Stereoselective Synthesis of 2-Oxazoline-4-carboxylates through Lewis Acid-Catalyzed Formal [3 + 2] Cycloadditions of 5-Alkoxyoxazoles with Aldehydes: Catalytic Effect of Methylaluminum β-Binaphthoxide on *Cis*-Selectivity

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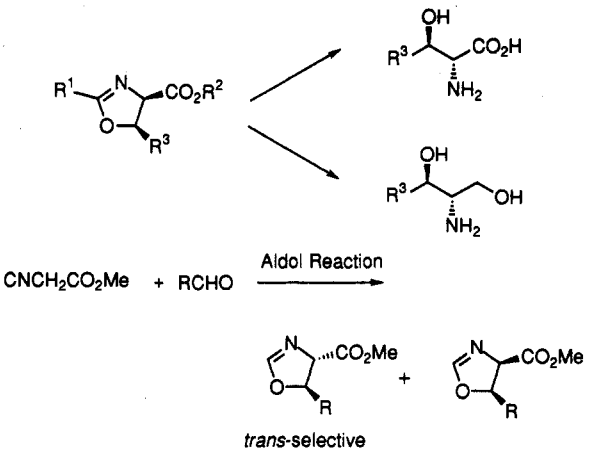
The formal [3 + 2] cycloadditions of 5-methoxy-2-(*p*-methoxyphenyl)oxazole with benzaldehyde, para- and meta-substituted benzaldehydes, propanal, cinnamaldehyde, and heterocyclic carboxaldehydes in the presence of methylaluminum β-binaphthoxide gave the corresponding methyl 5-alkyl-2-(*p*-methoxyphenyl)-2-oxazoline-4-carboxylates with high *cis*-selectivity (up to 98%). The use of ortho-substituted benzaldehydes resulted in a decrease in the *cis*-selectivity. The reaction of 5-methoxy-2-(*p*-methoxyphenyl)oxazole with benzaldehyde in the presence of titanium(IV) chloride or tin(IV) chloride gave the corresponding *trans*-2-oxazoline-4-carboxylate with 85–86% *trans*-selectivity. The reaction of ethyl glyoxylate with 5-ethoxy-2-phenyloxazole catalyzed by a 1:1 mixture of titanium(IV) chloride and titanium tetraisopropoxide gave diethyl 2-phenyl-2-oxazoline-4,5-dicarboxylate with a preference for *cis*-selectivity (*cis*/*trans* = 84:6). The *cis*-selectivity of the reaction in the presence of methylaluminum β-binaphthoxide can be explained by an antiperiplanar approach of the C4–C5 double bond of the oxazole to the aldehyde coordinated to the catalyst, followed by ring opening of the oxazole through a stepwise pathway involving zwitterionic intermediates.

Introduction

2-Oxazoline-4-carboxylates are versatile building blocks in organic synthesis as masked β-hydroxy amino acids or 2-amino 1,3-diols.[1-3] For example, on acid-catalyzed hydrolysis, *trans*-2-oxazoline-4-carboxylates are converted to *threo*-β-hydroxy amino acids, and *cis*-2-oxazoline-4-carboxylates are converted to *erythro*-β-hydroxy amino acids with retention of stereochemistry. Because of their synthetic utility, a general method for the stereoselective synthesis of 2-oxazoline-4-carboxylates is needed. *Trans*-isomers of 5-substituted 2-oxazoline-4-carboxylates have been selectively synthesized by the aldol reactions of isocyanoacetates with aldehydes under thermodynamic control.[1-3] For the synthesis of *trans*-2-oxazoline-4-carboxylates with high optical purity, a ferrocenylphosphine–gold(I) complex was found to be the most effective catalyst.[3] A *cis*-selective synthesis of 2-oxazoline-4-carboxylates is required for the preparation of *erythro*-β-hydroxy amino acids and their derivatives; however, a *cis*-selective synthesis has not been reported yet.

Recently we have found that oxazoles undergo formal [3 + 2] cycloadditions with strongly electron-deficient dienophiles through a stepwise pathway involving zwitterionic intermediates.[4] This cycloaddition has also been reported by others.[5] Although carbonyl compounds are usually inert to [3 + 2] cycloadditions with oxazoles,[5e,f] the reaction is expected to be activated by Lewis acids.[4]



trans-selective

In this paper,[6] we provide a full account of stereoselective syntheses of 2-oxazoline-4-carboxylates by means of the [3 + 2] cycloadditions of 5-alkoxyoxazoles with aldehydes in the presence of various Lewis acids and an explanation of the *cis*-selectivity found in the methylaluminum β-binaphthoxide-catalyzed reaction.

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(3) Enantioselective syntheses of *trans*-2-oxazoline-4-carboxylates: Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 645. *Idem. Tetrahedron Lett.* **1987**, *28*, 6215. *Ibid.* **1988**, *29*, 239. Ito, Y.; Sawamura, M.; Shirakawa, E.; Hayashizaki, K.; Hayashi, T. *Ibid.* **1988**, *29*, 235. *Idem. Tetrahedron* **1988**, *44*, 5253.

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(5) Kondrat'eva, Vedejs, Saalfrank, and Hassner also worked on this type of reaction: (a) Kondrat'eva, G. Y.; Aitzhanova, M. A.; Bogdanov, V. S.; Chizov, O. S. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1979**, 1313. (b) Bogdanov, V. S.; Kondrat'eva, G. Y.; Aitzhanova, M. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1980**, 1017. (c) Vedejs, E.; Fields, S. *J. Org. Chem.* **1988**, *53*, 4663. (d) Saalfrank, R. W.; Lurz, C.-J.; Hassa, J.; Danion, D.; Toupet, L. *Chem. Ber.* **1991**, *124*, 595. A few examples of thermal reactions of alkoxyoxazoles with carbonyl compounds have been reported. For example, the reaction of 5-ethoxy-4-phenyloxazole with diethyl oxomalonate in xylene (140 °C, 46 h) gave a mixture (1.2:1) of 2-oxazoline and 3-oxazoline. (e) Hassner, H.; Fischer, B. *Tetrahedron* **1989**, *45*, 3535. (f) *Idem. J. Org. Chem.* **1991**, *56*, 3419.

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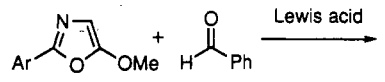
Table I. Reactions of Oxazole 1 with Benzaldehyde in the Presence of Lewis Acid[a]

run	Lewis acid (equiv)	solvent	temp (time)	total yield,[b] %	cis/trans[b]
1	$SnCl_4$ (1)	CH_2Cl_2	rt (21 h)	84	36:64
2	$SnCl_4$ (1)	MeCN	0 °C (120 h)	68	15:85
3	$TiCl_4$ (1)	CH_2Cl_2	0 °C (23 h)–rt (45 h)	77	14:86
4	$EtAlCl_2$ (1)	CH_2Cl_2–MeCN (1:1)	0 °C (93 h)	68	26:74
5	catalyst A[c] (1)	CH_2Cl_2	rt (66 h)	41[d]	80:20
6	catalyst B[c] (1)	CH_2Cl_2	0 °C (15 h)–rt (102 h)	43	63:37
7	catalyst C[c] (1)	CH_2Cl_2	0 °C (17 h)	61	52:48
8	catalyst D[e] (1)	CH_2Cl_2–MeCN (1:1)	0 °C (48 h)–rt (70 h)	2	50:50
9	catalyst E[e] (1)	CH_2Cl_2	0 °C (112 h)	87	38:62
10	MAD[e] (1)	CH_2Cl_2	rt (141 h)	8	15:85
11	catalyst A[c] (1)	MeCN	rt (112 h)	53	97:3
12	catalyst A[c] (2)	MeCN	rt (94 h)	87	98:2
13	catalyst A[c] (1)	CH_2Cl_2–MeCN (1:1)	0 °C (93 h)	78	98:2
14	catalyst F[c] (1)	CH_2Cl_2–MeCN (1:1)	0 °C (62 h)	71	90:10
15	catalyst G[c] (1)	CH_2Cl_2–MeCN (1:1)	0 °C (45 h)–rt (66 h)	7	52:48
16	catalyst H[c] (1)	CH_2Cl_2–MeCN (1:1)	0 °C (15.5 h)–rt (53 h)	70	64:36
17	catalyst I[f] (1)	CH_2Cl_2	rt (66 h)	36	39:61
18	catalyst J[g] (1)	CH_2Cl_2	0 °C (53 h)	69	13:87

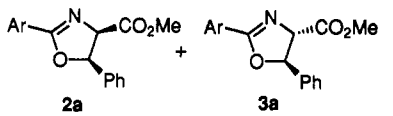
[a] The reaction was carried out under an argon atmosphere. [b] Determined by HPLC analysis using naphthalene as an internal standard. [c] Prepared in situ from $AlMe_3$ (0.99 M in hexane) and the corresponding binaphthol or biphenol derivative. [d] Isolated yield by column chromatography. [e] Prepared in situ from $AlMe_3$ (0.99 M in hexane) and 2 mol equiv of the corresponding phenol or naphthol derivative. [f] Prepared in situ by mixing (±)-2,2′-dihydroxy-1,1′-binaphthyl and Et_2AlCl (0.94 M in hexane) at rt for 1 h. [g] The catalyst was prepared in situ by mixing (±)-2,2′-dihydroxy-1,1′-binaphthyl and $TiCl_4$ in ether, removing the solvent in vacuo, adding toluene, and evaporating. Recovered oxazole 1:[b] run 1, 1%; run 2, 6%; run 3, 5%; run 4, 4%; run 5, 28%;[d] run 6, 47%; run 7, 21%; run 8, 79%; run 9, 1%; run 10, 40%; run 11, 29%; run 12, 0.1%; run 13, 5%; run 14, 6%; run 15, 23%; run 16, 0.6%; run 17, 34%; run 18, 6%. Catalysts A–J and MAD: see the figure in the text.

