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STUDIES OF C-H BOND CARBONYLATION AND DECARBONYLATIVE CLEAVAGE OF C-C BONDS CATALYZED BY RUTHENIUM COMPLEXES

Yutaka Ie

OSAKA UNIVERSITY

2000

STUDIES OF C-H BOND CARBONYLATION AND DECARBONYLATIVE CLEAVAGE OF C-C BONDS CATALYZED BY RUTHENIUM COMPLEXES

（ルテニウム触媒による炭素－水素結合のカルボニル化および炭素－炭素結合の脱カルボニル化的切断反応に関する研究）

Yutaka Ie

OSAKA UNIVERSITY

2000

Acknowledgments

The study presented in this thesis has been carried out under the direction of Professor Shinji Murai at the Department of Applied Chemistry, Faculty of Engineering, Osaka University from April, 1994 to March, 2000. The thesis is concerned with the ruthenium-catalyzed direct carbonylation at a C-H bond in the benzene ring and decarbonylative cleavage of C-C bonds of alkyl phenyl ketones.

I would like to express my utmost gratitude to Professor Shinji Murai for his guidance, suggestions, and hearty encouragement throughout this work. I was deeply impressed by not only his attitude toward chemistry but also his view of life. I shall be grateful to him.

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The destruction of Kobe city by Great Hannshin earthquake on January, 17, 1995 did serious damage to our lives, but dreams, hope, and cooperations enabled us to reconstruct Kobe. I am sure that we can apply this experience to our study of chemistry. We sometimes face with the failure or get stuck. Though the accomplishment of study will not be achieved alone, not only dreams, hope, efforts but also cooperations, suggestions from people, who have the same aim, will show us the bright future. I wish the study in this field would develop and shine as the Kobe Luminaries does every year.

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Suita, Osaka

March 2000

Yutaka Ie

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General Introduction

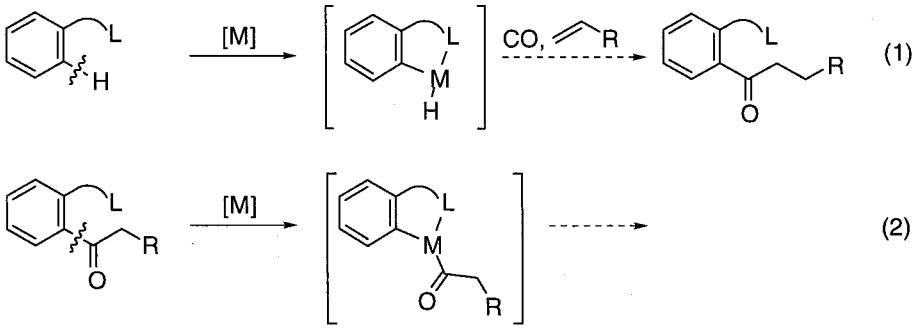
Considering attention has been focused on the development of the transition metal catalyzed reactions which involve the cleavage of unactivated bonds, such as C-H, C-F, and C-C bonds.[1] Despite their potential use in organic synthesis, the utilization of unactivated bonds as functional groups has not been explored extensively. Studies of C-C bond formation via unactivated bond cleavage would lead to a new category of chemistry. In addition, the use of traditionally unreactive molecules as synthetic precursors is becoming increasingly more attractive due to their abundance and low costs. However, the exploration of catalytic reactions which involve the cleavage of these bonds by transition metals remained a challenging task. One explanation could be the high C-H, C-F and C-C bond dissociation energies which have been calculated to 110, 115, and 93 kcal/mol for benzene, hexafluorobenzene, and toluene, respectively.

Recently, significant progress in catalytic reactions involving the cleavage of C-H bond has been made. In 1993, Murai reported the ruthenium-catalyzed addition reaction of *ortho* C-H bonds of acetophenones to olefins.[2] This prominent discovery was achieved by the cleavage of *ortho* C-H bond by use of the chelation assistance to form the cyclometalated complexes. Since this prominent discovery, a number of examples of catalytic additions of C-H bonds to olefins and acetylenes have been investigated for their potential utility.[3] While carbonylation reactions involving C-H bond cleavage would lead to aromatic carbonyl compounds directly from simple aromatic derivatives, there has been limited success in these reactions. Heteroaromatic rings heve been known to undergo carbonylation reactions of C-H bonds.[4-6] In contrast to the reactions of heteroaromatic rings, the direct carbonylation of C-H bonds in benzene rings is still rare.[7-9]

Catalytic reactions involving the cleavage of C-C bonds are also difficult to achieve. Although several catalytic reactions in which the cleavage of C-C bonds occur have already reported, most of them require the release of ring strain or the presence of an activating functionality.[10] Suggs and Jun reported the C-C bond cleavage of unstrained ketones which

utilize the chelation of sp^2 nitrogen such as quinoline and pyridine.[11, 12] In these reactions, the cleavage of C-C bonds were facilitated by the presence of directing group.

The prime objective of this thesis is to develop new catalytic reactions which involve the cleavage of C-H and C-C bonds by using of a directing group (a coordinating group) (eqs 1, 2). This thesis consists of the following three chapters.



Chapter 1 discusses the results of ruthenium-catalyzed reaction of pyridylbenzenes with CO and olefins. This reaction represents the first example of effective carbonylation of a benzene ring by cleavage of C-H bonds. The key feature of this catalytic reaction is the utilization of a directing group of the pyridine to the ruthenium.

Chapter 2 discusses the results of ruthenium-catalyzed reaction of 2-phenyloxazolines with CO and olefins. It is worth noting that the oxazoline ring also has a dramatic effect on both the reactivity and the site selectivity of the carbonylation of a C-H bond in a benzene ring. The details concerning the scope and limitation of the reaction, functional groups compatibility and discussion of the reaction mechanism are included.

Chapter 3 discusses the results of decarbonylative cleavage of a C-C bond of alkyl phenyl ketones. In this reaction, the presence of an oxazoline ring is necessary as a directing group to promote the reaction. Following the promotion is the site selective cleavage of C-C bond at the ortho position. The alkyl moieties in the alkyl phenyl ketones are converted into olefins, or ketenes if the formations of olefins are not possible for steric reasons.

References

(1) For a recent review on the cleavage of unreactive bonds, see: Murai, S. In *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S. Ed.; Springer: Berlin, 1999. For reviews on the cleavage of C-C bonds, see: Rybtchinski, B.; Milstein, D. *Angew. Chem. Int. Ed.* **1999**, *38*, 870. Jennings, P. W.; Johnson, L. L. *Chem. Rev.* **1994**, *94*, 2241. For reviews on the cleavage of C-H bonds, see: Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879. For a review on the cleavage of C-F bonds, see: Kiplinger, J. L.; Richmond, T. G.; Osterberg, C. E. *Chem. Rev.* **1994**, *94*, 373.

(2) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529.

(3) For a recent review fucused on catalytic reactions involving the cleavage of C-H bonds, see: Kakiuchi, F.; Murai, S. In *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S. Ed.; Springer: Berlin, 1999; pp. 47-80.

(4) Moore, E.; Pretzer, W. R.; O'Connell, T. J.; Harris, J.; LaBounty, L.; Chou, L.; Grimmer, S. S. *J. Am. Chem. Soc.* **1992**, *114*, 5888.

(5) Chatani, N.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1996**, *118*, 493.

(6) Fukuyama, T.; Chatani, N.; Tatsumi, J.; Kakiuchi, F. Murai, S. *J. Am. Chem. Soc.* **1998**, *120*, 11522

(7) Hong, P.; Yamazaki, H. *Chem. Lett.* **1979**, 1335.

(8) For transition metal-catalyzed carbonylation at a C-H bond under irradiation, see: Fisher, B. J.; Eisenberg, R. *Organometallics* **1983**, *2*, 764. Kunin, A. J.; Eisenberg, R. *J. Am. Chem. Soc.* **1986**, *108*, 535. Kunin, A. J.; Eisenberg, R. *Organometallics* **1988**, *7*, 2124. Gordon, E. M.; Eisenberg, R. *J. Mol. Catal.* **1988**, *45*, 57. Sakakura, T.; Tanaka, M. *Chem. Lett.* **1987**, 249. Sakakura, T.; Tanaka, M. *J. Chem. Soc., Chem. Commun.* **1987**, 758. Sakakura, T.; Sodeyama, T.; Sasaki, K.; Wada, K.; Tanaka, M. *J. Am. Chem. Soc.* **1990**, *112*, 7221. Boyd, S. E.; Field, L. D.; Partridge, M. G. *J. Am. Chem. Soc.* **1994**, *116*, 9492. Rosini, G. P.; Boese, W. T.; Goldman, A. S. *J. Am. Chem. Soc.* **1994**, *116*, 9498.

(9) Many examples have been reported for transition metal-catalyzed carbonylation which involves electrophilic substitution at the benzene ring to make carbon-transition metal bonds. For a recent review, see: Fujiwara, Y.; Takaki, K.; Taniguchi, Y. *Synlett* **1996**, 591.

(10) For a recent review fucused on catalytic reactions involving the cleavage of C-C bonds, see: Murakami, M.; Ito, Y. In *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S. Ed.; Springer: Berlin, 1999; pp. 97-129.

(11) Suggs, J. W.; Jun, C.-H. *J. Chem. Soc., Chem. Commun.* **1985**, 92.

(12) Jun, C.-H.; Lee, H. *J. Am. Chem. Soc.* **1999**, *121*, 880.

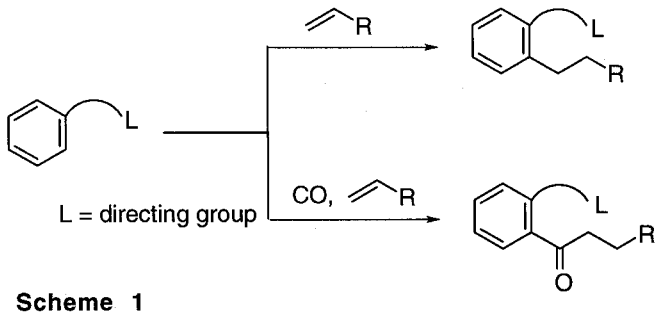
Chapter 1

Ruthenium-Catalyzed Reaction of Pyridylbenzenes with CO and olefins. Direct Carbonylation at a C-H Bond in the Benzene Ring

1.1 Introduction

Transition-metal-catalyzed carbonylation of a benzene ring represents a useful synthetic route for the production of aromatic carbonyl compounds.[1] A variety of compounds, such as PhI, PhOTf, PhN_2BF_4,[2] PPh_4Cl,[3] $(PhS)_2$,[4] $(PhSe)_2$,[4] $PhB(OH)_2$,[5] PhHg(OAc),[6] $PhTl(O_2CCF_3)_2$,[7] and Ph_4Pb[8] have been used as starting materials for the transition-metal-catalyzed carbonylation of a benzene ring. These reactions involve cleavage of C-I, C-O, C-N, C-P, C-S, C-Se, C-B, C-Hg, C-Tl, and C-Pb bonds, respectively, although the mechanism of cleavage of these bonds by transition metals are not the same for each case. Carbonylation of a benzene ring involving C-H bond fission has also been extensively studied, since this process would represent useful synthetic routes for aromatic carbonyl compounds directly from simple aromatic derivatives. The reactions can be classified into two types, depending on the mechanism of cleavage of the C-H bond; (i) oxidative addition (or its equivalent) of the C-H bond to a transition metal and (ii) electrophilic substitution at the benzene ring by a transition metal complex. Many examples have been reported for the latter case.[9, 10] In contrast, there has been only limited success in finding carbonylation reactions which involve C-H bond cleavage. Hong and Yamasaki reported that propiophenone was obtained as a minor product in the $Rh_4(CO)_{12}$-catalyzed reaction of benzene with ethylene under CO.[11] Eisenberg reported that $IrH_3(CO)(dppe)$ and $RhCl(CO)(PPh_3)_2$ promoted the carbonylation of benzene by photo-irradiation to give benzaldehyde.[12] Later Tanaka[13] found that $RhCl(CO)(PMe_3)_2$ was much more effective for the irradiation-catalyzed carbonylation of benzene.[14] In contrast to a benzene ring, heteroaromatic rings are known to undergo carbonylation reactions of a C-H bond. Moore reported that the catalytic carbonylation of pyridine involves the cleavage of a C-H bond α to the ring nitrogen atom.[15] We have reported on the $Ru_3(CO)_{12}$-catalyzed reaction of 1,2-disubstituted imidazoles with CO and olefins, in which carbonylation occurs at the C-H bond α to the sp^2-nitrogen.[16] We have quite recently found that benzimidazole derivatives underwent carbonylation reaction with the cleavage of a C-H bond β to the sp^2-nitrogen.[17] In contrast to these reactions of heteroaromatic rings, the direct carbonylation of a C-H bond in benzene rings is still rare.[11-14]

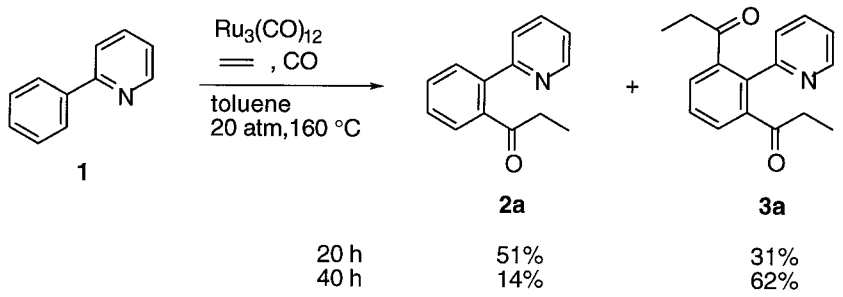
To attain both high efficiency and high site selectivity in the cleavage of a C-H bond in a benzene ring, the presence of a directing group[18] at an appropriate position is effective, in order to position metal close to the C-H bond. Indeed, several functional groups, such as ketones,[19-23] esters,[24] pyridine (*N*-heterocycle),[25-28] diazo,[29] and imine[30] have been found to promote C-C bond formation with the regioselective cleavage of C-H bonds. I wish to describe that carbonylation at a C-H bond in the benzene ring takes place during the $Ru_3(CO)_{12}$-catalyzed reaction of pyridylbenzenes with CO and olefins. The pyridine ring has a dramatic effect on both reactivity and selectivity on the carbonylation of a C-H bond in the benzene ring. The present reaction represents the first, effective catalytic carbonylation reaction involving cleavage of the benzene C-H bond.



Scheme 1

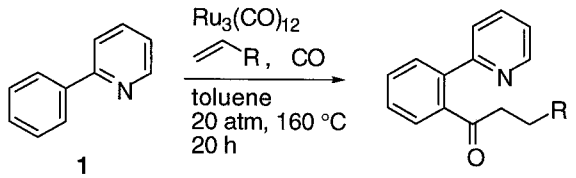
1.2 Carbonylation at a C-H Bond in the Benzene Ring of Pyridylbenzenes

The reaction of 2-phenylpyridine (**1**, 2 mmol) with ethylene (initial pressure 7 atm at 25 °C in 50-mL stainless autoclave) at 20 atm (initial pressure at 25 °C) of CO at 160 °C in toluene in the presence of $Ru_3(CO)_{12}$ (0.05 mmol) for 20 h gave 2-(2-propionylphenyl)pyridine (**2a**) in 51% isolated yield and 2-(2,6-di(propionyl)phenyl)pyridine (**3a**) in 31% isolated yield (eq 1). The benzene C-H bond reacted more rapidly. No carbonylation occurred at a C-H bond α to the aromatic nitrogen, although $Ru_3(CO)_{12}$ is known to catalyze the coupling of pyridine, CO, and olefins.[15] Carbonylation does not occur at a *meta* C-H bond or at a *para* C-H bond. The reaction proceeded beyond the mono propionylation stage. Prolonged reaction times (40 h) gave **3a** as a main product in 62% yield, along with **2a** in 14% yield. The catalytic activity of other complexes was then examined. Complexes such as $RhCl(PPh_3)_3$, $[RhCl(CO)_2]_2$, $Rh_6(CO)_{16}$ and $Ir_4(CO)_{12}$ proved to be totally inactive.



(1)

The reaction of **1** with 3,3-dimethylbutene was very slow, even when 0.1 mmol of $Ru_3(CO)_{12}$ was used, but interestingly, the mono coupling product **2b** was obtained as the sole product (34% yield). A reaction with trimethylvinylsilane gave **2c** in 50% yield, along with **2a** in 14% yield. Two possibilities exist for the formation of ethyl ketone **2a** from trimethylvinylsilane: 1) protodesilylation of the regioisomer of **2c** (α-silylethyl ketone) or 2) the coupling of **1**, CO, and ethylene, which could be formed by silyl group scrambling of the starting vinylsilane.[31] Although I have no detailed experimental evidence for the mechanism of the formation of ethyl ketone, the latter seems to be the more reasonable. When butyl vinyl ether was used as the olefin, **2a** was also obtained in 30% yield as the sole product and no corresponding product **2d** was detectable. Reaction of **1** with CO and olefins, such as 1-hexene, cyclohexene, allyltrimethylsilane, styrene, methyl methacrylate, vinyl acetate, triethoxyvinylsilane, and isopropenyltrimethylsilane did not afford the coupling products, and **1** was recovered.

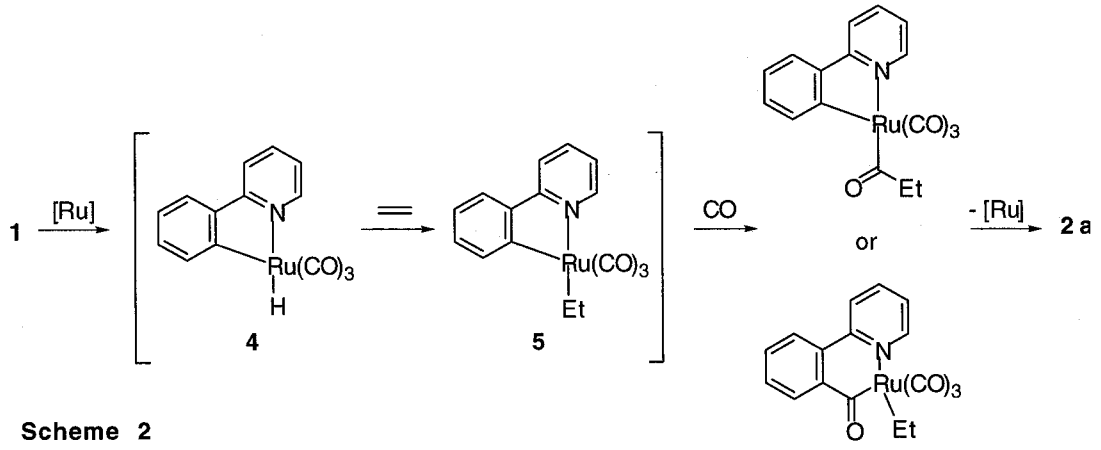


(2)

b:	R = Bu^t	34%
c:	R = $SiMe_3$	50% (also **2a** 14%)
d:	R = BuO	0% (**2a** 30%)

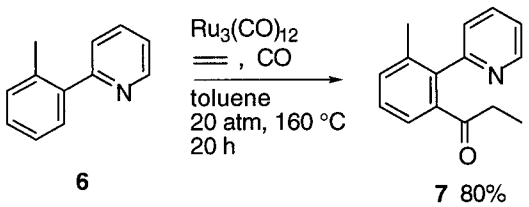
A cyclometalated complex, such as **4**, would be expected to play a key role for the formation of **2**. While no report of a stoichiometric reaction of **1** with $Ru_3(CO)_{12}$ has yet appeared, the related cyclometalated mononuclear ruthenium complexes were isolated as a result of a reaction of a benzaldehyde imine[32] or a benzo[h]quinoline[33] with $Ru_3(CO)_{12}$. The hydride complex, **4**, reacts with

ethylene to give the ethyl complex **5**, which undergoes CO insertion, followed by reductive elimination to give the final product **2a** (Scheme 2). Detail mechanism will be discussed in Chapter 2.



Scheme 2

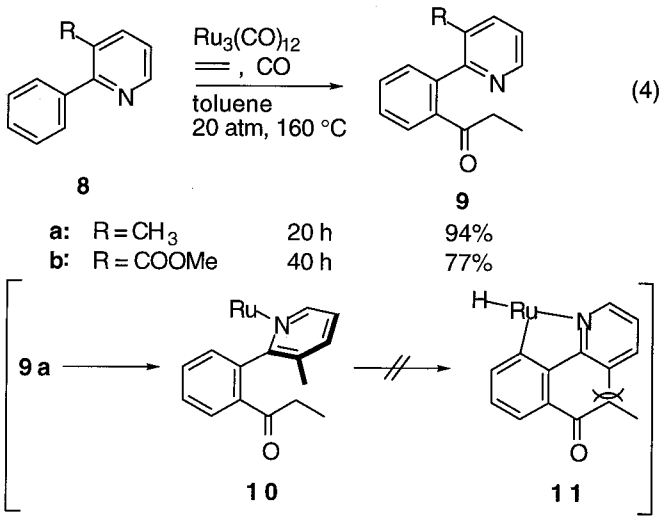
The reaction of 2-(2-methylphenyl)pyridine (**6**) with CO and ethylene proceed smoothly to give the corresponding mono ketone **7** in 80% yield (eq 3).



(3)

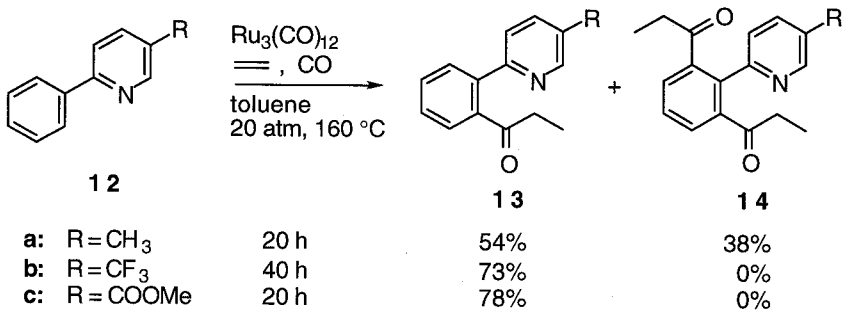
As was shown in eq 1, carbonylation did not stop at the mono-carbonylation step when a phenyl ring was used. Some attempts have been made to avoid the formation of a di-carbonylation product in a phenyl ring. It is noteworthy that the substitution of a methyl group at the 3-position on a pyridine ring gave a mono-carbonylation product selectively. The reaction of **8a** with CO and ethylene resulted in a clean reaction to exclusively give the mono-carbonylation product **9a** in high yield, with no di-carbonylation product being observed (eq 4). For **9a** to be converted to the di-carbonylation product, it would be required to adopt a conformation in which the plane of phenyl ring and that of pyridine ring are coplanar when the C-H bond undergoes cleavage. The presence of the methyl and propionyl group, as substituents, in **10** prevents the two rings from achieving coplanarity (leading to **11**) because of steric congestion. The reaction of phenylpyridine having an electron-

withdrawing group, such as a COOMe group, gave mono-carbonylation product **9b** exclusively, which also indicates the importance of steric factors at the 3-position on the pyridine ring.

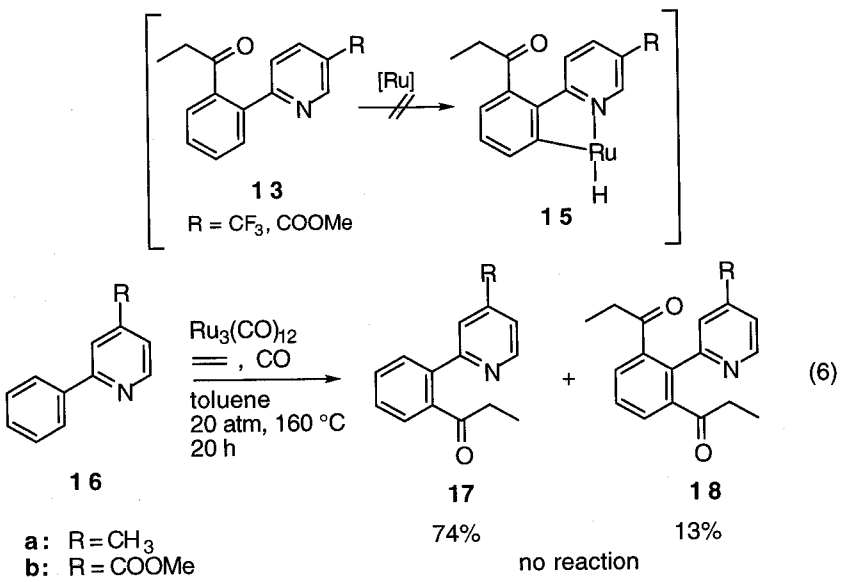


(4)

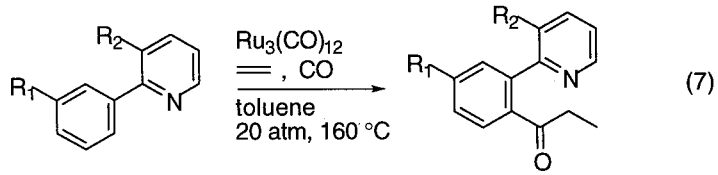
It was found that the product distribution can also be controlled by electronic factors on the pyridine ring. Firstly, when the reaction of phenyloxazolines bearing a methyl group at the 5-position (eq 5) or at the 4-position (eq 6) was run, the reaction could not stop at the mono-carbonylation stage and gave mixtures of mono-carbonylation product and di-carbonylation product. On the other hand, introduction of a CF_3 group at the 5-position on a pyridine ring resulted in a slow reaction (47% yield, 20 h) with the mono-carbonylation product **13b** being obtained exclusively (eq 5). The presence of electron-withdrawing groups, such as CF_3 and propionylphenyl groups, in **13** inhibit the coordination of nitrogen to the ruthenium from forming the complex **15**. Replacing a CF_3 group with a COOMe group also gave mono-carbonylation product **13c** selectively. However, introduction of a COOMe group at the 4-position on a pyridine ring did not undergo the carbonylation reaction and the starting materials were recovered (eq 6). The lack of reactivity illustrates the importance of coordination of the pyridine nitrogen to a ruthenium complex.



(5)

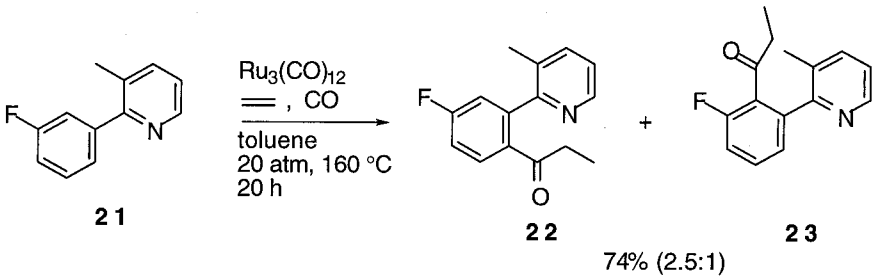


I next examined the effect of substituent groups on the site selectivity for the case of *meta*-substituted pyridylbenzenes (eq 7). When the reaction of 2-(3-methylphenyl)pyridine (**19a**) was run, coupling took place selectively at the 6-position and **20a** was obtained in high yield as a single product, with no di-carbonylation product being observed. Similarly, the reaction of 2-(3-methoxyphenyl)-3-methylpyridine (**19b**) gave mono-carbonylation product **20b** in 85% yield, along with its regioisomer (structure not shown) in 1% yield,[34] indicating a preferential cleavage of the less hindered C-H bond. The reaction of 2-(3-trifluoromethylphenyl)-3-methylpyridine (**19c**) also resulted in site selective carbonylation to give **20c** exclusively. The reaction of **19d** required more catalyst (0.2 mmol) and a longer reaction time (40 h) to achieve high yield of product (76% yield), while the reaction under standard reaction conditions (0.05 mmol of the catalyst, 20 h) led to the formation of **20d** in 22% yield. Carbonylation took place exclusively at the less hindered C-H bond, irrespective of the nature of the substituents. It is apparent that steric factors are more important for the control of site selectivity.



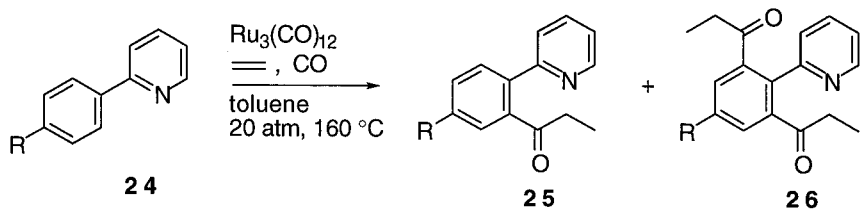
a:	$R_1 = CH_3$	$R_2 = H$	20 h	85%
b:	$R_1 = OMe$	$R_2 = CH_3$	40 h	85%
c:	$R_1 = CF_3$	$R_2 = H$	40 h	74%
d:	$R_1 = COOMe$	$R_2 = H$	40 h	76%

The reaction of 2-(3-fluorophenyl)-3-methylpyridine (**21**) gave the mono-carbonylation product **22** and its regioisomer **23** in a ratio of 2.5:1 (eq 8). This observation might suggest that steric factors do not play an important a role in determining the degree of site selectivity. In fact, the van der Waals radius of F (1.35 nm) is slightly larger than that of H (1.2 nm). In the case of **21**, the fluorine atom might show a directing effect, which could be attributed to the coordinating ability of the fluorine atom to the ruthenium.



(8)

Since it is interesting to pursue whether the product distribution can be controlled by electronic factors of substituents on the benzene ring, I investigated the reactivity of *para*-substituted phenylpyridines (eq 9). In the case of electron-donating group, such as methyl or methoxy group, the reaction gave mixtures of mono-carbonylation product and di-carbonylation product. In contrast, the reaction of phenylpyridines having an electron-withdrawing group were employed, mono-carbonylation product was yielded exclusively. The similar tendency of these electronic effects were observed in eq 5.

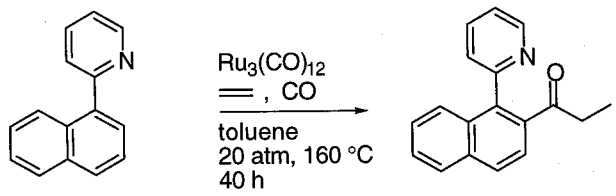


(9)

a:	R = CH_3	20 h	49%	44%
b:	R = OCH_3	20 h	55%	30%
c:	R = CF_3	20 h	81%	0%
d:	R = F	40 h	75%	0%

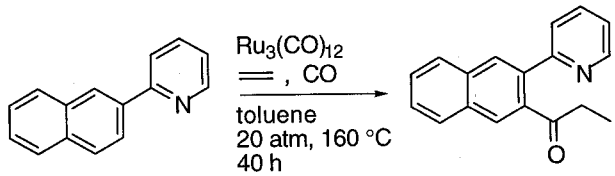
The present reaction can be applied to other aromatic systems. For example, the reaction of 2-(1'-naphtyl)pyridine (**27**) gave the corresponding ketone **28** in high yield (eq 10). Carbonylation of the β-isomer **29** took place regioselectively to give **30** as a single product (eq 11). Of the two different reaction sites in **29**, the C-H bond at the 3-position in the naphthalene ring underwent exclusive

cleavage and was carbonylated, presumably because of the steric hindrance of the peri-hydrogen on the naphtalene ring.[35]



(10)

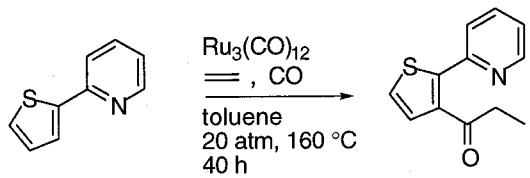
27 **28** 88%



(11)

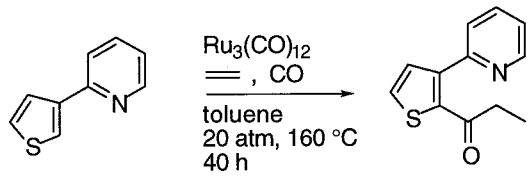
29 **30** 86%

The present carbonylation reaction at a C-H bond is also applicable to heteroaromatic compounds, such as thiophene and furan derivatives. The reaction of 2-(2-thienyl)pyridine (**31**) gave the corresponding ethyl ketone **32** in high yield (eq 12). The reaction of the β-isomer **33** afforded **34** exclusively, as a result of cleavage of a C-α-H bond (eq 13). The same selectivity was obtained in catalytic addition of a C-H bond in furan ring to alkenes[36] and alkynes[37] and in the stoichiometric cleavage of C-H bonds in furane ring by an iridium complex.[38]



(12)

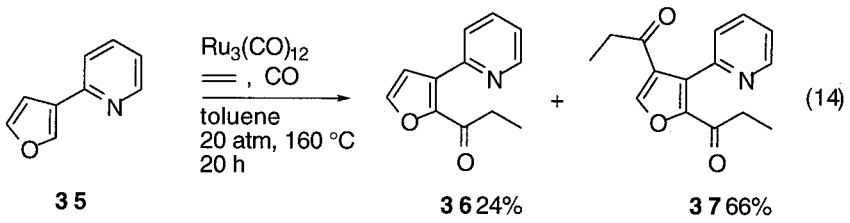
31 **32** 92%



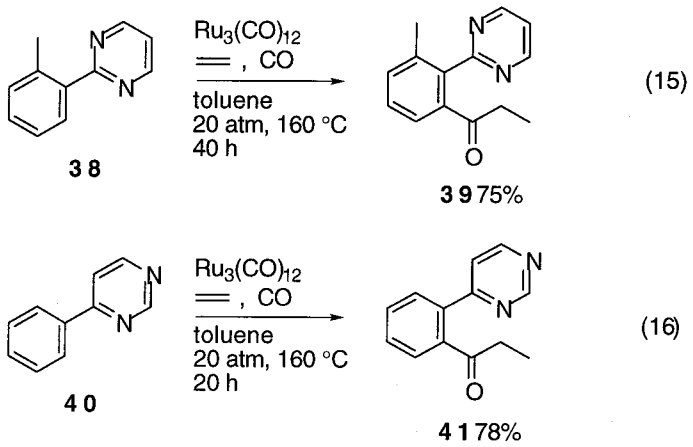
(13)

33 **34** 98%

By contrast with the site selectivity of **33**, the reaction of 2-(3-furanyl)pyridine (**35**) gave two products, mono-carbonylation product **36** and di-carbonylation product **37** (eq 14). The difference of reactivity between a thiophene ring and a furan ring is unclear at this point



Some six-membered heterocycles, other than pyridine, were also found to be an effective directing group for the carbonylation of a C-H bond in the benzene ring (eqs 15 and 16).



The substitution of acetylenes, such as phenylacetylene, 1-hexyne, 3-hexyne, and 1-trimethylsilyl-1-propyne or dienes such as isoprene for olefins failed to give any carbonylation products, and the starting pyridylbenzenes were recovered.

1.3 Conclusion

$Ru_3(CO)_{12}$ catalyzes the coupling of aromatic C-H bonds in pyridylbenzenes, CO and olefins. The present reaction represents the first clean example of effective carbonylation of a benzene ring with cleavage of the C-H bonds. Carbonylation takes place selectively at the *ortho* C-H bond in the phenyl ring. Carbonylation does not occur at a *meta* C-H bond, a *para* C-H bond, nor at the C-H bonds on the pyridine ring. Not only steric factors but also electronic factors of substituents control the efficiency of the reaction. The reaction is also applicable to naphthyl and thiophenyl and furanyl rings. Six-membered heterocycles, such as 2-pyrimidine and 4-pyrimidine, are also effective directing groups for carbonylation at a C-H bond in the benzene ring.

