at 0 °C.

In the preceding paper of this issue, we have synthesized several new chiral auxiliaries based on the control of relative conformational stability.[1] They include a C_2-symmetric 2,2-dimethylimidazolidine and 4-chiral 2,2-dialkyloxazolidines. Their *N*-acryloyl derivatives are expected to be especially useful for the asymmetric reactions performed without the aid of metal catalyst.

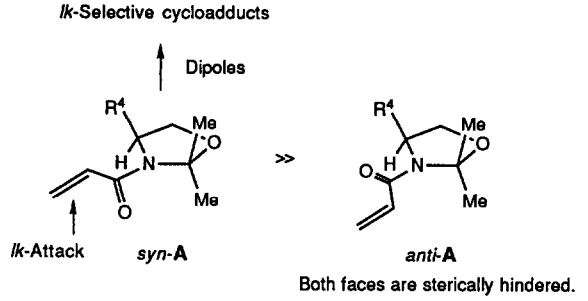


Figure 1. *lk*-Selective cycloaddition by the aid of conformation controlled chiral auxiliaries.

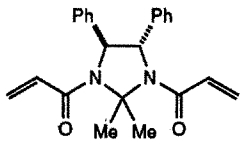
As shown in Fig. 1 with the example of 3-acryloyl-2,2-dimethyloxazolidines **A**, *syn*-conformers *syn*-**A** with respect to the amide nitrogen-carbonyl carbon bond are more highly stabilized than *anti*-**A**. The *s-cis*-conformation is more favored as to the rotation around the sp^2-sp^2 bond of *N*-acryloyl moiety. Accordingly, the sterically least hindered approach by a nucleophile (or a dipole) will occur from the side opposite to the R^4 substituent. The efficiency of chiral shielding by R^4 can be estimated with the magnetic shielding when R^4 is benzylic. Conformational analysis by ^1H NMR spectroscopy indicates that diphenylmethyl substituent as R^4 should work as a sufficient shielding substituent.

In the present paper, we have examined nitrile oxide dipolar cycloadditions to **A** in order to evaluate their utility in asymmetric synthesis in the absence of metal additive. Nitrile oxide is one of the most reactive dipoles and undergoes exclusively regioselective cycloadditions with terminal olefins to give 5-substituted 2-isoxazolines, e.g. 2-isoxazoline-5-carboxamides from **A**. Accordingly, nitrile oxide should behave as one of the least bulky dipoles to chiral acrylamide. Generally speaking, it has been quite difficult to establish highly diastereoselective nitrile oxide cycloadditions.

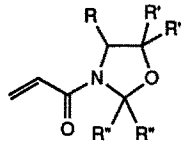
Nitrile oxide cycloaddition to olefinic dipolarophiles offers the best entry to 2-isoxazoline heterocycles whose synthetic utility is based on their transformation to β-hydroxy ketones (aldols) through the reductive cleavage of the oxygen-nitrogen bond.[2] This adds an important advantage to the asymmetric nitrile oxide cycloaddition methodology.

RESULTS AND DISCUSSION

The Curran's acrylamide[3] and the Oppolzer's chiral sultams[4,5] have demonstrated the exclusive or highly diastereoselective nitrile oxide cycloadditions, while the Evans' acrylamide and the Katsuki's C_2-symmetric amide were poor in selectivity.[1] Eleven acrylamides **1** and **2a-k** were employed in the present work (Scheme 1). Their synthesis, structural elucidation, and conformational analysis were already discussed in the preceding paper.[1]



(*S,S*)-**1**



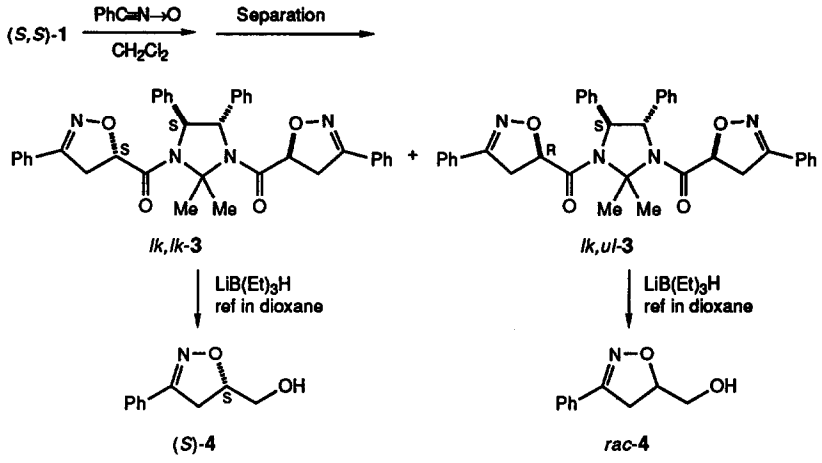
2a-k

a: R = Ph, R' = H, R" = Me
b: R = Ph, R' = H, R"$_2$ = $(CH_2)_5$
c: R = *i*-Pr, R' = H, R" = Me
d: R = $PhCH_2$, R' = H, R" = Me
e: R = $PhCH_2$, R' = R" = Me
f: R = $PhCH_2$, R' = Me, R" = Et
g: R = R" = $PhCH_2$, R' = Me
h: R = $PhCH_2$, R' = Me, R"$_2$ = $(CH_2)_5$
i: R = Ph_2CH, R' = H, R" = Me
j: R = Ph_2CH, R' = H, R"$_2$ = $(CH_2)_5$
k: R = 9-Fluorenyl, R' = H

Scheme 1.

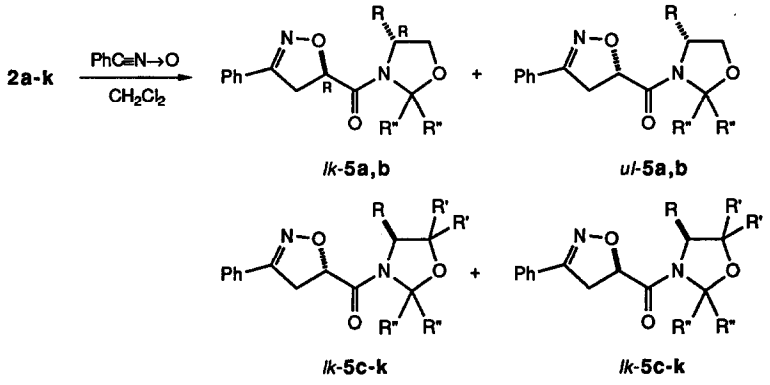
The reaction of optically pure 1,3-diacryloyl-2,2-dimethylimidazolidine (*S,S*)-**1** with excess benzonitrile oxide at –78 °C in dichloromethane gave an 83:17 mixture of diastereomeric cycloadducts **3** in 97% yield (Scheme 2 and Table 1, entry 1). Higher reaction temperatures (0 °C and room temperature) lowered selectivity, but only in a small degree (entries 2 and 3). These two diastereomeric cycloadducts, later assigned to be *lk,lk*-**3** and *lk,ul*-**3** on the basis of chemical transformations, were readily separated from each other in optically pure forms by a usual procedure of silica gel column chromatography. The major diastereomer was contained in a less polar eluent. Based on the ^1H NMR analysis, the major diasteromer *lk,lk*-**3** has a symmetric structure and the minor one *lk,ul*-**3** unsymmetric. Therefore, the total selectivity was calculated to be 91:9.

The imidazolidine chiral auxiliary was removed off from the optically pure major diastereomer *lk,lk*-**3** by treatment with lithium triethylborohydride to give (*S*)-3-phenyl-2-isoxazoline-5-methanol (*S*)-**4**. This removal procedure needed rather severe reaction conditions like heating under reflux in dioxane. The absolute configuration of (*S*)-**4** was determined by comparison of its optical rotation with the reported value.[6] To our



Scheme 2.

disappointment, however, some racemization occurred in this transformation (96% ee, checked by chiral HPLC using a Daicel Chiralcel^{R} OB with hexane - 2-propanol 3:1 v/v) and the yield of this transformation was poor (42%). This may be due to the severe reduction conditions employed. Use of tetrahydrofuran (THF) as solvent instead of dioxane in the reduction with lithium triethylborohydride, even under reflux, mostly recovered the starting *lk,lk*-**3**. Reduction with sodium borohydride, either at room temperature or under reflux in ethanol, also resulted in a quantitative recovery of *lk,lk*-**3**. Similar reduction of the minor diastereomer *lk,ul*-**3** gave *rac*-**4** (Scheme 2).



a: R = Ph, R" = Me
b: R = Ph, R"$_2$ = $(CH_2)_5$
c: R = *i*-Pr, R' = H, R" = Me
d: R = $PhCH_2$, R' = H, R" = Me
e: R = $PhCH_2$, R' = R" = Me
f: R = $PhCH_2$, R' = Me, R" = Et
g: R = R" = $PhCH_2$, R' = Me
h: R = $PhCH_2$, R' = Me, R"$_2$ = $(CH_2)_5$
I: R = Ph_2CH, R' = H, R" = Me
j: R = Ph_2CH, R' = H, R"$_2$ = $(CH_2)_5$
k: R = 9-Fluorenyl, R' = H

Scheme 3.

Substituents for the purpose of chiral shielding, attached at 4-position of the C_2-symmetric imidazolidine diacrylamide (*S,S*)-**1**, are phenyl groups. The oxazolidine acrylamides (*R*)-**2a** and *rac*-**2b**, derived from (*R*)- and *rac*-2,2-dimethyl-4-phenyloxazolidines, respectively, also bear a phenyl chiral shielding substituent. They showed almost equivalent diastereofacial selectivities in the reactions with benzonitrile oxide (ds = 87 to 85%, entries 4-6, Scheme 3). Little temperature dependence of selectivity was again observed in these cases (entries 4 vs 5). Acrylamide (*S*)-**2c** with an isopropyl substituent resulted in even worse selectivities (entry 7). Therefore, phenyl and isopropyl groups are not very suitable as a chiral shielding substituent.

