THE STUDY ON THE RUTHENIUM-CATALYZED CARBONYLATIVE CYCLOCOUPLING REACTIONS

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（ルテニウム触媒によるカルボニル化環化付加反応に関する研究）

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Preface

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. The thesis is concerned with the ruthenium-catalyzed carbonylative cyclocoupling reactions.

I would like to express his utmost gratitude to Professor Shinji Murai for his guidance, suggestion, and hearty encouragement throughout this work. I would like to express his deepest gratitude to Associate Professor Naoto Chatani for helpful suggestion and stimulating discussion.

I would like to acknowledge helpful discussion of Dr. Fumitoshi Kakiuchi and Dr. Yoshiya Fukumoto. I would like to express his gratitude to Associate Professor Kouichi Ohe and Dr. Sensuke Ogosshi for his kind help.

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Suita, Osaka

March 1999

Tsumoru Morimoto

List of Publications

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

(1) $Ru_3(CO)_{12}$-Catalyzed Cyclocarbonylation of 1,6-Enynes to Bicyclo[3.3.0]octenones
Tsumoru Morimoto, Naoto Chatani, Yoshiya Fukumoto, and Shinji Murai
J. Org. Chem. **1997**, *62*, 3762.

(2) $Ru_3(CO)_{12}$-Catalyzed Cyclocarbonylation of Yne-Aldehydes to Bicyclic α,β-Unsaturated γ-Butyrolactones
Naoto Chatani, Tsumoru Morimoto, Yoshiya Fukumoto, and Shinji Murai
J. Am. Chem. Soc. **1998**, *120*, 5335.

(3) $Ru_3(CO)_{12}$-Catalyzed Reaction of Yne-Imines with Carbon Monoxide Leading to Bicyclic α,β-Unsaturated Lactams
Naoto Chatani, Tsumoru Morimoto, Akihito Kamitani, Yoshiya Fukumoto, and Shinji Murai
J. Organomet. Chem. in press

(4) The First Catalytic Carbonylative [4+1] Cycloaddition to a 1,3-Conjugated System. A New Transformation of α,β-Unsaturated Imines to Unsaturated γ-Lactams Catalyzed by $Ru_3(CO)_{12}$
Tsumoru Morimoto, Naoto Chatani, and Shinji Murai
submitted for publication

Supplementary List of Publications

(1) Palladium-Catalyzed Reaction of Ketone α-Carbonates with Norbornenes. An Unusual Cyclopropanation

Sensuke Ogoshi, Tsumoru Morimoto, Ken-ichi Nishio, Kouichi Ohe, and Shinji Murai

J. Org. Chem. **1993**, *58*, 9.

(2) Preparation of Vinylgermanes and a Germole by the Pd-Catalyzed Reaction of Me_3GeCN with Acetylenes

Naoto Chatani, Tsumoru Morimoto, Toyoshige Muto, and Shinji Murai

J. Organomet. Chem. **1994**, *473*, 335.

(3) Nucleophilic Substitution at the Central Allyl Carbon Atom of a (π-Allyl)platinum Complex

Kouichi Ohe, Hideki Matsuda, Tsumoru Morimoto, Sensuke Ogoshi, Naoto Chatani, and Shinji Murai

J. Am. Chem. Soc. **1994**, *116*, 4125.

(4) Highly Selective Skeletal Reorganization of 1,6- and 1,7-Enynes to 1-Vinylcycloalkenes Catalyzed by $[RuCl_2(CO)_3]_2$

Naoto Chatani, Tsumoru Morimoto, Toyoshige Muto, and Shinji Murai

J. Am. Chem. Soc. **1994**, *116*, 6049.

Contents

General Introduction

Organic cycloaddition reactions are not only among the synthetically most useful reactions as a tool for the construction of cyclic sytems, but also among the theoretically and mechanistically best understood reactions.[1] Recently, the *organometallic* cycloaddition reactions also have been extensively studied.[2] Complexation of an olefin, a diene, or an acetylene, which can act as one component in the cycloaddition reaction, to a metal significantly modifies the reactivity of this moiety, opening the way for novel chemistry. Thus, the use of transition metal complexes in the reactions would provide new opportunities for highly efficient synthesis of the cyclic compounds.

The introduction of carbon monoxide as a one-carbon unit into the cycloaddition gives rise to the formation of cyclic carbonyl compounds. One of the most familiar examples is the Pauson-Khand reaction,[3] in which an alkyne, an alkene, and carbon monoxide undergo a formal [2+2+1] cycloaddition to form cyclopentenones. Use of this transformation would enable the construction of complex molecules in a convergent and efficient manner starting from structurally simple precursors. This strategy has been utilized for the synthesis of a wide variety of natural products and analogs,[4] although a stoichiometric amount of a transition metal complex is required. It is therefore not surprising that an increasing number of research groups are focusing on the further development of this reaction, especially on a catalytic process.[5]

The prime objective of this research is to develop new catalytic cycloaddition reactions using carbon monoxide as a one-carbon unit. The thesis consists of the following three chapters:

Chapter 1 deals with the ruthenium-catalyzed [2+2+1] cycloaddition reaction of enynes with carbon monoxide.

Chapter 2 deals with the ruthenium-catalyzed [2+2+1] cycloaddition reaction of yne-aldehydes with carbon monoxide.

Chapter 3 deals with the ruthenium-catalyzed [4+1] cycloaddition reaction of α,β-unsaturated imines with carbon monoxide.

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(5) Kim, J. W.; Chung, Y. K. *Synthesis* **1998**, 142 and references cited therein.

Chapter 1

Ruthenium-Catalyzed [2+2+1] Cycloaddition of Enynes with Carbon Monoxide

1.1 Introduction

The intramolecular Pauson-Khand reaction[1] is presently regarded as one of the most potent methods for the construction of bicyclo[3.3.0]octenones. While stoichiometric amounts of $Co_2(CO)_8$ were originally and generally used as the CO source,[1] several other metal carbonyl complexes such as $Fe(CO)_4$(acetone),[2] $W(CO)_5$(THF),[3] $W(CO)_5F^-$,[4] $Cr(CO)_5F^-$,[4] $Cp_2Mo_2(CO)_4$,[5] and $Mo(CO)_6$[6] have also been found to serve as a CO source in place of $Co_2(CO)_8$ for this reaction. In addition, a number of other different systems, such as Cp_2TiCl_2/CO,[7] Cp_2ZrCl_2/CO,[8] Cp_2TiCl_2/RNC,[7] Ni(COD)$_2$/PhNC,[9] $Cp_2Ti(PMe_3)_2$/R_3SiCN,[10] and Ni(COD)$_2$/$^iPr_3SiCN$[11] have been shown to be effective for the conversion of 1,6-enynes to bicyclo[3.3.0]octenone derivatives. In contrast to extensive studies of stoichiometric systems, no examples dealing with catalytic version of the intramolecular Pauson-Khand reaction have lately appeared. Recently, the catalytic versions have successively reported.[12-20] Jeong and coworkers reported that a catalytic reaction was attained in the case of $Co_2(CO)_8$/$P(OPh)_3$ (3-5 mol%/10-20 mol%) at 120 °C in an atmosphere of CO (4-5 atm).[12] Other cobalt-catalyzed systems, such as (indenyl)Co(COD), Co(acac)$_2$/$NaBH_4$,[13] and $Co_2(CO)_8$ in supercritical CO_2,[14] have also been reported, and Livinghouse reported a photochemical promotion using 10 mol% of $Co_2(CO)_8$ at 50-55 °C and 1 atm of CO pressure.[15] Chung reported that, under 150 °C and 10 atm of CO, the reaction of enynes was catalyzed by not only $Co_2(CO)_4$ but $Co_4(CO)_{12}$.[16] Furthermore, Sugihara reported $Co_3(CO)_9(\mu^3$-CH) also acted as a catalyst.[17] Buchwald reported that the treatment of enynes with a catalytic amount of $Cp_2Ti(CO)_2$ (5-20 mol%) in an atomosphere of CO (18 psig) gave rise to cyclopentenones.[18] Quite recently, Narasaka[19] and Jeong[20] reported the catalytic reactions of enynes at atmospheric CO using $[RhCl(CO)_2]_2$ and *trans*-$[RhCl(dppp)]_2$, respecttively. In this chapter, I describe the first use of a ruthenium

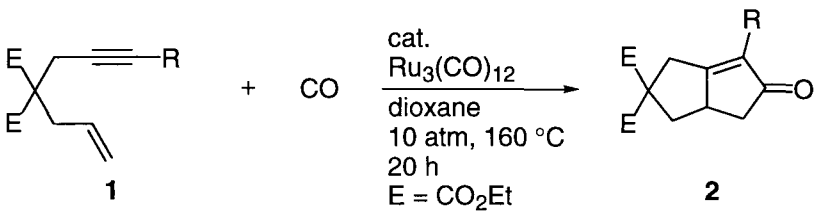
complex for a Pauson-Khand type reaction of enynes.[21] The new reaction appears to be catalytic in nature.

1.2 $Ru_3(CO)_{12}$-Catalyzed Cyclocarbonylation of 1,6-Enynes to Bicyclic Cyclopentenones

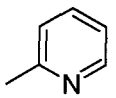
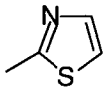
I initially examined the reaction of a trimethylsilyl-substituted enyne **1a**, because the silyl group can be converted into other functional groups in a variety of ways.[22] The reaction of **1a** (1 mmol) under 20 atm of CO at 160 °C in toluene in the presence of $Ru_3(CO)_{12}$ (0.02 mmol) for 20 h results in complete consumption of **1a** to give the 2-trimethylsilylbicyclo[3.3.0]octenone derivative **2a**[23] in 72% isolated yield, based on **1a**. When the reaction was run at 140 °C, the yield decreased to a 61% yield and 31% of **1a** was recovered. At 120 °C, no reaction observable occurred. The reaction is not as sensitive to CO pressure (20 atm 72% yield, 10 atm 70%, 5 atm 63%). Among the solvents examined (toluene 72%, cyclohexane 72%, $ClCH_2CH_2Cl$ 54%, CH_3OH 22%), dioxane (90% yield) or CH_3CN (86%) were the solvents of choice, when the reaction was run at 160 °C under 10 atm of CO for 20 h. This reaction represents the first use of $Ru_3(CO)_{12}$ as a catalyst for the cyclocarbonylation of enynes to cyclopentenones.

The reaction of phenyl-substituted enyne **1b** gave **2b** in 66% yield. Replacement of the phenyl group with a 2-pyridyl group, as in **1c**, led to higher yields. Although the $Co_2(CO)_8$-promoted Pauson-Khand reaction is known to tolerate a wide range of functionalities, no studies of reactions of enynes bearing pyridyl group have appeared, to my knowledge. The methyl-substituted enyne **1d** is also a reactive substrate and gave **2d** in 86% yield. The reaction of terminal alkyne **1e** gave **2e** in 47% yield, although **1e** was completely consumed. A decrease in reaction temperatures, shorter reaction times, and changing solvents failed to improve the yield of **2e**. The electron-deficient alkyne **1f** was, as anticipated, a poor substrate.[24] However, successful carbonylation of **1g** provides an alternative method for the preparation of bicyclo[3.3.0]octenone having a formyl or ester group at the 2-position.[25]

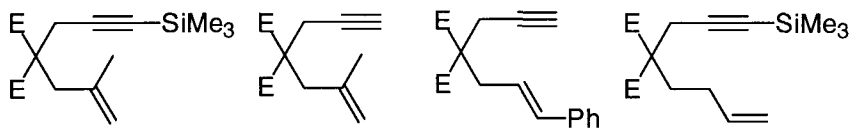
Scheme 1



1 2

1a:	R = $SiMe_3$	**2a:**	90%
1b:	R = Ph	**2b:**	66%
1c:	R = 	**2c:**	80%
1d:	R = Me	**2d:**	86%
1e:	R = H	**2e:**	47%
1f:	R = CO_2Et	**2f:**	0%
1g:	R = 	**2g:**	62%

The scope of the reaction with respect to the alkene is limited. This catalytic system lacks the ability to cyclocarbonylate 1,6-enynes containing substituted olefins and an 1,7-enyne, such as those shown below.

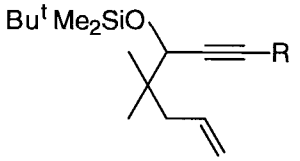
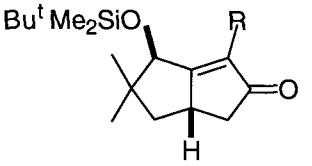
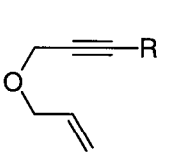
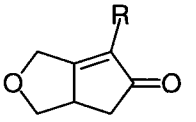
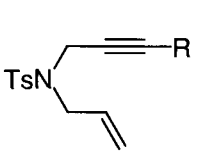
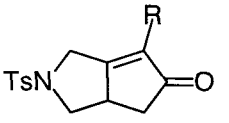


Some results for 1,6-enynes are shown in Table 1. The reaction of silyl-substituted enyne **3a** gave exclusively *cis*-**4a**, with no detectable *trans* isomer (entry 1). Magnus[26] observed a diastereomeric ratio of 26:1 of *cis*-**4a**:*trans*-**4a** for the $Co_2(CO)_8$-promoted cyclization of **3a** and Pearson[2b] observed a 13:1 ratio for a $Fe(CO)_5$-promoted reaction. The reaction of phenyl-substituted enyne **3b** gave **4b** in moderate yield with a high diastereosiomeric ratio (entry 2). When the reaction of **3c** was run at 140 °C, am improved yield was obtained (entry 4).[27] As shown by entries 1-3, it is clearly that the size of the group on the terminus of the acetylene has a controlling influence on the 1,3-diastereoselectivity.[28]

The reaction of an enyne having an oxygen atom in the tether **5a** afforded 2-timethylsilyl-7-oxabicylo[3.3.0]oct-1-en-3-one (**6a**) with significant efficiency (entry 5). The reaction of *N*-

ally-*N*-propargyl amides **7a** and **7b** gave the corresponding 7-azabicyclo[3.3.0]octenones **8a** and **8b** in nearly quantitative yield (entries 7 and 8). Introduction of a vinyl group into the siliy group had no effect on the yield (entry 8).

Table 1. Catalytic Cyclocarbonylation of 1,6-Enynes [a]

entry	enyne	product [b]
		
1	**3a:** R = $SiMe_3$	**4a** 65% (10:0)
2	**3b:** R = Ph	**4b** 44% (26:1)
3	**3c:** R = Me	**4c** 69% (2.4:1)
4	**3c**	**4c** 81% (1.5:1) [c]
		
5	**5a:** R = $SiMe_3$	**6a** 92%
6	**5b:** R = Ph	**6b** 57%
		
7	**7a:** R = $SiMe_3$	**8a** 95%
8	**7b:** R = $SiMe_2(CH{=}CH_2)$	**8b** 89%

[a] Reaction conditions: enyne (1 mmol), $Ru_3(CO)_{12}$ (0.02 mmol), dioxane (5 mL), CO (10 atm), 160 °C for 20 h. [b] Yields refer to chromatographically purified samples. Values in parentheses are the ratio of *cis*:*trans* isomers and were determined by GC analysis. [c] For a reaction at 140 °C.

While the exact course of this transformation is unclear, I propose that the reaction proceeds via a mechanism similar to the iron carbonyl promoted reaction.[2b] Thus, the reductive

cyclization of an enyne yields a metallacycle. The subsequent insertion of CO, and reductive elimination produce the cyclopentenone.

In summary, I have described the development of a $Ru_3(CO)_{12}$-catalyzed process for the transformation of 1,6-enynes to bicyclic cyclopentenones. The present reaction represents the first catalytic Pauson-Khand type reaction using a ruthenium complex as a catalyst. This transformation shows a high level of functional group compatibility, and the catalyst is commercially available and easily handled.

1.3 Experimental Section

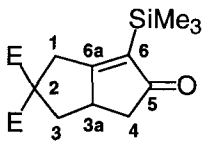
General Information. ^1H NMR and ^{13}C NMR were recorded on a JEOL JMN-270 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), coupling 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 instrument with ionization voltages of 70 eV. Elemental analyses were performed by the 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-14A gas chromatography, equipped with a flame ionization detector. Column chromatography was performed with SiO_2 (Wakogel).

Materials. Dioxane was distilled over CaH_2. $Ru_3(CO)_{12}$ was purchased from Aldrich Chemical Co. and used after recrystallization from hexane.

Typical Procedure. A 50-mL stainless autoclave was charged with diethyl 1-(trimethylsilyl)-6-hepten-1-yne-5,5-dicarboxylate (**1a**) (1 mmol, 310 mg), dioxane (5 mL), and $Ru_3(CO)_{12}$ (0.02 mmol, 13 mg). The system was flushed with 10 atmospheres of CO three times. Finally it was pressurized to 10 atm and immersed in an oil bath at 160 °C. After 20 hours had elapsed, the autoclave was removed from the oil bath and allowed to cool for 1 h. The CO was then released. The contents were transferred to a round bottomed flask with

CH_2Cl_2 and the volatiles removed in vacuo. The residue was subjected to column chromatography on silica gel (eluent; hexane/Et_2O = 2/1) to give 3,3a,4,5-tetrahydro-5-oxo-6-(trimethylsilyl)-2,2(1*H*)-pentalenedicarboxylic acid diethyl ester (**2a**) (334 mg, 90% yield) as a white solid.

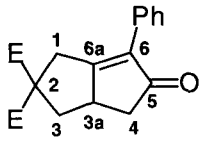
3,3a,4,5-Tetrahydro-5-oxo-6-(trimethylsilyl)-2,2(1*H*)-pentalenedicarboxylic acid diethyl ester (2a). White solid; mp 66-68 °C; R_f 0.22 (hexane/ether = 2/1); ^{1}H NMR ($CDCl_3$) δ 0.19 (s, 9H, $SiMe_3$), 1.25 (t, *J* = 7.3 Hz, 3H, CH_3), 1.28 (t, *J* = 7.3 Hz, 3H, CH_3), 1.66 (t, *J* = 12 Hz, 1H, 3-H), 2.06 (dd, *J* = 4.1 Hz, *J* = 18 Hz, 1H, 4-H), 2.57 (dd, *J* = 6.5 Hz, *J* = 18 Hz, 1H, 4-H), 2.78 (dd, *J* = 7.6 Hz, *J* = 12 Hz, 1H, 3-H), 2.95-3.09 (m, 1H, 3a-H), 3.22 (d, *J* = 19 Hz, 1H, 1-H), 3.32 (d, *J* = 19 Hz, 1H, 1-H), 4.20 (q, *J* = 7.3 Hz, 2H, CH_2), 4.24 (q, *J* = 7.3 Hz, 2H, CH_2); ^{13}C NMR ($CDCl_3$) δ -1.3 ($SiMe_3$), 14.0 (CH_3, two overlapping signals), 36.2 (1-C), 38.5 (3-C), 42.9 (4-C), 46.5 (3a-C), 60.8 (2-C), 61.9 (CH_2), 62.0 (CH_2), 136.6 (6-C), 171.0 (*C*OCH_2CH_3), 171.6 (*C*OCH_2CH_3), 192.4 (6a-C), 213.2 (5-C); IR (KBr) 2982 m, 2906 w, 1728 s, 1695 s, 1615 m, 1468 w, 1410 w, 1366 w, 1299 m, 1278 m, 1260 m, 1238 s, 1217 w, 1183 m, 1141 m, 1085 w, 1062 w, 1032 w, 1014 w, 927 w, 876 w, 865 w, 834 m, 754 w, 693 w, 667 w, 625 w; MS, *m/z* (relative intensity, %) 338 (M^+, 23), 323 (18), 265 (15), 264 (16), 249 (38), 237(30), 207 (10), 205 (26), 191 (28), 177 (20), 119 (22), 105 (10), 103 (17), 91 (15), 77 (22), 75 (100), 73 (97), 61 (12), 59 (22). Anal. Calcd for $C_{17}H_{26}O_5Si$: C, 60.33; H, 7.74. Found: C, 60.24; H, 7.63.



2a

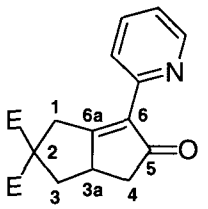
3,3a,4,5-Tetrahydro-5-oxo-6-phenyl-2,2(1*H*)-pentalenedicarboxylic acid diethyl ester (2b). Colorless oil; R_f 0.17 (hexane/ether = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.23 (t, *J* = 6.8 Hz, 3H, CH_3), 1.31 (t, *J* = 6.8 Hz, 3H, CH_3), 1.77 (t, *J* = 12 Hz, 1H, 3-H), 2.31 (dd, *J* = 3.2 Hz, *J* = 18 Hz, 1H, 4-H), 2.82 (dd, *J* = 6.5 Hz, *J* = 18 Hz, 1H, 4-H), 2.83 (dd, *J* = 7.6 Hz, *J* = 12 Hz, 1H, 3-H), 3.07-3.23 (m, 1H, 3a-H), 3.29 (d, *J* = 19 Hz, 1H, 1-H), 3.65 (d, *J* = 19 Hz, 1H, 1-H), 4.17 (dq, *J* = 1.9 Hz, *J* = 6.8 Hz, 2H, CH_2), 4.28 (q, *J* = 6.8

Hz, 2H, CH_2), 7.27-7.58 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 13.9 (CH_3), 14.0 (CH_3), 35.9 (1-C), 38.7 (3-C), 42.6 (4-C), 42.8 (3a-C), 61.3 (2-C), 61.9 (CH_2), 62.2 (CH_2), 128.2 (Ph), 128.4 (Ph, 6-C, two overlapping signals), 130.9 (Ph), 135.5 (Ph), 170.7 ($COCH_2CH_3$), 171.6 ($COCH_2CH_3$), 178.9 (6a-C), 207.1 (5-C); IR (neat) 2984 m, 2940 w, 1726 s, 1651 m, 1602 w, 1496 w, 1448 m, 1413 w, 1389 w, 1366 m, 1346 w, 1253 s, 1155s, 1114 w, 1093 w, 1059 m, 1036 w, 1014 w, 929 w, 885 w, 857 w, 761 m, 694 m, 602 m; MS, *m/z* (relative intensity, %) 342 (M^+, 24), 269 (16), 268 (81), 196 (17), 195 (100), 194 (11), 167 (49), 166 (17), 165 (29), 153 (14), 152 (22), 141 (11), 115 (16), 77 (12). Anal. Calcd for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 70.03; H, 6.48.



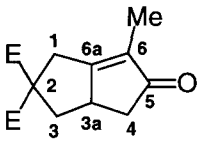
2b

3,3a,4,5-Tetrahydro-5-oxo-6-(2-pyridyl)-2,2(1*H*)-pentalenedicarboxylic acid diethyl ester (2c). White solid; mp 76-78 °C (hexane/ether); R_f 0.19 (hexane/ether = 1/1); ^1H NMR ($CDCl_3$) δ 1.24 (t, *J* = 7.0 Hz, 3H, CH_3), 1.30 (t, *J* = 7.0 Hz, 3H, CH_3), 1.74 (t, *J* = 13 Hz, 1H, 3-H), 2.32 (dd, *J* = 3.5 Hz, *J* = 18 Hz, 1H, 4-H), 2.85 (dd, *J* = 6.8 Hz, *J* = 18 Hz, 1H, 4-H), 2.88 (dd, *J* = 7.0 Hz, *J* = 13 Hz, 1H, 3-H), 3.13-3.28 (m, 1H, 3a-H), 3.78 (s, 2H, 1-H), 4.19 (q, *J* = 7.0 Hz, 2H, CH_2), 4.26 (dq, *J* = 1.9 Hz, *J* = 7.0 Hz, 2H, CH_2), 7.19 (dd, *J* = 1.9 Hz, *J* = 4.9 Hz, 1H, py-5-H), 7.70 (dt, *J* = 1.9 Hz, *J* = 7.8 Hz, 1H, py-4-H), 8.12 (d, *J* = 7.8 Hz, 1H, py-3-H), 8.64 (d, *J* = 4.9 Hz, 1H, py-6-H); ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3), 14.1 (CH_3), 37.5 (1-C), 38.7 (3-C), 42.9 (4-C), 43.4 (3a-C), 61.3 (2-C), 61.9 (CH_2), 62.0 (CH_2), 122.5 (py-5-C), 122.9 (py-3-C), 133.6 (6-C), 136.2 (py-4-C), 149.5 (py-6-C), 150.9 (py-2-C), 171.0 ($COCH_2CH_3$), 171.6 ($COCH_2CH_3$), 185.7 (6a-C), 206.7 (5-C); IR (KBr) 2990 w, 2932 w, 1730 s, 1699 s, 1649 m, 1584 w, 1563 w, 1474 m, 1432 m, 1407 w, 1366 w, 1320 w, 1273 s, 1249 s, 1190 m, 1175 m, 1118 w, 1093 w, 1060 m, 1032 w, 1016 w, 993 w, 938 w, 857 w, 786 w, 745 w, 700 w, 654 w, 602 w; MS, *m/z* (relative intensity, %) 343 (M^+, 30), 271 (19), 270 (100), 242 (28), 196 (23), 168 (26), 167 (27), 143 (10), 78 (15), 71 (19), 59 (34), 55 (15), 51 (11). Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.17; H, 6.16; N, 4.07.