Results and Discussion

Reaction of Oxazole 1 with Benzaldehyde in the Presence of Lewis Acids. The reaction of 5-methoxy-2-(*p*-methoxyphenyl)oxazole (1) with benzaldehyde was carried out in the presence of several kinds of Lewis acids (Table I). The results of reactions catalyzed by some commercially available Lewis acids in dichloromethane and/or acetonitrile are shown in runs 1–4. These Lewis acids catalyzed the production of methyl *cis*- and *trans*-2-(*p*-methoxyphenyl)-5-phenyl-2-oxazoline-4-carboxylates (**2a** and **3a**) in high to moderate yields. Tin(IV)



1: Ar=*p*-$MeOC_6H_4$



2a **3a**

chloride in acetonitrile and titanium(IV) chloride in dichloromethane both resulted in high *trans*-selectivity (85–86%).[7] The results of reactions catalyzed by some organoaluminum catalysts[8] prepared from trimethylaluminum and the appropriate phenol or naphthol derivatives are shown in runs 5–17. The bulky organoaluminum reagent methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD)[8a–d] was unsatisfactory in terms of reactivity (8% yield) and selectivity (*trans/cis* = 85:15, run 10). The use of catalyst E, which is derived from 2,4,6-tribromophenol and has higher Lewis acidity than MAD, increased the total yield to 87%. However, only low *trans*-selectivity (*trans/cis* = 62:38) was found (run 9). In contrast to the catalysts discussed so far, methylaluminum β-binaphthoxide (catalyst A), prepared from 2,2′-dihydroxy-1,1′-binaphthyl and trimethylaluminum, showed 80% *cis*-selectivity and a reasonable yield in dichloromethane (run 5). A 2,2′-dihydroxy-1,1′-biphenyl derivative (catalyst B) showed moderate *cis*-selectivity (run 6). A 5,5′-dibromo-2,2′-dihydroxy-1,1′-biphenyl derivative (catalyst C) showed increased reactivity relative to catalyst B but gave lower *cis*-selectivity (run 7). It is interesting to note that catalyst D, derived from β-naphthol, showed a lower yield and lower *cis*-selectivity (run 8) than did catalyst A. In order to find the optimum conditions for the highest yield and *cis*-selectivity, the effect of the solvent on the reaction in the presence of catalyst A was investigated (runs 11–13). Two molar equivalents of catalyst A in acetonitrile (run 12) and an equimolar amount of catalyst A in a 1:1 mixture of acetonitrile and dichloromethane (run 13) showed the highest *cis*-selectivities (*cis/trans* = 98:2 for both conditions) and high yields (87 and 78%, respectively). Thus, acetonitrile was found to be effective for increasing the *cis*-selectivity.

The dominant effect of the structure of the catalyst on the *cis*-selectivity was investigated with catalysts F–J (runs 14–18), which were prepared from binaphthol or substituted binaphthols. Whereas catalyst F (a 6,6′-dibromo derivative)[9] showed slightly decreased *cis*-selectivity (run 14) in comparison with run 13 (catalyst A), catalyst G (a 3,3′-dibromo derivative),[10] which has bulky bromo groups near the metal center, showed drastically decreased reactivity and *cis*-selectivity. Substitution of the methyl group on the Al center of catalyst A by a (trifluoromethyl)-

(7) *cis*-Oxazoline **2a** epimerized to a 81:19 mixture of **3a** and **2a** on treatment with an equimolar amount of $SnCl_4$ in CH_2Cl_2 at rt for 21 h. These results suggest that *trans*-oxazoline **3a** was selectively obtained by epimerization under $SnCl_4$ or $TiCl_4$ catalysis (runs 1–3). The initial selectivity of these reactions could not be ascertained.

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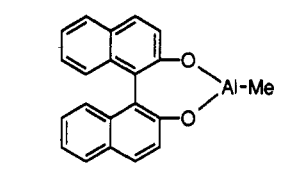
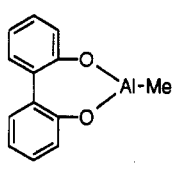
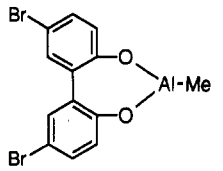


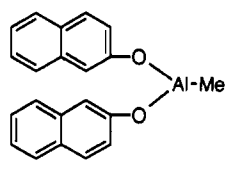
Catalyst A



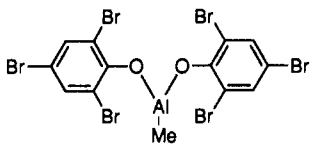
Catalyst B



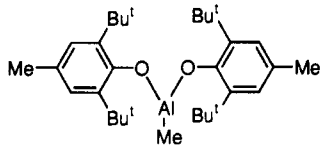
Catalyst C



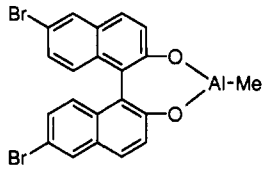
Catalyst D



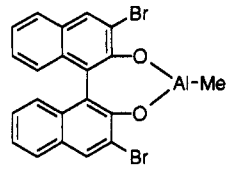
Catalyst E



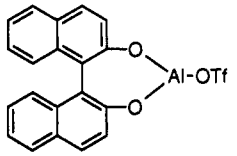
MAD



Catalyst F



Catalyst G



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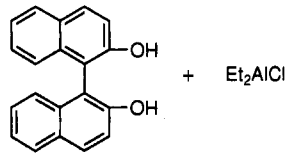
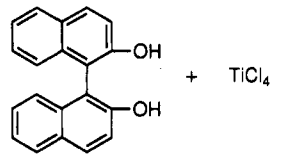


Catalyst I



Catalyst J

Table II. Reactions of Oxazole 1 with Aldehydes in the Presence of Catalyst A[a]

run	aldehyde	conditions[b]	temp (time)	products	total yield (%)[c]	*cis/trans*
1	PhCHO	A	0 °C (93 h)	**2a, 3a**	78	98:2
2	PhCHO	B	rt (94 h)	**2a, 3a**	87	98:2
3	*p*-$NO_2C_6H_4CHO$	A	0 °C (45 h)	**2b, 3b**	90	93:7
4	*m*-$NO_2C_6H_4CHO$	A	0 °C (43 h)	**2c, 3c**	87	85:15
5	*o*-$NO_2C_6H_4CHO$	A	0 °C (45 h)–rt (27 h)	**2d, 3d**	65	29:71
6	*p*-ClC_6H_4CHO	A	0 °C (66.5 h)	**2e, 3e**	82	98:2
7	2,4-$Cl_2C_6H_3CHO$	A	0 °C (23.5 h)–rt (70.5 h)	**2f, 3f**	76	45:55
8	2,6-$Cl_2C_6H_3CHO$	A	0 °C (24 h)–rt (120 h)	**2g, 3g**	36	39:61
9	*p*-MeC_6H_4CHO	B	rt (96 h)	**2h, 3h**	20	94:6
10	*m*-MeC_6H_4CHO	B	rt (171 h)	**2i, 3i**	49	92:8
11	*o*-MeC_6H_4CHO	B	rt (219 h)	**2j, 3j**	18	54:46
12	*p*-$MeOC_6H_4CHO$	A	0 °C (18 h)–rt (78 h)	**2k, 3k**	49	76:24
13	PhCH=CHCHO (*E*)	A	0 °C (18 h)–rt (51 h)	**2l, 3l**	27	78:22
14	EtCHO[d]	A	rt (52 h)	**2m, 3m**	15	85:15
15	3-pyridyl-CHO	B	rt (116 h)	**2n, 3n**	36	77:23
16	2-pyridyl-CHO	A	0 °C (17.7 h)–rt (76.5 h)	**2o, 3o**	28	79:21
17	3-furyl-CHO	B	rt (120 h)	**2p, 3p**	23	93:7
18	2-furyl-CHO	B	rt (45 h)	**2q, 3q**	67[e]	6:94

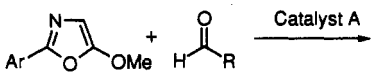
[a] The reaction was carried out in the presence of catalyst A (prepared by the method listed in Table I) under an argon atmosphere. [b] Condition A: equimolar amount of catalyst A in CH_2Cl_2–MeCN (1:1). Condition B: 2 mol equiv of catalyst A in MeCN. [c] Isolated yield by chromatography. [d] Two equivalents of EtCHO were used. [e] The ratio was determined by ^1H NMR. [f] Oxazole 1 was not recovered pure by chromatography, so the recovery was determined by HPLC. Recovered oxazole 1: run 2, 0.3%; run 3, 15%; run 4, 1%; run 6, 25%; run 7, 43%; run 8, 11%; run 9, 44%; run 10, 25%; run 11, 5%; run 12, 70%; run 13, 43%; run 14, 3%; run 15, 31%; run 16, 0.5%. Catalyst A: see the figure in the text.

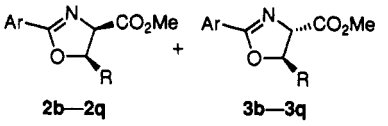
sulfonyl group (catalyst H) also lowered the *cis*-selectivity (run 16). Catalysts I and J, prepared by mixing 2,2′-dihydroxy-1,1′-binaphthyl with Et_2AlCl or $TiCl_4$, turned out to be *trans*-selective. These results suggest that the selectivity of the reaction is affected by even small changes in the structure, such as substituents on the binaphthol ring, the nature of the metal, and substituents on the metal. Catalyst A was found to be the optimum structure for the induction of high *cis*-selectivity.

Reaction of Oxazole 1 with Various Aldehydes. The reaction of oxazole 1 with electron-deficient and electron-rich para-substituted benzaldehydes in the presence of catalyst A gave 2-oxazolines with high *cis*-selectivity (98–76%, Table II, runs 3, 6, 9, and 12). These results suggest that the *cis*-selectivity is not dependent on the electronic effect of the para substituents. When electron-deficient para-substituted benzaldehydes were used, their high reactivity toward oxazole 1 resulted in high yields of 2-oxazoline (runs 3 and 6). In the case of electron-rich para-substituted benzaldehydes, the yields of 2-oxazolines were 20–49% (runs 9 and 12).