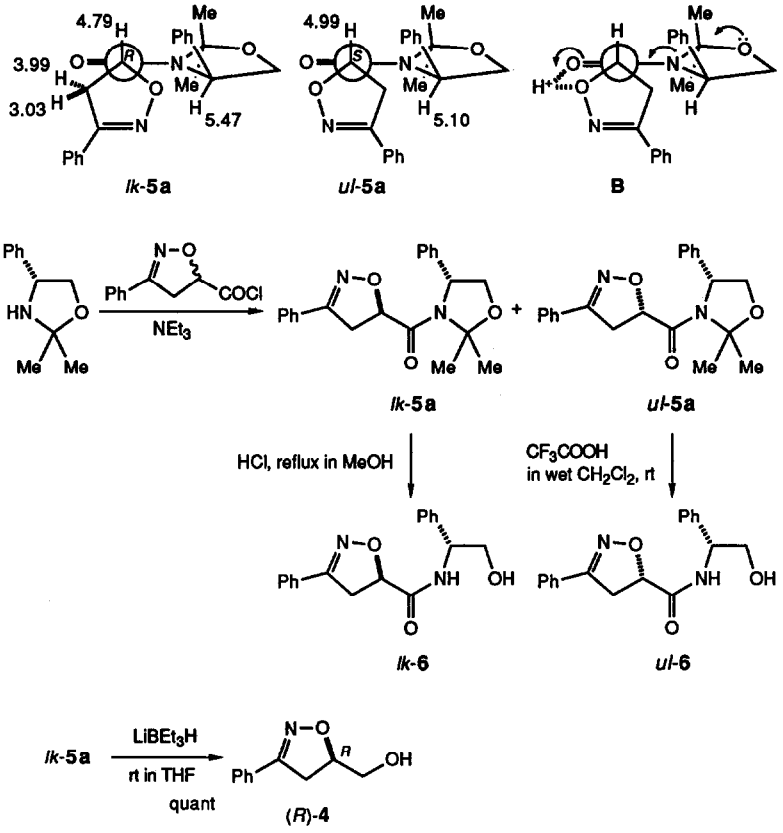
Table 1. Nitrile Oxide Cycloadditions of 1,3-Diacryloyl-2,2-dimethylimidazolidine **1** and 3-Acryloyl-2,2-dialkyloxazolidines **2a-k**[a]

Entry	Dipolarophile **1, 2a-k**	PhCNO[b] equiv	Temp/°C	Time/h	Product **3, 5a-k**	Yield/%[c]	Isomer ratio[d] *lk:ul*
1	**1**	3	–78	24	**3**	97	83:17 (91:9)[e]
2	**1**	3	0	5	**3**	quant	80:20 (90:10)[e]
3	**1**	3	rt	3	**3**	quant	80:20 (90:10)[e]
4	**2a**	2	–50	8	**5a**	95	87:13
5	**2a**	0.7	0	2	**5a**	quant[f]	85:15
6	**2b**	2	0	7	**5b**	97	87:13
7	**2c**	1.25	rt	0.5	**5c**	94	83:17
8	**2d**	1	0	8	**5d**	95	68:32
9[g]	**2d**	1	–30	41	**5d**	78 (23)	70:30
10[g]	**2e**	1	–30	42	**5e**	77 (21)	93:7
11	**2e**	1	0	16	**5e**	99	93:7
12[h]	**2e**	1	0	2	**5e**	99	93:7
13	**2f**	1	–50	83	**5f**	88	86:14
14	**2f**	1	0	5	**5f**	88	81:19
15[i]	**2f**	1	0	5.5	**5f**	87	82:18
16	**2g**	1	0	4	**5g**	99	83:17
17	**2h**	1	0	4	**5h**	87	93:7
18	**2h**	1	rt	1	**5h**	99	90:10
19	**2i**	1	0	3	**5i**	99	>99:1
20	**2j**	1	0	3	**5j**	quant	>99:1
21	**2j**	1	–50	70	**5j**	90	>99:1
22	**2k**	1	0	7	**5k**	quant	76:24

[a]All reactions were performed in dichloromethane unless otherwise stated. [b]Generated in situ from benzohydroximoyl chloride and triethylamine. [c]Yield of the isolated mixture of diastereomers. The yield in parenthesis is for the recovered **2**. [d]Determined by ^{1}H NMR spectrum (270 MHz) or HPLC (Hibar LiChrosorb[R] Si 60, Cica-Merck) of the crude reaction mixture. [e]Calculated diastereofacial selectivity. [f]Based on the benzohydroximoyl chloride used. [g]Quenched by 3-buten-2-one to trap the unreacted nitrile oxide. [h]Solvent: hexane. [i]Solvent: acetonitrile.

Structure of **5a** was determined on the basis of the discussion summarized in Scheme 4. The major and minor cycloadducts, assigned later as *lk*-**5a** and *ul*-**5a**, respectively, were readily separated from each other by silica gel column chromatography.[7] Although the minor diastereomer *ul*-**5a** underwent quick hydrolysis at room temperature in the presence of trifluoroacetic acid to give *ul*-**6**, the major one *lk*-**5a** resisted hydrolysis under the identical conditions. Reflux in methanol with concentrated HCl was needed to cause hydrolysis to lead to *lk*-**6**. Authentic samples of both *lk*-**5a** and *ul*-**5a** could be prepared by reaction of *rac*-3-phenyl-2-isoxazoline-5-carbonyl chloride with (*R*)-2,2-dimethyl-4-phenyloxazolidine in the presence of triethylamine. Such quick hydrolysis of the minor isomer *ul*-**5a** was conveniently applied to separate the major isomer *lk*-**5a**

from the mixture. The crude reaction mixture was simply treated with aqueous trifluoroacetic acid at room temperature in dichloromethane for a while. After evaporation of the solvents, the residue was filtered through a short silica gel column to give pure *lk*-**5a**. Such relative stability against hydrolysis holds true for other cycloadducts discussed in this work, and hence similar separation procedure can be applied as well.



Scheme 4.

The major diastereomer *lk*-**5a**, after being separated from the minor product *ul*-**5a** by column chromatography, was readily reduced by lithium triethylborohydride at room temperature in THF to give (*R*)-**4** in a quantitative yield (Scheme 4). No any racemization took place in this removal procedure. Such ready removal of the oxazolidine chiral auxiliary without racemization makes a striking contrast with the high stability of *lk,lk*-**3** mentioned in Scheme 2. This offers a high synthetic advantage of the oxazolidine chiral auxiliaries over the aforementioned imidazolidine controlling moiety.

However, a similar reduction of the minor cycloadduct *ul*-**5a** was unsuccessful, presumably due to its high susceptibility to the ring opening. Thus, (*R*)-3-phenyl-2-isoxazoline-5-methanol [(*R*)-**4**] is quantitatively available in an optically pure form from *lk*-**5a**. Its antipode (*S*)-**4** can be only obtained with the optical purity of 96% ee from *lk,lk*-**3**. Optical purities of these alcohol derivatives were confirmed by the chiral HPLC analysis employed above.

Inspection of ^{1}H NMR spectra of diastereomeric cycloadducts *lk*-**5a** and *ul*-**5a** provided us some important informations on the relative stability of conformers. Most favored conformations for *lk*-**5a** and *ul*-

5a are as follows: Based on the steric consideration, as already discussed in the preceding paper,[1] **5a** should occupy a *syn*-conformation with respect to the nitrogen-carbonyl carbon bond. To minimize the steric repulsion between the isoxazoline ring and the 4-phenyl substituent, the ring should stay with its major part away from the phenyl group. Such assumed conformation is well consistent with the following spectral data: Although both of 4-CH_2 of the isoxazoline ring of *ul*-**5a** are magnetically equivalent (H-4': δ = 3.48), those of *lk*-**5a** show very different chemical shifts (H-4': 3.99 and 4.79). The proton *trans* to H-5' (δ = 3.99), so close to the adjacent carbonyl oxygen, is much more deshielded than the other (3.03). This is due to the carbonyl anisotropy (Scheme 4). H-4 (5.47) of the oxazolidine ring of *lk*-**5a** is highly deshielded by the proximate isoxazoline oxygen, compared with that (5.10) of *ul*-**5a**. Such magnetic deshielding-conformational stability relationship can be conveniently applied to assign minor diastereomers of other cycloadducts. Chemical shifts for the indicator signals of diastereomers **5a-j** are listed in Table 2.

Table 2. ^{1}H NMR Spectra of the Major *lk*-**5a-k** and Minor Cycloadducts *ul*-**5a-k**.[a]

Product	Oxazolidine's ring protons			Isoxazoline's ring protons		
Major/minor	H-4	H-5 (*cis*)[b]	H-5 (*trans*)[b]	H-4' (*cis*)[c]	H-4' (*trans*)[c]	H-5'
lk-**5a**/*ul*-**5a**	5.47/5.10	4.44/4.41	3.97/3.98	3.03/3.48	3.99/3.48	4.79/4.99
lk-**5b**/*ul*-**5b**	5.47/5.08	4.39/4.37	3.94/3.96	3.00/3.49	3.98/3.49	4.80/4.98
lk-**5c**/*ul*-**5c**	4.23/3.90	3.99/3.98	3.99/3.98	3.36/3.46	4.12/3.87	5.35/5.23
lk-**5d**/*ul*-**5d**	4.61/4.27	3.97/3.80	3.89/3.94	3.04/3.50	3.98/4.12	4.78/5.41
lk-**5e**/*ul*-**5e**	4.27/4.25	–[d]	–[d]	2.47/3.47	3.69/3.88	3.84/5.16
lk-**5f**/*ul*-**5f**	4.39/–[e]	–[d]	–[d]	2.64/–[e]	3.79/–[e]	4.21/–[e]
lk-**5g**/*ul*-**5g**	4.51/4.12	–[d]	–[d]	3.23/3.59	4.22/3.99	5.01/5.33
lk-**5h**/*ul*-**5h**	4.22/4.20	–[d]	–[d]	2.44/3.46	3.66/3.84	3.88/5.15
lk-**5i**/*ul*-**5i**	4.98/–[f]	4.09/–[f]	3.86/–[f]	2.41/–[f]	3.59/–[f]	3.78/–[f]
lk-**5j**/*ul*-**5j**	4.94/–[f]	4.03/–[f]	3.83/–[f]	2.37/–[f]	3.55/–[f]	3.80/–[f]
lk-**5k**/*ul*-**5k**	4.25/4.63[g]	4.25/3.78[g]	4.25/3.28[g]	2.59/3.59[g]	3.81/3.91[g]	3.99/5.29[g]

[a]Measured at room temperature. [b]The proton *cis* (or *trans*) to H-5. [c]The proton *cis* (or *trans*) to H-5'. [d]No corresponding hydrogen exists. [e]Minor product shows broad signals due to restricted rotations. [f]The reaction was absolutely *lk*-selective, no minor cycloadduct being formed. [g]Signals of the *syn*-conformer are given for *ul*-**5k** .

