Direct Carbonylation at a C−H Bond in the Benzene Ring of 2-Phenyloxazolines Catalyzed by $Ru_3(CO)_{12}$. Scope, Limitations, and Mechanistic Aspects

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The ruthenium-catalyzed carbonylation at a C−H bond in the benzene ring of a 2-phenyloxazoline is described. The reaction of 2-phenyloxazolines with CO and ethylene in toluene in the presence of a catalytic amount of $Ru_3(CO)_{12}$ resulted in propionylation at an ortho C−H bond in the benzene ring. The presence of the oxazoline ring on the benzene ring is essential for the carbonylation to proceed. Other heterocycles, such as oxazine, oxazole, and thiazoline rings, also served as acceptable directing groups as did the oxazoline ring. A wide functional group compatibility was observed. The site selectivity of the carbonylation was examined using meta-substituted phenyloxazolines. It was found that the carbonylation took place exclusively at the less-hindered C−H bond, irrespective of the nature of substituents, indicating that the site selectivity was determined by steric factors. The reaction was also applicable, not only to a benzene ring, but also to naphthyl and thiophenyl rings. Olefins such as propene and trimethylvinylsilane in place of ethylene could also be used in the carbonylation reaction, while other olefins, such as 1-hexene, *tert*-butylethylene, vinylcyclohexane, isoprene, 1,5-hexadiene, cyclohexene, 1,5-cyclooctadiene, styrene, methyl acrylate, vinyl acetate, allyltrimethylsilane, and triethoxyvinylsilane did not afford the coupling products. An equilibrium between 2-phenyloxazolines, carbon monoxide, and olefins exists on one hand and the corresponding ketones on the other hand, and product composition is governed by the equilibrium thermodynamics of the system. The results of deuterium labeling experiments suggest that the catalysis involves a reversible C−H bond cleavage and that the rate-determining step is not the cleavage of a C−H bond. The results of kinetic study of the effects of CO pressure show that the reaction rate accelerates with decreasing CO pressure.

Introduction

Considering attention has been focused on the development of the transition-metal-catalyzed reactions which involve the cleavage of an unactivated C−H bond with respect to their potential use in organic synthesis.[1] Since the utilization of an unactivated C−H bond as a functional group has been the least studied, the study of C−C bond formation via C−H bond cleavage would lead to a new category of chemistry. Recently, a number of examples of the catalytic addition of a C−H bond to olefins[2−12] and acetylenes[13,14] has been investigated for their potential utility. In contrast, there has been only limited success in finding carbonylation reactions which involve C−H bond cleavage. This process, however, would represent useful synthetic routes for aromatic carbonyl compounds directly from simple aromatic derivatives. 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.[18−20]

We have already reported the $Ru_3(CO)_{12}$-catalyzed reaction of 2-pyridylbenzenes with CO and ethylene leading to ortho-propionylation products (eq 1).[21] 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

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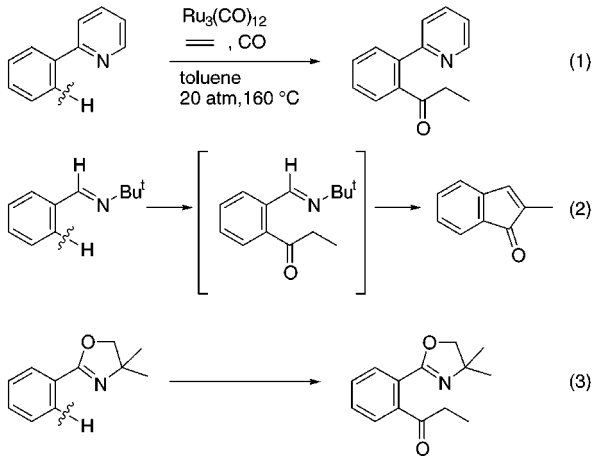
indicated that an effective directing group is required for the direct carbonylation at a C−H bond to take place.[22] In fact, the reaction of benzene, toluene, and anisole gave no carbonylation product at all. The coordination of the directing group to ruthenium brings the metal into close proximity 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.[23] 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 which were formed via intramolecular aldol-type reaction of the expected propionylation products in situ (eq 2).[24] Another candidate is an oxazoline ring, which is easily available from carboxylic acids and readily converted to carboxylic acids, esters, and aldehydes.[25] We now report 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. We further describe the full details concerning the scope and limitation of the reaction, and discuss the reaction mechanism.



Results

Carbonylation under CO Pressure. The reaction was run under the same reaction conditions as those used for the carbonylation of pyridylbenzenes.[21] 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**

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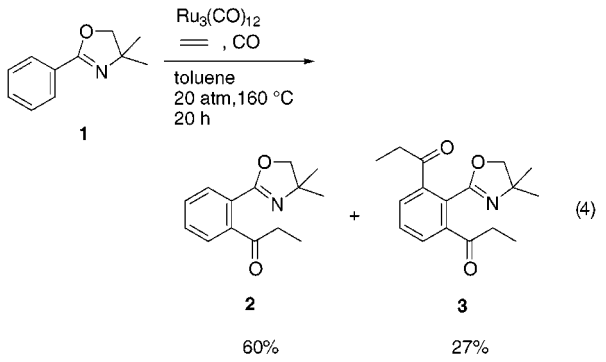
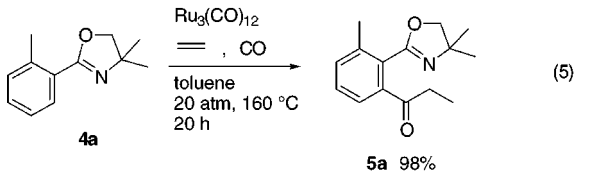
after column chromatography on silica gel (eq 4). The presence of the geminal dimethyl group on the oxazoline ring was critical for the success of this reaction. In fact, the reaction of 2-phenyloxazoline with no substituent at the 4-position on the oxazoline ring could not be stopped at the carbonylation 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,[22] 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.



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.



Prior to surveying a range of substrates, kinetic studies were conducted.[26] 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.

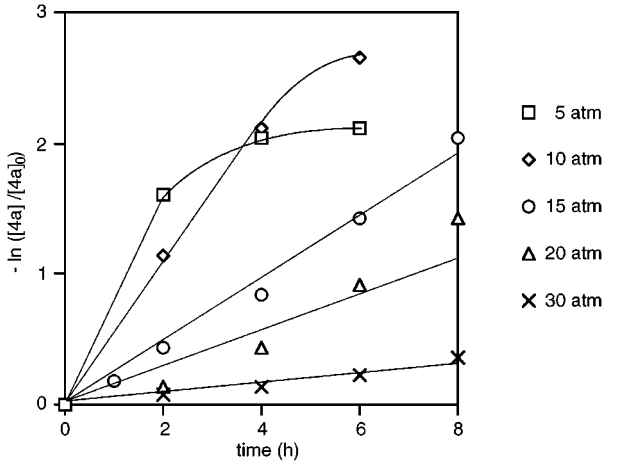


Figure 1. First-order rate plots for the reaction of **4a** (2 mmol) with CO and ethylene (7 atm) in the presence of $Ru_3(CO)_{12}$ (0.05 mmol) in toluene at 160 °C.