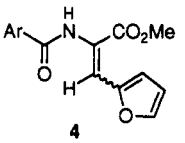
As in the case of the para-substituted benzaldehydes, *m*-nitro- and *m*-methylbenzaldehydes showed high *cis*-selectivity (85 and 92%, respectively, runs 4 and 10); however, *o*-nitro- and *o*-methylbenzaldehydes showed lower *cis*-selectivity (runs 5 and 11). Indeed, *o*-nitrobenzaldehyde gave high *trans*-selectivity (71%, run 5). It should be also noted that *cis*-2-oxazoline **2d** did not epimerize to the *trans*-isomer on treatment with an equimolar amount of catalyst A in acetonitrile–dichlo-

(10) Lingenfelter, D. S.; Helgeson, R. C.; Cram, D. J. *J. Org. Chem.* 1981, *46*, 393.





b: R=p-$NO_2C_6H_4$
c: R=m-$NO_2C_6H_4$
d: R=o-$NO_2C_6H_4$
e: R=p-ClC_6H_4
f: R=2,4-$Cl_2C_6H_3$
g: R=2,6-$Cl_2C_6H_3$
h: R=p-MeC_6H_4
i: R=m-MeC_6H_4
j: R=o-MeC_6H_4
k: R=p-$MeOC_6H_4$
l: R=PhCH=CH (*E*)
m: R=Et
n: R=3-pyridyl
o: R=2-pyridyl
p: R=3-furyl
q: R=2-furyl

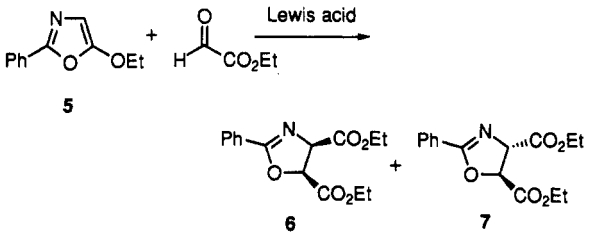


romethane (condition A). *o*-Chloro-substituted benzaldehydes show the same stereochemical trend. The *cis*-selectivity and the reactivity of benzaldehyde toward oxazole **1** were lowered by the *o*-chloro substitution (runs 7 and 8). Thus, the ortho-substitution lowers both the reactivity and the *cis*-selectivity. These results indicate that the *cis*-selectivity is governed by the steric environment of the substituted benzaldehyde.

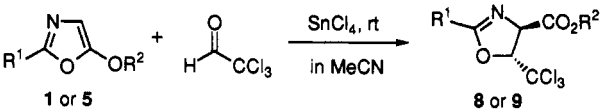
Cinnamaldehyde and propanal also underwent the *cis*-selective cycloaddition with oxazole **1** to give 2-oxazolines **2l** and **3l** (*cis*/*trans* = 78:22) and **2m** and **3m** (*cis*/*trans* = 85:15), respectively (runs 13 and 14). The reactions of heterocyclic carboxaldehydes with oxazole **1** gave the corresponding 2-oxazolines (runs 15–18). High *cis*-selectivity (93–77%) was found in the reactions of 3- and 2-pyridinecarboxaldehydes and 3-furaldehyde. However, the reaction of 2-furaldehyde under condition B (see Table II) resulted in high *trans*-selectivity and gave **2q** and **3q** together with ring-opened byproduct **4** (in 8% yield as a single isomer with undetermined geometry). When an equimolar amount of catalyst A was used in acetonitrile–dichloromethane (condition A; see Table II), *trans*-2-oxazoline **3q** was formed together with a 51% yield of **4**. Further, it is confirmed that *cis*-2-oxazoline **2q** was isomerized to give *trans*-2-oxazoline **3q** in 30% yield together with decomposition product **4** (in 26% yield) and unchanged **2q** (3%) when 2 mol equiv of catalyst A in acetonitrile were used. Therefore, 2-furaldehyde undergoes the cycloaddition in the *cis*-selective manner, and epimerization to thermodynamically stable *trans*-2-oxazoline **3q** follows. Thus, it was found that the *cis*-selectivity in the reaction is almost independent of the type of aldehyde (aromatic, aliphatic, α,β-unsaturated, and heterocyclic carboxy aldehydes) and is instead determined exclusively by the steric effects of the substituents on the aldehydes and the catalysts.

Reaction of 5-Ethoxy-2-phenyloxazole (5) with Ethyl Glyoxylate and Chloral. Like the reaction of **1** with benzaldehyde, the reaction of oxazole **5** with ethyl glyoxylate in the presence of tin(IV) chloride in acetonitrile gave *trans*-2-oxazoline (*trans*/*cis* = 85:15, run 1 in Table III). The reaction of oxazole **5** with ethyl glyoxylate in the presence of catalyst A resulted in less satisfactory *cis*-selectivity and reactivity (run 5). Titanium(IV) chloride, diethylaluminum chloride, and triisopropoxytitanium chloride were also unsatisfactory in terms of the selectivity (Table III, runs 3, 4, and 6). On the other hand, *cis*-2-oxazoline **6** was formed selectively (*cis*/*trans* = 84:16–73:27) in the presence of a 1:1 mixed catalyst of titanium(IV) chloride and titanium tetraalkoxide (runs 7–9).

It should be noted that *cis*-2-oxazoline **6** epimerizes to a 9:1 mixture of *trans*-2-oxazoline **7** and *cis*-2-oxazoline **6** on treatment with an equimolar amount of tin(IV) chloride in acetonitrile at room temperature for 24 h. This result suggests that the thermodynamically more stable *trans*-2-oxazoline **7** is formed in the presence of tin(IV) chloride through the epimerization of the initial *cis*-adduct under the reaction conditions.



Chloral reacted with oxazoles **1** and **5** in the presence of tin(IV) chloride at room temperature to give 2-oxazolines **8** and **9** in 65 and 56% yield, respectively. The formation of *trans*-2-oxazolines **8** and **9** as single products is ascribed to the thermodynamic instability of the *cis*-isomer due to the steric repulsion between the bulky trichloromethyl group at C-5 and the ester group at C-4.



1, **8**: R^1=p-$MeOC_6H_4$, R^2=Me
5, **9**: R^1=Ph, R^2=Et

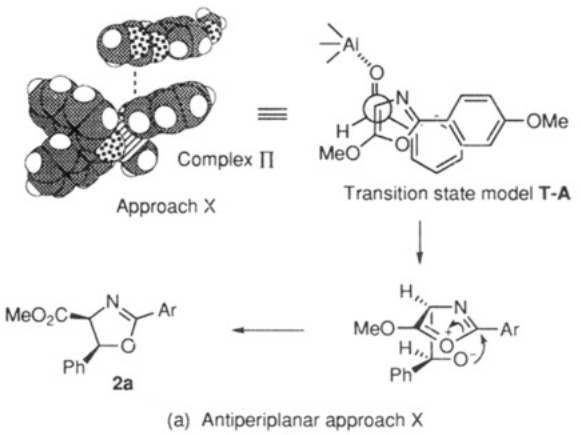
The Mechanism of *Cis*-Selectivity. It has been proposed that the formal [3 + 2] cycloadditions of oxazoles with tetracyanoethylene, 4-phenyl-3*H*-1,2,4-triazole-3,5-(4*H*)-dione (PTAD), and nitrosobenzene proceed through a stepwise pathway involving zwitterionic intermediates.[4a-e] Although reactions of 5-alkoxythiazoles with PTAD and diethyl azodicarboxylate (DEAD) generally gave formal [3 + 2] adducts, reactions of 5-methoxy-2-methylthiazole with DEAD and diethyl oxomalonate gave diethyl *N*-(5-methoxy-2-methyl-4-thiazolyl)bicarbamate and diethyl 2-(5-methoxy-2-methyl-4-thiazolyl)-2-hydroxymalonate, respectivly, by Friedel–Crafts-type electrophilic substitution.[4f] The results for oxazoles were expected to support the stepwise mechanism instead of a concerted mechanism. According to the interpretation of the stepwise pathway, the Lewis acid activates the aldehyde by accelerating the initial attack of the oxazole on the aldehyde in the reaction of a 5-alkoxyoxazole with an aldehyde. There are many precedents for Lewis acid-catalyzed Diels–Alder reactions. For example, the asymmetric hetero-Diels–Alder reaction of a siloxy diene with an aldehyde in the presence of a chiral organoaluminum reagent shows high enantioselectivity. This high selectivity is explained by an *endo*-approach of the diene to the 1:1 complex of the chiral catalyst and the aldehyde.[8f]

In the catalyst A-catalyzed reaction of oxazole **1** with benzaldehyde, a stable 1:1 complex of catalyst A with benzaldehyde may be the initial intermediate of the reaction. On the basis of the structure of this stable complex II,[12] we anticipate an antiperiplanar or synclinal approach of the C4–C5 double bond of oxazole **1** to the

Table III. Reactions of Oxazole 5 with Ethyl Glyoxylate[a]

run	conditions: Lewis acid	conditions: temp (time)	total yield (%)[b]	*cis*/*trans*
1	$SnCl_4$	rt (10.5 h)	68 (cis: 10%, trans: 55%)[c]	15:85
2	ZnI_2[d]	rt (140 h)	21[c]	29:71
3	$TiCl_4$	rt (10.5 h)	39	46:54
4	Et_2AlCl	rt (17 h)	38	58:42
5	catalyst A	0 °C (18.5 h)–rt (32 h)	43	28:72
6	$(i\text{-}PrO)_3TiCl$	rt (15 h)	18	55:45
7	$TiCl_4 + (i\text{-}PrO)_4Ti$	rt (13 h)	51 (cis: 40%, trans: 7%)[c]	84:16
8	$TiCl_4 + (i\text{-}PrO)_4Ti$[e]	rt (45 h)	38	84:16
9	$TiCl_4 + (EtO)_4Ti$	rt (20 h)	60	73:27

[a] The reaction was carried out with 2 mol equiv of ethyl glyoxylate in the presence of Lewis acid (an equimolar amount) in MeCN. [b] Determined by HPLC analysis. [c] Isolated yield by medium-pressure liquid chromatography over silica gel. [d] Five molar equivalents of ZnI_2 were used. [e] The reaction was carried out in toluene. Recovered oxazole 5:[b] run 1, 0.7%; run 2, detected by TLC but not recovered pure; run 3, 11%; run 4, 47%; run 5, detected by TLC but not recovered pure; run 6, 26%; run 9, 0.7%. Catalyst A: see the figure in the text.