2c

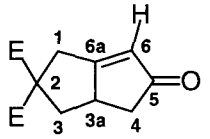
3,3a,4,5-Tetrahydro-5-oxo-6-methyl-2,2(1*H*)-pentalenedicarboxylic acid diethyl ester (2d). Colorless oil; R_f 0.11 (hexane/ether = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.25 (t, *J* = 7.3 Hz, 3H, CH_3), 1.27 (t, *J* = 7.3 Hz, 3H, CH_3), 1.63 (t, *J* = 13 Hz, 1H, 3-H), 1.70 (bs, 3H, CH_3), 2.07 (dd, *J* = 3.3 Hz, *J* = 18 Hz, 1H, 4-H), 2.63 (dd, *J* = 6.3 Hz, *J* = 18 Hz, 1H, 4-H), 2.77 (dd, *J* = 5.3 Hz, *J* = 13 Hz, 1H, 3-H), 2.89-3.03 (m, 1H, 3a-H), 3.14 (d, *J* = 19 Hz, 1H, 1-H), 3.23 (d, *J* = 19 Hz, 1H, 1-H), 4.19 (q, *J* = 7.3 Hz, 2H, CH_2), 4.23 (q, *J* = 7.3 Hz, 2H, CH_2); ^{13}C NMR ($CDCl_3$) δ 8.4 (CH_3), 13.9 (CH_3, two overlapping signals), 33.9 (1-C), 39.1 (3-C), 41.3 (4-C), 42.6 (3a-C), 60.9 (2-C), 61.8 (CH_2), 61.9 (CH_2), 132.8 (6-C), 170.9 (*C*OCH_2CH_3), 171.5 (*C*OCH_2CH_3), 177.7 (6a-C), 209.3 (5-C); IR (neat) 2986 m, 2926 w, 1723 s, 1672 s, 1448 m, 1414 w, 1366 m, 1267 s, 1188 m, 1151 m, 1091 w, 1061 m, 1036 w, 858 w; MS, *m/z* (relative intensity, %) 280 (M^+, 12), 206 (43), 178 (16), 134 (17), 133 (100), 132 (11), 105 (46), 91 (35), 79 (32), 77 (26), 65 (17), 55 (13), 53 (18), 51 (13); exact mass calcd for $C_{15}H_{20}O_5$ 280.1311, found 280.1311.



2d

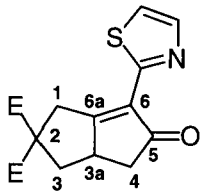
3,3a,4,5-Tetrahydro-5-oxo-2,2(1*H*)-pentalenedicarboxylic acid diethyl ester (2e). Colorless oil; R_f 0.17 (hexane/ether = 1/1); ^{1}H NMR ($CDCl_3$) δ 1.24 (t, *J* = 7.0 Hz, 3H, CH_3), 1.27 (t, *J* = 7.0 Hz, 3H, CH_3), 1.72 (t, *J* = 13 Hz, 1H, 3-H), 2.11 (dd, *J* = 3.5 Hz, *J* = 18 Hz, 1H, 4-H), 2.62 (dd, *J* = 6.2 Hz, *J* = 18 Hz, 1H, 4-H), 2.78 (dd, *J* = 7.8 Hz, *J* = 13 Hz, 1H, 3-H), 3.02-3.17 (m, 1H, 3a-H), 3.23 (d, *J* = 19 Hz, 1H, 1-H), 3.34 (d, *J* = 19 Hz, 1H, 1-H), 4.19 (q, *J* = 7.0 Hz, 2H, CH_2), 4.23 (q, *J* = 7.0 Hz, 2H, CH_2), 5.92 (d, *J* = 1.4 Hz, 1H, 6-H); ^{13}C NMR ($CDCl_3$) δ 13.9 (CH_3, two overlapping signals), 35.1 (1-C), 38.8 (3-C), 42.1 (4-C), 45.0 (3a-C), 60.7 (2-C), 61.9 (CH_2), 62.1 (CH_2), 125.5 (6-C), 170.7

($COCH_2CH_3$), 171.4 ($COCH_2CH_3$), 185.5 (6a-C), 209.5 (5-C); IR (neat) 2984 m, 1733 s, 1638 m, 1450 w, 1415 w, 1391 w, 1367 w, 1277 s, 1254 s, 1175 m, 1094 w, 1061 m, 1037 w, 1014 w, 898 w, 859 w, 820 w, 719 w; MS, *m/z* (relative intensity, %) 266 (M^+, 15), 193 (10), 192 (28), 165 (16), 164 (18), 163 (16), 120 (17), 119 (100), 92 (13), 91 (80), 79 (10), 77 (14), 65 (25), 55 (12), 53 (10), 51 (13). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.21; H, 6.96.



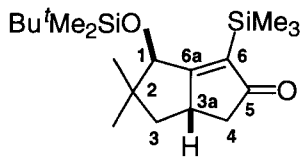
2e

3,3a,4,5-Tetrahydro-5-oxo-6-(2-thiazolyl)-2,2(1*H*)-pentalenedicarboxylic acid diethyl ester (2g). White solid; mp 79-81 °C (hexane/ether); R_f 0.10 (hexane/ether = 2/1); ^1H NMR ($CDCl_3$) δ 1.25 (t, *J* = 7.0 Hz, 3H, CH_3), 1.30 (t, *J* = 7.3 Hz, 3H, CH_3), 1.82 (t, *J* = 12 Hz, 1H, 3-H), 2.33 (dd, *J* = 3.5 Hz, *J* = 18 Hz, 1H, 4-H), 2.87 (dd, *J* = 6.2 Hz, *J* = 18 Hz, 1H, 4-H), 2.90 (dd, *J* = 7.3 Hz, *J* = 12 Hz, 1H, 3-H), 3.19-3.36 (m, 1H, 3a-H), 3.80 (t, *J* = 22 Hz, 2H, 1-H), 4.21 (dq, *J* = 0.81 Hz, *J* = 7.0 Hz, 2H, CH_2), 4.27 (q, *J* = 7.3 Hz, 2H, CH_2), 7.41 (d, *J* = 3.2 Hz, 1H, thiazolyl-5-H), 7.95 (d, *J* = 3.2 Hz, 1H, thiazolyl-4-H); ^{13}C NMR ($CDCl_3$) δ 13.9 (CH_3), 14.0 (CH_3), 37.1 (1-C), 38.7 (3-C), 41.7 (4-C), 43.9 (3a-C), 61.4 (2-C), 62.0 (CH_2), 62.1 (CH_2), 119.6 (thiazolyl-5-C), 129.0 (6-C), 142.9 (thiazolyl-4-C), 157.1 (thiazolyl-2-C), 170.6 ($COCH_2CH_3$), 171.4 ($COCH_2CH_3$), 183.4 (6a-C), 205.0 (5-C); IR (KBr) 2986 w, 1731 s, 1702 m, 1658 m, 1488 w, 1470 w, 1423 w, 1403 w, 1368 w, 1296 m, 1271 m, 1254 m, 1242 m, 1228 m, 1192 m, 1174 m, 1156 m, 1121 m, 1093 w, 1058 w, 1015 w, 984 w, 927 w, 839 w, 735 w, 654 w, 620 w; MS, *m/z* (relative intensity, %) 349 (M^+, 37), 277 (18), 276 (100), 275 (15), 248 (25), 247 (13), 246 (11), 204 (11), 203 (16), 202 (53), 201 (10), 175 (11), 174 (41), 173 (29), 77 (12), 59 (27), 58 (81), 51 (11). Anal. Calcd for $C_{17}H_{19}NO_5S$: C,58.44; H, 5.48; N, 4.01. Found: C, 58.45; H, 5.39; N, 4.04.



2g

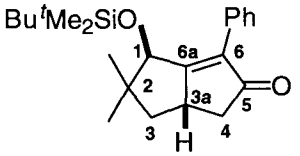
***cis*-5,5-Dimethyl-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-3-(trimethylsilyl)-2(1*H*)-pentalenone (4a).** Colorless oil; R_f 0.31 (hexane/ether = 10/1); ^{1}H NMR ($CDCl_3$) δ 0.02 (s, 3H, Si*Me*$_2$^{t}Bu), 0.11 (s, 3H, Si*Me*$_2$^{t}Bu), 0.22 (s, 9H, $SiMe_3$), 0.76 (s, 3H, CH_3), 0.88 (s, 3H, Si^{t}Bu), 1.05 (dd, *J* = 5.9 Hz, *J* = 12 Hz, 1H, 6-H), 1.13 (s, 3H, CH_3), 1.98 (dd, *J* = 4.0 Hz, *J* = 18 Hz, 1H, 1-H), 2.02 (t, *J* = 12 Hz, 1H, 6-H), 2.67 (dd, *J* = 6.9 Hz, *J* = 18 Hz, 1H, 1-H), 3.33-3.43 (m, 1H, 6a-H), 4.16 (s, 1H, 4-H); ^{13}C NMR ($CDCl_3$) δ -4.7 (Si*Me*$_2$^{t}Bu), -4.1 (Si*Me*$_2$^{t}Bu), -0.9 ($SiMe_3$), 18.2 (Si*C*$(CH_3)_3$), 24.1 (CH_3), 25.7 (SiC(*C*H_3)$_3$), 28.5 (CH_3), 42.1 (6-C), 42.2 (6a-C), 44.1 (5-C), 46.1 (1-C), 77.4 (4-C), 135.9 (3-C), 195.0 (3a-C), 215.7 (2-C); IR (neat) 2954 s, 2900 m, 2860 m, 1699 s, 1621 m, 1469 m, 1413 w, 1383 w, 1361 w, 1332 w, 1245 m, 1122 m, 1086 m, 1003 w, 937 w, 916 w, 838 s, 773 m, 707 w, 665 w; MS, *m/z* (relative intensity, %) 352 (M^+, 3), 147 (12), 131 (11), 91 (12), 75 (31), 73 (100), 59 (14). Anal. Calcd for $C_{19}H_{36}O_2Si_2$: C, 64.71; H, 10.29. Found: C 64.78; H 10.13.



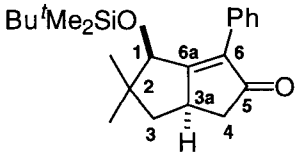
4a

5,5-Dimethyl-4-[[1,1-dimethylethyl)dimethylsilyl]oxy]-3-phenyl-4,5,6,6a-tetrahydro-2(1*H*)-pentalenone (4b). GC analysis of the crude reaction mixture showed that a mixture of *cis*-**4b** and *trans*-**4b** was produced in a ratio of 26:1. Both isomer can be separated easily by column chromatography on silica gel (hexane/ether = 5/1). (***cis*-4b**): White solid; mp 79-80 °C (hexane/ether); R_f 0.29 (hexane/ether = 5/1); ^{1}H NMR ($CDCl_3$) δ -0.18 (s, 3H, Si*Me*$_2$^{t}Bu), -0.07 (s, 3H, Si*Me*$_2$^{t}Bu), 0.83 (s, 9H, Si^{t}Bu), 0.93 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.21 (dd, *J* = 6.8 Hz, *J* = 13 Hz, 1H, 6-H), 2.13 (dd, *J* = 1.4 Hz, *J* = 13 Hz, 1H, 6-H), 2.20 (dd, *J* = 3.2 Hz, *J* = 18 Hz, 1H, 1-H), 2.90 (dd, *J* = 7.0 Hz, *J*

= 18 Hz, 1H, 1-H), 3.37-3.47 (m, 1H, 6a-H), 4.35 (s, 1H), 7.29-7.41 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ -5.0 (Si*Me*$_2$^{t}Bu), -4.7 (Si*Me*$_2$^{t}Bu), 18.1 (Si*C*$(CH_3)_3$), 24.1 (CH_3), 25.7 (SiC(CH_3)$_3$), 29.1 (CH_3), 39.1 (6a-C), 42.9 (6-C), 44.9 (1-C), 45.4 (5-C), 76.4 (4-C), 127.9 (Ph), 128.2 (Ph), 128.4 (Ph), 131.6 (Ph), 135.4 (3-C), 182.5 (3a-C), 209.2 (2-C); IR (KBr) 2958 m, 2860 m, 1712 s, 1670 w, 1601 w, 1497 w, 1472 w, 1416 w, 1387 w, 1360 w, 1322 w, 1294 w, 1248 m, 1199 w, 1153 w, 1123 m, 1090 s, 1001 w, 940 w, 906 w, 869 m, 836 m, 809 w, 771 m, 729 w, 701 m, 667 w; MS, *m/z* (relative intensity, %) 356 (M^+, 2), 301 (13), 300 (46), 299 (84), 285 (25), 141 (16), 115 (11), 91 (12), 75 (72), 73 (100), 59 (14), 57 (11). Anal. Calcd for $C_{22}H_{32}O_2Si$: C, 74.11; H, 9.05. Found: C, 74.09; H, 9.03. (***trans*-4b**): White solid; mp 99-101 °C (hexane/ether); R_f 0.10 (hexane/ether = 5/1); ^{1}H NMR ($CDCl_3$) δ -0.55 (s, 3H, $SiMe_2$), -0.03 (s, 3H, $SiMe_2$), 0.73 (s, 9H, Si^{t}Bu), 1.02 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.41 (dd, J = 5.4 Hz, J = 13 Hz, 1H, 6-H), 2.07 (dd, J = 2.7 Hz, J = 13 Hz, 1H, 6-H), 2.16 (dd, J = 3.5 Hz, J = 18 Hz, 1H, 1-H), 2.81 (dd, J = 7.0 Hz, J = 18 Hz, 1H, 1-H), 2.94-3.05 (m, 1H, 6a-H), 4.66 (s,1H, 4-H), 7.19-7.35 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ -5.1 (Si*Me*$_2$^{t}Bu), -5.0 (Si*Me*$_2$^{t}Bu), 18.1 (Si*C*$(CH_3)_3$), 25.0 (CH_3), 26.0 (SiC(CH_3)$_3$), 28.5 (CH_3), 35.2 (6a-C), 43.0 (6-C), 43.8 (5-C), 44.1 (1-C), 80.5 (4-C), 127.4 (Ph), 127.8 (Ph), 129.9 (Ph), 131.4 (Ph), 136.7 (3-C), 181.2 (3a-C), 208.6 (2-C); IR (KBr) 2958 m, 2860 m, 1713 s, 1673 m, 1602 w, 1495 w, 1471 m, 1445 w, 1418 w, 1388 w, 1363 w, 1328 w, 1293 w, 1252 m, 1169 m, 1133 s, 1068 w, 1002 w, 925 w, 884 w, 862 m, 835 m, 773 m, 730 m, 701 m, 668 w, 654 w, 624 w; MS, *m/z* (relative intensity, %) 356 (M^+, 0.2), 300 (34), 299 (72), 215 (13), 141 (14), 75 (53), 74 (10), 73 (100), 59 (16), 57 (12). Anal. Calcd for $C_{22}H_{32}O_2Si$: C, 74.11; H,9.05. Found: C, 74.04; H, 9.04.



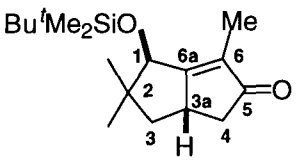
***cis*-4b**



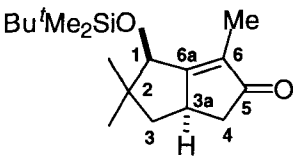
***trans*-4b**

4-[[1,1-Dimethylethyl)dimethylsilyl]oxy]-4,5,6,6a-tetrahydro-3,5,5-trimethyl-2(1*H*)-pentalenone (4c). GC analysis of the grude reaction mixture showed that a mixture of *cis*-**4c** and *trans*-**4c** was produced in a ratio of 2.4:1. Both isomer can be

separated easily by column chromatography on silica gel (hexane/ether = 7/1). (***cis*-4c**): Colorless oil; R_f 0.26 (hexane/ether = 7/1); ^{1}H NMR ($CDCl_3$) δ 0.01 (s, 3H, Si*Me*$_2$^{t}Bu), 0.10 (s, 3H, Si*Me*$_2$^{t}Bu), 0.80 (s, 3H, CH_3), 0.88 (s, 9H, Si^{t}Bu), 1.03 (dd, *J* = 7.0 Hz, *J* = 13 Hz, 1H, 6-H), 1.12 (s, 3H, CH_3), 1.75 (d, *J* = 2.4 Hz, 3H, CH_3), 1.99 (dd, *J* = 3.0 Hz, *J* = 18 Hz, 1H, 1-H), 2.00 (dd, *J* = 2.4 Hz, *J* = 13 Hz, 1H, 6-H), 2.71 (dd, *J* = 6.8 Hz, *J* = 18 Hz, 1H, 1-H), 3.16-3.32 (m, 1H, 6a-H), 4.09 (s, 1H, 4-H); ^{13}C NMR ($CDCl_3$) δ -4.9 (Si*Me*$_2$^{t}Bu), -4.7 (Si*Me*$_2$^{t}Bu), 8.9 (CH_3), 18.1 (Si*C*$(CH_3)_3$), 24.0 (CH_3), 25.7 (SiC(*C*$H_3)_3$), 29.0 (CH_3), 39.3 (6a-C), 43.0 (6-C), 44.0 (1-C), 45.1 (5-C), 76.2 (4-C), 131.9 (3-C), 180.8 (3a-C), 211.7 (2-C); IR (neat) 2932 m, 2860 m, 1712 s, 1678 m, 1467 w, 1412 w, 1383 w, 1362 w, 1300 w, 1251 m, 1145 m, 1086 m, 1064 m, 1005 w, 985 w, 938 w, 893 w, 857 m, 836 m, 773 m; MS, *m/z* (relative intensity, %) 294 (M^+, 1), 237 (24), 223 (10), 77 (10), 75 (100), 73 (79), 59 (13). Anal. Calcd for $C_{17}H_{30}O_2Si$: C, 69.33; H, 10.27. Found: C, 69.22; H, 10.26. (***trans*-4c**): Colorless oil; R_f 0.14 (hexane/ether = 7/1); ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 6H, Si*Me*$_2$^{t}Bu), 0.83 (s, 3H, CH_3), 0.95 (s, 9H, Si^{t}Bu), 1.15 (s, 3H, CH_3), 1.24 (dd, *J* = 4.9 Hz, *J* = 13 Hz, 1H, 6-H), 1.82 (t, *J* = 2.2 Hz, 3H), 1.94 (dd, *J* = 3.2 Hz, *J* = 13 Hz, 1H, 6-H), 1.96 (dd, *J* = 3.2 Hz, *J* = 18 Hz, 1H, 1-H), 2.63 (dd, *J* = 6.8 Hz, *J* = 18 Hz, 1H, 1-H), 2.72-2.87 (m, 1H, 6a-H), 4.57 (s, 1H); ^{13}C NMR ($CDCl_3$) δ -4.6 (Si*Me*$_2$^{t}Bu), -4.5 (Si*Me*$_2$^{t}Bu), 7.8 (CH_3), 18.0 (Si*C*$(CH_3)_3$), 24.6 (CH_3), 25.9 (SiC(*C*$H_3)_3$), 28.8 (CH_3), 35.2 (6a-C), 43.4 (1-C), 43.7 (5-C), 43.8 (6-C), 80.4 (4-C), 132.2 (3-C), 180.1 (3a-C), 210.9 (2-C); IR (neat) 2958 s, 2934 s, 2860 m, 1711 s, 1673 s, 1466 w, 1413 w, 1389 w, 1373 w, 1363 w, 1292 w, 1255 m, 1167 m, 1129 m, 1078 w, 1063 w, 1007 w, 961 w, 938 w, 853 m, 837 m, 773 m, 670 w; MS, *m/z* (relative intensity, %) 279 (M^+-15, 1), 238 (11), 237 (19), 223 (10), 75 (65), 73 (100), 59 (15). Anal. Calcd for $C_{17}H_{30}O_2Si$: C, 69.33; H, 10.27. Found: C, 69.19; H, 10.32.

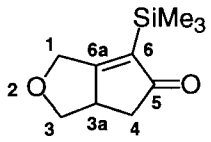


***cis*-4c**



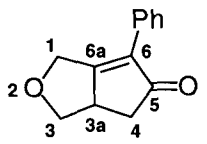
***trans*-4c**

3a,4-Dihydro-6-(trimethylsilyl)-1*H*-cyclopenta[c]furan-5(3*H*)-one (6a). Colorless oil; R_f 0.17 (hexane/ether = 2/1); ^{1}H NMR ($CDCl_3$) δ 0.18 (s, 9H, $SiMe_3$), 2.09 (dd, *J* = 3.8 Hz, *J* = 18 Hz, 1H, 4-H), 2.60 (dd, *J* = 5.1 Hz, *J* = 18 Hz, 1H, 4-H), 3.20-3.25 (m, 2H, 3-H, 3a-H), 4.30 (t, *J* = 14 Hz, 1H, 3-H), 4.47 (d, *J* = 16 Hz, 1H, 1-H), 4.65 (d, *J* = 16 Hz, 1H, 1-H); ^{13}C NMR ($CDCl_3$) δ -1.6 ($SiMe_3$), 40.2 (4-C), 47.0 (3a-C), 66.1 (1-C), 71.4 (3-C), 136.1 (6-C), 191.2 (6a-C), 212.7 (5-C); IR (neat) 2958 m, 2902 m, 2854 m, 1705 s, 1622 s, 1476 w, 1450 w, 1409 w, 1352 w, 1320 w, 1244 s, 1188 m, 1111 m, 1024 s, 995 w, 960 w, 926 m, 890 m, 837 s, 758 m, 735 w, 694 w, 662 w, 626 w; MS, *m/z* (relative intensity, %) 196 (M^+, 4), 181 (30), 180 (11), 151 (28), 123 (12), 83 (17), 77 (13), 75 (100), 73 (82), 69 (10), 61 (11), 59 (24), 55 (15), 53 (16); exact mass calcd for $C_{10}H_{16}O_2Si$ 196.0920, found 196.0913.



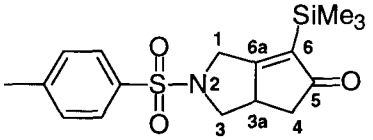
6a

3a,4-Dihydro-6-phenyl-1H-cyclopenta[c]furan-5(3*H*)-one (6b). Colorless oil; R_f 0.21 (hexane/ether = 1/1); ^{1}H NMR ($CDCl_3$) δ 2.34 (dd, *J* = 3.5 Hz, *J* = 18 Hz, 1H, 4-H), 2.85 (dd, *J* = 6.2 Hz, *J* = 18 Hz, 1H, 4-H), 3.20-3.39 (m, 2H, 3-H, 3a-H), 4.38 (t, *J* = 7.0 Hz, 1H, 3-H), 4.59 (d, *J* = 16 Hz, 1H, 1-H), 4.94 (d, *J* = 16 Hz, 1H, 1-H), 7.35-7.55 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 40.1 (4-C), 43.1 (3a-C), 66.1 (1-C), 71.2 (3-C), 127.9 (Ph), 128.4 (Ph, 6-C, two overlapping signals), 130.5 (Ph), 134.4 (Ph), 177.3 (6a-C), 206.7 (5-C); IR (neat) 2976 w, 2856 m, 1709 s, 1656 m, 1601 w, 1538 w, 1498 m, 1447 m, 1410 w, 1354 m, 1298 m, 1233 w, 1202 w, 1161 m, 1117 m, 1076 w, 1022 s, 966w, 904 m, 886 m, 764 m, 693 m, 657 w, 600 w; MS, *m/z* (relative intensity, %) 200 (M^+, 34), 170 (19), 169 (27), 158 (39), 143 (16), 142 (100), 129 (32), 128 (47), 127 (12), 116 (13), 115 (88), 105 (21), 103 (28), 91 (14), 89 (21), 78 (10), 77 (43), 76 (12), 75 (14), 74 (12), 70 (40), 65 (19), 64 (10), 63 (46), 62 (17), 57 (25), 55 (31), 52 (12), 51 (55), 50 (29). Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04.



6b

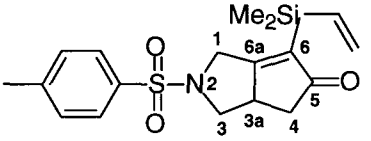
2,3,3a,4-Tetrahydro-2-[(4-methylphenyl)sulfonyl]-6-(trimethylsilyl)-cyclopenta[c]pyrrol-5(1*H*)-one (8a). White solid; mp 95-96 °C (hexane/ether); R_f 0.30 (hexane/ether = 1/2); ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 9H, $SiMe_3$), 1.97 (dd, *J* = 3.9 Hz, *J* = 17 Hz, 1H, 4-H), 2.39 (s, 3H, CH_3), 2.49 (dd, *J* = 6.8 Hz, *J* = 17 Hz, 1H, 4-H), 2.56 (dd, *J* = 1.4 Hz, *J* = 11 Hz, 1H, 3-H), 2.92-3.08 (m, 1H, 3a-H), 3.95 (t, *J* = 11 Hz, 1H, 3-H), 3.98 (d, *J* = 17 Hz, 1H, 1-H), 4.26 (d, *J* = 17 Hz, 1H, 1-H), 7.32 (d, *J* = 8.4 Hz, 2H, Ar), 7.69 (d, *J* = 8.4 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ -1.7 ($SiMe_3$), 21.4 (CH_3), 40.5 (4-C), 45.2 (3a-C), 48.1 (1-C), 52.0 (3-C), 127.2 (Ar), 129.8 (Ar), 133.4 (Ar), 137.8 (6-C), 143.9 (Ar), 185.3 (6a-C), 211.2 (5-C); IR (KBr) 2958 w, 2356 w, 1696 s, 1632 m, 1601 w, 1496 w, 1446 w, 1409 w, 1342 s, 1313 w, 1289 w, 1244 m, 1213 w, 1158 s, 1118 w, 1090 m, 1041 w, 1015 w, 986 w, 922 w, 865 w, 838 s, 749 w, 707 w, 680 m, 656 m, 612 w, 557 m; MS, *m/z* (relative intensity, %) 349 (M^+, 6), 334 (34), 194 (29), 178 (21), 167 (11), 166 (23), 151 (25), 149 (20), 139 (13), 91 (44), 77 (13), 75 (25), 73 (100), 65 (21), 59 (16). Anal. Calcd for $C_{17}H_{23}NO_3SSi$: C, 58.42; H, 6.63; N, 4.01. Found: C, 58.12; H, 6.69; N, 4.03.