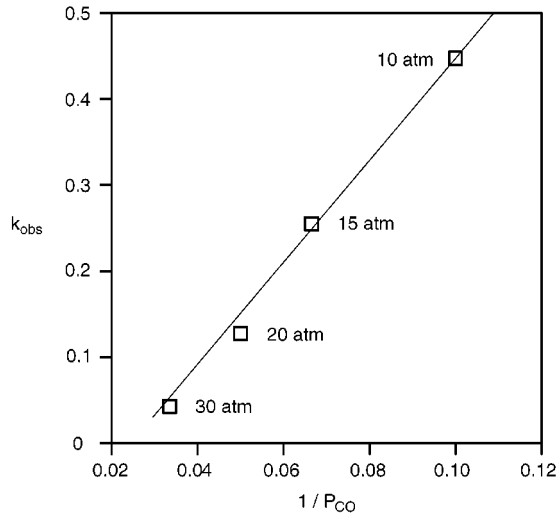


Figure 2. Plot of the first-order rate constant (k_{obs}) *vs*. $1/P_{CO}$ for the carbonylation of **4a**.

Carbonylation under 1 atm 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.[27] In an attempt to decrease the pressure of CO to 1 atm, 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

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

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

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

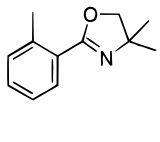
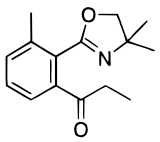
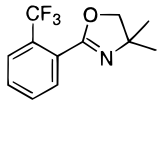
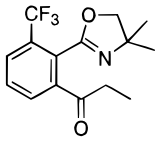
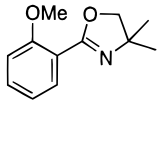
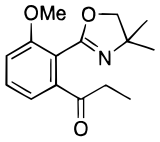
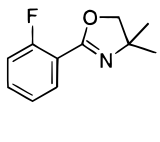
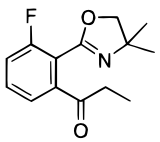
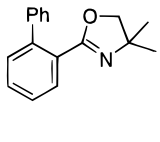
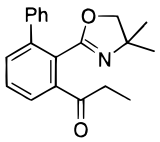
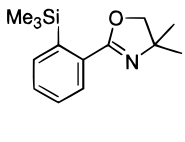
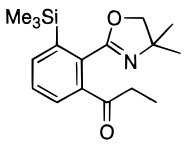
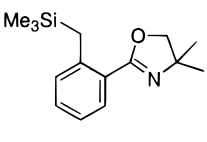
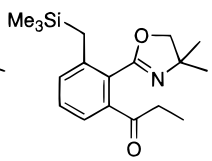
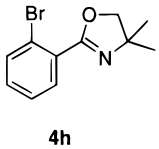
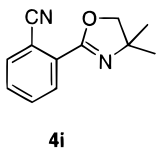
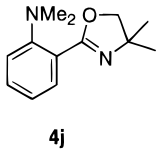
entry	$Ru_3(CO)_{12}$	temp.	solvent	yield of **5a** [b]
1	0.05 mmol	160 °C	toluene	36 %[c]
2		120 °C		66 %
3			THF	56 %
4			*N,N*-dimethylacetamide	68 %
5			DME	70 %
6			CH_3CN	89 %
7	0.1 mmol	120 °C	CH_3CN	98 %
8		100 °C		91 %
9		80 °C		17 %

[a] Reaction conditions: **4a** (2 mmol), ethylene (initial pressure 7 atm at rt), CO (iniital 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.

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).

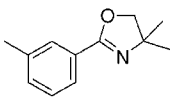
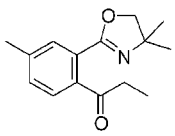
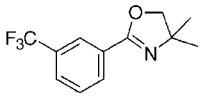
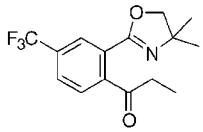
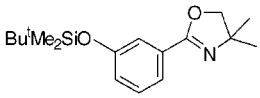
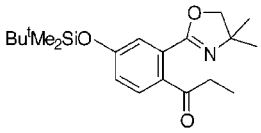
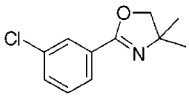
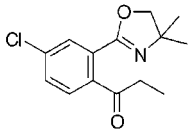
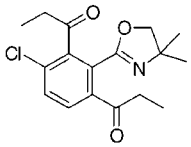
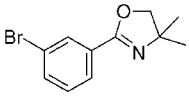
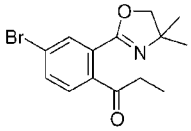
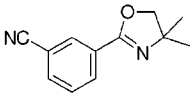
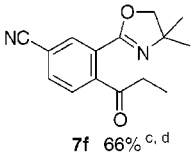
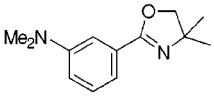
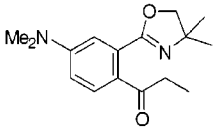
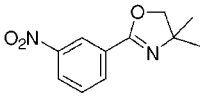
Carbonylation of Substituted 2-Phenyloxazolines. To examine functional group compatibility, a variety of ortho-substituted phenyloxazolines were treated with CO and ethylene (Table 2). The replacement of a methyl group with a trifluoromethyl group decreased the yield to 53%, along with 39% of the starting 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,[28] **5f** and **5g** would be expected to be amenable to further exploitation. In the case of *o*-bromo- **4h** or *o*-cyano-substituted oxazoline **4i**, carbonylation did not take place under the reaction conditions, and the starting materials were recovered (entries 8 and 9). The oxidative addition of the C−Br bond to ruthenium or the bidentate coordination of sp^2 nitrogen

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%
8	 **4h**	n.r.		
9	 **4i**	n.r.		
10	 **4j**	complicated		

[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 reactor 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]

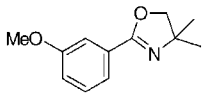
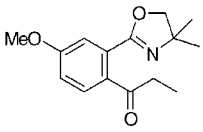
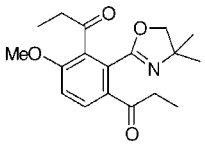
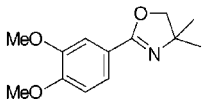
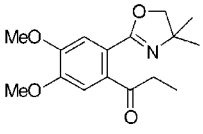
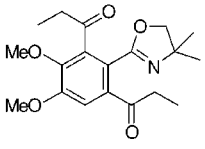
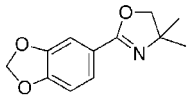
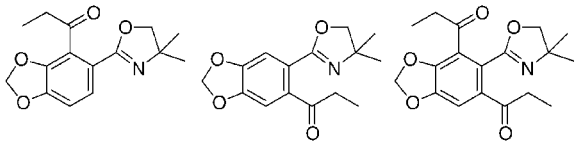
entry	2-phenyloxazolines	time	products [b]
1	 **6a**	20 h	 **7a** 91%
2	 **6b**	40 h	 **7b** 73% [c]
3	 **6c**	40 h	 **7c** 61%
4	 **6d**	40 h	 **7d** 74%  **8d** 9%
5	 **6e**	40 h	 **7e** 80%
6	 **6f**	20 h	 **7f** 66% [c, d]
7	 **6g**	40 h	 **7g** 57% [e]
8	 **6h**	20 h	n.r.

[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.

and a cyano group to ruthenium may have prevented **4h** or **4i** from undergoing cleavage of the C−H bonds, respectively. The reaction of 2-phenyloxazolines containing an *N*,*N*-dimethylamino group gave complex mixtures (entry 10).