1.4 Experimental Section

General Information. Boiling points (bp) refer to air bath temperatures for bulb-to-bulb distillation and are uncorrected. ^{1}H NMR and ^{13}C NMR were recorded on a JEOL JMN-270 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Data are reported as follows: chemical shift in ppm (d), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, m = multiplet, and c = complex), coupling constant (Hz), integration, and interpretation. Infrared spectra (IR) were obtained on a Hitachi 270-50 spectrometer; absorptions are reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained on a Shimadzu GCMS-QP 5000 with ionization voltages of 70 eV. Elemental analyses were performed by Elemental Analysis Section of Osaka University. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303. Analytical GC was carried out on a Shimadzu GC-14B gas chromatography, equipped with a flame ionization detector. Column chromatography was performed with SiO_2 (Wakogel).

Materials. Toluene was distilled with CaH_2. $Ru_3(CO)_{12}$ was purchased from Aldrich Chemical Co. and used after recrystallization from hexane. 2-Phenylpyridine (**1**), 3-methyl-2-phenylpyridine (**8a**) and 4-phenylpyrimidine (**40**) were purchased from Aldrich Chemical Co. and used after distillation or recrystallization. Substituted 2-arylpyridines such as **6**, **12a**, **12b**, , **16a**, **19a**, **19b**, **19c**, **21**, **24a**, **24b**, **24c**, **24d**, **27**, **29**, **31**, **35**, **38** were obtained by Ni-catalyzed coupling reaction of the corresponding heteroaromatic bromides with arylmagnesium bromides. Methyl 3-(2-pyridinyl)benzoate (**19d**) was prepared from the Pd-catalyzed coupling reaction of methyl-3-iodobenzoate with 2-tributylstannylpyridine. 2-(3-Thienyl)pyridine (**33**) was prepared from the Pd-catalyzed coupling of 2-bromopyridine with 3-thienylzinc bromide. Methyl ester, such as **8b**, **12c**, **16b**, were obtained by the oxidation of corresponding methyl substituted phenylpyridines **8a**, **12a**, and **16a** using $KMnO_4$, followed by esterification.

General Procedures. In a 50-mL stainless autoclave were placed $Ru_3(CO)_{12}$ (32 mg, 0.05 mmol), 2-phenylpyridine (**1**) (2 mmol), and toluene (6 mL). The autoclave was charged with ethylene to 7 atm and carbon monoxide to 20 atm at 25 °C, and then heated in an oil bath at 160 °C for 20 h. The autoclave was cooled and depressured. The solvent was removed in vacuo, and the coupling product was isolated by column chromatography on silica-gel with hexane/EtOAc as eluant. Analytical sample was obtained by bulb-to-bulb distillation or recrystallization.

1-[2-(2-Pyridinyl)phenyl]-1-propanone (2a). Pale yellow oil; Bp 120 ℃ (1 mmHg); R_f = 0.31 (hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$) δ 1.08 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.49 (q, *J* = 7.3 Hz 2H, $CH_2C(O)$), 7.21-7.26 (m, 1H, 5'-H), 7.44-7.67 (m, 5H, Ar, 3'-H), 7.77 (td, *J* = 7.6, 1.6 Hz, 1H, 4'-H), 8.62 (d, *J* = 4.9 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.50 ($CH_3CH_2C(O)$), 36.32 ($CH_2C(O)$), 122.10, 122.16, 127.24, 128.55, 128.73, 129.79, 136.66 (4'-C), 138.13, 141.78, 149.11 (6'-C), 157.18 (2'-C), 207.78 (CO); IR (neat) 3060 m, 2978 s, 2940 m, 2878 m, 2458 w, 1696 s, 1589 s, 1564 s, 1491 m, 1471 s, 1441 s, 1428 s, 1372 m, 1345 s, 1299 m, 1271 m, 1212 s, 1150 m, 1118 m, 1080 m, 1056 m, 1018 m, 989 m, 946 m, 797 m, 753 m, 615 m; MS, *m/z* (rel intensity) 211 (M^+, 0), 196 (M^+-CH_3, 3), 182 (100), 154 (8), 127 (19). Anal. Calcd for $C_{14}H_{13}NO$: C, 79.60; H, 6.20; N, 6.63. Found: C, 79.36; H, 6.34; N, 6.67.

4,4-Dimethyl-1-[2-(2-pyridinyl)phenyl]-1-pentanone (2b). Colorless oil; Bp 200 ℃ (1 mmHg); R_f = 0.09 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.74 (s, 9H, $(CH_3)_3C$), 1.50-1.56 (c, 2H, $CH_2CH_2C(O)$), 2.38-2.44 (c, 2H, $CH_2C(O)$), 7.22-7.27 (m, 1H, 5'-H), 7.45-7.67 (m, 5H, Ar, 3'-H), 7.77 (td, *J* = 6.3, 1.9 Hz, 1H, 4'-H), 8.62 (d, *J* = 3.8 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 28.95 ($(CH_3)_3C$), 29.60 ($C(CH_3)_3$), 37.95 ($CH_2CH_2C(O)$), 38.98 ($CH_2C(O)$), 122.17, 122.25, 127.35, 128.59, 128.79, 129.85, 136.69 (4'-C), 138.19, 141.94, 149.24 (6'-C), 157.30 (2'-C), 207.78 (CO); IR (neat) 3196 w, 3060 m, 2962 s, 2872 m, 1691 s, 1589 s, 1564 m, 1472 s, 1442 s, 1428 s, 1394 m, 1365 s, 1296 s, 1248 m, 1213 m, 1186 m, 1150 m, 1090 m, 1069 m, 1018 m, 987 m, 951 m, 909 s, 797 m, 751 s, 731 s, 643 m, 615 w; MS, *m/z* (rel intensity) 267 (M^+, 0), 252 (M^+-CH_3, 4), 183 (17), 182 (100), 127 (11). Anal. Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found C, 81.16; H, 7.85; N, 5.49.

1-[2-(2-Pyridinyl)phenyl]-3-trimethylsilyl-1-propanone (2c). Colorless oil; Bp 185-190 ℃ (1 mmHg); R_f = 0.15 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ -0.15 (s, 9H, $(CH_3)_3Si$), 0.75-0.81 (c, 2H, $CH_2CH_2C(O)$), 2.34-2.41 (c, 2H, $CH_2C(O)$), 7.23 (m, 1H, 5'-H), 7.45-7.67 (m, 5H, Ar, 3'-H), 7.76 (td, *J* = 7.6, 1.6 Hz, 1H, 4'-H), 8.62 (d, *J* = 4.6 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ -2.06 ($(CH_3)_3Si$), 10.95 ($CH_2CH_2C(O)$), 37.72 ($CH_2C(O)$), 122.21, 122.32, 127.48, 128.61, 128.81, 129.87, 136.69 (4'-C), 138.24, 141.69, 149.24 (6'-C), 157.36 (2'-C), 208.23 (CO); IR (neat) 3386 w, 3056 m, 2956 m, 2894 m, 1692 s, 1588 s, 1471 s, 1441 s, 1427 s,

1337 m, 1245 s, 1217 s, 1162 m, 1090 m, 1061 m, 1019 m, 974 m, 904 m, 856 s, 796 m, 752 s, 691 m, 615 w; MS, *m/z* (rel intensity) 282 (M^+, 0), 267 (M^+ -CH_3, 0.4), 182 (100), 127 (10), 73 (16). Anal. Calcd for $C_{17}H_{21}NOSi$: C, 72.04; H, 7.47; N, 4.94. Found C, 71.91; H, 7.41; N, 5.09.

1,1'-[2-(2-Pyridinyl)-1,3-phenylene]bis-1-propanone (3a). White solid; mp 102-104 °C (hexane); R_f = 0.11 (hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$) δ 0.96 (t, *J* = 7.3 Hz, 6H, $CH_3CH_2C(O)$), 2.36 (q, *J* = 7.3 Hz, 4H, $CH_2C(O)$), 7.26-7.32 (m, 2H, 3'-H, 5'-H), 7.52-7.58 (m, 3H, Ph), 7.72 (t, *J* = 7.6 Hz, 1H, 4'-H), 8.62 (d, *J* = 4.9 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.29 ($CH_3CH_2C(O)$), 36.14 ($CH_2C(O)$), 122.71, 124.82, 128.45, 128.66, 136.32, 142.28, 149.58, 156.55, 206.94 (CO); IR (KBr) 3254 m, 2982 s, 2940 m, 2904 m, 2880 m, 1697 s, 1590 s, 1567 s, 1476 s, 1457 s, 1427 s, 1408 s, 1375 s, 1344 s, 1293 m, 1272 m, 1247 m, 1227 s, 1177 s, 1150 m, 1119 s, 1051 s, 1022 m, 990 s, 903 m, 784 s, 755 s, 741 s, 659 m, 614 m; MS, *m/z* (rel intensity) 267 (M^+, 0), 252 (M^+-CH_3, 1), 238 (M^+-CH_2CH_3, 100), 181 (18), 153 (10). Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.17; H, 6.38; N, 5.52.

1-[3-Methyl-2-(2-pyridinyl)phenyl]-1-propanone (7). Light yellow oil; Bp 160 °C (5 mmHg); R_f = 0.09 (hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$) δ 0.94 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.18 (s, 3H, CH_3), 2.45 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.23-7.45 (m, 5H, Ar), 7.73 (td, *J* = 7.6, 1.6 Hz, 1H, 4'-H), 8.66 (d, *J* = 4.9 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 7.93 ($CH_3CH_2C(O)$), 19.70 (CH_3), 35.06 ($CH_2C(O)$), 121.60, 124.42, 124.67, 127.60, 132.27, 135.60, 136.37, 138.17, 140.50, 148.93, 158.11, 205.82 (CO); IR (neat) 3148 w, 3050 w, 2980 m, 2940 m, 1778 w, 1733 m, 1692 s, 1589 s, 1564 m, 1457 s, 1422 s, 1377 m, 1343 m, 1275 m, 1243 s, 1167 m, 1142 m, 1097 m, 1023 m, 987 m, 968 m, 850 w, 787 s, 749 s, 648 w, 618 w; MS, *m/z* (rel intensity) 225 (M^+, 1), 210 (M^+-CH_3, 2), 197 (15), 196 (M^+-CH_2CH_3, 100), 167 (18), 84 (12). Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.86; H, 6.73; N, 6.50.

1-[2-(3-Methyl-2-pyridinyl)phenyl]-1-propanone (9a). Colorless oil; Bp 135-140 °C (1 mmHg); R_f = 0.17 (hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$) δ 1.00 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.16 (s, 3H, CH_3), 2.58 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.19 (dd, *J* = 7.6, 4.6 Hz, 1H, 5'-H), 7.33 (dd, *J* = 7.6, 1.1 Hz, 1H, Ar), 7.44-7.58 (m, 3H, Ar), 7.72 (dd, *J* = 7.6, 1.5 Hz, 1H, 4'-H), 8.43 (d, *J* = 4.6 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.25 ($CH_3CH_2C(O)$), 19.36 (CH_3),

34.58 ($CH_2C(O)$), 122.35, 127.98, 128.10, 130.01, 130.82, 131.43, 137.72, 139.26, 139.87, 146.49, 158.94, 204.58 (CO); IR (neat) 3296 w, 3056 w, 2982 s, 1687 s, 1576 s, 1450 s, 1424 s, 1376 m, 1346 s, 1250 m, 1212 s, 1181 m, 1158 w, 1116 m, 1077 m, 1060 m, 1020 m, 988 m, 947 m, 877 w, 792 s, 754 s, 701 w, 641 w, 622 w; MS, *m/z* (rel intensity) 225 (M^+, 0), 210 (M^+-CH_3, 2), 197 (14), 196 (M^+-CH_2CH_3, 100), 167 (23), 83 (16). Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.97; H, 6.83; N, 6.31.

2-[2-(1-Oxopropyl)phenyl]-3-pyridinecarboxylic acid, methyl ester (9b). Yellow oil; Bp 190-195 °C (1 mmHg); ^{1}H NMR ($CDCl_3$) δ 1.03 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.79 (q, J = 7.3 Hz, 2H, $CH_2C(O)$), 3.67 (s, 3H, COOMe), 7.26 (dd, J = 7.3, 1.7 Hz, 1H, 3'-H), 7.36 (dd, J = 7.9, 4.9 Hz, 1H, 5-H), 7.45-7.58 (c, 2H, 4'-H, 5'-H), 7.81 (dd, J = 7.3, 1.7 Hz, 1H, 6'-H), 8.29 (dd, J = 7.7, 1.8 Hz, 1H, 4-H), 8.72 (dd, J = 4.6, 1.7 Hz, 1H, 6-H); ^{13}C NMR ($CDCl_3$) δ 8.14 ($CH_3CH_2C(O)$), 33.59 ($CH_2C(O)$), 52.11 ($COOCH_3$), 121.76 (5-C), 125.55, 128.07, 128.19 (6'-C), 129.78 (3'-C), 131.05, 137.36, 138.10 (4-C), 140.75, 151.57 (6-C), 160.88, 166.34 ($C(O)OCH_3$), 202.91 (CO); IR (KBr) 2978 w, 1725 s, 1683 s, 1570 s, 1492 w, 1428 s, 1376 w, 1352 w, 1272 s, 1212 m, 1131 m, 1091 m, 1076 m, 1060 m, 1021 w, 951 m, 833 w, 791 m, 759 m, 740 w, 669 w, 619 w, 559 w, 512 w; MS, *m/z* (rel intensity) 269 (M^+, 3), 241, (15), 240 (M^+-CH_2CH_3, 100), 181 (16), 167 (14), 153 (15), 127 (11), 126 (11), 104 (11), 90 (14), 76 (30), 63 (21), 59 (56), 57 (17), 51 (17), 50 (15). Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.10; H, 5.61; N, 5.20.

1-[2-(5-Methyl-2-pyridinyl)phenyl]-1-propanone (13a). Yellow oil; Bp 160 ℃ (1 mmHg); R_f = 0.17 (hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$) δ 1.09 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.37 (s, 3H, CH_3), 2.49 (q, J = 7.3 Hz, 2H, $CH_2C(O)$), 7.42-7.52 (c, 4H, Ph), 7.56 (dd, J = 7.9, 2.0 Hz, 1H, 4'-H), 7.63 (d, J = 7.6 Hz, 1H, 3'-H), 8.45 (s, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.47 ($CH_3CH_2C(O)$), 17.99 (CH_3), 36.25 ($CH_2C(O)$), 121.46, 127.08, 128.16, 128.46, 129.65, 131.70, 137.14 (4'-C), 137.97, 141.55, 149.43 (6'-C), 154.21, 207.92 (CO); IR (neat) 3064 w, 2978 m, 2938 m, 2324 w, 1893 w, 1692 s, 1599 m, 1476 m, 1442 m, 1410 w, 1376 m, 1346 m, 1297 w, 1270 w, 1212 m, 1135 w, 1114 w, 1078 w, 1017 w, 946 m, 835 m, 798 w, 773 m, 743 m, 564 w; MS, *m/z* (rel intensity) 225 (M^+, 0), 210 (M^+-CH_3, 2), 197 (15), 196 (M^+-CH_2CH_3, 100), 167 (13), 115 (11), 98 (14), 83 (20), 70 (13). Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.71; H, 6.73; N, 6.26.

1-[2-[5-(Trifluoromethyl)-2-pyridinyl]phenyl]-1-propanone (13b). Yellow oil; Bp 140 °C (1 mmHg); R_f = 0.34 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.14 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.67 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.50-7.59 (m, 3H, Ar), 7.59-7.66 (m, 1H, Ar), 7.71 (d, *J* = 8.3 Hz, 1H, 3'-H), 7.99 (dd, *J* = 8.3, 2.3 Hz, 1H, 4'-H), 8.86 (brs, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.39 ($CH_3CH_2C(O)$), 36.14 ($CH_2C(O)$), 121.87, 123.00 (q, *J* = 272 Hz), 124.90 (q, *J* = 33 Hz), 127.39, 129.27, 129.45, 130.12, 133.89, 137.04, 141.83, 145.90, 160.99, 206.97 (CO); IR (neat) 3062 w, 2980 m, 2942 m, 2884 w, 2506 w, 2324 w, 2030 w, 1966 w, 1871 w, 1694 s, 1606 s, 1580 m, 1564 m, 1498 w, 1479 w, 1462 m, 1445 w, 1413 w, 1385 m, 1330 s, 1301 m, 1274 w, 1213 s, 1162 s, 1127 s, 1080 s, 1013 s, 945 m, 849 m, 787 w, 747 s, 668 w, 631 w, 613 w; MS, *m/z* (rel intensity) 279 (M^+, 0), 264 (M^+-CH_3, 2), 251 (14), 250 (M^+-CH_2CH_3, 100), 202 (11), 75 (11). Anal. Calcd for $C_{15}H_{12}NOF_3$: C, 64.52; H, 4.33; N, 5.08. Found: C, 64.44; H, 4.49; N, 5.08.

6-[2-(1-Oxopropyl)phenyl]-3-pyridinecarboxylic acid, methyl ester (13c). Light red oil; Bp 180-185 °C (1 mmHg); ^{1}H NMR ($CDCl_3$) δ 1.13 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.62 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 3.97 (s, 3H, COOMe) 7.46-7.57 (c, 3H, Ar), 7.67-7.71 (c, 2H, Ph, 5-H), 8.36 (dd, *J* = 8.2, 2.3 Hz, 1H, 4-H), 9.20 (d, *J* = 2.3 Hz, 1H, 2-H); ^{13}C NMR ($CDCl_3$) δ 8.43 ($CH_3CH_2C(O)$), 36.25 ($CH_2C(O)$), 52.35 ($COOCH_3$), 121.60, 124.26, 127.31, 129.04, 129.36, 129.96, 137.20, 137.83 (4-C), 142.05, 150.19 (2-C), 161.01, 165.57 ($C(O)OCH_3$), 207.20 (CO); IR (neat) 3648 w, 3374 w, 3062 w, 2978 m, 1927 w, 1725 s, 1694 s, 1596 s, 1559 m, 1493 m, 1475 m, 1437 s, 1412 s, 1373 m, 1348 m, 1287 s, 1212 s, 1190 m, 1120 s, 1080 w, 1018 m, 947 m, 856 w, 832 w, 794 m, 754 s; MS, *m/z* (rel intensity) 269 (M^+, 0), 241 (17), 240 (M^+-CH_2CH_3, 100), 153 (11), 126 (10), 104 (14), 90 (13), 76 (34), 63 (25). Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.29; H, 5.69; N, 5.39.

1,1'-[2-(3-Methyl-2-pyridinyl)-1,3-phenylene]bis-1-propanone (14a). Brown solid; mp 90-92°C (hexane); R_f = 0.11 (hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$) δ 0.97 (t, *J* = 7.2 Hz, 6H, $CH_3CH_2C(O)$), 2.37 (q, *J* = 7.3 Hz, 4H, $CH_2C(O)$), 2.38 (s, 3H, CH_3), 7.19 (d, *J* = 7.8 Hz, 1H, 3'-H), 7.50-7.54 (m, 4H, Ar), 8.46 (s, 1H, 6'-H); ^{13}CNMR ($CDCl_3$) δ 8.32 ($CH_3CH_2C(O)$), 18.31 (CH_3), 36.16 ($CH_2C(O)$), 124.26, 128.23, 128.59, 132.44, 136.24, 136.91, 142.32, 150.06, 153.51, 207.22 (CO); MS, *m/z* (rel intensity) 281 (M^+, 0), 266 (M^+-CH_3, 1), 253

(19), 252 (M^+-CH_2CH_3, 100), 195 (21), 167 (11), 83 (15). Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.61; H, 6.83; N, 4.91.

1-[2-(4-Methyl-2-pyridinyl)phenyl]-1-propanone (17). Yellow oil; Bp 150-155 ℃ (1 mmHg); R_f = 0.17 (hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$) δ 1.08 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.41 (s, 3H, CH_3), 2.46 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.06 (d, *J* = 5.0 Hz, 1H, 5'-H), 7.43-7.51 (c, 4H, Ar), 7.63 (d, *J* = 7.6 Hz, 1H, 6-H), 8.46 (d, *J* = 5.0 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.61 ($CH_3CH_2C(O)$), 21.15 (CH_3), 36.39 ($CH_2C(O)$), 123.13, 123.27, 127.29, 128.50, 128.73, 129.81, 138.37, 141.89, 147.83, 148.98, 157.12, 208.01 (CO); IR (neat) 3052 w, 2978 m, 2938 m, 2882 w, 2362 w, 2200 w, 1693 s, 1605 s, 1557 m, 1461 m, 1441 m, 1375 w, 1344 m, 1294 w, 1278 w, 1213 m, 1102 w, 1080 w, 1035 w, 1012 w, 989 w, 945 m, 870 w, 826 m, 773 m, 745 m, 632 w, 591 w, 521 w; MS, *m/z* (rel intensity) 225 (M^+, 0), 210 (M^+-CH_3, 2), 197 (15), 196 (M^+-CH_2CH_3, 100), 167 (13), 115 (11), 98 (14), 83 (20), 70 (13). Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.67; H, 6.75; N, 6.28.

1,1'-[2-(4-Methyl-2-pyridinyl)-1,3-phenylene]bis-1-propanone (18). Brown solid; ^{1}H NMR ($CDCl_3$) δ 0.96 (t, *J* = 7.3 Hz, 6H, $CH_3CH_2C(O)$), 2.36 (q, *J* = 7.3 Hz, 4H, $CH_2C(O)$), 2.37 (s, 3H, CH_3), 7.11 (br, 2H, 3'-H, 5'-H), 7.48-7.56 (c, 3H, Ph), 8.48 (d, *d* = 5.0 Hz, 1H, 6'-H); ^{13}CNMR ($CDCl_3$) δ 8.34 ($CH_3CH_2C(O)$), 21.03 (CH_3), 36.16 ($CH_2C(O)$), 123.79, 125.66, 128.37, 128.61, 136.35, 142.34, 147.73, 149.33, 207.22 (CO); IR (KBr) 3056 w, 2984 m, 2942 m, 2290 w, 1949 w, 1694 s, 1604 s, 1574 m, 1556 m, 1477 m, 1457 m, 1410 m, 1372 m, 1351 m, 1292 w, 1272 m, 1251 m, 1225 m, 1191 w, 1173 m, 1113 m, 1095 m, 1082 m, 1037 m, 988 m, 946 m, 907 w, 872 w, 841 m, 804 m, 789 m, 777 m, 755 w, 738 w, 668 m, 572 w, 521 w, 505 w; MS, *m/z* (rel intensity) 281 (M^+, 0), 280 (5), 253 (16), 252 (M^+-CH_2CH_3, 100), 195 (22), 167 (13). Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.70; H, 6.80; N, 4.98.

1-[4-Methyl-2-(2-pyridinyl)phenyl]-1-propanone (20a). Light yellow oil; Bp 185 ℃ (1 mmHg); R_f = 0.34 (hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$) δ 1.05 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.44 (s, 3H, CH_3), 2.47 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.22-7.27 (m, 2H, Ar), 7.40 (d, *J* = 7.8 Hz, 1H, Ph), 7.44 (s, 1H, 6-H), 7.53 (d, *J* = 8.1 Hz, 1H, 3'-H), 7.75 (td, *J* = 7.7, 1.9 Hz, 1H, 4'-H), 8.63 (d, *J* = 4.6 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.65 ($CH_3CH_2C(O)$),

21.33 (CH_3), 36.16 ($CH_2C(O)$), 122.12, 122.44, 127.66, 129.16, 129.79, 136.53, 138.63, 138.78, 140.25, 149.22, 157.77, 207.38 (CO); IR (neat) 3282 w, 3228 w, 2976 m, 2936 m, 1691 s, 1609 m, 1588 s, 1564 m, 1473 s, 1461 s, 1429 s, 1373 m, 1345 m, 1308 w, 1293 w, 1271 m, 1218 s, 1189 m, 1149 m, 1080 w, 1054 w, 1039 w, 1014 m, 990 m, 948 m, 889 w, 824 m, 791 s, 746 m, 642 w; MS, *m/z* (rel intensity) 225 (M^+, 0), 210 (M^+-CH_3, 2), 197 (14), 196 (M^+-CH_2CH_3, 100), 167 (11). Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 80.10; H, 6.76; N, 6.30.

1-[4-Methoxy-2-(3-methyl-2-pyridinyl)phenyl]-1-propanone (20b). Yellow oil; Bp 175-180 °C (1 mmHg); R_f = 0.17 (hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$) δ 1.00 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.07 (s, 3H, CH_3), 2.61 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 3.86 (s, 3H, OCH_3), 6.79 (d, *J* = 2.7 Hz, 1H, 3-H), 6.96 (dd, *J* = 8.6, 2.7 Hz, 1H, 5-H), 7.20 (dd, *J* = 7.6, 4.6 Hz, 1H, 5'-H), 7.54 (d, *J* = 7.6 Hz, 1H, 4'-H), 7.81 (d, *J* = 8.4 Hz, 1H, 6-H), 8.44 (d, *J* = 4.6 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.32 ($CH_3CH_2C(O)$), 19.10 (CH_3), 33.55 ($CH_2C(O)$), 55.44 (OCH_3), 113.24, 115.40, 122.25, 130.53, 130.94, 131.14, 137.36, 142.75, 146.27, 159.48, 161.80, 201.62 (CO); IR (neat) 3150 w, 3058 w, 2974 w, 2942 w, 2840 w, 1681 s, 1603 s, 1563 s, 1461 s, 1432 s, 1377 s, 1346 s, 1320 s, 1301 s, 1260 s, 1220 s, 1172 s, 1135 m, 1113 m, 1079 m, 1060 m, 1026 s, 950 m, 883 m, 795 s, 694 w, 629 m, 601 m; MS, *m/z* (rel intensity) 255 (M^+, 0), 240 (M^+-CH_3, 1), 227 (15), 226 (M^+-CH_2CH_3, 100), 211 (11), 183 (16), 154 (17). Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.56; H, 6.74; N, 5.62.

1-[2-(2-Pyridinyl)-4-(trifluoromethyl)phenyl]-1-propanone (20c). Yellow oil; Bp 150-155 °C (I mmHg); R_f = 0.24 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.12 (t, *J* = 7.6 Hz, 3H, $CH_3CH_2C(O)$), 2.52 (q, *J* = 7.6 Hz, 2H, $CH_2C(O)$), 7.28 (dd, *J* = 7.9, 4.6 Hz, 1H, 5'-H), 7.52 (d, *J* = 7.9 Hz, 1H, 5-H or 6-H), 7.66-7.73 (m, 2H, 3-H, 5-H or 6-H), 7.81 (td, *J* = 7.9, 1.7 Hz, 1H, 4'-H), 7.94 (s, 1H, 3-H), 8.63 (d, *J* = 4.6 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.34 ($CH_3CH_2C(O)$), 36.48 ($CH_2C(O)$), 122.12, 122.95, 123.85 (q, *J* = 270 Hz), 125.46, 127.71, 131.78 (q, *J* = 33 Hz), 137.11, 138.62, 145.03, 149.34, 155.49, 206.83 (CO); IR (neat) 3064 w, 2982 m, 2944 m, 1704 s, 1617 w, 1590 s, 1497 m, 1477 m, 1414 s, 1375 w, 1334 s, 1304 m, 1285 s, 1263 s, 1212 m, 1167 s, 1132 s, 1084 s, 1034 m, 1015 m, 991 w, 949 w, 902 w, 833 m, 792 s, 745 m, 652 w, 618 w, 548 w; MS, *m/z* (rel intensity) 279 (M^+, 0), 264 (M^+-CH_3, 2), 251 (15), 250

(M^+-CH_2CH_3, 100), 153 (11), 125 (10). Anal. Calcd for $C_{15}H_{12}F_3NO$: C, 64.52; H, 4.33; N, 5.02. Found: C, 64.76; H, 4.38; N, 5.16.

4-(1-Oxopropyl)-3-(2-pyridinyl)-benzoic acid, methyl ester (20d). Colorless oil; Bp 190-195 °C (1 mmHg); R_f = 0.11 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.12 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.53 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 3.97 (s, 3H, OCH_3), 7.25-7.29 (m, 1H, 5'-H), 7.47 (d, *J* = 7.8 Hz, 1H, 5-H), 7.73 (d, *J* = 7.6 Hz, 1H, 3'-H), 7.82 (td, *J* = 7.6, 1.6 Hz, 1H, 4'-H), 8.11 (dd, *J* = 7.8, 1.6 Hz, 1H, 6-H), 8.37 (d, *J* = 1.6 Hz, 1H, 2-H), 8.61 (d, *J* = 4.6 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.38 ($CH_3CH_2C(O)$), 36.46 ($CH_2C(O)$), 52.36 (OCH_3), 121.98, 122.64, 127.28, 129.69, 131.20, 136.98, 138.06, 145.86, 149.13, 155.88, 166.13 ($C(O)OCH_3$), 207.33 (CO); IR (neat) 3230 w, 3058 m, 2980 s, 1729 s, 1611 m, 1589 s, 1575 s, 1475 s, 1431 s, 1408 s, 1372 s, 1347 s, 1310 s, 1253 s, 1209 s, 1148 m, 1111 s, 1041 m, 992 m, 970 m, 950 s, 915 m, 849 m, 793 s, 763 s, 748 s, 638 w, 618 w; MS, *m/z* (rel intensity) 269 (M^+, 0), 254 (M^+-CH_3, 2), 241 (15), 240 (M^+-CH_2CH_3, 100), 153 (12), 76 (16). Anal. Calcd for $C_{13}H_{22}N_2O_2$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.39; H, 5.72; N, 5.27.

1-[4-Fluoro-2-(3-methyl-2-pyridinyl)]phenyl]-1-propanone (22) and 1-[2-fluoro-6-(3-methyl-2-pyridinyl)]phenyl]-1-propanone (23). Spectral data were obtained from a mixture of **22** and **23**. Light yellow oil; Bp 160-65 °C (1 mmHg); R_f = 0.34 (hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$) δ 0.97-1.06 (m, 3H, $CH_3CH_2C(O)$), [2.16 (s, **22**), 2.25 (s, **23**), 3H, CH_3], [2.57 (q, *J* = 7.3 Hz, **22**), 2.78 (qd, *J* = 7.0, 1.8 Hz, **23**), 2H, $CH_2C(O)$], [7.03 (dd, *J* = 9.5, 2.7 Hz, **22**), 7.12-7.24 (m), 7.39-7.47 (m), 7.56-7.59 (m), 7.78 (dd, *J* = 8.6, 5.7 Hz, **22**), 5H, Ar], [8.39 (d, *J* = 4.6 Hz, **23**), 8.44 (d, *J* = 4.6 Hz, **22**), 1H, 6'-H]; ^{13}C NMR ($CDCl_3$) δ [7.64 (**23**), 8.18 (**22**), $CH_3CH_2C(O)$], [19.14 (**22**), 19.39 (**23**), CH_3], [34.31 (**22**), 37.94 (**23**), $CH_2C(O)$], 114.68, 114.99, 115.20, 115.53, 117.11, 117.43, 122.62, 122.68, 125.23, 125.28, 130.35, 130.48, 130.71, 130.85, 131.23, 131.84, 135.08, 135.11, 137.79, 138.15, 142.79, 142.91, 146.31, 146.52, 157.77, 161.83, 165.55, [202.64 (**22**), 203.65 (**23**), CO]; IR (neat) 3212 w, 3058 m, 2982 s, 2940 m, 2884 m, 1693 s, 1608 s, 1581 s, 1449 s, 1377 m, 1345 s, 1299 s, 1269 m, 1208 s, 1174 s, 1123 m, 1079 m, 1061 m, 1036 m, 1014 m, 951 s, 898 m, 878 m, 830 m, 794 s, 695 w, 629 m; MS, *m/z* (rel intensity) **22**: 243 (M^+, 0), 228 (M^+ -CH_3, 2), 215 (14), 214 (M^+-CH_2CH_3, 100), 185 (16), 92 (17); **23:** 243 (M^+, 0), 228 (M^+ -CH_3, 2), 215 (14), 214 (M^+-CH_2CH_3,

100), 185 (12), 92 (12). Anal. Calcd for $C_{15}H_{14}FNO$: C, 74.06; H, 5.80; N, 5.76. Found: C, 74.01; H, 5.93; N, 5.85.

1-[5-Methyl-2-(2-pyridinyl)phenyl]-1-propanone (25a). White solid; mp 115-120 °C (hexane); R_f = 0.37 (hexane/EtOAc = 2/3); ^{1}H NMR ($CDCl_3$) δ 1.08 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.42 (s, 3H, CH_3), 2.48 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.21 (ddd, *J* = 7.4, 4.9, 1.0 Hz, 1H, 5'-H), 7.23 (d, *J* = 1.0 Hz, 1H, 6-H), 7.31 (dd, *J* = 7.9, 1.0 Hz, 1H, 4-H), 7.55-7.60 (c, 2H, 3-H, 3'-H), 7.74 (td, *J* = 7.9, 2.0 Hz, 1H, 4'-H), 8.60 (ddd, *J* = 4.9, 1.7, 1.0 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.61 ($CH_3CH_2C(O)$), 21.10 (CH_3), 36.48 ($CH_2C(O)$), 121.89, 121.94, 127.89, 128.61, 130.48, 135.29, 136.62, 138.76, 141.83, 149.09, 157.11, 208.26 (CO); IR (KBr) 3068 w, 2970 m, 2934 m, 2898 m, 2874 m, 1980 w, 1923 w, 1690 s, 1591 s, 1558 m, 1502 w, 1472 m, 1430 s, 1409 m, 1371 m, 1342 m 1299 w, 1270 m, 1225 m, 1169 m, 1155 m, 1135 w, 1091 m, 1079 w, 1052 w, 1035 w, 1020 m, 989 m, 970 m, 890 w, 855 m, 834 m, 789 s, 749 m, 654 w, 621 w, 585 w, 565 w, 538 w, 501 w; MS, *m/z* (rel intensity) 225 (M^+, 1), 210 (M^+-CH_3, 3), 197 (14), 196 (M^+-CH_2CH_3, 100), 98 (10), 83 (17), 51 (12). Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.84; H, 6.74; N, 6.30.

1-[5-Methoxy-2-(3-methyl-2-pyridinyl)phenyl]-1-propanone (25b). Yellow oil; Bp 170-175 °C (1 mmHg); R_f = 0.11 (hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$) δ 1.09 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.45 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 3.86 (s, 3H, OCH_3), 6.92 (d, *J* = 2.6 Hz, 1H, 6-H), 7.01 (dd, *J* = 8.6, 2.6 Hz, 1H, 4-H), 7.17 (ddd, *J* = 7.6, 5.0, 1.0 Hz, 1H, 5'-H), 7.55 (d, *J* = 7.9 Hz, 1H, 3'-H), 7.61 (d, *J* = 8.6 Hz, 1H, 3-H), 7.72 (td, *J* = 7.7, 1.7 Hz, 1H, 4'-H), 8.57 (dd, *J* = 5.0, 1.0 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.57 ($CH_3CH_2C(O)$), 36.50 ($CH_2C(O)$), 55.47 (OCH_3), 112.49 (6-C), 115.36 (4-C), 121.46, 121.60 (5'-C), 129.92, 130.40, 136.62 (4'-C), 143.29, 149.98 (6'-C), 156.64, 159.86, 207.82 (CO); IR (KBr) 3058 w, 2978 m, 2938 m, 2878 w, 1686 s, 1608 s, 1587 s, 1563 m, 1509 m, 1470 s, 1429 s, 1408 m, 1371 m, 1345 m, 1316 s, 1287 m, 1232 s, 1199 m, 1182 m, 1152 m, 1115 m, 1098 w, 1054 m, 1038 m, 1011 m, 988 m, 874 m, 846 m, 823 w, 792 s, 746 m, 709 w, 654 w, 623 w, 602 w, 554 w, 506 w; MS, *m/z* (rel intensity) 241 (M^+, 1), 226 (M^+-CH_3, 1), 213 (15), 212 (M^+-CH_2CH_3, 100), 197 (22), 169 (27), 141 (14), 114 (10), 63 (11), 51 (13). Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81. Found: C, 74.56; H, 6.31; N, 5.76.