8a

2,3,3a,4-Tetrahydro-2-[(4-methylphenyl)sulfonyl]-6-(dimethylethenylsilyl)-cyclopenta[c]pyrrol-5(1*H*)-one (8b). White solid; mp 53-55 °C (hexane/ether); R_f 0.16 (hexane/ether = 1/1); ^{1}H NMR ($CDCl_3$) δ 0.21 (s, 3H, $SiMe_2$), 0.23 (s, 3H, $SiMe_2$), 1.99 (dd, *J* = 4.1 Hz, *J* = 18 Hz, 1H, 4-H), 2.43 (s, 3H, CH_3), 2.53 (dd, *J* = 6.5 Hz, *J* = 18 Hz, 1H, 4-H), 2.56 (dd, *J* = 1.6 Hz, *J* = 9.7 Hz, 1H, 3-H), 2.96-3.12 (m, 1H, 3a-H), 3.97 (t, *J* = 9.7 Hz, 1H, 3-H), 4.01 (d, *J* = 18 Hz, 1H, 1-H), 4.24 (d, *J* = 18 Hz, 1H, 1-H), 5.69 (dd, *J* = 4.3 Hz, *J* = 19 Hz, 1H, SiCH=C*H*$_2$), 6.02 (dd, *J* = 4.3 Hz, *J* = 15 Hz, 1H, SiCH=C*H*$_2$), 6.15 (dd, *J* = 15 Hz, *J* = 19 Hz, 1H, SiC*H*=CH$_2$), 7.34 (d, *J* = 8.4 Hz, 2H,

Ar), 7.71 (d, J = 8.4 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ -3.8 ($SiMe_2$), -3.5 ($SiMe_2$), 21.5 (CH_3), 40.5 (4-C), 45.4 (3a-C), 48.3 (1-C), 52.1 (3-C), 127.4 (Ar), 129.9 (Ar), 133.5 ($SiCH=CH_2$), 133.7 (Ar), 136.0 ($SiCH=CH_2$), 136.5 (6-C), 144.0 (Ar), 186.2 (6a-C), 211.1 (5-C); IR (KBr) 2966 w, 1698 s, 1630 s, 1599 w, 1494 w, 1477 w, 1444 w, 1404 w, 1346 s, 1308 w, 1236 m, 1213 w, 1161 s, 1118 w, 1089 m, 1047 w, 1012 w, 988 w, 925 w, 864 w, 838 w, 813 m, 774 w, 707 w, 681 w, 655 m, 610 w, 549 m; MS, 361 (M^+, 0.3), 207 (13), 206 (82), 179 (14), 178 59), 177 (10), 165 (14), 163 (16), 151 (14), 149 (19), 139 (17), 135 (12), 109 (12), 104 (25), 95 (13), 92 (11), 91 (89), 86 (10), 85 (55), 83 (10), 79 (10), 77 (18), 75 (36), 69 (10), 67 (10), 65 (39), 61 (14), 59 (100), 55 (15), 53 (11), 51 (11). Anal. Calcd for $C_{18}H_{23}NO_3SSi$: C, 59.80; H, 6.41; N, 3.87.



8b

1.4 References and Notes

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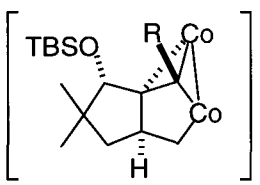
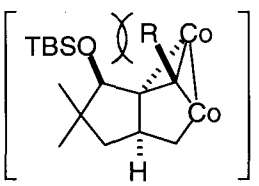
(27)For $Co_2(CO)_8$-mediated reaction, the ratio was 3:1.[26]

(28)Magnus reported that a similar tendency has also been observed in $Co_2(CO)_8$-mediated reaction.[26] He explained the 1,3-diastereoselectivity as follows. Thus, the newly formed five-membered ring, Co-metallacylce, is presumablly *cis*-fused. The metallacycle **A** minimizes the steric interactions between SiO- and R-, whereas **B** has a severe 1,3-*pseudo* diaxial interaction on the *endo*-face. Consequently, a large R-group (Me_3Si- > Ph- > Me-) would be expected to favor **A**.



A



B

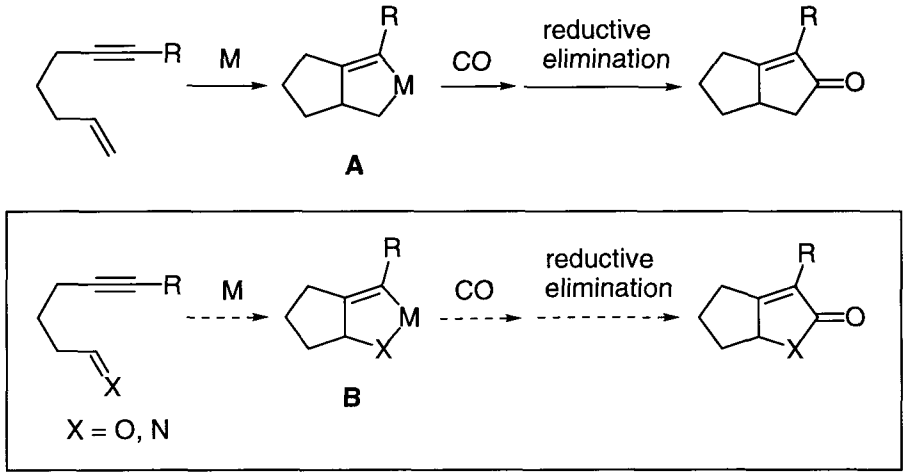
Chapter 2

Ruthenium-Catalyzed [2+2+1] Cycloaddition of Yne-Aldehydes and Imines with Carbon Monoxide

2.1 Introduction

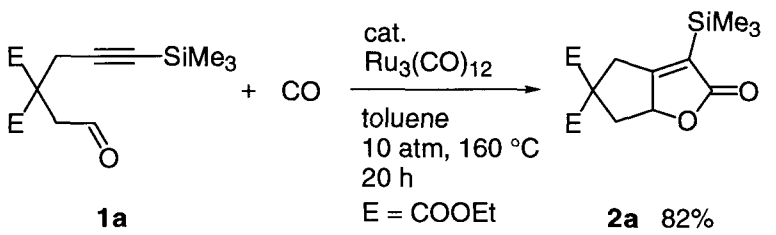
Metallacycles are involved as key species in many reactions such as olefin metathesis and a variety of cyclization reactions.[1] Metallacyclopentenes usually produced via the cycloaddition of a coordinated acetylene and an olefin. It is well established that the reaction of 1,6-enynes with a transition metal gives rise to bicyclic metallacyclopentene **A** or related complexes which may then undergo insertion of CO followed by reductive elimination to give cyclopentenones, i.e., the Pauson-Khand reaction. This transformation is accomplished by the presence of a stoichiometric amount of a variety of complexes which contain metals, such as Ti,[2] Zr,[3] W,[4,5] Cr,[5] Mo,[6] Fe,[7] and Co.[8] The catalytic transformation of enynes to bicyclic α,β-unsaturated ketones using $Co_2(CO)_8$,[9] $Co_4(CO)_{12}$,[10] $Co_3(CO)_9(\mu^3\text{-CH})$,[11] $Cp_2Ti(CO)_2$,[12] $Ru_3(CO)_{12}$,[13] $[RhCl(CO)_2]_2$[14], and *trans*-$[RhCl(dppp)]_2$[15] as catalysts are also believed to proceed via **A** or its related complexes. Although heteroatom-containing metallacyclopentenes **B**, which contain early transition metals such as Ti and Zr, are well known,[16,17] there are very few examples of **B** containing a late transition metal.[18] If the metallacyclopentene **B** is formed from the reaction of yne-aldehydes yne-imines with a late transition metal, it would be expected that **B** could undergo insertion of CO and the resultant carbonylated metallacycle could then undergo reductive elimination to give bicyclic α,β-unsaturated lactones and lactams, respectively. Such a catalytic transformation has not been observed. The use of a late transition metal complex could possibly make the sequence catalytic, while the strength of the early transition metal-heteroatom bond renders catalysis use difficult.[19] In this chapter, I describe the realization of the working hypothesis proposed above. This represents the first example of a transition metal catalyzed *hetero* Pauson-Khand reaction.

Scheme 1



2.2 $Ru_3(CO)_{12}$-Catalyzed Cyclocarbonylation of Yne-Aldehydes to Bicyclic α,β-Unsaturated γ-Butyrolactones

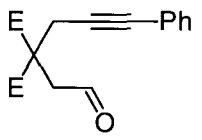
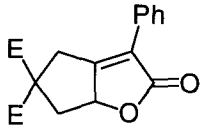
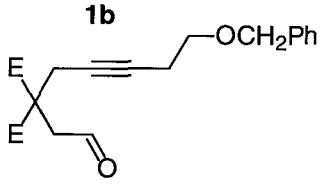
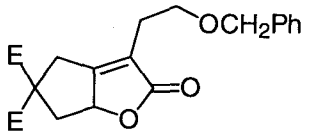
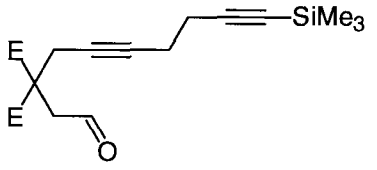
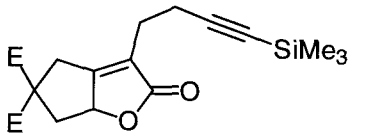
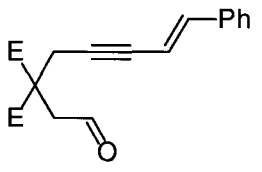
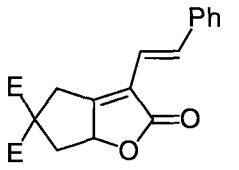
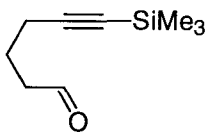
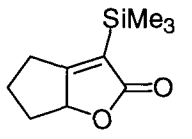
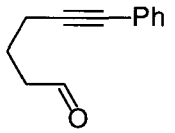
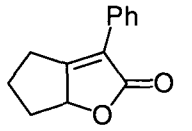
The reaction of yne-aldehyde **1a** (1 mmol) with CO (10 atm) in toluene (5 mL) in the presence of a catalytic amount of $Ru_3(CO)_{12}$ (0.02 mmol) at 160 °C gave a bicyclic lactone **2a** in 82% isolated yield (eq 1). When the reaction was carried out at 140 °C, no reaction was observed. The reaction also proceeded under 5 atm of CO (78% yield). A higher CO pressure (30 atm) decreased the yield to 30% yield with 38% of **1a** being recovered. Changing the solvent to dioxane (82%), CH_3CN (74%), or cyclohexane (78%) had no significant effect on the product yields. No reaction was observed when other complexes, such as $Ru(CO)_2(PPh_3)_3$, $[RuCl_2(CO)_3]_2$, $Ru(acac)_3$, Cp*RuCl(cod), $Co_2(CO)_8$, $Rh_4(CO)_{12}$, $[RhCl(CO)_2]_2$, $RhCl(PPh_3)_3$, and $Ir_4(CO)_{12}$ were used as catalysts. The standard reaction conditions established thus constitutes 2 mol% of $Ru_3(CO)_{12}$, 10 atm of CO, in toluene, and at 160 °C for 20 h.



1a **2a** 82% (1)

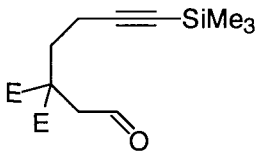
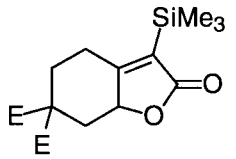
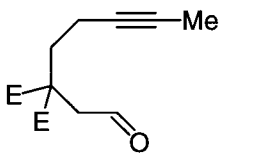
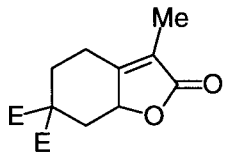
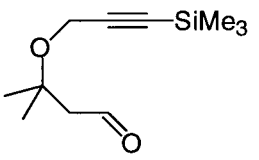
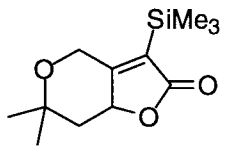
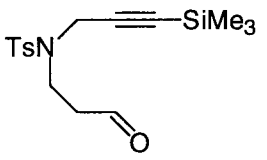
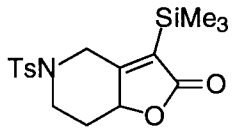
This reaction is the first catalytic transformation of yne-aldehydes to bicyclic α,β-unsaturated lactones. This reaction also represents the first reported catalytic synthesis of five-membered lactones via a [2+2+1] cyclocoupling reaction, incorporating the aldehyde π-bond, the alkyne π-bond, and the carbon atom of CO into a five-membered ring.[20]

Table 1. $Ru_3(CO)_{12}$-Catalyzed Cyclocarbonylation of Yne-aldehydes [a]

enrty	yne-aldehyde	lactone [b]
1	 **1b**	 **2b** 62%
2	 **1c**	 **2c** 80%
3	 **1d**	 **2d** 91%
4	 **1e**	 **2e** 83%
5	 **3a**	 **4a** 92%[c]
6	 **3b**	 **4b** 59%[c]

[a] Reaction conditions: yne-aldehyde (1 mmol), CO (10 atm), $Ru_3(CO)_{12}$ (0.02 mmol), toluene (5 mL) at 160 °C for 20 h. [b] Isolated yields. [c] The reaction was run at 180 °C.

Table 1. (Continued) [a]

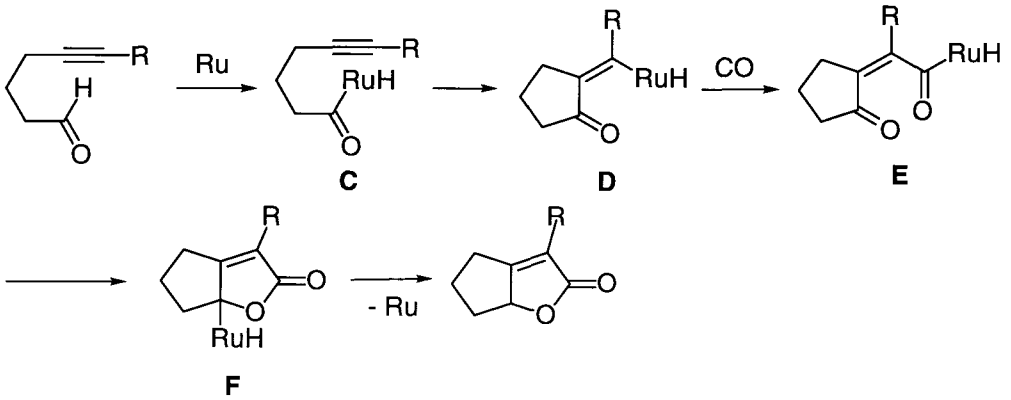
enrty	yne-aldehyde	lactone [b]
7	 **5a**	 **6a** 93%
8	 **5b**	 **6b** 69% [d]
9	 **7**	 **8** 89%
10	 **9**	 **10** 74%

[a] Reaction conditions: yne-aldehyde (1 mmol), CO (10 atm), $Ru_3(CO)_{12}$ (0.02 mmol), toluene (5 mL) at 160 °C for 20 h. [b] Isolated yields. [c] The reaction was run at 180 °C. [d] The reaction was run for 40 h.

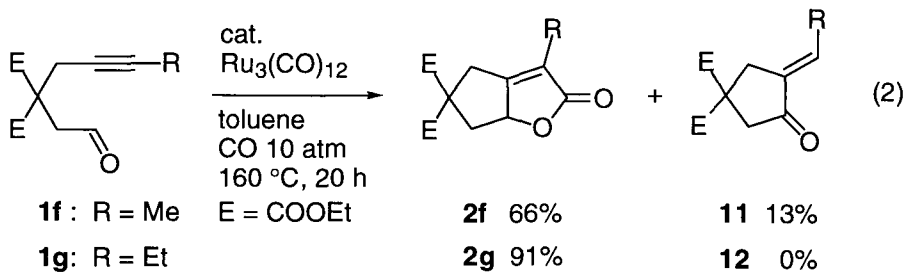
Selected results are shown in Table 1. The reaction of phenyl-substituted yne-aldehyde **1b** gave the corresponding lactone **2b** in 62% yield (entry 1). The alkyl substituents at the terminal acetylenic carbon had no significant effect on the reaction (entry 2). Interestingly, an olefinic and even acetylenic substituents remained intact under the reaction conditions (entries 3 and 4). An yne-aldehyde having a terminal acetylenic moiety failed to give desirable results.[21] The result of entries 5 and 6 shows that the presence of geminal substituents in the tether is not essential for the reaction to proceed, although higher reaction temperatures are required. The present reaction is applicable to the formation of a cyclohexane-fused γ-butyrolactone (entries 7 and 8). Yne-aldehydes containing heteroatoms, such as oxygen and nitrogen, in the tether worked well and heterocycle-fused γ-butyrolactones were obtained in high yields (entries 9 and

10). The formation of polyfunctional compounds such as **8** and **10** in a single step is also quite noteworthy, since they are amenable to further elaboration and no simple alternative methods are available to give these multifunctionalized compounds.

Scheme 2 Alternative Mechanism



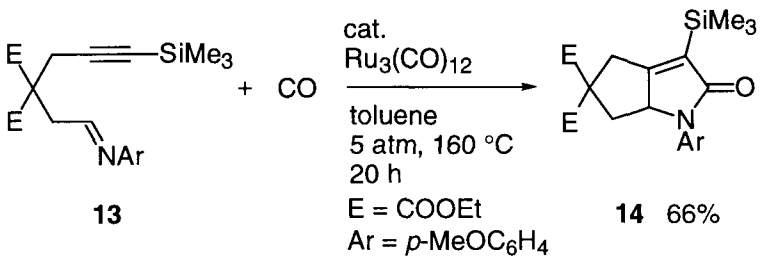
Although I initiated this study guided by my working hypothesis shown in Scheme 1, I wish to point out that another very interesting mechanistic alternative is also plausible. The mechanism involves the oxidative addition of an aldehyde C-H bond[22] by ruthenium, as shown in Scheme 2.[23,24] In fact, cleavage of an aldehyde C-H bond to ruthenium was proposed by Watanabe for the case of the $Ru_3(CO)_{12}$-catalyzed hydroacylation of benzaldehydes with intermolecular olefins.[22c] The reaction of **1f** with CO gave two products, one being the expected lactone **2f** and the other the exo-methylene ketone **11** (eq 2). While intermediate **B** in Scheme 1 can account for the route to **11**, the formation of **11** can also be rationalized by assuming a reductive elimination from a vinyl complex **D**. When R is a small group, such as a methyl group, a reductive elimination from **D** takes place to some extent. The more bulky R group facilitates the insertion of CO (**D** → **E**) because of release of steric congestion around the metal in **D**.[25] Indeed, even the ethyl isomer **1g** selectively gave only lactones.



2.3 $Ru_3(CO)_{12}$-Catalyzed Cyclocarbonylation of Yne-Imines to Bicyclic α,β-Unsaturated γ-Lactams

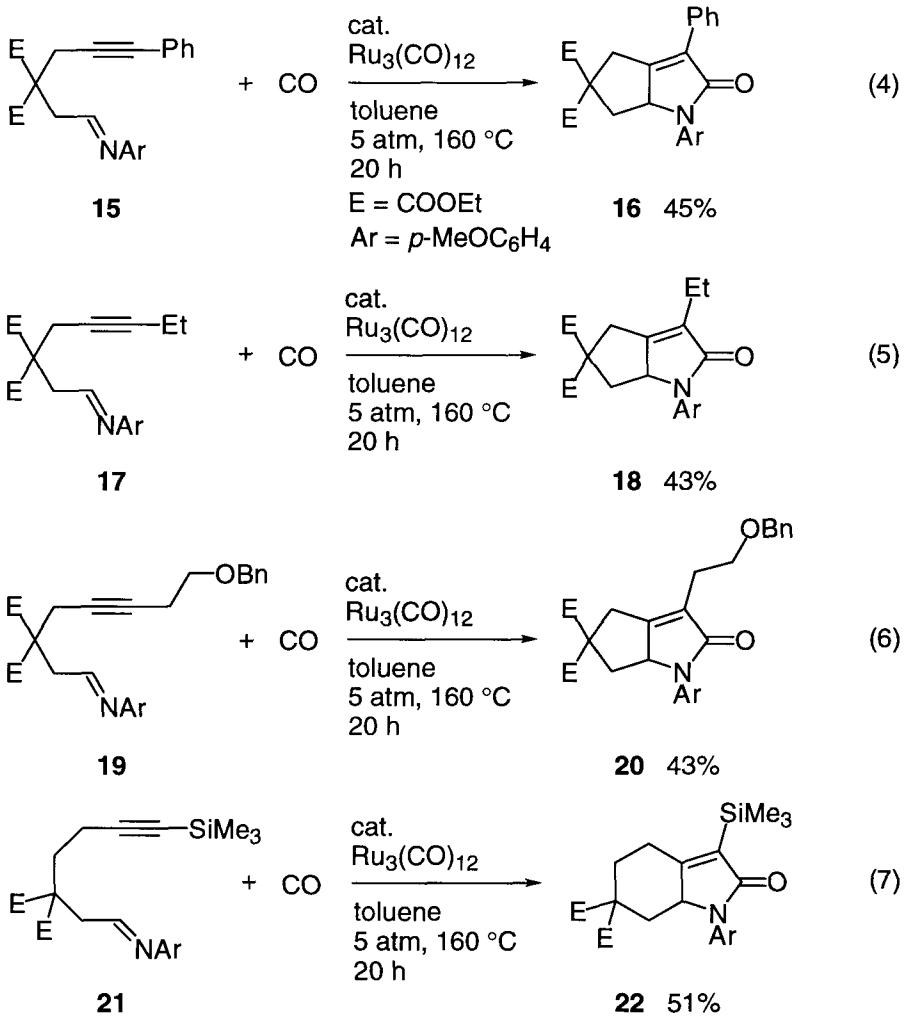
I next examined the possibility of extending this reaction to the synthesis of α,β-unsaturated lactams via the replacement of oxygen with nitrogen, since the lactam skeleton is one of the most important nitrogen heterocycles in pharmaceutical agents.[26] In this section, I describe the cyclocarbonylation of yne-imines in the presence of $Ru_3(CO)_{12}$ to give bicyclic α,β-unsaturated lactams.

The catalytic reaction proceeded smoothly and efficiently. Again $Ru_3(CO)_{12}$ exhibits catalytic activity for the desired carbonylation. The reaction of the yne-imine **13** (1 mmol), which was obtained by the condensation of the 5-hexynal derivative with *p*-anisidine in the presence of $MgSO_4$, and CO (5 atm) in the presence of $Ru_3(CO)_{12}$ (0.05 mmol) in toluene (5 mL) at 160 °C for 20 h gave a bicyclic α,β-unsaturated lactam **14** in 66% isolated yield (eq 3). A higher CO pressure (10 atm) decreased the yield to 43%. A comparable yield (64%) was obtained when cyclohexane replaced toluene as the solvent. The use of dioxane (51%) and CH_3CN (24%) as the solvents resulted in a decreased yield of **14**. When the reaction was carried out at 140 °C, the yield of **14** was decreased to 37% yield. The reaction at 180 °C gave a complex mixture. It was found that a *p*-$CH_3OC_6H_4$ group is the *N*-protecting group of choice. Replacement of the *p*-$CH_3OC_6H_4$ group with other *N*-protecting groups such as *n*-Bu (39%), *iso*-Pr (35%), Ph (28%), and *p*-$Me_2NC_6H_4$ (45%) gave decreased yields. The use of a *tert*-Bu group resulted in no product. This reaction is the first example the catalytic cyclocoupling of acetylenes, imines, and CO.[27]

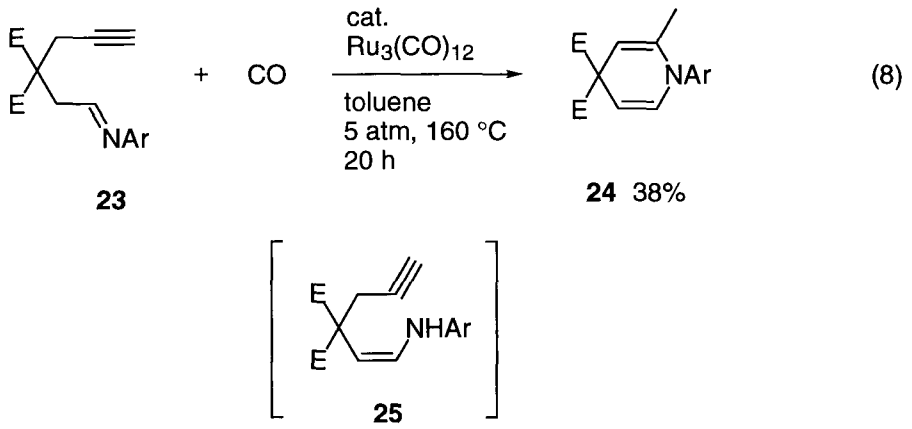


13 **14** 66% (3)

The reaction of phenyl-substituted yne-imine **15** gave the corresponding lactam **16** in 45% yield (eq 4). Alkyl-substituted yne-imines **17** and **19** also underwent cyclocarbonylation to give lactams **18** and **20** in good yields (eq 5 and 6). The reaction can also be applied to the formation of a cyclohaxane-fused γ-lactam (eq 7). In all cases, yields were somewhat lower than those in the case of yne-aldehydes.