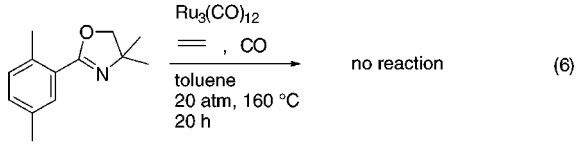
It would be interesting to study the substituents at the meta position, since two different C−H bonds are present. Table 3 lists the representative results obtained from the reaction of meta-substituted phenyloxazolines with CO and ethylene. When the reaction of 4,4-dimethyl-2-(3-methylphenyl)-2-oxazoline (**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 dicarbonylation 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.[21] 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, despite one remaining C−H bond at the ortho position (eq 6). The reaction of the chloro-isomer **6d** gave two products, the monocarbonylation product **7d** in 74%

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: 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 ^1H NMR.

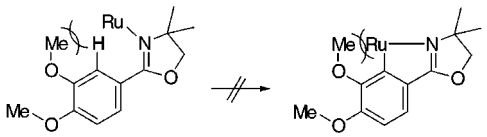
and dicarbonylation product **8d** in 9% yield (entry 4). However, the replacement of a chlorine atom by a bromine atom dramatically improved the selectivity, and the ketone **7e** was obtained as the sole product (entry 5). These results also show that the selectivity is controlled by steric factors. 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 (**4h** and **4i**) did not react completely (entries 8 and 9 in Table 2). 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).[29] 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).



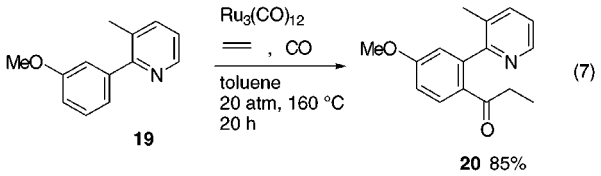
8

The reactivities of 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 monocarbonylation product **10** in 48% yield, along with its regioisomer (structure not shown) in 1% yield and the dicarbonylation product **11** in 46% yield (entry 1). We were interested in the position of the first carbonylation, at the hindered or less hindered C−H bond, when **11** was formed. As

Chart 1



we have already reported, the reaction of 2-(3-methoxyphenyl)-3-methylpyridine (**19**) gave the monocarbonylation product **20**, apparently indicating the exclusive cleavage of the less hindered C−H bond (eq 7).[21] From



19 **20** 85%

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 monocarbonylation product **13** was obtained in 72% yield and the dicarbonylation product **14** in 12% yield (entry 2). The observed improvement in site selectivity can be explained by a buttressing effect,[30] 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).[31] The result was not unexpected, since the acetal substituent is smaller than

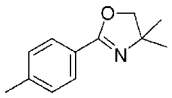
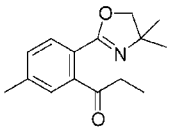
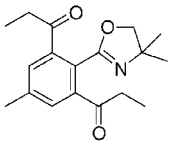
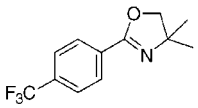
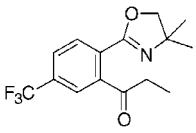
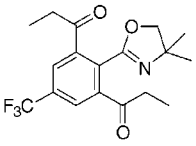
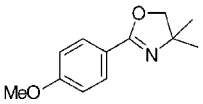
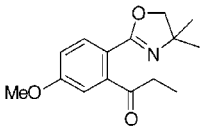
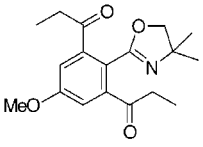
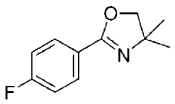
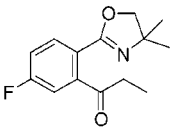
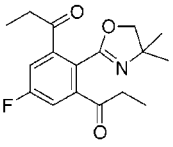
(28) For reviews, see: Colvin, E. W. *Silicon in Organic Synthesis*; Butterworth: London, 1981. Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: New York, 1983.

(29) In case of aromatic imines bearing a CF_3 group, ortho-ethylation product was obtained in 3%. See also ref 24.

(30) Kiplinger, J. L.; Richmond, T. G.; Osterberg, C. E. *Chem. Rev.* **1994**, *94*, 373. Similar phenomena were observed in our group. See ref 3.

(31) 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.

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

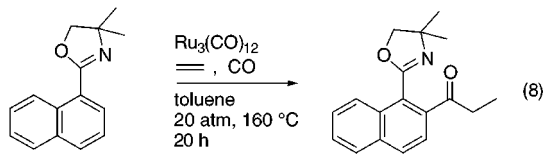
entry	2-phenyloxazolines	products [b]	
1	 **21a**	 **22a** 38%	 **23a** 47%
2	 **21b**	 **22b** 44%	 **23b** 16%
3	 **21c**	 **22c** 21%	 **23c** 73%
4	 **21d**	 **22d** 33%	 **23d** 41%

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

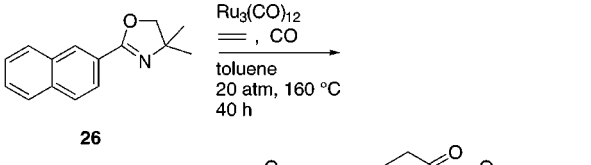
a methoxy group and the acetal oxygen also could coordinate to the ruthenium center.[32]

The results of para-substituted phenyloxazolines are shown in Table 5. In all cases, mixtures of the monocarbonylation and the dicarbonylation 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 dicarbonylation 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 monocarbonylation product preferentially (entry 2). The electron-donating substituents should have made the oxazoline-nitrogen a better coordinating group toward the ruthenium so that the second carbonylation took place prior to the dissociation of the monocarbonylation product from the ruthenium.[33] In the case of pyridylbenzenes, the product distribution is also controlled by electronic effects of substituents on a benzene or a pyridine ring.[21]

We 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 dicarbonylation 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 dicarbonylation product was not obtained in the reaction of β-naphthylpyridine, even after 40 h of reaction.[21] 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)



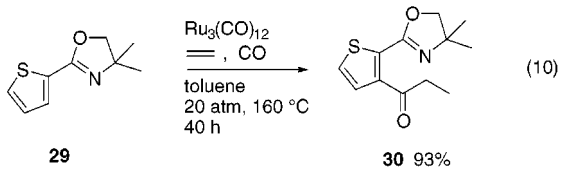
26 **27** 64% + **28** 17% (9)

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)-

(32) The similar effect was observed in Ru-catalyzed C−H/olefin coupling phenomena. See ref 3.

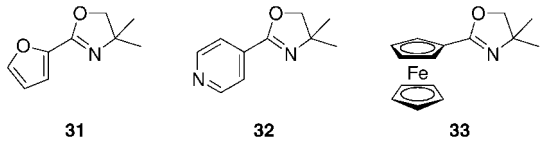
(33) A similar phenomena was observed in the reaction of acetophenone with vinylsilane. Thus, some parts of the second cleavage of C−H bonds take place without decomplexation of the carbonyl group from ruthenium throughout the reaction. See ref 2b, 2c.

oxazoline **29** gave the corresponding ethyl ketone **30** in high yield (eq 10).