With the suggested stable conformation, it is easy to understand that *ul*-**5a** was much more reactive than *lk*-**5a** in acid-catalyzed hydrolysis. Protonation to the amide carbonyl oxygen is accelerated by the proximate isoxazoline oxygen, in the case of stabilized conformation of *ul*-**5a**, to make it easy for the C(2)-N(3) bond to open the oxazolidine ring, as shown with model **B** (Scheme 4).

The efficiency of chiral shielding by a benzyl substituent at 4-position was next examined (Table 1, entries 8-19). Several 4-benzyloxazolidine derivatives (*S*)-**2d-h** were employed for this purpose (Scheme 3). When no substituent exists at 5-position as seen in (*S*)-**2d**, the selectivities *lk*-**5d**/*ul*-**5d** were extremely poor (*lk*:*ul* ≤ 70:30, entries 8 and 9). However, the reactions of 4-benzyloxazolidine (*S*)-**2e,h** bearing two methyl groups at 5-position afforded satisfactory selectivities (entries 10-12, 17 and 18). The best value was *lk*:*ul* = 93:7 at 0 °C, and the same ratio at –30 °C. Such improvement of selectivity is consistent with the expectation, made in the previous paper on the basis of conformational analysis, that two methyl substituents at 5-position will stablize the synclinal conformation (with respect to the rotation around the C(4)-C(α) bond) more than the antiperiplanar conformation.[1] Acrylamides (*S*)-**2e,h** carrying methyl and pentamethylene substituents at 2-position, respectively, showed the identical diastereoselectivities (entries 11 and 17).

The 4-benzyloxazolidine (*S*)-**2f** bearing ethyl groups at 2-position showed much lower selectivities (ds = 86-81%, entries 13-15). It was expected at the early stage of this work that bulky substituents at 2-position

would increase the *syn/anti* conformer ratio and decrease the reaction rate in the *anti*-conformation. Therefore, the both factors would work to improve diastereoselectivity in favor for *lk*-attack. However, the conformer ratio of (*S*)-**2f** was as poor as 81:19 at –30 °C and the magnetic shielding by the 4-benzyl moiety was insufficient.[1] Consequently, it came out that the observed poor diastereoselectivities were again predictable on the basis of the result of conformational analysis.

The acrylamide (*S*)-**2g** bearing benzyl groups at 2-position was single conformer in the temperature range from room temperature to –80 °C, but magnetic shielding by the 4-benzyl substituent was not effective. This was explained by the steric instability of the flat amide structure.[1] Its cycloaddition reaction with benzonitrile oxide was actually very poor in selectivity (ds = 83%, entry 16), indicating that the distorted ground state structure is not useful to accomplish a high diastereofacial selectivity.

The acrylamide *rac*-**2k** bearing a 9-fluorenyl substituent exists as a 71:29 *syn/anti* conformer mixture at 0 °C (checked by ^{1}H NMR). Its reaction with benzonitrile oxide at the same temperature resulted in the diastereoselectivity of 76:24 (entry 22). It is certain that not only the low *syn/anti* conformer ratio but also the insufficient magnetic shielding by the 4-(9-fluorenyl) substituent lowered the diastereoselectivity.

To our great delight, 3-acryloyl-4-(diphenylmethyl)oxazolidines *rac*-**2i,j** recorded the absolute diastereoselectivities in favor of the formation of *lk*-**5i,j** when the reactions with benzonitrile oxide were performed at 0 °C or below (entries 19-21). These isoxazolines *lk*-**5i,j** were used as racemates because optical resolution of *rac*-**2i,j** was not successful yet. Their optical resolution is under way and the result will be soon reported elsewhere.

It was found that polarity of reaction solvent was not so important in the above asymmetric nitrile oxide cycloadditions. The benzonitrile oxide employed in this work was generated in situ from benzohydroximoyl chloride and triethylamine. Since most of cycloadditions were performed in dichloromethane solution, the reaction was homogeneous and the triethylammonium chloride was always in solution. Use of hexane or acetonitrile as reaction solvent gave essentially the equivalent results (entries 12 and 15). A more polar medium certainly stabilizes the polarized amide structure so that the rotation barrier with respect to the amide nitrogen-carbonyl carbon bond may increase. In the asymmetric nitrile oxide cycloadditions using acrylamides **1** and **2**, however, the most important is the efficiency of chiral shielding by the 4-substituent. It is not surprising that no polarity effect is working in the conformation of such nonfunctionalized 4-substituents. Probably, the charge transfer from the benzylic substituent at 4-position to the *N*-acryloyl moiety is not important in the present reactions.

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EXPERIMENTAL

General. Melting points were recorded on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken with JASCO IRA-1 and A-702 spectrometers. ^{1}H and ^{13}C NMR spectra were recorded with JEOL JNM EX-90 (^{1}H NMR: 90 MHz) and JEOL GSX-270 (270 MHz for ^{1}H NMR and 67.94 MHz for ^{13}C NMR) instruments. Chemical shifts are reported in parts per million downfield (δ) from internal tetramethylsilane at 27 °C unless otherwise stated. Mass spectra were recorded with a JEOL-01SG-2 spectrometer. Ionization energy of 75 eV was employed unless otherwise stated. Elemental analyses were performed with a Hitachi 026 CHN analyzer. Optical rotations were recorded with a Horiba SEPA-200 polarimeter. High performance liquid chromatography (HPLC) was performed on TOSOH SC-8010 or JASCO FAMILIC-300S equipped with a column Hibar LiChrosorb^R Si 60 (Cica MERCK). Chiral HPLC was performed with Chiralcel^R OB and OD (both Dicel). Flash chromatography was performed with an Eyera EF-10 apparatus on a 20 x 180 mm column packed with 0.04-0.063 mm silica gel 60. For preparative column chromatography, Merck silica gel 60 was used.

Cycloaddition of Benzonitrile Oxide with (S,S)-1 Leading to lk,lk-3 and lk,ul-3. To a solution of benzohydroximoyl chloride (0.104 g, 0.9 mmol) in CH_2Cl_2 (5 ml) was added at 0 °C Et_3N (0.13 ml, 0.9 mmol). After 10 min at 0 °C, (*S,S*)-1 (0.108 g, 0.3 mmol) in CH_2Cl_2 (5 ml) was added. The mixture was stirred at room temperature for 8 h (the reaction was monitored by silica gel TLC), poured to saturated aqueous NH_4Cl, and then extracted with CH_2Cl_2 (3 x 15 ml). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue was chromatographed on silica gel to give the major cycloadduct *lk,lk*-3 (0.147 g, 83%) when eluted with CH_2Cl_2-EtOAc (35:1 v/v) and the minor product *lk,ul*-3 (0.036 g, 17%) when eluted with CH_2Cl_2-EtOAc (20:1 v/v). According to the ^1H NMR analysis of the crude reaction mixture, the diastereoselectivity was 83:17.

(4S,5S)-2,2-Dimethyl-4,5-diphenyl-1,3-bis[(5S)-3-phenyl-2-isoxazoline-5-carbonyl]imidazolidine (lk,lk-3): Colorless prisms (chloroform); mp 309-310 °C; $[\alpha]_D^{25} = -406.5°$ (c = 1.08, $CHCl_3$); IR (KBr) 2900, 1625, 1350, 1280, 890, 840, 750, and 650 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 2.23 (6H, s, Me), 3.01 (2H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(cis)}$ = 11.7 Hz, one of H-4'), 4.01 (2H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(trans)}$ = 7.3 Hz, the other of H-4'), 4.79 (2H, dd, $J_{5'\text{-}4'}$ = 11.7 and 7.3 Hz, H-5'), 5.69 (2H, s, H-4 and H-5), and 7.35-7.61 (20H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 24.23 (each Me), 36.25 (C-4'), 68.64 (C-4 and C-5), 79.13 (C-5'), 84.88 (C-2), 126.17, 126.86, 128.66, 128.69, 128.91, 129.61, 130.38, 140.80 (each Ph), 157.14 (C-3'), and 165.88 (NCO); MS (rel intensity, %) *m/z* 598 (M^+, 3), 584 (28), 583 (68), 410 (26), 279 (14), 237 (27), 222 (51), 146 (base peak), 118 (28), 103 (30), and 77 (37). Anal. Calcd for $C_{37}H_{34}N_4O_4$: C, 74.23; H, 5.72; N, 9.36%. Found: C, 73.78; H, 5.75; N, 9.35%.

(4S,5S)-2,2-Dimethyl-4,5-diphenyl-1-[(5R)-3-phenyl-2-isoxazoline-5-carbonyl]-3-[(5S)-3-phenyl-2-isoxazolin-5-carbonyl]imidazolidine (lk,ul-3): Colorless needles (*i*-PrOH); mp 220-221 °C; $[\alpha]_D^{24} = 118.8°$ (c = 0.73, $CHCl_3$); IR (KBr) 2900, 1630, 1350, 1280, 880, 850, 740, and 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 2.12, 2.26 (each 3H, s, Me), 3.06 (1H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 3.28-3.47 (2H, m, H-4'), 4.03 (1H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(trans)}$ = 7.7 Hz, the other of H-4'), 4.82 (1H, dd, $J_{5'\text{-}4'}$ = 11.0 and 7.7 Hz, one of H-5'), 5.02 (1H, m, the other of H-5'), 5.41 (1H, br, H-4 or H-5), 5.94 (1H, d, $J_{4\text{-}5}$ = 2.2 Hz, H-5 or H-4), 7.33-7.78 (20H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 24.55, 29.70 (each Me), 36.28, 39.35 (each C-4'), 67.44, 69.03 (C-4 and C-5), 78.03, 79.26 (each C-5'), 84.33 (C-2), 125.84, 126.10, 126.84, 126.88, 128.59, 128.64, 128.72, 129.30, 129.63, 130.29, 130.44, 139.58, 141.00 (each Ph), 155.47, 157.19 (each C-3'), 165.19, and 167.69 (each NCO); MS (rel intensity, %) *m/z* 598 (M^+, 7), 584 (29), 583 (70), 425 (21), 424 (51), 423 (13), 368 (16), 320 (28), 279 (25), 277 (10), 222 (13), 180 (22), 147 (29), 146 (base peak), and 103 (21). Anal. Calcd for $C_{37}H_{34}N_4O_4$: C, 74.23; H, 5.72; N, 9.36%. Found: C, 74.59; H, 5.92; N, 9.52%.

