DIASTEREOSELECTIVE 1,3-DIPOLAR CYCLOADDITION OF 2-(α,β-UNSATURATED) ACYL-3-PHENYL-*l*-MENTHOPYRAZOLES†

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Abstract— The 1,3-dipolar cycloadducts of *N*-(α,β-unsaturated) acylpyrazoles (**2**) with benzonitrile oxide or nitrones were afforded in good yield. In the cases of nitrones, the addition of $MgBr_2$ or $ZnBr_2$ promoted the stereoselectivity as well as the acceleration of the reaction rate. In the reaction of **2f** and **2g**, the big jump on the diastereoselectivity was accomplished by the addition of $MgBr_2$, and (3'*S*,4'*R*,5'*S*)-**8** was obtained as optically pure form in over 90% yield. These isoxazolidinecarbonylpyrazoles were converted into azetidinones in moderate yield with the retention of their stereo structures.

Recently we have developed the preparation and the utilities of 3-phenyl-*l*-menthopyrazole (**1**) as a new chiral auxiliary,[1] which has some unique structure and properties different from the conventional chiral auxiliaries.[2] The most important characteristic of this auxiliary is that the substrate terminates to heteroaromatic pyrazole ring and is surrounded by the chiral atmosphere. Especially the steric hindrance of **1** is relaxed by twisting the benzene ring, which overlays on one side of the terminal nitrogen atom.[1] This structural characteristic causes the diastereofacial effect in the reactions on the substrate moiety. Moreover, lone pair electrons of adjacent nitrogen take a role of Lewis base to form the chelation of N···Mg···O=C in the mixture of *N*-acylpyrazoles and $MgBr_2$.[3] Similar chelation of N···Li-O is perceived in the lithium enolate derived from *N*-acylpyrazoles. These chelations freeze the bond rotation of acyl group fixing to *Z*-configuration. As the result, the chirality of (4*R*)-

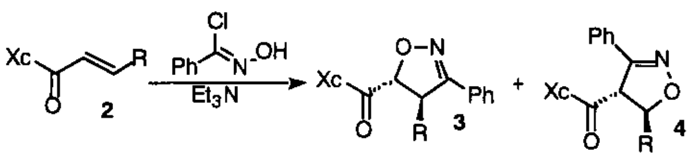
† This paper is dedicated to Professor Shigeru Oae on the occasion of his 77th birthday for his brilliant achievement in the field of heteroatom and heterocyclic chemistry.

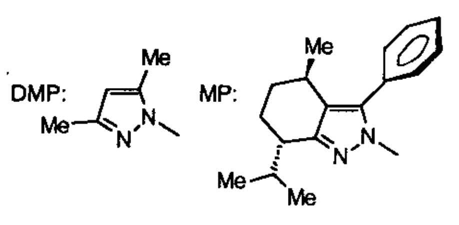
methyl group of **1** causes the high asymmetric induction in the reactions on acyl group of 2-acyl-3-phenyl-*l*-menthopyrazoles such as α–alkylation[4] and α–sulfenylation.[5] Otherwise, *N*-acyl substituted heteroaromatics such as *N*-acylimidazoles are easily converted into various acyl derivatives by the action of nucleophiles especially under acidic conditions.[6] The similar chemical behaviors are observed likely in the reactions of *N*-acylpyrazoles with alcohols,[7] amines,[8] Grignard reagents,[9] or organozinc compounds[10] under very mild conditions.

These facts demonstrated the excellent utility of **1** as a new chiral auxiliary. For the further extension of the utility of **1**, a wide variety of the diastereoselective reaction on the acyl moiety of 2-acyl-3-phenyl-*l*-menthopyrazoles is highly desired. Here, we report the diastereofacial 1,3-dipolar cycloaddition of a nitrile oxide and nitrones on 2-(α,β-unsaturated) acyl-3-phenyl-*l*-menthopyrazoles (**2**, Xc=MP).

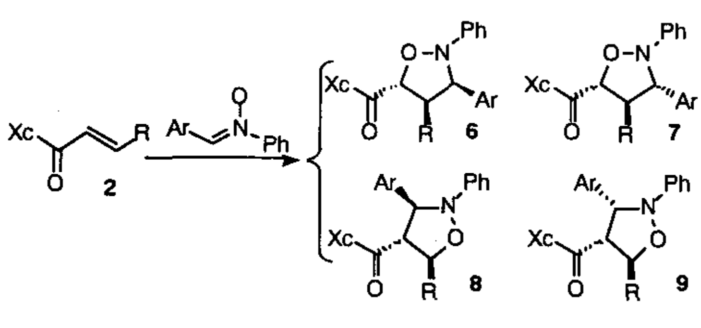
Firstly 1-(α,β-unsaturated) acyl-3,5-dimethylpyrazoles (**2**, Xc=DMP) were treated with benzonitrile oxide, which was generated *in situ* from 1-chlorobenzaldoxime and triethylamine. In the short reaction time at chilled temperature, 1,3-dipolar cycloaddi-tion of 1-acryloyl-3,5-dimethyl-pyrazole (**2a**) was performed regioselectively with benzonitrile oxide to give 1-(3'-phenyl-2'-isoxazoline-5'-carbonyl)-3,5-dimethylpyrazole (**3a**) in good yield. In the case of 1-cin-namoyl-3,5-dimethylpyrazole (**2c**), the longer reaction time and higher temperature are required to afford the mixture of 3c and its regioisomer (**4c**). Table 1 showed that the yield and the regioselectivity were decrease in the more polar solvent. The substituent effect of the dipolarophile was slightly revealed in the yields and the regioselectivity in **2c**~**e**.

Under the similar conditions, 2-acryloyl-3-phenyl-*l*-menthopyrazole (**2f**) afforded predominantly 1,3-





a: Xc=DMP, R=H
b: Xc=DMP, R=Me
c: Xc=DMP, R=Ph
d: Xc=DMP, R=p-ClC$_6$H$_4$
e: Xc=DMP, R=p-Tol
f: Xc=MP, R=H
g: Xc=MP, R=Me
h: Xc=MP, R=Ph



a: Xc=DMP, R=H, Ar=Ph
b: Xc=DMP, R=Me, Ar=Ph
c: Xc=DMP, R=Ph, Ar=Ph
f: Xc=MP, R=H, Ar=Ph
g: Xc=MP, R=Me, Ar=Ph
h: Xc=MP, R=Ph, Ar=Ph
i: Xc=MP, R=Me, Ar=p-Tol
j: Xc=MP, R=Me, Ar=p-Anis

Table 1. The 1,3-Dipolar Cycloaddition of 2 with Benzonitrile Oxide

Substrate			Solvent	Conditions	Yield	Ratio[a]	de (%)[a]	
	Xc[b]	R			(%)	(3 : 4)	3	4
2a	DMP	H	CH_2Cl_2	0°C, 1 h	90	100 : 0	—	—
2a	DMP	H	THF	0°C, 2 h	84	100 : 0	—	—
2b	DMP	Me	CH_2Cl_2	20°C, 16 h	69	53 : 47	—	—
2c	DMP	Ph	CH_2Cl_2	20°C, 24 h	79	29 : 71	—	—
2c	DMP	Ph	THF	20°C, 24 h	69	35 : 65	—	—
2c	DMP	Ph	THF-HMPA	20°C, 35 h	65	39 : 61	—	—
2c	DMP	Ph	Benzene	20°C, 24 h	36	47 : 53	—	—
2d	DMP	*p*-ClC_6H_4	CH_2Cl_2	20°C, 20 h	74	31 : 69	—	—
2e	DMP	*p*-Tol	CH_2Cl_2	20°C, 36 h	85	27 : 73	—	—
2f	MP	H	CH_2Cl_2	0°C, 1 h	85	100 : 0	24 (5'*R*)	—
2g	MP	Me	CH_2Cl_2	20°C, 24 h	84	52 : 48	12 (5'*R*)	31 (4'*R*)
2h	MP	Ph	CH_2Cl_2	20°C, 24 h	78	21 : 79	1 (5'*R*)	29 (4'*R*)

a: Isomer ratio and configuration were determined by ^1H nmr.