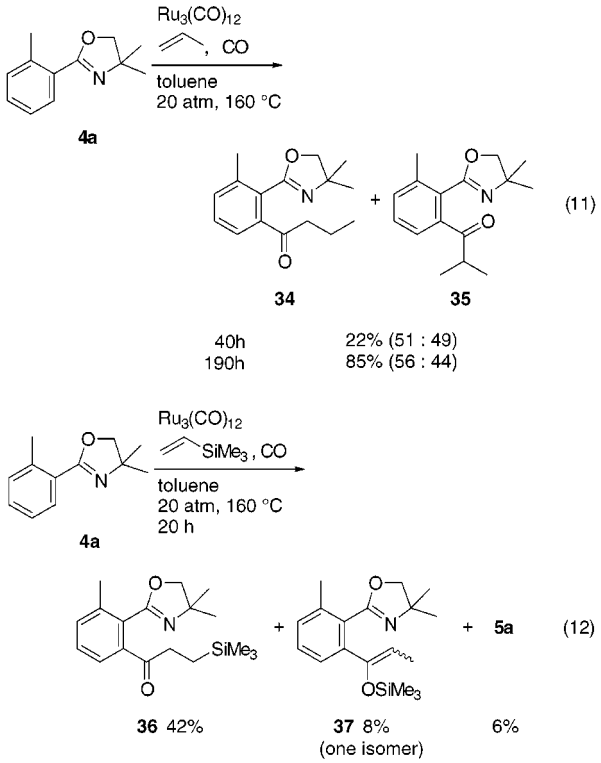
29 **30** 93% (10)

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**

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 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

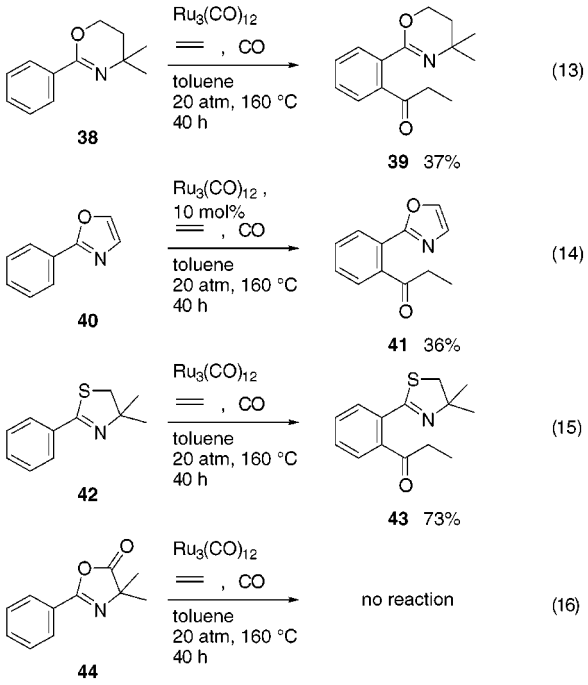


(11)

(12)

37 would be formed via silyl migration from carbon to oxygen in the branched isomer, α-silyl ketone.[34,35] The minor product **5a** appears to be formed by the reaction **4a** with CO and ethylene, which is generated in situ from the vinylsilane.[36] Reactions of **4a** with CO and olefins, such as 1-hexene, *tert*-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.

We 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, we were 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 monocarbonylation product **41** was obtained, with 54% of recovery of **40** (eq 14). A 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 monocarbonylation 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 monocarbonylation 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 (eq 16).



(13)

(14)

(15)

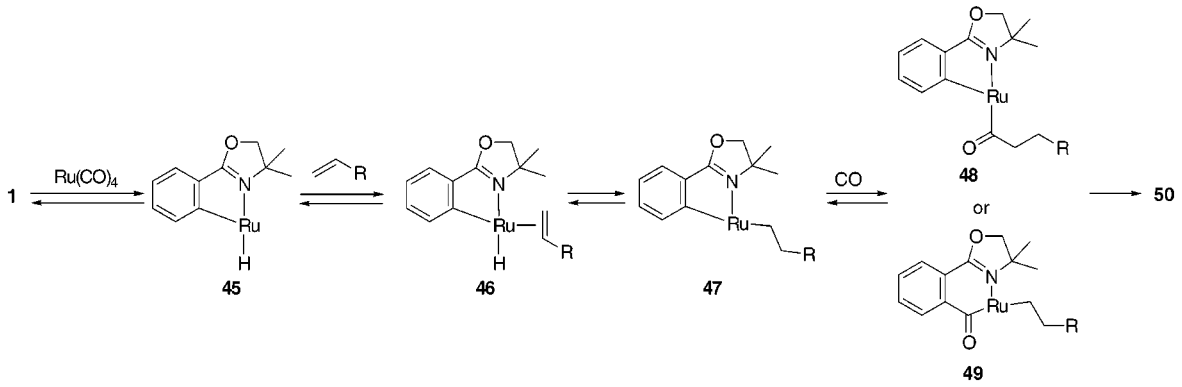
(16)

Deuterium Labeling Experiment. We carried out the reaction using phenyloxazoline-d_5 (**1**-d_5), to obtain information concerning the reaction mechanism. Triethoxyvinylsilane was selected as an olefin for this deuterium labeling experiment. The reaction was run at

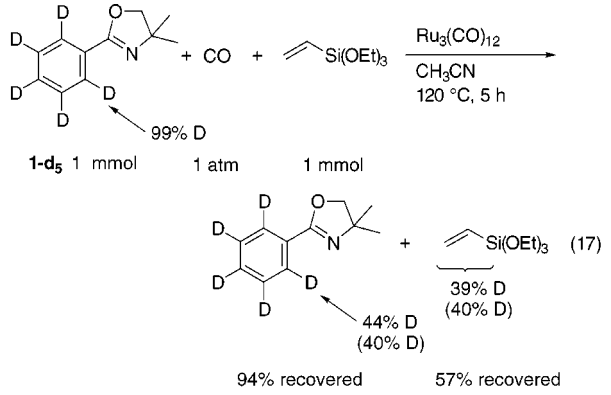
(34) MacRae studied the thermal isomerization of α-silyl ketones to enol silyl ethers in detail. Brook, A. G.; MacRae, D. M.; Bassindale, A. R. *J. Organomet. Chem.* **1975**, *86*, 185.

(35) 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 22b.

Scheme 1



120 °C under 1 atm of CO, to avoid the conversion of triethoxyvinylsilane to ethylene and disilylethylene.[36] The reaction of **1**-d_5 (1 mmol) with CO (initial pressure 1 atm at 25 °C in 50-mL stainless autoclave) and 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 17). 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 parentheses. The moderate yield of the recovered triethoxyvinylsilane was due to loss during purification by distillation. The mechanism based on these data will be discussed later.[37]



Discussion

The structure of the catalytically active species is poorly understood. To date we 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), we followed Laine's kinetic criteria.[38] Using this criteria, the turnover frequency decreases with increasing catalyst concentration which indicates that fragment catalytic species are responsible for the catalysis. A plot of turnover frequency vs $Ru_3(CO)_{12}$ concentration was constructed (see Supporting Information). 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,[21] 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,[39] while no report of a stoichiometric reaction of **1** with $Ru_3(CO)_{12}$ has yet appeared. The intermediancy of the cyclometalated complex,[40] 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**.

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.

(36) 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. See also ref 21.