1-[2-(2-Pyridinyl)-5-(trifluoromethyl)phenyl]-1-propanone (25c). Yellow oil; Bp 160-165 °C (1 mmHg); R_f = 0.29 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.11 (t, *J* = 7.6 Hz, 3H, $CH_3CH_2C(O)$), 2.52 (q, *J* = 7.6 Hz, 2H, $CH_2C(O)$), 7.30 (dd, *J* = 7.6, 4.6 Hz, 1H, 5'-H), 7.64-7.68 (m, 2H, Ar), 7.73-7.85 (m, 3H, 4'-H, Ar), 8.64 (d, *J* = 5.0 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.09 ($CH_3CH_2C(O)$), 36.14 ($CH_2C(O)$), 122.20, 122.82 (5'-C), 123.50 (q, *J* = 272 Hz), 123.98 (q, *J* = 3.7 Hz), 126.17 (d, *J* = 3.7 Hz), 128.90, 130.30 (q, *J* = 33 Hz), 136.89, 141.06, 142.25, 149.00 (6-C), 155.17, 206.14 (CO); IR (neat) 3072 w, 2982 w, 2942 w, 2634 w, 2574 w, 2276 w, 1701 s, 1616 m, 1591 m, 1567 m, 1503 w, 1470 m, 1434 m, 1411 m, 1327 s, 1305 m, 1261 m, 1202 s, 1169 s, 1125 s, 1080 s, 1019 w, 990 w, 965 w, 901 w, 843 m, 790 m, 747 m, 651 w, 619 w, 544 w, 500 w; MS, *m/z* (rel intensity) 279 (M^+, 0), 264 (M^+-CH_3, 2), 251 (14), 250 (M^+-CH_2CH_3, 100), 153 (10). Anal. Calcd for $C_{15}H_{12}F_3NO$: C, 64.52; H, 4.33; N, 5.02. Found: C, 64.40; H, 4.47; N, 5.06.

1-[5-Fluoro-2-(2-pyridinyl)phenyl]-1-propanone (25d). Yellow oil; Bp 150-155 ℃ (1 mmHg); R_f = 0.19 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.09 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.47 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.12-7.27 (c, 3H, Ar), 7.58 (d, *J* = 7.9 Hz, 1H, 3'-H), 7.65 (dd, *J* = 8.4, 5.1 Hz, 1H, 3-H), 7.75 (td, *J* = 6.8, 2.0 Hz, 1H, 4'-H), 8.60 (d, *J* = 4.0 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.34 ($CH_3CH_2C(O)$), 36.19 ($CH_2C(O)$), 114.33 (d, *J* = 23 Hz), 116.46 (d, *J* = 22 Hz), 121.74 (3'-C), 122.16 (5'-C), 130.49 (d, *J* = 7 Hz), 134.09 (2-C), 136.77 (4'-C), 143.67 (d, *J* = 6 Hz), 149.00 (6'-C), 155.94 (2'-C), 162.51 (d, *J* = 250 Hz), 206.20 (CO); IR (KBr) 3038 m, 2964 m, 2906 m, 2356 w, 1914 w, 1823 w, 1697 s, 1609 m, 1591 s, 1563 m, 1497 w, 1465 s, 1450 m, 1433 s, 1412 m, 1371 m, 1342 m, 1304 m, 1270 m, 1217 s, 1171 s, 1152 m, 1114 m, 1091 w, 1053 m, 1032 w, 1016 m, 988 m, 909 m, 866 w, 833 s, 804 m, 785 s, 748 s, 733 m, 711 m, 653 w, 608 w, 595 w, 563 m, 541 w, 503 m; MS, *m/z* (rel intensity) 229 (M^+, 0), 214 (M^+-CH_3, 2), 201 (14), 200 (M^+-CH_2CH_3, 100), 145 (14). Anal. Calcd for $C_{14}H_{12}FNO$: C, 73.35; H, 5.28; N, 6.11. Found: C, 73.36; H, 5.32; N, 6.09.

1,1'-[5-Methyl-2-(2-pyridinyl)-1,3-phenylene]bis-1-propanone (26a). Brown solid; mp 74-76 °C (hexane); R_f = 0.20 (hexane/EtOAc = 2/3); ^{1}H NMR ($CDCl_3$) δ 0.95 (t, *J* = 7.3 Hz, 6H, $CH_3CH_2C(O)$), 2.32 (q, *J* = 7.3 Hz, 4H, $CH_2C(O)$), 2.45 (s, 3H, CH_3), 7.29-7.33 (m, 2H, 3'-H, 5'-H), 7.34 (s, 2H, 4-H, 6-H), 7.70 (td, *J* = 7.6, 1.6 Hz, 1H, 4'-H), 8.62 (d, *J* = 4.6

Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.32 ($CH_3CH_2C(O)$), 21.04 (CH_3), 36.17 ($CH_2C(O)$), 122.55, 124.78, 129.18, 133.55, 136.28 (4'-C), 138.69, 142.36, 149.56 (6'-C), 156.55, 207.35 (CO); IR (KBr) 3054 w, 2976 m, 2934 m, 2428 w, 2318 w, 1697 s, 1591 s, 1560 s, 1483 m, 1455 s, 1429 s, 1405 s, 1373 m, 1342 s, 1283 m, 1242 m, 1128 s, 1054 s, 1025 m, 988 m, 885 m, 821 m, 790 s, 748 s, 660 w, 619 w, 597 w, 579 w, 520 w; MS, *m/z* (rel intensity) 281 (M^+, 1), 253 (19), 252 (M^+-CH_2CH_3, 100), 195 (11), 167 (14), 166 (10), 84 (13). Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.69; H, 6.87; N, 4.96.

1,1'-[5-Methoxy-2-(2-pyridinyl)-1,3-phenylene]bis-1-propanone (26b). Brown solid; mp 130-135 °C (hexane); R_f = 0.05 (hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$) δ 0.95 (t, *J* = 7.3 Hz, 6H, $CH_3CH_2C(O)$), 2.31 (q, *J* = 7.3 Hz, 4H, $CH_2C(O)$), 3.87 (s, 3H, OCH_3), 7.03 (s, 2H, 4-H, 6-H), 7.23-7.29 (m, 2H, 3'-H, 5'-H), 7.70 (td, *J* = 7.7, 1.9 Hz, 1H, 4'-H), 8.61 (dd, *J* = 5.0, 1.0 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.30 ($CH_3CH_2C(O)$), 36.19 ($CH_2C(O)$), 55.71 (OCH_3), 114.20 (4-C, 6-C), 122.41, 124.76, 128.59, 136.33 (4'-C), 143.83, 149.56 (6'-C), 156.21, 159.34, 207.04 (CO); IR (KBr) 3066 w, 2980 m, 2942 m, 2886 m, 2842 w, 1691 s, 1599 s, 1573 s, 1457 s, 1432 s, 1382 s, 1354 s, 1310 s, 1290 s, 1268 s, 1219 m, 1178 m, 1166 s, 1117 s, 1099 m, 1072 m, 1044 m, 1023 s, 986 m, 897 m, 876 m, 858 m, 825 w, 795 s, 757 m, 697 w, 620 w, 582 w, 509 w; MS, *m/z* (rel intensity) 297 (M^+, 0), 269 (18), 268 (M^+-CH_2CH_3, 100), 196 (17), 140 (20). Anal. Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.52; H, 6.50; N, 4.66.

1-[1-(2-Pyridinyl)-2-naphtalenyl]-1-propanone (28). Colorless oil; R_f = 0.10 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 0.98 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.46 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.34-7.39 (m, 1H, 5'-H), 7.42-7.48 (m, 2H, 7'-H, 3'-H), 7.54 (td, *J* = 7.4, 1.4 Hz, 1H, 6-H), 7.64 (d, *J* = 8.6 Hz, 1H, 8-H), 7.66 (d, *J* = 8.6 Hz, 1H, 4-H), 7.83 (td, *J* = 7.8, 1.9 Hz, 1H, 4'-H), 7.91 (d, *J* = 7.9 Hz, 1H, 5-H), 7.95 (d, *J* = 8.6 Hz, 1H, 3-H), 8.79 (d, *J* = 4.3 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.02 ($CH_3CH_2C(O)$), 35.56 ($CH_2C(O)$), 122.16, 123.59, 125.66, 126.24, 126.70, 126.77, 127.71, 128.48, 131.18, 134.02, 135.81, 136.51, 137.48, 149.27, 157.12, 205.98 (CO); IR (neat) 2986 m, 2942 m, 2716 w, 1923 w, 1856 w, 1691 s, 1622 w, 1589 s, 1566 m, 1474 m, 1431 m, 1377 m, 1350 m, 1214 m, 1147 w, 1091 m, 1035 w, 993 w, 955 w, 867 w, 819 m, 792 m, 748 s, 663 w, 577 w; MS, *m/z* (rel intensity) 261 (M^+, 0), 233 (19),

232 (M^+-CH_2CH_3, 100), 204 (10), 203 (14), 176 (12), 115 (13), 101 (37), 88 (19). Exact mass calcd for $C_{18}H_{15}NO_2$ 260.1075, found for 260.1079.

1-[3-(2-Pyridinyl)-2-naphtalenyl]-1-propanone (30). Colorless oil; R_f = 0.29 (hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$) δ 1.14 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.62 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.26-7.29 (m, 1H, 5'-H), 7.53-7.61 (m, 2H, 6-H, 7-H), 7.74 (brd, *J* = 7.8 Hz, 1H, 3'-H), 7.82 (dt, *J* = 7.8, 4.3 Hz, 1H, 4'-H), 7.90-7.94 (m, 2H, 5-H, 8-H), 7.98 (s, 1H, 4-H), 8.11 (s, 1H, 1-H), 8.61 (d, *J* = 4.9 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.72 ($CH_3CH_2C(O)$), 36.28 ($CH_2C(O)$), 122.07, 122.26, 127.24, 127.55, 127.60, 128.14, 128.39, 128.75, 132.51, 133.57, 136.03, 136.77, 139.53, 149.18, 157.57, 207.19 (CO); IR (neat) 3058 m, 2978 m, 2938 m, 2822 w, 1730 m, 1693 s, 1630 m, 1591 s, 1568 m, 1480 s, 1462 s, 1443 m, 1428 s, 1373 m, 1346 m, 1289 m, 1272 m, 1244 m, 1179 s, 1148 m, 1128 m, 1079 m, 1050 m, 1023 m, 995 m, 934 m, 892 s, 876 m, 788 s, 743 s, 641 w, 620 w; MS, *m/z* (rel intensity) 261 (M^+, 0), 246 (M^+ -CH_3, 2), 233 (18), 232 (M^+-CH_2CH_3, 100), 176 (12), 115 (22), 101 (14), 87 (20). Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.40; H, 5.82; N, 5.42.

1-[2-(2-Pyridinyl)-3-thienyl]-1-propanone (32). Yellow oil; Bp 125 °C (1 mmHg); R_f = 0.13 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.15 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.76 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.22-7.27 (m, 1H, 5'-H), 7.32-7.37 (m, 2H, thienyl-H), 7.67-7.75 (m, 2H, 3'-H, 4'-H), 8.61 (d, *J* = 5.1 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.29 ($CH_3CH_2C(O)$), 35.94 ($CH_2C(O)$), 122.82 (5'-C), 123.41, 126.25, 128.77, 136.39, 138.67, 146.56, 149.36 (6'-C), 151.90, 199.89 (CO); IR (neat) 3074 m, 2980 m, 2940 m, 1686 s, 1585 s, 1568 m, 1521 s, 1467 s, 1439 s, 1422 s, 1377 s, 1334 m, 1267 s, 1212 s, 1159 m, 1119 m, 1089 m, 1048 m, 995 m, 868 s, 779 s, 731 m, 652 m, 614 m; MS, *m/z* (rel intensity) 217 (M^+, 0.3), 202 (M^+-CH_3, 12), 189 (16), 188 (M^+-CH_2CH_3, 100), 116 (16), 89 (20), 78 (10). Anal. Calcd for $C_{12}H_{11}NOS$: C, 66.33; H, 5.10; N, 6.45. Found: C, 66.14; H, 5.24; N, 6.51.

1-[3-(2-Pyridinyl)-2-thienyl]-1-propanone (34). Yellow oil; Bp 165 °C (1 mmHg); R_f = 0.43 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.15 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.76 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.22-7.26 (m, 1H, 5'-H), 7.33-7.37 (m, 2H, thienyl, 3'-H), 7.65-7.75 (m, 2H, thienyl, 4'-H), 8.62 (d, *J* = 4.6 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.29 ($CH_3CH_2C(O)$), 35.94 ($CH_2C(O)$), 122.82, 123.41, 126.24, 128.70, 136.37, 138.65, 146.59, 149.38, 151.91, 199.91 (CO); IR (neat) 3104 w, 3054 w, 2980 m, 2938 w, 1684 s, 1584 s, 1568

m, 1519 m, 1467 s, 1438 m, 1422 m, 1377 m, 1333 w, 1265 m, 1215 m, 1150 w, 1118 w, 1087 w, 1046 w, 996 w, 868 m, 779 s, 733 m, 655 w, 614 w; MS, *m/z* (rel intensity) 217 (M^+, 0), 202 (M^+-CH_3, 12), 189 (14), 188 (M^+-CH_2CH_3, 100), 134 (10), 133 (10), 116 (22), 94 (10), 89 (32), 77 (17), 63 (19). Anal. Calcd for $C_{12}H_{11}NOS$: C, 66.33; H, 5.10; N, 6.45. Found: C, 66.48; H, 5.16; N, 6.50.

1-[3-(2-Pyridinyl)-2-furanyl]-1-propanone (36). Colorless oil; Bp 140 °C (1 mmHg); R_f = 0.23 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.19 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.98 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.08 (d, *J* = 1.7 Hz, 1H, 4-H), 7.25 (ddd, *J* = 7.6, 4.6, 1.5 Hz, 1H, 5'-H), 7.55 (d, *J* = 1.7 Hz, 1H, 5-H), 7.75 (td, *J* = 7.6, 1.6 Hz, 1H, 4'-H), 8.28 (d, *J* = 8.3 Hz, 1H, 3'-H), 8.66 (d, *J* = 4.6 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 7.68 ($CH_3CH_2C(O)$), 32.90 ($CH_2C(O)$), 114.84 (4-C), 123.00 (5'-C), 125.19 (3'-C), 132.10 (2-C), 136.15 (4'-C), 144.21 (5-C), 147.76 (2'-C), 149.22 (6'-C), 150.60 (3-C), 191.84 (CO); IR (neat) 3058 w, 2978 m, 2940 w, 2342 w, 2278 w, 2200 w, 1679 s, 1590 s, 1568 s, 1493 s, 1462 s, 1441 s, 1390 m, 1344 w, 1288 m, 1215 m, 1152 m, 1093 m, 1068 m, 1018 m, 917 m, 883 s, 772 m, 694 w, 614 w; MS, *m/z* (rel intensity) 201 (M^+, 8), 187 (11), 186 (M^+-CH_3, 83), 173 (12), 172 (M^+-CH_2CH_3, 100), 116 (41), 90 (11), 89 (52), 86 (13), 63 (40), 62 (13), 52 (10), 51 (26), 50 (13). Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.47; H, 5.54; N, 7.00.

1,1'-[3-(2-Pyridinyl)-2-furanylene]bis-1-propanone (37). Light red oil; Bp 160 °C (1 mmHg); R_f = 0.13 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.94-1.10 (m, 6H, $CH_3CH_2C(O)$), 2.58 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 2.68 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.34 (ddd, *J* = 7.6, 5.0, 1.3 Hz, 1H, 5'-H), 7.48 (dd, *J* = 7.6, 1.0 Hz, 1H, 3'-H), 7.78 (td, *J* = 7.6, 1.6 Hz, 1H, 4'-H), 8.10 (s, 1H, 5-H), 8.67 (dd, *J* = 5.0, 1.0 Hz, 1H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 7.17 ($CH_3CH_2C(O)$), 7.46 ($CH_3CH_2C(O)$), 32.81 ($CH_2C(O)$), 34.56 ($CH_2C(O)$), 123.07 (5'-C), 125.07 (3'-C), 128.57, 129.21, 136.06 (4'-C), 147.85 (5-C), 149.33 (6'-C), 149.53, 150.84, 190.71 (CO), 195.18 (CO); IR (neat) 3056 w, 2982 m, 2942 m, 2910 w, 2658 w, 2354 w, 2100 w, 1865 w, 1685 s, 1598 m, 1571 m, 1524 m, 1465 m, 1433 m, 1390 s, 1283 w, 1206 m, 1160 w, 1107 m, 1053 w, 1004 w, 989 w, 890 s, 788 m, 745 w, 616 w, 566 w, 506 w; MS, *m/z* (rel intensity) 257 (M^+, 0), 242 (M^+-CH_3, 17), 229 (15), 228 (M^+-CH_2CH_3, 100), 172 (25), 116 (22), 115 (13), 89 (22), 63 (14), 62 (11), 57 (35), 55 (13). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 70.30; H, 5.99; N, 5.55.

1-[3-Methyl-2-(2-pyrimidinyl)phenyl]-1-propanone (39). Red oil; Bp 160 °C (1 mmHg); R_f = 0.34 (hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$) δ 1.06 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.20 (s, 3H, CH_3), 2.79 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.26 (t, *J* = 5.0 Hz, 1H, 5'-H), 7.37-7.45 (m, 2H, Ar), 7.63 (dd, *J* = 6.8, 1.9 Hz, 1H, Ar), 8.81 (d, *J* = 5.0 Hz, 2H, 4'-H, 6'-H); ^{13}C NMR ($CDCl_3$) δ 8.20 ($CH_3CH_2C(O)$), 19.70 (CH_3), 33.95 ($CH_2C(O)$), 118.80, 125.80, 128.39, 133.68, 137.30, 138.22, 138.56, 156.77, 168.10, 203.56 (CO); IR (neat) 3034 m, 2978 m, 2936 m, 1692 s, 1621 w, 1558 s, 1445 s, 1408 s, 1377 m, 1344 m, 1285 m, 1236 s, 1168 m, 1101 m, 1039 m, 971 m, 951 m, 805 s, 772 s, 748 m, 714 m, 655 w, 629 m; MS, *m/z* (rel intensity) 226 (M^+, 0), 211 (M^+-CH_3, 2), 198 (15), 197 (M^+-CH_2CH_3, 100), 169 (11), 89 (13). Anal. Calcd for $C_{13}H_{14}N_2O$: C, 74.31; H, 6.24; N, 12.38. Found: C, 74.36; H, 6.27; N, 12.53.

1-[2-(4-Pyrimidinyl)phenyl]-1-propanone (41). Light red oil; Bp 135 °C (1 mmHg); R_f = 0.34 (hexane/EtOAc = 1/4); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.72 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.48-7.61 (m, 4H, Ar), 7.66-7.69 (m, 1H, Ar), 8.79 (d, *J* = 5.1 Hz, 1H, 5'-H), 9.19 (s, 1H, 2'-H); ^{13}C NMR ($CDCl_3$) δ 8.27 ($CH_3CH_2C(O)$), 36.03 ($CH_2C(O)$), 118.92, 127.28, 129.04, 130.01, 130.08, 135.45, 141.74, 151.27, 158.10, 164.42, 206.56 (CO); IR (neat) 3192 w, 3154 w, 3036 w, 2980 m, 2938 m, 2900 m, 1696 s, 1577 s, 1539 s, 1488 m, 1469 s, 1442 s, 1409 m, 1387 s, 1347 s, 1306 s, 1274 m, 1214m, 1160 m, 1116 m, 1079 m, 1012 m, 988 m, 947 s, 878 w, 846 m, 793 m, 753 s, 674 w, 640 m, 623 m; MS, *m/z* (rel intensity) 212 (M^+, 0), 197 (M^+-CH_3, 2), 184 (13), 183 (M^+-CH_2CH_3, 100), 128 (18), 101 (12). Anal. Calcd for $C_{13}H_{12}N_2O$: C, 73.57; H, 5.70; N, 13.20. Found: C, 73.38; H, 5.73; N, 13.22.

1.5 References and Notes

(1) For recent reviews on carbonylation, see: Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation*; Plenum Press: New York, 1991. Tkatchenko, I. *Comprehensive Organometallic Chemistry*; Wilkinson, G.; Stone, F. G. A.; Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; pp 101-223.

(2) Nagira, K.; Kikukawa, K.; Wada, F.; Matsuda, T. *J. Org. Chem.* **1980**, *45*, 2365.

(3) Sakamoto, M.; Shimizu, I.; Yamamoto, A. *Chem. Lett.* **1995**, 1101.

(4) Antebi, S.; Alper, H. *Tetrahedron Lett.* **1985**, *26*. 2609. Uemura, S.; Takahashi, H.; Ohe, K.; Sugita, N. *J. Organomet. Chem.* **1989**, *361*, 63.

(5) Miyaura, N.; Suzuki, A. *Chem. Lett.* **1981**, 879. Cho, C. S.; Ohe, K.; Uemura, S. *J. Organomet. Chem.* **1995**, *496*, 221.

(6) Barlow, L. R.; Davidson, J. M. *Chem. Ind.* **1965**, 1656. Heck, R. F. *J. Am. Chem. Soc.* **1986**, *90*, 5546.

(7) Larock, R. C.; Fellows, C. A. *J. Org. Chem.* **1980**, *45*, 363. Larock, R. C.; Fellows, C. A. *J. Am. Chem. Soc.* **1982**, *104*, 1900.

(8) Henry, P. M. *Tetrahedron Lett.* **1968**, 2285.

(9) For Pd(II)-catalyzed carbonylation of a benzene ring, see: Fujiwara, Y.; Kawauchi, T.; Taniguchi, H.; *J. Chem. Soc., Chem. Commun.* **1980**, 220. Taniguchi, Y.; Yamaoka, Y.; Nakata, K.; Takai, K.; Fujiwara, Y. *Chem. Lett.* **1995**, 345. For a recent review, see: Fujiwara, Y.; Takaki, K.; Taniguchi, Y. *Synlett* **1996**, 591.

(10) For recent examples of transition metal catalyzed carbonylative cyclization, see: Joh, T.; Doyama, K.; Fujiwara, K.; Maeshima, K.; Takahashi, S. *Organometallics* **1991**, *10*, 508. Ishii, Y.; Hidai, M. *J. Organomet. Chem.* **1992**, *428*, 279. Takeuchi, R.; Yasue, H. *J. Org. Chem.* **1993**, *58*, 5386. Kokubo, K.; Matsumasa, K.; Miura, M.; Nomura, M. *J. Org. Chem.* **1996**, *61*, 6941.

(11) Hong, P.; Yamazaki, H. *Chem. Lett.* **1979**, 1335.

(12) Fisher, B. J.; Eisenberg, R. *Organometallics* **1983**, *2*, 764. Kunin, A. J.; Eisenberg, R. *J. Am. Chem. Soc.* **1986**, *108*, 535. Kunin, A. J.; Eisenberg, R. *Organometallics* **1988**, *7*, 2124. Gordon, E. M.; Eisenberg, R. *J. Mol. Catal.* **1988**, *45*, 57.

(13) Sakakura, T.; Tanaka, M. *Chem. Lett.* **1987**, 249. Sakakura, T.; Tanaka, M. *J. Chem. Soc., Chem. Commun.* **1987**, 758. Sakakura, T.; Sodeyama, T.; Sasaki, K.; Wada, K.; Tanaka, M. *J. Am. Chem. Soc.* **1990**, *112*, 7221.

(14) Boyd, S. E.; Field, L. D.; Partridge, M. G. *J. Am. Chem. Soc.* **1994**, *116*, 9492. Rosini, G. P.; Boese, W. T.; Goldman, A. S. *J. Am. Chem. Soc.* **1994**, *116*, 9498.

(15) Moore, E.; Pretzer, W. R.; O'Connell, T. J.; Harris, J.; LaBounty, L.; Chou, L.; Grimmer, S. S. *J. Am. Chem. Soc.* **1992**, *114*, 5888. Moore, E.; Pretzer, W. R. U.S. Patent 5,081,250 1992; Chem. Abstr. **1992**, *116*, 174011.

(16) Chatani, N.; Fukuyama, T.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1996**, *118*, 493.

(17) Fukuyama, T.; Chatani, N.; Tatsumi, J.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1998**, *120*, 11522 .

(18) Bruce, M. I. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 73. Newkome, G. R.; Puckett, W. E.; Gupta, V. K.; Kiefer, G. E. *Chem. Rev.* **1986**, *86*, 451. Ryabov, A. D. *Chem. Rev.* **1990**, *90*, 403.

(19) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Nature* **1993**, *366*, 529. Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Pure & Appl. Chem.* **1994**, *66*, 1527. Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 62. Kakiuchi, F.; Tanaka, Y.; Sato, T.; Chatani, N.; Murai, S. *Chem. Lett.* **1995**, 679. Kakiuchi, F.; Yamamoto, Y.; Chatani, N.; Murai, S. *Chem. Lett.* **1995**, 681. Sonoda, M.; Kakiuchi, F.; Chatani, N.; Murai, S. *J. Organomet. Chem.* **1995**, *504*, 151. Murai, S.; Chatani, N.; Kakiuchi, F. *Pure Appl. Chem.* **1997**, *69*, 589. Sonoda, M.; Kakiuchi, F.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 3117. Sato, T.; Kakiuchi, F.; Chatani, N.; Murai, S. *Chem. Lett.* **1998**, 893. Kakiuchi, F.; Sato, T.; Tsujimoto, T.; Yamauchi, M.; Chatani, N.; Murai, S. *Chem. Lett.* **1998**, 1053.

(20) Guo, H.; Weber, W. P. *Polymer Bull.* **1994**, *32*, 525. Guo, H.; Tapsak, M. A.; Weber, W. P. *Polymer Bull.* **1994**, *33*, 417. Guo, H.; Tapsak, M. A.; Weber, W. P. *Polymer Bull.* **1995**, *34*, 49. Guo, H.; Weber, W. P. *Polymer Bull.* 1995, *35*, 259. Tapsak, M. A.; Guo, H.; Weber, W. P. *Polymer Prep.* **1995**, *36*, 451. Guo, H.; Tapsak, M. A.; Weber, W. P. *Polymer Prep.* **1995**, *36*, 705. Guo, H.; Tapsak, M. A.; Weber, W. P. *Macromolecules* **1995**, *28*, 4714. Guo, H.; Wang, G.; Tapsak, M. A.; Weber, W. P. *Macromolecules* **1995**, *28*, 5686. Wang, G.; Guo, H.; Weber, W. P. *J. Organomet. Chem.* **1996**, *521*, 351. Lu, P.; Paulasaari, J. K.; Weber, W. P. *Macromolecules* **1996**, *29*, 8583. Wang, G.; Guo, H.; Weber, W. P. *Polymer Bull.* **1996**, *37*, 169. Guo, H.; Wang, G.; Weber, W. P. *Polymer Bull.* **1996**, *37*, 423. Guo, H.; Tapsak, M. A.; Wang, G.; Weber, W. P. *ACS Symp. Ser.* **1996**, *624*, 99. Wang, G.; Tongco, E.; Guo, H.; Prakash, G. K. S.; Weber, W. P. *Polymer Prep.* **1996**, *37*, 329. Lu, P.; Paulasaari, J.; Weber, W. P. *Polymer Prep.* **1996**, *37*, 342. Guo, H.; Weber, W. P. *Polymer Prep.* **1996**, *37*, 344. Londergan, T. M.; Weber, W. P. *Macromol. Rapid. Commun.* **1997**, *18*, 207. Londergan, T. M.; Weber, W. P. *Polymer Prep.* **1997**, *38*, 184. Paulasaari, J. K.; Jyri, K.; Weber, W. P. *Macromolecules* **1998**, *31*, 7105. Kepler, C. L.; Londergan, T. M.; Lu, J.; Paulasaari, J.; Weber, W. P.*Polymer* **1998**, *40*, 765. Londergan, T. M.; You, Y.; Thompson, M. E.; Weber, W. P. *Polymer Prep.* **1998**, *39*, 270. Londergan, T. M.; Paulasaari, J.; Weber, W. P. *Polymer Prep.* **1998**, *39*, 272. Sargent, J. R.; Weber, W. P. *Polymer Prep.* **1998**, *39*, 274. Kepler, C. L.; Lu, J.; Weber, W. P. *Polymer Prep.* **1998**, *39*, 276. Weber, W. P. Guo, H.; Kepler, C.; Londergan, T.

M.; Tapsak, M. A.; Wang, G. *Polymer Prep.* **1998**, *39*, 454. Huang, D.; Weber, W. P. *Polymer Prep.* **1999**, *40*, 70. Gupta, S.; Londergan, T. M.; Paulasaari, J. K.; Sargent, J. R.; Weber, W. P *Polym. Mater. Sci. Eng.* **1999**, *80*, 445.

(21) Harris, P. W. R.; Woodgate, P. D. *J. Organomet. Chem.* **1996**, *506*, 339. Harris, P. W. R.; Woodgate, P. D. *J. Organomet. Chem.* **1997**, *530*, 211.

(22) Grigg, R.; Savic, V. *Tetrahedron Lett.* **1997**, *38*, 5737.

(23) Lenges, C. P.; Brookhart, M. *J. Am. Chem. Soc.* **1999**, *121*, 6616.

(24) Trost, B. M.; Imi, K.; Davies, I. W. *J. Am. Chem. Soc.* **1995**, *117*, 5371. Sonoda, M.; Kakiuchi, F.; Chatani, N.; Murai, S. *Chem. Lett.* **1996**, 109

(25) Usefulness of a pyridine ring as a directing group for formation of C-C bond has been described. Murai, S. *J. Synth. Org. Chem. Jpn.* **1994**, *52*, 992.

(26) Fujii, N.; Kakiuchi, F.; Chatani, N.; Murai, S. *Chem. Lett.* **1996**, 939. Fujii, N.; Kakiuchi, F.; Yamada, A.; Chatani, N.; Murai, S. *Chem. Lett.* **1997**, 425. Fujii, N.; Kakiuchi, F.; Yamada, A.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 285. Kakiuchi, F.; Sato, T.; Yamauchi, M.; Chatani, N.; Murai, S. *Chem. Lett.* **1999**, 19.

(27) Jordan, R. F.; Taylor, D. F. *J. Am. Chem. Soc.* **1989**, *111*, 778. Rodewald, S.; Jordan, R. F. *J. Am. Chem. Soc.* **1994**, *116*, 4491.

(28) Lim, Y.-G.; Kim, Y. H.; Kang, J.-B. *J. Chem. Soc., Chem. Commun.* **1994**, 2267. Lim, Y.-G.; Kim, Y. H.; Kang, J.-B. *J. Chem. Soc., Perkin 1* **1996**, 2201. Lim, Y.-G.; Kang, J.-B.; Kim, Y. H. *J. Chem. Soc., Chem. Commun.* **1996**, 585. Lim, Y.-G.; Kang, J.-B.; Kim, Y. H. *J. Chem. Soc., Perkin Trans. 1.* **1998**, *4*, 699.

(29) Halbritter, G.; Knoch, F.; Wolski, A.; Kisch, H. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1603. Halbritter, G.; Knoch, F.; Wolski, A.; Kisch, H. *J. Organomet. Chem.* **1995**, *492*, 87. Aulwurm, U. R.; Melchinger, J. U.; Kisch, H. *Organometallics* **1995**, *14*, 3385. Westernacher, S.; Kisch, H. *Monatsh. Chem.* **1996**, *127*, 469. Dürr, U.; Heinemann, F. W.; Kisch, H. *J. Organomet. Chem.* **1997**, *541*, 307. For a review, see: Dürr, U.; Kisch, H. *Synlett* **1997**, 1335.

(30) Kakiuchi, F.; Yamauchi, M.; Chatani, N.; Murai, S. *Chem. Lett.* **1996**, 111.

(31) The ruthenium-catalyzed conversion of vinylsilanes to ethylene and disilylethylene is known. Wakatuki, Y.; Yamazaki, H.; Nakano, M.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 703. Marciniec, B.; Pietraszuk, C. *J. Organomet. Chem.* **1991**, *412*, C1. See also Seki, Y.; Takeshita, K.; Kawamoto, K. *J. Organomet. Chem.* **1989**, *369*, 117. Wakatsuki, Y.; Yamazaki, H.; Nakano, M.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 703. Marciniec, B.;

Pietraszuk, C. *J. Organomet. Chem.* **1991**, *412*, C1. Marciniec, B.; Pietraszuk, C.; *J. Chem. Soc., Chem. Commun.* **1995**, 2003.

(32) Bennett, R. L.; Bruce, M. I.; Goodall, B. L.; Iqbal, M. Z.; Stone, F. G. A. *J. Chem. Soc., Dalton* **1972**, 1787.

(33) Bruce, M. I.; Goodall, B. L.; Stone, F. G. A. *J. Organomet. Chem.* **1973**, *60*, 343.

(34) GC analysis of the crude reaction mixture indicated that they were formed in a ratio of 21:1.

(35) The reaction of 2-acetylnaphtalene with vinylsilane in the presence of $RuH_2(CO)(PPh_3)_3$ resulted in formation of C-C bond at 1-position. The difference between the two reactions in regioselectivity may suggest the difference in the mechanism of C-C bond forming step.

(36) Yamazaki, H.; Wakatsuki, Y. *J. Organomet. Chem.* **1978**, *149*, 377. Yamazaki, H.; Hong, P. *J. Mol. Catal.* **1983**, *21*, 133.

(37) Boese, R.; Harvey, D. F.; Malaska, M. J.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1994**, *116*, 11153.

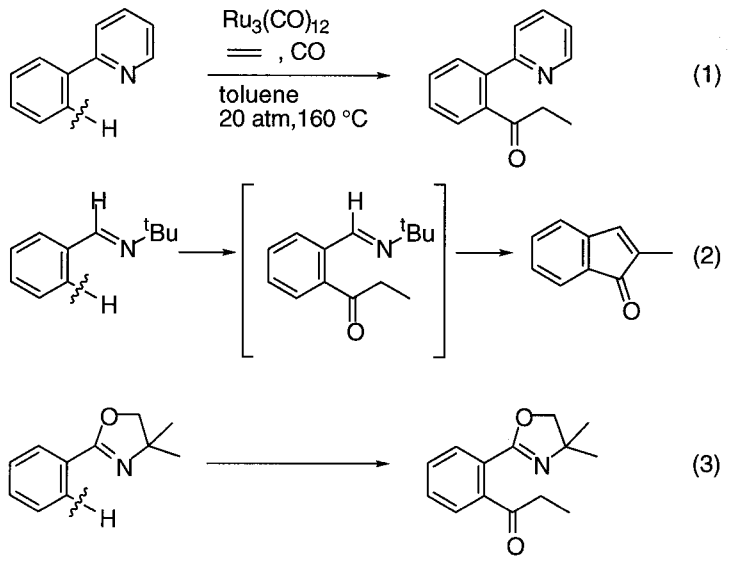
(38) Selnau, H. E.; Merola, J. S. *Organometallics* **1993**, *12*, 1583.

Chapter 2

Ruthenium-Catalyzed Direct Carbonylation at a C-H Bond in the Benzene Ring of 2-Phenyloxazolines.

2.1 Introduction

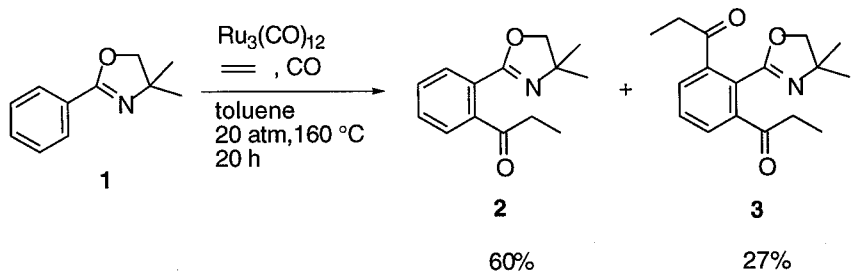
In chapter 1, I described the $Ru_3(CO)_{12}$-catalyzed reaction of 2-pyridylbenzenes with CO and ethylene leading to *ortho*-propionylation products (eq 1). The reaction involves the direct carbonylation at a C-H bond in the benzene ring and the carbonylation takes place site selectively at an *ortho* C-H bond. The experiments indicated that an effective directing group is required for the direct carbonylation at a C-H bond to take place.[1] In fact, the reaction of benzene, toluene, and anisole gave no carbonylation product at all. The coordination of the directing group to ruthenium brings the metal into close proximity to the ortho C-H bond, which may cleave. In terms of synthetic organic chemistry, a directing (coordinating) group should be introduced readily and removed or functionalized readily. In this context, the pyridyl group is not a suitable directing group for further useful transformations. One of the directing groups which fulfills all these requirements is an imino group, which is readily prepared from an aldehyde functionality and is readily deprotected to the original aldehyde.[2] However, the imino group does not survive under conditions of carbonylation. The reaction of benzaldehyde imines with CO and ethylene in the presence of $Ru_3(CO)_{12}$ did not stop at the carbonylation stage and the expected propionylation products were not obtained, but rather indenone derivatives constituted the final products and which were formed via intramolecular aldol-type reaction of the expected propionylation products in situ (eq 2).[3] Another candidate is an oxazoline ring, which is easily available from carboxylic acids and readily converted to carboxylic acids, esters, and aldehydes.[4] In this chapter, I wish to present the $Ru_3(CO)_{12}$-catalyzed reaction of 2-phenyloxazolines with CO and olefins (eq 3). It is noteworthy that the oxazoline ring has also a dramatic effect on both the reactivity and the site selectivity of the carbonylation at a C-H bond in a benzene ring. I further describe the full details concerning the scope and limitation of the reaction, and discuss the reaction mechanism.