Removal of the Chiral Auxiliary from lk,lk-3 Leading to (S)-4. To a solution of *lk,lk*-3 (0.147 g, 0.25 mmol) in dry dioxane (2 ml) was added, at room temperature under nitrogen, $LiB(Et)_3H$ (1 M solution in THF, 1 ml, 1 mmol) by the aid of a syringe. The mixture was heated under reflux for 0.5 h and the addition of water (2 ml) and aqueous H_2O_2 (30%, 2 ml) was followed. The resulting mixture was stirred at room temperature for 0.5 h and extracted with CH_2Cl_2 (3 x 15 ml). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue was chromatographed on silica gel with hexane-EtOAc (2:1 v/v) to give (*S*)-4 (0.037 g, 84%). Optical purity of this sample (*S*)-4 was determined to be 98:2 (96% ee) by a chiral HPLC on Dicel Chiralcel^R OB (hexane-*i*-PrOH 3:1 v/v). Its spectral data are described below together with those of (*R*)-4.

Removal of the Chiral Auxiliary from lk-5a Leading to (R)-4. To a solution of *lk*-5a (0.105 g, 0.3 mmol) in dry THF (2 ml) was added, at room temperature under nitrogen, $LiB(Et)_3H$ (1 M solution in THF, 1.8 ml, 1.8 mmol) by the aid of a syringe. The mixture was stirred at room temperature for 5 min and the addition of water (2 ml) and aqueous H_2O_2 (30%, 2 ml) was followed. The resulting mixture was stirred at room temperature for 0.5 h and extracted with CH_2Cl_2 (3 x 15 ml). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue was chromatographed on silica gel with hexane-EtOAc (2:1 v/v) to give optically pure (*S*)-4 (0.06 g, quant, checked by the same chiral HPLC as above).

(5S)- and (5R)-3-Phenyl-2-isoxazoline-5-methanol [(S)-4 and (R)-4]: Colorless plates (hexane); mp 78-79 °C; (*S*)-4 (96% ee): $[\alpha]_D^{25} = 169.1°$ (c = 0.41, $CHCl_3$); (*R*)-4: $[\alpha]_D^{25} = -172.8°$ (c = 0.63, $CHCl_3$); IR (KBr) 3300, 1440, 1350, 1040, 910, 890, 800, 750, and 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 2.48 (1H, br, OH), 3.28 (1H, dd, J_{gem} = 16.5 and $J_{4\text{-}5(trans)}$ = 8.1 Hz, one of H-4), 3.38 (1H, dd, J_{gem} = 16.5 and $J_{4\text{-}5(cis)}$ = 10.4 Hz, the other of H-4), 3.68 (1H, dd, J_{gem} = 12.1 and $J_{CH2\text{-}5}$ = 4.8 Hz, one of 5-CH_2), and 3.86 (1H, dd, J_{gem} = 12.1 and $J_{CH2\text{-}5}$ = 3.1 Hz, the other of 5-CH_2), 4.86 (1H, dddd, $J_{5\text{-}4}$ = 10.4, 8.1, $J_{5\text{-}CH2}$ = 4.8, and 3.1 Hz, H-5), 7.36-7.43, and 7.62-7.69 (5H, m,

Ph); ^{13}C NMR ($CDCl_3$) δ = 36.33 (C-4), 63.63 (CH_2), 81.29 (C-5) 126.72, 128.72, 129.28, and 130.20 (each Ph); MS (rel intensity, %) *m/z* 177 (M^+, 71), 146 (75), 145 (11), 118 (87), 117 (13), 104 (12), 103 (12), 91 (25), 78 (13), 77 (base peak), and 51 (28). Anal. Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90%. Found: C, 67.89; H, 6.37; N, 7.93%.

General Procedure for the Nitrile Oxide Cycloadditions of 2a-k Leading to 5a-k. As a typical example the reaction of (*R*)-**5a** is presented. To a solution of benzohydroximoyl chloride (0.156 g, 1 mmol) in CH_2Cl_2 (8 ml) was added at 0 °C Et_3N (0.14 ml, 1 mmol). After 10 min at 0 °C, the resulting mixture was transfered, by the use of a syringe, to the cooled flask (–50 °C) containing (*R*)-**5a** (0.116 g, 0.5 mmol) in CH_2Cl_2 (4 ml). The mixture was stirred at –50 °C for 8 h (the reaction was monitored by silica gel TLC), poured to saturated aqueous NH_4Cl, and then extracted with CH_2Cl_2 (3 x 15 ml). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue was chromatographed on silica gel to give the major cycloadduct *lk*-**5a** (0.149 g, 85%) when eluted with hexane-EtOAc (6:1 v/v) and *ul*-**5a** (0.018 g, 10%) when eluted with hexane-EtOAc (3:1 v/v). According to the ^1H NMR analysis of crude reaction mixture, the diastereoselectivity was 87:13.

Other cycloadditions were performed under the reaction conditions shown in Table 1. The yields as well as the diastereoselectivities are also summarized in Table 1.

(4R)-2,2-Dimethyl-4-phenyl-3-[(5R)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (lk-5a): Colorless prisms (hexane); mp 45-46 °C; $[\alpha]_D^{25}$ = –412.1° (*c* = 1.01, $CHCl_3$); IR (KBr) 2900, 1640, 1410, 1350, 1230, 1060, 880, 840, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.65, 1.90 (each 3H, s, Me), 3.03 (1H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(cis)}$ = 11.4 Hz, one of H-4'), 3.97 (1H, dd, J_{gem} = 9.0 and $J_{5\text{-}4(trans)}$ = 2.2 Hz, one of H-5), 3.99 (1H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(trans)}$ = 7.3 Hz, the other of H-4'), 4.44 (1H, dd, J_{gem} = 9.0 and $J_{5\text{-}4(cis)}$ = 6.6 Hz, the other of H-5), 4.89 (1H, dd, $J_{5'\text{-}4'}$ = 11.4 and 7.3 Hz, H-5'), 5.47 (1H, dd, $J_{4\text{-}5}$ = 6.6 and 2.2 Hz, H-4), 7.31-7.41, and 7.60-7.65 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 22.94, 25.23 (each Me), 36.20 (C-4'), 60.43 (C-5), 71.59 (C-4), 79.18 (C-5'), 96.70 (C-2), 126.40, 126.91, 128.13, 128.68, 128.78, 129.14, 130.33, 141.18 (each Ph), 157.14 (C-3'), and 165.16 (NCO); MS (rel intensity, %) *m/z* 351 (M^+ + 1, 10), 350 (M^+, 34), 319 (30), 205 (19), 177 (9), 147 (15), and 146 (base peak). Anal. Calcd for $C_{21}H_{22}N_2O_3$: C, 71.98; H, 6.33; N, 7.99%. Found: C, 71.93; H, 6.56; N, 7.81%.

(4R)-2,2-Dimethyl-4-phenyl-3-[(5S)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (ul-5a): Colorless needles (*i*-PrOH); mp 162-163 °C; $[\alpha]_D^{24}$ = –19.2° (*c* = 0.97, $CHCl_3$); IR (KBr) 2980, 1655, 1410, 1355, 1240, 890, 840, and 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.67, 1.91 (each 3H, s, Me), 3.48 (2H, d, $J_{4'\text{-}5'}$ = 9.7 Hz, H-4'), 3.98 (1H, dd, J_{gem} = 9.0 and $J_{5\text{-}4(trans)}$ = 2.2 Hz, one of H-5), 4.41 (1H, dd, J_{gem} = 9.0 and $J_{5\text{-}4(cis)}$ = 6.2 Hz, the other of H-5), 4.99 (1H, t, $J_{5'\text{-}4'}$ = 9.7 Hz, H-5'), 5.10 (1H, dd, $J_{4\text{-}5}$ = 6.2 and 2.2 Hz, H-4), and 7.26-7.58 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 23.17, 25.21 (each Me), 39.37 (C-4'), 61.01 (C-5), 71.83 (C-4), 78.59 (C-5'), 97.06 (C-2), 125.97, 126.85, 128.19, 128.61, 129.01, 129.08, 130.22, 140.56 (each Ph), 155.29 (C-3'), and 166.38 (NCO); MS (20 eV, rel intensity, %) *m/z* 351 (M^+ + 1, 11), 350 (M^+, 43), 319 (30), 205 12), 147 (16), and 146 (base peak). Anal. Calcd for $C_{21}H_{22}N_2O_3$: C, 71.98; H, 6.33; N, 7.99%. Found: C, 71.82; H, 6.31; N, 7.98%.

The authentic samples of *lk*-**5a** and *ul*-**5a** were prepared as follows: A solution of *rac*-3-phenyl-2-isoxazoline-5-carboxylic acid (0.105 g, 0.59 mmol) in thionyl chloride (3 ml) was stirred at room temperature for 6 h. The excess thionyl chloride was removed by evaporation in vacuo. The residue was dissolved in CH_2Cl_2 (1 ml) and the resulting solution was added to a mixture of (*R*)-2,2-dimethyl-4-phenyloxazolidine (0.106 g, 0.6 mmol) and Et_3N (0.17 ml, 1.2 mmol) in CH_2Cl_2 (1 ml). The mixture was stirred at 0 °C for 10 min, neutralized with saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2 (3 x 15 ml). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue was chromatographed on silica gel with hexane-EtOAc to give *lk*-**5a** (0.044 g, 20%) and *ul*-**5a** (0.037 g, 19%).