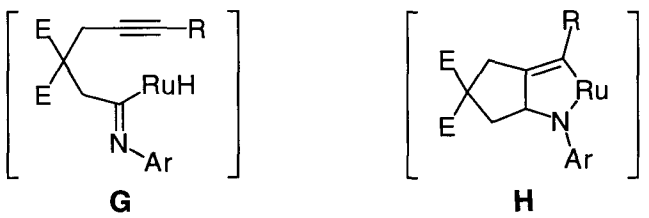


The reaction of an yne-imine having a terminal acetylenic moiety gave the dihydropyridine derivative **24** (eq 8), rather than the expected lactam. Although the mechanism is presently not clear, **24** would have been formed via an intramolecular hydroamination[28] of **25**, which is the enamine-form of **23**, followed by the isomerization of the *exo* olefinic bond to an *endo* isomer. When a substituent is present on the terminal acetylenic carbon, cyclocarbonylation takes place because the addition of N-H bond to an acetylene is retarded by steric hindrance.



(8)

The mechanism of the cyclocarbonylation reactions examined herein should be similar to that which operates in the reaction of yne-aldehydes in section 2.1. Thus, the key step in the present reaction is the oxidative addition of an imine C-H bond to ruthenium, to give **G**. In contrast to aldehyde C-H bonds,[29] however, no example of the oxidative addition of imine C-H bonds to a transition metal complex has been reported, except for limited cases.[30,31] Suggs reported the chelation assisted oxidative addition of imine C-H bonds in 2-aminopyridyl aldimines to $Rh(PPh_3)_3Cl$.[30] Jun developed some Rh-catalyzed reactions which involve the oxidative addition of imine C-H bonds in 2-aminopyridyl aldimines to a rhodium complex as the key step.[31] To my knowledge, no report of the oxidative addition of a simple imine C-H bond to a transition metal complex exsists. On the other hand, an alternative mechanism for the present catalytic reaction involves the oxidative cyclization of an yne-imine to a ruthenium leading to metallacycle **H**. This also has no precedent, to my knowledge.



In summary, I have demonstrated a new Ru-catalyzed cyclocarbonylation of yne-aldehydes. This reaction is the first catalytic transformation of yne-aldehydes with CO to bicyclic γ-butenolides. Furthermore, I have demonstrated a new $Ru_3(CO)_{12}$-catalyzed cyclocarbonylation of yne-imines leading to α,β-unsaturated lactams. This is the first example of the catalytic cyclocoupling of acetylenes, imines, and CO.

2.4 Experimental Section

General Information. ^{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 (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, and m = multiplet), 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 instrument with ionization voltages of 70 eV. Elemental analyses were performed by the 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, dioxane, CH_3CN, and cyclohexane was distilled from CaH_2. $Ru_3(CO)_{12}$ was purchased from Aldrich Chemical Co. and used after recrystallization from hexane. Yne-aldehydes were prepared as described below. All yne-imines were prepared by the reaction of the corresponding yne-aldehydes with *p*-anisidine in the presence of $MgSO_4$.[32]

(2-Oxoethyl)-[3-(trimethylsilyl)-2-propynyl]propanedioic Acid Diethyl Ester (1a). In ethanol (250mL) was dissolved sodium (8.4 g, 355 mmol), and diethyl malonate (56 mL, 370 mmol) was added dropwise over 15 min at 55-60 °C. Then, bromoacetaldehyde diethylacetal (53 mL, 350 mmol) was added dropwise to the mixture over 1.5 h at 55-60 °C, and the whole was stirred at reflux for 3 days. The reaction mixture was concentrated *in vacuo*, ether (200 mL) and water (150 mL) were added to the concentrate, and an organic layer was separated. The aqueous layer was extracted with ether, and the combined organic layers were washed with brine and dried over $MgSO_4$. After removal of the volatile, the residue was distilled under reduced pressure (bp. 106-107 °C/0.7 mmHg) to give (2,2-diethoxyethyl)propanedioic acid diethyl ester as a colorless liquid (52.8 g, 52 %).

To a suspension of NaH (0.96 g, 24 mmol) in THF (50 mL) was added (2,2-diethoxyethyl)-propanedioic acid diethyl ester (5.5 g, 20 mmol) at 0 °C, and the mixture was stirred at room temperature until evolution of hydrogen gas subsided. 3-Bromo-1-(trimethylsilyl)-1-propyne[33] (5.7 g, 30 mmol) was added dropwise to the mixture at 0 °C and the mixture was stirred at room temperature for 12 h. To the reaction mixture was added water (40 mL), and an organic layer was separated. The aqueous layer was extracted with ether, and the combined organic layers were washed brine and dried over $MgSO_4$. After removal of the volatile, the residue was distilled under reduced pressure (bp. 106-107 °C/0.6 mmHg) to give (2,2-diethoxyethyl)-[3-(trimethylsilyl)-2-propynyl]propanedioic acid diethyl ester as a colorless liquid (7.5 g, 97 %).

A solution of (2,2-diethoxyethyl)-[3-(trimethylsilyl)-2-propynyl]propanedioic acid diethyl ester (3.9 g, 10 mmol), *p*-toluenesulfonic acid (95 mg, 0.5 mmol) and water (0.5 mL) in acetone (40 mL) was stirred at room temperature for 5 h. The reaction mixture was concentrated *in vacuo*, and ether (30 mL) and saturated $NaHCO_3$ aqueous solution (5 mL) was added to the concentrate. An organic layer was separated, the aqueous layer was extracted with ether, and the combined organic layers were washed with brine and dried over $MgSO_4$. After removal of the volatile, the residue was purified by column chromatography on silica gel to give (2-oxoethyl)-[3-(trimethylsilyl)-2-propynyl]propanedioic acid diethyl ester (**1a**) (2.7 g, 87 %). Colorless oil; R_f 0.17 (hexane/ether = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.13 (s, 9H), 1.25 (t, J = 6.8 Hz, 6H), 2.97 (s, 2H), 3.18 (d, J = 0.81 Hz, 2H), 4.20 (q, J = 6.8 Hz, 2H), 4.21 (q, J = 6.8 Hz, 2H), 9.76 (t, J = 0.81 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ -0.2, 13.9, 25.2, 46.1, 54.2, 62.2, 89.0, 100.9, 168.8, 198.8; IR (neat) 2966 m, 2908 w, 2742 w, 2180 m, 1746 s, 1557 m, 1469 m, 1450 m, 1429 m, 1392 m, 1369 m, 1282 s, 1250 s, 1196 s, 1095 s, 1033 s, 945 w, 847 s, 761 m, 700 w, 640 w; MS, *m/z* (relative intensity, %) 312 (M^+, 0.1), 240 (11), 239 (51), 223 (11), 211 (13), 195 (24), 179 (15), 173 (39), 151 (21), 149 (12), 127 (31), 121 (33), 103 (14), 99 (14), 93 (24), 83 (16), 77 (13), 75 (72), 73 (100), 61 (15), 59 (13), 55 (10); exact mass calcd for $C_{15}H_{24}O_5Si$ 312.1393, found 312.1406.

(2-Oxoethyl)-(3-phenyl-2-propynyl)propanedioic Acid Diethyl Ester (1b). 3-Bromo-1-phenyl-1-propyne was prepared by the treatment of 3-phenyl-2-propyn-1-ol[34] with

PBr_3 using a modification of the method of Brandsma.[35] (2-Oxoethyl)-(3-phenyl-2-propynyl)propanedioic acid diethyl ester (**1b**) was prepared by the reaction of (2,2-diethoxyethyl)propanedioic acid diethyl ester with 3-bromo-1-phenyl-1-propyne, followed by hydrolysis, by a procedure similar to that used for **1a**. Colorless oil; R_f 0.20 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.0 Hz, 6H), 3.19 (s, 2H), 3.28 (d, J = 1.1 Hz, 2H), 4.24 (q, J = 7.0 Hz, 2H), 4.25 (q, J = 7.0 Hz, 2H), 7.26-7.38 (m, 5H), 9.81 (t, J = 1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.9, 24.8, 46.2, 54.4, 62.2, 84.0, 84.1, 122.8, 128.1, 128.2, 131.6, 168.9, 198.7; IR (neat) 3058 w, 2986 m, 2940 w, 2844 w, 2744 w, 1735 s, 1627 w, 1600 w, 1575 w, 1494 m, 1468 w, 1447 m, 1433 w, 1391 m, 1369 m, 1285 m, 1199 s, 1093 m, 1070 m, 1052 m, 1020 m, 918 w, 860 w, 758 m, 692 m; MS, *m/z* (relative intensity, %) 316 (M^+, 1), 243 (26), 242 (35), 215 (18), 199 (11), 197 (16), 185 (14), 173 (13), 171 (24), 170 (19), 169 (34), 153 (12), 143 (13), 142 (12), 141 (40), 139 (12), 129 (11), 128 (13), 127 (21), 117 (15), 116 (13), 115 (100), 105 (31), 89 (12), 77 (11), 63 (12); exact mass calcd for $C_{18}H_{20}O_5$ 316.1311, found 316.1316.

(5-Benzyloxy-2-pentynyl)-(2-oxoethyl)propanedioic Acid Diethyl Ester (1c). To a suspension of NaH (5.6 g, 140 mmol) in THF (200 mL) was added 3-butyn-1-ol (9.1 mL, 120 mmol) dropwise at 0°C, and the mixture was stirred at room temperature until evolution of hydrogen gas subsided. Benzyl bromide (16.6 mL, 140 mmol) was added dropwise at 0 °C, and then tetrabutylammonium iodide (50 g, 135 mmol) was added at the same temperature. The reaction mixture was stirred at 0 °C for 30 min and then at room temperature for 12 h. After filtration of the reaction mixture, the filtrate was poured into water (300 mL). An organic layer was separated and the aqueous layer was etracted with ether. The combined organic layers were dried over $MgSO_4$. After removal of the volatile, the residue was distilled under reduced pressure (78-79 °C/3 mmHg) to give 1-(benzyloxy)-3-butyne as a colorless liquid (18.2 g, 95 %).

5-(Benzyloxy)-2-pentyn-1-ol was prepared from 1-(benzyloxy)-3-butyne using a modification of the method of Denis.[34] 5-(Benzyloxy)-1-bromo-2-pentyne was prepared by the treatment of the corresponding alcohol with PBr_3 using a modification of the method of Brandsma.[35]

(5-Benzyloxy-2-pentynyl)-(2-oxoethyl)propanedioic acid diethyl ester (**1c**) was prepared by the reaction of (2,2-diethoxyethyl)propanedioic acid diethyl ester with 5-(benzyloxy)-1-bromo-2-pentyne, followed by hydrolysis, by a procedure similar to that used for **1a**. Colorless oil; R_f 0.09 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.24 (t, J = 7.3 Hz, 6H), 2.44 (tt, J = 2.2 Hz, J = 7.0 Hz, 2H), 2.93 (t, J = 2.2 Hz, 2H), 3.17 (s, 2H), 3.53 (t, J = 7.0 Hz, 2H), 4.20 (q, J = 7.3 Hz, 4H), 4.53 (s, 2H), 7.27-7.35 (m, 5H), 9.72 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 13.9, 20.0, 24.3, 46.0, 54.3, 62.0, 68.5, 72.9, 75.4, 81.1, 127.6, 128.4, 138.0, 169.1, 198.9; IR (neat) 3068 w, 3032 w, 2986 m, 2940 m, 2866 m, 2740 w, 1739 s, 1499 w, 1457 m, 1391 m, 1368 m, 1284 m, 1199 s, 1096 s, 1053 m, 1023 m, 908 w, 860 w, 825 w, 740 m, 698 m, 610 w; MS, *m/z* (relative intensity, %) 374 (M^+, 0.1), 173 (15), 91 (100), 65 (11); exact mass calcd for $C_{21}H_{26}O_6$ 374.1729, found 374.1739.

(2-Oxoethyl)-[7-(trimethylsilyl)-2,6-heptadiynyl]propanedioic Acid Diethyl Ester (1d). 7-(Trimethylsilyl)-2,6-heptadiyn-1-ol was prepared, using a modification of the method of Corey, as described below.[36] To a solution of 1-(trimethylsilyl)-1-propyne (4.7 g, 42 mmol) in THF (80 mL) was added dropwise butyllithium (28.0 mL, 42 mmol) as a 1.50 M solution in hexane at -30 °C over 30 min, and the mixture was stirred at same temperature for 30 min. The above solution was added at 0 °C to a solution of 4-chloro-2-butyn-1-yl tetrahydro-2-pyranyl ether (7.9 g, 42 mmol), which was prepared by the reaction of 4-chloro-2-butyn-1-ol[37] with 3,4-dihydro-2*H*-pyran, and the mixture was stirred at 0 °C for 2 h. The reaction mixture was poured into water, and an organic layer was separated. The aqueous layer was extracted with ether, and the combined organic layers were dried over $MgSO_4$. After removal of the volatile, the crude ether was diluted in methanol (50 mL). To the solution was added *p*-toluenesulfonic acid (200 mg), and the mixture was stirred at room temperature for 6 h. To the reaction mixture was added saturated $NaHCO_3$ aqueous solution (5 mL). After removal of the volatile *in vacuo*, the concentrate was diluted in ether (150 mL) and the solution was dried over $MgSO_4$. After removal of the volatile, the residue was purified by column chromatography on silica gel (hexane/ether = 3/1, R_f 0.13) to give 7-(trimethylsilyl)-2,6-heptadiyn-1-ol as a light yellow liquid (4.1 g, 55 %).

6-Bromo-1-(trimethylsilyl)-1,5-heptadiyne was prepared by the reaction of the corresponding alcohol with PBr_3 using a modification of the method of Brandsma.[35]

(2-Oxoethyl)-[7-(trimethylsilyl)-2,6-heptadiynyl]propanedioic acid diethyl ester (**1d**) was prepared by the reaction of (2,2-diethoxyethyl)propanedioic acid diethyl ester with 6-bromo-1-(trimethylsilyl)-1,5-heptadiyne, followed by hydrolysis, by a procedure similar to that used for **1a**. Colorless oil; R_f 0.17 (hexane/ether = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.15 (s, 9H), 1.25 (t, J = 7.3 Hz, 6H), 2.31-2.38 (m, 4H), 2.93 (t, J = 2.2 Hz, 2H), 3.19 (d, J = 1.1 Hz, 2H), 4.22 (q, J = 7.3 Hz, 4H), 9.77 (t, J = 1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.0, 13.9, 18.8, 20.1, 24.2, 46.0, 54.3, 62.0, 75.3, 82.5, 85.4, 105.2, 169.0, 198.8; IR (neat) 2964 m, 2844 w, 2740 w, 2176 m, 1739 s, 1469 w, 1448 w, 1434 w, 1390 w, 1369 w, 1283 s, 1249 s, 1194 s, 1092 m, 1045 m, 1021 m, 874 m, 844 s, 761 m, 699 w, 638 w; MS, *m/z* (relative intensity, %) 364 (M^+, 0.1), 291 (14), 275 (12), 201 (11), 173 (35), 157 (10), 145 (10), 129 (14), 127 (23), 83 (14), 77 (13), 75 (52), 73 (100), 59 (15), 55 (12); exact mass calcd for $C_{19}H_{28}O_5Si$ 364.1706, found 364.1712.

(2-Oxoethyl)-[5-(*E*)-phenyl-4-penten-2-ynyl]propanedioic Acid Diethyl Ester (1e). (2,2-Diethoxyethyl)-[5-(*E*)-phenyl-4-penten-2-ynyl]propanedioic acid diethyl ester was prepared using a modification of the method of Hagihara, as follows.[38] A mixture of (2,2-diethoxyethyl)-2-propynylpropanedioic acid diethyl ester (9.4 g, 30 mmol), *trans*-b-bromostyrene[39] (6.3 g, 34.5 mmol), $PdCl_2(CH_3CN)_2$ (156 mg, 2mol %), triphenylphosphine (315 mg, 4 mol%), CuI (229 mg, 4 mol %) and diethylamine (50 mL) was stirred at room temperature for 12 h. After filtration, the filtrate was concentrated *in vacuo*, and the concentrate was purified by column chromatography on silica gel (hexane/ether = 5/1, R_f 0.16) to give (2,2-Diethoxyethyl)-[5-(*E*)-phenyl-4-penten-2-ynyl]propanedioic acid diethyl ester as a pale yellow liquid (11.9 g, 95 %).

(2-Oxoethyl)-[5-(*E*)-phenyl-4-penten-2-ynyl]propanedioic acid diethyl ester (**1e**) was prepared by hydrolysis of (2,2-diethoxyethyl)-[5-(*E*)-phenyl-4-penten-2-ynyl]propanedioic acid diethyl ester, by a procedure similar to that used for **1a**. Colorless liquid; R_f 0.07 (hexane/ether = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.3 Hz, 6H), 3.16 (d, J = 2.4 Hz, 2H), 3.25 (d, J = 1.1 Hz, 2H), 4.25 (q, J = 7.3 Hz, 4H), 6.08 (td, J = 2.4 Hz, J = 16 Hz, 1H),

6.87 (d, J = 16 Hz, 1H), 7.28-7.37 (m, 5H), 9.80 (t, J = 1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.9, 25.0, 46.1, 54.3, 62.2, 83.2, 86.1, 107.7, 126.1, 128.5, 128.6, 136.0, 141.3, 168.9, 198.7; IR (neat) 3062 w, 3030 w, 2986 m, 2940 w, 2912 w, 2840 w, 2742 w, 2216 w, 1960 w, 1888 w, 1730 s, 1657 w, 1600 w, 1578 w, 1495 w, 1468 m, 1451 m, 1431 w, 1391 m, 1368 m, 1285 s, 1206 s, 1092 s, 1052 m, 1018 m, 957 m, 859 m, 749 m, 692 m, 608 w; MS, *m/z* (relative intensity, %) 342 (M^+, 1), 269 (18), 268 (31), 251 (15), 250 (24), 241 (10), 224 (11), 223 (28), 222 (10), 207 (13), 196 (12), 195 (46), 194 (16), 181 (10), 180 (11), 179 (25), 178 (13), 173 (13), 168 (14), 167 (65), 166 (28), 165 (62), 155 (10), 153 (19), 152 (42), 143 (17), 142 (17), 141 (78), 140 (13), 139 (23), 131 (26), 129 (12), 128 (34), 127 (29), 119 (21), 116 (13), 115 (100), 103 (10), 99 (12), 91 (29), 89 (11), 83 (22), 77 (12), 65 (11), 63 (17), 55 (15), 51 (14); exact mass calcd for $C_{20}H_{22}O_5$ 342.1467, found 342.1460.

(2-Butynyl)-(2-oxoethyl)propanedioic Acid Diethyl Ester (1f). This compound **1f** was prepared by the reaction of (2,2-diethoxyethyl)propanedioic acid diethyl ester with 1-bromo-2-butyne,[40] followed by hydrolysis, by a procedure similar to that used for **1a**. Colorless oil; R_f 0.24 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.25 (t, J = 7.3 Hz, 6H), 1.75 (t, J = 2.4 Hz, 3H), 2.90 (q, J = 2.4 Hz, 2H), 3.17 (d, J = 1.4 Hz, 2H), 4.22 (q, J = 7.3 Hz, 4H), 9.77 (t, J = 1.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 3.3, 13.8, 24.3, 46.0, 54.3, 62.0, 73.2, 79.6, 169.1, 198.9; IR (neat) 2986 m, 2928 m, 2860 w, 2744 w, 2314 w, 2232 w, 1733 s, 1469 m, 1449 m, 1391 m, 1369 m, 1286 s, 1195 s, 1135 w, 1093 s, 1053 m, 1019 m, 945 w, 862 m, 777 w, 716 w, 669 w; MS, *m/z* (relative intensity, %) 254 (M^+, 2), 211 (26), 181 (61), 173 (90), 165 (45), 153 (33), 152 (19), 137 (27), 136 (11), 135 (57), 127 (100), 125 (19), 124 (60), 123 (12), 109 (21), 108 (14), 107 (54), 99 (38), 97 (21), 96 (43), 95 (17), 91 (11), 83 (11), 82 (11), 81 (22), 80 (10), 79 (60), 78 (24), 77 (78), 69 (17), 67 (13), 65 (13), 57 (48), 56 (10), 55 (39), 54 (12), 53 (79), 52 (23), 51 (35); exact mass calcd for $C_{13}H_{18}O_5$ 254.1155, found 254.1150.

(2-Oxoethyl)-(2-pentynyl)propanedioic Acid Dietyl Ester (1g). 1-Bromo-2-pentyne was prepared by the treatment of 2-pentyn-1-ol with PBr_3 using a modification of the method of Brandsma.[35] (2-Oxoethyl)-(2-pentynyl)propanedioic acid dietyl ester (**1g**) was prepared by the reaction of (2,2-diethoxyethyl)propanedioic acid diethyl ester with 1-bromo-2-

pentyne, followed by hydrolysis, by a procedure similar to that used for **1a**. Colorless oil; R_f 0.17 (hexane/ether = 5/1); ^{1}H NMR ($CDCl_3$) δ 1.08 (t, J = 7.3 Hz, 3H), 1.25 (t, J = 7.3 Hz, 6H), 2.12 (tq, J = 2.4 Hz, J = 7.3 Hz, 2H), 2.91 (t, J = 2.4 Hz, 2H), 3.17 (d, J = 1.1 Hz, 2H), 4.22 (q, J = 7.3 Hz, 2H), 4.23 (q, J = 7.3 Hz, 2H), 9.77 (t, J = 1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 12.2, 13.9, 14.0, 24.3, 46.1, 54.5, 62.0, 73.4, 85.8, 169.1, 199.0; IR (neat) 2982 s, 2942 m, 2882 w, 2852 w, 2742 w, 1740 s, 1468 m, 1449 m, 1390 m, 1369 m, 1322 m, 1284 s, 1192 s, 1093 s, 1052 m, 1020 m, 861 w, 783 w, 667 w; MS, m/z (relative intensity, %) 268 (M+, 3), 225 (13), 195 (46), 179 (40), 173 (63), 167 (30), 166 (12), 151 (21), 150 (14), 149 (37), 139 (10), 138 (45), 127 (100), 123 (21), 121 (32), 110 (21), 109 (14), 105 (10), 99 (38), 97 (10), 96 (10), 95 (42), 93 (44), 92 (13), 91 (50), 83 (14), 81 (18), 79 (33), 78 (16), 77 (87), 72 (12), 71 (41), 69 (29), 67 (42), 66 (15), 65 (49), 63 (12), 57 (39), 55 (65), 53 (48), 52 (19), 51 (35); exact mass calcd for $C_{14}H_{20}O_5$ 268.1310, found 268.1303.

6-(Trimethylsilyl)-5-hexynal (3). This compound **3** was prepared by Swern oxidation[41] of 6-(trimethylsilyl)-5-hexyn-1-ol, which was prepared by the treatment of 5-hexyn-1-ol with chlorotrimethylsilane using a modification of the method of Kita.[42] Colorless oil; R_f 0.17 (hexane/ether = 20/1); ^{1}H NMR ($CDCl_3$) δ 0.15 (s, 9H), 1.85 (tt, J = 7.0 Hz, J = 7.0 Hz, 2H), 2.30 (t, J = 7.0 Hz, 2H), 2.58 (dt, J = 1.4 Hz, J = 7.0 Hz, 2H), 9.81 (t, J = 1.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 0.0, 19.2, 21.0, 42.6, 85.8, 105.8, 201.7; IR (neat) 2962 s, 2902 m, 2828 w, 2726 w, 2176 s, 1729 s, 1455 w, 1434 w, 1412 m, 1393 w, 1346 w, 1327 w, 1249 s, 1212 w, 1050 w, 1035 w, 995 w, 946 w, 915 w, 851 s, 760 s, 698 w, 638 w; MS, *m/z* (relative intensity, %) 153 (M^+-15, 19), 116 (14), 101 (17), 97 (54), 83 (12), 81 (11), 75 (100), 73 (40), 69 (14), 61 (12), 59 (23), 55 (20), 53 (15); exact mass calcd for $C_9H_{16}OSi$ 153.0736, found 153.0743.

(2-Oxoethyl)-[4-(trimethylsilyl)-3-butynyl]propanedioic Acid Diethyl Ester (5). This compound **5** was prepared by the reaction of (2,2-diethoxyethyl)propanedioic acid diethyl ester with 4-(trimethylsilyl)-3-butynyl methanesulfonate,[42] followed by hydrolysis, by a procedure similar to that used for **1a**. Colorless oil; R_f 0.17 (hexane/ether = 4/1); ^{1}H NMR ($CDCl_3$) δ 0.13 (s, 9H), 1.26 (t, J = 7.0 Hz, 6H), 2.26 (s, 4H), 3.04 (d, J = 1.1 Hz, 2H), 4.21 (q, J = 7.0 Hz, 2H), 4.22 (q, J = 7.0 Hz, 2H), 9.72 (t, J = 1.1 Hz, 1H); ^{13}C NMR

($CDCl_3$) δ -0.1, 13.9, 15.6, 32.4, 46.1, 54.3, 61.9, 85.6, 105.4, 169.8, 198.4; IR (neat) 2966 m, 2908 w, 2736 w, 2358 w, 2178 m, 1732 s, 1450 w, 1411 w, 1369 w, 1249 s, 1194 s, 1097 m, 1069 w, 1019 m, 933 w, 849 m, 760 m, 698 w, 641 w; MS, *m/z* (relative intensity, %) 326 (M^+, 7), 253 (27), 179 (11), 173 (56), 136 (12), 135 (100), 127 (15), 107 (11), 91 (12), 83 (13), 79 (11), 77 (22), 75 (50), 73 (71), 69 (10), 57 (10), 55 (13); exact mass calcd for $C_{16}H_{26}O_5$ 326.1549, found 326.1537.