2.2 Carbonylation at a C-H Bond in the Benzene Ring of Phenyloxazolines

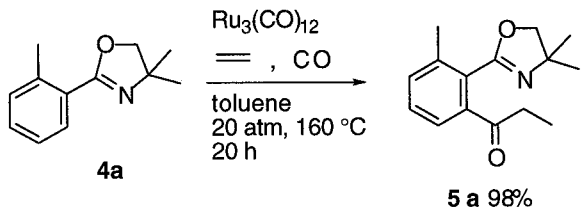
Carbonylation under CO pressure. The reaction was run under the same reaction conditions as those used for the carbonylation of pyridylbenzenes. The reaction of 4,4-dimethyl-2-phenyl-2-oxazoline (**1**, 2 mmol) with ethylene (initial pressure 7 atm at 25 °C in 50-mL stainless autoclave) at 20 atm (initial pressure at 25 °C) of CO at 160 °C in toluene (6 mL) in the presence of $Ru_3(CO)_{12}$ (0.05 mmol) for 20 h gave 1-[2-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-propanone (**2**) in 60% isolated yield and 1,1'-[2-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)-1,3-phenylene]-bis-1-propanone (**3**) in 27% isolated yield, along with 11% of the starting material **1** after column chromatography on silica gel (eq 4). The presence of the geminal dimethyl group on the oxazoline ring was critical for the success of this reaction. In fact, the reaction of 2-phenyloxazoline with no substituent at the 4-position on the oxazoline ring could not be stopped at the carbonylation stage, and further reactions, such as an aldol-type reaction similar to that in eq 2, took place to give mixtures. When the 2-(2-methylphenyl)oxazoline, which has an isopropyl group at the 4-position on the oxazoline ring, was used as the substrate, the corresponding ethyl ketone was obtained in low yield (33%), along with the starting material in 33% yield, along with unidentified products (equation not shown). A variety of transition metal complexes were examined for their ability to catalyze the carbonylation. Other complexes such as $RhCl(PPh_3)_3$, $[RhCl(CO)_2]_2$, $Co_2(CO)_8$, $RuH_2(CO)(PPh_3)_3$ and $Ir_4(CO)_{12}$ proved to be totally inactive. Although $Rh_4(CO)_{12}$ showed a high catalytic activity for the carbonylation at the C-H bond in *N*-(2-pyridyl)enamines,[1] it was not effective for the

carbonylation of phenyloxazolines. It was found that 2-benzyloxazoline, a one carbon homologue between a benzene ring and an oxazoline ring, was completely unreactive.



(4)

The reaction of 4,4-dimethyl-2-(2-methylphenyl)-2-oxazoline (**4a**) with CO and ethylene proceeded cleanly to give the corresponding ketone **5a** in 98% yield (eq 5). The rate of carbonylation of **4a** was found to be about 3 times faster than the corresponding 2-pyridyltoluene. Thus, the oxazoline ring is a more efficient directing group than a pyridine ring.



(5)

Prior to surveying a range of substrates, kinetic studies were conducted.[5] The effect of CO in the carbonylation reaction was monitored by quantification of the coupling products **5a** and the starting material **4a** by GC. The rate of formation of **5a** was measured independently with various pressures of CO, as shown in Figure 1. The rates which were measured under 15, 20, and 30 atm of CO show a least-squares fit to the data points. On the other hand, the rates under 5 and 10 atm of CO were linear during the initial reaction period but then deviated from the expected first-order and become slower. This deviation might be attributed to the decomposition of the catalyst during the reaction under the low CO pressure at high reaction temperature. A plot of k_{obs} vs. $1/P_{co}$ is linear in the range of 10 and 30 atm of CO which were used in these studies. These plots demonstrate that the rate of carbonylation shows an essentially first-order in $1/P_{co}$, as shown in Figure 2.

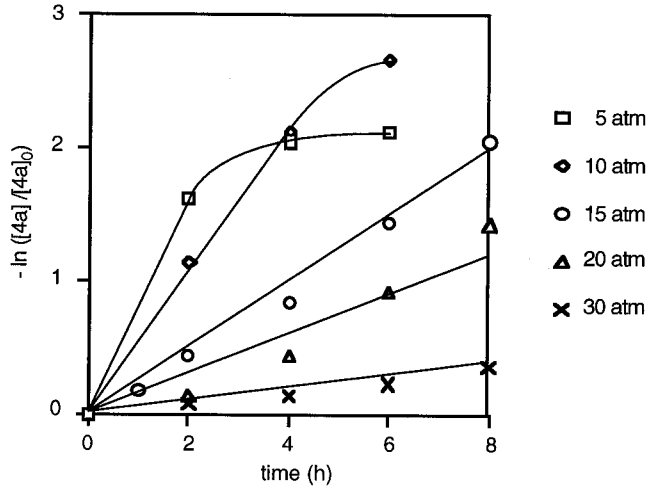


Figure 1. First-order rate plots for the reaction of **4a** (2 mmol) with CO and ethylene (7 atm) in the presence of $Ru_3(CO)_{12}$ (0.05 mmol) in toluene at 160 °C.

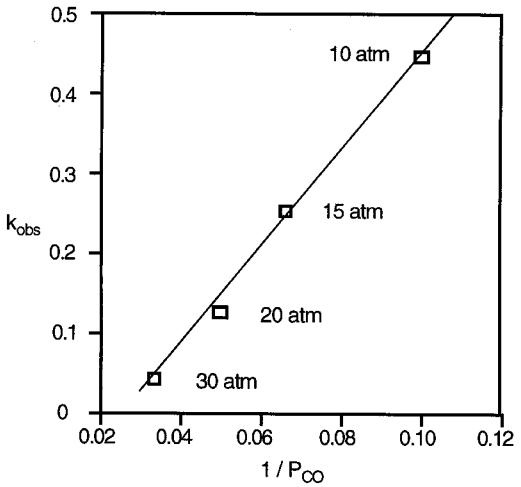


Figure 2. Plot of the first-order rate constant ($k_{obs.}$) *vs.* $1/P_{CO}$ for the carbonylation of **4a**

Carbonylation under 1atm of CO. The results of the kinetic study with respect to CO pressure showed that as the pressure of CO decreased, the reaction rate accelerates.[6] In an attempt to decrease the pressure of CO to 1 atm, in order to further accelerate the reaction rate and thus avoid the harsh reaction conditions, we reexamined the reaction conditions for the reaction of **4a** (Table 1). An initial effort involved the treatment of **4a** with 1 atm of CO under the same reaction conditions as eq 3, and provided **5a** in 36% yield, along with numerous byproducts, the formation of which can be ascribed to the decomposition of active catalytic species under low CO pressure at high temperatures, such as 160 °C (entry 1). It is important to note that the reaction proceeds cleanly without apparent decomposition of the catalysts when the reaction is carried out in toluene at 120 °C (entry 2). An

investigation of solvents revealed that acetonitrile is the most effective solvent for the carbonylation. Indeed, the reaction of **4a** (2 mmol) with ethylene (initial pressure 7 atm at 25 °C in 50-mL stainless autoclave) at 1 atm (initial pressure at 25 °C) of CO at 120 °C in acetonitrile (6 mL) in the presence of $Ru_3(CO)_{12}$ (0.05 mmol) for 20 h gave **5a** in 89% GC yield (entry 6). The use of a large amount of the catalyst (0.1 mmol) resulted in a quantitative yield of **5a** (entry 7).

Table 1. Carbonylation of **4a** with CO (1 atm) and Ethylene[a]

entry	$Ru_3(CO)_{12}$	temp.	solvent	yield of **5a** [b]
1	0.05 mmol	160 °C	toluene	36 %[c]
2		120 °C		66 %
3			THF	56 %
4			*N,N*-dimethylacetamide	68 %
5			DME	70 %
6			CH_3CN	89 %
7	0.1 mmol	120 °C	CH_3CN	98 %
8		100 °C		91 %
9		80 °C		17 %

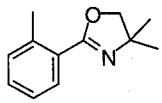
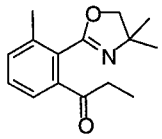
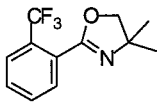
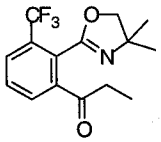
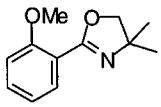
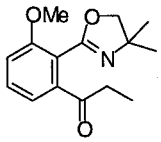
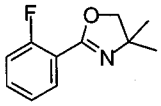
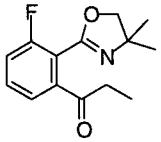
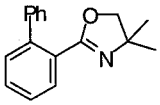
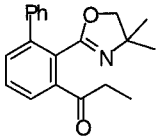
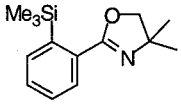
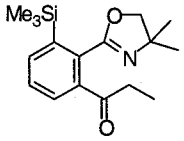
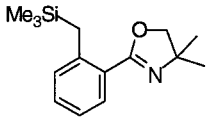
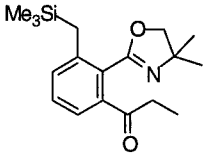
[a] Reaction conditions: **4a** (2 mmol), ethylene (initial pressure 7 atm at rt), CO (initial pressure 1 atm at rt), solvent (6 mL), 20 h in a 50-mL stainless steel autoclave.[b] GC yield. [c] Many other products were obtained.

Carbonylation of *ortho*-Substituted 2-Phenyloxazolines. In order to examine functional group compatibility, a variety of *ortho*-substituted 2-phenyloxazolines were treated with CO and ethylene (Table 2). The replacement of a methyl group with a trifluoromethyl group decreased the yield to 53%, along with 39% of the starting material **4b** (entry 2). The yield increased to 82% when the reaction was run for 40 h. 2-Phenyloxazolines which contain a methoxy, a fluoro, or a phenyl group also reacted to give the products **5c**, **5d** or **5e** in good yields (entries 3-5). It was found that the reaction of 2-phenyloxazolines which contain an electron-withdrawing group on the phenyl ring, did not afford satisfactory results when the reaction was carried out under 1 atm of CO at 120 °C (entries 2 and 4). When 4,4-dimethyl-2-(2-trimethylsilylphenyl)-2-oxazoline (**4f**) was used, the coupling product **5f** was obtained in moderate yield (entry 6). The reaction of **4g**, containing a silylmethyl group at the ortho position gave **5g**, resulted in an increased yield of 70% (entry 7). Since phenylsilanes and benzylsilanes are known to be useful synthetic intermediates,[7] **5f** and **5g** would be expected to be amenable to further exploitation. In the case of *o*-bromo- or *o*-cyano- substituted oxazoline, carbonylation did not take place under the reaction

conditions and the starting materials were recovered (structure not shown). The oxidative addition of the C-Br bond to ruthenium or the bidentate coordination of sp^2 nitrogen and a cyano group to ruthenium may have prevented or from undergoing cleavage of the C-H bonds, respectively. The reaction of 2-phenyloxazolines containing an *N, N*-dimethylamino group gave complex mixtures (structure not shown).

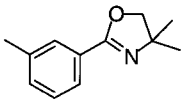
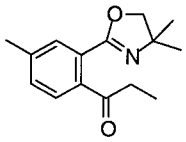
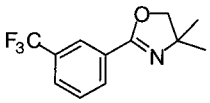
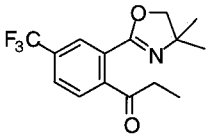
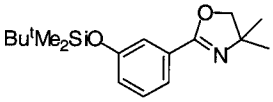
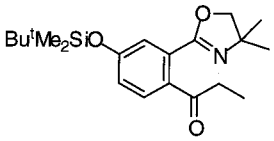
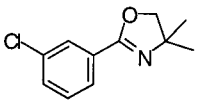
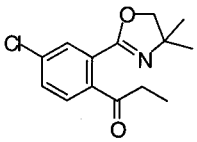
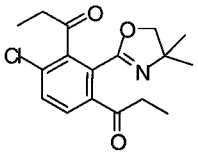
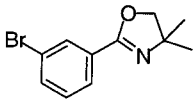
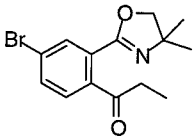
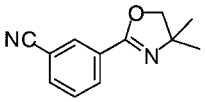
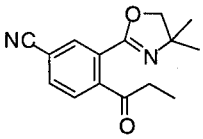
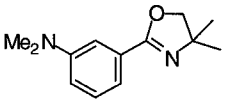
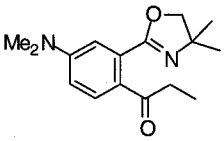
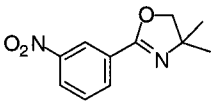
Carbonylation of *meta*-Substituted 2-Phenyloxazolines. It would be interesting to study the substituents at the *meta* position, since two different C-H bonds are present. Table 3 lists the representative results obtained from the reaction of *meta*-substituted 2-phenyloxazolines with CO and ethylene. When the reaction of 4,4-dimethyl-2-(3-methylphenyl)-2-oxazoline (**6a**) was carried out, the coupling reaction took place selectively at the less hindered C-H bond to give the corresponding ketone **7a** in 91% yield, and its regioisomer or the di-carbonylation product were not observed (entry 1). The reaction of 4,4-dimethyl-2-(3-trifluoromethylphenyl)-2-oxazoline (**6b**) also resulted in a site selective carbonylation to give **7b** exclusively (entry 2). A similar site selectivity was also observed in the reaction of the $Ru_3(CO)_{12}$-catalyzed *meta*-substituted pyridylbenzenes with CO and ethylene.[8] It is apparent that steric factors are important in controlling site selectivity. For example, the introduction of methyl groups at the 2- and 5-position on the benzene ring resulted in no reaction, in spite of one remaining C-H bond at the ortho position (eq 6). The reaction of the chloro-isomer **6d** gave two products, the mono-carbonylation product **7d** in 74% and di-carbonylation product **8d** in 9% yield (entry 4). However, the replacement of a chlorine atom by a bromine atom dramatically improved the selectivity and the ketone **7e** was obtained as the sole product (entry 5). These results also show that the selectivity is controlled by steric factors. Interestingly, phenyloxazolines containing a bromo **6e** or a cyano **6f** group at the meta position gave the corresponding ketones in high yields (entries 5 and 6), while the corresponding ortho-substituted phenyloxazolines did not react completely. The reaction of phenyloxazolines containing an electron-withdrawing group at the meta position gave a small amount (ca. 2-5%) of *ortho*-ethylation products (entries 2 and 6).[9] Other functional groups such as an *N,N*-dimethylamino group was tolerable in this reaction (entry 7). In case of *m*-nitro substituted oxazoline **6h**, carbonylation did not take place and the starting material was recovered (entry 8).

Table 2. $Ru_3(CO)_{12}$-Catalyzed Reaction of *ortho*-Substituted 2-Phenyloxazolines with CO and Ethylene [a]

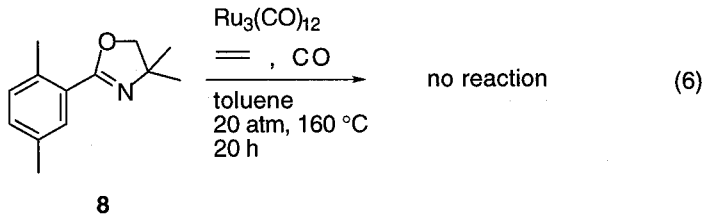
entry	2-phenyloxazoline	product	time	yield [b]
1	 **4a**	 **5a**	20 h	98% (98%)
2	 **4b**	 **5b**	20 h 40 h 40 h	53% 82% (70%)
3	 **4c**	 **5c**	20 h	74% (75%)
4	 **4d**	 **5d**	20 h	78% (49%)
5	 **4e**	 **5e**	20 h	77% (76%)
6	 **4f**	 **5f**	20 h	42% [c]
7	 **4g**	 **5g**	20 h	70%

[a] Reaction conditions: 2-phenyloxazolines (2 mmol), ethylene (initial pressure 7 atm at rt), CO (initial pressure 20 atm at rt), toluene (6 mL), $Ru_3(CO)_{12}$ (0.05 mmol), 160 °C in a 50-mL stainless steel autoclave. The numbers in parentheses are the yields at the following reaction conditions: CO (initial pressure 1 atm at rt), acetonitrile (6 mL), 120 °C. [b] Isolated yields based on the phenyloxazoline. [c] **4f** was recovered in 41% yield.

Table 3. $Ru_3(CO)_{12}$-Catalyzed Reaction of *meta*-Substituted 2-Phenyloxazolines with CO and Ethylene [a]

entry	2-phenyloxazolines	time	products [b]
1	 **6a**	20 h	 **7a** 91%
2	 **6b**	40 h	 **7b** 73% [c]
3	 **6c**	40 h	 **7c** 61%
4	 **6d**	40 h	 **7d** 74%  **8d** 9%
5	 **6e**	40 h	 **7e** 80%
6	 **6f**	20 h	 **7f** 66% [c, d]
7	 **6g**	40 h	 **7g** 57% [e]
8	 **6h**	20 h	n.r.

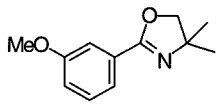
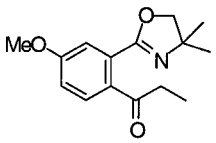
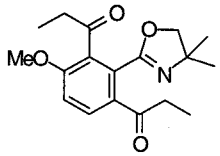
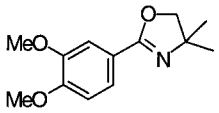
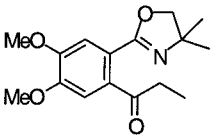
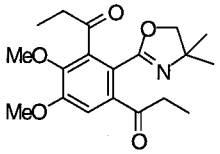
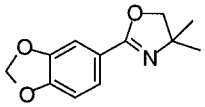
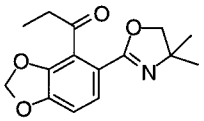
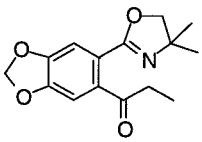
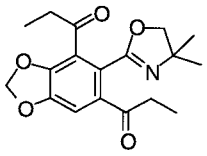
[a] Reaction conditions: phenyloxazolines (2 mmol), ethylene (initial pressure 7 atm at rt), CO (initial pressure 20 atm at rt), toluene (6 mL), $Ru_3(CO)_{12}$ (0.05 mmol), 160 °C in a 50-mL stainless steel autoclave. [b] Isolated yields based on the phenyloxazoline. [c] A small amount (ca. 2-5%) of ortho-ethylation products were detected by GC-MS. [d] **6f** was recovered in 31% yield. [e] **6g** was recovered in 43% yield.



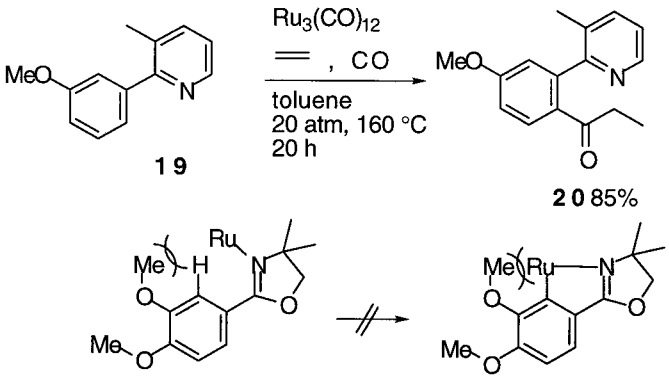
(6)

The reactivities of 2-phenyloxazolines having an ether-functionality (OMe, $-OCH_2O-$) on the benzene ring are shown in Table 4. The reaction of 4,4-dimethyl-2-(3-methoxyphenyl)-2-oxazoline (**9**) gave the mono-carbonylation product **10** in 48% yield, along with its regioisomer (structure not shown) in 1% yield and the di-carbonylation product **11** in 46% yield (entry 1). I was interested in the position of the first carbonylation, at the hindered or less hindered C-H bond, when **11** was formed. As I have already reported, the reaction of 2-(3-methoxyphenyl)-3-methylpyridine (**19**) gave the mono-carbonylation product **20**, apparently indicating the exclusive cleavage of the less hindered C-H bond (eq 7).[10] From this result, it should be expected that the formation of **11** also proceeds with the preferential cleavage of the less hindered C-H bond first and that the second carbonylation then took place at the hindered C-H bond to give **11**. When 4,4-dimethyl-2-(3,4,-dimethoxyphenyl)-2-oxazoline (**12**) was used, the selectivity was improved, in that the mono-carbonylation product **13** was obtained in 72% yield and the di-carbonylation product **14** in 12% yield (entry 2). The observed improvement in site selectivity can be explained by a buttressing effect,[11] which inhibits ruthenium from approaching to a C-H bond at the 2-position because of steric hindrance of methoxy groups (Chart 1). Interestingly, the carbonylation of **15** occurred preferentially at a C-H bond at the 2-position (a hindered position) (entry 3).[12] The result was not unexpected, since the acetal substituent is smaller than a methoxy group and the acetal oxygen also could coordinate to the ruthenium center.[13]

Table 4. $Ru_3(CO)_{12}$-Catalyzed Reaction of *Ether*-Substituted 2-Phenyloxazolines with CO and Ethylene [a]

entry	2-phenyloxazolines	time	products [b]	
1	 **9**	20 h	 **10** 48%	 **11** 46%
2	 **12**	20 h	 **13** 72%	 **14** 12%
3	 **15**	5 h	  **16, 17** 62% (85 : 15)[c]	 **18** 21%

[a] Reaction conditions: 2-phenyloxazolines (2 mmol), ethylene (initial pressure 7 atm at rt), CO (initial pressure 20 atm at rt), toluene (6 mL), $Ru_3(CO)_{12}$ (0.05 mmol), 160 °C in a 50-mL stainless steel autoclave. [b] Isolated yields based on the phenyloxazoline. [c] The ratio was determined by ^{1}HNMR.



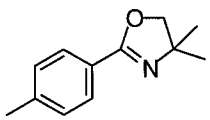
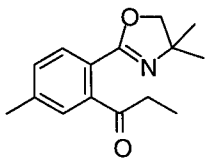
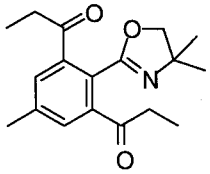
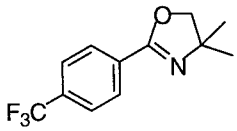
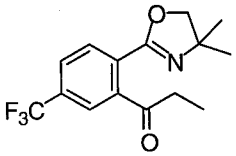
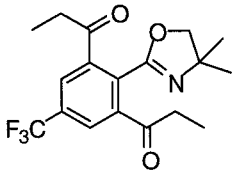
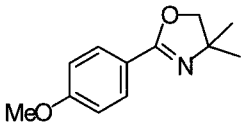
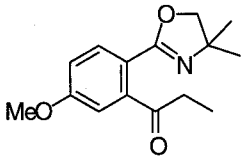
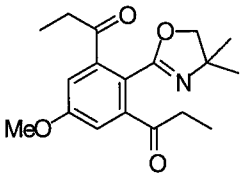
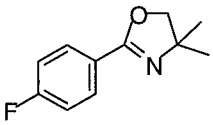
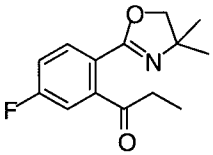
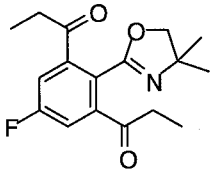
(7)

Chart 1

Carbonylation of *para*-Substituted 2-Phenyloxazolines. The results of *para*-substituted 2-phenyloxazolines are shown in Table 5. In all cases, mixtures of the mono-carbonylation and the di-carbonylation products were obtained. The ratio of these two products is affected by the electronic effect of the substituent on the benzene ring. The preferential formation of di-carbonylation products was observed in the reaction of phenyloxazolines having electron-donating groups (entries 1 and 3). In contrast, the reaction of a phenyloxazoline having an electron-withdrawing group yielded the mono-carbonylation product preferentially (entry 2). The electron

donating substituents should have made the oxazoline-nitrogen a better coordinating group towards the ruthenium so that the second carbonylation took place prior to the dissociation of the mono-carbonylation product from the ruthenium. In the case of pyridylbenzenes, the product distribution is also controlled by electronic effects of substituents on a benzene or a pyridine ring.[14]

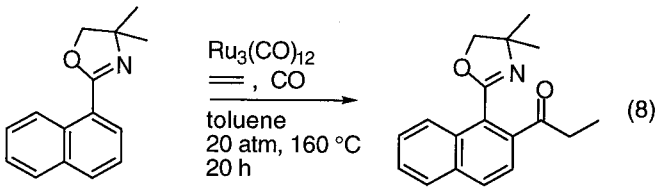
Table 5. $Ru_3(CO)_{12}$-Catalyzed Reaction of*para*-Substituted 2-Phenyloxazolines with CO and Ethylene[a]

entry	2-phenyloxazolines	products[b]	
1	 **21a**	 **22a** 38%	 **23a** 47%
2	 **21b**	 **22b** 44%	 **23b** 16%
3	 **21c**	 **22c** 21%	 **23c** 73%
4	 **21d**	 **22d** 33%	 **23d** 41%

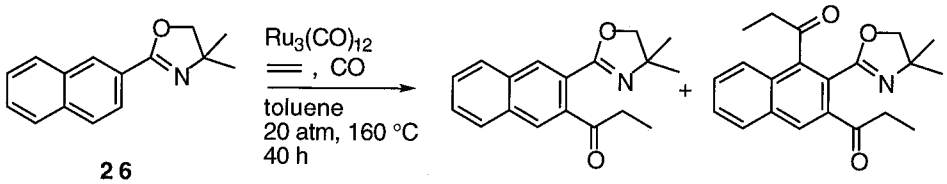
[a] Reaction conditions: 2-phenyloxazolines (2 mmol), ethylene (initial pressure 7 atm at rt), (initial pressure 20 atm at rt), $Ru_3(CO)_{12}$ (0.05 mmol), toluene (6 mL), 160 °C, 20h in a 50-mL stainless steel autoclave.[b] Isolated yields based on the phenyloxazoline.

I next examined other aromatic systems. The use of 2-(1'-naphthyl)oxazoline **24** as a substrate gave the corresponding ketone **25** in good yield (eq 8). Carbonylation of the β-isomer **26** took place site selectively to give **27**, along with di-carbonylation product **28** (eq 9). Despite the presence of the two different reaction sites in **26**, the C-H bond at the 3-position in the naphthalene ring underwent preferential cleavage and was carbonylated, presumably because of the steric hindrance of the peri-hydrogen on the naphthalene ring. In contrast to **26**, a di-carbonylation product was not obtained in the reaction of β-naphthylpyridine, even after 40 h of reaction.[15] One possible

explanation of the difference between oxazoline system and pyridine system is the higher strength of coordination ability of oxazoline nitrogen to ruthenium, compared to the pyridine nitrogen. This may be consistent with the observation that the phenyloxazolines bearing an electron-donating group is more reactive. Another possibility is that the relatively small size of an oxazoline ring compared to a pyridine ring may make the approach of ruthenium at the 1-position considerably easier.

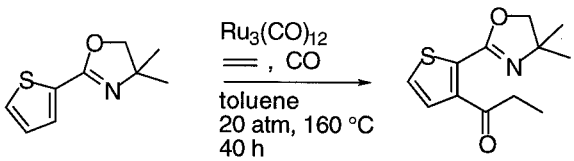


24 **25** 65% (8)



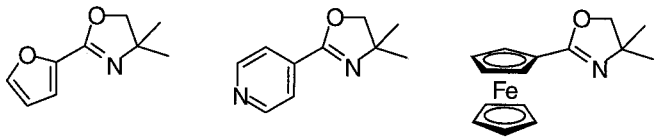
26 **27** 64% + **28** 17% (9)

The present carbonylation reaction at a C-H bond is also applicable to heteroaromatic compounds, such as thiophene derivatives. The reaction of 2-(2'-thiophenyl)oxazoline **29** gave the corresponding ethyl ketone **30** in high yield (eq 10).



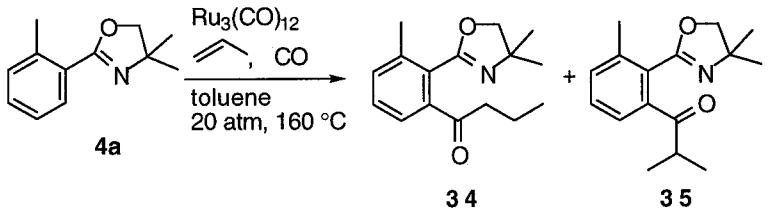
29 **30** 93% (10)

In the case of 2-(2-furanyl)oxazoline **31** and 2-(4-pyridinyl)oxazoline **32**, the coupling reaction did not take place and starting materials were recovered. The reaction of ferrocenyloxazoline **33** gave no corresponding product, but rather unidentified products.



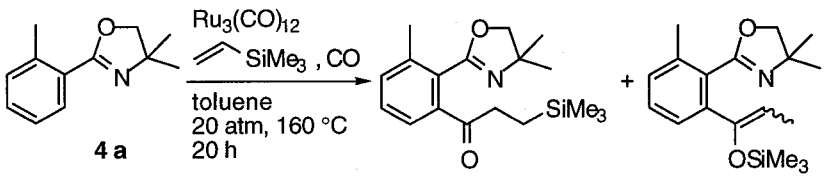
31 **32** **33**

In order to extend the scope of this reaction, a survey of the reactivity of several olefins toward **4a** with CO was carried out. In the case of propene, a mixture of linear and branched isomers **34** and **35**, were obtained in 22% total yields in a 51 : 49 ratio of **34** : **35** after 40 h (eq 11). Prolonging the reaction times from 40 h to 190 h improved the yield of products from 22% to 85%, and the ratios of **34** : **35** remained the same. A reaction with trimethylvinylsilane gave the coupling product **36** in 42% yield, accompanied by **37** as a single stereoisomer and **5a** in 8% and 6% yields, respectively (eq 12). The minor product **37** would be formed via silyl migration from carbon to oxygen in the branched isomer, α-silyl ketone.[16,17] The minor product **5a** appears to be formed by the reaction **4a** with CO and ethylene, which is generated in situ from the vinylsilane.[18] Reactions of **4a** with CO and olefins, such as 1-hexene, t-butylethylene, vinylcyclohexane, isoprene, 1,5-hexadiene, cyclohexene, 1,5-cyclooctadiene, styrene, methyl acrylate, vinyl acetate, allyltrimethylsilane and triethoxyvinylsilane did not afford the coupling products, and **4a** was recovered quantitatively. The reaction with a terminal alkyne, such as 1-hexyne, or with an internal alkyne, such as 3-hexyne, gave complex mixtures.



(11)

40h 22% (51 : 49)
190h 85% (56 : 44)

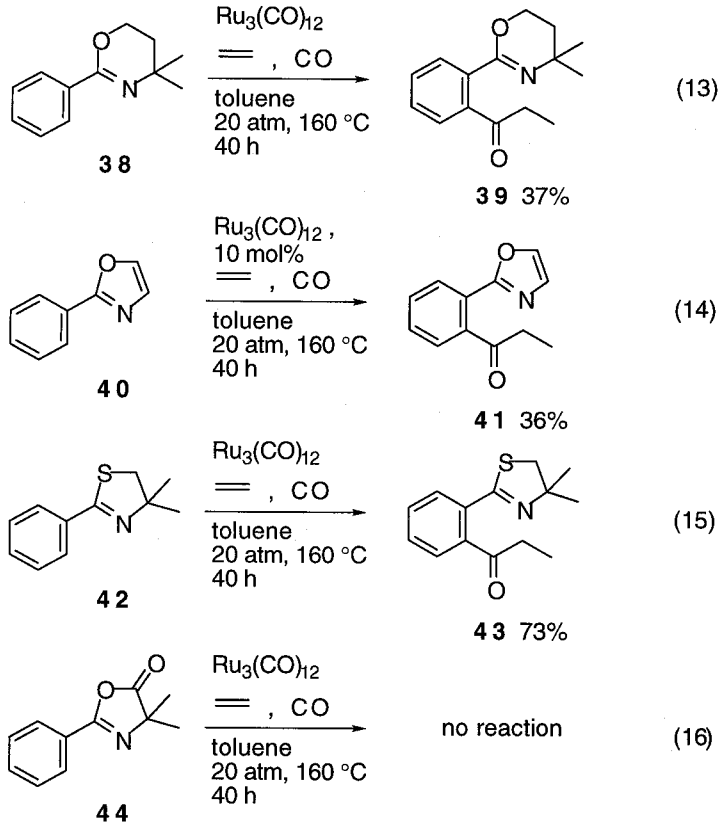


(12)

36 42% 37 8% (one isomer) 6%

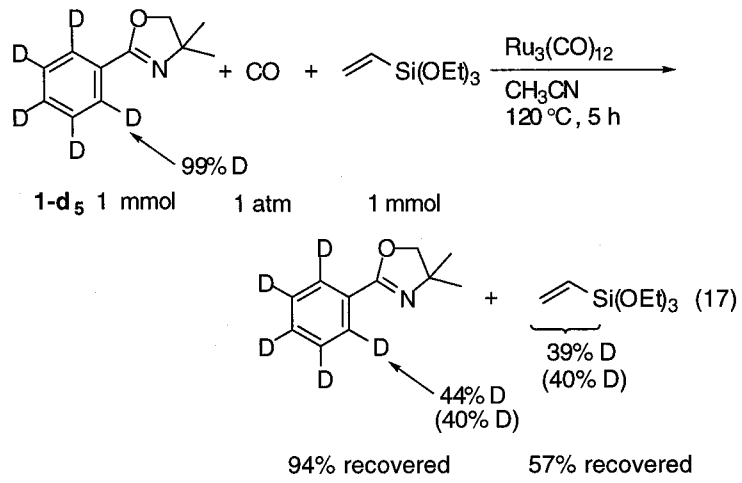
I examined the issue of whether other five- or six-membered heterocycles can be utilized as a directing group for present carbonylation reaction. As a result, I was pleased to discover that some heterocycles bearing an sp^2-nitrogen in the ring also work well as directing groups for the carbonylation of a C-H bond. Selected results are shown in eqs 13-15. The reaction of

phenyloxazine **38**, a six-membered analogue, gave the coupling product **39** in moderate yield (eq 13). When 2-phenyloxazole (**40**) was reacted in the presence of 10 mol% of catalyst, the mono-carbonylation product **41** was obtained, with 54% of recovery of **40** (eq 14). Thiazoline ring was also found to be an effective directing group for the carbonylation of a C-H bond in the benzene ring. In fact, phenylthiazoline **42** gave the mono-carbonylation product **43** as the sole product (eq 15). From this result, it is clear that the presence of sulfur has a profound effect on the production of the mono-carbonylation product selectively, even if the details of this effect are unclear at this point. The reaction of 2-phenyl-5-oxazolone **44** did not afford a coupling product.