(4RS)-2,2-Pentamethylene-4-phenyl-3-[(5RS)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (lk-5b): Separated and purified by silica gel column chromatography using hexane-EtOAc (10:1 v/v). Colorless prisms (*i*-PrOH); mp 168-169 °C; IR (KBr) 2950, 1655, 1410, 1360, 1080, 890, 760, and 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.22-1.40, 1.49-1.84, 1.90-2.00 (8H, m, CH_2), 2.39 (1H, ddd, *J* = 13.2, 13.0, and 4.8 Hz, CH_2), 2.81 (1H, dt, *J* = 13.2, 13.2, and 5.1 Hz, CH_2), 3.00 (1H, dd, J_{gem}= 16.5 and $J_{4'\text{-}5'(cis)}$ = 11.2 Hz, one of H-4'), 3.94 (1H, dd, J_{gem} = 9.0 and $J_{5\text{-}4(trans)}$ = 2.0 Hz, one of H-5), 3.98 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(trans)}$ = 7.3 Hz, the other of H-4'), 4.39 (1H, dd, J_{gem} = 9.0 and $J_{5\text{-}4(cis)}$ = 6.4 Hz, the other of H-5), 4.80 (1H, dd, $J_{5'\text{-}4'}$ = 11.2 and 7.3 Hz, H-5'), 5.47 (1H, dd,

$J_{4\text{-}5}$ = 6.4 and 2.0 Hz, H-4), 7.26-7.41, and 7.60-7.64 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 23.02, 23.44, 24.69, 29.53, 33.38 (each CH_2), 36.18 (C-4'), 60.34 (C-5), 71.32 (C-4), 79.38 (C-5'), 98.37 (C-2), 126.37, 126.88, 128.03, 128.65, 128.81, 129.05, 130.28, 141.42 (each Ph), 157.12 (C-3'), and 165.37 (NCO); MS (rel intensity, %) *m/z* 391 (M^+ + 1, 17), 390 (M^+, 63), 347 (24), 245 (18), 244 (30), 217 (16), 216 (26), 175 (21), 174 (base peak), 161 (36), 146 (80), 145 (25), 128 (28), 120 (33), 119 (24), 118 (30), 104 (74), 103 (26), 99 (46), 91 (29), 81 (13), and 77 (49). Anal. Calcd for $C_{24}H_{26}N_2O_3$: C, 73.82; H, 6.71; N, 7.17%. Found: C, 73.99; H, 6.74; N, 7.27%.

(4RS)-2,2-Pentamethylene-4-phenyl-3-[(5SR)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (ul-5b): Separated and purified by silica gel column chromatography using hexane-EtOAc (4:1 v/v). Colorless prisms (*i*-PrOH); mp 194 -195 °C; IR (KBr) 2900, 1650, 1410, 1360, 1080, 890, 760, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.20-1.41, 1.48-1.84, 1.91-2.40 (8H, m, CH_2), 2.51 (1H, ddd, *J* = 13.2, 12.8, and 4.2 Hz, CH_2), 2.84 (1H, dt, *J* = 13.2, 13.2, and 4.8 Hz, CH_2), 3.49 (2H, d, $J_{4'\text{-}5'}$ = 9.9 Hz, H-4'), 3.96 (1H, dd, J_{gem} = 8.8 and $J_{5\text{-}4(trans)}$ = 2.2 Hz, one of H-5), 4.37 (1H, dd, J_{gem}= 8.8 and $J_{5\text{-}4(cis)}$ = 6.2 Hz, the other of H-5), 4.98 (1H, t, $J_{5'\text{-}4'}$ = 9.9 Hz, H-5'), 5.08 (1H, dd, $J_{4\text{-}5}$ = 6.2 and 2.2 Hz, H-4), and 7.26-7.59 (10H, m, Ph); MS (20 eV, rel intensity, %) *m/z* 391 (M^+ + 1, 15), 390 (M^+, 50), 347 (16), 240 (31), 217 (23), 216 (26), 174 (base peak), 161 (30), 146 (72), 128 (28), 120 (26), 118 (26), 104 (41), 99 (35), and 77 (42). Anal. Calcd for $C_{24}H_{26}N_2O_3$: C, 73.82; H, 6.71; N, 7.17%. Found: C, 73.82; H, 6.68; N, 7.15%.

(4S)-4-Isopropyl-2,2-dimethyl-3-[(5S)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (lk-5c): Separated and purified by silica gel column chromatography using hexane-EtOAc (13:1 v/v). Colorless liquid; $[\alpha]_D^{24}$ = 337.0° (*c* = 1.03, $CHCl_3$); IR (neat) 2980, 1660, 1420, 1355, 1240, 1070, 895, 760, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.99, 1.00 (each 3H, d, *J* = 7.0 Hz, *i*-Pr), 1.53, 1.69 (each 3H, s, Me), 2.05 (1H, m, *i*-Pr), 3.36 (1H, dd, J_{gem} = 16.7 and $J_{4'\text{-}5'(cis)}$ = 11.2 Hz, one of H-4'), 3.99 (2H, m, H-5), 4.12 (1H, dd, J_{gem} = 16.7 and $J_{4'\text{-}5'(trans)}$ = 7.3 Hz, the other of H-4'), 4.23 (1H, m, H-4), 5.35 (1H, dd, $J_{5'\text{-}4'}$ = 11.2 and 7.3 Hz, H-5'), 7.37-7.42, and 7.67-7.71 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 17.71, 19.88 (*i*-Pr), 22.61, 25.80 (each Me), 31.73 (*i*-Pr), 36.87 (C-4'), 61.77 (C-5), 64.94 (C-4), 79.18 (C-5'), 95.81 (C-2), 126.94, 128.71, 128.85, 130.35 (each Ph), 157.17 (C-3'), and 165.28 (NCO); MS (rel intensity, %) *m/z* 316 (M^+, 40), 301(21), 285 (33), 273 (37), 170 (27), 146 (base peak), 128 (36), 118 (26), 112 (51), 100 (44), 77 (35), and 59 (50). Anal. Calcd for $C_{18}H_{24}N_2O_3$: C, 68.33; H, 7.65; N, 8.85%. Found: C, 68.19; H, 7.63; N, 8.29%..

(4S)-4-Isopropyl-2,2-dimethyl-3-[(5R)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (ul-5c): Separated and purified by silica gel column chromatography using hexane-EtOAc (4:1 v/v). Colorless needles (hexane); mp 67-68 °C; $[\alpha]_D^{24}$ = –305.6° (*c* = 0.86, $CHCl_3$); IR (KBr) 2950, 1630, 1410, 1345, 1230, 1055, 880, and 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.98, 1.02 (each 3H, d, *J* = 7.0 Hz, *i*-Pr), 1.53, 1.73 (each 3H, s, Me), 2.36 (1H, m, *i*-Pr), 3.46 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(cis)}$ = 10.6 Hz, one of H-4'), 3.87 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(trans)}$ = 8.1 Hz, the other of H-4'), 3.90 (1H, m, H-4), 3.98 (2H, m, H-5), 5.23 (1H, dd, $J_{5'\text{-}4'}$ = 10.6 and 8.1 Hz, H-5'), 7.36-7.42, and 7.66-7.70 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 16.52, 19.94 (*i*-Pr), 22.69, 25.40 (each Me), 31.66 (*i*-Pr), 38.78 (C-4'), 62.43 (C-5), 63.94 (C-4), 78.54 (C-5'), 96.08 (C-2), 126.97, 128.71, 128.91, 130.29 (each Ph), 156.38 (C-3'), and 166.13 (NCO); MS (rel intensity, %) *m/z* 316 (M^+, 26), 301 (8), 285 (22), 273 (39), 170 (22), 146 (base peak), 128 (24), 118 (27), 112 (42), 100 (42), 77 (33), and 59 (45). Anal. Calcd for $C_{18}H_{24}N_2O_3$: C, 68.33; H, 7.65; N, 8.85%. Found: C, 68.22; H, 8.13; N, 8.29%.

(4S)-4-Benzyl-2,2-dimethyl-3-[(5S)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (lk-5d): Separated and purified by silica gel column chromatography using hexane-EtOAc (10:1 v/v). Colorless prisms (hexane); mp 46-48 °C; $[\alpha]_D^{24}$ = 204.8° (*c* = 1.58, $CHCl_3$); IR (KBr) 2950, 1640, 1420, 1355, 1240, 890, and 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.56, 1.80 (each 3H, s, Me), 2.92 (1H, dd, J_{gem} = 13.6 and $J_{CH2\text{-}4}$ = 8.3 Hz, one of $PhCH_2$), 3.04 (1H, dd, J_{gem} = 16.7 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 3.05 (1H, dd, J_{gem} =13.6 and $J_{CH2\text{-}4}$ = 6.6 Hz, the other of $PhCH_2$), 3.89 (1H, d, J_{gem} = 9.2 Hz, one of H-5), 3.97 (1H, dd, J_{gem} = 9.2 and $J_{5\text{-}4(cis)}$ = 4.8 Hz, the other of H-5), 3.98 (1H, dd, J_{gem} = 16.7 and $J_{4'\text{-}5'(trans)}$ = 7.3 Hz, the other of H-4'). 4.61 (1H, ddd, $J_{4\text{-}CH2}$ = 8.3, 6.6, and $J_{4\text{-}5(cis)}$ = 4.8 Hz, H-4), 4.78 (1H, dd, $J_{5'\text{-}4'}$ = 11.0 and 7.3 Hz, H-5'), 7.23-7.42, and 7.62-7.68 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 22.78, 26.84 (each Me), 36.51 (C-4'), 40.95 ($PhCH_2$), 58.46 (C-5), 67.56 (C-4), 79.08 (C-5'), 96.04 (C-2), 126.92, 127.07, 128.69, 128.79, 129.01, 129.51, 130.35, 137.32 (each Ph), 157.23 (C-3'), and 164.65 (NCO); MS (rel intensity, %) *m/z* 364 (M^+, 13), 274 (17), 276 (base peak), 160 (91), 146 (36), 118 (29), 117 (14), 103 (10), 100

(55), 91 (46), 83 (17), and 77 (26). Anal. Calcd for $C_{22}H_{24}N_2O_3$: C, 72.51; H, 6.64; N, 7.69%. Found: C, 72.54; H, 6.60; N, 7.77%.