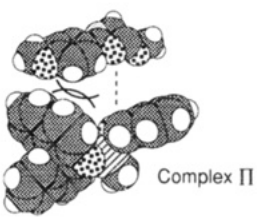
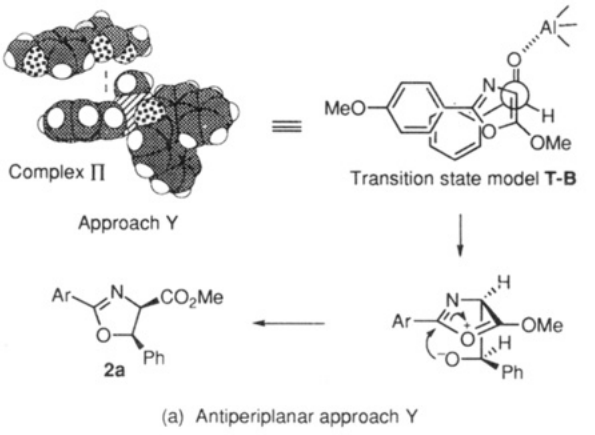


Figure 1. *Re*-face attack of the oxazole on the Lewis acid–aldehyde complex.



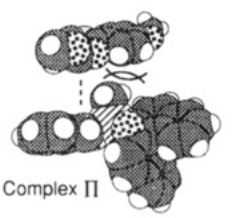


Figure 2. *Si*-face attack of the oxazole on the Lewis acid–aldehyde complex.

carbonyl group of complex Π.[11] In the *re*-face attack on complex Π, the sterically less-hindered approach X seems to be most favorable. Approach X corresponds to an antiperiplanar attack of the C4–C5 double bond of oxazole **1** on the carbonyl group of the aldehyde as shown in transition state model **T-A**, and this approach gives *cis*-2-oxazoline **2a** through a stepwise pathway (Figure 1). Approaches such as X′ are unfavorable because of steric hindrance between the naphthyl moiety and the *p*-methoxyphenyl group of oxazole **1**. In the case of *si*-face attack, antiperiplanar approach Y, which gives *cis*-2-oxazoline **2a** through the stepwise pathway, seems to be more favorable than an approach such as Y′ because of the steric repulsion between the methyl group of aluminum center and the *p*-methoxyphenyl group of oxazole **1** (Figure 2). Approach X seems to be more favorable than approach Y, but the actual selectivity could not be proven because we used racemic catalyst A in the above reactions.

The steric effect of the substituent on the benzaldehyde and the structural effect of the catalyst may be explained as follows. Ortho-substitution on the benzaldehyde changes the favorable conformation of the complex between the aldehyde and catalyst A because of the steric interaction between the ortho-substituents and the catalyst. Changing the favorable mode of the approach decreases the *cis*-selectivity and the reactivity. The lower activity of catalyst G, which has 3,3′-dibromo substituents on binaphthol, is explained by interference to approaches X and Y caused by the steric repulsion of bulky bromo substituents. Because the use of catalysts B, C, F, and H changes the stable conformation of complex II between the catalyst and benzaldehyde, the *cis*-selectivity of the reaction is governed by only a small change in the structure of the catalyst.

(11) A similar type of approach was proposed for ene reactions and for the reactions of enol silanes: Gennari, C. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds; Pergamon Press: Oxford, New York, Seoul, Tokyo, 1991; Vol. 2, Chapt. 2.4, pp 629–660. Reetz, M. T.; Hüllmann, H.; Massa, H.; Berger, S.; Rademacher, P.; Heymanns, P. *J. Am. Chem. Soc.* **1986**, *108*, 2405. Heathcock, C. H.; Davidson, S. K.; Hug, K. T.; Flippin, L. A. *J. Org. Chem.* **1986**, *51*, 3027. Mikami, K.; Loh, T. -P.; Nakai, T. *Tetrahedron Asymmetry* **1990**, *1*, 13 and refs cited therein.

(12) Only the structure of the (*R*)-form of complex **A** was drawn, but the racemic complex is probably formed.

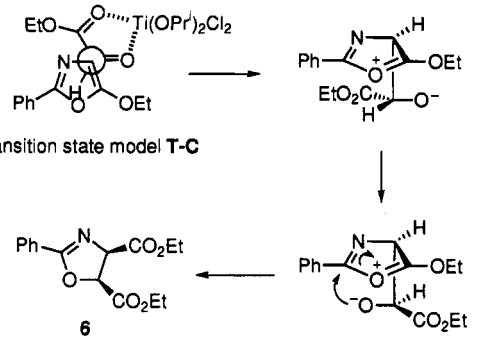


Figure 3. Synclinal approach.

In the reaction of oxazole **5** with ethyl glyoxylate, which is catalyzed by $Ti(OPr^i)_2Cl_2$ generated *in situ* by mixing $TiCl_4$ and $Ti(OPr^i)_4$, the high *cis*-selectivity is explained by another transition state model, **T-C** (Figure 3). Ethyl glyoxylate forms a chelate with $Ti(OPr^i)_2Cl_2$, and the sterically less-hindered synclinal attack of the C4–C5 double bond of oxazole 1 on the formyl group of ethyl glyoxylate seems to be favorable. After the nucleophilic attack of the oxazole, the zwitterionic intermediate cyclizes to afford *cis*-2-oxazoline **6** selectively through the proposed stepwise pathway involving the oxazole ring opening.

In conclusion, the above-described methodology involving the methylaluminum β-binaphthoxide-catalyzed formal [3 + 2] cycloaddition of 5-alkoxyoxazoles with aldehydes has the advantage of high *cis*-selectivity over the previous methods for the synthesis of 2-oxazoline-4-carboxylates.[1-3] The dramatic dependence of the *cis*-selectivity on the structure of the catalyst and the bulkiness of the substituents on the aldehyde makes it probable that the *cis*-selectivity arises from an antiperiplanar approach of the C4–C5 double bond to the aldehyde carbonyl group by a stepwise pathway. Asymmetric versions of this formal [3 + 2] cycloaddition of a 5-alkoxyoxazole with an aldehyde are now under study with chiral catalysts. The results of these studies will be reported in due time.

Experimental Section

General Procedures. Melting points are uncorrected. ^1H NMR spectra were run at 270 or 500 MHz. ^{13}C NMR spectra were determined at 67.8 or 125.7 MHz. Medium-pressure liquid chromatography was carried out on a column packed with silica gel 60 (Merck, size: 0.040–0.063 mm). High-performance liquid chromatography (HPLC) was performed with a Nova-Pak C18 column (Waters). All reactions were carried out under an argon atmosphere in dried glassware.

5-Methoxy-2-(*p*-methoxyphenyl)oxazole (1) and 5-ethoxy-2-phenyloxazole (**5**) were synthesized by the methods described in a literature.[13] MeCN and CH_2Cl_2 were purified by the methods reported previously.[4e]

Typical Procedure for the Reaction of Oxazole 1 with Benzaldehyde in the Presence of the Commercially Available Lewis Acids: Formation of Methyl 2-(*p*-Methoxyphenyl)-5-phenyl-2-oxazoline-4-carboxylate (2a and 3a). To a solution of oxazole 1 (0.205 g, 1.0 mmol or 0.103 g, 0.5 mmol) and benzaldehyde (0.106 g, 0.10 mL, 1.0 mmol or 0.054 g, 0.052 mL, 0.5 mmol) in CH_2Cl_2 and/or MeCN (10 mL or 5 mL) at −20 °C to −78 °C was added a commercially available Lewis acid (1.0 mmol or 0.5 mmol). After the mixture was stirred at the temperature for the time listed in Table I, the catalyst was quenched with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (30 mL × 3). After the organic layer was dried over anhyd $MgSO_4$, removal of the solvent afforded a crude product. This product was analyzed by HPLC using naphthalene as an internal standard.

Typical Procedure for the Reaction of Oxazole 1 with an Aldehyde in the Presence of Catalyst A: Method A. To a solution of (±)-2,2′-dihydroxy-1,1′-binaphthyl (0.205 g, 1.0 mmol) in CH_2Cl_2 (5 mL) was added a 0.99 M hexane solution of Me_3Al (1.0 mL, 1.0 mmol). The resulting solution was stirred at rt for 1 h. After the mixture was cooled to −78 °C, a solution of oxazole 1 (0.205 g, 1.0 mmol) and benzaldehyde (0.106 g, 0.10 mL, 1.0 mmol) in MeCN (5 mL) was added to the solution. The mixture, after stirring at 0 °C for 93 h, was quenched with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (30 mL × 3), the separated organic layer was dried over anhyd $MgSO_4$, and the solvent was removed from the organic solution under reduced pressure. The crude product was analyzed by HPLC using naphthalene as an internal standard. **Method B.** To a solution of (±)-2,2′-dihydroxy-1,1′-binaphthyl (0.293 g, 1.02 mmol) in MeCN (3 mL) was added a 0.99 M hexane solution of Me_3Al (1.03 mL, 1.02 mmol), and the resulting solution was stirred at rt for 1 h. After the mixture was cooled to −20 °C, a solution of oxazole 1 (0.105 g, 0.51 mmol) and benzaldehyde (0.054 g, 0.052 mL, 0.51 mmol) in MeCN (2.5 mL) was added to the solution. The mixture, after stirring at rt for 94 h, was quenched with saturated solution of $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (30 mL × 3), the separated organic layer was dried over anhyd $MgSO_4$, and the solvent was removed from the organic solution under reduced pressure. The crude product was analyzed by HPLC with naphthalene as an internal standard. 2-Oxazolines **3a** and **2a** were isolated in that order by medium-pressure liquid chromatography on silica gel with hexane–ethyl acetate (7:1) and (33:7) as an eluent, respectively.