Deuterium Labeling Experiment. I carried out the reaction using phenyloxazoline-d_5 (**1**-d_5), in order to obtain information concerning the reaction mechanism. Triethoxyvinylsilane was selected as an olefin for this deuterium labeling experiment. The reaction was run at 120 °C under 1 atm of CO, in order to avoid the conversion of triethoxyvinylsilane to ethylene and disilylethylene.[18] The reaction of **1**-d_5 (1 mmol), with CO (initial pressure 1 atm at 25 °C in 50-mL stainless autoclave), triethoxyvinylsilane (1 mmol), in acetonitrile (3 mL) at 120 °C for 20 h gave no carbonylation product and **1**-d_5 was recovered in 94% (eq 16). Deuterium incorporation was

determined by integration of ^{1}H NMR spectrum. The deuterium atoms at the *ortho* position of the recovered **1**-d_5 were scrambled, which corresponds to a 55% incorporation of protio label into these sites. In contrast, no deuterium incorporation at the *meta* and *para* position was observed. H/D exchange delivered deuterium from **1**-d_5 into triethoxyvinylsilane. All three vinyl protons of the recovered triethoxyvinylsilane were also 39% deuterated. The observed values were close to the theoretical values calculated for the case of complete scrambling over five positions, which are shown in parenthesis. The moderate yield of the recovered triethoxyvinylsilane was due to loss during purification by distillation. The mechanism based on this data will be discussed later.[19]

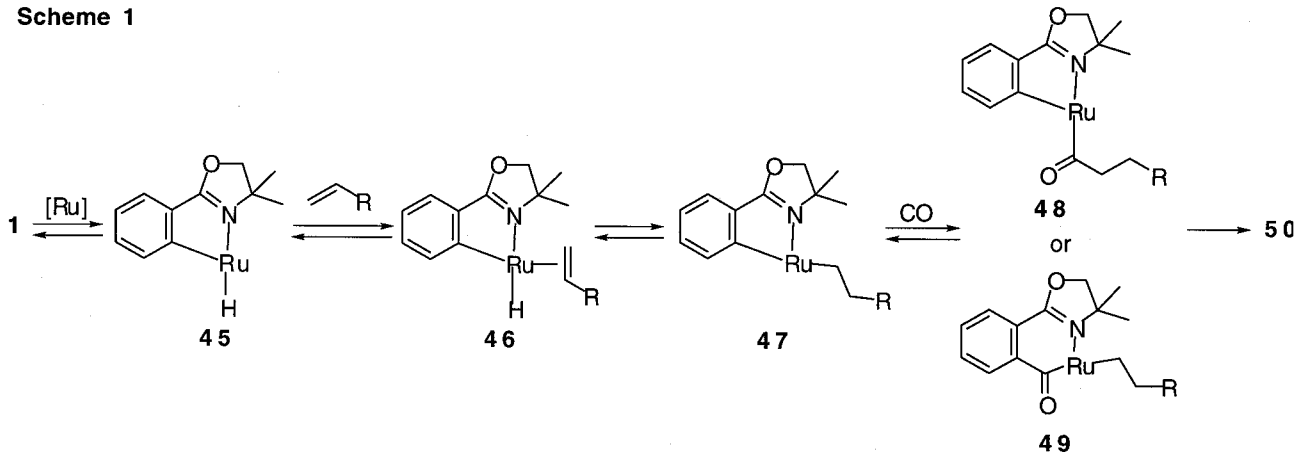


2.3 Mechanistic Discussion

The structure of the catalytically active species is poorly understood. To date I have been unsuccessful in characterizing or isolating the active species. To determine the molecularity of the true catalytic species, intact clusters (trinuclear ruthenium species) or fragment catalytic species (dinuclear or mononuclear ruthenium species), I followed Laine's kinetic criteria.[20] Using this criteria, the turnover frequency decreases with increasing catalyst concentration indicates that fragment catalytic species are responsible for the catalysis. A plot of turnover frequency vs. $Ru_3(CO)_{12}$ concentration was constructed (see experimental section). The resulting curve showed that, as the catalyst loading is increased, a slight decrease in the TOF value occurs, indicating that the active catalytic species is not $Ru_3(CO)_{12}$ but a lower nuclearity species, such as $Ru(CO)_n$ (where n = 4 or 5).

The mechanism for this transformation is believed to be analogous to the one proposed for the reaction of pyridylbenzenes, as shown in Scheme 1. The catalytic cycle may start with the formation of a five-membered metallacycle **45** in the first step. The related cyclometalated mononuclear ruthenium complexes were isolated,[21] while no report of a stoichiometric reaction of **1** with $Ru_3(CO)_{12}$ has yet appeared. The intermediancy of the cyclometalated complex[22], such as **45**, is invoked for the present carbonylation. Thus, the coordination of the nitrogen on the oxazoline ring to ruthenium would be essential for achieving the C-H bond cleavage to give the hydride complex **45**. The successive insertion of an olefin gives the alkyl complex **47**, by way of two steps, i.e., olefin coordination to ruthenium (**46**) followed by hydride migration to olefin. Complex **47** then undergoes CO insertion (**48** or **49**), followed by reductive elimination to give the coupling product **50**.

Scheme 1

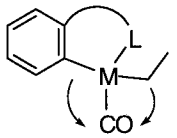


In the deuterium labeling experiment, H/D exchange occurred between the C-H bonds at the ortho position in the benzene ring and vinylic protons in the olefin (eq 17). Because a nearly complete scramble was observed at these positions, the cleavage of a C-H bond is reversible and olefin insertion/β-hydride elimination occurs faster than conversion to products. Thus, the cleavage of a C-H bond is not the rate-determining step in this reaction and a rapid equilibrium between **1** and **47** exists.

A comparison of the rates of the carbonylation of phenyloxazoline and pyridylbenzene was made. It was found that the rate of carbonylation of **4a** is roughly 3 times faster than the corresponding pyridine derivative. In a previous report on the carbonylation of a β-C-H bond in benzimidazole derivatives, I found that the reactivity of the substrates corresponds to the p*Ka* values

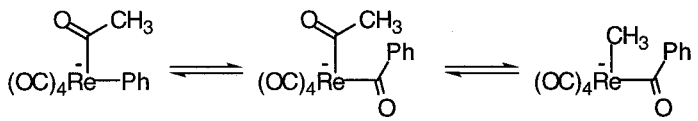
of the conjugated acids.[23] While the p*K*a values of the directing groups are not necessarily proportional to the binding strength to metal, these results suggest that the coordination of the substrates to a ruthenium complex is a necessary prerequisite for the carbonylation to proceed. There is, however, no correlation between reactivity and p*K*a values for the carbonylation at a γ-C-H bond as in the cases of phenyloxazolines and pyridylbenzenes, which is contrary to the results obtained for benzimidazole derivatives.[24] This distinct difference between the carbonylation at C-H bonds in benzene rings and heteroaromatic rings could be due to the differences in the rate-determining steps for the carbonylation.

The issue of whether CO insertion occurs into an alkyl-Ru bond or a phenyl-Ru bond in **47** is not presently known. Although insertion-deinsertion of CO into alkyl-metal or aryl-metal bond have been extensively studied,[25] comparison between these two bonds are limited. Furthermore, to the best of our knowledge, studies of CO insertion into five-membered metallacycles such as **A**, have not been done. Casey has established the studies of decarbonylation from (acyl)(aroyl)rhenium complex **C**.[26] It has been reported that the complex **B** is the thermodynamic product and the complex **D** is the kinetic one (Scheme 2). Carmona reported that the regioselective insertion of CO into the alkyl-Ni bond in the cyclometalated complex **E**, followed by reductive elimination gives an indanone derivative **F** (Scheme 2).[27] In both examples, the thermodynamically favored complexes involve an aryl-metal bond and alkyl-C(O)-metal bond. I recently reported that the decarbonylative cleavage of the C-C bonds in alkyl phenyl ketones, which is the reverse of the carbonylation reaction being considered here.[28] An investigation of the reaction pathway revealed that the reverse reaction is likely to proceed by way of **48** as an intermediate. Thus, by microscopic reversibility, we currently favor the intermediacy of **48** in the Ru-catalyzed carbonylation of phenyloxazolines.

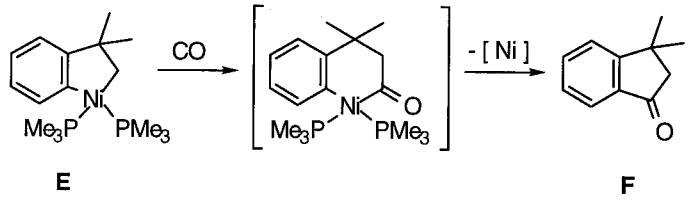


A

L = a directing group

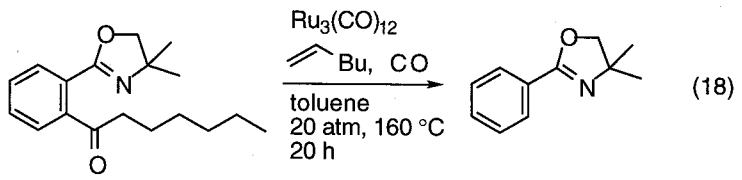


B thermodynamic | **C** | **D** kinetic

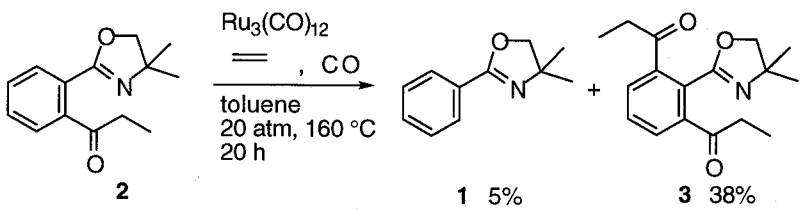


Scheme 2

One of the limitations of the present carbonylation reaction is the applicability of a narrow range of olefins. As mentioned above, the present reaction involved the reverse pathway. This means that an equilibrium between 2-phenyloxazoline and its carbonylation product (**1** ⇌ **50**) exists. Control experiments provided important information concerning the mechanism of carbonylation. Hexyl ketone **51** under the same conditions as in eq 12 underwent decarbonyltion to give **1** in 82% yield (eq 18). In contrast, for the reaction of **2**, **1** was obtained in only 5% yield, along with the di-carbonylation product, **3** in 38% yield and a 49% of the recovered **2**. Considering the difference in reactivity between 1-hexene and ethylene, it seems reasonable that the reaction is governed by the thermodynamics of the equilibrium system. It should be noted that 1-hexene is 4.6 kcal/mol more stable than ethylene. In addition, 1-hexene is isomerized to internal hexenes under the reaction conditions, thus permitting an equilibrium shift to 2-phenyloxazoline **1**. In contrast, in the case of ethylene, the equilibrium lies preferentially in favor of the ethyl ketone **2**.



(18)



(19)

2.4 Conclusion

I have demonstrated that $Ru_3(CO)_{12}$ catalyzes the coupling of aromatic C-H bonds in phenyloxazolines, CO, and olefins. The series of reactions described here demonstrates that an oxazoline ring can be an effective directing group in the direct carbonylation at a C-H bond. In fact, the presence of an oxazoline ring has a strong influence on site selectivity and reactivity. Carbonylation takes place selectively at the *ortho* C-H bond in the benzene ring. Furthermore, the wide range of compatibility of functional groups would be advantageous for organic synthesis. The H/D labeling experiment showed that the cleavage of a C-H bond is not the rate-determining step. The carbonylation reaction rate followed first-order kinetics as a function of $1/P_{co}$.

2.5 Experimental Section

General Information. Boiling points (bp) refer to air bath temperatures for bulb-to-bulb distillation and are uncorrected. ^{1}H NMR and ^{13}C NMR were recorded on a JEOL JMN-270 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Data are reported as follows: chemical shift in ppm (d), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and c = complex), coupling constant (Hz), integration, and interpretation. Infrared spectra (IR) were obtained on a Hitachi 270-50 spectrometer; absorptions are reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained on a Shimadzu GCMS-QP 5000 with ionization voltages of 70 eV. Elemental analyses were performed by Elemental Analysis Section of Osaka University. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303. Analytical GC was carried out on a Shimadzu GC-14B gas chromatography, equipped with a flame ionization detector. Column chromatography was performed with SiO_2 (Wakogel or Merk SilicaGel 60 (230-400mesh)).

Materials. Toluene was distilled over CaH_2. $Ru_3(CO)_{12}$ was purchased from Aldrich Chemical Co. and used after recrystallization from hexane. 4,5-dihydro-4,4-dimethyl-2-phenyl-2-oxazoline (**1**) were purchased from Aldrich Chemical Co. Substituted 2-aryloxazolines (**4a-4g**, **6a-6h**, **8**, **9**, **12**, **15**, **21a-21d**, **24**, **26**, **29**, **31**, **32**, **33**), 2-phenyloxazines (**38**) and phenylthiazoline (**42**) were obtained by corresponding substituted benzoyl chlorides and aminoalcohols or thioalcohol according to Meyers procedure.[4] 2-Phenyloxazole (**40**) was obtained

from dehydrogenation of 4,5-dihydro-2-phenyloxazoline by using of DDQ. 2-Phenyl-5-oxazolone (**44**) was synthesized from benzoyl chloride and oxamic acid, followed by acid-mediated cyclization. All substrates were used after distillation or recrystallization.

General Procedures for Carbonylation. In a 50-mL stainless autoclave were placed $Ru_3(CO)_{12}$ (32 mg, 0.05 mmol), 4,5-dihydro-4,4-dimethyl-2-(2-methylphenyl)oxazoline (**4a**) (2 mmol), and toluene (6 mL). The autoclave was charged with ethylene to 7 atm and carbon monoxide to 20 atm at 25 °C, and then heated in an oil bath at 160 °C for 20 h. The autoclave was cooled and depressured. The solvent was removed in vacuo, and the resulting residue was subjected to column chromatography on silica-gel with hexane/EtOAc as eluant to give 1-[2-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)-3-methylphenyl]-1-propanone (**5a**) as yellow oil. An analytical sample was obtained by bulb-to-bulb distillation.

Kinetic Study. The kinetics were monitored by the area of integration of GC. The condition of the GC analysis used are as follows. Shimadzu GC-14B which equipped with capillary column CBP-10 (25 m X 0.2 mm). Typical initial CO pressure were in the range of 5 atm - 30 atm. The data, which was obtained under 15-30 atm of CO, could convincingly fit (R>0.97) by least squares.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-propanone (2). Yellow oil; Bp 95 °C (4 mmHg); R_f = 0.29 (hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$) δ 1.20 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.36 (s, 6H, $C(CH_3)_2$), 2.78 (q, J = 7.3 Hz, 2H, $CH_2C(O)$), 4.07 (s, 2H, OCH_2), 7.30-7.33 (m, 1H, 3-H or 6-H), 7.42-7.52 (c, 2H, 4,5-H), 7.82-7.85 (m, 1H, 3-H or 6-H); ^{13}C NMR ($CDCl_3$) δ 8.27 ($CH_3CH_2C(O)$), 28.00 ($C(CH_3)_2$), 36.23 ($CH_2C(O)$), 67.98 ($C(CH_3)_2$), 79.34 (OCH_2), 125.25 (1-C or 2-C), 126.15 (3-C or 6-C), 129.20 (3-C or 6-C), 129.38 (4-C or 5-C), 130.67 (4-C or 5-C), 142.32 (1-C or 2-C), 161.01 (C=N), 206.49 (CO); IR (neat) 3072 w, 2974 m, 2896 w, 2756 w, 2574 w, 2402 w, 2338 w, 2018 w, 1704 s, 1651 s, 1596 w, 1575 w, 1462 m, 1409 w, 1351 s, 1310 m, 1214 m, 1186 w, 1124 w, 1082 w, 1052 m, 1033 m, 962 m, 869 w, 799 w, 773 w, 741 w; MS, *m/z* (rel intensity) 231 (M^+, 0), 216 (M^+-CH_3, 20), 203 (12), 202 (96), 198 (14), 186 (23), 160 (39), 148 (46), 144 (12), 131 (10), 130 (100), 115 (13), 104 (13), 103 (15),

102 (29), 77 (17), 76 (27), 75 (10), 57 (10), 55 (54), 51 (15), 50 (17). Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.60; H, 7.44; N, 6.12.

1,1'-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-1,3-phenylene]-bis-1-propanone (3). Orange solid; Mp 75-78 °C (4 mmHg); R_f = 0.09 (hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, *J* = 7.3 Hz, 6H, $CH_3CH_2C(O)$), 1.34 (s, 6H, $C(CH_3)_2$), 2.86 (q, *J* = 7.3 Hz, 4H, $CH_2C(O)$), 4.07 (s, 2H, OCH_2), 7.52-7.58 (c, 3H, 4, 5, 6-H); ^{13}CNMR ($CDCl_3$) δ 8.02 ($CH_3CH_2C(O)$), 27.46 ($C(CH_3)_2$), 35.29 ($CH_2C(O)$), 68.25 ($C(CH_3)_2$), 79.91 (OCH_2), 124.98 (2-C), 128.27 (4-C, 6-C), 129.88 (5-C), 141.98 (1-C, 3-C), 160.52 (C=N), 204.04 (CO); IR (KBr) 2974 m, 2938 m, 1702 s, 1659 s, 1576 w, 1461 m, 1413 w, 1354 m, 1297 m, 1250 w, 1232 w, 1211 w, 1171 m, 1115 m, 1082 w, 1061 w, 1039 m, 953 m, 920 w, 869 w, 803 w, 786 w, 765 w, 707 w; MS, *m/z* (rel intensity) 287 (M^+, 0), 272 (M^+-CH_3, 25), 258 (M^+-CH_2CH_3, 54), 242 (13), 186 (32), 143 (14), 130 (10), 115 (16), 103 (13), 102 (10), 77 (13), 76 (16), 75 (24), 57 (100), 56 (13), 55 (88), 53 (10), 51 (11), 50 (11). Anal. Calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.88. Found: C, 70.99; H, 7.41; N, 4.83.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3-methylphenyl]-1-propanone (5a). Yellow oil; Bp 150-155 °C (4 mmHg); R_f = 0.20 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.17 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.40 (s, 6H, $C(CH_3)_2$), 2.42 (s, 3H, CH_3), 2.89 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.12 (s, 2H, OCH_2), 7.33-7.35 (c, 2H), 7.45-7.49 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 8.20 ($CH_3CH_2C(O)$), 19.37 (CH_3), 27.93 ($C(CH_3)_2$), 34.14 ($CH_2C(O)$), 67.93 ($C(CH_3)_2$), 79.32 (OCH_2), 124.94 (4-C or 5-C or 6-C), 127.71 (1-C or 2-C or 3-C), 129.25 (4-C or 5-C or 6-C), 132.94 (4-C or 5-C or 6-C), 138.45 (1-C or 2-C or 3-C), 139.78 (1-C or 2-C or 3-C), 161.78 (C=N), 203.22 (CO); IR (neat) 3130 w, 2972 s, 2934 s, 2750 w, 2700 w, 2654 w, 2492 w, 2438 w, 2314 w, 2238 w, 2084 w, 1957 w, 1700 s, 1667 s, 1590 m, 1544 w, 1460 s, 1380 m, 1346 s, 1294 s, 1243 s, 1209 m, 1171 m, 1103 m, 1042 s, 962 s, 918 m, 867 w, 845 w, 777 s, 705 w; MS, *m/z* (rel intensity) 245 (M^+, 1), 230 (M^+-CH_3, 11), 217(12), 216 (M^+-CH_2CH_3, 91), 212 (11), 200 (20), 174 (36), 162 (47), 158 (15), 145 (12), 144 (100), 117 (13), 116 (29), 115 (13), 91 (16), 90 (18), 89 (42), 77 (11), 65 (13), 63 (19), 57 (19), 55 (74), 51 (12). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.54; H, 7.86; N, 5.74.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3-(trifluoromethyl)phenyl]-1-propanone (5b). Yellow oil; Bp 120-125 °C (4 mmHg); R_f = 0.23 (hexane/EtOAc = 3/1); ^{1}H

NMR ($CDCl_3$) δ 1.18 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.36 (s, 3H, $C(CH_3)_2$), 2.92 (q, J = 7.3 Hz, 2H, $CH_2C(O)$), 4.16 (s, 2H, OCH_2), 7.62 (t, J = 7.9 Hz, 1H, 5-H), 7.77 (d, J = 7.3 Hz, 1H, 4-H or 6-H), 7.82 (d, J = 7.9 Hz, 1H, 4-H or 6-H); ^{13}C NMR ($CDCl_3$) δ 7.77 ($CH_3CH_2C(O)$), 27.28 ($C(CH_3)_2$), 34.76 ($CH_2C(O)$), 68.12 ($C(CH_3)_2$), 80.02 (OCH_2), 123.10 (q, J = 274.7 Hz, CF_3), 126.63 (2-C), 128.23 (q, J = 4.9 Hz, 4-C), 129.85 (5-C), 130.06 (6-C), 130.35 (q, J = 31.8 Hz, 3-C), 141.69 (1-C), 159.23 (C=N), 202.28 (CO); IR (neat) 3084 w, 2976 s, 2938 s, 2900 m, 2712 w, 2614 w, 2546 w, 2384 w, 2230 w, 1919 w, 1824 w, 1706 s, 1667 s, 1587 s,1508 m, 1462 s, 1410 m, 1381 m, 1351 s, 1312 s, 1243 s, 1134 s, 1079 s, 1046 s, 959 s, 921 m, 869 m, 793 s, 758 s, 714 m; MS, *m/z* (rel intensity) 299 (M^+, 0), 284 (M^+-CH_3, 29), 271 (14), 270 (M^+-CH_2CH_3, 87), 264 (27), 254 (66), 250 (15), 228 (16), 216 (11), 213 (13), 210 (11), 198 (26), 196 (28), 170 (17), 151 (13), 125 (13), 75 (16), 70 (14), 57 (35), 56 (16), 55 (100), 53 (11). Anal. Calcd for $C_{15}H_{16}NO_2F_3$: C, 60.20; H, 5.39; N, 4.68. Found: C, 60.04; H, 5.51; N, 4.70.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3-methoxyphenyl]-1-propanone (5c). Yellow oil; Bp 130 °C (4 mmHg); R_f = 0.21 (hexane/EtOAc = 1/1); ^1H NMR ($CDCl_3$) δ 1.17 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.38 (s, 6H, $C(CH_3)_2$), 2.89 (q, J = 7.3 Hz, 2H, $CH_2C(O)$), 3.85 (s, 3H, OCH_3), 4.13 (s, 2H, OCH_2), 7.05 (d, J = 8.6 Hz, 1H, 4-H or 6-H), 7.23 (d, J = 7.9 Hz, 1H, 4-H or 6-H), 7.43 (t, J = 8.0 Hz, 1H, 5-H); ^{13}C NMR ($CDCl_3$) δ 8.07 ($CH_3CH_2C(O)$), 27.80 ($C(CH_3)_2$), 34.25 ($CH_2C(O)$), 56.34 (OCH_3), 67.71 ($C(CH_3)_2$), 79.34 (OCH_2), 114.00 (4-C or 5-C or 6-C), 117.61 (1-C or 2-C or 3-C), 119.52 (4-C or 5-C or 6-C), 130.80 (4-C or 5-C or 6-C), 140.83 (1-C or 2-C or 3-C), 158.36, 159.86, 202.55 (CO); IR (neat) 3252 w, 2972 s, 2942 m, 2894 w, 2736 w, 2574 w, 2312 w, 2224 w, 1947 w, 1698 s, 1671 s, 1582 m, 1461 s, 1440 m, 1411 w, 1350 s, 1270 s, 1235 m, 1209 m, 1184 m, 1100 w, 1041 s, 1016 m, 964 m, 918 w, 870 w, 841 w, 784 m, 748 m; MS, *m/z* (rel intensity) 261 (M^+, 0), 246 (M^+-CH_3, 24), 233 (15), 232 (M^+-CH_2CH_3, 100), 216 (24), 190 (22), 178 (39), 175 (12), 161 (12), 160 (86), 132 (11), 117 (21), 108 (11), 104 (10), 103 (12), 102 (11), 91 (17), 90 (12), 89 (13), 77 (32), 76 (24), 75 (11), 65 (10), 63 (20), 62 (12), 57 (55), 56 (13), 55 (99), 53 (11), 51 (16), 50 (14). Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.68; H, 7.38; N, 5.47.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3-fluorophenyl]-1-propanone (5d). Yellow oil; Bp 120 °C (4 mmHg); R_f = 0.37 (hexane/EtOAc = 1/1); ^1H NMR ($CDCl_3$) δ 1.19 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.40 (s, 6H, $C(CH_3)_2$), 2.88 (q, J = 7.3 Hz, 2H, $CH_2C(O)$),

4.13 (s, 2H, OCH_2), 7.23 (d, J = 9.2 Hz, 1H, 4-H), 7.39 (d, J = 7.9 Hz 1H, 6-H), 7.44-7.52 (m, 1H, 5-H); ^{13}C NMR ($CDCl_3$) δ 7.98 ($CH_3CH_2C(O)$), 27.80 ($C(CH_3)_2$), 34.54 ($CH_2C(O)$), 68,11 ($C(CH_3)_2$), 79.44 (OCH_2), 116.15 (d, J = 15.9 Hz, 2-C), 118.47 (d, J = 21.9 Hz, 4-C), 122.92 (d, J = 3.7 Hz, 6-C), 131.53 (d, J = 8.6 Hz, 5-C), 141.83 (1-C), 157.45 (C=N), 160.74 (d, J = 253.9 Hz, 3-C), 202.03 (CO); IR (neat) 3058 w, 2976 m, 2940 m, 2890 m, 2640 w, 2334 w, 2260 w, 2070 w, 1956 w, 1906 w, 1700 s, 1673 s, 1609 m, 1576 m, 1523 w, 1463 s, 1412 w, 1351 s, 1300 s, 1254 s, 1211 w, 1186 m, 1091 m, 1058 m, 1030 m, 961 m, 921 w, 859 m, 788 m, 755 w; MS, *m/z* (rel intensity) 249 (M^+, 0), 234 (M^+-CH_3, 27), 221 (10), 220 (M^+-CH_2CH_3, 82), 216 (12), 204 (34), 178 (30), 166 (40), 164 (13), 163 (21), 160 (10), 148 (61), 135 (10), 133 (12), 122 (12), 121 (13), 120 (22), 101 (13), 95 (14), 94 (22), 75 (15), 70 (12), 57 (32), 56 (16), 55 (100), 53 (10), 50 (11). Anal. Calcd for $C_{14}H_{16}NO_2F$: C, 67.46; H, 6.47; N, 5.62. Found: C, 67.44; H, 6.54; N, 5.82.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3-(phenyl)phenyl]-1-propanone (5e). Yellow oil; Bp 150 °C (1 mmHg); R_f = 0.09 (hexane/EtOAc = 3/1); ^1H NMR ($CDCl_3$) δ 1.14 (s, 6H, $C(CH_3)_2$), 1.20 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.96 (q, J = 7.3 Hz, 2H, $CH_2C(O)$), 3.85 (s, 2H, OCH_2), 7.35-7.39 (c, 5H), 7.47-7.55 (c, 2H), 7.63 (dd, J = 6.9, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.11 ($CH_3CH_2C(O)$), 27.32 ($C(CH_3)_2$), 34.38 ($CH_2C(O)$), 67.60 ($C(CH_3)_2$), 79.39 (OCH_2), 126.16, 127.21, 127.46, 127.82, 128.75, 129.31, 132.44, 139.78, 139.93, 143.06, 161.37 (C=N), 203.04 (CO); IR (neat) 2974 s, 2936 m, 2894 w, 1699 s, 1667 s, 1584 w, 1500 w, 1462 s, 1438 m, 1411 w, 1379 m, 1364 m, 1349 s, 1295 s, 1272 m, 1232 m, 1210 m, 1179 m, 1124 m, 1100 m, 1042 s, 986 m, 964 s, 920 m, 870 w, 794 m, 761 s, 700 s, 633 w, 613 w, 533 w; MS, *m/z* (rel intensity) 307 (M^+, 18), 306 (100), 292 (M^+-CH_3, 13), 278 (M^+-CH_2CH_3, 42), 236 (15), 234 (17), 207 (10), 206 (56), 179 (10), 178 (31), 177 (20), 165 (20), 164 (11), 152 (31), 151 (40), 150 (13), 77 (14), 76 (15), 57 (31), 55 (57), 51 (11). Anal. Calcd for $C_{20}H_{21}NO_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 77.85; H, 7.00; N, 4.60.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3-(trimethylsilyl)phenyl]-1-propanone (5f). Colorless oil; Bp 120 °C (1 mmHg); R_f = 0.40 (hexane/EtOAc = 3/1); ^1H NMR ($CDCl_3$) δ 0.32 (s, 9H, $Si(CH_3)_3$), 1.17 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.38 (s, 6H, $C(CH_3)_2$), 2.89 (q, J = 7.3 Hz, 2H, $CH_2C(O)$), 4.11 (s, 2H, OCH_2), 7.39-7.47 (c, 2H), 7.66 (dd, J = 6.8, 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.15 ($Si(CH_3)_3$), 8.07 ($CH_3CH_2C(O)$), 27.94 ($C(CH_3)_2$), 35.22

($CH_2C(O)$), 68.12 ($C(CH_3)_2$), 79.41 (OCH_2), 126.94 (4-C or 5-C or 6-C), 128.61 (4-C or 5-C or 6-C), 132.49 (1-C or 2-C or 3-C), 136.44 (4-C or 5-C or 6-C), 140.88 (1-C or 2-C or 3-C), 141.58 (1-C or 2-C or 3-C), 162.61 (C=N), 205.28 (CO); IR (neat) 2974 s, 2904 m, 1707 s, 1656 s, 1569 w, 1461 w, 1410 w, 1376 m, 1365 m, 1352 m, 1296 s, 1273 w, 1249 s, 1212 w, 1187 w, 1173 w, 1156 w, 1099 m, 1082 m, 1062 m, 1041 m, 1026 m, 985 w, 971 m, 960 m, 920 w, 871 m, 839 s, 793 w, 782 w, 771 m, 753 m, 717 w; MS, *m/z* (rel intensity) 303 (M^+, 0), 288 (M^+-CH_3, 28), 275 (22), 274 (M^+-CH_2CH_3, 100), 272 (12), 259 (10), 258 (50), 218 (10), 217 (10), 216 (42), 204 (16), 202 (25), 145 (12), 133 (27), 130 (21), 119 (11), 115 (14), 108 (12), 93 (18), 91 (10), 83 (10), 75 (40), 73 (50), 70 (12), 59 (21), 57 (16), 55 (51), 53 (14). Anal. Calcd for $C_{17}H_{25}NO_2Si$: C, 67.28; H, 8.30; N, 4.62. Found: C, 67.20; H, 8.30; N, 4.65.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3-[(trimethylsilyl)methyl]phenyl]-1-propanone (5g). Yellow oil; Bp 140 °C (1 mmHg); R_f = 0.49 (hexane/EtOAc = 5/1); ^1H NMR ($CDCl_3$) δ -0.01 (s, 9H, $Si(CH_3)_3$), 1.16 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.39 (s, 6H, $C(CH_3)_2$), 2.39 (s, 2H, $CH_2Si(CH_3)_3$), 2.86 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.06 (s, 2H, OCH_2), 7.18 (m, 1H), 7.29-7.31 (c, 2H); ^{13}C NMR ($CDCl_3$) δ -1.45 ($Si(CH_3)_3$), 8.18 ($CH_3CH_2C(O)$), 23.90 ($CH_2Si(CH_3)_3$), 27.98 ($C(CH_3)_2$), 34.27 ($CH_2C(O)$), 67.94 ($C(CH_3)_2$), 78.92 (OCH_2), 123.15 (4-C or 5-C or 6-C), 125.54 (1-C or 2-C or 3-C), 128.82 (4-C or 5-C or 6-C), 131.61 (4-C or 5-C or 6-C), 140.63 (1-C or 2-C or 3-C), 141.78 (1-C or 2-C or 3-C), 161.74 (C=N), 203.81 (CO); IR (neat) 3062 w, 2968 s, 2898 m, 1704 s, 1666 s, 1586 m, 1462 s, 1418 s, 1347 s, 1296 s, 1247 s, 1210 m, 1159 s, 1082 m, 1048 s, 964 s, 920 m, 858 s, 793 m, 762 m; MS, *m/z* (rel intensity) 317 (M^+, 5), 302 (M^+-CH_3, 16), 260 (21), 230 (12), 75 (16), 74 (10), 73 (100), 59 (10), 55 (19). Anal. Calcd for $C_{18}H_{27}NO_2Si$: C, 68.09; H, 8.57; N, 4.41. Found: C, 68.05; H, 8.66; N, 4.47.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-4-methylphenyl]-1-propanone (7a). Orange solid; Mp 160 °C (4 mmHg); R_f = 0.29 (hexane/EtOAc = 5/2); ^1H NMR ($CDCl_3$) δ 1.18 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.36 (s, 6H, $C(CH_3)_2$), 2.39 (s, 3H, CH_3), 2.76 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.06 (s, 2H, OCH_2), 7.27 (s, 2H), 7.64 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 8.43 ($CH_3CH_2C(O)$), 21.03 (CH_3), 28.07 ($C(CH_3)_2$), 35.94 ($CH_2C(O)$), 67.93 ($C(CH_3)_2$), 79.50 (OCH_2), 125.73 (1-C or 2-C or 4-C), 126.65 (3-C or 5-C or 6-C), 130.05 (3-C or 5-C or 6-C), 131.25 (3-C or 5-C or 6-C), 139.19 (1-C or 2-C or 4-C), 140.07 (1-C or 2-C or 4-C), 161.71

(C=N), 206.00 (CO); IR (KBr) 3374 w, 2976 s, 2938 m, 2270 w, 1693 s, 1645 s, 1605 s, 1570 w, 1498 w, 1461 m, 1410 m, 1386 w, 1356 s, 1312 s, 1282 m, 1251 w, 1220 s, 1189 s, 1138 w, 1080 m, 1050 s, 1022 m, 967 s, 949 m, 935 w, 896 w, 826 w, 809 m, 796 m, 764 w, 729 w; MS, *m/z* (rel intensity) 245 (M^+, 0), 230 (M^+-CH_3, 19), 217 (15), 216 (M^+-CH_2CH_3, 100), 212 (15), 200 (17), 174 (35), 162 (46), 145 (13), 144 (100), 118 (10), 117 (13), 116 (30), 115 (14), 91 (19), 90 (20), 89 (45), 77 (12), 65 (15), 63 (21), 57 (15), 55 (69), 53 (10), 51 (14). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.50; H, 7.88; N, 5.75.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-4-(trifluoromethyl)phenyl]-1-propanone (7b). White solid; Mp 125-130 °C (4 mmHg); R_f = 0.54 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.22 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.36 (s, 6H, $C(CH_3)_2$), 2.77 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.10 (s, 2H, OCH_2), 7.39 (d, *J* = 7.9 Hz, 1H, 6-H), 7.75 (d, *J* = 7.9 Hz, 1H, 5-H), 8.14 (s, 1H, 3-H); ^{13}C NMR ($CDCl_3$) δ 8.11 ($CH_3CH_2C(O)$), 28.02 ($C(CH_3)_2$), 36.57 ($CH_2C(O)$), 68.47 ($C(CH_3)_2$), 79.61 (OCH_2), 123.29 (q, *J* = 272.6 Hz, CF_3), 125.88, 126.30 (q, *J* = 3.7 Hz, 3-C), 126.65 (6-C), 127.54 (q, *J* = 3.6 Hz, 5-C), 131.49 (q, *J* = 33.4 Hz, 4-C), 145.82, 159.59 (C=N), 205.73 (CO); IR (KBr) 3294 w, 2974 w, 2278 w, 1694 s, 1656 m, 1463 w, 1416 m, 1387 w, 1362 m, 1337 s, 1304 w, 1283 w, 1267 w, 1213 m, 1165 s, 1127 s, 1079 s, 1054 m, 1019 w, 966 m, 911 w, 888 w, 839 m, 801 w, 763 w, 736 w; MS, *m/z* (rel intensity) 299 (M^+, 0), 284 (M^+-CH_3, 13), 270 (M^+-CH_2CH_3, 49), 254 (14), 228 (18), 216 (18), 198 (27), 170 (13), 75 (12), 57 (17), 56 (14), 55 (100). Anal. Calcd for $C_{15}H_{16}NO_2F_3$: C, 60.20; H, 5.39; N, 4.68. Found: C, 60.06; H, 5.38; N, 4.78.