(4S)-4-Benzyl-2,2-dimethyl-3-[(5R)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (ul-5d): Separated and purified by silica gel column chromatography using hexane-EtOAc (5:1 v/v). Colorless prisms (*i*-PrOH); mp 132-133 °C; $[\alpha]_D^{24} = -433.2°$ (c = 0.42, $CHCl_3$); IR (KBr) 3000, 1640, 1420, 1350, 1250, and 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.59, 1.74 (each 3H, s, Me x 2), 2.91 (1H, dd, J_{gem} = 13.2 and $J_{CH2\text{-}4}$ = 11.4 Hz, one of $PhCH_2$), 3.45 (1H, ddd, J_{gem} = 13.2, $J_{CH2\text{-}4}$ = 2.9, and $J_{CH2\text{-}5}$ = 1.8 Hz, the other of $PhCH_2$), 3.50 (1H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 3.80 (1H, ddd, J_{gem} = 9.2, $J_{5\text{-}4(cis)}$ = 4.8, and $J_{5\text{-}CH2}$ = 1.8 Hz, one of H-5), 3.94 (1H, d, J_{gem} = 9.2 Hz, the other of H-5), 4.12 (1H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(trans)}$ = 7.5 Hz, the other of H-4'), 4.27 (1H, ddd, $J_{4\text{-}CH2}$ = 11.4, 2.9, and $J_{4\text{-}5(cis)}$ = 4.8 Hz, H-4), 5.41 (1H, dd, $J_{5'\text{-}4'(cis)}$ = 11.0 and $J_{5'\text{-}4'(trans)}$ = 7.5 Hz, H-5'), 7.21-7.43, and 7.69-7.68 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 22.97, 26.62 (each Me), 38.11 (C-4'), 40.59 ($PhCH_2$), 60.04 (C-5), 66.45 (C-4), 79.77 (C-5'), 96.14 (C-2), 126.79, 127.01, 128.78, 129.53, 130.44, 138.14, (each Ph), 157.04 (C-3'), and 164.89 (NCO); MS (rel intensity, %) *m/z* 364 (M^+, 9), 274 (19), 273 (base peak), 160 (8), 146 (32), 118 (20), 117 (11), 100 (40), 91 (31), and 77 (19). Anal. Calcd for $C_{22}H_{24}N_2O_3$: C, 72.51; H, 6.64; N, 7.69%. Found: C, 72.18; H, 6.61; N, 7.70%.

(4S)-4-Benzyl-2,2,5,5-tetramethyl-3-[(5S)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (lk-5e): Separated and purified by silica gel column chromatography using hexane-EtOAc (12:1 v/v). Colorless prisms (hexane); mp 133-134 °C; $[\alpha]_D^{25} = -162.4°$ (c = 1.09, $CHCl_3$); IR (KBr) 2930, 1630, 1340, 890, 750, and 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.40, 1.48, 1.71, 1.82 (each 3H, s, Me), 2.47 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 2.88 (1H, dd, J_{gem} = 13.6 and $J_{CH2\text{-}4}$ = 10.6 Hz, one of $PhCH_2$), 3.01 (1H, dd, J_{gem} =13.6 and $J_{CH2\text{-}4}$ = 4.0 Hz, the other of $PhCH_2$), 3.69 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(trans)}$ = 7.5 Hz, the other of H-4'), 3.84 (1H, dd, $J_{5'\text{-}4'}$ = 11.0 and 7.5 Hz, H-5'), 4.27 (1H, dd, $J_{4\text{-}CH2}$ = 10.6 and 4.0 Hz, H-4), 7.20-7.37, and 7.54-7.59 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 23.96, 27.52, 28.57, 28.88 (each Me), 35.79 (C-4'), 38.27 ($PhCH_2$), 66.13 (C-4), 78.35 (C-5), 80.92 (C-5'), 94.78 (C-2), 126.82, 126.98, 128.59, 128.94, 129.11, 129.90, 130.15, 137.98, 157.12, and 165.64 (NCO); MS (rel intensity, %) *m/z* 392 (M^+, 15), 302 (21), 301 (base peak), and 243 (14). Anal. Calcd for $C_{24}H_{28}N_2O_3$: C, 73.44; H, 7.19; N, 7.14%. Found: C, 73.52; H, 7.22; N, 6.96%.

(4S)-4-Benzyl-2,2,5,5-tetramethyl-3-[(5R)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (ul-5e): Separated and purified by silica gel column chromatography using hexane-EtOAc (10:1 v/v). Colorless prisms (hexane); mp 46-47 °C; $[\alpha]_D^{24} = -309.4°$ (c = 0.57, $CHCl_3$); IR (KBr) 2980, 1660, 1415, 1360, 1070, 895, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.20, 1.36, 1.72, 1.74 (each 3H, s, Me), 3.10 (1H, dd, J_{gem} = 14.4 and $J_{CH2\text{-}4}$ = 19.5 Hz, one of $PhCH_2$), 3.30 (1H, dd, J_{gem} =14.4 and $J_{CH2\text{-}4}$ = 3.8 Hz, the other of $PhCH_2$), 3.47 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 3.88 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(trans)}$ = 7.7 Hz, the other of H-4'), 4.25 (1H, dd, $J_{4\text{-}CH2}$ = 9.5 and 3.8 Hz, H-4), 5.16 (1H, dd, $J_{5'\text{-}4'}$ = 11.0 and 7.7 Hz, H-5'), 7.15-7.40, and 7.64-7.68 (10H, m, Ph); MS (rel intensity, %) *m/z* 392 (M^+, 9), 377 (9), 302 (21), 301 (base peak), 243 (34), 204 (8), 173 (8), 162 (5), 146 (28), 128 (12), 118 (13), 91 (33), and 70 (15). Anal. Calcd for $C_{24}H_{28}N_2O_3$: C, 73.44; H, 7.19; N, 7.14%. Found: C, 73.52; H, 7.05; N, 7.15%.

(4S)-4-Benzyl-2,2-diethyl-5,5-dimethyl-3-[(5S)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (lk-5f): Separated and purified by silica gel column chromatography using hexane-EtOAc (15:1 v/v). Colorless prisms (hexane); mp 44-45 °C; $[\alpha]_D^{24} = 173.8°$ (c = 1.03, $CHCl_3$); IR (neat) 3000, 1655, 1420, 1360, 1150, 895, 735, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.92, 1.10 (each 3H, t, J = 7.5 Hz, Et), 1.37, 1.47 (each 3H, s, Me), 1.85 (1H, sex, J = 7.5 Hz, CH_2 of Et), 2.02-2.25 (2H, m, CH_2 of Et), 2.45 (1H, sex, J = 7.5 Hz, CH_2 of Et), 2.64 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 2.96 (1H, dd, J_{gem} = 13.9 and $J_{CH2\text{-}4}$ = 8.8 Hz, one of $PhCH_2$), 3.06 (1H, dd, J_{gem} =13.9 and $J_{CH2\text{-}4}$ = 5.5 Hz, the other of $PhCH_2$), 3.79 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(trans)}$ = 7.3 Hz, the other of H-4'), 4.21 (1H, dd, $J_{5'\text{-}4'}$ = 11.0 and 7.3 Hz, H-5'), 4.39 (1H, dd, $J_{4\text{-}CH2}$ = 8.8 and 5.5 Hz, H-4), 7.24-7.36, and 7.57-7.61 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 8.96, 9.42 (each Et), 24.68, 29.57 (each Me), 30.12, 32.83 (each Et), 36.01 (C-4'), 38.96 ($PhCH_2$), 65.83 (C-4), 78.73 (C-5), 80.80 (C-5'), 100.07 (C-2), 126.88, 126.94, 128.62, 128.97, 129.08, 129.60, 130.20, 138.08 (each Ph), 157.24 (C-3'), and 165.91 (NCO); MS (20 eV, rel intensity, %) m/z 420 (M+, 1), 392 (26), 391 (base peak), 329 (33), 243 (16), 218 (15), and 146 (5). Anal. Calcd for $C_{26}H_{32}N_2O_3$: C, 74.26; H, 7.67; N, 6.66%. Found: C, 74.51; H, 7.72; N, 6.71%.

The minor cycloadduct *ul-5f* is the mixture of rotational isomers based on the ^1H NMR spectrum recorded in $CDCl_3$ at room temperature. The data other than ^1H and ^{13}C NMR spectra are as follows: Separated and purified by silica gel column chromatography using hexane-EtOAc (8:1 v/v). Colorless liquid; $[\alpha]_D^{24} = -314.8$ ($c = 0.26$, $CHCl_3$); IR (neat) 2990, 1650, 1420, 1360, 1150, 900, 770, 740, and 700 cm^{-1}; MS (20 eV, rel intensity, %) *m/z* 420 (M^+, 1), 392 (26), 391 (base peak), 329 (33), 243 (7), 218 (11), 188 (3), and 146 (3). Anal. Calcd for $C_{26}H_{32}N_2O_3$: C, 74.26; H, 7.67; N, 6.66%. Found: C, 74.33; H, 7.63; N, 6.41%.

(4S)-2,2,4-Tribenzyl-5,5-dimethyl-3-[(5S)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (lk-5g): Separated and purified by silica gel column chromatography using hexane-EtOAc (12:1 v/v). Colorless prisms (hexane); mp 73-74 °C; $[\alpha]_D^{25} = 70.9°$ ($c = 1.01$, $CHCl_3$); IR (KBr) 3000, 1650, 1415, 1360, 1300, 1050, 900, 770, and 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.02, 1.46 (each 3H, s, Me), 1.41 (1H, dd, J_{gem} = 15.8 and $J_{CH2\text{-}4}$ =10.3 Hz, one of 4-$PhCH_2$), 1.88 (1H, dd, J_{gem} = 15.8 and $J_{CH2\text{-}4}$ = 3.7 Hz, the other of 4-$PhCH_2$), 2.85, 3.23, 3.54, 3.83 (each 1H, d, J_{gem} = 13.9 and 13.5 Hz, 2-$PhCH_2$), 3.23 (1H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 4.22 (1H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(trans)}$ = 7.0 Hz, the other of H-4'), 4.51 (1H, dd, $J_{4\text{-}CH2}$ = 10.3 and 3.7 Hz, H-4), 5.01 (1H, dd, $J_{5'\text{-}4'}$ = 11.0 and 7.0 Hz, H-5'), 6.91-6.94, 7.11-7.44, and 7.70-7.75 (15H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 24.75, 30.94 (each Me), 36.49 (C-4'), 37.19, 41.91, 43.33 (each $PhCH_2$), 64.35 (C-4), 79.25 (C-5'), 82.13 (C-5), 99.55 (C-2), 126.40, 126.78, 126.97, 127.93, 127.97, 128.45, 128.69, 128.78, 128.85, 129.48, 130.42, 131.36, 131.73, 137.16, 137.56, 138.12 (each Ph), 157.24 (C-3'), and 165.96 (NCO); MS (20 eV, rel intensity, %) *m/z* 456 (M^+, 1), 454 (33), 453 (base peak), 283 (2), 280 (9), and 162 (1). Anal. Calcd for $C_{36}H_{36}N_2O_3$: C, 79.38; H, 6.66; N, 5.14%. Found: C, 79.31; H, 6.76; N, 4.81%.