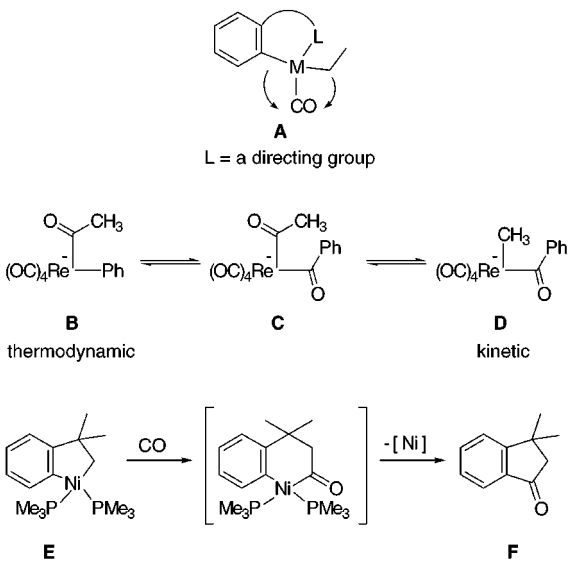
(37) The reaction of **1**-d_5 with CO and ethylene was also run (equation not shown). After 2 h, a 75% of **1**-d_5 was recovered, along with a 16% of **4a**. In this case, the deuterium atoms of recovered **1**-d_5 were also scrambled at the ortho position, which occurred 6% incorporation of protio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

(38) Laine, R. M. *J. Mol. Catal.* **1982**, *14*, 137.

(39) 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.

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

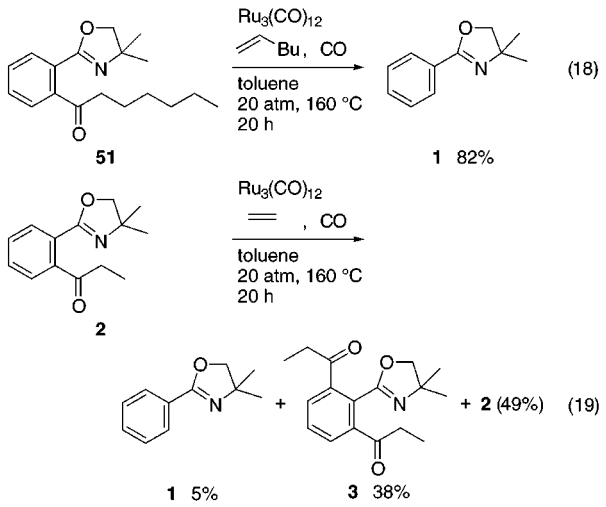
Scheme 2



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, we found that the reactivity of the substrates corresponds to the pK_a values of the conjugated acids.[17] While the pK_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 pK_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. 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,[41] 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**.[42] 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).[43] In both examples, the thermodynamically favored complexes involve an aryl−metal bond and alkyl−C(O)−metal bond. We 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.[44] 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.

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 dicarbonylation product, **3**, in 38% yield and a 49% recovery of **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.[45] 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**.



Conclusion

We 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-

(41) 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.
(42) Casey, C. P.; Scheck, D. M. *J. Am. Chem. Soc.* **1980**, *102*, 2723.
(43) Campora, J.; Gutierrez, E.; Monge, A.; Palma, P.; Poveda, M. L.; Ruiz, C.; Carmona, E. *Organometallics* **1994**, *13*, 1728.
(44) Chatani, N.; Ie, Y.; Kakiuchi, F.; Murai, S. *J. Am. Chem. Soc.* **1999**, *121*, 8645.
(45) This value was calculated by the difference of standard enthalpy of formation between ethylene (16.2 kcal/mol) and 1-hexene (20.8 kcal/mol).

determining step. The carbonylation reaction rate followed first-order kinetics as a function of $1/P_{co}$. Additional studies are currently underway to investigate and explore further applications of the chelation-assisted carbonylation to other catalytic systems.