b: DMP and MP were represented to be 3,5-dimethylpyrazole and 3-phenyl-*l*-menthopyrazole rings, respectively.

dipolar cycloadduct (**3f**), while 2-cinnamoyl-3-phenyl-*l*-menthopyrazole (**2h**) gave the regioisomeric mixture of **3h** and **4h**. The diastereoselectivities in these reactions of 3-phenyl-*l*-menthopyrazole derivatives were observed in some extent, summarized in Table 1. The 1,3-cycloadduct (**4h**) was derived into 3-phenyl-5-hydroxymethyl-isoxazoline (**5**) by removal of the chiral auxiliary according to L-selectride® reduction. By the comparison of specific rotation of **5**,[11] the absolute configuration of the preferable adducts was postulated to have (5*R*)-isoxazoline ring. For the promotion of the diastereoselectivity, the 1,3-dipolar cycloaddition of benzonitrile oxide was attempted in the presence of $MgBr_2$, which was expected to freeze the bond rotation between acyl group and pyrazole ring.[3] However any remarkable promotion was not observed in the addition of $MgBr_2$, where the additive must be quenched by triethylamine contaminated in the solution.

Next, cycloaddition of **2** was performed with α,*N*-diphenylnitrone, which was facile 1,3-dipolar substance as a pure form. When **2a** was treated with α,*N*-diphenylnitron at refluxing temperature in THF, the mixture of 4 cycloadduct isomers (**6a**, **7a**, **8a**, and **9a**) was obtained along the regio- and stereo-isomerism. These adducts were treated with sodium methoxide in methanol for the conversion into methyl isoxazolidinecarboxylates, the nmr data of which were compared with the authentic data for the structural determination.[12] Since the reaction rate, regioselectivity and stereoselectivity were strongly dependent on the molecular structure of dipolarophiles, the effects of solvent, additives[13] and substituents on β-position were examined. Any remarkable difference on the selectivity was not observed in the reaction in benzene. The Table 2 showed that the addition of some Lewis acid accelerated the rate of 1,3-dipolar cycloaddition with α,*N*-diphenylnitrone. This acceleration due to the chelation was convinced by the electron deficiency on 1,3-dipolarophiles. The introduction of the substituent group on β-position depressed the formation of **6** and **7**, and the mixture of **8** and **9** was obtained regioselectively, summarized in Table 3. Moreover, the addition of divalent Lewis acids such as $MgBr_2$ and $ZnBr_2$ caused the change in the stereoselectivity, while no change was observed in stereoselectivity in the presence of tributylborane. The promotion of the stereoselectivity was reasonably interpreted by the formation of chelate complex, in which the bond rotation between pyrazole and acyl group of *N*-acylpyrazole was frozen.[3]

Table 2. The Reaction Rate of **2b** with α,*N*-Diphenylnitrone.

Lewis Acid	$\tau_{1/2}$ (h)
none	64
LiBr	82
$MgBr_2$	2.6
$ZnBr_2$	3.2

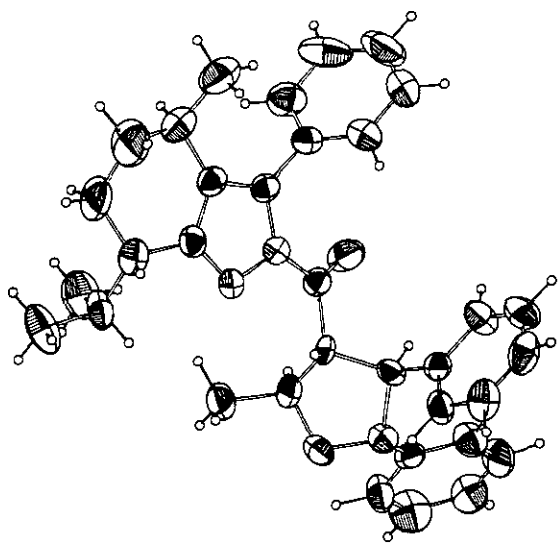


Figure 1. The ORTEP Diagram of **8g**

Finally the diastereofacial 1,3-dipolar cycloaddition of α,*N*-diphenylnitrone was carried out using chiral *N*-(α,β-unsaturated) acylpyrazoles (**2f~h**) summarized in Table 3. Although 16 isomers due to the stereo-, regio- and diastereo-isomerism are expected for the 1,3-dipolar cycloadduct of **2g** and α,*N*-diphenylnitrone, 2-(5'-methyl-2',3'-diphenylisoxazolidine-4'-carbonyl)-3-phenyl-*l*-menthopyrazole (**8g**) was predominantly formed

Table 3. The 1,3-Dipolar Cycloaddition of **2** with Nitrones

Substrate			Nitrone	Additive	Conditions[a]	Yield	Isomer Ratio[b]	De (%)[b]	
	Xc[c]	R	Ar			(%)	6 : 7 : 8 : 9	8	9
2a	DMP	H	Ph	none	reflux, 10 h	93	15 : 40 : 26 : 19	—	—
2a	DMP	H	Ph	none	reflux,[d] 12 h	88	16 : 39 : 27 : 18	—	—
2a	DMP	H	Ph	$MgBr_2$	reflux, 4 h	62	3 : 7 : 67 : 23	—	—
2b	DMP	Me	Ph	none	reflux, 16 h	92	0 : 0 : 73 : 27	—	—
2b	DMP	Me	Ph	none	reflux,[d] 17 h	95	0 : 0 : 75 : 25	—	—
2b	DMP	Me	Ph	$MgBr_2$	reflux, 1 h	94	0 : 0 : 48 : 52	—	—
2b	DMP	Me	Ph	$ZnBr_2$	reflux, 2 h	90	0 : 0 : 20 : 80	—	—
2b	DMP	Me	Ph	BBu_3	reflux, 13 h	41	0 : 0 : 73 : 27	—	—
2c	DMP	Ph	Ph	none	reflux, 17 h	66	0 : 0 : 89 : 11	—	—
2c	DMP	Ph	Ph	none	130°C,[d] 18 h	82	0 : 0 : 80 : 20	—	—
2c	DMP	Ph	Ph	$MgBr_2$	reflux, 6 h	25	0 : 0 : 64 : 36	—	—
2f	MP	H	Ph	$MgBr_2$	reflux, 1 h	79	0 : 0 : 83 : 17	>95(4'*R*)	22(4'*R*)
2g	MP	Me	Ph	none	reflux, 24 h	93	0 : 0 : 86 : 14	34(4'*R*)	10(4'*R*)
2g	MP	Me	Ph	$MgBr_2$	reflux, 1 h	94	0 : 0 : 91 : 9	>95(4'*R*)	48(4'*R*)
2g	MP	Me	*p*-Tol	$MgBr_2$	reflux, 1 h	99	0 : 0 : 86 : 14	>95(4'*R*)	50(4'*R*)
2g	MP	Me	*p*-Anis	$MgBr_2$	reflux, 1 h	85	0 : 0 : 89 : 11	>95(4'*R*)	25(4'*R*)
2g	MP	Me	Ph	LiBr	reflux, 25h	85	0 : 0 : 87 : 13	29(4'*R*)	19(4'*R*)
2g	MP	Me	Ph	$ZnBr_2$	reflux, 1.5 h	100	0 : 0 : 47 : 53	66(4'*R*)	27(4'*R*)
2h	MP	Ph	Ph	none	reflux, 24 h	32	0 : 0 : e : e	37(4'*R*)	e
2h	MP	Ph	Ph	$MgBr_2$	reflux, 24 h	0	—	—	—