(4S)-2,2,4-Tribenzyl-5,5-dimethyl-3-[(5R)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (ul-5g): Separated and purified by silica gel column chromatography using hexane-EtOAc (12:1 v/v). Colorless prisms (*i*-PrOH); mp 93-94 °C; $[\alpha]_D^{24} = -244.2°$ ($c = 1.02$, $CHCl_3$); IR (KBr) 3000, 1650, 1500, 1410, 1355, 1300, 1260, 1175, 1145, 1090, 900, 850, 740, and 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 0.98, 1.39 (each 3H, s, Me), 1.21 (1H, dd, J_{gem} = 16.1 and $J_{CH2\text{-}4}$ = 11.7 Hz, one of 4-$PhCH_2$), 2.44 (1H, dd, J_{gem} = 16.1 and $J_{CH2\text{-}4}$ = 1.8 Hz, the other of 4-$PhCH_2$), 2.81, 3.18, 3.60, 3.91 (each 1H, d, J_{gem} = 13.9 and 13.6 Hz, 2-$PhCH_2$), 3.59 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 3.99 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(trans)}$ = 8.1 Hz, the other of H-4'), 4.12 (1H, dd, $J_{4\text{-}CH2}$ = 11.7 and 1.8 Hz, H-4), 5.33 (1H, dd, $J_{5'\text{-}4'}$ = 11.0 and 8.1 Hz, H-5'), 6.86-6.89, 7.08-7.44, and 7.70-7.75 (15H, m, Ph); MS (20 eV, rel intensity, %) *m/z* 456 (M^+, 1), 454 (34), 453 (base peak), 281 (2), 280 (12), and 162 (2). Anal. Calcd for $C_{36}H_{36}N_2O_3$: C, 79.38; H, 6.66; N, 5.14%. Found: C, 78.89; H, 6.67; N, 4.80%.

(4S)-4-Benzyl-5,5-dimethyl-2,2-pentamethylene-3-[(5S)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (lk-5h): Separated and purified by silica gel column chromatography using hexane-EtOAc (12:1 v/v). Colorless prisms (*i*-PrOH); mp 180-181 °C; $[\alpha]_D^{25} = 149.4°$ ($c = 1.06$, $CHCl_3$); IR (KBr) 2940, 1645, 1410, 1145, 900, 760, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ =1.41, 1.46 (each 3H, s, Me), 1.56-1.91, 2.51-2.76 (10H, m, CH_2), 2.44 (1H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 2.88 (1H, dd, J_{gem} = 13.6 and $J_{CH2\text{-}4}$ = 10.8 Hz, one of $PhCH_2$), 3.00 (1H, dd, J_{gem} =13.6 and $J_{CH2\text{-}4}$ = 4.0 Hz, the other of $PhCH_2$), 3.66 (1H, dd, J_{gem} = 16.9 and $J_{4'\text{-}5'(trans)}$ = 7.7 Hz, the other of H-4'), 3.88 (1H, dd, $J_{5'\text{-}4'}$ = 11.0 and 7.7 Hz, H-5'), 4.22 (1H, dd, $J_{4\text{-}CH2}$ = 10.8 and 4.0 Hz, H-4), 7.28-7.37, and 7.55-7.60 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 23.28, 23.40, 24.30, 24.88, 28.84, 33.26, 35.74 (each Me and CH_2), 37.48 (C-4'), 38.73 ($PhCH_2$), 66.92 (C-4), 78.74 (C-5), 80.62 (C-5'), 96.69 (C-2), 126.84, 126.94, 128.59, 129.07, 130.02, 130.13, 138.15 (each Ph), 157.17 (C-3'), and 165.97 (NCO); MS (20 eV, rel intensity, %) *m/z* 433 ($M^+ + 1$, 31), 432 (M^+, base peak), 404 (12), 389 (10), 342 (11), 341 (47), 329 (18), 287 (18), 285 (16), 259 (10), 168 (44), 146 (10), and 145 (23). Anal. Calcd for $C_{27}H_{32}N_2O_3$: C, 74.97; H, 7.46; N, 6.48%. Found: C, 75.07; H, 7.55; N, 6.26%.

(4S)-4-Benzyl-5,5-dimethyl-2,2-pentamethylene-3-[(5R)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (ul-5h): Separated and purified by silica gel column chromatography using hexane-EtOAc (12:1 v/v). Colorless liquid; $[\alpha]_D^{24}$ = –242.4° ($c = 1.04$, $CHCl_3$); IR (KBr) 2940, 1640, 1410, 1135, 890, 720, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.21, 1.34 (each 3H, s, Me), 1.50-1.78, 2.38-2.88 (10H, m, CH_2), 3.09 (1H, dd, J_{gem} = 14.7 and $J_{CH2\text{-}4}$ = 9.2 Hz, one of $PhCH_2$), 3.28 (1H, dd, J_{gem} = 14.7 and $J_{CH2\text{-}4}$ = 4.0 Hz, the other of $PhCH_2$), 3.46 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(cis)}$ = 11.4 Hz, one of H-4'), 3.84 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(trans)}$ = 7.7 Hz, the other of H-4'), 4.20 (1H, dd, $J_{4\text{-}CH2}$ = 9.2 and 4.0 Hz, H-4), 5.15 (1H, dd, $J_{5'\text{-}4'}$ = 11.4 and 7.7 Hz, H-5'), 7.31-7.40, and 7.64-7.67 (10H,

m, Ph); ^{13}C NMR ($CDCl_3$) δ = 23.08, 23.53, 24.81, 29.57, 33.78, 36.75 (each Me and CH_2), 38.53 (C-4'), 39.64 ($PhCH_2$), 66.22 (C-4), 79.28 (C-5), 80.92 (C-5'), 96.63 (C-2), 126.58, 126.94, 128.68, 128.79, 128.89, 129.07, 130.26, 138.47 (each Ph), 156.28 (C-3'), and 165.96 (NCO); MS (rel intensity, %) *m/z* 433 (M^+ + 1, 23), 432 (M^+, 74), 389 (25), 341 (59), 329 (20), 287 (21), 286 (31), 258 (20), 243 (30), 216 (52), 168 (base peak), 162 (26), 146 (45), 145 (72), 118 (25), and 91 (98). Anal. Calcd for $C_{27}H_{32}N_2O_3$: C, 74.97; H, 7.46; N, 6.48%. Found: C, 74.78; H, 7.53; N, 6.45%.

(4RS)-2,2-Dimethyl-4-diphenylmethyl-3-[(5RS)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (lk-5i): Purified by silica gel column chromatography using hexane-EtOAc (10:1 v/v). Colorless prisms (hexane); mp 155-156 °C; IR (KBr) 2950, 1640, 1410, 1235, 1055, 890, 745, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.57, 1.97 (each 3H, s, Me), 2.41 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 3.59 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(trans)}$ = 7.3 Hz, the other of H-4'), 3.78 (1H, dd, $J_{5'\text{-}4'}$ = 11.0 and 7.3 Hz, H-5'), 3.86 (1H, d, J_{gem} = 9.2 Hz, one of H-5), 4.09 (1H, dd, J_{gem} = 9.2 and $J_{5\text{-}4(cis)}$ = 4.8 Hz, the other of H-5), 4.27 (1H, d, $J_{CH\text{-}4}$ = 11.4 Hz, Ph_2CH), 4.98 (1H, dd, $J_{4\text{-}CH}$ = 11.4 and $J_{4\text{-}5(cis)}$ = 4.8 Hz, H-4), 7.21-7.43, and 7.54-7.58 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 22.91, 27.21 (each Me), 36.05 (C-4'), 54.30 (Ph_2CH), 61.06 (C-5), 67.96 (C-4), 78.27 (C-5'), 96.45 (C-2), 126.86, 127.18, 127.21, 128.61, 128.78, 128.88, 129.70, 130.22, 140.41, 141.06 (each Ph), 157.20 (C-3'), and 166.01 (NCO); MS (20 eV, rel intensity, %) *m/z* 440 (M^+, 0.8), 275 (20), 274 (18), 273 (base peak), 146 (3), and 100 (7). Anal. Calcd for $C_{28}H_{28}N_2O_3$: C, 76.34; H, 6.41; N, 6.36%. Found: C, 76.55; H, 6.53; N, 6.30%.

(4RS)-2,2-Pentamethylene-4-diphenylmethyl-3-[(5RS)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (lk-5j): Purified by silica gel column chromatography using hexane-EtOAc (12:1 v/v). Colorless prisms (hexane); mp 160-161 °C; IR (KBr) 2940, 1640, 1425, 1090, 890, 760, and 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.20-2.96 (10H, m, CH_2), 2.37 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 3.55 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(trans)}$ = 7.0 Hz, the other of H-4'), 3.80 (1H, dd, $J_{5'\text{-}4'}$ = 11.0 and 7.0 Hz, H-5'), 3.83 (1H, d, J_{gem} = 9.2 Hz, one of H-5), 4.03 (1H, dd, J_{gem} = 9.2 and $J_{5\text{-}4(cis)}$ = 4.4 Hz, the other of H-5), 4.27 (1H, d, $J_{CH\text{-}4}$ = 11.4 Hz, Ph_2CH), 4.94 (1H, dd, $J_{4\text{-}CH}$ = 11.4 and $J_{4\text{-}5(cis)}$ = 4.4 Hz, H-4), 7.15-7.45, and 7.50-7.60 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 23.17, 23.53, 24.65, 28.70, 35.97 (each CH_2), 36.03 (C-4'), 54.44 (Ph_2CH), 60.91 (C-5), 67.66(C-4), 78.50 (C-5'), 98.11(C-2), 126.86, 127.12, 127.17, 128.58, 128.71, 128.92, 128.98, 129.82, 130.18, 140.41, 141.06 (each Ph), 157.20 (C-3'), and 166.20 (NCO); MS (20 eV, rel intensity, %) *m/z* 384 (M^+, 1), 314 (21), 313 (base peak), 191 (1), 167 (1), and 140 (5). Anal. Calcd for $C_{31}H_{32}N_2O_3$: C, 77.47; H, 6.71; N, 5.83%. Found: C, 77.17; H, 6.92; N, 5.14%.