2a: colorless prisms (benzene–hexane); mp 124.7–128.0 °C; IR (KBr) 1749, 1648 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.22 (3H, s), 3.88 (3H, s), 5.29 (1H, d, J = 10.6 Hz), 5.92 (1H, d, J = 10.6 Hz), 6.95–6.98 (2H, m), 7.29–7.34 (5H, m), 8.04–8.08 (2H, m); ^{13}C NMR ($CDCl_3$) δ 51.6, 55.4, 74.1, 82.7, 113.8, 126.3, 128.2, 128.5, 130.6, 119.2, 136.1, 162.7, 166.4, 169.7. Anal. Found: C, 69.21; H, 5.58; N, 4.53%. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50%.

3a: colorless prisms (benzene–hexane); mp 62.5–65.5 °C; IR (KBr) 1738, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.83 (3H, s), 3.84 (3H, s), 4.79 (1H, d, J = 7.6 Hz), 5.87 (1H, d, J = 7.6 Hz), 6.91–6.95 (2H, m), 7.37 (5H, s), 8.00–8.04 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.8 (q), 55.4 (q), 76.8 (d), 83.0 (d), 113.8, 125.6, 128.6, 128.9, 130.6 (each d), 119.2 (s), 139.7 (s), 162.6 (s), 165.3 (s), 171.5 (s). Anal. Found: C, 69.22; H, 5.57; N, 4.60%. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50%.

A procedure similar to method A or B was employed for the formation of 2-oxazolines **2b–q** and **3b–q**. Although some trace products did not give satisfactory analytical data in a few of cases, these products could be characterized by ^1H NMR.

Methyl 2-(*p*-methoxyphenyl)-5-(*p*-nitrophenyl)-*cis*-2-oxazoline-4-carboxylate (2b): colorless needles (benzene–hexane); mp 155.3–156.0 °C; IR (KBr) 1739, 1646, 1513, 1348 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.27 (3H, s), 3.88 (3H, s), 5.35 (1H, d, J = 10.9 Hz), 5.98 (1H, d, J = 10.9 Hz), 6.95–7.01 (2H, m), 7.46–7.51 (2H, m), 8.00–8.06 (2H, m), 8.18–8.23 (2H, m); ^{13}C NMR ($CDCl_3$) δ 51.9 (q), 55.5 (q), 74.2 (d), 81.5 (d), 114.0, 123.4, 127.27, 130.6 (each d), 118.7 (s), 143.5 (s), 147.9 (s), 163.0 (s), 166.2 (s), 169.2 (s). Anal. Found: C, 60.93; H, 4.61; N, 7.86%. Calcd for $C_{18}H_{16}N_2O_6$: C, 60.67; H, 4.53; N, 7.86%.

Methyl 2-(*p*-methoxyphenyl)-5-(*p*-nitrophenyl)-*trans*-2-oxazoline-4-carboxylate (3b): pale yellow prisms (benzene–hexane); mp 146.2–147.2 °C; IR (KBr) 1723, 1647, 1516, 1341 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.87 (3H, s), 3.89 (3H, s), 4.76 (1H, d, J = 7.6 Hz), 5.98 (1H, d, J = 7.6 Hz), 6.93–7.01 (2H, m), 7.55–7.61 (2H, m), 7.98–8.05 (2H, m), 8.23–8.29 (2H, m); ^{13}C NMR ($CDCl_3$) δ 53.1 (q), 55.5 (q), 76.9 (d), 81.7 (d), 114.0, 124.2, 126.3, 130.6 (each d), 118.7 (s), 146.9 (s), 147.9 (s), 162.9 (s), 165.1 (s), 171.0 (s). Anal. Found: C, 60.98; H, 4.63; N, 7.87%. Calcd for $C_{18}H_{16}N_2O_6$: C, 60.67; H, 4.53; N, 7.86%.

Methyl 2-(*p*-methoxyphenyl)-5-(*m*-nitrophenyl)-*cis*-2-oxazoline-4-carboxylate (2c): colorless prisms (benzene–hexane); mp 121.2–123.3 °C; IR (KBr) 1731, 1644 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.26 (3H, s), 3.86 (3H, s), 5.35 (1H, d, J = 10.6 Hz), 6.00 (1H, d, J = 10.6 Hz), 6.92–7.00 (2H, m), 7.53 (1H, t, J = 7.6 Hz), 7.65

(13) Grifanti, M.; Sein, M. L. *Ann. Chim. (Rome)* **1965**, *55*, 578.

(1H, d, J = 7.6 Hz), 8.00–8.07 (2H, m), 8.15–8.18 (2H, m); ^{13}C NMR ($CDCl_3$) δ 51.8 (q), 55.5 (q), 74.1 (d), 81.4 (d), 114.0, 130.6 (each d), 118.7 (s), 121.4, 123.5, 129.4, 132.2 (each d), 138.5, 148.1 (each s), 163.0 (s), 166.2 (s), 169.2 (s). Anal. Found: C, 60.62; H, 4.59; N, 7.76%. Calcd for $C_{18}H_{16}N_2O_6$: C, 60.67; H, 4.53; N, 7.86%.

Methyl 2-(*p*-methoxyphenyl)-5-(*m*-nitrophenyl)-*trans*-2-oxazoline-4-carboxylate (3c): yellow viscous oil; ^{1}H NMR ($CDCl_3$) δ 3.87 (3H, s), 3.89 (3H, s), 4.77 (1H, d, J = 7.6 Hz), 5.97 (1H, d, J = 7.6 Hz), 6.92–7.00 (2H, m), 7.59 (1H, t, J = 7.9 Hz), 7.74 (1H, d, J = 7.9 Hz), 7.98–8.05 (2H, m), 8.21 (1H, d, J = 8.3 Hz), 8.26 (1H, s).

Methyl 2-(*p*-methoxyphenyl)-5-(*o*-nitrophenyl)-*cis*-2-oxazoline-4-carboxylate (2d): yellow prisms (benzene–hexane); mp 152.2–154.3 °C; ^{1}H NMR ($CDCl_3$) δ 3.22 (3H, s), 3.88 (3H, s), 5.53 (1H, d, J = 10.2 Hz), 6.59 (1H, d, J = 10.2 Hz), 6.94–7.00 (2H, m), 7.49–7.81 (3H, m), 8.00–8.08 (2H, m), 8.22 (1H, d, J = 8.3 Hz).

Methyl 2-(*p*-methoxyphenyl)-5-(*o*-nitrophenyl)-*trans*-2-oxazoline-4-carboxylate (3d): yellow prisms (benzene–hexane); mp 113.3–116.5 °C; IR (KBr) 1744, 1637 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.86 (3H, s), 3.88 (3H, s), 4.70 (1H, d, J = 5.6 Hz), 6.46 (1H, d, J = 5.6 Hz), 6.94–6.98 (2H, m), 7.48–7.70 (3H, m), 8.00–8.05 (2H, m), 8.15 (1H, dd, J = 8.2, 1.3 Hz); ^{13}C NMR ($CDCl_3$) δ 53.0 (q), 55.5 (q), 77.2 (d), 79.7 (d), 113.9, 130.6 (each d), 118.7 (s), 125.4, 126.8, 129.1, 134.5 (each d), 136.2, 146.1 (each s), 162.8 (s), 165.4 (s), 171.2 (s). Anal. Found: C, 60.69; H, 4.56; N, 7.92%. Calcd for $C_{18}H_{16}N_2O_6$: C, 60.67; H, 4.53; N, 7.86%.

Methyl 5-(*p*-chlorophenyl)-2-(*p*-methoxyphenyl)-*cis*-2-oxazoline-4-carboxylate (2e): colorless prisms (benzene–hexane); mp 157.2–160.0 °C; IR (KBr) 1750, 1648 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.27 (3H, s), 3.85 (3H, s), 5.26 (1H, d, J = 10.9 Hz), 5.85 (1H, d, J = 10.9 Hz), 6.92–7.00 (2H, m), 7.20–7.24 (2H, m), 7.28–7.32 (2H, m), 7.89–8.05 (2H, m); ^{13}C NMR ($CDCl_3$) δ 51.8 (q), 55.4 (q), 74.0 (d), 82.0 (d), 113.9, 130.6 (each d), 119.1 (s), 127.7, 128.4 (each d), 134.4 (s), 134.7 (s), 162.8 (s), 166.3 (s), 169.5 (s). Anal. Found: C, 62.80; H, 4.77; N, 4.02%. Calcd for $C_{18}H_{16}NO_4Cl$: C, 62.52; H, 4.66; N, 4.05%.

Methyl 5-(*p*-chlorophenyl)-2-(*p*-methoxyphenyl)-*trans*-2-oxazoline-4-carboxylate (3e): yellow viscous oil; IR (neat) 1735, 1636 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.85 (3H, s), 3.87 (3H, s), 4.73 (1H, d, J = 7.6 Hz), 5.84 (1H, d, J = 7.6 Hz), 6.90–6.98 (2H, m), 7.30–7.38 (4H, m), 7.96–8.04 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.9, 55.4, 76.8, 82.2, 113.8, 130.5, 119.0, 127.0, 129.1, 134.4, 138.2, 162.7, 165.2, 171.3; MS found M$^+$, 345.0758, calcd for $C_{18}H_{16}NO_4Cl$ M$^+$, 345.0768.