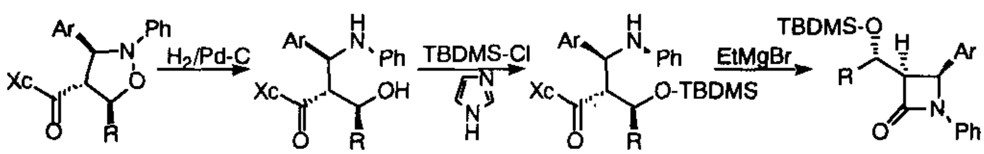
a: Reaction was carried out in THF. b: Isomer ratio and configuration were determined by ^1H NMR.

c: DMP and MP were represented to be 3,5-dimethylpyrazolyl and 3-phenyl-*l*-menthopyrazolyl, respectively.

d: Reaction was carried out in benzene. e: Product ratio cannot be evaluated due to the very complicated reaction mixture.

with poor diastereoselectivity. By the addition of $ZnBr_2$, the big jump on the diastereoselectivity was observed either in **8g** and **9g**, which were isolated exclusively by the simple column chromatography. The addition of $MgBr_2$ instead of $ZnBr_2$ afforded only one diastereomer (**8g**) in over 90% yield. From the X-ray structural analysis shown the ORTEP diagram in Figure 1, the isolated 1,3-dipolar cycloadduct was deduced to be (3'*S*,4'*R*,5'*S*)-**8g**. Similarly, optically pure 1,3-dipolar cycloadduct (**8f**) was obtained from **2f** and α,*N*-diphenylnitrone in good yield using $MgBr_2$ as a catalyst. In the case of **2h**, the cycloaddition is extremely inhibited by their steric hindrance and desired products were afforded in poor yields without recovery of **2h**. Further, α−(p-substituted)phenyl-*N*-phenylnitrones were treated with **2g** to give the corresponding 1,3-dipolar cycloadducts in good yield with high regio-, stereo- and diastereoselectivity.

The predominant isomers (**8** and **9**) were converted into azetidinones, which were paid much attention as the antibiotics. In the first step, isoxazolidine ring of **8b** was cleaved by hydrogenation to afford amino alcohol derivative (**10b**). After the protection of hydroxyl group with *tert*-butyldimethylsilyl chloride (TBDMS-Cl), **11b** was cyclized by the intramolecular aminolysis catalyzed by ethylmagnesium bromide. The TBDMS derivative of 3,4-*cis*-(1'-anti-hydroxyethyl)-1,4-diphenyl-2-azetidinone (3,4-*cis*-**12b**), which was identified by the comparison with the authentic data,[14] was obtained in 29% overall yield. Isomer (**9b**) was similarly converted into desired azetidinone (3,4-*trans*-**12b**) with the retention of stereo structure in 13% overall yield. However, the formation of **12b** from 3'*S*,4'*R*,5'*S*-**8g** was unsuccessful because of the steric hindrance of **11g**.



In conclusion, the 1,3-dipolar cycloadducts from **2** with benzonitrile oxide were formed in good yield. In the cases of 2-acyl-3-phenyl-*l*-menthopyrazoles, the remarkable promotion of the diastereoselectivity was not observed under various reaction conditions. On the contrary, the cycloaddition of **2** with nitrones was successful to give isoxazolidinecarbonylpyrazoles (**6**, **7**, **8**, and **9**). The addition of $MgBr_2$ or $ZnBr_2$ promoted the stereoselectivity as well as the acceleration of the reaction rate. In the reaction of **2f** and **2g**, the big jump on the diastereoselectivity was accomplished by the addition of $MgBr_2$, and (3'*S*,4'*R*,5'*S*)-**8** was obtained as optically pure form in over 90% yield. These isoxazolidinecarbonylpyrazoles were converted into azetidinones in moderate yield with the retention of their stereo structures.

EXPERIMENTAL

Nmr spectra were recorded on JEOL JNM-EX270 (270 MHz) spectrometers in $CDCl_3$ with TMS as an internal standard. Ir spectrum was measured by Shimadzu IR-460 spectrophotometer. Specific rotations were measured on a JASCO DIP-360 digital polarimeter. Hplc chromatograms were recorded by JASCO BIP-I chromatograph with uv-detector (254 nm) using SIL-C18 (24 cm) column. THF was dried over benzophenone ketyl radical generated from benzophenone and sodium metal, and distilled just before use. *N*-Acyl-3,5-dimethylpyrazoles (**2a~e**), and 2-acyl-3-phenyl-*l*-menthopyrazoles (**2f~h**) were prepared from the corresponding pyrazoles according to the method reported in the previous paper.[1,4,7]

General Procedure of Reaction with Benzonitrile Oxide.

Triethylamine (120 mg, 1.2 mmol) was added slowly to the solution of *N*-(α,β-unsaturated) acylpyrazole (**2**, 1.0 mmol) and 1-chlorobenzaldoxime (187 mg, 1.2 mmol) in CH_2Cl_2 (6 ml), and the mixture was stirred under nitrogen atmosphere. After the reaction was quenched with water, the organic layer was washed with 1N HCl, water, 1% $NaHCO_3$ and 3% NaCl , dried over anhydrous $MgSO_4$, and concentrated. The residue was chromatographed on silica gel with benzene or benzene-ethyl acetate (10 : 1 v/v) mixture. The isomer ratios were evaluated by ^{1}H nmr.

1-(3'-Phenyl-2'-isoxazoline-5'-carbonyl)-3,5-dimethylpyrazole (**3a**). ^{1}H-Nmr ($CDCl_3$) δ 2.24 (3H, s), 2.51 (3H, s), 3.69 (2H, ABX, J = 7.3, 11.6, 17.2 Hz), 5.99 (1H, s), 6.21 (dd, J = 7.3, 11.6 Hz), 7.27-7.47 (3H. m), 7.61-7.68 (2H, m). Anal. Calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60. Found: C, 66.91; H, 5.47; N, 15.55.

*1-(4',5'-*trans*-4'-Methyl-3'-phenyl-2'-isoxazoline-5'-carbonyl)-3,5-dimethylpyrazole* (**3b**). ^{1}H-Nmr ($CDCl_3$) δ 1.58 (3H, d, J = 6.9 Hz), 2.27 (3H, s), 2.54 (3H, d, J = 1.0 Hz), 3.97 (1H, dq, J = 3.6, 6.9 Hz), 5.87 (1H, d, J = 3.6 Hz), 6.02 (1H, d, J = 1.0 Hz), 7.32-7.42 (3H, m), 7.63-7.73 (m, 2H). Anal. Calcd for $C_{16}H_{17}N_3O_2$: C, 67.83; H, 6.05; N, 14.83. Found: C, 68.03; H, 6.08; N, 14.94.