(4RS)-4-(9-Fluorenyl)-2,2-dimethyl-3-[(5RS)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (lk-5k): Separated and purified by silica gel column chromatography using hexane-EtOAc (8:1 v/v). Colorless plates (hexane); mp 143-144 °C; IR (KBr) 3000, 1640, 1420, 1355, 1240, 1130, 890, and 730 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.63, 1.96 (each 3H, s, Me), 2.59 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(cis)}$ = 10.6 Hz, one of H-4'), 3.81 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(trans)}$ = 7.7 Hz, the other of H-4'), 3.99 (1H, dd, $J_{5'\text{-}4'}$ = 10.5 and 7.7 Hz, H-5'), 4.25 (3H, m, H-5), 4.37 (2H, d, $J_{CH\text{-}4}$ = 8.4 Hz, fluorenyl CH), 7.24-7.57, and 7.74-7.80 (13H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 22.63, 23.08 (each Me), 36.21 (C-4'), 50.37 (fluorenyl CH), 60.26 (C-5), 67.90 (C-4), 79.02 (C-5'), 96.33 (C-2), 120.53, 120.63, 124.72, 126.49, 126.85, 127.05, 127.48, 128.10, 128.20, 128.59, 128.76, 130.23, 141.06, 141.58, 143.51, and 143.80 (Ph and Ar), 157.14 (C-3'), and 165.88 (NCO); MS (20 eV, rel intensity, %) *m/z* 439 (M^+, 2), 438 (M^+, 6), 274 (17), 273 (base peak), 178 (2), 146 (3), and 100 (8). Anal. Calcd for $C_{28}H_{26}N_2O_3$: C, 76.69; H, 5.98; N, 6.39%. Found: C, 77.34; H, 6.12; N, 6.09%.

(4RS)-4-(9-Fluorenyl)-2,2-dimethyl-3-[(5SR)-3-phenyl-2-isoxazoline-5-carbonyl]oxazolidine (ul-5k): Separated and purified by silica gel column chromatography using hexane-EtOAc (3:1 v/v). Colorless needles (*i*-PrOH); mp 210-211 °C; IR (KBr) 2990, 1650, 1430, 1355, 1080, 890, and 745 cm^{-1}; ^1H NMR ($CDCl_3$) *syn*: δ = 1.54, 1.72 (each 3H, s, Me), 3.28 (1H, dd, J_{gem} = 9.5 and $J_{5\text{-}4(trans)}$ = 2.6 Hz, one of H-5), 3.59 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(cis)}$ = 11.0 Hz, one of H-4'), 3.78 (1H, dd, J_{gem} = 9.5 and $J_{5\text{-}4(cis)}$ = 6.6 Hz, the other of H-5), 3.91 (1H, dd, J_{gem} = 16.5 and $J_{4'\text{-}5'(trans)}$ = 8.1 Hz, the other of H-4'), 4.63 (1H, m, H-4), 4.71 (1H, d, $J_{CH\text{-}4}$ = 5.5 Hz, fluorenyl CH), 5.29 (1H, dd, $J_{5'\text{-}4'}$ = 11.0 and 8.1 Hz, H-5'), 7.31-7.46, and 7.64-7.79 (13H, m, Ar). *anti*: δ = 1.57, 1.63 (each 3H, s, Me), 2.76 (1H, br t, H-5), 3.57 (2H, br, H-5), 3.64 (1H, dd, J_{gem} = 15.8 and $J_{4'\text{-}5'(cis)}$ = 9.9 Hz, one of H-4'), 4.13 (1H, dd, J_{gem} = 15.8 and $J_{4'\text{-}5'(trans)}$ =7.3 Hz, the other of H-4'), 5.04 (2H, br, H-4 and fluorenyl CH), and 5.49 (1H,

br dd, H-5'). Other signals are ovelapping with those of *syn*-conformer; MS (20 eV, rel intensity, %) *m/z* 439 (M^+ + 1, 3), 438 (M^+, 7), 274 (18), 273 (base peak), 178 (8), 146 (4), and 100 (12). Anal. Calcd for $C_{28}H_{26}N_2O_3$: C, 76.69; H, 5.98; N, 6.39%. Found: C, 77.39; H, 6.05; N, 5.91%.

Acid Hydrolysis of lk-5a Leading to lk-6. To a solution of *lk*-**5a** (0.055 g, 0.16 mmol) in aqueous MeOH (2 ml, MeOH-water 3:1 v/v) was added conc HCl (5 drops). The mixture was heated under reflux for 5 h. The mixture was neutralized with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (5 x 15 ml). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo to give *lk*-**6** (0.04 g, 81%). Purification by silica gel column chromatography with EtOAc gave pure *lk*-**6**.

N-[(1R)-2-Hydroxy-1-phenylethyl]-(5R)-3-phenyl-2-isoxazoline-5-carboxamide (lk-6): Colorless needles (*i*-PrOH); mp 191-192 °C; $[\alpha]_D^{24} = -211.1°$ (*c* = 1.07, EtOH); IR (KBr) 3400, 3350, 1650, 1510, 1030, 890, 860, 760, and 700 cm^{-1}; ^1H NMR (DMSO-d_6) δ = 3.53 (1H, dd, J_{gem} = 17.2, and $J_{4\text{-}5(trans)}$ = 6.9 Hz, one of H-4), 3.64 (2H, d, $J_{CH2\text{-}CH}$ = 5.9 Hz, CH_2O), 3.70 (1H, dd, J_{gem} = 17.2 and $J_{4\text{-}5(cis)}$ = 11.4 Hz, the other of H-4), 4.91 (1H, dd, $J_{5\text{-}4(cis)}$ = 11.4 and 6.9 Hz, H-5), 4.98 (1H, t, $J_{CH\text{-}CH2}$ = 5.9 Hz, PhCH), 7.17-7.33, 7.41-7.57, 7.67-7.73, and 8.56-8.59 (10H, m, Ph); ^{13}C NMR (DMSO-d_6) δ = 38.36 (C-4), 55.06 (CH_2O), 64.30 (PhCH), 79.03 (C-5), 126.66, 126.71, 126.78, 128.00, 128.56, 128.78, 130.29, 140.61 (each Ph), 156.54 (C-3), 169.18 (NCO); MS (20 eV, rel intensity, %) *m/z* 310 (M^+, 7), 297 (10), 296 (9), 280 (52), 279 (base peak), 148 (21), and 106 (8). Anal. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03%. Found: C, 69.95; H, 5.91; N, 9.04%.

Acid Hydrolysis of ul-5a Leading to ul-6. A solution of *ul*-**5a** (0.018 g, 0.05 mmol) in wet CH_2Cl_2 (2 ml, MeOH-water 3:1 v/v) containing CF_3COOH (4 drops) was stirred at room temperature for 0.5 h. The mixture was neutralized with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (3 x 15 ml). The combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue was purified by silica gel column chromatography with hexane-EtOAc (3:2 v/v) to give *ul*-**6** (0.016 g, quant).

N-[(1R)-2-Hydroxy-1-phenylethyl]-(5S)-3-phenyl-2-isoxazoline-5-carboxamide (ul-6): Colorless prisms (*i*-PrOH); mp 179 -180 °C; $[\alpha]_D^{25} = 80.6°$ (*c* = 0.65, $CHCl_3$); IR (KBr) 3350, 1650, 1500, 1350, 1060, 1040, 880, 750, and 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.70-2.50 (2H, br, NH and OH), 3.67 (1H, dd, J_{gem} = 17.2 and $J_{4\text{-}5(cis)}$ = 11.0 Hz, one of H-4), 3.76 (1H, dd, J_{gem} = 17.2, and $J_{4\text{-}5(trans)}$ = 6.6 Hz, the other of H-4), 3.85 (2H, d, $J_{CH2\text{-}CH}$ = 5.1 Hz, CH_2O), 5.06 (1H, dt, $J_{CH\text{-}NH}$ = 7.7 and $J_{CH\text{-}CH2}$ = 5.1 Hz, PhCH), 5.15 (1H, dd, $J_{5\text{-}4}$ = 11.0 and 6.6 Hz, H-5), 7.29-7.47, and 7.66-7.70 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 39.71 (C-4), 55.87 (CH_2), 66.28 (PhCH), 78.95 (C-5), 126.78, 127.09, 128.15, 128.25, 128.92, 128.98, 130.90, 138.24 (each Ph), 157.36 (C-3), and 171.31(NCO); MS (20 eV, rel intensity, %) *m/z* 310 (M^+, 2), 281 (7), 280 (46), 279 (base peak), 173 (2), 148 (29), and 106 (8). Anal. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03%. Found: C, 69.32; H, 5.88; N, 8.86%.

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6. Optical rotations of (*S*)-4 (96% ee): $[\alpha]_D^{25} = 169.1°$ (*c* = 0.41, $CHCl_3$); (*R*)-4: $[\alpha]_D^{25} = -172.8°$ (*c* = 0.63, $CHCl_3$). The reported value[4a] for a 95:5 diastereomer mixture of (*R*)-4: $[\alpha]_D^{25} = -161°$ (*c* = 1.0, $CHCl_3$).
7. In silica gel column chromatography, the major isomer *lk*-**5a** was obtained from the less polar eluent (hexane-EtOAc: 6:1 v/v). Change of polarity of the solvent was needed to get the minor one *ul*-**5a** (hexane-EtOAc: 3:1 v/v). This tendency is general for the other cycloadducts discussed in this report.