Methyl 5-(2,4-dichlorophenyl)-2-(*p*-methoxyphenyl)-*cis*-2-oxazoline-4-carboxylate (2f): pale yellow prisms (benzene–hexane); mp 130.3–131.9 °C; IR (KBr) 1753, 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.28 (3H, s), 3.85 (3H, s), 5.33 (1H, d, J = 10.6 Hz), 6.14 (1H, d, J = 10.6 Hz), 6.92–6.98 (2H, m), 7.23 (1H, dd, J = 8.2, 2.0 Hz), 7.37 (1H, d, J = 5.3 Hz), 7.39 (1H, s), 7.97–8.05 (2H, m); ^{13}C NMR ($CDCl_3$) δ 51.8 (q), 55.4 (q), 72.6 (d), 79.6 (d), 113.9, 130.6 (each d), 119.0 (s), 127.2, 128.3, 128.9 (each d), 132.8, 133.0, 134.7 (each s), 162.9 (s), 166.3 (s), 169.3 (s). Anal. Found: C, 56.82; H, 4.03; N, 3.70%. Calcd for $C_{18}H_{15}NO_4Cl_2$: C, 56.86; H, 3.98; N, 3.68%.

Methyl 5-(2,4-dichlorophenyl)-2-(*p*-methoxyphenyl)-*trans*-2-oxazoline-4-carboxylate (3f): yellow viscous oil; ^{1}H NMR ($CDCl_3$) δ 3.83 (3H, s), 3.84 (3H, s), 4.66 (1H, d, J = 6.6 Hz), 6.19 (1H, d, J = 6.6 Hz), 6.90–6.97 (2H, m), 7.21–7.31 (2H, m), 7.41 (1H, d, J = 1.7 Hz), 7.97–8.04 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.9, 55.5, 76.2, 79.9, 113.9, 130.6, 118.9, 127.6, 127.7, 129.8, 132.3, 134.8, 136.0, 162.8, 165.3, 171.0; MS found M$^+$, 379.0368, calcd for $C_{18}H_{15}NO_4Cl_2$ M$^+$, 379.0378.

Methyl 5-(2,6-dichlorophenyl)-2-(*p*-methoxyphenyl)-*cis*-2-oxazoline-4-carboxylate (2g): yellow prisms (benzene–hexane); IR (KBr) 1750, 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.43 (3H, s), 3.85 (3H, s), 5.41 (1H, d, J = 12.2 Hz), 6.61 (1H, d, J = 12.2 Hz), 6.90–6.96 (2H, m), 7.15–7.33 (3H, m), 7.98–8.04 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.0 (q), 55.4 (q), 72.5 (d), 78.6 (d), 113.8, 130.6 (each d), 119.5 (s), 129.8 (d), 131.8 (s), 162.6 (s), 165.7 (s), 169.6 (s); MS found M$^+$, 379.0360, calcd for $C_{18}H_{15}NO_4Cl_2$ M$^+$, 379.0378.

Methyl 5-(2,6-dichlorophenyl)-2-(*p*-methoxyphenyl)-*trans*-2-oxazoline-4-carboxylate (3g): pale yellow prisms (benzene–hexane); mp 169.5–173.3 °C; IR (KBr) 1742, 1641 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.84 (3H, s), 3.85 (3H, s), 5.06 (1H, d, J = 9.6 Hz), 6.60 (1H, d, J = 9.6 Hz), 6.88–6.95 (2H, m), 7.21–7.39 (3H, m), 7.92–8.00 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.8 (q), 55.4 (q), 74.1 (d), 79.1 (d), 113.7, 130.5 (each d), 119.2 (s), 129.4, 130.4 (each d), 132.5, 136.0 (each s), 162.5 (s), 165.2 (s), 171.4 (s). Anal. Found: C, 57.19; H, 4.05; N, 3.80%. Calcd for $C_{18}H_{15}NO_4Cl_2$: C, 56.86; H, 3.98; N, 3.68%.

Methyl 2-(*p*-methoxyphenyl)-5-(*p*-tolyl)-*cis*-2-oxazoline-4-carboxylate (2h): colorless prisms (benzene–hexane); mp 124.8–127.1 °C; IR (KBr) 1749, 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.32 (3H, s), 3.24 (3H, s), 3.85 (3H, s), 5.25 (1H, d, J = 10.6 Hz), 5.86 (1H, d, J = 10.6 Hz), 6.92–6.96 (2H, m), 7.11–7.18 (4H, m), 8.01–8.04 (2H, m); ^{13}C NMR ($CDCl_3$) δ 21.2 (q), 51.6 (q), 55.4 (q), 74.0 (d), 82.8 (d), 113.8, 130.6 (each d), 119.4 (s), 126.2, 128.9 (each d), 133.1 (s), 138.4 (s), 162.7 (s), 166.4 (s), 169.8 (s). Anal. Found: C, 70.02; H, 5.90; N, 4.26%. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.30%.

Methyl 2-(*p*-methoxyphenyl)-5-(*p*-tolyl)-*trans*-2-oxazoline-4-carboxylate (3h): yellow oil; ^{1}H NMR ($CDCl_3$) δ 2.35 (3H, s), 3.85 (3H, s), 3.92 (3H, s), 4.77 (1H, d, J = 7.3 Hz), 5.82 (1H, d, J = 7.3 Hz), 6.91–6.95 (2H, m), 7.18–7.37 (4H, m), 8.01–8.04 (2H, m).

Methyl 2-(*p*-methoxyphenyl)-5-(*m*-tolyl)-*cis*-2-oxazoline-4-carboxylate (2i): colorless prisms (benzene–hexane); mp 94.8–98.8 °C; IR (KBr) 1756, 1645 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.31 (3H, s), 3.22 (3H, s), 3.83 (3H, s), 5.23 (1H, d, J = 10.9 Hz), 5.84 (1H, d, J = 10.9 Hz), 6.90–6.98 (2H, m), 7.05–7.30 (4H, m), 8.00–8.08 (2H, m); ^{13}C NMR ($CDCl_3$) δ 21.4, 51.6, 55.4, 74.1, 82.8, 113.8, 119.3, 123.4, 126.8, 128.1, 129.4, 130.6, 136.0, 137.9, 162.7, 166.5, 169.8. Anal. Found: C, 70.15; H, 5.87; N, 4.22%. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.30%.

Methyl 2-(*p*-methoxyphenyl)-5-(*m*-tolyl)-*trans*-2-oxazoline-4-carboxylate (3i): yellow oil; ^{1}H NMR ($CDCl_3$) δ 2.36 (3H, s), 3.85 (3H, s), 3.86 (3H, s), 4.78 (1H, d, J = 7.6 Hz), 5.83 (1H, d, J = 7.6 Hz), 6.90–6.98 (2H, m), 7.14–7.31 (4H, m), 7.97–8.05 (2H, m).

Methyl 2-(*p*-methoxyphenyl)-5-(*o*-tolyl)-*cis*-2-oxazoline-4-carboxylate (2j): colorless prisms (benzene–hexane); mp 127.7–130.3 °C; IR (KBr) 1749, 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.39 (3H, s), 3.15 (3H, s), 3.87 (3H, s), 5.27 (1H, d, J = 10.6 Hz), 6.08 (1H, d, J = 10.6 Hz), 6.93–7.00 (2H, m), 7.12–7.22 (3H, m), 7.33 (1H, d, J = 7.3 Hz), 8.01–8.08 (2H, m); ^{13}C NMR ($CDCl_3$) δ 19.2 (q), 51.5 (q), 55.4 (q), 73.0 (d), 80.3 (d), 113.9, 130.5 (each d), 119.4 (s), 125.4, 125.9, 128.2, 130.0 (each d), 134.4, 134.9 (each s), 162.7 (s), 166.7 (s), 169.7 (s). Anal. Found: C, 70.37; H, 5.91; N, 4.35%. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.30%.

Methyl 2-(*p*-methoxyphenyl)-5-(*o*-tolyl)-*trans*-2-oxazoline-4-carboxylate (3j): pale yellow viscous oil; ^{1}H NMR ($CDCl_3$) δ 2.38 (3H, s), 3.84 (3H, s), 3.86 (3H, s), 4.73 (1H, d, J = 6.9 Hz), 6.11 (1H, d, J = 6.9 Hz), 6.91–6.97 (2H, m), 7.18–7.29 (4H, m), 7.99–8.04 (2H, m); ^{13}C NMR ($CDCl_3$) δ 19.2 (q), 52.8 (q), 55.4 (q), 76.2 (d), 80.7 (d), 113.8, 130.6 (each d), 119.3 (s), 125.5, 126.5, 128.4, 130.9 (each d), 135.0, 137.6 (each s), 162.6 (s), 165.4 (s), 171.7 (s); MS found M$^+$, 325.1300, calcd for $C_{19}H_{19}NO_4$ M$^+$, 325.1314.

Methyl 2,5-bis(*p*-methoxyphenyl)-*cis*-2-oxazoline-4-carboxylate (2k): colorless prisms (benzene–hexane) mp 147.5–150.4 °C; IR (KBr) 1749, 1646 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.26 (3H, s), 3.77 (3H, s), 3.81 (3H, s), 5.22 (1H, d, J = 10.6 Hz), 5.85 (1H, d, J = 10.6 Hz), 6.80–6.87 (2H, m), 6.91–6.97 (2H, m), 7.17–7.23 (2H, m), 7.99–8.05 (2H, m); ^{13}C NMR ($CDCl_3$) δ 51.7 (q), 55.3 (q), 55.4 (q), 74.0 (d), 82.6 (d), 113.6, 113.8, 127.7, 130.6 (each d), 119.4, 128.2 (each s), 159.8, 162.7 (each s), 166.4 (s), 169.9 (s). Anal. Found: C, 66.93; H, 5.64; N, 4.07%. Calcd for $C_{19}H_{19}NO_5$: C, 66.85; H, 5.61; N, 4.10%.