1-[4-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-propanone (7c). Yellow oil; Bp 180 °C (4 mmHg); R_f = 0.11 (hexane/EtOAc = 10/1); ^{1}H NMR ($CDCl_3$) δ 0.22 (s, 6H, $Si(CH_3)_2C(CH_3)_3$), 0.98 (s, 9H, $Si(CH_3)_2C(CH_3)_3$), 1.18 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.36 (s, 6H, $C(CH_3)_2$), 2.77 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.07 (s, 3H, OCH_3), 6.90 (dd, *J* = 8.4, 2.5 Hz, 1H, 5-H), 7.20 (d, *J* = 2.3 Hz, 1H, 3-H), 7.33 (d, *J* = 8.3 Hz, 1H, 3-H); ^{13}C NMR ($CDCl_3$) δ -4.44 ($Si(CH_3)_2C(CH_3)_3$), 8.59 ($CH_3CH_2C(O)$), 18.12 ($Si(CH_3)_2C(CH_3)_3$), 25.54 ($Si(CH_3)_2C(CH_3)_3$), 28.05 ($C(CH_3)_2$), 35.56 ($CH_2C(O)$), 68.07 ($C(CH_3)_2$), 79.53 (OCH_2), 121.22 (3-C), 121.51 (5-C), 128.27, 128.75 (6-C), 134.65, 157.16, 161.49, 204.87 (CO); IR (neat) 2960 s, 2936 s, 2894 m, 2862 m, 2750 w, 2334 w, 2162 w, 1698 s, 1654 s, 1600 s, 1562 m, 1499 m, 1465 m, 1423 m, 1392 w, 1349 s, 1313 s, 1278

s, 1236 s, 1199 s, 1127 w, 1082 w, 1044 m, 980 s, 949 m, 917 m, 867 s, 838 s, 781 s; MS, *m/z* (rel intensity) 361 (M^+, 0), 346 (M^+-CH_3, 14), 333 (18), 332 (M^+-CH_2CH_3, 78), 278 (12), 260 (20), 232 (36), 75 (26), 74 (11), 73 (100), 59 (23), 57 (62), 56 (10), 55 (62). Anal. Calcd for $C_{20}H_{31}NO_3Si$: C, 66.44; H, 8.64; N, 3.87. Found: C, 66.69; H, 8.72; N, 3.94.

1-[4-Chloro-2-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-propanone (7d). Yellow oil; Bp 90 °C (4 mmHg); R_f = 0.66 (hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$) δ 1.19 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.35 (s, 6H, $C(CH_3)_2$), 2.75 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.08 (s, 2H, OCH_2), 7.26 (d, *J* = 7.6 Hz, 1H, 6-H), 7.45 (dd, *J* = 8.3, 2.0 Hz, 1H, 5-H), 7.83 (d, *J* = 2.3 Hz, 1H, 3-H); ^{13}C NMR ($CDCl_3$) δ 8.32 ($CH_3CH_2C(O)$), 28.07 ($C(CH_3)_2$), 36.34 ($CH_2C(O)$), 68.30 ($C(CH_3)_2$), 79.64 (OCH_2), 127.19 (1-C or 2-C or 4-C), 127.78 (6-C), 129.40 (3-C), 130.75 (5-C), 135.62 (1-C or 2-C or 4-C), 140.56 (1-C or 2-C or 4-C), 160.05 (C=N), 205.44 (CO); IR (neat) 3076 w, 2974 s, 2936 m, 2900 m, 2292 w, 1705 s, 1653 s, 1589 s, 1563 m, 1487 m, 1463 m, 1409 m, 1349 s, 1306 s, 1272 m, 1212 s, 1134 w, 1097 s, 1050 s, 1014 m, 964 s, 885 m, 827 m, 799 m, 783 m, 754 w; MS, *m/z* (rel intensity) 265 (M^+, 0), 252 (13), 250 (M^+-CH_3, 11), 238 (29), 237 (15), 236 (M^+-CH_2CH_3, 89), 232 (14), 220 (18), 194 (41), 184 (14), 182 (48), 179 (10), 166 (27), 165 (10), 164 (77), 138 (15), 137 (13), 136 (19), 115 (12), 111 (12), 110 (15), 102 (16), 100 (10), 75 (28), 57 (18), 56 (13), 55 (100), 53 (11), 51 (10), 50 (12). Anal. Calcd for $C_{14}H_{16}NO_2Cl$: C, 63.28; H, 6.07; N, 5.27. Found: C, 63.32; H, 6.05; N, 5.41.

1,1'-[4-Chloro-2-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)-1,3-phenylene]-bis-1-propanone (8d). Orange oil; R_f = 0.63 (hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.21 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.31 (s, 6H, $C(CH_3)_2$), 2.81 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 2.94 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.00 (s, 2H, OCH_2), 7.42 (d,*J* = 8.1 Hz, 1H), 7.50 (d, *J* = 7.3 Hz, 2H).

1-[4-Bromo-2-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-propanone (7e). Yellow oil; Bp 105 °C (4 mmHg); R_f = 0.11 (hexane/EtOAc = 15/1); ^{1}H NMR ($CDCl_3$) δ 1.19 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.35 (s, 6H, $C(CH_3)_2$), 2.75 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.08 (s, 2H, OCH_2), 7.19 (d, *J* = 8.3 Hz, 1H, 6-H), 7.62 (dd, *J* = 7.9, 2.0 Hz, 1H, 5-H), 8.00 (d, *J* = 1.7 Hz, 1H, 3-H); ^{13}C NMR ($CDCl_3$) δ 8.30 ($CH_3CH_2C(O)$), 28.07 ($C(CH_3)_2$), 36.34 ($CH_2C(O)$), 68.30 ($C(CH_3)_2$), 79.64 (OCH_2), 123.61 (1-C or 2-C or 4-C), 127.26 (1-C or 2-C or 4-C), 127.87 (6-C), 132.26 (3-C), 133.73 (5-C), 141.04 (1-C or 2-C or 4-C), 159.91 (C=N), 205.52

(CO); IR (neat) 3068 w, 2972 s, 2938 m, 2896 m, 2572 w, 2252 w, 1704 s, 1652 s, 1584 s, 1559 m, 1486 w, 1462 m, 1407 m, 1349 s, 1303 s, 1271 m, 1211 s, 1136 w, 1083 s, 1049 s, 1013 m, 962 s, 893 w, 878 w, 825 m, 798 w, 773 w, 751 w; MS, *m/z* (rel intensity) 310 (M^+, 0), 296 (11), 294 (M^+-CH_3, 11), 282 (64), 281 (12), 280 (M^+-CH_2CH_3, 68), 266 (10), 264 (10), 240 (21), 238 (25), 228 (24), 226 (30), 210 (42), 208 (42), 182 (12), 141 (14), 115 (11), 102 (20), 101 (12), 100 (13), 75 (33), 74 (12), 57 (18), 56 (11), 55 (100), 51 (10). Anal. Calcd for $C_{14}H_{16}NO_2Br$: C, 54.21; H, 5.20; N, 4.52. Found: C, 54.33; H, 5.26; N, 4.58.

1-[4-Cyano-2-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-propanone (7f). Yellow oil; Bp 120 °C (4 mmHg); R_f = 0.54 (hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$) δ 1.22 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.35 (s, 6H, $C(CH_3)_2$), 2.76 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.10 (s, 6H, OCH_2), 7.37 (d, *J* = 7.9 Hz, 1H, 6-H), 7.77 (dd, *J* = 7.8, 1.5 Hz, 1H, 5-H), 8.17 (d, *J* = 1.0 Hz, 1H, 3-H); ^{13}C NMR ($CDCl_3$) δ 8.02 ($CH_3CH_2C(O)$), 27.98 ($C(CH_3)_2$), 36.53 ($CH_2C(O)$), 68.52 ($C(CH_3)_2$), 79.64 (OCH_2), 113.33, 117.31, 126.16, 126.85 (6-C), 132.79 (3-C), 134.07 (5-C), 146.36, 158.83 (C=N), 205.23 (CO); IR (neat) 3078 w, 2974 s, 2940 m, 2902 m, 2334 w, 2232 m, 1704 s, 1657 s, 1603 m, 1557 w, 1462 m, 1403 m, 1352 s, 1314 s, 1275 m, 1247 m, 1210 s, 1188 s, 1084 m, 1052 s, 1014 m, 969 s, 951 m, 931 m, 907 m, 841 m, 802 m, 760 w; MS, *m/z* (rel intensity) 256 (M^+, 0), 241 (M^+-CH_3, 26), 228 (11), 227 (M^+-CH_2CH_3, 80), 223 (13), 211 (29), 185 (49), 173 (47), 170 (11), 155 (52), 140 (11), 129 (12), 128 (14), 127 (21), 101 (19), 75 (10), 57 (15), 56 (12), 55 (100), 50 (15). Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.93. Found: C, 70.33; H, 6.36; N, 11.02.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-4-(dimethylamino)phenyl]-1-propanone (7g). Orange oil; Bp 105 °C (4 mmHg); R_f = 0.06 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.17 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.42 (s, 6H, $C(CH_3)_2$), 2.81 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 3.04 (s, 6H, $N(CH_3)_2$), 4.11 (s, 2H, OCH_2), 6.66 (dd, *J* = 8.9, 2.6 Hz, 1H, 5-H), 6.88 (d, *J* = 2.6 Hz, 1H, 3-H), 7.58 (d, *J* = 8.9 Hz, 1H, 6-H); ^{13}C NMR ($CDCl_3$) δ 8.92 ($CH_3CH_2C(O)$), 28.09 ($C(CH_3)_2$), 33.52 ($CH_2C(O)$), 40.06 ($N(CH_3)_2$), 67.71 ($C(CH_3)_2$), 79.68 (OCH_2), 111.81 (5-C), 112.97 (3-C), 126.38 (1-C or 2-C or 4-C), 129.97 (1-C or 2-C or 4-C), 130.31 (6-C), 151.73 (1-C or 2-C or 4-C), 163.97 (C=N), 201.44 (CO); IR (KBr) 2974 m, 2900 m, 2818 w, 2324 w, 2032 w, 1688 s, 1645 m, 1603 s, 1516 m, 1490 w, 1450 m, 1404 w, 1370 s, 1290 m, 1275 m, 1234 s, 1211 m, 1167 m, 1085 m, 1060 m, 1044 m, 1017 w, 980 m, 947 m, 923 w, 885 w, 857 w,

826 m, 796 w, 753 w; MS, *m/z* (rel intensity) 274 (M^+, 9), 259 (M^+-CH_3, 24), 245 (M^+-CH_2CH_3, 41), 203 (18), 191 (31), 174 (13), 173 (100), 115 (12), 114 (10), 77 (11), 55 (29). Anal. Calcd for $C_{16}H_{22}N_2O_2$: C, 70.05; H, 8.08; N, 10.21. Found: C, 69.99; H, 8.09; N, 10.25.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-4-methoxyphenyl]-1-propanone (10). Yellow solid; Mp 70-72 °C (4 mmHg); R_f = 0.09 (hexane/EtOAc = 4/1); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.39 (s, 6H, $C(CH_3)_2$), 2.78 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 3.87 (s, 3H, OCH_3), 4.09 (s, 2H, OCH_2), 6.98 (dd, *J* = 8.6, 2.6 Hz, 1H, 5-H), 7.26 (d, *J* = 2.6 Hz, 1H, 3-H), 7.42 (d, *J* = 8.3 Hz, 1H, 6-H); ^{13}C NMR ($CDCl_3$) δ 8.57 ($CH_3CH_2C(O)$), 28.03 ($C(CH_3)_2$), 35.33 ($CH_2C(O)$), 55.55 (OCH_3), 68.02 ($C(CH_3)_2$), 79.61 (OCH_2), 114.39 (3-C), 116.30 (5-C), 128.46 (1-C or 2-C or 4-C), 128.99 (6-C), 133.75 (1-C or 2-C or 4-C), 160.74, 161.87, 204.31 (CO); IR (KBr) 3078 w, 2972 s, 2902 m, 2848 w, 1939 w, 1764 w, 1694 s, 1650 s, 1603 s, 1568 m, 1498 m, 1466 m, 1452 s, 1421 w, 1400 w, 1374 w, 1354 s, 1296 s, 1230 s, 1199 s, 1172 s, 1146 m, 1085 w, 1040 s, 966 m, 928 m, 881 m, 840 m, 809 w, 795 w, 756 w, 705 w; MS, *m/z* (rel intensity) 261 (M^+, 0), 246 (M^+-CH_3, 12), 233(11), 232 (M^+-CH_2CH_3, 77), 190(29), 178 (41), 161 (12), 160 (99),117 (14), 108 (11), 102 (11), 77 (27), 63 (32), 57 (18), 56 (11), 55 (100), 53 (13), 51 (11). Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.68; H, 7.22; N, 5.34.

1,1'-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-4-methoxy-1,3-phenylene]-bis-1-propanone (11). Orange oil; Bp 150 °C (4 mmHg); R_f = 0.03 (hexane/EtOAc = 4/1); ^{1}H NMR ($CDCl_3$) δ 1.15 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.17 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.32 (s, 6H, $C(CH_3)_2$), 2.84 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 2.89 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 3.87 (s, 3H, OCH_3), 4.03 (s, 2H, OCH_2), 6.98 (d, *J* = 8.9 Hz, 1H, 5-H or 6-H), 7.65 (d, *J* = 8.9 Hz, 1H, 5-H or 6-H); ^{13}C NMR ($CDCl_3$) δ 7.33 ($CH_3CH_2C(O)$), 8.45 ($CH_3CH_2C(O)$), 27.48 ($C(CH_3)_2$), 34.00 ($CH_2C(O)$), 37.68 ($CH_2C(O)$), 55.99 (OCH_3), 68.11 ($C(CH_3)_2$), 79.77 (OCH_2), 111.54 (5-C or 6-C), 126.85, 130.06 (5-C or 6-C), 132.24, 133.53, 157.66, 160.54, 201.38 (CO), 205.48 (CO); IR (neat) 3264 w, 2976 s, 2942 s, 2304 w, 1707 s, 1667 s, 1579 s, 1461 s, 1411 m, 1346 s, 1301 s, 1236 s, 1189 m, 1173 m, 1138 m, 1115 m, 1035 s, 986 m, 966 m, 930 m, 803 m, 713 w; MS, *m/z* (rel intensity) 317 (M^+, 11), 302 (M^+-CH_3, 17), 289 (15), 288 (M^+-CH_2CH_3, 100), 282 (12), 272 (11), 270 (23), 264 (14), 226 (13), 217 (11), 216 (61), 207 (11), 189 (12), 173 (27), 160 (17), 129 (12), 117 (10), 115 (13), 103 (15), 102 (12), 101 (10), 77 (19), 76 (16), 75 (16), 63

(11), 57 (61), 55 (100), 53 (13). Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30; N, 4.41. Found: C, 67.87; H, 7.33; N, 4.59.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-4,5-dimethoxyphenyl]-1-propanone (13). White solid; Mp 82-85 °C (4 mmHg); R_f = 0.06 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.36 (s, 6H, $C(CH_3)_2$), 2.74 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 3.91 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.05 (s, 2H, OCH_2), 6.83 (s, 1H, 3-H or 6-H), 7.30 (s, 1H, 3-H or 6-H); ^{13}C NMR ($CDCl_3$) δ 8.43 ($CH_3CH_2C(O)$), 27.94 ($C(CH_3)_2$), 36.14 ($CH_2C(O)$), 55.85 (OCH_3), 55.94 (OCH_3), 67.78 ($C(CH_3)_2$), 79.23 (OCH_2), 109.42 (3-C or 6-C), 111.52 (3-C or 6-C), 118.33, 135.42, 149.38, 150.42, 161.02 (C=N), 205.71 (CO); IR (KBr) 2970 s, 2940 m, 1699 s, 1651 s, 1603 s, 1579 m, 1530 s, 1466 s, 1401 m, 1387 m, 1367 s, 1295 m, 1268 s, 1223 s, 1197 s, 1157 s, 1087 m, 1022 m, 992 m, 969 m, 938 m, 912 w, 890 w, 870 m, 847 w, 824 w, 802 w, 781 w, 747 w, 722 w; MS, *m/z* (rel intensity) 291 (M^+, 0), 276 (M^+-CH_3, 43), 263 (12), 262 (M^+-CH_2CH_3, 81), 221 (12), 220 (18), 208 (27), 191 (11), 190 (81), 123 (16), 104 (11), 93 (10), 91 (11), 79 (10), 77 (21), 65 (11), 57 (51), 56 (12), 55 (100), 53 (17), 51 (12), 50 (17). Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 65.69; H, 7.22; N, 4.76.

1,1'-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-4,5-dimethoxy-1,3-phenylene]-bis-1-propanone (14). Orange solid; R_f = 0.14 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.17 (t, *J* = 7.3 Hz, 6H, $CH_3CH_2C(O)$), 1.29 (s, 6H, $C(CH_3)_2$), 2.77 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 2.81 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 3.82 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 3.97 (s, 2H, OCH_2), 6.93 (s, 1H, 6-H); ^{13}C NMR ($CDCl_3$) δ 7.46 ($CH_3CH_2C(O)$), 8.29 ($CH_3CH_2C(O)$), 27.64 ($C(CH_3)_2$), 35.62 ($CH_2C(O)$), 37.74 ($CH_2C(O)$), 55.99 (OCH_3), 61.67 (OCH_3), 68.23 ($C(CH_3)_2$), 79.48 (OCH_2), 110.91 (6-C), 115.81, 138.49, 138.54 146.00, 153.69, 159.37, 204.22 (CO), 204.87 (CO); IR (neat) 3402 w, 2976 s, 2942 s, 1711 s, 1662 s, 1586 s, 1465 s, 1410 s, 1352 s, 1315 s, 1294 s, 1247 s, 1217 m, 1194 s, 1154 s, 1116 s, 1074 m, 1057 m, 1022 s, 977 m, 932 m, 865 w, 811 w, 704 w, 661 w, 623 w, 533 w; MS, *m/z* (rel intensity) 347 (M^+, 0), 332 (M^+-CH_3, 18), 319 (18), 318 (M^+-CH_2CH_3, 100), 300 (14), 246 (41), 203 (15), 77 (13), 57 (48), 55 (56). Anal. Calcd for $C_{19}H_{25}NO_5$: C, 65.69; H, 7.25; N, 4.03. Found: C, 65.60; H, 7.19; N, 3.93.

1-[6-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-2,3-methylenedioxyphenyl]-1-propanone (16). and 1-[6-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)-3,4-methylenedioxyphenyl]-1-propanone (17). Spectral data were obtained from a mixture of **16**

and **17**. Colorless oil; Bp 120 °C (1 mmHg); R_f = 0.14 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ [1.17 (t, *J* = 7.3 Hz, **17**), 1.20 (t, *J* = 7.3 Hz, **16**), 3H, $CH_3CH_2C(O)$], [1.32 (s, **16**), 1.36 (s, **17**), 6H, $C(CH_3)_2$], [2.71 (q, *J* = 7.3 Hz, **17**), 2.80 (q, *J* = 7.3 Hz, **16**), 2H, $CH_2C(O)$], 4.01 (s, 2H, OCH_2, **16**), 4.04 (s, 2H, OCH_2, **17**), 6.04 (s, 2H, OCH_2O, **16**, **17**), 6.79 (s, 1H, **17**), 6.82 (d, *J* = 8.3 Hz, 1H, **16**), 7.25 (s, 1H, **17**), 7.39 (d, *J* = 7.9 Hz, 1H, **16**); ^{13}C NMR ($CDCl_3$) δ [7.87 (**17**), 8.52 (**16**), ($CH_3CH_2C(O)$], 28.03 ($C(CH_3)_2$), [36.26 (**16**), 37.29 (**17**), $CH_2C(O)$], 67.81 ($C(CH_3)_2$), [79.21 (**16**), 79.41 (**17**), (OCH_2)], 102.01, 106.96, 108.45, 109.24, 119.28, 123.97, 119.28, 123.97, 144.29, 149.79, 160.52, 202.64 (CO); IR (neat) 3402 w, 2974 s, 2936 s, 2902 s, 2792 w, 1712 s, 1651 s, 1627 s, 1598 m, 1505 m, 1456 s, 1408 m, 1352 s, 1306 s, 1253 s, 1217 s, 1190 s, 1148 w, 1116 m, 1095 m, 1034 s, 992 m, 972 s, 929 s, 908 m, 881 w, 824 m, 796 w, 761 w, 742 w, 709 m, 621 w, 562 w; MS, *m/z* (rel intensity) **16**: 275 (M^+, 1), 260 (M^+ -CH_3, 6), 247 (13), 260 (M^+ - CH_2CH_3, 90), 204 (19), 192 (33), 175 (13), 174 (100), 130 (11), 116 (11), 115 (13), 91 (11), 90 (10), 89 (12), 77 (10), 55 (33). Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.24; H, 6.07; N, 5.17.

1,1'-[6-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3,4-methylenedioxy-1,3-phenylene]-bis-1-propanone (18). Colorless solid; Mp 40 °C (4 mmHg) R_f = 0.03 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.16 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.17 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.31 (s, 6H, $C(CH_3)_2$), 2.79 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 2.89 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.03 (s, 2H, OCH_2), 6.11 (s, 2H, OCH_2O), 7.00 (s, 1H, 6-H); ^{13}C NMR ($CDCl_3$) δ 8.08 ($CH_3CH_2C(O)$), 8.75 ($CH_3CH_2C(O)$), 27.93 ($C(CH_3)_2$), 35.49 ($CH_2C(O)$), 37.59 ($CH_2C(O)$), 68.57 ($C(CH_3)_2$), 80.34 (OCH_2), 103 11 (6-C), 114.02, 120.72, 132.17, 136.84, 149.43, 160.83, 201.28 (CO), 202.95 (CO); IR (neat) 2987 w, 2940 w, 1704 s, 1616 w, 1504 w, 1465 s, 1378 s, 1289 m, 1259 s, 1143 s, 1032 m, 969 m, 812 w, 733 w; MS, *m/z* (rel intensity) 331 (M^+, 4), 316 (M^+-CH_3, 34), 302 (M^+-CH_2CH_3, 100), 284 (13), 260 (12), 244 (11), 231 (15), 230 (48), 187 (16), 174 (19), 147 (10), 115 (10), 91 (10), 89 (16), 77 (14), 72 (12), 63 (14), 57 (62), 56 (12), 55 (71), 53 (15), 51 (10). HRMS calcd for $C_{18}H_{21}NO_5$: 331.1420. Found: 331.1439.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-5-methylphenyl]-1-propanone (22a). Yellow oil; Bp 130 °C (1 mmHg); R_f = 0.31 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.19 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.34 (s, 6H, $C(CH_3)_2$), 2.39 (s, 3H, CH_3), 2.75 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.04 (s, 2H, OCH_2), 7.10 (s, 1H, 6-H), 7.24 (d, *J* = 8.1 Hz, 1H, 3-H or 4-H),

7.73 (d, J = 7.9 Hz, 1H, 3-H or 4-H); ^{13}C NMR ($CDCl_3$) δ 8.39 ($CH_3CH_2C(O)$), 21.33 (CH_3), 28.12 ($C(CH_3)_2$), 36.44 ($CH_2C(O)$), 67.98 ($C(CH_3)_2$), 79.35 (OCH_2), 122.41 (1-C or 2-C or 5-C), 126.81 (6-C), 129.31 (3-C or 4-C), 130.06 (3-C or 4-C), 141.28 (1-C or 2-C or 5-C), 142.55 (1-C or 2-C or 5-C), 161.13 (C=N), 207.08 (CO); IR (neat) 2974 s, 2934 m, 2896 m, 2534 w, 2322 w, 2114 w, 1700 s, 1651 s, 1609 m, 1571 w, 1499 w, 1461 m, 1408 m, 1350 s, 1310 s, 1238 m, 1213 w, 1170 s, 1141 w, 1084 m, 1051 s, 963 m, 920 w, 873 w, 831 m, 798 w, 756 w, 725 w; MS, *m/z* (rel intensity) 245 (M^+, 0), 230 (M^+-CH_3, 30), 217 (16), 216 (M^+-CH_2CH_3, 100), 212 (16), 200 (18), 174 (34), 162 (44), 145 (11), 144 (98), 117 (12), 116 (28), 115 (11), 101 (12), 91 (16), 90 (17), 89 (38), 77 (11), 65 (14), 63 (18), 57 (20), 56 (10), 55 (77), 53 (10), 51 (12). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.28; H, 7.86; N, 5.81.

1,1'-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-5-methyl-1,3-phenylene]-bis-1-propanone (23a). Orange solid; Mp 115-120 ℃ (4 mmHg); R_f = 0.17 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, J = 7.3 Hz, 6H, $CH_3CH_2C(O)$), 1.33 (s, 6H, $C(CH_3)_2$), 2.42 (s, 3H, CH_3), 2.83 (q, J = 7.3 Hz, 4H, $CH_2C(O)$), 4.04 (s, 2H, OCH_2), 7.31 (s, 2H, 4-H, 6-H); ^{13}C NMR ($CDCl_3$) δ 8.07 ($CH_3CH_2C(O)$), 21.28 (CH_3), 27.55 ($C(CH_3)_2$), 35.47 ($CH_2C(O)$), 68.25 ($C(CH_3)_2$), 79.82 (OCH_2), 121.80, 128.70 (4-C, 6-C), 140.47, 142.28, 160.50 (C=N), 204.58 (CO); IR (KBr) 2978 m, 2938 m, 1703 s, 1668 m, 1650 m, 1600 w, 1572 w, 1461 m, 1406 w, 1349 m, 1304 m, 1283 m, 1237 w, 1213 w, 1183 w, 1131 m, 1094 w, 1050 s, 961 m, 919 w, 883 w, 826 w, 800 w; MS, *m/z* (rel intensity) 301 (M^+, 0), 296 (11), 286 (M^+-CH_3, 28), 273 (16), 272 (M^+-CH_2CH_3, 82), 256 (12), 200 (30), 157 (14), 129 (11), 117 (11), 115 (11), 89 (16), 72 (10), 63 (13), 57 (100), 56 (12), 55 (67). Anal. Calcd for $C_{18}H_{23}NO_3$: C, 71.74; H, 7.69; N, 4.65. Found: C, 71.54; H, 7.72; N, 4.62

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-4-(trifluoromethyl)phenyl]-1-propanone (22b). White solid; Mp 75-78 ℃ (4 mmHg); R_f = 0.19 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.22 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.36 (s, 6H, $C(CH_3)_2$), 2.80 (q, J = 7.3 Hz, 2H, $CH_2C(O)$), 4.10 (s, 2H, OCH_2), 7.55 (s, 1H, 6-H), 7.70 (d, J = 8.3 Hz, 1H, 3-H or 4-H), 7.97 (d, J = 8.2 Hz, 1H, 3-H or 4-H); ^{13}C NMR ($CDCl_3$) δ 8.16 ($CH_3CH_2C(O)$), 28.03 ($C(CH_3)_2$), 36.48 ($CH_2C(O)$), 68.48 ($C(CH_3)_2$), 79.64 (OCH_2), 123.21 (q, J = 3.6 Hz, 6-C), 123.28 (q, J = 272.6 Hz, CF_3), 126.10 (q, J = 3.7 Hz, 4-C), 128.57 (1-C or 2-C), 129.88 (3-C), 132.68 (q, J = 33.4 Hz, 5-C), 143.18 (1-C or 2-C), 159.82 (C=N), 205.26 (CO); IR (KBr) 3050 w, 2982 m, 2948 w, 2900 w, 2360 w, 2288 w, 1710 s, 1651 m, 1615 m, 1578 w, 1503

w, 1464 m, 1411 m, 1353 m, 1328 s, 1290 m, 1273 m, 1252 w, 1198 m, 1161 s, 1115 s, 1082 m, 1066 m, 1043 m, 1022 m, 968 m, 918 m, 871 w, 853 m, 823 w, 796 w, 767 w, 734 w; MS, *m/z* (rel intensity) 299 (M^+, 0), 284 (M^+-CH_3, 11), 270 (M^+-CH_2CH_3, 38), 254 (12), 228 (19), 216 (19), 198 (27), 57 (16), 56 (12), 55 (100). Anal. Calcd for $C_{15}H_{16}NO_2F_3$: C, 60.20; H, 5.39; N, 4.68. Found: C, 60.15; H, 5.40; N, 4.71.

1,1'-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-4-trifluoromethyl-1,3-phenylene]-bis-1-propanone (23b). Brown solid; Mp 125-128 °C (4 mmHg); R_f = 0.10 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.21 (t, *J* = 7.3 Hz, 6H, $CH_3CH_2C(O)$), 1.34 (s, 6H, $C(CH_3)_2$), 2.99 (q, *J* = 7.3 Hz, 4H, $CH_2C(O)$), 4.08 (s, 2H, OCH_2), 7.76 (s, 2H, 4-H 6-H); ^{13}C NMR ($CDCl_3$) δ 7.80 ($CH_3CH_2C(O)$), 27.41 ($C(CH_3)_2$), 35.47 ($CH_2C(O)$), 68.66 ($C(CH_3)_2$), 80.15 (OCH_2), 122.83 (q, *J* = 273.0 Hz, CF_3), 124.71 (q, *J* = 3.6 Hz, 4-C 6-C), 128.14 (2-C), 132.15 (q, *J* = 33.4 Hz, 5-C), 143.05 (1-C 3-C), 159.26 (C=N), 202.84 (CO); IR (KBr) 3080 w, 2980 m, 2940 w, 1706 s, 1673 m, 1616 w, 1570 m, 1462 m, 1406 m, 1382 m, 1350 m, 1330 m, 1303 m, 1228 m, 1171 s, 1132 s, 1112 s, 1051 m, 989 w, 964 m, 926 w, 829 w, 805 w, 712 w; MS, *m/z* (rel intensity) 355 (M^+, 0), 340 (M^+-CH_3, 40), 326 (M^+-CH_2CH_3, 53), 310 (13), 254 (18), 70 (12), 57 (74), 56 (16), 55 (100), 53 (10). Anal. Calcd for $C_{18}H_{20}NO_3F_3$: C, 60.84; H, 5.67; N, 3.94. Found: C, 60.92; H, 5.69; N, 3.97.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-5-methoxyphenyl]-1-propanone (22c). Yellow oil; Bp 160 °C (1 mmHg); R_f = 0.14 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.19 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.33 (s, 6H, $C(CH_3)_2$), 2.74 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 3.84 (s, 3H, OCH_3), 4.03 (s, 2H, OCH_2), 6.76 (d, *J* = 2.6 Hz, 1H, 6-H), 6.93 (dd, *J* = 8.6, 2.6 Hz, 1H, 4-H), 7.79 (d, *J* = 8.6 Hz, 1H, 3-H); ^{13}C NMR ($CDCl_3$) δ 8.38 ($CH_3CH_2C(O)$), 28.16 ($C(CH_3)_2$), 36.61 ($CH_2C(O)$), 55.49 (OCH_3), 67.93 ($C(CH_3)_2$), 79.28 (OCH_2), 111.61, 114.57, 117.31, 131.05, 144.49, 160.68, 161.42, 206.86 (CO); IR (neat) 3282 w, 3070 w, 2972 s, 2444 w, 1708 s, 1649 s, 1604 s, 1570 s, 1500 s, 1462 s, 1408 m, 1352 s, 1314 s, 1280 s, 1242 s, 1192 s, 1124 m, 1083 m, 1057 m, 1025 s, 965 m, 920 w, 872 w, 843 m, 755 w, 723 w; MS, *m/z* (rel intensity) 261 (M^+, 2), 247 (11), 246 (M^+-CH_3, 75), 233 (14), 232 (M^+-CH_2CH_3, 100), 228 (12), 216 (22), 191 (11), 190 (36), 178 (35), 175 (10), 161 (12), 160 (84), 132 (11), 117 (18), 108 (11), 102 (15), 91 (12), 89 (11), 77 (29), 75 (10), 63 (37), 62 (12), 57 (39), 56 (10), 55 (84), 53 (13), 51 (11). Anal. Calcd for $C_{15}H_{19}NO_3$ C, 68.94; H, 7.33; N, 5.36. Found: C, 68.84; H, 7.34; N, 5.46.

1,1'-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-5-methoxy-1,3-phenylene]-bis-1-propanone (23c). Orange oil; Bp 160 °C (1 mmHg); R_f = 0.06 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, *J* = 7.3 Hz, 6H, $CH_3CH_2C(O)$), 1.31 (s, 6H, $C(CH_3)_2$), 2.80 (q, *J* = 7.3 Hz, 4H, $CH_2C(O)$), 3.86 (s, 3H, OCH_3), 4.01 (s, 2H, OCH_2), 6.94 (s, 2H, 4,6-H); ^{13}C NMR ($CDCl_3$) δ 8.04 ($CH_3CH_2C(O)$), 27.59 ($C(CH_3)_2$), 35.67 ($CH_2C(O)$), 55.67 (OCH_3), 68.23 ($C(CH_3)_2$), 79.66 (OCH_2), 113.23 (4, 6-C), 115.92, 144.26, 160.02, 160.47, 204.58 (CO); IR (neat) 3386 w, 2976 s, 2940 s, 2896 m, 2846 w, 1709 s, 1661 s, 1598 s, 1464 s, 1422 s, 1353 s, 1317 s, 1282 s, 1248 m, 1226 m, 1197 s, 1171 s, 1125 s, 1093 s, 1059 s, 1029 s, 964 s, 920 m, 874 m, 810 m, 769 w, 702; MS, *m/z* (rel intensity) 317 (M^+, 2), 302 (M^+-CH_3, 23), 289 (17), 288 (M^+-CH_2CH_3, 100), 216 (18), 57 (44), 55 (26). Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30; N, 4.41. Found: C, 68.03; H, 7.32; N, 4.59.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-5-fluorophenyl]-1-propanone (22d). Yellow oil; Bp 100 °C (4 mmHg); R_f = 0.20 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.20 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.34 (s, 6H, $C(CH_3)_2$), 2.76 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.06 (s, 2H, OCH_2), 6.99 (dd, *J* = 8.6, 2.6 Hz, 1H, 6-H), 7.13 (td, *J* = 8.6, 2.6 Hz, 1H, 4-H), 7.85 (dd, *J* = 8.6, 5.3 Hz, 1H, 3-H); ^{13}C NMR ($CDCl_3$) δ 8.25 ($CH_3CH_2C(O)$), 28.09 ($C(CH_3)_2$), 36.41 ($CH_2C(O)$), 68.20 ($C(CH_3)_2$), 79.50 (OCH_2), 113.59 (d, *J* = 23.2 Hz, 6-C), 116.30 (d, *J* = 21.9 Hz, 4-C), 121.32 (d, *J* = 3.7 Hz, 2-C), 131.69 (d, *J* = 8.6 Hz, 3-C), 144.94 (d, *J* = 7.3 Hz, 1-C), 160.05 (C=N), 163.76 (d, *J* = 253.9 Hz, 5-C), 205.25 (CO); IR (neat) 3068 w, 2972 m, 2938 m, 1698 s, 1655 s, 1607 m, 1582 s, 1495 m, 1461 m, 1408 s, 1384 m, 1353 s, 1312 s, 1295 w, 1266 m, 1245 w, 1229 s, 1184 m, 1168 s, 1117 m, 1080 m, 1050 s, 1020 m, 962 m, 923 w, 895 w, 877 m, 857 w, 828 m, 796 w, 756 w, 724 w; MS, *m/z* (rel intensity) 249 (M^+, 0), 234 (M^+-CH_3, 25), 226 (13), 224 (12), 220 (M^+-CH_2CH_3, 58), 216 (12), 205 (13), 204 (27), 178 (33), 171 (13), 166 (29), 163 (10), 160 (10), 151 (11), 148 (56), 122 (18), 121 (13), 120 (23), 95 (16), 94 (24), 75 (11), 57 (21), 56 (12), 55 (100). Anal. Calcd for $C_{14}H_{16}NO_2F$: C, 67.46; H, 6.47; N, 5.62. Found: C, 67.20; H, 6.45; N, 5.69.