*1-(4',5'-*trans*-3',4'-Diphenyl-2'-isoxazoline-5'-carbonyl)-3,5-dimethylpyrazole* (**3c**). ^{1}H-Nmr ($CDCl_3$) δ 2.23 (3H, s), 2.54 (3H, s), 5.05 (1H, d, J = 3.3 Hz), 6.01 (1H, s), 6.02 (1H, d, J = 3.3 Hz), 7.14-7.94 (10H, m). Anal. Calcd for $C_{21}H_{19}N_3O_2$: C, 73.03; H, 5.54; N, 12.17. Found: C, 72.86; H, 5.82; N, 11.83.

*1-[4',5'-*trans*-4'-(*p*-Chlorophenyl)-3'-phenyl-2'-isoxazoline-5'-carbonyl]-3,5-dimethylpyrazole* (**3d**). ^{1}H-Nmr ($CDCl_3$) δ 2.24 (3H, s), 2.55 (3H, s), 5.01 (1H, d, J = 3.3 Hz), 5.97 (1H, d, J = 3.3 Hz), 6.03 (1H, s), 7.25-7.68 (9H, m). Anal. Calcd for $C_{21}H_{18}N_3O_2Cl$: C, 66.40; H, 4.78; N, 11.06. Found: C, 66.51; H, 4.75; N, 11.01.

*1-[4',5'-*trans*-4'-(*p*-Methylphenyl)-3'-phenyl-2'-isoxazoline-5'-carbonyl)-3,5-dimethylpyrazole* (**3e**). ^{1}H-Nmr ($CDCl_3$) δ 2.24 (3H, s), 2.32 (3H, s), 2.55 (3H, s), 5.00 (1H, d, J = 3.6 Hz), 5.99 (1H, d, J = 3.6 Hz), 6.02 (1H, s), 7.11-7.90 (9H, m). Anal. Calcd for $C_{22}H_{21}N_3O_2$: C, 73.52; H, 5.89; N, 11.69. Found: C, 73.37; H, 6.01; N, 11.60.

*2-(4',5'-*trans*-3'-Phenyl-2'-isoxazoline-5'-carbonyl)-3-phenyl-*l*-menthopyrazole* (**3f**). Anal. Calcd for $C_{27}H_{29}N_3O_2$: C, 75.85; H, 6.84; N, 9.83. Found: C, 75.89; H, 6.89; N, 9.81.

5'S-Diastereomer ^{1}H-Nmr ($CDCl_3$) δ 0.74 (3H, d, J = 6.9 Hz), 0.97 (3H, d, J = 6.9 Hz), 1.09 (3H, d, J = 6.9 Hz), 1.18-1.33 (1H, m), 1.42-1.61 (1H, m), 1.87-2.04 (2H, m), 2.38-2.52 (1H, m), 2.60-2.86 (2H, m), 3.59-3.86 (2H, m), 6.28 (1H, dd, J = 8.2, 10.9 Hz), 7.29-7.54 (6H, m), 7.59-7.80 (4H, m).

5'R-Diastereomer ^{1}H-Nmr ($CDCl_3$) δ 0.72 (3H, d, J = 6.9 Hz), 0.97 (3H, d, J = 6.9 Hz), 1.11 (3H, d, J = 6.9 Hz), 1.18-1.33 (1H, m), 1.42-1.61 (1H, m), 1.87-2.04 (2H, m), 2.38-2.52 (1H, m), 2.60-2.86 (2H, m), 3.59-3.86 (2H, m), 6.33 (1H, dd, J = 7.3, 11.2 Hz), 7.29-7.54 (6H, m), 7.59-7.80 (4H, m).

*2-(4',5'-*trans*-4'-Methyl-3'-phenyl-2'-isoxazoline-5'-carbonyl)-3-phenyl-*l*-menthopyrazole* (**3g**). Anal. Calcd for $C_{28}H_{31}N_3O_2$: C, 76.16; H, 7.08; N, 9.52. Found: C, 76.08; H, 7.08; N, 9.41.

5'S-Diastereomer ^{1}H-Nmr ($CDCl_3$) δ 0.71 (3H, d, J = 6.9 Hz), 0.96 (3H, d, J = 6.9 Hz), 1.13 (3H, d, J = 6.9 Hz), 1.18-1.33 (2H, m), 1.56 (3H, d, J = 7.3 Hz), 1.90-2.06 (2H, m), 2.35-2.87 (3H, m), 3.88 (1H, dq, J = 7.3, 3.6 Hz), 5.95 (1H, d, J = 3.6 Hz), 7.25-7.43 (8H, m), 7.58-7.72 (2H, m).

5'R-Diastereomer ^{1}H-Nmr ($CDCl_3$) δ 0.75 (3H, d, J = 6.6 Hz), 0.98 (3H, d, J = 6.9 Hz), 1.11 (3H, d, J = 6.9 Hz), 1.18-1.33 (2H, m), 1.58 (3H, d, J = 7.3 Hz), 1.90-2.06 (2H, m), 2.35-2.87 (3H, m), 4.08 (1H, dq, J=7.3, 4.0 Hz), 5.89 (1H, d, J = 4.0 Hz), 7.25-7.43 (8H, m), 7.58-7.72 (2H, m)

*1-(4',5'-*trans*-5'-Methyl-3'-phenyl-2'-isoxazoline-4'-carbonyl)-3,5-dimethylpyrazole* (**4b**). ^{1}H-Nmr ($CDCl_3$) δ 1.58 (3H, d, J = 6.3 Hz), 2.28 (3H, s), 2.49 (3H, d, J = 1.0 Hz), 5.00 (1H, dq, J = 5.6, 6.3 Hz), 5.55 (1H, d, J = 5.6 Hz), 6.05 (1H, d, J = 1.0 Hz), 7.33-7.38 (3H, m), 7.63-7.67 (2H, m). Anal. Calcd for $C_{16}H_{17}N_3O_2$: C, 67.83; H, 6.05; N, 14.83. Found: C, 68.02; H, 6.28; N, 14.31.

*1-(4',5'-*trans*-4',5'-Dihydro-3',5'-diphenyl-2'-isoxazoline-4'-carbonyl)-3,5-dimethylpyrazole* (**4c**). ^{1}H-Nmr ($CDCl_3$) δ 2.26 (3H, s), 2.50 (3H, s), 5.93 (2H, AB, J = 5.0 Hz), 6.06 (1H, s), 7.14-7.94 (10H, m). Anal. Calcd for $C_{21}H_{19}N_3O_2$: C, 73.03; H, 5.54; N, 12.17. Found: C, 72.96; H, 5.51; N, 12.26.

*1-[4',5'-*trans*-5'-(*p*-Chlorophenyl)-3'-phenyl-2'-isoxazoline-4'-carbonyl]-3,5-dimethylpyrazole* (**4d**). ^{1}H-Nmr ($CDCl_3$) δ 2.28 (3H, s), 2.51 (3H, d, J = 0.7 Hz), 5.87 (2H, AB, J = 4.6 Hz), 6.07 (1H, d, J = 0.7 Hz), 7.23-7.38 (5H, m), 7.49-7.58 (2H, m), 7.64-7.69 (2H, m). Anal. Calcd for $C_{21}H_{18}N_3O_2Cl$: C, 66.4; H, 4.78; N, 11.06. Found: C, 66.28; H, 4.72; N, 10.99.