Experimental Section

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**) was purchased from Aldrich Chemical Co. Substituted 2-aryloxazolines (**4a**−**j**, **6a**−**h**, **8**, **9**, **12**, **15**, **21a**−**d**, **24**, **26**, **29**, **31**, **32**, **33**), 2-phenyloxazines (**38**), and phenylthiazoline (**42**) were obtained by corresponding substituted benzoyl chlorides and amino alcohols or thioalcohol according to Meyers procedure.[25] 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 was equipped with capillary column CBP-10 (25 m × 0.2 mm). Typical initial CO pressure was in the range of 5−30 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), 1.36 (s, 6H), 2.78 (q, J = 7.3 Hz, 2H), 4.07 (s, 2H), 7.30−7.33 (m, 1H), 7.42−7.52 (c, 2H), 7.82−7.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 8.27, 28.00, 36.23, 67.98, 79.34, 125.25, 126.15, 129.20, 129.38, 130.67, 142.32, 161.01, 206.49; IR (neat) 1704, 1651; MS, *m*/*z* (rel intensity) 231 (M^+, 0), 216 ($M^+ - CH_3$, 20), 130 (100). 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), 1.34 (s, 6H), 2.86 (q, J = 7.3 Hz, 4H), 4.07 (s, 2H), 7.52−7.58 (c, 3H); ^{13}CNMR ($CDCl_3$) δ 8.02, 27.46, 35.29, 68.25, 79.91, 124.98, 128.27, 129.88, 141.98, 160.52, 204.04; IR (KBr) 1702, 1659; MS, *m*/*z* (rel intensity) 287 (M^+, 0), 272 ($M^+ - CH_3$, 25), 57 (100). 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), 1.40 (s, 6H), 2.42 (s, 3H), 2.89 (q, J = 7.3 Hz, 2H), 4.12 (s, 2H), 7.33−7.35 (c, 2H), 7.45−7.49 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 8.20, 19.37, 27.93, 34.14, 67.93, 79.32, 124.94, 127.71, 129.25, 132.94, 138.45, 139.78, 161.78, 203.22; IR (neat) 1700, 1667; MS, *m*/*z* (rel intensity) 245 (M^+, 1), 144 (100). 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), 1.36 (s, 3H), 2.92 (q, J = 7.3 Hz, 2H), 4.16 (s, 2H), 7.62 (t, J = 7.9 Hz, 1H), 7.77 (d, J = 7.3 Hz, 1H), 7.82 (d, J = 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.77, 27.28, 34.76, 68.12, 80.02, 123.10 (q, J = 274.7 Hz), 126.63, 128.23 (q, J = 4.9 Hz), 129.85, 130.06, 130.35 (q, J = 31.8 Hz), 141.69, 159.23, 202.28; IR (neat) 1706, 1667; MS, *m*/*z* (rel intensity) 299 (M^+, 0), 284 ($M^+ - CH_3$, 29), 55 (100). 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); ^{1}H NMR ($CDCl_3$) δ 1.17 (t, J = 7.3 Hz, 3H), 1.38 (s, 6H), 2.89 (q, J = 7.3 Hz, 2H), 3.85 (s, 3H), 4.13 (s, 2H), 7.05 (d, J = 8.6 Hz, 1H), 7.23 (d, J = 7.9 Hz, 1H), 7.43 (t, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.07, 27.80, 34.25, 56.34, 67.71, 79.34, 114.00, 117.61, 119.52, 130.80, 140.83, 158.36, 159.86, 202.55; IR (neat) 1698, 1671; MS, *m*/*z* (rel intensity) 261 (M^+, 0), 246 ($M^+ - CH_3$, 24), 232 ($M^+ - CH_2CH_3$, 100). 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); ^{1}H NMR ($CDCl_3$) δ 1.19 (t, J = 7.3 Hz, 3H), 1.40 (s, 6H), 2.88 (q, J = 7.3 Hz, 2H), 4.13 (s, 2H), 7.23 (d, J = 9.2 Hz, 1H), 7.39 (d, J = 7.9 Hz 1H), 7.44−7.52 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 7.98, 27.80, 34.54, 68,11, 79.44, 116.15 (d, J = 15.9 Hz), 118.47 (d, J = 21.9 Hz), 122.92 (d, J = 3.7 Hz), 131.53 (d, J = 8.6 Hz), 141.83, 157.45, 160.74 (d, J = 253.9 Hz), 202.03; IR (neat) 1700, 1673; MS, *m*/*z* (rel intensity) 249 (M^+, 0), 234 ($M^+ - CH_3$, 27), 55 (100). 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); ^{1}H NMR ($CDCl_3$) δ 1.14 (s, 6H), 1.20 (t, J = 7.3 Hz, 3H), 2.96 (q, J = 7.3 Hz, 2H), 3.85 (s, 2H), 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, 27.32, 34.38, 67.60, 79.39, 126.16, 127.21, 127.46, 127.82, 128.75, 129.31, 132.44, 139.78, 139.93, 143.06, 161.37, 203.04; IR (neat) 1699, 1667; MS, *m*/*z* (rel intensity) 307 (M^+, 18), 306 (100). 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); ^{1}H NMR ($CDCl_3$) δ 0.32 (s, 9H), 1.17 (t, J = 7.3 Hz, 3H), 1.38 (s, 6H), 2.89 (q, J = 7.3 Hz, 2H), 4.11 (s, 2H), 7.39−7.47 (c, 2H), 7.66 (dd, J = 6.8, 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.15, 8.07, 27.94, 35.22, 68.12, 79.41, 126.94, 128.61, 132.49, 136.44, 140.88, 141.58, 162.61, 205.28; IR (neat) 1707, 1656; MS, *m*/*z* (rel intensity) 303 (M^+, 0), 288 ($M^+ - CH_3$, 28), 274 ($M^+ - CH_2CH_3$, 100). 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); ^{1}H NMR ($CDCl_3$) δ −0.01 (s, 9H), 1.16 (t, J = 7.3 Hz, 3H), 1.39 (s, 6H), 2.39 (s, 2H), 2.86 (q, J = 7.3 Hz, 2H), 4.06 (s, 2H), 7.18 (m, 1H), 7.29−7.31 (c, 2H); ^{13}C NMR ($CDCl_3$) δ −1.45, 8.18, 23.90, 27.98, 34.27, 67.94, 78.92, 123.15, 125.54, 128.82, 131.61, 140.63, 141.78, 161.74, 203.81; IR (neat) 1704, 1666; MS, *m*/*z* (rel intensity) 317 (M^+, 5), 73 (100). 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); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, J = 7.3 Hz, 3H), 1.36 (s, 6H), 2.39 (s, 3H), 2.76 (q, J = 7.3 Hz, 2H), 4.06 (s, 2H), 7.27 (s, 2H), 7.64 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 8.43, 21.03, 28.07, 35.94, 67.93, 79.50, 125.73, 126.65, 130.05, 131.25, 139.19, 140.07, 161.71, 206.00; IR (KBr) 1693, 1645; MS, *m*/*z* (rel intensity) 245 (M^+, 0), 230 ($M^+ - CH_3$, 19), 216 ($M^+ - CH_2CH_3$, 100). 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), 1.36 (s, 6H), 2.77 (q, J = 7.3 Hz, 2H), 4.10 (s, 2H), 7.39 (d, J = 7.9 Hz, 1H), 7.75 (d, J = 7.9 Hz, 1H), 8.14 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 8.11, 28.02, 36.57, 68.47, 79.61, 123.29 (q, J = 272.6 Hz), 125.88, 126.30 (q, J = 3.7 Hz), 126.65, 127.54 (q, J = 3.6 Hz), 131.49 (q, J = 33.4 Hz), 145.82, 159.59, 205.73; IR (KBr) 1694; MS, *m*/*z* (rel intensity) 299 (M^+, 0), 284 ($M^+ - CH_3$, 13), 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), 0.98 (s, 9H), 1.18 (t, J = 7.3 Hz, 3H), 1.36 (s, 6H), 2.77 (q, J = 7.3 Hz, 2H), 4.07 (s, 3H), 6.90 (dd, J = 8.4, 2.5 Hz, 1H), 7.20 (d, J = 2.3 Hz, 1H), 7.33 (d, J = 8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ −4.44, 8.59, 18.12, 25.54, 28.05, 35.56, 68.07, 79.53, 121.22, 121.51, 128.27, 128.75, 134.65, 157.16, 161.49, 204.87; IR (neat) 1698, 1654; MS, *m*/*z* (rel intensity) 361 (M^+, 0), 346 ($M^+ - CH_3$, 14), 73 (100). 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), 1.35 (s, 6H), 2.75 (q, J = 7.3 Hz, 2H), 4.08 (s, 2H), 7.26 (d, J = 7.6 Hz, 1H), 7.45 (dd, J = 8.3, 2.0 Hz, 1H), 7.83 (d, J = 2.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.32, 28.07, 36.34, 68.30, 79.64, 127.19, 127.78, 129.40, 130.75, 135.62, 140.56, 160.05, 205.44; IR (neat) 1705, 1653; MS, *m*/*z* (rel intensity) 265 (M^+, 0), 250 ($M^+ - CH_3$, 11), 55 (100). 