1,1'-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-5-fluoro-1,3-phenylene]-bis-1-propanone (23d). Orange solid; R_f = 0.09 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.19 (t, *J* = 7.3 Hz, 6H, $CH_3CH_2C(O)$), 1.33 (s, 6H, $C(CH_3)_2$), 2.83 (q, *J* = 7.3 Hz, 4H, $CH_2C(O)$), 4.05 (s, 2H, OCH_2), 7.21 (d, *J* = 7.9 Hz, 2H, 4-H 6-H); ^{13}C NMR ($CDCl_3$) δ 7.93 ($CH_3CH_2C(O)$),

27.50 ($C(CH_3)_2$), 35.44 ($CH_2C(O)$), 68.41 ($C(CH_3)_2$), 79.97 (OCH_2), 115.32 (d, J = 23.2 Hz, 4-C 6-C), 120.67, (d, J = 3.6 Hz, 2-C), 144.65 (d, J = 6.1 Hz, 1-C 3-C), 159.60 (C=N), 162.61 (d, J = 255.2 Hz, 5-C), 202.86 (CO); IR (KBr) 3072 m, 2978 m, 2884 m, 2582 w, 2334 w, 1981 w, 1704 s, 1658 s, 1597 m, 1459 m, 1423 w, 1404 m, 1343 m, 1305 m, 1286 m, 1244 w, 1214 m, 1182 w, 1162 m, 1115 m, 1088 m, 1055 m, 984 w, 962 m, 922 w, 908 m, 862 w, 823 w, 807 w, 793 w, 767 w; MS, *m/z* (rel intensity) 305 (M^+, 0), 290 (M^+-CH_3, 38), 277 (10), 276 (M^+-CH_2CH_3, 71), 260 (17), 219 (10), 204 (26), 161 (13), 148 (11), 133 (14), 121 (14), 120 (10), 94 (10), 93 (13), 70 (13), 57 (98), 56 (17), 55 (100), 53 (12). Anal. Calcd for $C_{17}H_{20}NO_3F$: C, 66.90; H, 6.60; N, 4.59. Found: C, 66.69; H, 6.57; N, 4.61.

1-[1-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-2-naphthalenyl]-1-propanone (25). Yellow solid; Mp 65-70 °C (4 mmHg); R_f = 0.26 (hexane/EtOAc = 2/1); ^1H NMR ($CDCl_3$) δ 1.22 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.50 (s, 6H, $C(CH_3)_2$), 2.97 (q, J = 7.3 Hz, 4H, $CH_2C(O)$), 4.21 (s, 2H, OCH_2), 7.52-7.64 (c, 3H), 7.83-7.86 (m, 1H), 7.93 (d, J = 8.6 Hz, 1H), 8.26-8.30 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 8.20 ($CH_3CH_2C(O)$), 28.12 ($C(CH_3)_2$), 34.86 ($CH_2C(O)$), 68.43 ($C(CH_3)_2$), 79.43 (OCH_2), 123.18, 125.52, 126.29, 127.53, 127.68, 127.94, 130.30, 131.14, 134.05, 137.83, 160.88 (C=N), 203.88 (CO); IR (KBr) 3074 w, 2970 s, 2934 s, 2884 m, 1925 w, 1778 w, 1697 s, 1655 s, 1591 m, 1562 w, 1503 w, 1465 s, 1432 w, 1411 w, 1392 w, 1375 m, 1363 m, 1333 m, 1276 m, 1258 s, 1221 m, 1201 s, 1171 m, 1138 m, 1117 m, 1094 s, 1046 m, 1004 s, 972 m, 955 m, 929 m, 911 m, 871 m, 855 w, 820 s, 787 m, 748 m; MS, *m/z* (rel intensity) 281 (M^+, 0), 253 (17), 252 (M^+-CH_2CH_3, 97), 210 (31), 198 (35), 181 (12), 180 (81), 155 (14), 153 (19), 152 (51), 127 (20), 126 (26), 125 (11), 77 (13), 76 (12), 75 (11), 63 (15), 57 (24), 56 (11), 55 (100), 51 (11). Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.59; H, 6.78; N, 4.96.

1-[3-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-2-naphthalenyl]-1-propanone (27). Yellow oil; Bp 150 °C (0.8 mmHg); R_f = 0.20 (hexane/EtOAc = 3/1); ^1H NMR ($CDCl_3$) δ 1.25 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.40 (s, 6H, $C(CH_3)_2$), 2.88 (q, J = 7.3 Hz, 4H, $CH_2C(O)$), 4.12 (s, 2H, OCH_2), 7.56-7.61 (c, 2H), 7.84 (s, 1H, 1-H or 4-H), 7.86-7.91 (m, 2H), 8.34 (s, 1H, 1-H or 4-H); ^{13}C NMR ($CDCl_3$) δ 8.57 ($CH_3CH_2C(O)$), 28.12 ($C(CH_3)_2$), 36.10 ($CH_2C(O)$), 68.12 ($C(CH_3)_2$), 79.52 (OCH_2), 123.11, 126.67, 127.73, 128.07, 128.28, 128.45, 130.17, 132.88, 133.41, 138.89, 161.46 (C=N), 205.91 (CO); IR (neat) 3060 w, 2974 s, 2938 m,

2896 m, 1704 s, 1653 s, 1629 s, 1593 m, 1500 m, 1465 s, 1447 s, 1410 m, 1384 m, 1350 s, 1330 m, 1308 s, 1286 s, 1245 m, 1221 m, 1193 s, 1129 s, 1084 s, 1042 s, 1006 s, 965 s, 894 s, 845 m, 800 m, 754 s; MS, *m/z* (rel intensity) 281 (M^+, 0), 266 (M^+-CH_3, 25), 253 (18), 252 (M^+-CH_2CH_3, 100), 248 (11), 210 (29), 198 (36), 195 (11), 181 (15), 180 (90), 165 (10), 153 (16), 152 (48), 127 (15), 126 (26), 125 (12), 118 (15), 77 (11), 63 (15), 57 (24), 55 (64). Anal. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.69; H, 7.00; N, 5.15.

1,1'-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-1,3-naphthalenylene]-bis-1-propanone (28). Yellow solid; Mp 106-110 °C (4 mmHg); R_f = 0.11 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.24 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.27 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.36 (s, 6H, $C(CH_3)_2$), 2.91-3.01 (c, 4H, $CH_2C(O)$), 4.06 (s, 2H, OCH_2), 7.59-7.68 (c, 2H), 7.91-7.94 (m, 2H), 8.01 (s, 1H, 1-H); ^{13}C NMR ($CDCl_3$) δ 7.51 ($CH_3CH_2C(O)$), 8.41 ($CH_3CH_2C(O)$), 27.73 ($C(CH_3)_2$), 35.02 ($CH_2C(O)$), 38.78 ($CH_2C(O)$), 68.48 ($C(CH_3)_2$), 79.73 (OCH_2), 119.95, 125.16, 128.18, 128.81, 129.08, 129.38, 133.03, 137.43, 142.43, 160.31 (C=N), 203.72 (CO), 207.26 (CO); IR (KBr) 2976 m, 2938 m, 2024 w, 1941 w, 1701 s, 1660 s, 1570 w, 1501 w, 1461 m, 1407 m, 1378 m, 1346 m, 1298 m, 1281 m, 1222 w, 1190 m, 1161 m, 1139 s, 1117 m, 1094 m, 1047 m, 962 m, 941 w, 904 w, 865 w, 837 w, 810 w, 754 m; MS, *m/z* (rel intensity) 337 (M^+, 4), 322 (M^+-CH_3, 11), 309 (20), 308 (100), 290 (20), 280 (12), 252 (25), 236 (31), 193 (15), 180 (25), 165 (16), 153 (16), 152 (23), 151 (10), 126 (14), 125 (15), 57 (65), 55 (54). Anal. Calcd for $C_{18}H_{19}NO_2$: C, 74.75; H, 6.87; N, 4.15. Found: C, 74.48; H, 6.91; N, 4.16.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3-thienyl]-1-propanone (30). Colorless oil; Bp 120 °C (0.8 mmHg); R_f = 0.14 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.37 (s, 6H, $C(CH_3)_2$), 2.88 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.10 (s, 2H, OCH_2), 7.15 (d, *J* = 5.0 Hz, 1H, 4-H or 5-H), 7.36 (d, *J* = 5.3 Hz, 1H, 4-H or 5-H); ^{13}C NMR ($CDCl_3$) δ 8.12 ($CH_3CH_2C(O)$), 28.00 ($C(CH_3)_2$), 36.23 ($CH_2C(O)$), 68.27 ($C(CH_3)_2$), 79.71 (OCH_2), 127.84 (4-C or 5-C), 128.19 (4-C or 5-C), 129.56 (2-C or 3-C), 143.83 (2-C or 3-C), 156.86 (C=N), 200.93 (CO); IR (neat) 3108 w, 2976 s, 2938 m, 2900 m, 1696 s, 1647 s, 1521 m, 1463 m, 1432 s, 1379 s, 1348 m, 1288 s, 1227 s, 1206 s, 1185 m, 1111 m, 1084 w, 1030 s, 992 w, 957 m, 916 m, 883 m, 864 w, 829 w, 811 w, 745 m; MS, *m/z* (rel intensity) 237 (M^+, 6), 223 (10), 222 (M^+-CH_3, 67), 204 (23), 166 (23), 154 (16), 151 (15), 150 (11), 138 (10), 137 (11), 136

(100), 110 (13), 109 (10), 83 (11), 64 (15), 57 (23), 55 (44). Anal. Calcd for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.91. Found: C, 60.63; H, 6.26; N, 5.96.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3-methylphenyl]-1-butanone (34). Colorless oil; Bp 110 °C (1 mmHg); R_f = 0.30 (hexane/EtOAc = 4/1); ^{1}H NMR ($CDCl_3$) δ 0.97 (t, *J* = 7.3 Hz, 6H, $CH_3CH_2CH_2C(O)$), 1.39 (s, 6H, $C(CH_3)_2$), 1.65-1.78 (m, 2H, $CH_2CH_2C(O)$), 2.41 (s, 3H, CH_3), 2.85 (t, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.12 (s, 2H, OCH_2), 7.33-7.38 (c, 2H, Ph), 7.46-7.49 (m, 1H, Ph); ^{13}C NMR ($CDCl_3$) δ 13.68 ($CH_3CH_2CH_2C(O)$), 17.65 ($CH_3CH_2C(O)$), 19.30 (CH_3), 27.89 ($C(CH_3)_2$), 42.73 ($CH_2C(O)$), 67.89 ($C(CH_3)_2$), 79.26 (OCH_2), 125.09 (4-C, 5-C, 6-C), 127.78 (1-C, 2-C, 3-C), 129.20 (4-C, 5-C, 6-C), 132.96 (4-C, 5-C, 6-C), 138.44 (1-C, 2-C, 3-C), 139.78 (1-C, 2-C, 3-C), 161.76 (C=N), 202.66 (CO); IR (neat) 2970 m, 1694 s, 1667 s, 1592 m, 1464 s, 1383 m, 1364 s, 1296 s, 1239 m, 1211 m, 1172 m, 1117 m, 1045 s, 990 m, 964 m, 920 m, 869 w, 785 m, 758 m, 618 w, 504 w; MS, *m/z* (rel intensity) 259 (M^+, 0), 244 (M^+-CH_3, 3), 217 (13), 216 (M^+-Pr, 100), 200 (21), 174 (32), 172 (10), 162 (43), 160 (11), 158 (15), 145 (12), 144 (99), 119 (13), 118 (10), 117 (14), 116 (31), 115 (18), 91 (18), 90 (18), 89 (42), 77 (10), 65 (11), 63 (16), 55 (48). Anal. Calcd for $C_{16}H_{21}NO_3$: C, 74.10; H, 8.16; N, 5.40. Found: C, 73.99; H, 8.20; N, 5.44.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3-methylphenyl]-2-methyl-1-propanone (35). Colorless oil; Bp 110 °C (1 mmHg); R_f = 0.31 (hexane/EtOAc = 4/1); ^{1}H NMR ($CDCl_3$) δ 0.97 (t, *J* = 7.3 Hz, 6H, $CH_3CH_2CH_2C(O)$), 1.39 (s, 6H, $C(CH_3)_2$), 1.65-1.78 (m, 2H, $CH_2CH_2C(O)$), 2.41 (s, 3H, CH_3), 2.85 (t, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.12 (s, 2H, OCH_2), 7.33-7.38 (c, 2H, Ph), 7.46-7.49 (m, 1H, Ph); ^{13}C NMR ($CDCl_3$) δ 18.69 ($(CH_3)_2CCH_2C(O)$), 19.50 (CH_3), 27.96 ($C(CH_3)_2$), 38.17 ($(CH_3)_2CCH_2C(O)$), 67.96 ($C(CH_3)_2$), 79.23 (OCH_2), 124.69 (4-C, 5-C, 6-C), 127.84 (1-C, 2-C, 3-C), 129.18 (4-C, 5-C, 6-C), 132.69 (4-C, 5-C, 6-C), 138.49 (1-C, 2-C, 3-C), 140.05 (1-C, 2-C, 3-C), 161.65 (C=N), 207.15 (CO); IR (neat) 2972 s, 2934 s, 2876 m, 1758 w, 1696 s, 1667 s, 1592 m, 1465 s, 1384 m, 1365 m, 1348 m, 1296 s, 1248 s, 1211 m, 1186 m, 1108 m, 1082 m, 1045 s, 990 m, 964 s, 920 m, 891 w, 870 w, 829 w, 817 w, 797 m, 762 m, 743 w, 724 w, 698 w, 665 w, 617 w, 569 w; MS, *m/z* (rel intensity) 259 (M^+, 1), 244 (M^+-CH_3, 5), 217 (14), 216 (M^+-Pr, 100), 174 (24), 162 (35), 149 (61), 116 (16), 90 (10), 89 (20), 55 (32). Anal. Calcd for $C_{16}H_{21}NO_3$: C, 74.10; H, 8.16; N, 5.40. Found: C, 73.83; H, 8.03; N, 5.28.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-3-methylphenyl]-3-(trimethylsilyl)-1-propanone (36). Yellow oil; Bp 140 °C (1 mmHg); R_f = 0.20 (hexane/EtOAc = 4/1); ^{1}H NMR ($CDCl_3$) δ 0.02 (s, 9H, $SiMe_3$), 0.83-0.89 (m, 2H, $CH_2CH_2C(O)$), 1.39 (s, 6H, $C(CH_3)_2$), 2.42 (s, 3H, CH_3), 2.79-2.85 (m, 2H, $CH_2C(O)$), 4.12 (s, 2H, OCH_2), 7.34-7.36 (c, 2H, Ph), 7.44-7.48 (m, 1H, Ph); ^{13}C NMR ($CDCl_3$) δ -1.81 ($SiMe_3$), 10.68 ($CH_2CH_2C(O)$), 19.43 (CH_3), 27.96 ($C(CH_3)_2$), 35.58 ($CH_2C(O)$), 67.93 ($C(CH_3)_2$), 79.30 (OCH_2), 124.98 (4-C or 5-C or 6-C), 127.76 (1-C or 2-C or 3-C), 129.25 (4-C or 5-C or 6-C), 132.90 (4-C or 5-C or 6-C), 138.51 (1-C or 2-C or 3-C), 139.73 (1-C or 2-C or 3-C), 161.76 (C=N), 203.59 (CO); IR (neat) 3066 w, 2960 s, 2896 s, 1697 s, 1669 s, 1591 m, 1464 s, 1440 m, 1383 m, 1364 m, 1346 s, 1295 s, 1247 s, 1210 m, 1177 s, 1099 m, 1081 m, 1043 s, 986 m, 964 m, 919 m, 860 s, 838 s, 784 m, 762 s; MS, *m/z* (rel intensity) 317 (M^+, 0), 230 (16), 217 (14), 216 (99), 174 (37), 162 (44), 144 (63), 116 (17), 89 (16), 75 (61), 74 (10), 73 (100), 59 (14), 55 (74). Anal. Calcd for $C_{18}H_{27}NO_2Si$: C, 68.09; H, 8.57; N, 4.41. Found C, 67.80; H, 8.45; N, 4.62.

4,5-Dihydro-4,4-dimethyl-2-[6-methyl-2-[1-(trimethylsilyl)oxy]-1-propenyl]phenyl]oxazoline (37). Yellow oil; R_f = 0.23 (hexane/EtOAc = 4/1); ^{1}H NMR ($CDCl_3$) δ 0.23 (s, 9H, $SiMe_3$), 1.55 (s, 6H, $C(CH_3)_2$), 1.67 (d, J = 7.0 Hz, 3H, $CHC(CH_3)$), 2.55 (s, 3H, 3-H), 4.18 (s, 2H, OCH_2), 5.14 (q, J = 7.3 Hz, 1H, $CHC(CH_3)$), 7.24-7.27 (m, 3H).

1-[2-(5,6-Dihydro-4,4-dimethyl-4*H*-1,3-oxazin-2-yl)phenyl]-1-propanone (39). Yellow oil Bp 110 °C (4 mmHg); R_f = 0.23 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.19 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.27 (s, 6H, $C(CH_3)_2$), 1.80 (t, J = 7.8 Hz, 2H, $CH_2C(CH_3)_2$), 2.83 (q, J = 7.3 Hz, 2H, $CH_2C(O)$), 4.26 (t, J = 5.8 Hz, 2H, OCH_2), 7.26-7.30 (m, 1H), 7.39-7.42 (m, 2H), 7.71-7.74 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 8.29 ($CH_3CH_2C(O)$), 30.03 ($C(CH_3)_2$), 34.00 ($CH_2C(CH_3)_2$), 36.05 ($CH_2C(O)$), 49.08 ($C(CH_3)_2$), 62.48 (OCH_2), 126.15, 128.41, 129.36, 129.54, 132.44 (1-C or 2-C), 141.53 (1-C or 2-C), 153.10 (C=N), 206.65 (CO); IR (neat) 3166 w, 2972 s, 2442 w, 2162 w, 1972 w, 1701 s, 1656 s, 1598 w, 1575 w, 1463 w, 1410 w, 1344 w, 1295 s, 1258 m, 1211 m, 1191 m, 1164 m, 1091 m, 948 m, 869 m, 766 m, 741 m; MS, *m/z* (rel intensity) 245 (M^+, 0), 230 (M^+-CH_3, 17), 217 (17), 216 (93), 205 (11), 188 (21), 162 (14), 161 (53), 160 (15), 148 (34), 133 (31), 131 (11), 130 (41), 117 (10), 115 (14), 105 (28), 104 (13), 103 (13), 102 (26), 91 (14), 84 (32), 77 (22), 76 (30), 75 (10), 70 (10), 69 (100), 66 (31), 57 (14), 56

(10), 55 (18), 53 (10), 52 (15), 51 (17), 50 (11). Anal. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71. Found: C, 72.57; H, 8.00; N, 5.57.

1-(2-Oxazolylphenyl)-1-propanone (41). Colorless oil Bp 120-130 ℃ (1 mmHg); R_f = 0.27 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.21 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 2.73 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 7.24 (s, 1H, 4-H), 7.33-7.37 (m, 1H), 7.47-7.55 (m, 2H), 7.70 (s, 1H, 5-H), 7.96-8.00 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 8.23 ($CH_3CH_2C(O)$), 36.48 ($CH_2C(O)$), 123.92 (1-C or 2-C), 126.45, 128.10, 128.55, 129.63, 130.12, 138.94, 141.35 (1-C or 2-C), 160.25 (C=N), 207.13 (CO); IR (neat) 3068 w, 2984 m, 2942 m, 2882 w, 1702 s, 1604 w, 1585 w, 1562 m, 1519 m, 1487 m, 1462 m, 1437 m, 1418 m, 1359 m, 1257 m, 1213 s, 1140 m, 1104 m, 1075 m, 1029 m, 949 m, 922 m, 858 w, 777 s, 741 s, 714 s, 688 w, 642 w, 559 w; MS, *m/z* (rel intensity) 201 (M^+, 3), 186 (11), 173 (16), 172 (100), 144 (10), 116 (17), 89 (28), 63 (16), 62 (10), 50 (10). Anal. Calcd for $C_{12}H_{11}NO_3$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.72; H, 5.68; N, 6.95.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-thiazolyl)phenyl]-1-propanone (43). Yellow oil Bp 110 °C (1 mmHg); R_f = 0.09 (hexane/EtOAc = 10/1); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.42 (s, 6H, $C(CH_3)_2$), 2.76 (q, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 3.23 (s, 2H, SCH_2), 7.28-7.31 (m, 1H), 7.41-7.48 (m, 2H), 7.59-7.62 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 8.30 ($CH_3CH_2C(O)$), 27.14 ($C(CH_3)_2$), 36.48 ($CH_2C(O)$), 45.54 (SCH_2), 79.39 ($C(CH_3)_2$), 126.42, 129.40, 129.74, 130.30, 130.87 (1-C or 2-C), 141.89 (1-C or 2-C), 162.50 (C=N), 206.76 (CO); IR (neat) 3066 w, 2974 s, 2936 s, 2878 m, 1704 s, 1611 s, 1594 s, 1571 m, 1483 m, 1462 s, 1443 m, 1409 m, 1379 m, 1361 s, 1348 s, 1263 s, 1214 s, 1171 s, 1120 w, 1079 m, 1014 m, 953 s, 880 w, 799 m, 765 s, 737 m; MS, *m/z* (rel intensity) 247 (M^+, 0), 218 (M^+-CH_2CH_3, 55), 186 (12), 160 (11), 130 (20), 102 (28), 88 (82), 76 (10), 73 (13), 60 (28), 59 (13), 55 (100), 54 (70), 53 (10), 51 (10). Anal. Calcd for $C_{14}H_{17}NOS$: C, 67.98; H, 6.93; N, 5.66. Found: C, 67.99; H, 6.91; N, 5.83.

A plot of turnover frequency vs. catalyst concentration (Laine's kinetic criteria) was shown in Figure.

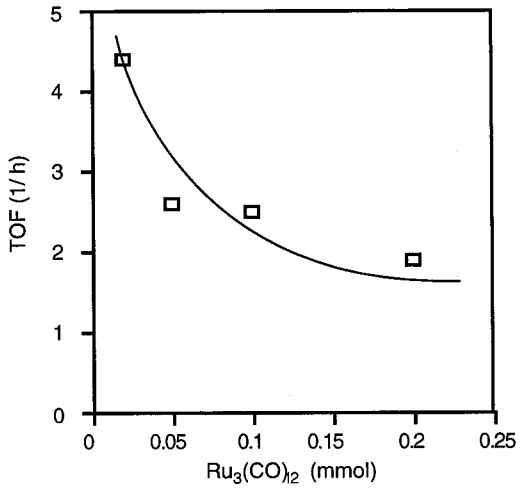


Figure. Plots of TOF vs catalyst loading for the reaction of **4a** (2 mmol) with CO (20 atm) and ethylene (7 atm) in the presence of $Ru_3(CO)_{12}$ in toluene (6 mL) at 160 °C for 5 h.

2.6 References and Notes

(1) For related carbonylation reactions promoted by a pyridine ring as a directing group, see: (a) Ishii, Y.; Chatani, N.; Kakiuchi, F.; Murai, S. *Organometallics* **1997**, *16*, 3615. (b) Chatani, N.; Ishii, Y.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1998**, *63*, 5129.

(2) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, 1991.

(3) Fukuyama, T.; Chatani, N.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1997**, *62*, 5647.

(4) Frump, J. A. *Chem. Rev.* **1971**, *71*, 483. Reuman, M.; Meyers, A. I. *Tetrahedron* **1985**, *41*, 387.

(5) Although the kinetics for ethylene pressure, catalyst concentration, and substrate concentration were also studied, the reproducibility was invariably poor.

(6) The similar trend was observed in the Rh-catalyzed transformation of 4-pentynylcyclopropanes, see: Koga, Y.; Narasaka, K. *Chem. Lett.* **1999**,705.

(7) For reviews, see: Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981. Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: New York, 1983.

(8) See: Chapter 1, pp. 10-11 (eqs 7, 8).

(9) In case of aromatic imines bearing a CF_3 group, ortho-ethylation product was obtained in 3%. See also ref. 3.

(10) See: Chapter 1, pp. 10-11 (eq 7).

(11) (a) Kiplinger, J. L.; Richmond, T. G.; Osterberg, C. E. *Chem. Rev.***1994**, *94*, 373. Similar phenomena were observed in our group. (b) Sonoda, M.; Kakiuchi, F.; Chatani, N.; Murai, S. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 3117.

(12) When the reaction times prolonged to 20 h, **16** and **17** were not detected and the product **18** was obtained in 45% yield, along with complex mixtures.

(13) The similar effect was observed in Ru-catalyzed C-H/olefin coupling.phenomena. See ref. 11b.

(14) See: Chapter 1, pp. 11 (eq 9).

(15) See: Chapter 1, pp. 12 (eq 11).

(16) MacRae studied the thermal isomerization of α-silyl ketones to enol silyl ethers in detail. Brook, A. G.; MacRae, D. M.; Bassindale, A. R. *J. Organomet. Chem.* **1975**, *86*, 185.

(17) The formation of enol silyl ether was observed in the $Ru_3(CO)_{12}$-catalyzed reaction of *N*-(2-pyridyl)enamine with CO and trimethylvinylsilane. See: ref. 1b

(18) The ruthenium-catalyzed conversion of vinylsilanes to ethylene and disilylethylene is known, see: Marciniec, B.; Gulinski, J. *J. Organomet. Chem.* **1984**, *266*, C19. Seki, Y.; Takeshita, K.; Kawamoto, K. *J. Organomet. Chem.* **1989**, *369*, 117. Wakatsuki, Y.; Yamazaki, H.; Nakano, M.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 703. Marciniec, B.; Pietraszuk, C. *J. Organomet. Chem.* **1991**, *412*, C1. Marciniec, B.; Pietraszuk, C.; *J. Chem. Soc., Chem. Commun.* **1995**, 2003.

(19) The reaction of **1**-d_5 with CO and ethylene was also run (equation not shown). After 2 h, a 75% of **1**-d_5 was recovered, along with a 16% of **4a**. In this case, the deuterium atoms of recovered **1**-d_5 were also scrambled at the *ortho* position, which occurred 6% incorporation of protio label into these sites.

(20) Laine, R. M. *J. Mol. Cat.* **1982**, *14*, 137.

(21) A stoichiometric reaction of benzaldehyde imine or benzo[h]quinoline with $Ru_3(CO)_{12}$ has appeared. Bennett, R. L.; Bruce, M. I.; Goodall, B. L.; Iqbal, M. Z.; Stone, F. G. A. *J. Chem. Soc., Dalton Trans.* **1972**, 1787. Bruce, M. I.; Goodall, B. L.; Stone, F. G. A. *J. Organomet. Chem.* **1973**, *60*, 343.

(22) Newkome, G. R.; Puckett, W. E.; Gupta, V. K.; Kiefer, G. E. *Chem. Rev.* **1986**, *86*, 451.

(23) Fukuyama, T.; Chatani, N.; Tatsumi, J.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1998**, *120*, 11522 .

(24) The p*K*a value of 2-picoline is 7.98. The p*K*a value of 4,4-dimethyl-2-methyl-2-oxazoline is 5.59.

(25) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; Chapter 6.

(26) Casey, C. P.; Scheck, D. M. . *J. Am. Chem. Soc.* **1980**, *102*, 2723.

(27) Campora, J.; Gutierrez, E.; Monge, A.; Palma, P.; Poveda, M. L.; Ruiz, C.; Carmona, E. *Organometallics* **1994**, *13*, 1728.

(28) I will describe the detail in chapter 3. See also, Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1999**, *121*, 8645.

Chapter 3

Ruthenium-Catalyzed Decarbonylative Cleavage of a C-C Bond of Alkyl Phenyl Ketones

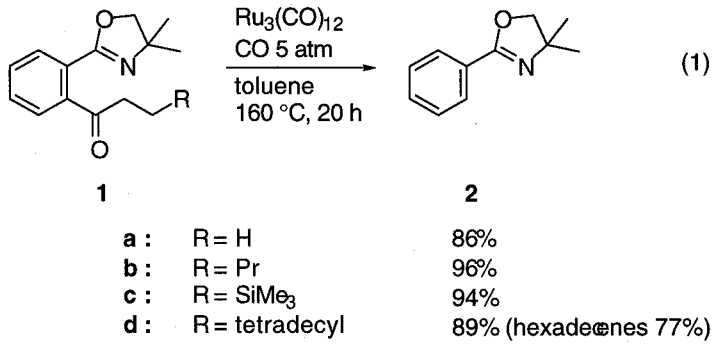
3.1 Introduction

The cleavage of unreactive bonds, such as C-H, C-C, C-F, for example, by transition metals has received considerable attention over the past decades.[1] Although substantial progress has been made in this field, most studies have involved stoichiometric reactions. Recently, significant developments in catalytic reactions involving the cleavage of C-H bonds has been achieved via the use of Ru,[2,3] Rh,[4] and Co[5] complexes as catalysts. In contrast, the cleavage of C-C bonds remains limited. In this context, the exploration of catalytic reactions which enable the cleavage of a C-C bond represents a challenging topic of considerable synthetic interest.[6] While several catalytic reactions in which the cleavage of a C-C bond occurs have already been reported, most involve reactions of strained substrates and are based on the methodology which takes advantage of the release of ring strain and/or the presence of an activating functionality, such as a carbonyl group. Strained ketones, such as cyclopropenones,[7] cyclobutanones,[8] and cyclobutenones[9] are known to undergo C-C bond cleavage via catalysis by transition metal complexes. On the other hand, analogous catalytic reactions of unstrained ketones are rare. Kaneda reported the Rh-catalyzed decarbonylation of diketones to monoketones.[10] Suggs and Jun found that rhodium complexes promote an exchange reaction of alkyl groups in the reaction of 8-quinolinyl alkyl ketones[11] or in situ generated *N*-pyridyl imines with olefins.[12] These results strongly suggest that chelation represents a promising approach to the cleavage of unstrained C-C bonds. In this chapter, I wish to describe a new type of catalytic reaction, which involves the $Ru_3(CO)_{12}$-catalyzed decarbonylative cleavage of a C-C bond in aromatic ketones.

A substrate for the exploration of C-C bond breaking reactions was designed, in which chelation can be utilized to bring a C-C bond into a coordination sphere, thus permitting cleavage of the C-C bond. I choose alkyl phenyl ketones bearing an oxazoline or pyridine on the phenyl group as model systems so as to directly observe unstrained C-C bond cleavage. The utility of these directing groups for the cleavage of C-H bonds has already been discussed.[13]

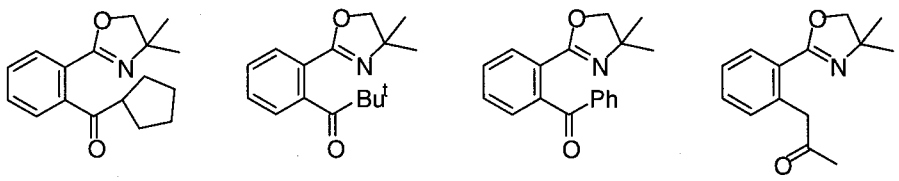
3.2 Decarbonylative Cleavage of a C-C Bond of Alkyl Phenyl Ketones

Treatment of 1-[2-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-propanone (**1a**) with 5 mol% of $Ru_3(CO)_{12}$ under an atmosphere of nitrogen at 135 °C in toluene in a 50-mL screw-capped vial resulted in decarbonylation to give **2** in 62% yield, along with **1a** in 25% yield. The color of the solution became black, indicating the decomposition of the catalyst. After optimizing the reaction conditions, I discovered that CO pressure maintains the catalyst in an active form, thus eliminating color formation. When the reaction of **1a** (0.5 mmol) under 5 atm of CO at 160 °C in toluene in the presence of $Ru_3(CO)_{12}$ (0.025 mmol) for 20 h in a 50-mL stainless autoclave gave **2** in 86% isolated yield, the color of the final reaction solution was orange (eq 1).



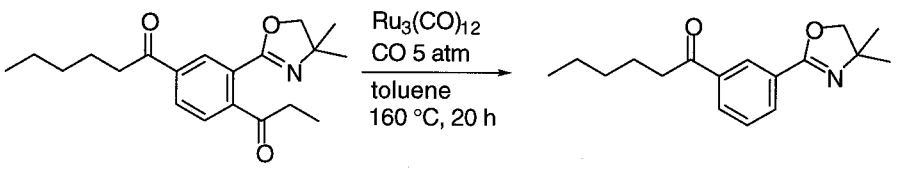
(1)

The pentyl ketone **1b** and β-silylethyl ketone **1c** underwent decarbonylation to give **2** in high yields. The reaction of hexadecyl ketone **1d** afforded **2** in 89% yield, along with hexadecenes in 77% yield. The recovered olefins were comprised of at least five isomers of hexadecenes. The corresponding cyclopentyl ketone, *tert*-butyl ketone, and phenyl ketone failed to react. This may be due to the steric bulkiness in the vicinity of the keto moiety. The reaction of methyl benzyl ketone also failed to react.



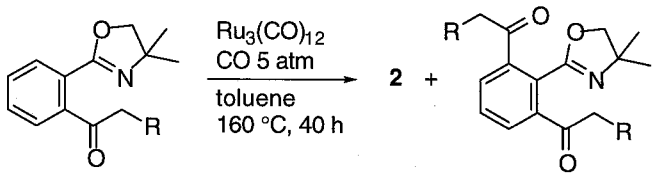
The use of a pyridine ring in place of an oxazoline ring as the directing group also gave good results. For example, the reaction of the corresponding pyridine isomer of **1a** gave 2-phenylpyridine in 81% yield under identical conditions (the equation not shown). It is noteworthy that the presence

of a directing group is critical for the decarbonylation reaction to proceed. Of additional importance is the fact that the directing group caused a site-selective reaction. Indeed, the reaction of diketone **3** involved site-selective decarbonylation at the ortho position to give decarbonylated product **4** in high yield (eq 2).