3-Methyl-3-[3-(trimethylsilyl)-2-propynyloxy]butanal (7). To a suspension of NaH (2.4 g, 60 mmol) in THF (40 mL) was added dropwise a solution of 3-hydroxy-3-methylbutyl tetrahydro-2-pyranyl ether (9.4 g, 50 mmol), which was prepared by the reaction of 3-methyl-1,3-butanediol with 3,4-dihydro-2*H*-pyran, in THF (10 mL) at 0 °C, and the mixture was stirred at room temperature for 2 h. 1-Bromo-2-propyne (5.4 mL, 60 mmol) was added dropwise at 0 °C, and the mixture was stirred at reflux for 12 h. After filtration, the filtrate was concentrated *in vacuo*, and the concentrate, *p*-toluenesulfonic acid and methanol was stirred at room temperature for 2 h. After addition of saturated $NaHCO_3$ aqueous solution, follwed by filtration and concentration, the concentrate was diluted in ether, and the etherial solution was washed with water and dried over $MgSO_4$. After removal of the volatile, the residue was purified by column chromatography on silica gel (hexane/ether = 1/1, R_f 0.15) to give 3-methyl-3-(2-propynyloxy)butanol as a colorless liquid (1.3 g, 18 %).

After preparation of ethylmagnesium bromide (25 mL of 0.88 M THF solution, 22 mmol), a solution of 3-methyl-3-(2-propynyloxy)butanol (1.3 g, 9.1 mmol) in THF (5 mL) was added dropwise at 0 °C, and the mixture was stirred at room temperature for 3 h. Trimethylsilyl chloride (3.8 mL, 30 mmol) was added dropwise to the solution at 0 °C, and the mixture was stirred at room temperature for 12 h. To the reaction mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the mixture was stirred at room temperature for 1 h. An organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to give crude product, which was purified by column chromatography on silica gel (hexane/ether = 2/1, R_f 0.15) to afford 3-methyl-3-[3-(trimethylsilyl)-2-propynyloxy]butanol as a colorless oil (1.0 g, 52 %).

3-Methyl-3-[3-(trimethylsilyl)-2-propynyloxy]butanal (**7**) was prepared by Swern oxidation[41] of 3-methyl-3-[3-(trimethylsilyl)-2-propynyloxy]butanol. Colorless oil; R_f 0.16 (hexane/ether = 10/1); ^{1}H NMR ($CDCl_3$) δ 0.17 (s, 9H), 1.35 (s, 6H), 2.56 (d, J = 2.7 Hz, 2H), 4.16 (s, 2H), 9.87 (t, J = 2.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ -0.3, 25.9, 51.2, 53.7, 75.3, 90.4, 102.9, 202.2; IR (neat) 2976 m, 2906 w, 2864 w, 2748 w, 2180 w, 1726 s, 1472 w, 1412 w, 1388 m, 1372 m, 1304 w, 1251 s, 1223 w, 1176 w, 1150 m, 1069 s, 1000 m, 849 s, 762 m, 701 w, 646 w; MS, *m/z* (relative intensity, %) 197 (M^+-15, 1), 169 (15), 139 (11), 113 (23), 112 (13), 111 (83), 109 (22), 99 (14), 86 (34), 85 (45), 84 (19), 83 (100), 81 (12), 79 (16), 77 (13), 75 (47), 73 (75), 71 (26), 69 (11), 67 (11), 61 (27), 59 (26), 57 (20), 56 (54), 55 (35), 53 (24); exact mass calcd for $C_{10}H_{17}O_2Si$ 197.0998, found 197.0995.

4-Methyl-*N*-(3-oxopropyl)-*N*-[3-(trimethylsilyl)-2-propynyl]-benzenesulfonamide (9). To a mixture of *N*-(3-hydroxypropyl)phthalimide (6.2 g, 30 mmol), *p*-toluenesulfonic acid (57 mg, 1 mol %) and CH_2Cl_2 (50 mL) was added dropwise 3,4-dihydro-2*H*-pyran (4.2 mL, 45 mmol) at 0 °C, and the mixture was stirred at 0 °C for 2 h. To the reaction mixture was added 10 mL of saturated $NaHCO_3$ aqueous solution, and an organic layer was separated and was dried over $MgSO_4$. After removal of the volatile, the residue was purified by column chromatography on silica gel (hexane/AcOEt = 5/1, R_f 0.14) to give *N*-[3-(tetrahydro-2-pyranyloxy)propyl]phthalimide as a white solid (8.7 g, 100 %). A mixture of *N*-[3-(tetrahydro-2-pyranyloxy)propyl]phthalimide (8.7 g, 30 mmol), hydrazine monohydrate (3.0 mL, 60 mmol) and methanol (70 mL) was stirred at 70 °C for 12 h. After filtration, the filter cake was washed with methanol, and the filtrate was concentrated *in vacuo*. The concentrate was washed with ether, followed by filtration, and the filtrate was concentrated *in vacuo*. The operation (filtration of the concentrate and evaporation of the filtrate) was repeated twice to give 3-(tetrahydro-2-pyranyloxy)propylamine (4.8 g, 100 %).

To a mixture of 3-(tetrahydro-2-pyranyloxy)propynlamine (4.8 g, 30 mmol) and pyridine (40 mL) was added portionwise *p*-toluenesulfonyl chloride (6.7 g, 35 mmol) at 0 °C, and the mixture was stirred at room temperature for 12 h. After filtration of the reaction mixture, the filtrate was concentrated *in vacuo*, and the concentrate was diluted with ethyl acetate (200 mL). The solution was washed with water and saturated $NaHCO_3$ aqueous solution, dried over

$MgSO_4$, and concentrated *in vacuo* to give crude product, which was purified by column chromatography on silica gel (hexane/AcOEt = 2/1, R_f 0.20) to afford 4-methyl-*N*-[3-(tetrahydro-2-pyranyloxy)propyl]benzenesulfonamide as a white solid (9.1 g, 97 %).

A mixture of 4-methyl-*N*-[3-(tetrahydro-2-pyranyloxy)propyl]benzenesulfonamide (7.9 g, 25 mmol), 3-bromo-1-(trimethylsilyl)-1-propyne (9.8 g, 50 mmol), K_2CO_3 (6.9 g, 50 mmol) and CH_3CN (30 mL) was stirred at 60 °C for 15 h. The reaction mixture was filered, and the filtrate was concentrated *in vacuo* to give crude product, which was purified by column chromatography on silica gel (hexane/AcOEt = 10/1, R_f 0.14) to afford 4-methyl-*N*-[3-(tetrahydro-2-pyranyl)propyl]-*N*-[3-(trimethylsilyl)-2-propynyl]benzenesulfonamide as a white solid (9.7 g, 91 %).

A mixture of the above sulfonamide (9.7g, 23 mmol), *p*-toluenesulfonic acid (219 mg, 5 mol%) and methanol (40 mL) was stirred at room temperature for 3 h. To the reaction mixture was added 3 mL of saturated $NaHCO_3$ aqueous solution, and, after filtration, the filtrate was concentrated *in vacuo*. The concentrate was diluted in ethyl acetate (200 mL), and the solution was washed with water and dried over $MgSO_4$. After removal of the volatile, the residue was purified by column chromatography on silica gel (hexane/AcOEt = 4/1, R_f 0.09) to give 4-methyl-*N*-(3-hydroxypropyl)-*N*-[3-(trimethylsilyl)-2-propynyl]benzenesulfonamide as a white solid (7.7 g, 99 %).

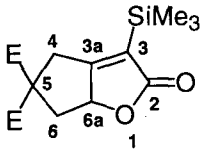
4-Methyl-*N*-(3-oxopropyl)-*N*-[3-(trimethylsilyl)-2-propynyl]benzenesulfonamide (**9**) was prepared using a modification of the method of Mori.[43] 4-Methyl-*N*-(3-hydroxypropyl)-*N*-[3-(trimethylsilyl)-2-propynyl]benzenesulfonamide (3.6 g, 10.5 mmol) in CH_2Cl_2 (60 mL) was added portionwise PCC supported on alumina (24.8 g, 24.8 mmol), and the mixture was stirred at room temperature for 24 h. The reaction mixture was filtered through Florisil, and the Florisil was washed with ether. The filtrate was concentrated *in vacuo*, and the concentrate was purified by column chromatography on silica gel to give 4-methyl-*N*-(3-oxopropyl)-*N*-[3-(trimethylsilyl)-2-propynyl]benzenesulfonamide **9** as a white solid (1.2 g, 33 %) and recover the starting material (2.1 g, 59 %). White solid; mp 64-65 °C (hexane/ether); R_f 0.19 (hexane/AcOEt = 4/1); ^{1}H NMR ($CDCl_3$) δ 0.00 (s, 9H), 2.43 (s, 3H), 2.85 (dt, J = 1.1 Hz, J = 7.0 Hz, 2H), 3.51 (t, J = 7.0 Hz, 2H), 4.14 (s, 2H), 7.30 (d, J = 8.1 Hz, 2H), 7.74 (d, J =

8.1 Hz, 2H), 9.81 (t, J = 1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ -0.5, 21.5, 38.4, 40.5, 43.0, 91.2, 97.8, 127.8, 129.6, 135.3, 143.7, 200.1; IR (KBr) 2966 m, 2906 w, 2844 w, 2746 w, 2180 w, 1923 w, 1722 s, 1652 w, 1600 w, 1497 w, 1448 w, 1420 w, 1394 m, 1384 m, 1344 s, 1332 s, 1306 m, 1281 m, 1252 m, 1246 m, 1223 w, 1167 s, 1139 m, 1112 m, 1088 w, 1071 w, 1024 m, 993 m, 928 w, 905 w, 842 s, 813 w, 800 w, 772 m, 762 m, 699 w, 667 s, 640 w, 600 m; MS, *m/z* (relative intensity, %) 337 (M^+, 0.1), 266 (20), 183 (10), 182 (63), 155 (23), 154 (42), 149 (19), 140 (10), 139 (24), 138 (21), 111 (13), 97 (10), 92 (12), 91 (100), 83 (35), 75 (14), 73 (76), 69 (10), 66 (12), 65 (37), 59 (20), 56 (10), 55 (17). Anal. Calcd for $C_{16}H_{23}NO_3SSi$: C, 56.95; H, 6.88; N, 4.15. Found: C, 56.83; H, 6.79; N, 4.15.

Typical Procedure for Cyclocarbonylation of Yne-Aldehydes and Imines. A 50-mL stainless autoclave was charged with (2-oxoethyl)-[3-(trimethylsilyl)-2-propynyl]propanedioic acid diethyl ester (**1a**) (1 mmol, 312 mg), toluene (5 mL), and $Ru_3(CO)_{12}$ (0.02 mmol, 13 mg). The system was flushed with 10 atmospheres of CO three times. Finally it was pressurized to 10 atm and immersed in an oil bath at 160 °C. After 20 hours had elapsed, the autoclave was removed from the oil bath and allowed to cool for 1 h. The CO was then released. The contents were transferred to a round bottomed flask with ether and the volatiles removed in vacuo. The residue was subjected to column chromatography on silica gel (eluent; hexane/Et_2O = 3/1) to give 4,5,6,6a-tetrahydro-3-(trimethylsilyl)-2*H*-cyclopenta[b]furan-2-one-5,5-dicarboxylic acid diethyl ester (**2a**) (275 mg, 81% yield) as colorless oil.

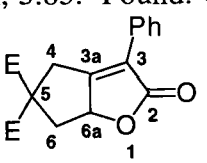
4,5,6,6a-Tetrahydro-3-(trimethylsilyl)-2*H*-cyclopenta[b]furan-2-one-5,5-dicarboxylic Acid Diethyl Ester (2a). Colorless oil; R_f 0.18 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 0.26 (s, 9H, $SiMe_3$), 1.25 (t, J = 7.3 Hz, 3H, CH_3), 1.28 (t, J = 7.3 Hz, 3H, CH_3), 1.74 (dd, J = 11 Hz, J = 13 Hz, 1H, 6-H), 2.94 (dd, J = 7.6 Hz, J = 13 Hz, 1H, 6-H), 3.17 (d, J = 18 Hz, 1H, 4-H), 3.34 (dd, J = 1.1 Hz, J = 18 Hz, 1H, 4-H), 4.16-4.31 (m, 4H, CH_2), 5.03 (dd, J = 7.6 Hz, J = 11 Hz, 1H, 6a-H); ^{13}C NMR ($CDCl_3$) δ -1.7 ($SiMe_3$), 13.9 (CH_3, two overlapping signals), 32.1 (4-C), 36.6 (6-C), 59.7 (5-C), 62.3 (CH_2), 62.4 (CH_2), 83.3 (6a-C), 124.9 (3-C), 169.9 ($COCH_2CH_3$), 170.9 ($COCH_2CH_3$), 177.3 (2-C), 181.0 (3a-C); IR (neat) 2984 m, 1754 s, 1645 m, 1450 w, 1368 w, 1236 m, 1183 m, 1129 w, 1097 w,

1062 w, 1045 w, 1014 w, 949 w, 880 w, 845 m, 784 w, 699 w, 628 w, 603 w; MS, *m/z* (relative intensity, %) 340 (M^+, 20), 326 (19), 325 (87), 295 (20), 267 (31), 252 (11), 251 (58), 223 (26), 207 (16), 195 (12), 179 (26), 177 (21), 153 (16), 149 (13), 140 (15), 135 (13), 133 (18), 125 (14), 121 (11), 105 (14), 103 (12), 97 (10), 91 (13), 84 (11), 83 (11), 77 (19), 75 (100), 73 (86), 61 (11), 59 (14). Anal. Calcd for $C_{16}H_{24}O_6Si$: C, 56.45; H, 7.11. Found: C, 56.17; H, 6.89.



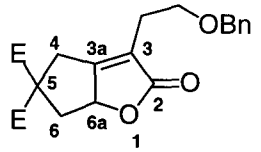
2a

4,5,6,6a-Tetrahydro-3-phenyl-2*H*-cyclopenta[b]furan-2-one-5,5-dicarboxylic Acid Diethyl Ester (2b). White solid; mp 87-89 °C (hexane/ether); R_f 0.13 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.23 (t, *J* = 7.3 Hz, 3H, CH_3), 1.31 (t, *J* = 7.3 Hz, 3H, CH_3), 1.85 (dd, *J* = 11 Hz, *J* = 13 Hz, 1H, 6-H), 2.98 (dd, *J* = 7.6 Hz, *J* = 13 Hz, 1H, 6-H), 3.38 (dd, *J* = 1.3 Hz, *J* = 19 Hz, 1H, 4-H), 3.53 (d, *J* = 19 Hz, 1H, 4-H), 4.18 (q, *J* = 7.3 Hz, 2H, CH_2), 4.29 (q, *J* = 7.3 Hz, 2H, CH_2), 5.18-5.25 (m, 1H, 6a-H), 7.35-7.49 (m, 3H, Ph), 7.69-7.77 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$) δ 13.9 (CH_3), 14.0 (CH_3), 32.4 (4-C), 36.8 (6-C), 60.3 (5-C), 62.3 (CH_2), 62.6 (CH_2), 81.1 (6a-C), 124.6 (3-C), 128.2 (Ph), 128.7 (Ph), 129.1 (Ph), 129.3 (Ph), 165.0 (3a-C), 169.6 ($COCH_2CH_3$), 170.9 ($COCH_2CH_3$), 172.8 (2-C); IR (KBr) 2990 w, 1762 s, 1731 s, 1544 w, 1500 w, 1469 w, 1450 w, 1431 w, 1391 w, 1369 w, 1338 w, 1278 s, 1239 m, 1205 w, 1186 m, 1155 w, 1134 w, 1098 w, 1076 w, 1063 w, 1048 w, 1015 w, 989 w, 973 w, 951 w, 929 w, 899 w, 859 w, 790 w, 752 w, 701 w, 695 w, 670 w, 655 w, 640 w; MS, *m/z* (relative intensity, %) 344 (M+, 19), 270 (37), 242 (15), 241 (15), 225 (10), 198 (13), 197 (65), 170 (11), 169 (30), 153 (18), 152 (15), 144 (23), 142 (16), 141 (49), 139 (12), 129 (15), 128(15), 127 (10), 116 (42), 115 (100), 105 (28), 102 (18), 91 (12), 89 (13), 77 (19), 76 (10), 65 (13), 63 (17), 57 (10), 55 (21), 51 (17). Anal. Calcd for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 66.02; H, 5.82.



2b

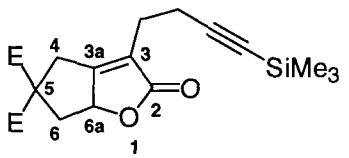
4,5,6,6a-Tetrahydro-3-(2-benzyloxyethyl)-2*H*-cyclopenta[b]furan-2-one-5,5-dicarboxylic Acid Diethyl Ester (2c). Colorless oil; R_f 0.23 (hexane/ether = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.23 (t, *J* = 7.3 Hz, 3H, CH_3), 1.28 (t, *J* = 7.3 Hz, 3H, CH_3), 1.76 (dd, *J* = 11 Hz, *J* = 13 Hz, 1H, 6-H), 2.48-2.69 (m, 2H, $CH_2CH_2OCH_2Ph$), 2.91 (dd, *J* = 7.3 Hz, *J* = 13 Hz, 1H, 6-H), 3.10 (d, *J* = 18 Hz, 1H, 4-H), 3.35 (d, *J* = 18 Hz, 1H, 4-H), 3.57-3.72 (m, 2H, $CH_2CH_2OCH_2Ph$), 4.17 (q, *J* = 7.3 Hz, 2H, CH_2), 4.24 (q, *J* = 7.3 Hz, 2H, CH_2), 4.50 (s, 2H), 5.06 (dd, *J* = 7.3 Hz, *J* = 11 Hz, 1H, 6a-H), 7.24-7.36 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 13.9 (CH_3), 14.0 (CH_3), 25.1 ($CH_2CH_2OCH_2Ph$), 30.7 (4-C), 37.0 (6-C), 59.9 (5-C), 62.2 (CH_2), 62.4 (CH_2), 67.4 ($CH_2CH_2OCH_2Ph$), 72.9 (CH_2Ph), 81.5 (6a-C), 123.0 (3-C), 127.6 (Ph, two overlapping signals), 128.4 (Ph), 138.1 (Ph), 166.5 (3a-C), 169.8 ($COCH_2CH_3$), 171.0 ($COCH_2CH_3$), 175.0 (2-C); IR (neat) 2984 m, 2936 m, 2870 m, 1767 s, 1731 s, 1499 w, 1456 m, 1390 w, 1367 m, 1341 w, 1265 s, 1238 s, 1189 s, 1143 s, 1096 s, 1049 s, 985 w, 904 w, 885 w, 859 w, 740 m, 699 m; MS, *m/z* (relative intensity, %) 402 (M^+, 8), 223 (13), 97 (16), 96 (11), 91 (100), 84 (10), 83 (19), 82 (10), 72 (32), 71 (15), 70 (13), 69 (22), 67 (10), 65 (11), 60 (13), 59 (90), 57 (49), 56 (19), 55 (63), 54 (14). Anal. Calcd for $C_{22}H_{26}O_7$: C, 65.66; H, 6.51. Found: C, 65.38; H, 6.56.



2c

4,5,6,6a-Terahydro-3-[(4-trimethylsilyl)-3-butynyl]-2*H*-cyclopenta[b]-furan-2-one-5,5-dicarboxylic Acid Diethyl Ester (2d). Colorless oil; R_f 0.10 (hexane/ether = 2/1); ^{1}H NMR ($CDCl_3$) δ 0.13 (s, 9H, $SiMe_3$), 1.25 (t, *J* = 7.3 Hz, 3H, CH_3), 1.27 (t, *J* = 7.3 Hz, 3H, CH_3), 1.73 (dd, *J* = 11 Hz, *J* = 12 Hz, 1H, 6-H), 2.34-2.62 (m, 4H, $CH_2CH_2CCSiMe_3$), 2.94 (dd, *J* = 7.3 Hz, *J* = 12 Hz, 1H, 6-H), 3.16 (d, *J* = 18 Hz, 1H, 4-H), 3.37 (d, *J* = 18 Hz, 1H, 4-H), 4.20 (q, *J* = 7.3 Hz, 2H, CH_2), 4.24 (dq, *J* = 1.6 Hz, *J* = 7.3 Hz, 2H, CH_2), 5.08 (dd, *J* = 7.3 Hz, *J* = 11 Hz, 1H, 6a-H); ^{13}C NMR ($CDCl_3$) δ -0.1 ($SiMe_3$), 13.9 (CH_3, two overlapping signals), 18.5 ($CH_2CH_2CCSiMe_3$), 23.7 ($CH_2CH_2CCSiMe_3$), 30.9 (4-C), 36.9 (6-C), 59.9 (5-C), 62.3 (CH_2), 62.4 (CH_2), 81.5 (6a-C), 85.8 ($CH_2CH_2CCSiMe_3$), 105.6 ($CH_2CH_2CCSiMe_3$), 124.0 (3-C), 166.3 (3a-C), 169.8

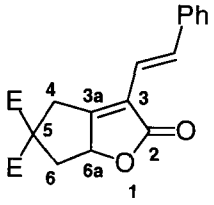
($COCH_2CH_3$), 170.9 ($COCH_2CH_3$), 174.8 (2-C); IR (neat) 2964 m, 2910 m, 2178 m, 1768 s, 1738 s, 1704 m, 1469 w, 1448 w, 1392 w, 1368 w, 1342 w, 1253 s, 1187 m, 1142 m, 1096 w, 1049 m, 949 w, 845 s, 761 m, 699 w, 638 w; MS, *m/z* (relative intensity, %) 392 (M^+, 7), 377 (10), 129 (11), 128 (11), 127 (10), 96 (13), 83 (19), 81 (20), 79 (11), 77 (17), 75 (76), 74 (10), 73 (100), 59 (17), 55 (16), 53 (15); exact mass calcd for $C_{20}H_{28}O_6Si$ 392.1655, found 392.1657.



2d

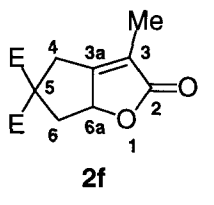
4,5,6,6a-Tetrahydro-3-[(*E*)-2-phenylethenyl]-2*H*-cyclopenta[b]furan-2-one-5,5-dicarboxylic Acid Diethyl Ester (2e). White solid; mp 87-89 ℃ (hexane/ether); R_f 0.15 (hexane/ether = 3/1); ^1H NMR ($CDCl_3$) δ 1.26 (t, J = 7.3 Hz, 3H, CH_3), 1.31 (t, J = 7.3 Hz, 3H, CH_3), 1.82 (dd, J = 11 Hz, J = 13 Hz, 1H, 6-H), 2.98 (dd, J = 7.3 Hz, J = 13 Hz, 1H, 6-H), 3.34 (d, J = 19 Hz, 1H, 4-H), 3.45 (dd, J = 1.6 Hz, J = 19 Hz, 1H, 4-H), 4.22 (q, J = 7.3 Hz, 2H, CH_2), 4.29 (q, J = 7.3 Hz, 2H, CH_2), 5.15-5.22 (m, 1H, 6a-H), 6.78 (d, J = 16 Hz, 1H, C*H*Ph), 7.28-7.40 (m, 3H, Ph), 7.37 (d, J = 16 Hz, 1H, C*H*=CHPh), 7.49-7.52 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$) δ 13.9 (CH_3), 14.0 (CH_3), 31.6 (4-C), 37.0 (6-C), 60.4 (5-C), 62.3 (CH_2), 62.5 (CH_2), 81.5 (6a-C), 115.7 (*C*HPh), 122.7 (3-C), 126.8 (Ph), 128.6 (Ph), 128.7 (Ph), 135.5 (*C*H=CHPh), 136.4 (Ph), 163.3 (3a-C), 169.6 ($COCH_2CH_3$), 170.9 ($COCH_2CH_3$), 173.1 (2-C); IR (KBr) 2988 w, 1766 m, 1748 m, 1728 s, 1632 w, 1497 w, 1453 w, 1392 w, 1370 w, 1340 w, 1297 w, 1265 m, 1237 m, 1188 m, 1145 m, 1119 w, 1094 w, 1044 m, 1015 w, 972 w, 924 w, 858 w, 747 m, 691 w, 669w; MS, *m/z* (relative intensity, %) 370 (M^+, 50), 325 (15), 324 (17), 306 (11), 297 (18), 296 (60), 279 (13), 278 (20), 267 (14), 252 (11), 251 (36), 250 (69), 235 (11), 234 (26), 233 (15), 224 (15), 223 (69), 222 (47), 207 (12), 206 (12), 205 (11), 196 (20), 195 (45), 194 (17), 181 (11), 180 (11), 179 (43), 178 (37), 177 (12), 171 (18), 170 (86), 169 (36), 168 (15), 167 (55), 166 (27), 165 (73), 155 (15), 154 (12), 153 (21), 152 (47), 142 (20), 141 (100), 139 (18), 131 (12), 129 (11), 128 (35), 127 (27), 116 (12), 115 (77), 113 (14), 105

(74), 102 (10), 99 (10), 91 (34), 89 (17), 83 (17), 77 (29), 65 (14), 63 (15), 55 (15), 51 (17). Anal. Calcd for $C_{21}H_{22}O_6$: C, 68.08; H, 5.99. Found: C, 67.90; H, 6.03.