Methyl 2,5-bis(*p*-methoxyphenyl)-*trans*-2-oxazoline-4-carboxylate (3k): yellow oil; ^{1}H NMR ($CDCl_3$) δ 3.80 (3H, s), 3.83 (3H, s), 3.85 (3H, s), 4.77 (1H, d, J = 7.6 Hz), 5.80 (1H, d, J = 7.6 Hz), 6.88–6.95 (4H, m), 7.28–7.34 (2H, m), 7.87–8.03 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.8 (q), 55.3 (q), 55.4 (q), 76.7 (d), 83.0 (d), 113.7, 114.3, 127.3, 130.5 (each d), 119.4, 131.6 (each s), 159.9, 162.6 (each s), 165.3 (s), 171.6 (s); MS found M$^+$, 341.1259, calcd for $C_{19}H_{19}NO_5$ M$^+$, 341.1263.

Methyl 2-(*p*-methoxyphenyl)-5-(2(*E*)-phenylethenyl)-*cis*-2-oxazoline-4-carboxylate (2l): colorless prisms (benzene–hexane) mp 123.0–125.4 °C; IR (KBr) 1730, 1638 cm^{-1}; ^{1}H NMR

($CDCl_3$) δ 3.66 (3H, s), 3.83 (3H, s), 5.10 (1H, d, J = 10.2 Hz), 5.45 (1H, dd, J = 10.2, 7.9 Hz), 6.21 (1H, dd, J = 15.8, 7.9 Hz), 6.73 (1H, d, J = 15.8 Hz), 6.90–6.97 (2H, m), 7.26–7.38 (5H, m), 7.95–8.02 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.2 (q), 55.4 (q), 72.7 (d), 82.0 (d), 113.8, 130.5 (each d), 119.4 (s), 122.9 (d), 126.8, 128.4, 128.7 (each d), 134.7 (d), 135.8 (s), 162.6 (s), 166.2 (s), 170.2 (s). Anal. Found: C, 71.41; H, 5.77; N, 4.14%. Calcd for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15%.

Methyl 2-(*p*-methoxyphenyl)-5-(2(*E*)-phenylethenyl)-*trans*-2-oxazoline-4-carboxylate (3l): yellow oil; ^1H NMR ($CDCl_3$) δ 3.83 (3H, s), 3.85 (3H, s), 4.69 (1H, d, J = 7.6 Hz), 5.48 (1H, t, J = 7.6 Hz), 6.29 (1H, dd, J = 15.8, 7.6 Hz), 6.77 (1H, d, J = 15.8 Hz), 6.90–6.95 (2H, m), 7.26–7.43 (5H, m), 7.94–8.00 (2H, m).

Methyl 5-ethyl-2-(*p*-methoxyphenyl)-*cis*-2-oxazoline-4-carboxylate (2m): pale yellow oil; IR (neat) 1749, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (3H, t, J = 7.3 Hz), 1.62–1.73 (2H, m), 3.76 (3H, s), 3.85 (3H, s), 4.78 (1H, ddd, J = 5.9, 7.9 Hz, J_{5-4} = 10.2 Hz), 4.96 (1H, d, J_{4-5} = 10.2 Hz), 6.89–6.94 (2H, m), 7.91–7.97 (2H, m); ^{13}C NMR ($CDCl_3$) δ 10.7 (q), 24.0 (t), 52.1 (q), 55.4 (q), 71.2 (d), 83.0 (d), 113.7, 130.4 (each d), 119.8 (s), 162.5 (s), 166.1 (s), 170.7 (s). Anal. Found: C, 63.61; H, 6.59; N, 5.10%. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32%.

Methyl 5-ethyl-2-(*p*-methoxyphenyl)-*trans*-2-oxazoline-4-carboxylate (3m): colorless oil; IR (neat) 1741, 1636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (3H, t, J = 7.3 Hz), 1.81 (2H, dq, J = 14.5, 7.3 Hz), 3.81 (3H, s), 3.85 (3H, s), 4.49 (1H, d, J_{4-5} = 6.9 Hz), 4.81 (1H, dt, J_{5-4} = 6.9, J = 6.6 Hz), 6.87–6.95 (2H, m), 7.90–7.98 (3H, dt, J = 8.9, 2.6 Hz); ^{13}C NMR ($CDCl_3$) δ 9.0 (q), 28.2 (t), 52.6 (q), 55.4 (q), 73.1 (d), 83.6 (d), 113.7 130.3 (each d), 119.7 (s), 162.5 (s), 165.5 (s), 172.0 (s). Anal. Found: C, 62.83; H, 6.54; N, 5.36%. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32%.

Methyl 2-(*p*-methoxyphenyl)-5-(3-pyridyl)-*cis*-2-oxazoline-4-carboxylate (2n): colorless prisms (benzene–hexane); mp 132.4–135.6 °C; IR (KBr) 1747, 1647 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.27 (3H, s), 3.88 (3H, s), 5.33 (1H, d, J = 10.9 Hz), 5.94 (1H, d, J = 10.9 Hz), 6.94–7.00 (2H, m), 7.28 (1H, dd, J = 7.9, 4.6 Hz), 7.63 (1H, d, J = 7.9 Hz), 8.00–8.06 (2H, m), 8.57 (2H, brs); ^{13}C NMR ($CDCl_3$) δ 51.9 (q), 55.4 (q), 74.0 (d), 80.3 (d), 113.9, 130.6 (each d), 118.8 (s), 123.2, 133.9, 147.9, 150.0 (d), 132.0 (s), 162.8 (s), 166.3 (s), 169.4 (s). Anal. Found: C, 65.46; H, 5.28; N, 8.87%. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.38; H, 5.16; N, 8.97%.

Methyl 2-(*p*-methoxyphenyl)-5-(3-pyridyl)-*trans*-2-oxazoline-4-carboxylate (3n): yellow oil; IR (neat) 1738 , 1642 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.872 (3H, s), 3.875 (3H, s), 4.79 (1H, d, J = 7.6 Hz), 5.91 (1H, d, J = 7.6 Hz), 6.94–6.98 (2H, m), 7.35 (1H, dd, J = 7.9, 5.0 Hz), 7.72 (1H, d, J = 7.9 Hz), 7.97–8.03 (2H, m), 8.62–8.68 (2H, m); ^{13}C NMR ($CDCl_3$) δ 53.0, 55.4, 76.7, 80.7, 113.9, 130.6, 118.8, 123.8, 133.4, 135.3, 147.4, 150.0, 162.8, 165.2, 171.1; MS found M^+, 312.1108, calcd for $C_{17}H_{16}N_2O_4$ M^+, 312.1110.

Methyl 2-(*p*-methoxyphenyl)-5-(2-pyridyl)-*cis*-2-oxazoline-4-carboxylate (2o): yellow prisms (benzene); mp 98.0–99.6 °C; IR (KBr) 1743, 1647 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.33 (3H, s), 3.87 (3H, s), 5.40 (1H, d, J = 10.6 Hz), 6.00 (1H, d, J = 10.6 Hz), 6.92–7.00 (2H, m), 7.22 (1H, ddd, J = 7.9, 4.6, 1.0 Hz), 7.43 (1H, d, J = 7.9 Hz), 7.70 (1H, dt, J = 1.0, 7.9 Hz), 8.00–8.08 (2H, m), 8.57 (1H, d, J = 4.6 Hz); ^{13}C NMR ($CDCl_3$) δ 51.9 (q), 55.4 (q), 73.3 (d), 82.9 (d), 113.8, 130.6 (each d), 119.1 (s), 120.9, 123.1, 136.7, 149.0 (each d), 156.7 (s), 162.7 (s), 166.2 (s), 169.9 (s). Anal. Found: C, 65.17; H, 5.25; N, 8.83%. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.38; H, 5.16; N, 8.97%.

Methyl 2-(*p*-methoxyphenyl)-5-(2-pyridyl)-*trans*-2-oxazoline-4-carboxylate (3o): colorless oil; ^1H NMR ($CDCl_3$) δ 3.86 (6H, s), 5.13 (1H, d, J = 6.6 Hz), 6.00 (1H, d, J = 6.6 Hz), 6.91–6.97 (2H, m), 7.24–7.29 (1H, m), 7.45 (1H, d, J = 7.9 Hz), 7.72 (1H, dt, J = 1.7, 7.9 Hz), 7.99–8.05 (2H, m), 8.65 (1H, d, J = 5.0 Hz); ^{13}C NMR ($CDCl_3$) δ 52.9, 55.4, 75.0, 82.8, 113.8, 130.6, 119.2, 120.8, 123.3, 137.0, 149.9, 158.3, 162.6, 165.0, 171.5; MS found M^+, 312.1086, calcd for $C_{17}H_{16}N_2O_4$ M^+, 312.1110.

Methyl 5-(3-furyl)-2-(*p*-methoxyphenyl)-*cis*-2-oxazoline-4-carboxylate (2p): colorless prisms (benzene–hexane); mp 111.3–114.0 °C; ^1H NMR ($CDCl_3$) δ 3.49 (3H, s), 3.85 (3H, s), 5.17 (1H, d, J = 10.6 Hz), 5.88 (1H, d, J = 10.6 Hz), 6.32 (1H, d, J = 1.7 Hz), 6.92–6.97 (2H, m), 7.37 (1H, t, J = 1.7 Hz), 7.48 (1H, brs), 7.96–8.02 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.0 (q), 55.4 (q), 73.0 (d), 76.2 (d), 108.6 (d), 113.8, 130.5 (each d), 119.2 (s), 121.1 (s), 140.8, 143.6 (each d), 162.7 (s), 166.1 (s), 170.0 (s). Anal. Found: C, 63.50; H, 5.07; N, 4.64%. Calcd for $C_{16}H_{15}O_5N$: C, 63.78; H, 5.02; N, 4.65%.

Methyl 5-(3-furyl)-2-(*p*-methoxyphenyl)-*trans*-2-oxazoline-4-carboxylate (3p): yellow oil; ^1H NMR ($CDCl_3$) δ 3.84 (3H, s), 3.85 (3H, s), 4.79 (1H, d, J = 7.6 Hz), 5.84 (1H, d, J = 7.6 Hz), 6.43 (1H, d, J = 1.7 Hz), 6.89–6.95 (2H, m), 7.45 (1H, t, J = 1.7 Hz), 7.55 (1H, brs), 7.92–7.99 (2H, m).