*1-[4',5'-*trans*-5'-(*p*-Methylphenyl)-3'-phenyl-2'-isoxazoline-4'-carbonyl)]3,5-dimethylpyrazole* (**4e**). ^{1}H-Nmr ($CDCl_3$) δ 2.28 (3H, s), 2.35 (3H, s), 2.53 (3H, d, J = 1.0 Hz), 5.90 (2H, AB, J = 5.0 Hz), 6.06 (1H, d, J = 1.0 Hz), 7.17-7.69 (9H, m). Anal. Calcd for $C_{22}H_{21}N_3O_2$: C, 73.52; H, 5.89; N, 11.69. Found: C, 73.42; H, 5.88; N, 11.68.

*2-(4',5'-*trans*-5'-Methyl-3'-phenyl-2'-isoxazoline-4'-carbonyl)-3-phenyl-*l*-menthopyrazole* (**4g**). Anal. Calcd for $C_{28}H_{31}N_3O_2$: C, 76.16; H, 7.08; N, 9.52. Found: C, 76.18; H, 7.05; N, 9.37.

*4'*S*-Diastereomer* ^{1}H-Nmr ($CDCl_3$) δ 0.72 (3H, d, J = 6.6 Hz), 0.93 (3H, d, J = 6.9 Hz), 1.13 (3H, d, J = 6.9 Hz), 1.22-1.34 (1H, m), 1.42-1.70 (1H, m), 1.58 (3H, d, J = 6.6 Hz), 1.88-2.06 (2H, m), 2.46-2.59 (1H, m), 2.67-2.87 (2H, m), 4.93 (1H, quint, J = 6.3 Hz), 5.55 (1H, d, J = 6.3 Hz), 7.17-7.48 (8H, m), 7.57-7.70 (2H, m).

*4'*R*-Diastereomer* ^{1}H-Nmr ($CDCl_3$) δ 0.72 (3H, d, J = 6.6 Hz), 1.03 (3H, d, J = 6.9 Hz), 1.15 (3H, d, J = 6.9 Hz), 1.22-1.34 (1H, m), 1.42-1.70 (1H, m), 1.58 (3H, d, J = 6.3 Hz), 1.88-2.06 (2H, m), 2.46-2.59 (1H, m), 2.67-2.87 (2H, m), 5.09 (1H, quint, J = 6.3 Hz), 5.65 (1H, d, J = 5.6 Hz), 7.17-7.48 (8H, m), 7.57-7.70 (2H, m).

*2-(4',5'-*trans*-3',5'-Diphenyl-2'-isoxazoline-4'-carbonyl)-3-phenyl-*l*-menthopyrazole* (**4h**). Anal. Calcd for $C_{33}H_{33}N_3O_2$: C, 78.70; H, 6.60; N, 8.34. Found: C, 78.46; H, 6.88; N, 8.05.

*4'*S*-Diastereomer* ^{1}H-Nmr ($CDCl_3$) δ 0.71 (3H, d, J = 6.6 Hz), 0.82 (3H, d, J = 6.9 Hz), 0.85-0.92 (1H, m), 1.01 (3H, d, J = 6.9 Hz), 1.42-1.57 (1H, m), 1.86-2.03 (2H, m), 2.35-2.50 (1H, m), 2.63-2.84 (2H, m), 6.00 (2H, AB, J = 6.3 Hz), 7.14-7.70 (15H, m).

*4'*R*-Diastereomer* ^{1}H-Nmr ($CDCl_3$) δ 0.74 (3H, d, J = 6.9 Hz), 0.85-0.92 (1H, m), 0.95 (3H, d, J = 6.9 Hz), 1.09 (3H, d, J = 6.9 Hz), 1.42-1.57 (1H, m), 1.86-2.03 (2H, m), 2.35-2.50 (1H, m), 2.63-2.84 (2H, m), 6.02 (2H, AB, J = 5.6 Hz), 7.14-7.70 (15H, m).

Conversion of 4h into 5 by L-Selectride®.

To a solution of **4h** (333 mg, 0.66 mmol, 24% de) in THF (10 ml) under nitrogen atmosphere, L-selectride® (1.0 M in THF, 1.5 ml) was added dropwise at room temperature. After stirring for 30 min, the mixture was quenched with aqueous hydrogen peroxide (30%, 1 ml) and 1N aq-NaOH (2 ml). The product was extracted with CH_2Cl_2, the organic layer washed with 3% NH_4Cl, dried over anhydrous $MgSO_4$ and concentrated. The residue was chromatographed on silica gel with benzene-ethyl acetate (2 : 1 v/v) to isolate 4,5-*trans*-5-hydroxymethyl-3-phenyl-2-isoxazoline (**5**); yield 53%; $[\alpha]_D^{26}$ -39.8 [c 1.46, $CHCl_3$, 24% ee (*R*)];[15] ^{1}H-nmr ($CDCl_3$) δ 2.64 (1H, br s), 3.22-3.45 (2H, m), 3.68 (1H, dd, J=12.2, 7.6 Hz), 3.85 (1H, dd, J=12.2, 3.3 Hz), 4.85 (1H, m), 7.26-7.40 (3H, m), 7.61-7.82 (2H, m); ^{13}C-nmr ($CDCl_3$) δ (DEPT) 36.2 (CH2), 63.5 (CH2), 81.2 (CH), 126.6 (CH), 128.6 (CH), 129.2 (C), 130.1 (CH), 157.0 (C). Also 3-phenyl-*l*-menthopyrazole was recovered in 99% yield.

General Procedure of Reaction with Nitrone.

The solution of *N*-(α,β-unsaturated) acylpyrazole (**2**, 3.0 mmol), nitrone (3.3 mmol) and additive (3.0 mmol) in THF (15 ml) was refluxed under nitrogen atmosphere. After the reaction was quenched with water, the mixture was extracted with CH_2Cl_2. The organic layer was washed with 1N HCl, water, 1% $NaHCO_3$ and 3% NaCl, dried over anhydrous $MgSO_4$, and concentrated. The residue was chromatographed on silica gel with benzene-hexane (2 : 1 v/v) mixture. The isomer ratios were evaluated by ^{1}H nmr.

1-(2',3'-Diphenylisoxazolidine-5'-carbonyl)-3,5-dimethylpyrazole. Anal. Calcd for $C_{21}H_{21}N_3O_2$: C, 72.6; H, 6.09; N, 12.1. Found: C, 72.68; H, 6.16; N, 11.93.

*3',5'-*trans *Isomer* (**6a**) ^{1}H-Nmr ($CDCl_3$) δ 2.19 (3H, s), 2.56 (3H, s), 2.47-3.70 (1H, m), 3.35-3.48 (1H, m), 4.71 (1H, t, J = 7.4 Hz), 5.76 (1H, t, J = 7.9 Hz), 5.95 (1H, s), 6.89-7.52 (10H, m).

*3',5'-*cis *Isomer* (**7a**). ^{1}H-Nmr ($CDCl_3$) δ 2.22 (3H, s), 2.47 (3H, s), 2.91-3.08 (2H, m), 4.77 (1H, t, J = 7.4 Hz), 5.90 (1H, dd, J = 5.3, 7.9 Hz), 5.97 (1H, s), 6.89-7.52 (10H, m).

1-(2',3'-Diphenylisoxazolidine-4'-carbonyl)-3,5-dimethylpyrazole. Anal. Calcd for $C_{21}H_{21}N_3O_2$: C, 72.60; H, 6.09; N, 12.10. Found: C, 72.64; H, 6.15; N, 12.02.