2e

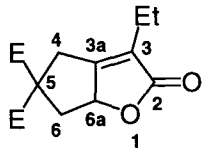
4,5,6,6a-Tetrahydro-3-methyl-2*H*-cyclopenta[b]furan-2-one-5,5-dicarboxylic Acid Diethyl Ester (2f). Colorless oil; R_f 0.09 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.25 (t, *J* = 7.3 Hz, 3H, CH_3), 1.27 (t, *J* = 7.3 Hz, 3H, CH_3), 1.73 (dd, *J* = 11 Hz, *J* = 13 Hz, 1H, 6-H), 1.84 (d, *J* = 0.8 Hz, 3H, CH_3), 2.91 (dd, *J* = 7.6 Hz, *J* = 13 Hz, 1H, 6-H), 3.07 (d, *J* = 18 Hz, 1H, 4-H), 3.25 (d, *J* = 18 Hz, 1H, 4-H), 4.20 (q, *J* = 7.3 Hz, 2H, CH_2), 4.24 (q, *J* = 7.3 Hz, 2H, CH_2), 4.99-5.09 (m, 1H, 6a-H); ^{13}C NMR ($CDCl_3$) δ 9.1 (CH_3), 13.9 (CH_3, two overlapping signals), 30.2 (4-C), 37.0 (6-C), 59.9 (5-C), 62.2 (CH_2), 62.4 (CH_2), 81.3 (6a-C), 121.8 (3-C), 164.4 (3a-C), 169.9 ($COCH_2CH_3$), 170.9 ($COCH_2CH_3$), 175.4 (2-C); IR (neat) 2986 m, 2940 w, 1736 s, 1450 w, 1388 w, 1368 w, 1345 w, 1271 s, 1191 s, 1147 m, 1093 m, 1045 s, 982 w, 871 w, 760 w, 695 w, 652 w; MS, *m/z* (relative intensity, %) 282 (M^+, 6), 208 (21), 180 (13), 179 (16), 163 (18), 152 (15), 137 (14), 136 (16), 135 (86), 124 (11), 119 (13), 110 (10), 109 (12), 108 (16), 107 (30), 91 (27), 83 (10), 82 (79), 81 (26), 80 (16), 79 (70), 78 (16), 77 (64), 69 (10), 67 (16), 65 (23), 63 (10), 55 (33), 54 (52), 53 (100), 52 (29), 51 (40), 50 (13). Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43. Found: C, 59.64; H, 6.40.



2f

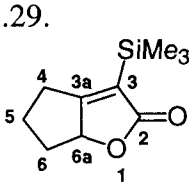
4,5,6,6a-Tetrahydro-3-ethyl-2*H*-cyclopenta[b]furan-2-one-5,5-dicarboxylic acid diethyl ester (2g). Colorless oil; R_f 0.10 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.14 (t, *J* = 7.6 Hz, 3H, CH_3), 1.24 (t, *J* = 7.0 Hz, 3H, CH_3CH_2CO), 1.27 (t, *J* = 7.0 Hz, 3H, CH_3CH_2CO), 1.72 (dd, *J* = 11 Hz, *J* = 12 Hz, 1H, 6-H), 2.17-2.42 (m, 2H, CH_2), 2.91 (dd, *J* = 7.3 Hz, *J* = 12 Hz, 1H, 6-H), 3.10 (d, *J* = 18 Hz, 1H, 4-H), 3.32

(d, J = 18 Hz, 1H, 4-H), 4.20 (dq, J = 0.54 Hz, J = 7.0 Hz, 2H, CH_3CH_2CO), 4.24 (dq, J = 0.54 Hz, J = 7.0 Hz, 2H, CH_3CH_2CO), 4.96-5.07 (m, 1H, 6a-H); ^{13}C NMR ($CDCl_3$) δ 12.1 (CH_3), 13.9 (CH_3CH_2CO, two overlapping signals), 17.9 (CH_2), 30.4 (4-C), 36.9 (6-C), 60.1 (5-C), 62.2 (CH_3CH_2CO), 62.4 (CH_3CH_2CO), 81.2 (6a-C), 127.2 (3-C), 163.6 (3a-C), 169.9 ($COCH_2CH_3$), 170.9 ($COCH_2CH_3$), 175.0 (2-C); IR (neat) 2982 m, 2942 m, 2884 w, 1765 s, 1731 s, 1704 m, 1467 m, 1449 m, 1391 w, 1368 m, 1337 w, 1266 s, 1238 s, 1190 s, 1145 m, 1097 m, 1045 s, 1016 w, 984 w, 957 w, 938 w, 899 w, 884 w, 859 w, 782 w, 765 w, 699 w, 652 w; MS, *m/z* (relative intensity, %) 296 (M^+, 36), 251 (22), 223 (25), 222 (38), 195 (15), 194 (20), 193 (50), 178 (10), 177 (29), 176 (14), 165 (14), 151 (15), 150 (18), 149 (100), 148 (17), 133 (10), 127 (11), 121 (31), 105 (17), 96 (55), 95 (17), 93 (20), 91 (26), 81 (13), 79 (25), 77 (37), 67 (25), 65 (18), 55 (19), 53 (24), 51 (12). Anal. Calcd for $C_{15}H_{20}O_6$: C, 60.78; H, 6.81. Found: C, 60.76; H, 6.72.



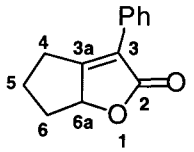
2g

4,5,6,6a-Tetrahydro-3-(trimethylsilyl)-2-cyclopenta[b]furan-2-one (4a). Colorless oil; R_f 0.17 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 0.25 (s, 9H, $SiMe_3$), 1.31 (dq, J = 8.9 Hz, J = 11 Hz, 1H, 6-H), 1.98-2.30 (m, 3H, 5-H, 6-H), 2.47-2.69 (m, 2H, 4-H), 4.90 (dd, J = 7.3 Hz, J = 11 Hz,1H, 6a-H); ^{13}C NMR ($CDCl_3$) δ -1.7 ($SiMe_3$), 23.3 (4-C), 23.7 (5-C), 29.1 (6-C), 85.7 (6a-C), 123.3 (3-C), 178.3 (2-C), 186.9 (3a-C); IR (neat) 2962 m, 2900 w, 1747 s, 1635 m, 1532 w, 1454 w, 1429 w, 1339 w, 1309 w, 1299 w, 1248 s, 1204 w, 1165 m, 1126 s, 1107 s, 1021 m, 989 m, 950 w, 916 m, 869 s, 844 s, 783 m, 754 w, 722 w, 698 w, 642 w, 625 w; MS, *m/z* (relative intensity, %) 196 (M^+, 3), 181 (42), 153 (28), 137 (15), 136 (14), 135 (11), 125 (20), 107 (26), 97 (12), 83 (13), 77 (31), 75 (100), 73 (36), 69 (18), 67 (10), 61 (44), 59 (39), 55 (18), 53 (22). Anal. Calcd for $C_{10}H_{16}O_2Si$: C, 61.18; H, 8.21. Found: C, 60.99; H, 8.29.



4a

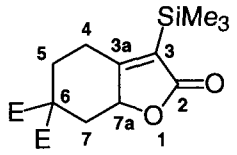
4,5,6,6a-Tetrahydro-3-phenyl-2-cyclopenta[b]furan-2-one (4b). White solid; mp 56-58 °C (hexane); R_f 0.17 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.36 (q, J = 11 Hz, 1H, 6-H), 2.14-2.42 (m, 3H, 5-H, 6-H), 2.67 (dtd, J = 1.1 Hz, J = 8.6 Hz, J = 19 Hz, 1H, 4-H), 2.86 (ddd, J = 6.5 Hz, J = 9.2 Hz, J = 19 Hz, 1H, 4-H), 5.07 (dd, J = 7.0 Hz, J = 11 Hz,1H, 6a-H), 7.33-7.46 (m, 3H, Ph), 7.73-7.77 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$) δ 23.7 (4-C), 24.2 (5-C), 29.1 (6-C), 83.3 (6a-C), 123.3 (3-C), 127.9 (Ph), 128.4 (Ph), 128.5 (Ph), 130.0 (Ph), 170.8 (3a-C), 173.8 (2-C); IR (KBr) 2982 w, 2950 w, 2886 w, 1746 s, 1658 w, 1562 w, 1498 w, 1469 w, 1450 w, 1422 w, 1336 w, 1305 w, 1294 w, 1273 w, 1197 w, 1163 w, 1125 m, 1084 m, 1025 w, 999 w, 960 m, 931 w, 912 w, 787 m, 757 w, 699 m, 670 w, 655 w, 633 w; MS, *m/z* (relative intensity, %) 200 (M^+, 75), 173 (10), 172 (86), 171 (13), 144 (89), 130 (16), 129 (17), 128 (25), 117 (15), 116 (85), 115 (100), 102 (13), 89 (14), 77 (12), 76 (10), 71 (15), 65 (11), 63 (22), 57 (10), 55 (12), 51 (21), 50 (12). Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.97; H, 6.04. Found: C, 77.85; H, 6.18.



4b

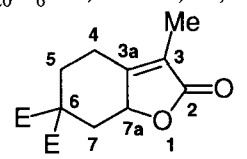
5,6,7,7a-Tetrahydro-3-(trimethylsilyl)-2(4*H*)-benzofuranone-6,6-dicarboxylic Acid Diethyl Ester (6a). Colorless oil; R_f 0.14 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 0.26 (s, 9H, $SiMe_3$), 1.24 (t, J = 7.3 Hz, 3H, CH_3), 1.29 (t, J = 7.3 Hz, 3H, CH_3), 1.59 (dd, J = 12 Hz, J = 13 Hz, 1H, 7-H), 1.78 (dt, J = 4.6 Hz, J = 14 Hz, 1H, 5-H), 2.42 (dt, J = 4.6 Hz, J = 14 Hz, 1H, 4-H), 2.61 (quintd, J = 2.3 Hz, J = 14 Hz, 1H, 4-H), 2.93 (qd, J = 2.3 Hz, J = 14 Hz, 1H, 5-H), 3.06 (ddd, J = 2.3 Hz, J = 6.3 Hz, J = 13 Hz, 1H, 7-H), 4.18 (q, J = 7.3 Hz, 2H, CH_2), 4.26 (q, J = 7.3 Hz, 2H, CH_2), 4.81 (dd, J = 6.3 Hz, J = 12 Hz, 1H, 7a-H); ^{13}C NMR ($CDCl_3$) δ -1.0 ($SiMe_3$), 13.9 (CH_3), 14.0 (CH_3), 24.9 (4-C), 32.0 (5-C), 38.4 (7-C), 54.3 (6-C), 62.0 (CH_2), 62.1 (CH_2), 78.7 (7a-C), 123.6 (3-C), 169.8 ($COCH_2CH_3$), 170.0 ($COCH_2CH_3$), 175.9 (2-C), 177.0 (3a-C); IR (neat) 2982 m, 2904 w, 1753 s, 1732 s, 1628 m, 1451 w, 1392 w, 1369 w, 1333 w, 1296 m, 1246 m, 1174 m, 1126 w, 1096 m, 1023 m, 974 w, 898 w, 845 m, 787 w, 750 w, 697 w, 669 w, 635 w, 609 w; MS, *m/z* (relative intensity, %) 354 (M^+, 17), 309 (10), 280 (18), 265 (16), 263 (10),

219 (12), 207 (11), 191 (10), 183 (12), 182 (84), 173 (24), 145 (12), 127 (11), 91 (11), 77 (16), 75 (81), 73 (100), 59 (13). Anal. Calcd for $C_{17}H_{26}O_6Si$: C, 57.60; H, 7.39. Found: C, 57.44; H, 7.29.



6a

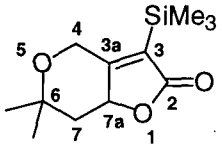
5,6,7,7a-Tetrahydro-3-methyl-2(4*H*)-benzofuranone-6,6-dicarboxylic Acid Diethyl Ester (6b). White solid; mp 57-58 °C (hexane/ether); R_f 0.17 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.22 (t, J = 7.3 Hz, 3H, CH_3), 1.28 (t, J = 7.3 Hz, 3H, CH_3), 1.53 (dd, J = 12 Hz, J = 13 Hz, 1H, 7-H), 1.73 (dt, J = 4.6 Hz, J = 14 Hz, 1H, 5-H), 1.79 (t, J = 1.3 Hz, 3H, CH_3), 2.33 (tdt, J = 2.0 Hz, J = 4.6 Hz, J = 15 Hz, 1H, 4-H), 2.58 (quintd, J = 2.3 Hz, J = 14 Hz, 1H, 5-H), 2.79 (ddd, J = 2.0 Hz, J = 4.6 Hz, J = 15 Hz, 1H, 4-H), 3.06 (ddd, J = 2.3 Hz, J = 5.9 Hz, J = 13 Hz, 1H, 7-H), 4.16 (q, J = 7.3 Hz, 2H, CH_2), 4.25 (q, J = 7.3 Hz, 2H, CH_2), 4.82 (dd, J = 5.9 Hz, J = 12 Hz, 1H, 7a-H); ^{13}C NMR ($CDCl_3$) δ 8.2 (CH3), 13.9 (CH_3), 14.0 (CH_3), 22.5 (4-C), 31.2 (5-C), 38.0 (7-C), 54.5 (6-C), 62.0 (CH_2), 62.1 (CH_2), 76.9 (7a-C), 120.6 (3-C), 160.1 (3a-C), 169.8 ($COCH_2CH_3$), 170.0 ($COCH_2CH_3$), 174.2 (2-C); IR (KBr) 2984 m, 2944 w, 1766 s, 1692 m, 1525 w, 1451 m, 1391 w, 1368 w, 1329 w, 1295 m, 1244 s, 1185 s, 1113 m, 1093 s, 1065 w, 1033 s, 960 w, 939 w, 862 m, 813 w, 765 w, 749 w, 706 w, 669 w, 649 w; MS, *m/z* (relative intensity, %) 296 (M^+, 11), 223 (11), 222 (43), 194 (14), 193 (53), 177 (10), 173 (64), 150 (14), 149 (100), 127 (57), 121 (15), 99 (11), 93 (12), 91 (19), 82 (13), 79 (10), 77 (22), 55 (15), 54 (15), 53 (31). Anal. Calcd for $C_{15}H_{20}O_6$: C, 60.78; H, 6.81. Found: C, 60.77; H, 6.69.



6b

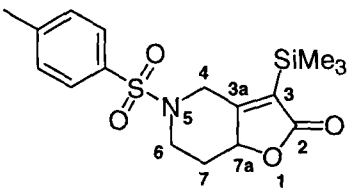
7,7a-Dihydro-6,6-dimethyl-3-(trimethylsilyl)-4*H*-furo[3,2-c]pyran-2(6*H*)-one (8). White solid; mp 103-105 °C (hexane); R_f 0.17 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 9H, $SiMe_3$), 1.29 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.51 (t, J = 12 Hz,

1H, 7-H), 2.38 (dd, J = 6.3 Hz, J = 12 Hz, 1H, 7-H), 4.42 (d, J = 14 Hz, 1H, 4-H), 4.67 (d, J = 14 Hz, 4-H), 4.86 (dd, J = 6.3 Hz, J = 12 Hz, 1H, 7a-H); ^{13}C NMR ($CDCl_3$) δ -1.2 ($SiMe_3$), 22.4 (CH_3), 30.1 (CH_3), 45.0 (7-C), 59.8 (4-C), 72.7 (6-C), 77.8 (7a-C), 124.8 (3-C), 172.8 (3a-C), 175.6 (2-C); IR (KBr) 2958 w, 2856 w, 1735 s, 1633 m, 1542 w, 1457 w, 1387 w, 1373 w, 1357 w, 1302 w, 1280 w, 1250 m, 1235 w, 1211 w, 1188 w, 1140 m, 1098 m, 1047 m, 1027 w, 1014 w, 999 w, 983 w, 969 w, 861 m, 845 m, 790 w, 770 w, 760 w, 750 w, 735 w, 717 w, 702 w; MS, *m/z* (relative intensity, %) 240 (M^+, 3), 225 (11), 209 (11), 169 (15), 168 (34), 167 (37), 154 (21), 139 (14), 123 (56), 111 (11), 97 (15), 95 (17), 85 (16), 84 (12), 83 (31), 77 (12), 75 (100), 73 (90), 69 (11), 59 (24), 57 (18), 55 (16), 53 (16). Anal. Calcd for $C_{12}H_{20}O_3Si$: C, 59.96; H, 8.39. Found: C, 59.89; H, 8.25.



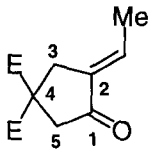
8

5,6,7,7a-Tetrahydro-5-[(4-methylphenyl)sufonyl]-3-(trimethylsilyl)-furo[3,2-c]pyridin-2(4*H*)-one (10). White solid; mp 144-146 °C (hexane/AcOEt); R_f 0.14 (hexane/AcOEt = 3/1); ^{1}H NMR ($CDCl_3$) δ 0.32 (s, 9H, $SiMe_3$), 1.55 (dq, J = 4.6 Hz, J = 12 Hz, 1H, 7-H), 2.40 (tt, J = 2.7 Hz, J = 6.5 Hz, 1H, 7-H), 2.45 (s, 3H, CH_3), 2.65 (dt, J = 2.7 Hz, J = 13 Hz, 1H, 6-H), 3.28 (d, J = 14 Hz, 1H, 4-H), 3.97 (tdd, J = 2.2 Hz, J = 4.6 Hz, J = 13 Hz, 1H, 6-H), 4.55 (dd, J = 6.5 Hz, J = 12 Hz, 1H, 7a-H), 4.89 (dd, J = 2.2 Hz, J = 14 Hz, 1H, 4-H), 7.35 (d, J = 7.8 Hz, 2H, Ar), 7.68 (d, J = 7.8 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ -1.3 ($SiMe_3$), 21.5 (CH_3), 32.5 (7-C), 42.9 (6-C), 45.4 (4-C), 79.5 (7a-C), 126.7 (3-C), 127.5 (Ar), 130.0 (Ar), 133.5 (Ar), 144.3 (Ar), 168.7 (3a-C), 175.2 (2-C); IR (KBr) 2960 w, 2858 w, 1755 s, 1738 s, 1640 m, 1599 w, 1496 w, 1461 w, 1447 w, 1352 s, 1335 m, 1305 w, 1289 w, 1271 m, 1246 m, 1183 m, 1164 s, 1144 m, 1120 m, 1085 m, 1039 w, 1018 w, 1005 m, 975 w, 965 w, 948 m, 907 w, 861 m, 844 s, 815 m, 790 w, 760 w, 743 m, 709 w, 683 m, 654 w, 634 w, 621 w; MS, *m/z* (relative intensity, %) 365 (M^+, 0.9), 352 (11), 351 (23), 350 (100), 194 (16), 176 (21), 149 (16), 139 (10), 120 (20), 91 (60), 75 (22), 73 (45), 65 (21), 59 (10). Anal. Calcd for $C_{17}H_{23}NO_4SSi$: C, 55.87; H, 6.35; N, 3.84. Found: C, 55.91; H, 6.17; N. 3.77.



10

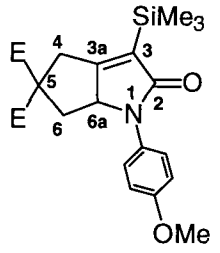
2-(*E*)-Ethylidenecyclopentane-4,4-dicarboxylic Acid Diethyl Ester (11) Colorless oil; R_f 0.16 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.26 (t, J = 7.3 Hz, 6H, CH_3), 1.83 (td, J = 1.9 Hz, J = 7.3 Hz, 3H, $CHCH_3$), 2.91 (s, 2H, 5-H), 3.16 (qd, J = 1.9 Hz, J = 2.7 Hz, 2H, 3-H), 4.22 (q, J = 7.3 Hz, CH_2), 6.69 (tq, J = 2.7 Hz, J = 7.3 Hz, 1H, $CHCH_3$); ^{13}C NMR ($CDCl_3$) δ 13.9 (CH_3), 15.2 ($CHCH_3$), 34.1 (3-C), 45.3 (5-C), 54.1 (4-C), 62.0 (CH_2), 133.2 ($CHCH_3$), 135.4 (2-C), 170.8 ($COCH_2CH_3$), 200.9 (1-C); IR (neat) 2986 m, 2942 m, 1731 s, 1659 s, 1469 m, 1449 m, 1396 m, 1369 m, 1284 s, 1242 s, 1207 s, 1157 m, 1135 m, 1096 m, 1067 m, 1040 m, 1010 w, 968 w, 931 w, 900 w, 862 w, 836 w, 790 w, 735 w, 610 w; MS, *m/z* (relative intensity, %) 254 (M^+, 23), 209 (10), 181 (51), 180 (100), 153 (39), 152 (68), 135 (15), 134 (21), 124 (24), 109 (10), 107 (22), 106 (21), 96 (16), 81 (20), 80 (13), 79 (61), 77 (30), 68 (10), 55 (17), 54 (23), 53 (31), 52 (10), 51 (13); exact mass calcd for $C_{13}H_{18}O_5$ 254.1155, found 254.1146.



11

4,5,6,6a-Tetrahydro-1-(4-methoxyphenyl)-3-(trimethylsilyl)-2*H*-cyclopenta[b]pyrrol-2-one-5,5-dicarboxylic acid diethyl ester (14). White solid; mp 86-87 °C (hexane); R_f 0.16 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 0.29 (s, 9H, $SiMe_3$), 1.24 (t, J = 7.3 Hz, 3H, CH_3), 1.31 (t, J = 7.3 Hz, 3H, CH_3), 1.67 (t, J = 12 Hz, 1H, 6-H), 3.03 (dd, J = 7.3 Hz, J = 12 Hz, 1H, 6-H), 3.19 (d, J = 18 Hz, 1H, 4-H), 3.39 (d, J = 18 Hz, 1H, 4-H), 3.79 (s, 3H, OCH_3) 4.20 (dq, J = 2.7 Hz, J = 7.3 Hz, 2H, CH_2), 4.28 (dq, J = 2.7 Hz, J = 7.3 Hz, 2H, CH_2), 4.76 (dd, J = 7.3 Hz, J = 12 Hz, 1H, 6a-H), 6.88 (d, J = 8.4 Hz, 2H, Ar), 7.31 (d, J = 8.4 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ -1.3 ($SiMe_3$), 13.9 (CH_3), 14.0 (CH_3), 32.7 (4-C), 37.2 (6-C), 55.5 (OCH_3), 60.8 (5-C), 62.1 (CH_2), 62.3

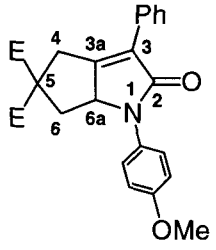
(CH_2), 66.7 (6a-C), 114.2 (Ar), 121.3 (Ar), 131.3 (Ar), 132.2 (3-C), 156.1 (Ar), 170.2 ($COCH_2CH_3$), 171.0 (3a-C), 171.4 ($COCH_2CH_3$), 174.7 (2-C); IR (KBr) 2964 m, 2906 m, 2844 w, 1742 s, 1674 s, 1639 m, 1515 s, 1461 m, 1449 m, 1427 m, 1373 m, 1320 m, 1300 s, 1274 s, 1249 s, 1180 s, 1159 s, 1133 m, 1114 m, 1089 m, 1080 m, 1055 m, 1036 m, 1024 m, 1009 m, 911 w, 842 s, 829 s, 780 m, 767 m, 743 w, 687 w, 669 w, 630 w, 618 w; MS, *m/z* (relative intensity, %) 445 (M^+, 36), 372 (12), 134 (11), 77 (18), 75 (34), 73 (100), 59 (10). Anal. Calcd for $C_{23}H_{31}NO_6Si$: C, 62.00; H, 7.02; N, 3.15. Found: C, 61.87; H, 7.02; N, 3.09.



14

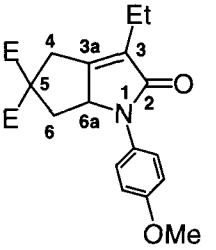
4,5,6,6a-Tetrahydro-1-(4-methoxyphenyl)-3-phenyl-2*H*-cyclopenta[b]pyrrol-2-one-5,5-dicarboxylic acid diethyl ester (16). White solid; mp 97-98 °C (hexane); R_f 0.20 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.21 (t, *J* = 7.0 Hz, 3H, CH_3), 1.33 (t, *J* = 7.0 Hz, 3H, CH_3), 1.76 (t, *J* = 12 Hz, 1H, 6-H), 3.05 (dd, *J* = 6.8 Hz, *J* = 12 Hz, 1H, 6-H), 3.48 (d, *J* = 18 Hz, 1H, 4-H), 3.53 (d, *J* = 18 Hz, 1H, 4-H), 3.82 (s, 3H, OCH_3) 4.16 (q, *J* = 7.0 Hz, 2H, CH_2), 4.31 (q, *J* = 7.0 Hz, 2H, CH_2), 4.86 (dd, *J* = 7.0 Hz, *J* = 12 Hz, 1H, 6a-H), 6.94 (d, *J* = 8.9 Hz, 2H, Ar), 7.36-7.47 (m, 3H, Ar), 7.76 (d, *J* = 8.9 Hz, 2H, Ar), 7.78 (d, *J* = 7.8 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ 13.4 (CH_3), 13.5 (CH_3), 32.2 (4-C), 36.9 (6-C), 55.0 (OCH_3), 60.9 (5-C), 61.7 (CH_2), 61.9 (CH_2), 63.6 (6a-C), 113.9 (Ar), 121.7 (Ar), 127.9 (Ar), 128.0 (Ar),129.3 (3-C), 130.5 (Ar), 131.5 (Ar), 155.5 (3a-C), 156.2 (Ar), 169.4 ($COCH_2CH_3$), 169.7 (2-C), 170.9 ($COCH_2CH_3$); IR (KBr) 2982 m, 2840 w, 2220 w, 1735 s, 1693 s, 1583 w, 1515 s, 1470 m, 1447 m, 1371 m, 1296 m, 1266 m, 1243 s, 1182 m, 1147 m, 1136 m, 1092 m, 1056 m, 1022 m, 959 w, 858 w, 829 w, 788 m, 757 w, 701 w, 669 m, 654 m, 610 w; MS, *m/z* (relative intensity, %) 449 (M^+, 71), 421 (26), 420 (76), 346 (28), 303 (21), 302 (100), 274 (14), 153 (15), 152 (14), 141 (15),

134 (36), 122 (11), 115 (36), 108 (25), 107 (20), 92 (19), 77 (48), 64 (16). Anal. Calcd for $C_{26}H_{27}NO_6$: C, 69.46; H, 6.06; N, 3.12. Found: C, 69.31; H, 6.06; N, 3.16.