Methyl 5-(2-furyl)-2-(*p*-methoxyphenyl)-*cis*-2-oxazoline-4-carboxylate (2q): yellow oil; ^1H NMR ($CDCl_3$) δ 3.54 (3H, s), 3.85 (3H, s), 5.22 (1H, d, J = 10.9 Hz), 5.90 (1H, d, J = 10.9 Hz), 6.36 (1H, dd, J = 3.3, 2.0 Hz), 6.43 (1H, brd, J = 3.3 Hz), 6.91–6.95 (2H, m), 7.39 (1H, dd, J = 2.0, 1.0 Hz), 7.97–8.00 (2H, m).

Methyl 5-(2-furyl)-2-(*p*-methoxyphenyl)-*trans*-2-oxazoline-4-carboxylate (3q): yellow oil; ^1H NMR ($CDCl_3$) δ 3.78 (3H, s), 3.80 (3H, s), 5.09 (1H, d, J = 7.6 Hz), 5.89 (1H, d, J = 7.6 Hz), 6.36 (1H, dd, J = 3.3, 2.0 Hz), 6.50 (1H, d, J = 3.3 Hz), 6.85–6.92 (2H, m), 7.44 (1H, d, J = 2.0 Hz), 7.90–7.98 (2H, m); ^{13}C NMR ($CDCl_3$) δ 52.8 (q), 55.3 (q), 72.7 (d), 76.2 (d), 109.9, 110.6 (each d), 113.7, 130.5 (each d), 119.2 (s), 143.8 (d), 150.4 (s), 162.6 (s), 164.9 (s), 171.0 (s).

Methyl 3-(2-furyl)-2-[(*p*-methoxybenzoyl)amino]propenoate (4): brown prisms (benzene); mp 132.6–135.8 °C; IR (KBr) 3423, 3225, 1724 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.79 (3H, s), 3.84 (3H, s), 6.43 (1H, dd, J = 3.0, 1.7 Hz), 6.56 (1H, d, J = 3.6 Hz), 6.90–6.98 (2H, m), 7.03 (1H, s), 7.46 (1H, d, J = 1.7 Hz), 7.85–7.92 (2H, m), 8.33 (1H, brs); ^{13}C NMR ($CDCl_3$) δ 52.5 (q), 55.4 (q), 112.3, 115.2 (each d), 113.9, 129.5 (each d), 116.4 (d), 123.3 (s), 125.8 (s), 144.4 (d), 150.0 (s), 162.8 (s), 165.3 (s), 165.5 (s). Anal. Found: C, 63.69; H, 5.07; N, 4.54%. Calcd for $C_{16}H_{15}NO_5$: C, 63.78; H, 5.02; N, 4.65%.

Epimerization of *cis*-2-Oxazoline 2q in the Presence of Catalyst A. To a solution of (±)-2,2′-dihydroxy-1,1′-binaphthyl (0.112 g, 0.392 mmol) in MeCN (5 mL) was added a 0.99 M hexane solution of Me_3Al (0.396 mL, 0.392 mmol). The resulting solution was stirred at rt for 1 h. After the mixture was cooled to −20 °C, a solution of **2q** (0.059 g, 0.196 mmol) in MeCN (5 mL) was added to the solution. The mixture, after stirring at rt for 48 h, was quenched with a saturated solution of $NaHCO_3$. After the aqueous layer was extracted with CH_2Cl_2 (20 mL × 3), the separated organic layer was dried over anhyd $MgSO_4$. Removal of the solvent from the organic solution under reduced pressure gave a residue. This residue was chromatographed over silica gel with hexane–ethyl acetate (23:13) to give *trans*-2-oxazoline **3q** (0.018 g, 30%) and a mixture (0.018 g) of **2q** (3%) and **4** (26%). The yields of **2q** and **4** were determined by ^1H NMR.

Typical Procedure for the Reaction of Oxazole 5 with Ethyl Glyoxylate in the Presence of Commercially Available Lewis Acids: Method Using $SnCl_4$. To a solution of oxazole **5** (0.189 g, 1.0 mmol) and ethyl glyoxylate (0.204 g, 2.0 mmol) in MeCN (10 mL) at −20 °C was added $SnCl_4$ (0.12 mL, 1.0 mmol). The mixture was stirred at rt for 10.5 h and quenched with a saturated solution of $NaHCO_3$. After the aqueous layer was extracted with CH_2Cl_2 (30 mL × 3), the separated organic layer was dried over anhyd $MgSO_4$. Removal of the solvent under reduced pressure gave a crude product, which was analyzed by HPLC using naphthalene as an internal standard.

Method Using $TiCl_4$ and $Ti(i\text{-}PrO)_4$. To $Ti(i\text{-}PrO)_4$ (0.30 mL, 1.0 mmol) at 0 °C was added $TiCl_4$ (0.11 mL, 1.0 mmol). After the resulting solution was stirred at rt for 5 min, a solution of oxazole **5** (0.378 g, 2.0 mmol) and ethyl glyoxylate (0.442 g, 4.0 mmol) in MeCN (20 mL) was added. The mixture was stirred for 13 h and quenched with a saturated solution of $NaHCO_3$. After the aqueous layer was extracted with CH_2Cl_2 (30 mL × 3), the separated organic layer was dried over anhyd $MgSO_4$, and the solvent was removed under reduced pressure. The crude product obtained was analyzed by HPLC using naphthalene as an internal standard. 2-Oxazolines **6** and **7** were isolated on medium-pressure liquid chromatography on silica gel by elution with a mixed solvent of hexane–ethyl acetate, 19:1 and 9:1, respectively.

Diethyl *cis*-2-phenyl-2-oxazoline-4,5-dicaboxylate (6): colorless prisms (ether–hexane); mp 96.9–97.9 °C; IR (KBr) 1759, 1736, 1656 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.290 (3H, t, J = 7.3 Hz), 1.292 (3H, t, J = 7.3 Hz), 4.18–4.29 (4H, m), 5.20 (1H, d, J = 10.8 Hz), 5.26 (1H, d, J = 10.8 Hz), 7.27–7.53 (3H, m),

8.01–8.04 (2H, m); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 14.03, 14.06, 61.83, 61.86, 72.2, 78.4, 126.5, 128.4, 128.9, 132.2, 166.2, 168.0, 168.9. Anal. Found: C, 61.81; H, 5.93; N, 4.77%. Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81%.

Diethyl *trans*-2-phenyl-2-oxazoline-4,5-dicaboxylate (7): colorless prisms (ether–hexane); mp 58.8–60.1 °C; IR (KBr) 1735, 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.32 (3H, t, J = 7.1 Hz), 1.35 (3H, t, J = 7.1 Hz), 4.25–4.34 (4H, m), 4.98 (1H, d, J = 6.7 Hz), 5.38 (1H, d, J = 6.7 Hz), 7.41–7.53 (3H, m), 8.01–8.04 (2H, m); ^{13}C NMR ($CDCl_3$, 125.7 MHz) δ 14.13, 14.15, 62.2, 62.3, 73.1, 78.4, 126.5, 128.9, 132.2, 165.5, 169.2, 169.8. Anal. Found: C, 61.87; H, 5.92; N, 4.81%. Calcd for $C_{15}H_{17}O_5N$: C, 61.85; H, 5.88; N, 4.81%.

Methyl 2-(*p*-Methoxyphenyl)-5-(trichloromethyl)-*trans*-2-oxazoline-4-carboxylate (8). To a solution of oxazole 1 (0.205 g, 1.0 mmol) and chloral (0.295 g, 2.0 mmol) in MeCN (10 mL) at −20 °C was added $SnCl_4$ (0.23 mL, 2.0 mmol). The mixture, after stirring at rt for 45 h, was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (30 mL × 3), and the separated organic layer was dried over anhyd $MgSO_4$. Removal of the solvent from the organic solution under reduced pressure gave a residue. This residue was chromatographed over silica gel with hexane–ethyl acetate (37:3) to give *trans*-2-oxazoline 8 (0.230 g, 65%) and unchanged 1 (0.017 g, 8.3%): colorless needles (hexane); mp 76.7–77.6 °C; IR (KBr) 1739, 1646 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.85 (3H, s), 3.87 (3H, s), 4.98 (1H, d, J = 5.6 Hz), 5.52 (1H, d, J = 5.6 Hz), 6.90–6.98 (2H, m), 7.93–8.01 (2H, m); ^{13}C NMR ($CDCl_3$) δ 53.2, 55.4 (each q), 72.7 (d), 89.7 (d), 98.0 (s), 113.9, 130.6 (each d), 118.1 (s), 163.0 (s), 164.7 (s), 169.7 (s). Anal. Found: C, 44.40; H, 3.39; N, 4.02%. Calcd for $C_{13}H_{12}NO_4Cl_3$: C, 44.28; H, 3.43; N, 3.97%.

Ethyl 2-Phenyl-5-(trichloromethyl)-*trans*-2-oxazoline-4-carboxylate (9). A similar procedure using oxazole 5 (0.189 g, 1.0 mmol) at rt for 42 h gave *trans*-2-oxazoline 9 (0.189 g, 56%) and unchanged 5 (0.049 g, 26%) after chromatography over silica gel with hexane–ethyl acetate (19:1): colorless prisms (hexane); mp 61.9–64.4 °C; IR (KBr) 1740, 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.37 (3H, t, J = 6.9 Hz), 4.24–4.42 (2H, m), 4.99 (1H, d, J = 5.9 Hz), 5.54 (1H, d, J = 5.9 Hz), 7.42–7.58 (3H, m), 8.01–8.05 (2H, m); ^{13}C NMR ($CDCl_3$) δ 14.1 (q), 62.5 (t), 72.9 (d), 89.9 (d), 98.0 (s), 125.8 (s), 128.5, 128.8, 132.4 (each d), 164.8 (s), 169.0 (s). Anal. Found: C, 46.37; H, 3.63; N, 4.18%. Calcd for $C_{13}H_{12}NO_2Cl_3$: C, 46.39; H, 3.59; N, 4.16%.

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