*3',4'-*trans *Isomer* (**8a**). ^{1}H-Nmr ($CDCl_3$) δ 2.17 (3H, s), 2.47 (3H, s), 4.20-4.24 (1H, m), 4.63-4.76 (2H, m), 5.32 (1H, d, J = 5.0 Hz), 5.93 (1H, s), 6.90-7.59 (10H, m).

*3',4'-*cis *Isomer* (**9a**). ^{1}H-Nmr ($CDCl_3$) δ 2.03 (3H, s), 2.26 (3H, s), 4.38 (1H, t, J = 8.4 Hz), 4.74 (1H, t, J = 7.8 Hz), 5.08 (1H, q, J = 8.6 Hz), 5.29 (1H, d, J = 9.2 Hz), 5.82 (1H, s), 6.93-7.38 (10H, m).

*1-(4',5'-*trans*-5'-Methyl-2',3'-triphenylisoxazolidine-4'-carbonyl)-3,5-dimethylpyrazole.* Anal. Calcd for $C_{22}H_{23}N_3O_2$: C, 73.11; H, 6.41; N, 11.63. Found: C, 72.94; H, 6.47; N, 11.65.

*3',4'-*trans *Isomer* (**8b**). ^{1}H-Nmr ($CDCl_3$) δ 1.56 (3H, d, J = 5.9 Hz), 2.13 (3H, s), 2.48 (3H, d, J = 0.7 Hz), 4.50-4.66 (2H, m), 5.31 (1H, d, J = 6.3 Hz), 5.94 (1H, s), 6.88-8.41 (10H, m).

*3',4'-*cis *Isomer* (**9b**). ^{1}H-Nmr ($CDCl_3$) δ 1.50 (3H, d, J = 5.9 Hz), 2.02 (3H, s), 2.25 (3H, s), 4.50-4.66 (1H, m), 4.96-5.02 (1H, m), 5.06 (1H, d, J = 10.6 Hz), 5.80 (1H, s), 6.88-8.41 (10H, m).

*1-(4',5'-*trans*-2',3',5'-Triphenylisoxazolidine-4'-carbonyl)-3,5-dimethylpyrazole.* Anal. Calcd for $C_{27}H_{25}N_3O_2$: C, 76.57; H, 5.95; N, 9.92. Found: C, 77.09; H, 6.03; N, 9.57.

*3',4'-*trans *Isomer* (**8c**). ^{1}H-Nmr ($CDCl_3$) δ 1.93 (3H, s), 2.47 (3H, s), 5.02-5.07 (1H, m), 5.38 (1H, d, J = 5.9 Hz), 5.59 (1H, d, J = 7.3 Hz), 5.87 (1H, s), 6.93-7.61 (10H, m).

*3',4'-*cis *Isomer* (**9c**). ^{1}H-Nmr ($CDCl_3$) δ 1.99 (3H, d, J = 0.7 Hz), 2.21 (3H, s), 5.02-5.07 (1H, m), 5.24 (1H, d, J = 7.9 Hz), 5.75 (1H, s), 5.92 (1H, d, J = 10.2 Hz), 6.93-7.61 (10H, m).

*2-(3'S,4'R-2',3'-Diphenylisoxazolidine-4'-carbonyl)-3-phenyl-*l*-menthopyrazole* (**8f**). ^{1}H-Nmr ($CDCl_3$) δ 0.66 (3H, d, J = 6.9 Hz), 0.90 (3H, d, J = 6.9 Hz), 1.12 (3H, d, J = 6.9 Hz), 1.15-1.28 (1H, m), 1.43-1.56 (1H, m), 1.77-1.99 (2H, m), 2.34-2.46 (1H, m), 2.54-2.61 (1H, m), 2.68-2.81 (1H, m), 4.16-4.24 (1H, m), 4.67-4.82 (2H, m), 5.32 (1H d, J = 4.6 Hz), 6.87-7.91 (15H, m). Anal. Calcd for $C_{33}H_{35}N_3O_2$: C, 78.38; H, 6.98; N, 8.31. Found: C, 78.38; H, 7.00; N, 8.41.

*2-(2',3'-Diphenyl-5'-methylisoxazolidine-4'-carbonyl)-3-phenyl-*l*-menthopyrazole.* Anal. Calcd for $C_{34}H_{37}N_3O_2$: C, 78.58; H, 7.18; N, 8.09. Found: C, 78.62; H, 7.22; N, 8.10.

3'S,4'R,5'S Isomer (**8g**). ^{1}H-Nmr ($CDCl_3$) δ 0.67 (3H, d, J = 6.9 Hz), 0.84 (3H, d, J = 6.9 Hz), 1.05 (3H, d, J = 6.9 Hz), 1.11-1.26 (1H, m), 1.39-1.59 (1H, m), 1.52 (3H, d, J = 6.3 Hz), 1.81-1.97 (2H, m), 2.34-2.59 (2H, m), 2.66-2.77 (1H, m), 4.46 (1H, dq, J = 6.3, 6.9 Hz), 4.68 (1H, t, J = 6.9 Hz), 5.27 (1H, d, J = 6.9 Hz), 6.84-7.89 (15H, m).

3'R,4'R,5'S Isomer (**9g**). ^{1}H-Nmr ($CDCl_3$) δ 0.69 (3H, d, J = 6.6 Hz), 0.76 (3H, d, J = 6.9 Hz), 0.94 (3H, d, J = 6.9 Hz), 1.14-1.27 (1H, m), 1.38-1.48 (1H, m), 1.59 (3H, d, J = 5.9 Hz), 1.82-1.98 (2H, m), 2.19-2.22 (1H, m), 2.51-2.60 (1H, m), 2.69-2.77 (1H, m), 4.59 (1H, dq, J = 7.9, 5.9 Hz), 4.75 (1H, dd, J = 7.9, 6.9 Hz), 5.19 (1H, d, J = 6.9 Hz), 6.84-7.59 (15H, m).

*2-(3',4'-*trans*-2',3',5'-Triphenylisoxazolidine-4'-carbonyl)-3-phenyl-*l*-menthopyrazole.* Anal. Calcd for $C_{39}H_{39}N_3O_2$: C, 80.52; H, 6.76; N, 7.22. Found: C, 80.54; H, 6.86; N, 7.22.

3'S,4'R,5'S Isomer (**8h**). ^{1}H-Nmr ($CDCl_3$) δ 0.61 (3H, d, J = 6.6 Hz), 0.66 (3H, d, J = 6.9 Hz), 0.89 (3H, d, J = 7.3 Hz), 1.06-1.48 (2H, m), 1.75-1.92 (2H, m), 2.05-2.22 (1H, m), 2.41-2.48 (1H, m), 2.62-2.71 (1H, m), 5.11 (1H, t, J = 6.6 Hz), 5.38 (1H, d, J = 5.6 Hz), 5.63 (1H, d, J = 7.3 Hz), 6.87-7.68 (20H, m).

3'R,4'R,5'S Isomer (**9h**). ^{1}H-Nmr ($CDCl_3$) δ 0.61 (3H, d, J = 6.6 Hz), 0.66 (3H, d, J = 6.9 Hz), 0.83 (3H, d, J = 7.3 Hz), 1.06-1.48 (2H, m), 1.75-1.92 (2H, m), 1.96-2.02 (1H, m), 2.29-2.37 (1H, m), 2.62-2.71 (1H, m), 5.19 (1H, t, J = 7.3 Hz), 5.30 (1H, d, J = 6.6 Hz), 5.54 (1H, d, J = 8.2 Hz), 6.87-7.68 (20H, m).