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), 1.21 (t, J = 7.3 Hz, 3H), 1.31 (s, 6H), 2.81 (q, J = 7.3 Hz, 2H), 2.94 (q, J = 7.3 Hz, 2H), 4.00 (s, 2H), 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), 1.35 (s, 6H), 2.75 (q, J = 7.3 Hz, 2H), 4.08 (s, 2H), 7.19 (d, J = 8.3 Hz, 1H), 7.62 (dd, J = 7.9, 2.0 Hz, 1H), 8.00 (d, J = 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.30, 28.07, 36.34, 68.30, 79.64, 123.61, 127.26, 127.87, 132.26, 133.73, 141.04, 159.91, 205.52; IR (neat) 1704, 1652; MS, *m*/*z* (rel intensity) 310 (M^+, 0), 294 ($M^+ - CH_3$, 11), 100 (13). 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), 1.35 (s, 6H), 2.76 (q, J = 7.3 Hz, 2H), 4.10 (s, 6H), 7.37 (d, J = 7.9 Hz, 1H), 7.77 (dd, J = 7.8, 1.5 Hz, 1H), 8.17 (d, J = 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.02, 27.98, 36.53, 68.52, 79.64, 113.33, 117.31, 126.16, 126.85, 132.79, 134.07, 146.36, 158.83, 205.23; IR (neat) 1704, 1657; MS, *m*/*z* (rel intensity) 256 (M^+, 0), 241 ($M^+ - CH_3$, 26), 55 (100). 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), 1.42 (s, 6H), 2.81 (q, J = 7.3 Hz, 2H), 3.04 (s, 6H), 4.11 (s, 2H), 6.66 (dd, J = 8.9, 2.6 Hz, 1H), 6.88 (d, J = 2.6 Hz, 1H), 7.58 (d, J = 8.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.92, 28.09, 33.52, 40.06, 67.71, 79.68, 111.81, 112.97, 126.38, 129.97, 130.31, 151.73, 163.97, 201.44; IR (KBr) 1688, 1603; MS, *m*/*z* (rel intensity) 274 (M^+, 9), 173 (100). 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), 1.39 (s, 6H), 2.78 (q, J = 7.3 Hz, 2H), 3.87 (s, 3H), 4.09 (s, 2H), 6.98 (dd, J = 8.6, 2.6 Hz, 1H), 7.26 (d, J = 2.6 Hz, 1H), 7.42 (d, J = 8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.57, 28.03, 35.33, 55.55, 68.02, 79.61, 114.39, 116.30, 128.46, 128.99, 133.75, 160.74, 161.87, 204.31; IR (KBr) 1694, 1650; MS, *m*/*z* (rel intensity) 261 (M^+, 0), 246 ($M^+ - CH_3$, 12), 55 (100). 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), 1.17 (t, J = 7.3 Hz, 3H), 1.32 (s, 6H), 2.84 (q, J = 7.3 Hz, 2H), 2.89 (q, J = 7.3 Hz, 2H), 3.87 (s, 3H), 4.03 (s, 2H), 6.98 (d, J = 8.9 Hz, 1H), 7.65 (d, J = 8.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 7.33, 8.45, 27.48, 34.00, 37.68, 55.99, 68.11, 79.77, 111.54, 126.85, 130.06, 132.24, 133.53, 157.66, 160.54, 201.38, 205.48; IR (neat) 1707, 1667; MS, *m*/*z* (rel intensity) 317 (M^+, 11), 288 ($M^+ - CH_2CH_3$, 100). 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), 1.36 (s, 6H), 2.74 (q, J = 7.3 Hz, 2H), 3.91 (s, 3H), 3.95 (s, 3H), 4.05 (s, 2H), 6.83 (s, 1H), 7.30 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 8.43, 27.94, 36.14, 55.85, 55.94, 67.78, 79.23, 109.42, 111.52, 118.33, 135.42, 149.38, 150.42, 161.02, 205.71; IR (KBr) 1699, 1651; MS, *m*/*z* (rel intensity) 291 (M^+, 0), 276 ($M^+ - CH_3$, 43), 55 (100). 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), 1.29 (s, 6H), 2.77 (q, J = 7.3 Hz, 2H), 2.81 (q, J = 7.3 Hz, 2H), 3.82 (s, 3H), 3.92 (s, 3H), 3.97 (s, 2H), 6.93 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 7.46, 8.29, 27.64, 35.62, 37.74, 55.99, 61.67, 68.23, 79.48, 110.91, 115.81, 138.49, 138.54 146.00, 153.69, 159.37, 204.22, 204.87; IR (KBr) 1711, 1662; MS, *m*/*z* (rel intensity) 347 (M^+, 0), 332 ($M^+ - CH_3$, 18), 318 ($M^+ - CH_2CH_3$, 100). 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], [1.32 (s, **16**), 1.36 (s, **17**), 6H], [2.71 (q, J = 7.3 Hz, **17**), 2.80 (q, J = 7.3 Hz, **16**), 2H], 4.01 (s, 2H, **16**), 4.04 (s, 2H, **17**), 6.04 (s, 2H, **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**)], 28.03, [36.26 (**16**), 37.29 (**17**)], 67.81, [79.21 (**16**), 79.41 (**17**)], 102.01, 106.96, 108.45, 109.24, 119.28, 123.97, 119.28, 123.97, 144.29, 149.79, 160.52, 202.64; IR (neat) 1712, 1651, 1627; MS, *m*/*z* (rel intensity) **16**: 275 (M^+, 1), 260 ($M^+ - CH_3$, 6), 174 (100). 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), 1.17 (t, J = 7.3 Hz, 3H), 1.31 (s, 6H), 2.79 (q, J = 7.3 Hz, 2H), 2.89 (q, J = 7.3 Hz, 2H), 4.03 (s, 2H), 6.11 (s, 2H), 7.00 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 8.08, 8.75, 27.93, 35.49, 37.59, 68.57, 80.34, 103 11, 114.02, 120.72, 132.17, 136.84, 149.43, 160.83, 201.28, 202.95; IR (neat) 1704; MS, *m*/*z* (rel intensity) 331 (M^+, 4), 302 ($M^+ - CH_2CH_3$, 100). 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), 1.34 (s, 6H), 2.39 (s, 3H), 2.75 (q, J = 7.3 Hz, 2H), 4.04 (s, 2H), 7.10 (s, 1H), 7.24 (d, J = 8.1 Hz, 1H), 7.73 (d, J = 7.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.39, 21.33, 28.12, 36.44, 67.98, 79.35, 122.41, 126.81, 129.31, 130.06, 141.28, 142.55, 161.13, 207.08; IR (neat) 1700, 1651; MS, *m*/*z* (rel intensity) 245 (M^+, 0), 230 ($M^+ - CH_3$, 30), 216 ($M^+ - CH_2CH_3$, 100). 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 °C (4 mmHg); R_f = 0.17 (hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.18 (t, J = 7.3 Hz, 6H), 1.33 (s, 6H), 2.42 (s, 3H), 2.83 (q, J = 7.3 Hz, 4H), 4.04 (s, 2H), 7.31 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 8.07, 21.28, 27.55, 35.47, 68.25, 79.82, 121.80, 128.70, 140.47, 142.28, 160.50, 204.58; IR (KBr) 1703, 1050; MS, *m*/*z* (rel intensity) 301 (M^+, 0), 286 ($M^+ - CH_3$, 28), 57 (100). 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 °C (4 mmHg); R_f = 0.19 (hexane/EtOAc = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.22 (t, J = 7.3 Hz, 3H), 1.36 (s, 6H), 2.80 (q, J = 7.3 Hz, 2H), 4.10 (s, 2H), 7.55 (s, 1H), 7.70 (d, J = 8.3 Hz, 1H), 7.97 (d, J = 8.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.16, 28.03, 36.48, 68.48, 79.64, 123.21 (q, J = 3.6 Hz), 123.28 (q, J = 272.6 Hz), 126.10 (q, J = 3.7 Hz), 128.57, 129.88, 132.68 (q, J = 33.4 Hz), 143.18, 159.82, 205.26; IR (KBr) 1710; MS, *m*/*z* (rel intensity) 299 (M^+, 0), 284 ($M^+ - CH_3$, 11), 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), 1.34 (s, 6H), 2.99 (q, J = 7.3 Hz, 4H), 4.08 (s, 2H), 7.76 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 7.80, 27.41, 35.47, 68.66, 80.15, 122.83 (q, J = 273.0 Hz), 124.71 (q, J = 3.6 Hz), 128.14, 132.15 (q, J = 33.4 Hz), 143.05, 159.26, 202.84; IR (KBr) 1706; MS, *m*/*z* (rel intensity) 355 (M^+, 0), 340 ($M^+ - CH_3$, 40), 55 (100). 