(2)

I next used ketones which contain no hydrogen β to the ketone, in order to circumvent the formation of alkenes, in the expectation that it would lead to new reactions. These substrates, however, again gave **2** (eq 3). The reaction of methyl ketone **5a** gave **2** in 81% yield.[14] No other products were detected by GC-MS and ^{1}HNMR of the crude reaction mixture. Benzyl ketone **5b** provided **2** in 86% yield. Interestingly, when the solvent was changed to CH_3OH, **2** (73%) and $PhCH_2C(O)OMe$ (31%) were formed. The formation of $PhCH_2C(O)OMe$ suggests the generation of phenylketene, which is captured by CH_3OH. The reaction of **5c** gave quite unexpected results, giving **2** and diketone **6** in 34% and 10% yields respectively, and **5c** was recovered in 49%.[15]



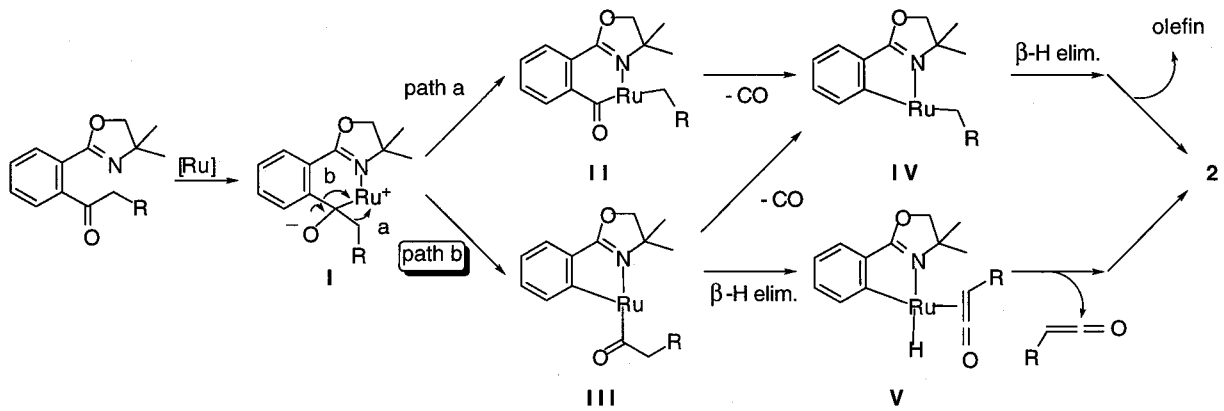
(3)

a:	R = H	81%	0%
b:	R = Ph	86%	0%
c:	R = Bu^t	34%	10%

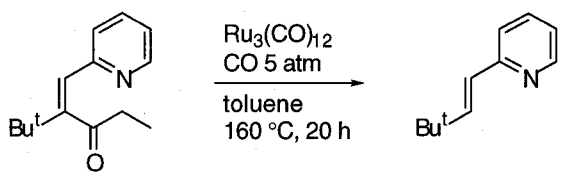
I propose a reaction mechanism, as shown in Scheme 1. Coordination of the nitrogen to ruthenium provides the metal with a more nucleophilic character, as well as bringing it close to the ketonic carbon. The coordinated ruthenium attacks the carbonyl group to generate **I**. The first C-C bond cleavage to form **II** or **III** (via path a or path b), followed by decarbonylation (second C-C bond cleavage) would generate Ru-alkyl intermediate **IV**. At the present time, it is not clear which C-C bond

(aryl-carbonyl or alkyl-carbonyl) cleave first. If an aryl group rearranges in **I**, the five-membered metallacycle **III**, which might be more stable than a six-membered metallacycle **II**, is formed. With the support of this hypothesis, the formation of methyl phenylacetate and **6** in eq 3 suggest that path b is the more likely. The Ru-alkyl intermediate **IV** undergoes β-hydrogen elimination followed by reductive elimination to give **2** and olefins. Based on the results in eq 3, another pathway involving β-hydrogen elimination from intermediate **III** to give **V** is also possible when β-hydrogen elimination is not possible for steric reason.[16] Methyl phenylacetate, which is derived from the reaction of **5b** is probably formed by the capture of phenylketene with methanol.[17] In addition, the formation of **6c** can be explained by reaction of **5c** with *tert*-butyl ketene.[18]

Scheme 1



The present reaction is applicable, not only to alkyl phenyl ketones, but also to α,β-unsaturated ketones. The reaction of α, β–unsaturated ketone **7** gave 2-[(E)-3,3-dimethyl-1-butenyl]pyridine (**8**) in high yield (eq 4).



7 **8** 90% (4)

3.3 Conclusion

In summary, I describe a new catalytic reaction involving decarbonylative C-C bond cleavage. Although the decarbonylation of aldehydes, acyl halides, acyl cyanide, acyl phosphonates, and acylsilanes are well known,[19] analogous reaction of ketones appears to be limited to specific substrates.[8a, 8b,10] The reaction involves double cleavage of a C-C bond. The presence of a directing group, such as oxazoline or pyridine, is critical for the decarbonylation reaction to proceed. The alkyl moiety in the alkyl aryl ketones is converted into olefins, or ketene if the formation of olefins are not possible for steric reason. The reaction is applicable, not only to alkyl aryl ketones, but also to an α,β-unsaturated ketone. A key feature is the utilization of the chelation of nitrogen to Ru, which assists in the formation of a metallacycle during the cleavage of the C-C bond.[20]

3.4 Experimental Section

General Information. Boiling points (bp) refer to air bath temperatures for bulb-to-bulb distillation and are uncorrected. ^{1}H NMR and ^{13}C NMR were recorded on a JEOL JMN-270 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Data are reported as follows: chemical shift in ppm (d), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and c = complex), coupling constant (Hz), integration, and interpretation. Infrared spectra (IR) were obtained on a Hitachi 270-50 spectrometer; absorptions are reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were obtained on a Shimadzu GCMS-QP 5000 with ionization voltages of 70 eV. Elemental analyses were performed by Elemental Analysis Section of Osaka University. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-DX303. Analytical GC was carried out on a Shimadzu GC-14B gas chromatography, equipped with a flame ionization detector. Column chromatography was performed with SiO_2 (Wakogel or Merk SilicaGel 60 (230-400mesh)).

Materials. Toluene was distilled over CaH_2. $Ru_3(CO)_{12}$ was purchased from Aldrich Chemical Co. and used after recrystallization from hexane. Alkyl phenyl ketones (**1a**, **1c** and **3**) and (Z)-5,5-dimethyl-4-[(2-pyridyl)methylene]hexan-3-one (**7**) were prepared by the carbonylation of corresponding benzene ring or vinyl group with CO and olefins (ethylene or teimethylvinylsilane).[13, 21] Alkyl phenyl ketones (**1b**, **1d**, **5a** and **5c**) were obtained by Evans's procedure.[22] 1-[2-(4,5-Dihydro-

4,4-dimethyl-2-oxazolyl)phenyl]-2-phenyl-ethanone (**5b**) was synthesized via ortho lithiation of 4,4-dimethyl-2-phenyl-2-oxazoline followed by the reaction with ethyl phenylacetate.

General Procedure. In a 50-mL stainless autoclave were placed $Ru_3(CO)_{12}$ (16 mg, 0.025 mmol), 1-[2-(4,5-dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-propanone (**1a**) (0.05 mmol), and toluene (1 mL). The autoclave was charged with carbon monoxide to 5 atm at 25 °C, and then heated in an oil bath at 160 °C for 20 h. The autoclave was cooled and depressured. The solvent was removed in vacuo, and the resulting residue was subjected to column chromatography on silica-gel with hexane/EtOAc as eluant to give 4,5-dihydro-4,4-dimethyl-2-phenyl-2-oxazoline (**2**) as yellow oil. An analytical sample was obtained by bulb-to-bulb distillation.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-propanone (1a). Yellow oil; Bp 95 °C (4 mmHg); R_f = 0.29 (hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$) δ 1.20 (t, J = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.36 (s, 6H, $C(CH_3)_2$), 2.78 (q, J = 7.3 Hz, 2H, $CH_2C(O)$), 4.07 (s, 2H, OCH_2), 7.30-7.33 (m, 1H, 3-H or 6-H), 7.42-7.52 (c, 2H, 4,5-H), 7.82-7.85 (m, 1H, 3-H or 6-H); ^{13}C NMR ($CDCl_3$) δ 8.27 ($CH_3CH_2C(O)$), 28.00 ($C(CH_3)_2$), 36.23 ($CH_2C(O)$), 67.98 ($C(CH_3)_2$), 79.34 (OCH_2), 125.25 (1-C or 2-C), 126.15 (3-C or 6-C), 129.20 (3-C or 6-C), 129.38 (4-C or 5-C), 130.67 (4-C or 5-C), 142.32 (1-C or 2-C), 161.01 (C=N), 206.49 (CO); IR (neat) 3072 (w), 2974 (m), 2896 (w), 2756 (w), 2574 (w), 2402 (w), 2338 (w), 2018 (w), 1704 (s), 1651 (s), 1596 (w), 1575 (w), 1462 (m), 1409 (w), 1351 (s), 1310 (m), 1214 (m), 1186 (w), 1124 (w), 1082 (w), 1052 (m), 1033 (m), 962 (m), 869 (w), 799 (w), 773 (w), 741 (w); MS, *m/z* (rel intensity) 231 (M^+, 0), 216 (M^+-CH_3, 20), 203 (12), 202 (96), 198 (14), 186 (23), 160 (39), 148 (46), 144 (12), 131(10), 130 (100), 115 (13), 104 (13), 103 (15), 102 (29) 77 (17), 76 (27), 75 (10), 57 (10), 55 (54), 51 (15), 50 (17). Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.60; H, 7.44; N, 6.12.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-hexanone (1b). Colorless oil; Bp 150-155 °C (1 mmHg); R_f = 0.24 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J = 6.9 Hz, 3H, $CH_3CH_2CH_2CH_2CH_2C(O)$), 1.33 (c, 4H, $CH_2CH_2CH_2CH_2C(O)$), 1.36 (s, 6H, $C(CH_3)_2$), 1.69 (c, 2H, $CH_2CH_2C(O)$), 2.77 (t, J = 7.4 Hz, 2H, $CH_2C(O)$), 4.06 (s, 2H, OCH_2), 7.33 (dd, J = 6.9, 2.0 Hz, 1H, Ph), 7.42-7.49 (m, 2H, Ph), 7.83 (dd, J = 6.6, 2.3 Hz, 1H, Ph); ^{13}C

NMR ($CDCl_3$) δ 13.91 ($CH_3CH_2CH_2CH_2CH_2C(O)$), 22.46 ($CH_2CH_2CH_2CH_2C(O)$), 23.96 ($CH_2CH_2C(O)$), 28.12 ($C(CH_3)_2$), 31.36 ($CH_2CH_2CH_2C(O)$), 43.04 ($CH_2C(O)$), 68.11 ($C(CH_3)_2$), 79.48 (OCH_2), 125.52 (1-C or 2-C), 126.40, 129.43, 129.54, 130.73, 142.43 (1-C or 2-C), 161.29 (C=N), 206.02 (CO); IR (neat) 3064 (w), 2964 (s), 2934 (s), 2872 (s), 1784 (m), 1705 (s), 1652 (s), 1598 (m), 1576 (m), 1465 (s), 1405 (m), 1365 (s), 1352 (s), 1312 (s), 1266 (m), 1245 (m), 1202 (m), 1189 (m), 1127 (m), 1112 (w), 1057 (s), 1039 (s), 987 (m), 966 (s), 923 (m), 871 (w), 819 (w), 775 (s), 760 (m), 723 (m); MS, *m/z* (rel intensity) 273 (M^+, 0), 258 (M^+ -CH_3, 5), 216 (17), 203 (14), 202 (100), 186 (16), 160 (36), 158 (16), 148 (43), 146 (10), 131 (12), 130 (81), 129 (10), 104 (12), 103 (15), 102 (24), 77 (13), 76 (17), 55 (54). Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found C, 74.70; H, 8.70; N, 5.10.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-3-(trimethylsilyl)-1-propanone (1c). Yellow oil; Bp 120 °C (1 mmHg); R_f = 0.31 (hexane/EtOAc = 3/1); ^1H NMR ($CDCl_3$) δ 0.01 (s, 9H, $SiMe_3$), 0.86-0.92 (m, 2H, $CH_2CH_2C(O)$), 1.35 (s, 6H, $C(CH_3)_2$), 2.68-2.75 (m, 2H, $CH_2C(O)$), 4.06 (s, 2H, OCH_2), 7.29-7.33 (m, 1H, Ph), 7.42-7.52 (c, 2H, Ph), 7.82-7.86 (m, 1H, Ph); ^{13}C NMR ($CDCl_3$) δ -1.85 ($SiMe_3$), 10.73 ($CH_2CH_2C(O)$), 28.16 ($C(CH_3)_2$), 37.77 ($CH_2C(O)$), 68.07 ($C(CH_3)_2$), 79.46 (OCH_2), 125.27 (1-C or 2-C), 126.40, 129.36, 129.42, 130.76, 142.41 (1-C or 2-C), 161.11 (C=N), 207.17 (CO); IR (neat) 3068 (w), 2960 (s), 2898 (m), 1706 (s), 1653 (s), 1597 (m), 1576 (w), 1465 (m), 1445 (m), 1408 (m), 1385 (w), 1352 (s), 1313 (s), 1247 (s), 1222 (s), 1188 (m), 1131 (w), 1111 (w), 1060 (m), 1041 (s), 978 (s), 922 (m), 905 (m), 864 (s), 838 (s), 775 (m), 760 (m), 746 (s), 712 (w); MS, *m/z* (rel intensity) 303 (M^+, 0), 288 (M^+ -CH_3, 13), 216 (16), 203 (13), 202 (95), 160 (34), 158 (12), 148 (46), 130 (72), 115 (12), 103 (10), 102 (13), 77 (11), 76 (15), 75 (59), 74 (10), 73 (100), 59 (13), 56 (10), 55 (70). Anal. Calcd for $C_{17}H_{25}NO_2Si$: C, 67.28; H, 8.30; N, 4.62. Found C, 67.04; H, 8.26; N, 4.82.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-heptadecanone (1d). White solid; Mp 63 °C (1 mmHg); R_f = 0.46 (hexane/EtOAc = 5/1); ^1H NMR ($CDCl_3$) δ 0.88 (t, J = 6.4 Hz, 3H, CH_3CH_2), 1.20-1.30 (m, 26H, alkyl), 1.36 (s, 6H, $C(CH_3)_2$), 1.69 (c, 2H, $CH_2CH_2C(O)$), 2.76 (t, J = 7.6 Hz, 2H, $CH_2C(O)$), 4.06 (s, 2H, OCH_2), 7.33 (dd, J = 6.6, 2.0 Hz, 1H, Ph), 7.42-7.49 (m, 2H, Ph), 7.83 (dd, J = 6.6, 2.3 Hz, 1H, Ph); ^{13}C NMR ($CDCl_3$) δ 14.07 (CH_3CH_2), 22.64, 24.28 ($CH_2CH_2C(O)$), 28.12 ($C(CH_3)_2$), 29.18, 29.31, 29.44, 29.49, 29.62,

29.65, 31.88, 43.07 ($CH_2C(O)$), 68.09 ($C(CH_3)_2$), 79.50 (OCH_2), 125.52 (1-C or 2-C), 126.40, 129.45, 129.54, 130.73, 142.41 (1-C or 2-C), 161.31 (C=N), 206.00 (CO); IR (KBr) 2962 (s), 2927 (s), 2852 (s), 1699 (s), 1651 (s), 1597 (m), 1577 (w), 1471 (s), 1442 (m), 1405 (m), 1355 (m), 1335 (m), 1315 (m), 1299 (m), 1281 (m), 1257 (w), 1237 (w), 1218 (m), 1201 (m), 1178 (m), 1160 (w), 1125 (w), 1093 (w), 1069 (w), 1051 (m), 1042 (s), 999 (w), 988 (m), 967 (m), 919 (w), 868 (w), 819 (w), 779 (s), 755 (m), 735 (m), 721 (m); MS, *m/z* (rel intensity) 427 (M^+, 0.5), 216 (15), 203 (15), 202 (100), 160 (11), 148 (12), 130 (26), 55 (17). Anal. Calcd for $C_{28}H_{45}NO_2$: C, 78.64; H, 10.61; N, 3.28. Found C, 78.30; H, 10.79; N, 3.24.

1-[3-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-4-(1-oxopropyl)phenyl]-1-hexanone (3). Colorless oil; Bp countless; R_f = 0.12 (hexane/EtOAc = 5/1); ^1H NMR ($CDCl_3$) δ 0.93 (t, *J* = 6.9 Hz, 3H, $CH_3CH_2CH_2CH_2CH_2C(O)$), 1.21 (t, *J* = 7.3 Hz, 3H, $CH_3CH_2C(O)$), 1.37 (s, 6H, $C(CH_3)_2$), 1.38 (c, 4H, $CH_2CH_2CH_2CH_2C(O)$), 1.70 (c, 2H, $CH_2CH_2C(O)$), 2.78 (q, *J* = 7.3 Hz, 2H, $CH_3CH_2C(O)$), 2.99 (t, *J* = 7.3 Hz, 2H, $CH_2C(O)$), 4.10 (s, 2H, OCH_2), 7.37 (d, *J* = 7.9 Hz, 1H, 5-H), 8.06 (dd, *J* = 8.1, 1.8 Hz, 1H, 6-H), 8.37 (d, *J* = 1.7 Hz, 1H, 2-H); ^{13}C NMR ($CDCl_3$) δ 8.21 ($CH_3CH_2C(O)$), 13.91 ($CH_3CH_2CH_2CH_2CH_2C(O)$), 22.46 ($CH_2CH_2CH_2CH_2C(O)$), 23.72 ($CH_2CH_2C(O)$), 28.11 ($C(CH_3)_2$), 31.38 ($CH_2CH_2CH_2C(O)$), 36.50 ($CH_3CH_2C(O)$), 38.73 ($CH_2C(O)$), 68.41 ($C(CH_3)_2$), 79.59 (OCH_2), 125.68, 126.56 (5-C), 128.95 (2-C), 130.19 (6-C), 137.63, 146.20, 160.22 (C=N), 199.14 ($CH_2C(O)$), 206.20 ($CH_3CH_2C(O)$); IR (neat) 2968 (s), 2936 (s), 2874 (m), 1693 (s), 1656 (s), 1607 (w), 1567 (w), 1464 (m), 1409 (s), 1352 (s), 1315 (s), 1213 (s), 1189 (s), 1085 (m), 1051 (s), 1016 (m), 966 (s), 952 (s), 880 (w), 835 (w), 801 (w), 758 (m), 703 (w); MS, *m/z* (rel intensity) 329 (M^+, 0), 314 (M^+ -CH_3, 21), 301 (14), 300 (77), 258 (17), 246 (18), 228 (18), 129 (13), 103 (11), 75 (11), 57 (21), 56 (11), 55 (100). Anal. Calcd for $C_{20}H_{27}NO_3$: C, 72.92; H, 8.26; N, 4.25. Found C, 72.76; H, 8.39; N, 4.36.

1-[3-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-1-hexanone (4). Colorless oil; Bp countless; R_f = 0.22 (hexane/EtOAc = 5/1); ^1H NMR ($CDCl_3$) δ 0.92 (t, *J* = 6.9 Hz, 3H, $CH_3CH_2CH_2CH_2CH_2C(O)$), 1.37 (c, 4H, $CH_2CH_2CH_2CH_2C(O)$), 1.41 (s, 6H, $C(CH_3)_2$), 1.75 (c, 2H, $CH_2CH_2C(O)$), 3.01 (t, *J* = 7.4 Hz, 2H, $CH_2C(O)$), 4.15 (s, 2H, OCH_2), 7.51 (t, *J* = 7.8 Hz, 1H, 5-H), 8.07 (d, *J* = 7.9 Hz, 1H, 4-H or 6-H), 8.13 (d, *J* = 7.6 Hz, 1H, 4-H or 6-H), 8.47 (s, 1H, 2-H); ^{13}C NMR ($CDCl_3$) δ 13.93 ($CH_3CH_2CH_2CH_2CH_2C(O)$), 22.50 ($CH_2CH_2CH_2CH_2C(O)$), 23.79

($CH_2CH_2C(O)$), 23.38 ($C(CH_3)_2$), 31.43 ($CH_2CH_2CH_2C(O)$), 38.65 ($CH_2C(O)$), 67.82 ($C(CH_3)_2$), 79.25 (OCH_2), 127.80, 128.64, 130.44, 132.38, 137.25, 161.29 (C=N), 199.89 (CO); IR (neat) 2966 (s), 2934 (s), 2872 (m), 1692 (s), 1652 (s), 1607 (m), 1580 (m), 1465 (m), 1439 (m), 1354 (m), 1321 (m), 1248 (m), 1189 (s), 1083 (m), 1060 (m), 990 (m), 968 (m), 923 (w), 879 (w), 809 (m), 715 (s); MS, *m/z* (rel intensity) 273 (M^+, 9), 258 (48), 230 (10), 217 (19), 203 (15), 202 (100), 174 (18), 129 (20), 103 (19), 102 (16), 76 (19), 75 (10), 57 (13), 55 (21). Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found C, 74.50; H, 8.59; N, 5.37.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-ethanone (5a). Colorless oil; Bp 130-135 °C (4 mmHg); R_f = 0.23 (hexane/EtOAc = 5/1); ^1H NMR ($CDCl_3$) δ 1.38 (s, 6H, $C(CH_3)_2$), 2.52 (s, 3H, $CH_3C(O)$), 4.09 (s, 2H, OCH_2), 7.41-7.51 (m, 3H, Ph), 7.79-7.82 (m, 1H, Ph); ^{13}C NMR ($CDCl_3$) δ 28.07 ($C(CH_3)_2$), 30.17 ($CH_3C(O)$), 68.14 ($C(CH_3)_2$), 79.62 (OCH_2), 125.95 (1-C or 2-C), 126.74, 129.60, 130.08, 130.76, 141.78 (1-C or 2-C), 161.51 (C=N), 202.80 (CO); IR (neat) 2974 (m), 2930 (w), 2898 (w), 1703 (s), 1653 (s), 1597 (m), 1575 (m), 1465 (m), 1354 (s), 1312 (s), 1270 (m), 1242 (s), 1213 (m), 1188 (m), 1128 (m), 1086 (m), 1047 (s), 966 (m), 922 (m), 871 (w), 818 (w), 776 (m), 759 (m); MS, *m/z* (rel intensity) 217 (M^+, 1), 203 (13), 202 (100), 187 (11), 160 (12), 148 (12), 146 (13), 131 (46), 130 (36), 128 (32), 103 (14), 102 (19), 77 (14), 76 (20), 55 (16), 51 (17), 50 (17). Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 7.07. Found: C, 71.82; H, 7.07; N, 6.43.

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-2-phenyl-ethanone (5b). Yellow oil; R_f = 0.25 (hexane/EtOAc = 5/1); ^1H NMR ($CDCl_3$) δ 1.38 (s, 6H, $C(CH_3)_3$), 4.10 (s, 2H, OCH_2), 4.13 (s, 2H, $PhCH_2C(O)$), 7.17-7.31 (m, 6H, Ph), 7.44 (m, 2H, Ph), 7.88 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$) δ 28.16 ($C(CH_3)_2$), 49.90 (CH_2Ph), 68.18 ($C(CH_3)_3$), 79.37 ($CH_2C(O)$), 125.05, 126.72, 126.81, 128.36, 129.27, 129.51, 129.95, 130.69, 134.14, 141.96, 160.84 (C=N), 203.31 (CO); IR (neat) 2972 (s), 2932 (s), 2898 (m), 1947 (w), 1706 (s), 1653 (s), 1597 (s), 1576 (m), 1499 (s), 1457 (s), 1403 (m), 1385 (s), 1353 (s), 1313 (s), 1246 (s), 1215 (s), 1191 (m), 1122 (m), 1057 (s), 1041 (s), 1005 (s), 990 (s), 966 (s), 923 (m), 870 (m), 819 (m), 775 (s), 756 (s), 733 (s), 700 (s), 647 (w), 601 (m); MS, *m/z* (rel intensity) 293 (M^+, 4), 202 (67), 160 (27), 148 (39), 131 (10), 130 (100), 102 (21), 91 (17), 76 (13), 65 (12), 55 (45); exact mass calcd for $C_{19}H_{19}NO_2$ 293.1427, found for 293.1389

1-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)phenyl]-3,3-dimethyl-1-butanone (5c). Colorless oil; Bp 135-140 °C (1 mmHg); R_f = 0.31 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.03 (s, 9H, $C(CH_3)_3$), 1.38 (s, 6H, $C(CH_3)_2$), 2.74 (s, 2H, $CH_2C(O)$), 4.06 (s, 2H, OCH_2), 7.36-7.48 (m, 3H, Ph), 7.78-7.81 (m, 1H, Ph); ^{13}C NMR ($CDCl_3$) δ 28.12 ($C(CH_3)_2$), 29.74 ($C(CH_3)_3$), 31.36 ($C(CH_3)_3$), 54.79 ($CH_2C(O)$), 68.14 ($C(CH_3)_2$), 79.53 (OCH_2), 125.98 (1-C or 2-C), 126.86, 129.63, 129.67, 130.67, 143.20 (1-C or 2-C), 161.72 (C=N), 204.65 (CO); IR (neat) 2962 (s), 2872 (m), 1711 (s), 1656 (s), 1597 (m), 1576 (w), 1481 (m), 1466 (m), 1385 (m), 1364 (s), 1351 (s), 1312 (s), 1264 (m), 1230 (m), 1182 (m), 1121 (w), 1072 (m), 1057 (m), 1043 (m), 1007 (m), 988 (m), 966 (m), 911 (m), 870 (w), 818 (w), 770 (m), 744 (w); MS, *m/z* (rel intensity) 273 (M^+, 0), 258 (M^+ -CH_3, 8), 216 (17), 203 (13), 202 (100), 186 (47), 160 (27), 148 (39), 146 (11), 131 (14), 130 (83), 104 (12), 103 (12), 102 (24), 77 (11), 76 (19), 57 (28), 56 (21), 55 (55). Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.58; H, 8.70; N, 5.19.

1,1'-[2-(4,5-Dihydro-4,4-dimethyl-2-oxazolyl)-1,3-phenylene]-bis-3,3-dimethyl-1-butanone (6). Dark green oil; Bp countless; R_f = 0.31 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 18H, $C(CH_3)_3$), 1.38 (s, 6H, $C(CH_3)_2$), 2.78 (s, 4H, $CH_2C(O)$), 4.09 (s, 2H, OCH_2), 7.51-7.61 (m, 3H, Ph); ^{13}C NMR ($CDCl_3$) δ 27.53 ($C(CH_3)_2$), 29.74 ($C(CH_3)_3$), 31.52 ($C(CH_3)_3$), 53.73 ($CH_2C(O)$), 80.07 (OCH_2), 129.04, 129.69, 142.97, 202.66 (CO); IR (neat) 2960 (s), 2908 (s), 2874 (s), 1695 (s), 1576 (m), 1481 (m), 1467 (s), 1387 (s), 1366 (s), 1349 (s), 1298 (s), 1251 (m), 1212 (m), 1181 (m), 1097 (s), 1047 (s), 988 (m), 963 (m), 920 (w), 870 (w), 818 (w), 760 (m), 708 (m); MS, *m/z* (rel intensity) 371 (M^+, 0), 356 (M^+- CH_3, 13), 300 (36), 284 (12), 244 (13), 173 (10), 172 (15), 57 (100), 56 (10), 55 (38); exact mass calcd for $C_{19}H_{19}NO_2$ 371.2461, found for 371.2465.

2-[(1E)-3,3-Dimethyl-1-butenyl]pyridine (8). Colorless oil; Bp 75-80 °C (1 mmHg); R_f = 0.29 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 9H, $C(CH_3)_3$), 6.41 (d, J = 16.2 Hz, 1H, $CHC(CH_3)_3$), 6.77 (d, J = 15.8 Hz, 1H, PyC*H*), 7.08 (ddd, J = 7.3, 4.9, 1.1 Hz, 1H, 5-H), 7.26 (d, J = 7.6 Hz, 1H, 3-H), 7.60 (td, J = 7.6, 1.9 Hz, 1H, 4-H), 8.53 (d, J = 4.6 Hz, 1H, 6-H); ^{13}C NMR ($CDCl_3$) δ 29.33 ($C(CH_3)_3$), 33.46 ($C(CH_3)_3$), 121.11 (3-C), 121.47 (5-C), 124.85 ($CHC(CH_3)_3$), 136.41 (4-C), 146.29 (Py*C*H), 149.25 (6-C), 156.33 (2-C); IR (neat) 3048 (m), 3004 (m), 2962 (s), 2908 (s), 2868 (s), 1727 (m), 1651 (s), 1586 (s), 1567 (s), 1472 (s), 1432 (s), 1391 (m), 1364 (s), 1305 (m), 1267 (s), 1147 (m), 1091 (w), 1047 (m), 1023 (w), 977 (s), 943 (s), 921 (m), 887 (w),

854 (m), 766 (s), 741 (m), 638 (w), 613 (m), 534 (w); MS, *m/z* (rel intensity) 161 (M^+, 13), 160 (12), 147 (10), 146 (100), 144 (10), 132 (10), 131 (55), 130 (39), 118 (13), 117 (12), 93 (13), 78 (13), 77 (10), 65 (17), 52 (14), 51 (28), 50 (11); Anal. Calcd for $C_{11}H_{15}N$: C, 81.94; H, 9.38; N, 8.69. Found: C, 81.72; H, 9.20; N, 8.70.

3.5 References and Notes

(1) For a recent review on the cleavage of unreactive bonds, see: Murai, S. In *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S. Ed.; Springer: Berlin, 1999. For reviews on the cleavage of C-C bonds, see: Rybtchinski, B.; Milstein, D. *Angew. Chem. Int. Ed.* **1999**, *38*, 870. Jennings, P. W.; Johnson, L. L. *Chem. Rev.* **1994**, *94*, 2241. For reviews on the cleavage of C-H bonds, see: Shilov, A. E.; Shul'pin, G. B. *Chem. Rev.* **1997**, *97*, 2879. For a review on the cleavage of C-F bonds, see: Kiplinger, J. L.; Richmond, T. G.; Osterberg, C. E. *Chem. Rev.* **1994**, *94*, 373.

(2) Kakiuchi, F.; Sato, T.; Tsujimoto, T.; Yamauchi, M.; Chatani, N.; Murai, S. *Chem. Lett.* **1998**, 1053 and reference cited therein.

(3) Fukuyama, T.; Chatani, N.; Tatsumi, J.; Kakiuchi, F. Murai, S. *J. Am. Chem. Soc.* **1998**, *120*, 11522 and reference cited therein.

(4) Lim, Y.-G.; Kim, Y. H.; Kang, J.-B. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2201 and reference cited therein.

(5) Dürr, U.; Heinemann, F. W.; Kisch, H. *J. Organomet. Chem.* **1997**, *541*, 307 and reference cited therein.

(6) For a recent review fucused on catalytic reactions involving the cleavage of C-C bonds, see: Murakami, M.; Ito, Y. In *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S. Ed.; Springer: Berlin, 1999; pp. 97-129.

(7) Baba, A.; Oshiro, Y.; Agawa, T. *J. Organomet. Chem.* **1976**, *110*, 121.

(8) (a) Murakami, M.; Amii, H.; Ito, Y. *Nature* **1994**, *370*, 540. (b) Murakami, M.; Amii, H.; Shigeto, K.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 8285. (c) Murakami, M.; Takahashi, K.; Amii, H.; Ito, Y. *J. Am. Chem. Soc.* **1997**, *119*, 9307. (d) Murakami, M.; Itahashi, H.; Amii, H.; Ito, Y. *J. Am. Chem. Soc.* **1998**, *120*, 9949.

(9) Huffman, M. A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 4895.

(10) Kaneda, K.; Azuma, H.; Wayaku, M.; Teranishi, S. *Chem. Lett.* **1974**, 215.

(11) Suggs, J. W.; Jun, C.-H. *J. Chem. Soc., Chem. Commun.* **1985**, 92.

(12) Jun, C.-H.; Lee, H. *J. Am. Chem. Soc.* **1999**, *121*, 880.

(13) Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1997**, *62*, 2604.

(14) The reaction of **5a** under an atmosphere of nitrogen at 160 °C in toluene in a 8-mL screw-capped vial also resulted in decarbonylation to give **2** in ca.60% yield.

(15) The reaction of cyclopropylketone under same reaction condition also gave **2** and diketone **6** in 58% and 18% yields respectively.

(16) Tanaka, H.; Abdul Hai, A. K. M.; Sadakane, M.; Okumoto, H.; Torii, S. *J. Org. Chem.* **1994**, *59*, 3040.

(17) Other possibility to form $PhCH_2C(O)OMe$ is the direct methanolysis of intermediate **III**.

(18) The reaction of benzene with diphenylketene in the presence of $Rh_4(CO)_{12}$ resulted in the addition of the C-H bond in benzene to the ketene to give diphenylmethyl phenyl ketone. Hong, P.; Yamazaki, H.; Sonogashira, K.; Hagihara, K. *Chem. Lett.* **1978**, 535. Yamazaki, H.; Hong, P. *J. Mol. Catal.* **1983**, *21*, 133.

(19) For a review on decarbonylation, see: Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. Carbonylation; Plenum: New York, 1991; Chapter 11.

(20) Suggs, J. W.; Jun, C.-H. *J. Am. Chem. Soc.* **1984**, *106*, 3054. Suggs, J. W.; Cox, S. D. *J. Organomet. Chem.* **1981**, *221*, 199. Suggs, J. W.; Jun, C.-H. *J. Am. Chem. Soc.* **1986**, *108*, 4679. Jun, C.-H.; Kang, J.-B.; Lim, Y.-G. *Tetrahedron Lett.* **1995**, *36*, 277. Jun, C.-H. *Organometallics* **1996**, *15*, 895.

(21) Chatani, N.; Ishii, Y.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Org. Chem.* **1998**, *63*, 5129.

(22) Evans, P. A.; Nelson, J. D.; Stanley, A. L. *J. Org. Chem.* **1995**, *60*, 2298.

Conclusion

In this thesis, ruthenium-catalyzed direct carbonylation at C-H bonds in the benzene ring and ruthenium-catalyzed decarbonylative cleavage of C-C bonds in alkyl phenyl ketones are discussed. The results in each chapter of this thesis are summarized as follows.

The ruthenium-catalyzed carbonylation of pyridylbenzenes occur exclusively at *ortho* C-H bonds in the benzene ring. Chapter 1 gives a detailed discussion of this reaction. It represents the first, effective catalytic carbonylation reaction involving the cleavage of a benzene C-H bond. Not only steric factors but also electronic factors of substituents control the efficiency of the reaction. The reaction is also applicable to naphthyl, thiophenyl and furanyl rings. Six-membered heterocycles such as 2-pyrimidine and 4-pyrimidine, are also effective directing groups for carbonylation at a C-H bond in the benzene ring.

Ruthenium-catalyzed reaction of 2-phenyloxazolines with CO and olefins are discussed in Chapter 2. It demonstrates that an oxazoline ring can also be an effective directing group in the direct carbonylation at a C-H bond in the benzene ring. The wide range of functional compatibility would be advantageous for organic synthesis. The H/D labeling experiment shows that the cleavage of a C-H bond is not the rate-determining step.

In Chapter 3, a new catalytic reaction, which involves the ruthenium-catalyzed decarbonylative cleavage of a C-C bond in alkyl phenyl ketones, is described. It is interesting to note that the presence of a directing group, such as oxazoline or pyridine, is critical for the decarbonylation reaction to proceed. The alkyl moieties in the alkyl aryl ketones are converted into olefins, or ketenes if the formation of olefins are not possible for steric reasons. A key feature is the utilization of the chelation of nitrogen to ruthenium, which assists in the formation of a metallacycle during the cleavage of the C-C bond.

Present studies of these new catalytic reactions, namely the carbonylation at C-H bonds in the benzene ring and the decarbonylative cleavage of C-C bond in alkyl phenyl ketones, may offer a new efficient method involving the cleavage of unreacted bonds and will undoubtedly be an important and a rewarding area for organic syntheses and homogeneous catalysis.

List of Publications

The contents of this thesis are composed of the following papers.

(1) $Ru_3(CO)_{12}$-Catalyzed Reaction of Pyridylbenzenes with Carbon Monoxide and Olefins. Carbonylation at a C-H Bond in the Benzene Ring
Naoto Chatani, Yutaka Ie, Fumitoshi Kakiuchi, and Shinji Murai
J. Org. Chem. **1997**, *62*, 2604.

(2) $Ru_3(CO)_{12}$-Catalyzed Decarbonylative Cleavage of a C-C Bond of Alkyl Phenyl Ketones.
Naoto Chatani, Yutaka Ie, Fumitoshi Kakiuchi, Shinji Murai
J. Am. Chem. Soc. **1999**, *121*, 8645.

(3) Direct Carbonylation at a C-H Bond in the Benzene Ring of 2-Phenyloxazolines Catalyzed by $Ru_3(CO)_{12}$. Scope and Limitations and Mechanistic Aspects
Yutaka Ie, Naoto Chatani, Takashi Ogo, Daniel R. Marshall, Fumitoshi Kakiuchi, and Shinji Murai
J. Org. Chem. in press.

Supplementary List of Publications

(1) $Ru_3(CO)_{12}$- and $Rh_4(CO)_{12}$-Catalyzed Reactions of Pyridylolefins or *N*-(2-Pyridyl)enamines with CO and Olefins. Carbonylation at Olefinic C-H Bonds
Naoto Chatani, Yutaka Ishii, Yutaka Ie, Fumitoshi Kakiuchi, and Shinji Murai
J. Org. Chem. **1998**, *63*, 5129.

(2) A New Benchmark for the Non-Enzymatic Enantioselective Acylation of Amines. Use of a Planar-Chiral Derivative of 4-Pyrrolidinopyridine as the Acylating Agent
Yutaka Ie, Gregory C. Fu
Chem. Commun., in press.