*2-[3'S,4'R,5'S-5'-Methyl-3'-(*p*-methylphenyl)-2'-phenylisoxazolidine-4'-carbonyl]-3-phenyl-*l*-menthopyrazole* (**8i**). ^{1}H-Nmr ($CDCl_3$) δ 0.67 (3H, d, J = 6.6 Hz), 0.84 (3H, d, J = 6.6 Hz), 1.05 (3H, d, J = 6.6 Hz), 1.14-1.27 (1H, m), 1.39-1.60 (1H, m), 1.52 (3H, d, J = 5.9 Hz), 1.82-1.98 (2H, m), 2.36 (3H, s), 2.40-2.77 (3H, m), 4.45 (1H, dq, J = 7.6, 5.9 Hz), 4.67 (1H, t, J = 7.3 Hz), 5.23 (1H, d, J = 6.9 Hz), 6.84-7.47 (15H, m). Anal. Calcd for $C_{35}H_{39}N_3O_2$: C, 78.77; H, 7.37; N, 7.87. Found: C, 78.61; H, 7.39; N, 7.96.

*2-[5'-Methyl-3'-(*p*-methoxyphenyl)-2'-phenylisoxazolidine-4'-carbonyl]-3-phenyl-*l*-menthopyrazole.* Anal. Calcd for $C_{35}H_{39}N_3O_3$: C, 76.47; H, 7.15; N, 7.64. Found: C, 76.32; H, 7.22; N, 7.61.

3'S,4'R,5'S Isomer (**8j**). ^{1}H-Nmr ($CDCl_3$) δ 0.67 (3H, d, J=6.6 Hz), 0.85 (3H, d, J=6.6 Hz), 1.06 (3H, d, J=6.9 Hz), 1.17-1.39 (1H, m), 1.52 (3H, d, J=6.3 Hz), 1.43-1.56 (1H, m), 1.82-1.98 (2H, m), 2.39-2.48 (1H, m), 2.53-2.69 (1H, m), 2.71-2.77 (1H, m), 3.81 (3H, s), 4.40-4.50 (1H, dq, J=6.3, 7.6 Hz), 4.65 (1H, t, J=7.3 Hz), 5.19 (1H, d, J=6.9 Hz), 6.85-7.49 (14H, m).

3'R,4'R,5'S Isomer (**9j**). ^{1}H-Nmr ($CDCl_3$) δ 0.58 (3H, d, J=6.6 Hz), 0.94 (3H, d, J=6.6 Hz), 1.09 (3H, d, J=6.9 Hz), 1.17-1.39 (1H, m), 1.43 (3H, d, J=6.3 Hz), 1.43-1.56 (1H, m), 1.82-1.98 (2H, m), 2.39-2.48 (1H, m), 2.53-2.69 (1H, m), 2.71-2.77 (1H, m), 3.79 (3H, s), 4.55 (1H, t, J=7.3 Hz), 4.78-4.93 (1H, dq, J=6.3, 7.6 Hz), 5.06 (1H, d, J=6.9 Hz), 6.85-7.49 (14H, m).

Single-Crystal X-ray Diffraction Analysis of 8g.

The crystal data for **8g** are as follows: Monoclinic; space group $P2_1$ with *a*=11.792 (5), *b*=8.377 (2), *c*=15.297 (6) Å, β=104.86 (1)°, V=1460.6 Å^3, and Z=2. The empirical formula is $C_{34}H_{37}N_3O_2$, molecular weight is 519.68, and calculated density is 1.18 g/cm^3. The three-dimensional X-ray data were collected by the use of graphite-monochromated Mo Ka radiation (l=0.71073 Å) using the ω-2θ scan technique to a maximum 2θ of 46.0°. A total of 2283 reflections was collected, of which 2282 were unique and not systematically absent. Lorentz and polarization corrections were applied to the data. The linear absorption coefficient is 0.7 cm^{-1} for Mo K radiation. The structure was solved by direct methods. The remaining atoms were located in succeeding difference Fourier syntheses. Hydrogen atoms were located. The structure was refined in full-matrix least-squares and converged to a conventional R factor of 0.068. Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited with the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Evaluation of Reaction Rate with Diphenylnitrone.

The solution of α,*N*-diphenylnitrone (96 mg, 0.49 mmol), **2b** (80 mg, 0.49 mmol) and additive (LiBr, $MgBr_2$ or $ZnBr_2$, 0.50 mmol) in THF (5 ml) was heated at 40.0°C in the presence of naphthalene (*ca.* 100 mg) as an internal standard. The decrease of **2b** was traced with time by hplc eluting with H_2O-MeOH (3 : 1 v/v, flow rate 1.5 ml / min) mixture.

Methanolysis of *8* and *9* in the Presence of Sodium Methoxide.

Sodium methoxide (54 mg, 1.0 mmol) in methanol (2 ml) was added to a solution of isoxazolidinecarbonylpyrazole (**8** or **9**, 1 mmol) in methanol (8 ml) at room temperature and the stirring was continued for 30 min under a nitrogen atmosphere. The mixture was quenched with water and extracted with CH_2Cl_2. The organic layer was washed with 1N HCl, water, 1% $NaHCO_3$, 3% NaCl, dried over anhydrous $MgSO_4$, and concentrated. The residue was chromatographed on silica gel with hexane-ethyl acetate (10 : 1 v/v) mixture. In the case of **8g**, **1** was recovered by the elution from the column with ethyl acetate in 75% yield.

Methyl 2,3-Diphenyl-4-isoxazolidinecarboxylate.[12] Yield 37%.

*3,4-*trans *Isomer.* ^{1}H-Nmr ($CDCl_3$) δ 3.57 (1H, q, J=7.0 Hz), 3.69 (3H, s), 4.29-4.44 (2H, m), 5.00 (1H, d, J=5.6 Hz), 6.91-7.06 (2H, m), 7.19-7.56 (8H, m).

*3,4-*cis *Isomer.* ^{1}H-Nmr ($CDCl_3$) δ 3.28 (3H, s), 3.80 (1H, q, J=8.4 Hz), 4.29-4.44 (1H, m), 4.50-4.58 (1H, m), 5.02 (1H, d, J=5.6 Hz), 6.91-7.06 (2H, m), 7.19-7.56 (8H, m).

*Methyl 4,5-*trans*-5-Methyl-2,3-diphenylisoxazolidine-4-carboxylate.*[16]

*3,4-*trans *Isomer.* Yield 74% from **8g**; ^{1}H-nmr ($CDCl_3$) δ 1.41 (3H, d, J=7.0 Hz), 3.21 (1H, dd, J=9.2, 7.0 Hz), 3.71 (3H, s), 4.41-4.49 (1H, m), 5.18 (1H, d, J=7.0 Hz), 6.88-7.00 (3H, m), 7.15-7.55 (7H, m).

*3,4-*cis *Isomer.* Yield 80% from **9b**; ^{1}H-Nmr ($CDCl_3$) δ 1.21 (3H, d, J=7.0 Hz), 3.27 (3H, s), 3.38 (1H, t, J=9.4 Hz), 4.83-4.88 (1H, m), 4.86 (1H, d, J=10.6 Hz), 6.88-7.00 (3H, m), 7.15-7.55 (7H, m).

Conversion of 9 into Azetidinones.