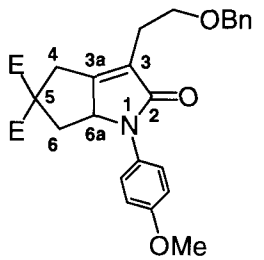
16

4,5,6,6a-Tetrahydro-3-ethyl-1-(4-methoxyphenyl)-2*H*-cyclopenta[b]pyrrol-2-one-5,5-dicarboxylic acid diethyl ester (18). White solid; mp 87-88 °C (hexane); R_f 0.07 (hexane/ether = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.16 (t, J = 7.8 Hz, 3H, CH_3), 1.22 (t, J = 7.3 Hz, 3H, CH_3), 1.29 (t, J = 7.3 Hz, 3H, CH_3), 1.62 (t, J = 12 Hz, 1H, 6-H), 2.22-2.46 (m, 2H, CH_2), 3.00 (dd, J = 6.8 Hz, J = 12 Hz, 1H, 6-H), 3.10 (d, J = 18 Hz, 1H, 4-H), 3.36 (d, J = 18 Hz, 1H, 4-H), 3.78 (s, 3H, OCH_3) 4.18 (dq, J = 2.2 Hz, J = 7.3 Hz, 2H, CH_2), 4.26 (dq, J = 2.7 Hz, J = 7.3 Hz, 2H, CH_2), 4.67 (dd, J = 6.8 Hz, J = 12 Hz, 1H, 6a-H), 6.88 (d, J = 8.9 Hz, 2H, Ar), 7.51 (d, J = 8.9 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ 12.5 (CH_3), 13.8 (CH_3), 13.9 (CH_3), 18.0 (CH_2), 30.6 (4-C), 37.5 (6-C), 55.4 (OCH_3), 61.2 (5-C), 62.0 (CH_2), 62.2 (CH_2), 63.9 (6a-C), 114.2 (Ar), 121.1 (Ar), 132.3 (3-C), 132.6 (Ar), 153.8 (3a-C), 156.2 (Ar), 170.2 ($COCH_2CH_3$), 171.4 ($COCH_2CH_3$), 171.8 (2-C); IR (KBr) 2972 w, 2840 w, 1732 s, 1689 s, 1582 w, 1512 s, 1470 w, 1448 w, 1434 w, 1383 m, 1296 m, 1242 s, 1190 m, 1144 m, 1115 w, 1092 m, 1062 m, 1029 m, 960 w, 859 w, 835 m, 792 w, 762 w, 725 w, 669 w, 624 w; MS, *m/z* (relative intensity, %) 401 (M^+, 100), 373 (24), 372 (14), 356 (17), 328 (14), 300 (11), 299 (19), 298 (76), 282 (12), 255 (17), 254 (89), 226 (17), 214 (24), 200 (12), 134 (26), 122 (11), 108 (18), 107 (14), 105 (14), 92 (17), 91 (18), 79 (15), 78 (11), 77 (48), 65 (12). Anal. Calcd for $C_{22}H_{27}NO_6$: C, 65.82; H, 6.78; N, 3.49. Found: C, 65.79; H, 6.82; N, 3.56.



18

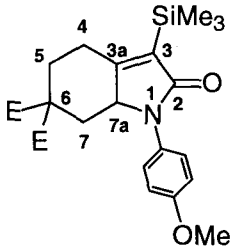
4,5,6,6a-Tetrahydro-3-(2-benzyloxyethyl)-1-(4-methoxyphenyl)-2*H*-cyclopenta[b]pyrrol-2-one-5,5-dicarboxylic acid diethyl ester (20). Yellow oil; R_f 0.10 (hexane/ether = 1/1); ^{1}H NMR ($CDCl_3$) δ 1.22 (t, J = 7.0 Hz, 3H, CH_3), 1.29 (t, J = 7.0 Hz, 3H, CH_3), 1.65 (t, J = 12 Hz, 1H, 6-H), 2.53-2.77 (m, 2H, CH_2CH_2OBn), 3.00 (dd, J = 7.0 Hz, J = 12 Hz, 1H, 6-H), 3.11 (d, J = 18 Hz, 1H, 4-H), 3.36 (d, J = 18 Hz, 1H, 4-H), 3.60-3.77 (m, 2H, CH_2CH_2OBn), 3.80 (s, 3H, OCH_3) 4.16 (q, J = 7.0 Hz, 2H, CH_2), 4.26 (dq, J = 1.4 Hz, J = 7.0 Hz, 2H, CH_2), 4.53 (s, 2H, OCH_2Ph), 4.71 (dd, J = 7.0 Hz, J = 12 Hz, 1H, 6a-H), 6.90 (d, J = 8.9 Hz, 2H, Ar), 7.22-7.37 (m, 5H, Ph), 7.51 (d, J = 8.9 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ 13.8 (CH_3), 13.9 (CH_3), 25.3 (CH_2CH_2OBn), 30.9 (4-C), 37.5 (6-C), 55.4 (OCH_3), 61.0 (5-C), 62.0 (CH_2), 62.2 (CH_2), 64.1 (6a-C), 67.9 (CH_2CH_2OBn), 72.8 (OCH_2Ph), 114.2 (Ar), 121.2 (Ar), 127.4 (Ar), 127.8 (Ph), 128.0 (Ar), 128.1 (Ph), 132.2 (3-C), 138.3 (Ph), 156.2 (Ar), 156.6 (3a-C), 170.0 ($COCH_2CH_3$), 171.4 ($COCH_2CH_3$), 171.7 (2-C); IR (neat) 2982 m, 2936 m, 2866 m, 1730 s, 1686 s, 1612 s, 1585 m, 1513 s, 1457 s, 1376 s, 1248 s, 1184 s, 1140 s, 1103 s, 1035 s, 910 w, 860 m, 830 m, 778 m, 737 m, 698 m; MS, *m/z* (relative intensity, %) 507 (M^+, 8), 416 (18), 410 (11), 342 (11), 92 (11), 91 (100), 77 (13), 65 (12).



20

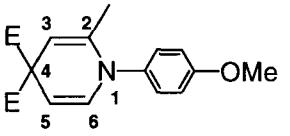
5,6,7,7a-Tetrahydro-1-(4-methoxyphenyl)-3-(trimethylsilyl)-3*H*-indol-2-one-6,6-dicarboxylic acid diethyl ester (22). White solid; mp 106-108 °C (hexane); R_f 0.10 (hexane/ether = 4/1); ^{1}H NMR ($CDCl_3$) δ 0.30 (s, 9H, $SiMe_3$), 1.21 (t, J = 7.0 Hz, 3H, CH_3), 1.35 (t, J = 7.0 Hz, 3H, CH_3), 1.40 (t, J = 12 Hz, 1H, 7-H), 1.92 (dt, J = 4.9 Hz, J = 14 Hz, 1H, 5-H), 2.38 (dt, J = 4.9 Hz, J = 14 Hz, 1H, 4-H), 2.60-2.71 (m, 1H, 5-H), 2.93-3.05 (m, 2H, 4-H, 7-H), 3.80 (s, 3H, OCH_3), 4.04-4.22 (m, 2H, CH_2), 4.23-4.42 (m, 2H, CH_2), 4.57 (dd, J = 5.1 Hz, J = 12 Hz, 1H, 7a-H), 6.91 (d, J = 9.2 Hz, 2H, Ar), 7.47 (d, J = 9.2 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ -0.48 ($SiMe_3$), 13.9 (CH_3), 14.1 (CH_3), 25.2 (4-C),

33.0 (5-C), 37.7 (7-C), 54.3 (6-C), 55.5 (OCH_3), 60.3 (7a-C), 61.9 (CH_2), 62.0 (CH_2), 114.2 (Ar), 122.4 (Ar), 130.4 (3-C), 130.5 (Ar), 156.3 (Ar), 167.1 (3a-C), 170.2 ($COCH_2CH_3$), 170.4 ($COCH_2CH_3$), 172.7 (2-C); IR (KBr) 2980 m, 2836 w, 1747 s, 1673 s, 1627 w, 1516 s, 1455 w, 1384 m, 1336 m, 1297 m, 1241 s, 1189 m, 1161 w, 1092 w, 1043 w, 1018 w, 841 m, 813 m, 781 w, 693 w, 629 w; MS, *m/z* (relative intensity, %) 459 (M^+, 46), 288 (20), 287 (100), 77 (13), 75 (21), 73 (67). Anal. Calcd for $C_{24}H_{33}NO_6Si$: C, 62.72; H, 7.24; N, 3.05. Found: C, 62.57; H, 7.18; N, 3.10.



22

1,4-Dihydro-1-(4-methoxyphenyl)-2-methyl-pyridine-4,4-dicarboxylic acid diethyl ester (24). Yellow oil; R_f 0.11 (hexane/ether = 3/1); ^1H NMR ($CDCl_3$) δ 1.26 (t, J = 7.0 Hz, 6H, CH_3), 1.64 (d, J = 1.1 Hz, 3H, CH_3), 4.20 (q, J = 7.0 Hz, 4H, CH_2), 4.69 (dd, J = 1.1 Hz, J = 2.7 Hz, 1H, 3-H), 4.80 (dd, J = 2.7 Hz, J = 7.8 Hz, 1H, 5-H), 6.23 (d, J = 7.8 Hz, 1H, 6-H), 6.84 (d, J = 8.9 Hz, 2H, Ar), 7.05 (d, J = 8.9 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3), 20.4 (CH_3), 55.1 (4-C), 55.4 (OCH_3), 61.4 (CH_2), 94.0 (3-C), 94.8 (5-C), 114.1 (Ar), 128.9 (Ar), 133.0 (6-C), 136.3 (Ar), 136.9 (2-C), 158.3 (Ar), 171.5 ($COCH_2CH_3$); IR (neat) 2986 m, 2938 m, 2842 w, 2056 w, 1981 w, 1733 s, 1684 s, 1622 m, 1583 w, 1515 s, 1468 m, 1448 m, 1408 m, 1388 m, 1363 m, 1273 s, 1248 s, 1194 s, 1175 s, 1107 s, 1063 m, 1032 s, 879 m, 840 m, 802 m, 772 m, 721 m, 664 w, 638 w, 607 w; MS, *m/z* (relative intensity, %) 345 (M^+, 1), 273 (12), 272 (100), 245 (10), 244 (62), 200 (10), 92 (12), 77 (17).



24

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Chapter 3

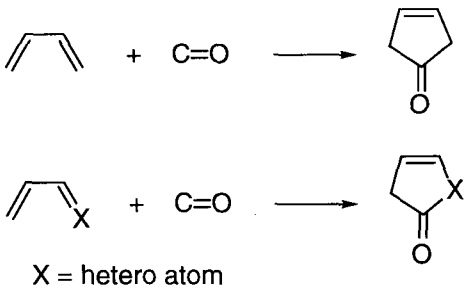
Ruthenium-Catalyzed [4+1] Cycloaddition of α,β-Unsaturated Imines with Carbon Monoxide

3.1 Introduction

Transition-metal-catalyzed cycloaddition reactions using carbon monoxide as one-carbon unit have been extensively studied.[1] One of the most familiar examples is the Pauson-Khand reaction,[2,3] in which an alkyne, an alkene, and carbon monoxide are condensed in a formal [2+2+1] cycloaddition to form cyclopentenones. This transformation has been the subject of intense investigation, both stoichiometrically and catalytically[3] because of its utility in the construction of five-membered cyclic systems. In terms of the construction of a five-membered ring system, the [4+1] mode, in which conjugated systems act as four-atom assembling units, is also attractive. In this mode, the reaction of 1,3-dienes with carbon monoxide would be expected to afford cyclopentenones, and the replacement of a terminal carbon by a heteroatom, such as oxygen and nitrogen, would give rise to unsaturated γ-lactones and γ-lactams, respectively (Scheme 1). Especially, the latter catalytic transformation using α,β-unsaturated imines would be useful in synthetic organic chemistry, because γ-lactam skeleton is one of the most important nitrogen heterocycles for pharmaceutical agents.[4,5] To my knowledge, however, such transformations of conjugated systems are known to proceed only with the η^4-diene iron carbonyl complex,[6] and no precedent for a catalytic reaction in this area has been reported. As a similar transformation, Et_2AlCl-mediated [4+1] cycloaddition of α,β-unsaturated carbonyl compounds with isocyanides, which are isoelectronic to carbon monoxide, has been reported.[7] Recently, a special class of catalytic [4+1] cycloaddition reactions using cumulene has been reported as well. The applicable substrates for these reactions are limited to particular molecules having cumulated double bonds, and include vinylallenes,[8] diallenes,[9] allenyl aldehydes/ketones,[10] and allenyl imines.[11] In this chapter, I

describe the first example of a [4+1] cycloaddition of structurally simple α,β-unsaturated imines with carbon monoxide.

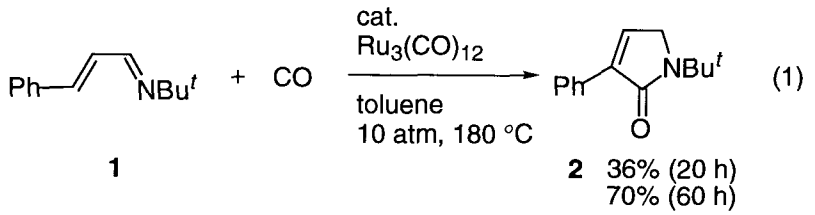
Scheme 1



3.2 $Ru_3(CO)_{12}$-Catalyzed Reaction of α,β-Unsaturated Imines with Carbon Monoxide Leading to Unsaturated γ-Lactams

The reaction of the α,β-unsaturated imine **1** (2 mmol), which was derived from the reaction of *trans*-cinnamaldehyde with *tert*-butylamine, with CO (10 atm) in toluene (3 mL) in the presence of a catalytic amount of $Ru_3(CO)_{12}$ (0.04 mmol) at 180 °C for 20 h gave a 1,5-dihydro-1-(1,1-dimethylethyl)-3-phenyl-2*H*-pyrrol-2-one (**2**) in 36% isolated yield (eq 1) with 47% of the imine being recovered as *trans*-cinnamaldehyde by silica-gel column chromatography. Prolongation of the reaction time (60 h) increased the yield of **2** to 70%. When the reaction was carried out at 160 °C, **2** was formed only in 7% yield, and 90% of the original aldehyde was recovered. Both a lower pressure (3 atm)[12] and a higher pressure (30 atm) decreased the yield to 26% and 12%, respectively. Among the solvents examined (dioxane 25% yield, CH_3CN 22%, cyclohexane 23%, pyridine 0%), toluene was solvent of choice, when the reaction was run at 180 °C under 10 atm of CO for 20 h. Changing the substituent on the nitrogen atom to *iso*-Pr, *n*-Bu, or *p*-$MeOC_6H_4$ resulted in no corresponding products being produced. No reaction was observed when other ruthenium complexes, such as Cp*RuCl(cod), $Ru(CO)_2(PPh_3)_3$, $[RuCl_2(CO)_3]_2$, $RuH_2(CO)(PPh_3)_3$, and $Ru(acac)_3$, were used as catalysts. $Rh_4(CO)_{12}$ and $[RhCl(CO)_2]_2$ exhibited catalytic activities to give the lactam **2** in 7% and 12% yields, respectively. The standard reaction conditions established are 2 mol%

of $Ru_3(CO)_{12}$, 10 atm of CO, in toluene, and at 180 °C. This reaction represents the first example of catalytic carbonylative [4+1] cycloaddition using a srructurally simple 1,3-diene system.[13]



1 2 36% (20 h) 70% (60 h) (1)

Table 1. $Ru_3(CO)_{12}$-Catalyzed [4+1]Cycloaddition of α,β-Unsaturated Imines with CO [a]

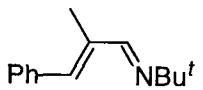
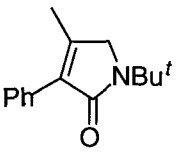
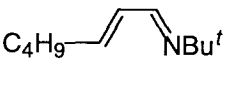
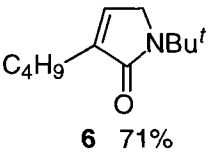
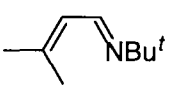
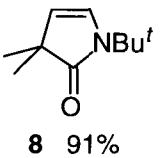
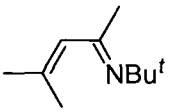
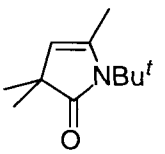
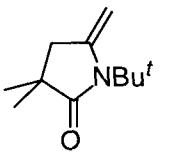
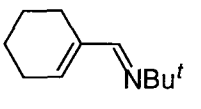
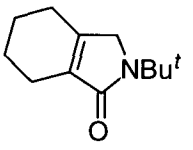
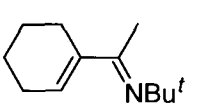
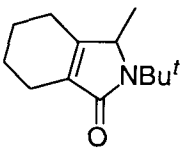
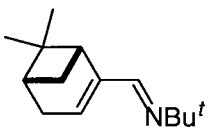
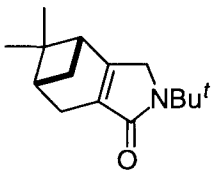
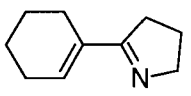
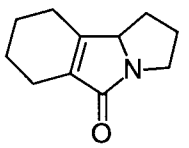
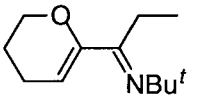
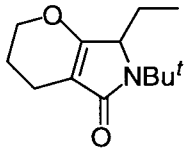
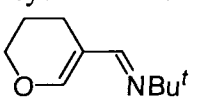
enrty	α,β-unsaturated imine	lactam [b]
1	 **3**	 **4** 51% (43%) 77% (13%) [c]
2	 **5**	 **6** 71%
3	 **7**	 **8** 91%
4	 **9**	  **10** 96% (*endo*/*exo*=20/80) [d]
5	 **11**	 **12** 81%
6	 **13**	 **14** 94%

Table 1. (Continued) [a]

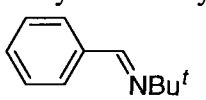
enrty	α,β-unsaturated imine	lactam [b]
7		
	15	**16** 60% (28%) 79% (7%) [c]
8		
	17	**18** 65% [c]
9		
	19	**20** 83%

[a] Reaction conditions: α,β-unsaturated imine (2 mmol), CO (10 atm), $Ru_3(CO)_{12}$ (0.04 mmol), toluene (3 mL) at 180 °C for 20 h. [b] Isolated yield. Values in parentheses are the yield of enimines recovered as the original aldehydes. [c] The reaction was run for 60 h. [d] The ratio of products is determined by ^1H NMR.

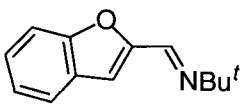
Selected results are shown in Table 1. The reaction of imine **3** of 2-methylcinnamaldehyde gave the corresponding lactam **4** in 77% yield (entry 1). Replacement of the phenyl group in **1** with an alkyl group, as in **5**, led to higher yield (entry 2). β,β-Disubstituted imines also worked well (entries 3 and 4). The reactions of imines having cyclic olefin counterparts also proceeded to give bicyclic γ-lactams (entries 5-7). Changing the aldimino group to a ketimino group permitted a more efficient transformation (entries 4 and 6).[14] Use of imine **15** derived from the commercially available, optically active aldehyde, (1*R*)-(-)-myrtenal, and cyclic imine **17** also gave rise to the formation of tricyclic γ-lactams (entries 7 and 8). The reaction of α-oxyimine **19**, which contains an oxygen-functionality at the α-carbon, gave the corresponding lactam **20** (entry 9), however, the β-oxyimine **21** failed to react. This catalytic system lacks the ability to carbonylate aromatic imines **22** and **23**.[13a]



21



22



23

The detail of the reaction mechanism, especially the molecularity of true catalyst, is unclear. It is in general difficult to establish with precision whether the cluster loaded itself or its fragment species are actually responsible for the catalytic phenomenon. Thus, the molecularity of catalyst is the long-standing unsolved subject in cluster chemistry. However, Laine demonstrated that studies of turnover frequency (TOF) as a function of total metal concentration can be a useful proof of catalysis mechanism.[15,16] Thus, as the total catalyst concentration increases, the TOF increases are indicative of cluster catalysis, and, conversely, the TOF decreases are indicative of lower nuclearity species catalysis. I followed his criteria, and constructed plots of TOF vs $Ru_3(CO)_{12}$ concentration (Table 2 and Figure 1), and the curve obtained shows that as the cluster concentration is increased, there is a decrease in the TOF, indicating that the active catalytic species is not intact $Ru_3(CO)_{12}$ but lower nuclearity species, such as $Ru(CO)_5$.

Table 2. Effect of $Ru_3(CO)_{12}$ concentration on the rate of formation of lactam **8**

entry	$[Ru_3(CO)_{12}]$ (x 10^{-4} M)	turnover frequency (h^{-1})
1	4.16	26.7
2	7.51	21.7
3	19.1	13.5
4	39.4	10.1
5	82.3	6.4

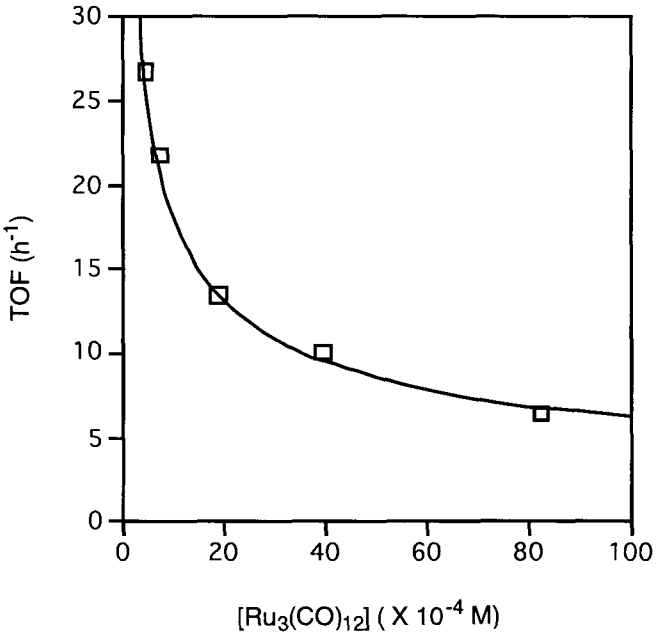


Figure 1. Plot of the rate of formation of lactam **8** turnover frequency (TOF) as a function of $Ru_3(CO)_{12}$ concentration.

The kinetics were investigated using the imine **7** as substrate in toluene at 180 °C and 10 atm of CO. The rate was found to be a 1/2 order in the catalyst concentration, $[Ru_3(CO)_{12}]$ (Figure 2). Variation of the CO pressure caused the rate to change. The rates decreased as the

pressure was increased from 7 to 30 atm (Figure 3). The reaction order with respect to CO pressure is not simple one, and I could not determine the reaction order.

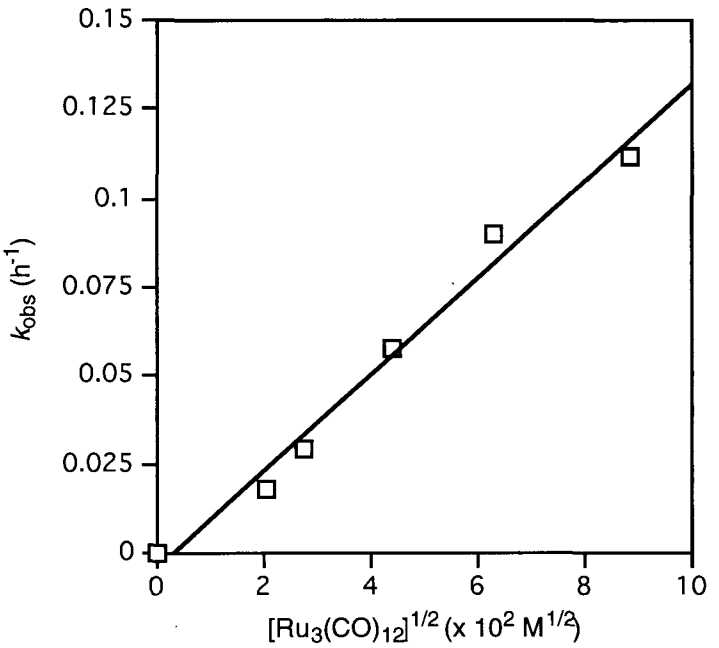


Figure 2. Plot of k_{obs} vs square root of $Ru_3(CO)_{12}$ concentration for the reaction of imine **7** with CO at varying $Ru_3(CO)_{12}$ concentration with [imine **7**]$_0$ = 0.4 M. The reactions were carried out in toluene at 180 °C.