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), 1.33 (s, 6H), 2.74 (q, J = 7.3 Hz, 2H), 3.84 (s, 3H), 4.03 (s, 2H), 6.76 (d, J = 2.6 Hz, 1H), 6.93 (dd, J = 8.6, 2.6 Hz, 1H), 7.79 (d, J = 8.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.38, 28.16, 36.61, 55.49, 67.93, 79.28, 111.61, 114.57, 117.31, 131.05, 144.49, 160.68, 161.42, 206.86; IR (neat) 1708, 1649; MS, *m*/*z* (rel intensity) 261 (M^+, 2), 232 ($M^+ - CH_2CH_3$, 100). 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), 1.31 (s, 6H), 2.80 (q, J = 7.3 Hz, 4H), 3.86 (s, 3H), 4.01 (s, 2H), 6.94 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 8.04, 27.59, 35.67, 55.67, 68.23, 79.66, 113.23, 115.92, 144.26, 160.02, 160.47, 204.58; IR (neat) 1709, 1661; MS, *m*/*z* (rel intensity) 317 (M^+, 2), 288 ($M^+ - CH_2CH_3$, 100). 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), 1.34 (s, 6H), 2.76 (q, J = 7.3 Hz, 2H), 4.06 (s, 2H), 6.99 (dd, J = 8.6, 2.6 Hz, 1H), 7.13 (td, J = 8.6, 2.6 Hz, 1H), 7.85 (dd, J = 8.6, 5.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.25, 28.09, 36.41, 68.20, 79.50, 113.59 (d, J = 23.2 Hz), 116.30 (d, J = 21.9 Hz), 121.32 (d, J = 3.7 Hz), 131.69 (d, J = 8.6 Hz), 144.94 (d, J = 7.3 Hz), 160.05, 163.76 (d, J = 253.9 Hz), 205.25; IR (neat) 1698, 1655; MS, *m*/*z* (rel intensity) 249 (M^+, 0), 234 ($M^+ - CH_3$, 25), 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), 1.33 (s, 6H), 2.83 (q, J = 7.3 Hz, 4H), 4.05 (s, 2H), 7.21 (d, J = 7.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 7.93, 27.50, 35.44, 68.41, 79.97, 115.32 (d, J = 23.2 Hz), 120.67, (d, J = 3.6 Hz), 144.65 (d, J = 6.1 Hz), 159.60, 162.61 (d, J = 255.2 Hz), 202.86; IR (KBr) 1704, 1658; MS, *m*/*z* (rel intensity) 305 (M^+, 0), 290 ($M^+ - CH_3$, 38), 55 (100). 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); ^{1}H NMR ($CDCl_3$) δ 1.22 (t, J = 7.3 Hz, 3H), 1.50 (s, 6H), 2.97 (q, J = 7.3 Hz, 4H), 4.21 (s, 2H), 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, 28.12, 34.86, 68.43, 79.43, 123.18, 125.52, 126.29, 127.53, 127.68, 127.94, 130.30, 131.14, 134.05, 137.83, 160.88, 203.88; IR (KBr) 1697, 1655; MS, *m*/*z* (rel intensity) 281 (M^+, 0), 252 ($M^+ - CH_2CH_3$, 97), 55 (100). 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); ^{1}H NMR ($CDCl_3$) δ 1.25 (t, J = 7.3 Hz, 3H), 1.40 (s, 6H), 2.88 (q, J = 7.3 Hz, 4H), 4.12 (s, 2H), 7.56−7.61 (c, 2H), 7.84 (s, 1H), 7.86−7.91 (m, 2H), 8.34 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 8.57, 28.12, 36.10, 68.12, 79.52, 123.11, 126.67, 127.73, 128.07, 128.28, 128.45, 130.17, 132.88, 133.41, 138.89, 161.46, 205.91; IR (neat) 1704, 1653, 1629; MS, *m*/*z* (rel intensity) 281 (M^+, 0), 266 ($M^+ - CH_3$, 25), 252 ($M^+ - CH_2CH_3$, 100). 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), 1.27 (t, J = 7.3 Hz, 3H), 1.36 (s, 6H), 2.91−3.01 (c, 4H), 4.06 (s, 2H), 7.59−7.68 (c, 2H), 7.91−7.94 (m, 2H), 8.01 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 7.51, 8.41, 27.73, 35.02, 38.78, 68.48, 79.73, 119.95, 125.16, 128.18, 128.81, 129.08, 129.38, 133.03, 137.43, 142.43, 160.31, 203.72, 207.26; IR (KBr) 1701, 1660; MS, *m*/*z* (rel intensity) 337 (M^+, 4), 308 (100). 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), 1.37 (s, 6H), 2.88 (q, J = 7.3 Hz, 2H), 4.10 (s, 2H), 7.15 (d, J = 5.0 Hz, 1H), 7.36 (d, J = 5.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.12, 28.00, 36.23, 68.27, 79.71, 127.84, 128.19, 129.56, 143.83, 156.86, 200.93; IR (neat) 1696, 1647; MS, *m*/*z* (rel intensity) 237 (M^+, 6), 136 (100). 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), 1.39 (s, 6H), 1.65−1.78 (m, 2H), 2.41 (s, 3H), 2.85 (t, J = 7.3 Hz, 2H), 4.12 (s, 2H), 7.33−7.38 (c, 2H), 7.46−7.49 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.68, 17.65, 19.30, 27.89, 42.73, 67.89, 79.26, 125.09, 127.78, 129.20, 132.96, 138.44, 139.78, 161.76, 202.66; IR (neat) 1694, 1667; MS, *m*/*z* (rel intensity) 259 (M^+, 0), 244 ($M^+ - CH_3$, 3), 216 ($M^+ - Pr$, 100). 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), 1.39 (s, 6H), 1.65−1.78 (m, 2H), 2.41 (s, 3H), 2.85 (t, J = 7.3 Hz, 2H), 4.12 (s, 2H), 7.33−7.38 (c, 2H), 7.46−7.49 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 18.69, 19.50, 27.96, 38.17, 67.96, 79.23, 124.69, 127.84, 129.18, 132.69, 138.49, 140.05, 161.65, 207.15; IR (neat) 1696, 1667; MS, *m*/*z* (rel intensity) 259 (M^+, 1), 216 ($M^+ - Pr$, 100). 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), 0.83−0.89 (m, 2H), 1.39 (s, 6H), 2.42 (s, 3H), 2.79−2.85 (m, 2H), 4.12 (s, 2H), 7.34−7.36 (c, 2H), 7.44−7.48 (m, 1H); ^{13}C NMR ($CDCl_3$) δ −1.81, 10.68, 19.43, 27.96, 35.58, 67.93, 79.30, 124.98, 127.76, 129.25, 132.90, 138.51, 139.73, 161.76, 203.59; IR (neat) 1697, 1669; MS, *m*/*z* (rel intensity) 317 (M^+, 0), 230 (16), 73 (100). 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), 1.55 (s, 6H), 1.67 (d, J = 7.0 Hz, 3H), 2.55 (s, 3H), 4.18 (s, 2H), 5.14 (q, J = 7.3 Hz, 1H), 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), 1.27 (s, 6H), 1.80 (t, J = 7.8 Hz, 2H), 2.83 (q, J = 7.3 Hz, 2H), 4.26 (t, J = 5.8 Hz, 2H), 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, 30.03, 34.00, 36.05, 49.08, 62.48, 126.15, 128.41, 129.36, 129.54, 132.44, 141.53, 153.10, 206.65; IR (neat) 1701, 1656; MS, *m*/*z* (rel intensity) 245 (M^+, 0), 230 ($M^+ - CH_3$, 17), 69 (100). 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 °C (1 mmHg); R_f = 0.27 (hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.21 (t, J = 7.3 Hz, 3H), 2.73 (q, J = 7.3 Hz, 2H), 7.24 (s, 1H), 7.33−7.37 (m, 1H), 7.47−7.55 (m, 2H), 7.70 (s, 1H), 7.96−8.00 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 8.23, 36.48, 123.92, 126.45, 128.10, 128.55, 129.63, 130.12, 138.94, 141.35, 160.25, 207.13; IR (neat) 1702; MS, *m*/*z* (rel intensity) 201 (M^+, 3), 172 (100). 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), 1.42 (s, 6H), 2.76 (q, J = 7.3 Hz, 2H), 3.23 (s, 2H), 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, 27.14, 36.48, 45.54, 79.39, 126.42, 129.40, 129.74, 130.30, 130.87, 141.89, 162.50, 206.76; IR (neat) 1704, 1611; MS, *m*/*z* (rel intensity) 247 (M^+, 0), 218 ($M^+ - CH_2CH_3$, 55), 55 (100). 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.

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Supporting Information Available: Full characterization data for all new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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