A mixture of **8** (0.58 mmol) and 5% Pd-C (55 mg) in THF (10 ml) was stirred for 24 h at room temperature under a hydrogen atmosphere (1 atmosphere pressure). After the catalyst was filtered off, the solvent was removed. The residue was purified by column chromatography on silica gel with benzene-ethyl acetate (30 : 1 v/v) mixture and recrystallization from hexane.

1-[2-(1-Hydroxy)ethyl-3-anilino-3-phenyl]propanoyl-3,5-dimethylpyrazole (**10b**).

2,3-trans *Isomer*. Yield 98%; ^{1}H-nmr ($CDCl_3$) δ 1.25 (3H, d, J=5.6 Hz), 2.24 (3H, s), 2.27 (3H, s), 4.53 (2H, AB-q, J=4.0 Hz), 5.08 (1H, d, J=6.9 Hz), 5.88 (1H, s), 6.61 (2H, d, J=7.6 Hz), 6.69 (1H, t, J=7.3 Hz), 7.07-7.36 (8H, m).

2,3-cis *Isomer*. ^{1}H-Nmr ($CDCl_3$) δ 1.252 (3H, d, J=5.9 Hz), 2.140 (3H, s), 2.431 (3H, d, J=1.0 Hz), 4.349 (1H, quint, J=6.3 Hz), 4.571 (1H, t, J=5.9 Hz), 5.107 (1H, d, J=5.6 Hz), 5.856 (1H, s), 6.58-6.71 (3H, m), 7.06-7.38 (7H, m).

2-[2,3-trans-*2-(1-Hydroxyethyl)-3-anilino-3-phenyl]propanoyl-3-phenyl*-l-*menthopyrazole* (**10g**). Yield 86%; ^{1}H-nmr ($CDCl_3$) δ 0.58 (3H, d, J=6.6 Hz), 0.95 (3H, d, J=6.6 Hz), 1.14 (3H, d, J=6.6 Hz), 1.21 (3H, d, J=5.9 Hz), 1.44-1.56 (2H, m), 1.87-1.98 (2H, m), 2.50-2.56 (1H, m), 2.65-2.74 (2H, m), 4.44-4.56 (2H, m), 4.62 (1H, br s), 5.00 (1H, d, J=7.9 Hz), 6.61-6.72 (5H, m), 7.07-7.31 (10H, m). Anal. Calcd for $C_{34}H_{39}N_3O_2$: C, 78.28; H, 7.54; N, 8.05. Found: C, 78.22; H, 7.64; N, 8.08.

The mixture of **10** (0.74 mmol), TBDMS-Cl (154 mg, 1.0 mmol), imidazole (115 mg, 1.7 mmol) and DMF (2 ml) in CH_2Cl_2 (5 ml) was stirred for 12 h at room temperature. The reaction mixture was quenched with water, and the mixture was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, and concentrated. The residue was chromatographed on silica gel with hexane-ethyl acetate (10 : 1 v/v) mixture and recrystallization from hexane.

*1-[2-(1-*t-*Butyldimethylsiloxy)ethyl-3-anilino-3-phenyl]propanoyl-3,5-dimethylpyrazole* (**11b**). Anal. Calcd for $C_{28}H_{39}N_3O_2Si$: C, 70.40; H, 8.23; N, 8.80. Found: C, 70.15; H, 8.22; N, 8.75.

2,3-trans *Isomer*. Yield 59%; ^{1}H-nmr ($CDCl_3$) δ 0.10 (3H, s), 0.12 (3H, s), 0.88 (9H, s), 1.26 (3H, d, J=6.3 Hz), 2.27 (3H, s), 2.28 (3H, s), 4.40-4.46 (1H, dq, J=6.3, 7.6 Hz), 4.53-4.58 (1H, dd, J=7.9, 5.6 Hz), 5.01 (1H, d, J=5.6 Hz), 5.88 (1H, s), 6.46 (2H, d, J=7.6 Hz), 6.59 (1H, t, J=7.3 Hz), 7.01-7.27 (8H, m).

2,3-cis *Isomer*. Yield 54%; ^{1}H-nmr ($CDCl_3$) δ -0.189 (3H, s), 0.000 (3H, s), 0.828 (9H, s), 1.221 (3H, d, J=5.9 Hz), 1.993 (3H, s), 2.417 (3H, s), 4.346 (1H, dq, J=8.2, 1.9 Hz), 4.57-4.63 (1H, m), 4.96 (1H, br s), 5.47 (1H, br s), 5.747 (1H, s), 6.44-6.57 (3H, m), 6.98-7.25 (7H, m).

2-[2,3-trans-*2-(1-*t-*Butyldimethylsiloxy)ethyl-3-anilino-3-phenyl]propanoyl-3-phenyl*-l-*menthopyrazole* (**11g**). Yield 92%; ^{1}H-nmr ($CDCl_3$) δ 0.07 (3H, s), 0.08 (3H, s), 0.62 (3H, d, J=4.0 Hz), 0.90 (9H, s), 1.00 (3H, d, J=6.9 Hz), 1.13 (3H, d, J=5.9 Hz), 1.17 (3H, d, J=6.9 Hz), 1.18-1.31 (1H, m), 1.45-1.54 (1H, m), 1.89-1.97 (2H, m), 2.51-2.58 (1H, m), 2.67-2.74 (2H, m), 4.30-4.38 (1H, m), 4.44-4.49 (1H, m), 5.08 (1H, d, J=4.3 Hz), 5.87 (1H, br s), 6.44 (2H, d, J=7.9 Hz), 6.58 (1H, t, J=7.3 Hz), 6.88 (2H, d, J=5.9 Hz), 7.04

(2H, t, J=7.6 Hz), 7.15-7.32 (11H, m). Anal. Calcd for $C_{40}H_{53}N_3O_2Si$: C, 75.54; H, 8.40; N, 6.61. Found: C, 75.25; H, 8.67; N, 6.51.

A solution of ethylmagnesium bromide (2.0 M in Et_2O, 0.36 ml) was added to **11** (0.25 mmol) in THF (5 ml) under a nitrogen atmosphere, and kept at 0°C with stirring for 5 h. After the addition of 3% NH_4Cl (2 ml), the mixture was extracted with CH_2Cl_2. The organic layer was washed with 3% NaCl, dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by column chromatography on silica gel with hexane-ethyl acetate (10 : 1 v/v) and recrystallization. In the case of **11g**, azetidinone (**12g**) was not detected at all.

*3-(1-*t*-Butyldimethylsiloxy)ethyl-1,4-diphenylazetidin-2-one* (**12b**).

*3,4-*cis *Isomer.* Yield 49%; ir (CHCl3) 1747 cm^{-1}; ^1H-nmr ($CDCl_3$) δ 0.119 (3H, s), 0.128 (3H, s), 0.954 (9H, s), 0.945 (3H, d, J=6.3 Hz), 2.792 (1H, t, J=4.3 Hz), 4.621 (1H, dq, J=6.3, 4.6 Hz), 5.150 (1H, d, J=4.6 Hz), 6.50-6.67 (3H, m), 7.04-7.49 (7H, m).

*3,4-*trans *Isomer.* Yield 24%; ir (CHCl3) 1747 cm^{-1}; ^1H-nmr ($CDCl_3$) δ 0.071 (3H, s), 0.103 (3H, s), 0.793 (9H, s), 1.290 (3H, dd, J=6.3, 0.7 Hz), 3.083 (1H, t, J=3.0 Hz), 4.382 (1H, dq, J=6.3, 5.9 Hz), 5.107, (1H, d, J=2.0 Hz), 6.98-7.04 (2H, m), 7.19-7.40 (8H, m).

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