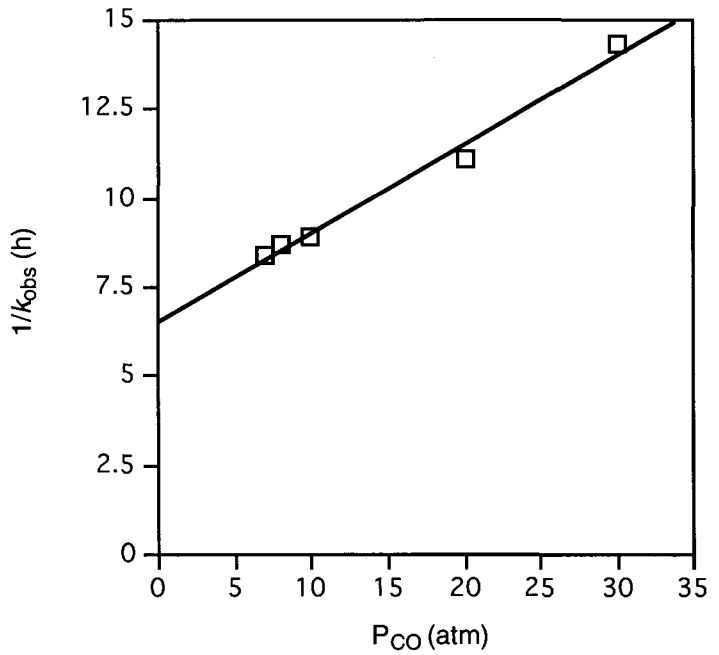
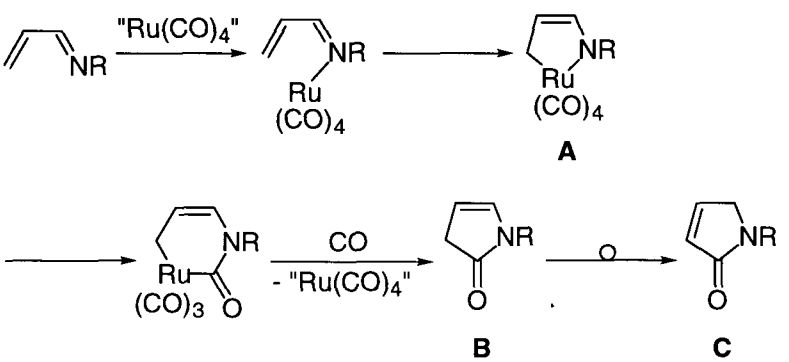


Figure 3. Plot of reciprocal k_{obs} vs CO pressure for the reaction of imine **7** with CO at varying CO pressure with [imine **7**]$_0$ = 0.4 M and $[Ru_3(CO)_{12}]$ = 0.008 M. The reactions were carried out in toluene at 180 °C.

At the present time, I cannot determine the structure of the true catalytic species from these kinetic studies, however I speculate that monoruthenium complex, $Ru(CO)_n$ (n = 4 or 5) is a key catalytic species.

I propose that the reaction proceeds via a pathway shown in Scheme 2. The coordination of a nitrogen to ruthenium allows the complex to be easily converted to metallacycle **A** via an oxidative cyclization of the α,β-unsaturated imine. No examples exist in which metallacycle **A** is formed by the reaction of a late transition metal complex with a α,β-unsaturated imine,[17,18] although it is well-known that metallacyclopenetenes which contain early transition metals, such as Ti and Zr, are formed by the reaction of "Cp_2Ti" and "Cp_2Zr" with α,β-unsaturated imines.[19] The subsequent insertion of CO and reductive elimination of ruthenium initially produce the β,γ-unsaturated γ-lactam **B**. For the reaction of imines which contain a β-hydrogen, **B** is transfered to the thermally more stable α,β-unsaturated isomer **C**. I speculate that the significant difference between the reactivity of imines **19** and **21** is due to the different direction of the resonance effect by the oxygen atom to π-system. The nitrogen in imine **21** partially loses, by the resonance effect, its sp^2-character which appears to be essential for the interaction between the α,β-unsaturated imine and ruthenium.[20]

Scheme 2.



In summary, I have demonstrated a new Ru-catalyzed [4+1] cycloaddition of α,β-unsaturated imines with carbon monoxide. The present reaction represents the first reported [4+1] cycloaddition of α,β-unsaturated imines.

3.3 Experimental Section

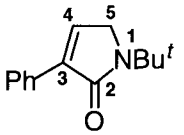
General Information. ^{1}H NMR and ^{13}C NMR were recorded on a JEOL JMN-270 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Data are reported as follows: chemical shift in ppm (d), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, and m = multiplet), 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 instrument with ionization voltages of 70 eV. Elemental analyses were performed by the 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 (MERCK).

Materials. Toluene, dioxane, CH_3CN, cyclohexane, and pyridine were distilled from CaH_2. $Ru_3(CO)_{12}$ was purchased from Aldrich Chemical Co. and used after recrystallization from hexane. Aldimines **1**,**3**,**5**,**7**,**11**,**15**, and **21**-**23** were obtained by the reaction of the corresponding aldehydes with *tert*-butylamine in the presence of $MgSO_4$.[21] Ketimines **9**,**13**, and **19** were prepared by the treatment of the corresponding ketones with *tert*-butylamine in the presence of $TiCl_4$.[22] Cyclic ketimine **17** was prepared by the reaction of methyl 1-cyclohexene-1-carboxylate with 1-vinyl-2-pyrrolidinone using a modification of the method of Cosford.[23]

Typical Procedure. A 50-mL stainless autoclave was charged with N-*tert*-butyl-*trans*-cinnamaldimine (**1**) (2 mmol, 360 mg), toluene (3 mL), and $Ru_3(CO)_{12}$ (0.04 mmol, 26 mg). The system was flushed with 10 atmospheres of CO three times. Finally it was pressurized to 10 atm and immersed in an oil bath at 180 °C. After 20 hours had elapsed, the autoclave was removed from the oil bath and allowed to cool for 1 h. The CO was then released. The contents were transferred to a round bottomed flask with ether and the volatiles removed in vacuo. The residue was subjected to column chromatography on silica gel (eluent; hexane/Et_2O

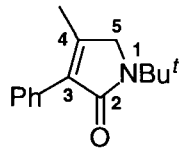
= 5/1) to give 1,5-dihydro-1-(1,1-dimethylethyl)-3-phenyl-2*H*-pyrrol-2-one (**2**) (148 mg, 36% yield) as a white solid.

1,5-Dihydro-1-(1,1-dimethylethyl)-3-phenyl-2*H*-pyrrol-2-one (2). White solid; mp 101-103 °C (hexane); R_f 0.14 (hexane/ether=5/1); ^{1}H NMR ($CDCl_3$) δ 1.52 (s, 9H), 4.06 (d, J = 2.2 Hz, 2H), 7.12 (t, J = 2.2 Hz, 1H), 7.27-7.42 (m, 3H), 7.81-7.88 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 27.9, 48.6, 54.1, 127.1, 128.2, 132.0, 134.5, 138.3, 170.2; IR (KBr) 2982 m, 2958 m, 2906 w, 2854 w, 1795 w, 1702 w, 1668 s, 1634 m, 1600 w, 1496 m, 1451 m, 1442 m, 1394 w, 1381 m, 1365 m, 1306 w, 1274 w, 1231 s, 1202 w, 1171 w, 1154 w, 1071 w, 1034 w, 1014 w, 993 w, 918 w, 896 m, 817 m, 803 w, 792 m, 744 m, 696 s, 683 w, 634 w; MS, *m/z* (relative intensity, %) 215 (M^+, 26), 200 (24), 172 (31), 160 (16), 159 (100), 131 (15), 130 (89), 115 (67), 103 (18), 102 (10), 100 (16), 78 (11), 77 (18), 70 (11), 63 (11), 57 (34), 56 (12), 55 (13), 51 (16). Anal. Calcd for $C_{14}H_{17}NO$: C, 78.09; H, 7.96; N, 6.51. Found: C, 78.02; H, 7.99; N, 6.54.



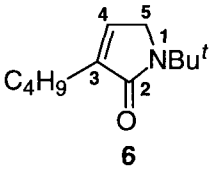
2

1,5-Dihydro-1-(1,1-dimethylethyl)-4-methyl-3-phenyl-2*H*-pyrrol-2-one (4). White solid; mp 64-66 °C (hexane); R_f 0.14 (hexane/ether = 3/1); ^{1}H NMR ($CDCl_3$) δ 1.50 (s, 9H), 2.12 (s, 3H), 3.95 (s, 2H), 7.27-7.49 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.0, 28.0, 52.8, 53.8, 127.4, 128.0, 129.2, 131.9, 133.6, 146.8, 171.0; IR (KBr) 2976 w, 1766 w, 1702 s, 1673 s, 1657 s, 1498 w, 1457 m, 1389 m, 1379 m, 1360 m, 1351 m, 1265 w, 1244 m, 1222 m, 1181 w, 1113 w, 1006 w, 996 w, 789 w, 744 w, 695 m, 654 w; MS, *m/z* (relative intensity, %) 229 (M+, 67), 215 (14), 214 (87), 187 (11), 186 (46), 174 (18), 173 (99), 172 (18), 158 (31), 145 (13), 144 (88), 131 (12), 130 (25), 129 (100), 128 (31), 127 (15), 117 (14), 116 (13), 115 (61), 107 (25), 104 (13), 103 (19), 91 (22), 89 (13), 86 (10), 78 (14), 77 (22), 70 (29), 65 (16), 64 (15), 63 (21), 58 (11), 57 (36), 56 (20), 55 (23), 51 (32); exact mass calcd for $C_{15}H_{19}NO$ 229.1467, found 229.1478.



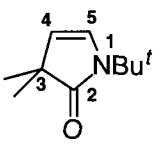
4

1,5-Dihydro-3-butyl-1-(1,1-dimethylethyl)-2*H*-pyrrol-2-one (6). Colorless oil; R_f 0.17 (hexane/ether = 5/1); ^{1}H NMR ($CDCl_3$) δ 0.92 (t, J = 6.8 Hz, 3H), 1.29-1.59 (m, 4H), 1.45 (s, 9H), 2.17-2.27 (m, 2H), 3.88 (q, J = 1.9 Hz, 2H), 6.54 (quint, J = 1.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.8, 22.5, 25.3, 27.9, 29.6, 49.0, 53.7, 132.8, 141.7, 172.0; IR (neat) 2964 m, 2932 m, 2874 w, 2260 w, 1679 s, 1452 m, 1384 s, 1366 s, 1271 w, 1240 s, 1158 w, 1141 w, 1081 w, 1032 w, 982 w, 934 w, 816 m, 667 w, 641 w; MS, *m/z* (relative intensity, %) 195 (M^+, 24), 181 (11), 180 (91), 153 (26), 152 (100), 140 (16), 124 (11), 110 (24), 97 (38), 96 (85), 95 (11), 84 (15), 83 (23), 82 (21), 81 (15), 70 (12), 69 (11), 68 (15), 67 (27), 65 (11), 58 (11), 57 (47), 56 (30), 55 (63), 54 (21), 53 (92), 52 (10), 51 (10); exact mass calcd for $C_{12}H_{21}NO$ 195.1623, found 195.1623.



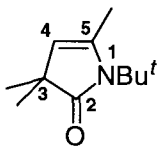
6

2,3-Dihydro-3,3-dimethyl-1-(1,1-dimethylethyl)-pyrrol-2-one (8). White solid; mp 96-98 °C (hexane); R_f 0.17 (hexane/ether = 10/1); ^{1}H NMR ($CDCl_3$) δ 1.13 (s, 3H), 1.45 (s, 9H), 5.25 (d, J = 4.9 Hz, 1H), 6.53 (d, J = 4.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 23.4, 28.2, 47.1, 53.9, 116.2, 128.3, 183.3; IR (KBr) 2972 m, 2932 w, 2872 w, 1687 s, 1605 w, 1539 w, 1462 m, 1395 m, 1369 w, 1290 m, 1271 m, 1222 w, 1183 w, 1167 w, 1092 w, 1030 w, 969 w, 935 w, 906 w, 805 w, 752 w, 697 m, 669 w; MS, *m/z* (relative intensity, %) 167 (M^+, 16), 111 (45), 110 (15), 96 (100), 83 (34), 82 (12), 68 (16), 57 (47), 55 (13), 53 (32) Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.37. Found: C, 71.52; H, 10.15; N, 8.45.

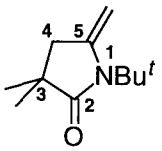


8

2,3-Dihydro-3,3-dimethyl-1-(1,1-dimethylethyl)-5-methyl-pyrrol-2-one (*endo*-10) and 3,3-dimethyl-1-(1,1-dimethylethyl)-5-methylene-pyrrolidin-2-one (*exo*-10). The products were obtained as a mixture of *endo*- and *exo*-isomer. Colorless oil; bp 115-117 °C (bulb-to-bulb distillation); ^{1}H NMR ($CDCl_3$) for *endo*-**10**: δ 1.08 (s, 6H), 1.54 (s, 9H), 2.13 (d, J = 1.9 Hz, 3H), 4.96 (q, J = 1.9 Hz, 1H); for *exo*-**10**: δ 1.11 (s, 6H), 1.56 (s, 9H), 2.33 (t, J = 1.1 Hz, 2H), 4.27 (q, J = 1.1 Hz, 1H), 4.48 (q, J = 1.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) for *endo*-**10**: δ 19.6, 23.7, 29.9, 44.7, 56.7, 116.2, 140.2, 185.4; for *exo*-**10**: δ 24.4, 28.6, 40.3, 43.6, 56.6, 90.4, 144.6, 181.7; IR (neat) for a mixture of *endo*- and *exo*-**10**: 2968 s, 2932 m, 2872 w, 2618 w, 2334 w, 1725 s, 1642 s, 1469 m, 1384 s, 1368 s, 1337 s, 1300 w, 1288 w, 1257 m, 1237 w, 1205 m, 1153 m, 1115 w, 1070 w, 1012 w, 981 w, 954 w, 933 w, 899 w, 824 w, 792 w, 758 w, 727 w, 660 w; MS, *m/z* (relative intensity, %) for *endo*-**10**: 181 (M^+, 5), 125 (24), 110 (100), 57 (17); for *exo*-**10**: 181 (M^+, 9), 126 (66), 125 (66), 110 (24), 98 (13), 96 (33), 83 (14), 82 (100), 69 (12), 67 (10), 57 (66), 56 (23), 55 (22), 53 (17). Anal. Calcd for $C_{11}H_{19}NO$: C, 72.87; H, 10.57; N, 7.73. Found: C, 73.01; H, 10.49; N, 7.71.

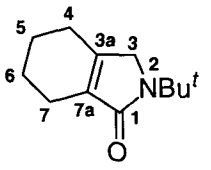


***endo*-10**



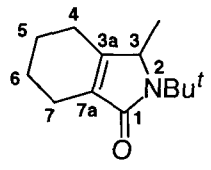
***exo*-10**

2,3,4,5,6,7-Hexahydro-2-(1,1-dimethylethyl)-1*H*-isoindol-1-one (12). White Solid; mp 74-76 °C (hexane); R_f 0.15 (hexane/ether = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.44 (s, 9H), 1.60-1.76 (m, 4H), 2.09-2.26 (m, 4H), 3.79 (br, 2H); ^{13}C NMR ($CDCl_3$) δ 20.1, 21.9, 22.2, 24.0, 28.1, 51.6, 53.4, 133.4, 148.4, 172.3; IR (KBr) 2976 m, 2928 s, 2862 m, 1680 s, 1652 s, 1621 w, 1451 m, 1443 m, 1422 w, 1394 m, 1383 m, 1360 m, 1284 w, 1267 w, 1253 m, 1236 m, 1196 w, 1183 w, 1161 w, 1145 m, 1127 w, 1098 w, 1051 w, 945 w, 930 w, 858 w, 814 w, 773 w, 757 m, 669 w, 654 w; MS, *m/z* (relative intensity, %) 193 (M^+, 4), 179 (11), 178 (100), 150 (41), 109 (19), 108 (10), 91 (14), 81 (10), 79 (13), 77 (19), 67 (12), 65 (10), 58 (17), 55 (11), 53 (17). Anal. Calcd for $C_{12}H_{19}NO$: C, 74.55; H, 9.91; N, 7.25. Found: C, 74.65; H, 9.81; N, 7.33.



12

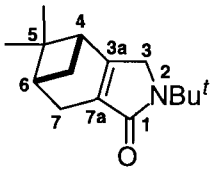
2,3,4,5,6,7-Hexahydro-2-(1,1-dimethylethyl)-3-methyl-1*H*-isoindol-1-one (14). Colorless oil; bp 145-147 °C / 2 mmHg (bulb-to-bulb distillation); R_f 0.17 (hexane/ether = 2/1); ^{1}H NMR ($CDCl_3$) δ 1.31 (d, J = 6.8 Hz, 3H), 1.49 (s, 9H), 1.52-1.80 (m, 4H), 2.00-2.26 (m, 4H), 3.97 (q, J = 6.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 19.9, 20.6, 21.9, 22.3, 22.8, 28.8, 54.2, 58.4, 131.3, 154.2, 172.2; IR (neat) 2972 s, 2936 s, 2284 w, 1672 s, 1484 w, 1462 m, 1442 m, 1401 s, 1370 s, 1360 s, 1298 w, 1278 w, 1249 m, 1226 s, 1184 w, 1164 m, 1100 w, 1078 w, 1064 w, 1054 w, 1035 w, 1008 w, 980 w, 948 w, 927 w, 899 w, 882 w, 850 w, 823 w, 759 m, 719 w, 662 w, 608 w; MS, *m/z* (relative intensity, %) 207 (M^+, 11), 193 (14), 192 (100), 164 (64), 136 (17), 123 (14), 122 (13), 108 (13), 91 (17), 81 (13), 79 (29), 77 (23), 67 (15), 65 (12), 58 (15), 57 (13), 56 (10), 55 (15), 53 (21), 52 (11), 51 (12). Anal. Calcd for $C_{13}H_{21}NO$: C, 75.32; H, 10.21; N, 6.76. Found: C, 75.20; H, 10.27; N, 7.04.



14

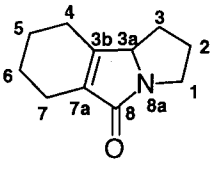
2,3,4,5,6,7-Hexahydro-5,5-dimethyl-2-(1,1-dimethylethyl)-1*H*-4,6-methanoisoindol-1-one (16) White solid; mp 77-79 °C (hexane); R_f 0.14 (hexane/ether = 2/1); ^{1}H NMR ($CDCl_3$) δ 0.76 (s, 3H), 1.24 (d, J = 8.9 Hz, 1H), 1.36 (s, 3H), 1.45 (s, 9H), 2.27 (sext, J = 3.0 Hz, 1H), 2.36 (t, J = 5.1 Hz, 1H), 2.39-2.48 (m, 1H), 2.57 (dt, J = 8.9 Hz, J = 5.9 Hz, 2H), 3.79 (dt, J = 19 Hz, J = 2.7 Hz, 1H), 3.95 (dt, J = 19 Hz, J = 2.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.2, 26.2 (two overlapping signals), 28.1, 32.0, 40.4, 40.9, 41.7, 50.5, 53.6, 129.6, 160.9, 172.4; IR (KBr) 2992 w, 2942 w, 2924 m, 1672 s, 1654 s, 1471 w, 1445 w, 1395 w, 1383 w, 1365 w, 1357 w, 1334 w, 1276 w, 1254 w, 1237 m, 1201 w, 1174 w, 1162 w, 1151 w, 1123 w, 1098 w, 1074 w, 766 w, 753 w, 669 w; MS, *m/z* (relative

intensity, %) 233 (M^+, 17), 218 (52), 177 (20), 176 (12), 174 (13), 162 (29), 148 (13), 134 (35), 133 (16), 122 (11), 119 (11), 105 (32), 97 (12), 93 (10), 91 (54), 79 (14), 77 (22), 65 (12), 58 (14), 57 (100), 56 (13), 55 (17), 53 (17), 51 (10); exact mass calcd for $C_{15}H_{23}NO$ 233.1779, found 233.1781.



16

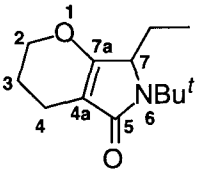
2,3,3a,4,5,6,7,8-Octahydro-1*H*-pyrrolo[1,2-a]isoindol-8-one (18). Colorless oil; R_f 0.15 (hexane/ether = 1/5); ^{1}H NMR ($CDCl_3$) δ 1.09 (dq, J = 7.3 Hz, J = 11 Hz, 1H), 1.59-1.78 (m, 4H), 2.04 (dquint, J = 1.9 Hz, J = 6.2 Hz, 1H), 2.10-2.35 (m, 6H), 3.24 (dt, J = 2.4 Hz, J = 8.4 Hz, 1H), 3.44 (dt, J = 11 Hz, J = 8.4 Hz, 1H), 4.00 (dd, J = 10 Hz, J = 6.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.2, 21.7, 21.9, 23.9, 28.4, 29.1, 41.9, 67.5, 131.9, 156.8, 176.7; IR (neat) 2940 s, 2886 s, 1682 s, 1488 w, 1441 m, 1398 m, 1366 m, 1327 m, 1303 m, 1279 m, 1250 m, 1203 m, 1173 w, 1137 w, 1122 w, 1104 w, 1055 w, 1008 w, 947 w, 927 w, 912 w, 881 w, 836 w, 821 w, 760 w, 739 w, 703 w, 693 w, 655 w, 618 w; MS, *m/z* (relative intensity, %) 177 (M^+, 92), 176 (13), 162 (11), 150 (10), 149 (100), 148 (97), 136 (13), 135 (22), 134 (36), 121 (44), 120 (59), 106 (18), 94 (16), 93 (27), 92 (10), 91 (27), 80 (17), 79 (42), 78 (12), 77 (38), 67 (14), 66 (14), 65 (26), 54 (10), 53 (31), 52 (27), 51 (35), 50 (11); exact mass calcd for $C_{11}H_{15}NO$ 177.1153, found 177.1151.



18

3,4,6,7-Tetrahydro-6-(1,1-dimethylethyl)-7-ethyl-pyrano[2,3-c]pyrrol-5(2*H*)-one (20). Colorless oil; bp 115-118 °C / 3 mmHg (bulb-to-bulb distillation); R_f 0.12 (hexane/ether = 1/1); ^{1}H NMR ($CDCl_3$) δ 0.72 (t, J = 7.3 Hz, 3H), 1.45 (s, 9H), 1.73-1.98 (m, 4H), 2.08-2.28 (m, 2H), 4.02-4.07 (m, 1H), 4.07-4.23 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 6.0, 16.2, 21.6, 24.2, 28.8, 54.4, 58.6, 68.6, 106.6, 167.6, 173.5; IR (neat) 2968 s, 1670 s, 1470 m, 1412 m, 1378 m, 1293 m, 1264 m, 1230 m, 1180 w, 1133 m, 1069 w, 1032 m,

956 m, 918 w, 875 w, 842 w, 791 w, 754 w, 668 w; MS, *m/z* (relative intensity, %) 223 (M^+, 3), 209 (13), 208 (100), 180 (27), 139 (46), 138 (52), 110 (17), 69 (17), 57 (23), 56 (19), 55 (42), 54 (16), 53 (21); exact mass calcd for $C_{13}H_{21}NO_2$ 223.1572, found 223.1575.



20

The Kinetic Studies. The reactions was run as described in " Typical Procedure ". The reaction was monitored by analyzing, on GC, a few drops of the reaction mixture which was quickly purged with CO pressure kept.

(1) Catalyst-Dependence Experiments. Each turnover frequency number at varying $Ru_3(CO)_{12}$ concentration was obtained by measurement of amount of product, lactam **8**, at 2 h after heating was started. The final conditions are as follows: imine **7**, 0.4 M (2 mmol of **7** in 5 mL of toluene); $[Ru_3(CO)_{12}]$, $4.16x10^{-4}$, $7.51x10^{-4}$, $19.1x10^{-4}$, $39.4x10^{-4}$, and $82.3x10^{-4}$ M; CO pressure 10 atm.

(2) CO-Dependence Experiments. The final conditions are as follows: imine **7**, 0.4 M (2 mmol of **7** in 5 mL of toluene); $Ru_3(CO)_{12}$ 0.008 M (0.04 mmol of $Ru_3(CO)_{12}$ in 5 mL of toluene); CO pressure, 7, 8, 10, 20, 30 atm.

3.4 References and Notes

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Conclusion

In this thesis, new ruthenium-catalyzed carbonylative cyclocoupling reactions have been studied. The results mentioned in each chapter of this thesis are summarized as follows.

In Chapter 1, ruthenium-catalyzed [2+2+1] cycloaddition reaction of enynes with carbon monoxide has been described. This reaction represents the first use of $Ru_3(CO)_{12}$ as a catalyst for the cyclocarbonylation of enynes to cyclopentenones. This transformation shows a high level of functional group compatibility.

In Chapter 2, it has been described that ruthenium-catalyzed [2+2+1] cycloaddition reaction of yne-aldehydes with carbon monoxide. This reaction is the first catalytic transformation of yne-aldehydes to bicyclic α,β-unsaturated γ-lactones. This reaction also represents the first catalytic synthesis of five-membered lactones via a [2+2+1] cyclocoupling reaction, incorporating the aldehyde π-bond, the alkyne π-bond, and the carbon atom of carbon monoxide into a five-membered ring. Furthermore, it was found that yne-imines, instead of yne-aldehydes, were applicable for this transformation to give bicyclic α,β-unsaturated γ-lactams. This is the first example of the catalytic cyclocoupling of acetylenes, imines, and carbon monoxide.

In Chapter 3, it has been described that ruthenium-catalyzed [4+1] cycloaddition reaction of α,β-unsaturated imines with carbon monoxide. This reaction is the first transformation of α,β-unsaturated imines to unsaturated γ-lactams. This reaction also represents the first catalytic carbonylative [4+1] cycloaddition using a structurally simple 1,3-diene system.

The present studies on the catalytic carbonylative cycloaddition reactions will provide a new efficient method for the construction of cyclic carbonyl compound skeletons, and will contribute to the development of homogeneous catalytic chemistry.