博士論文

オキサニッケラサイクル中間体を経由する炭素-炭素結合形成反応の開発研究

-環状ケトンとアルキンの分子内環化反応およびアレナミドへの二酸化炭素固定反応-

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略語表

本論文中で以下の略語を用いた。

Ac	: acetyl
acac	: acetylacetonate
Ar	: aryl
Bn	: benzyl
Boc	: *tert*-butoxycarbonyl
bpy	: 2,2´-bipyridyl
Bu	: butyl
cat.	: catalytic
cdt	: 1,5,9-cyclododecatriene
cod	: 1,5-cyclooctadiene
Cp	: cyclopentadienyl
Cy	: cyclohexyl
Cyp	: cyclopentyl
DBU	: 1,8-diazabicyo[5.4.0]undec-7-ene
DCPE	: 1,2-bis(dicyclohexylphosphino)ethane
DIAD	: diisopropyl azodicarboxylate
DIBAL-H	: diisobutylaluminum hydride
DMF	: *N*,*N*-dimethylformamide
equiv	: equivalent(s)
Et	: ethyl
EWG	: electron-withdrawing group
Fc	: ferrocenyl
h	: hour(s)
Hex	: hexane
HRMS	: high resolution mass spectroscopy
i	: iso
L	: ligand
LRMS	: low resolution mass spectroscopy
M	: metal
Me	: methyl
Mes	: mesityl
Ms	: methanesulfonyl
MS	: molecular sieves
NHC	: *N*-heterocyclic carbene

NMO : *N*-Methylmorpholine *N*-oxide
NMR : nuclear magnetic resonance analysis
NOE : nuclear Overhauser effect
NOESY : nuclear Overhauser and exchange spectroscopy
p : para
PCC : pyridinium chlorochromate
Ph : phenyl
Pr : propyl
quant : quantitative yield
rec. : recovery
t : tertiary
SM : starting material
TBS : *tert*-butyldimethylsilyl
TBDPS : *tert*-butyldiphenylsilyl
THF : tetrahydrofuran
THP : tetrahydropyranyl
TMEDA : *N,N,N′,N′*-tetramethylethylenediamine
TMS : trimethylsilyl
TPAP : Tetrapropylammonium perruthenate
Ts : *p*-toluenesulfonyl

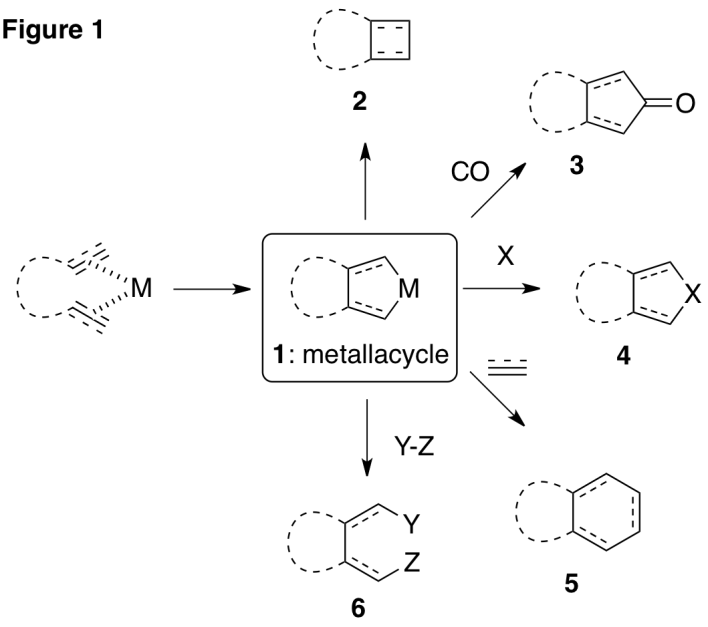
目次

序論

私たちは常日頃より農薬、医薬品、香料、染料など多くの有機化合物の恩恵に預かり生活している。これら有機化合物を扱う有機化学の分野の中で、有機合成化学は効率よく目的の有機化合物を合成するための反応や技術を開発する研究分野であり、その発展により現在では複雑な構造をもつ化合物も合成可能となってきている。有機合成化学における最も重要な課題の一つに、いかにして目的の炭素骨格を効率的に構築するかという点があり、有機合成化学が進歩した今なお多くの化学者が頭を悩ませている。さらに今日、有機合成化学者に要求される標的化合物の構造の複雑さは増していることから、立体選択性や位置選択性をより精密に制御できる新規反応の開発が必要である。この要求に対し、近年多くの有機化学者が遷移金属錯体を用いた触媒反応に注目し研究を行っている。遷移金属錯体はその酸化状態や配位子の選択により多様な反応性を示す。このため個々の目的物に合わせた反応条件の微調整が可能である。遷移金属錯体を用いた反応の研究の結果、クロスカップリング反応やメタセシス反応など効率的な合成法が数多く開発され、現在これらの反応は機能性材料の開発や、高度に官能基化された天然物合成の鍵工程にも利用されている。

遷移金属錯体を用いた反応の大きな特徴として、多重結合間で容易に炭素-炭素結合を形成させ得ることが挙げられる。特に、炭素-炭素多重結合が低原子価の遷移金属錯体に酸化的環化付加して生成する「メタラサイクル」は、図 1 に示すように多様な反応性を示し、様々な化合物へ変換できることから、有機合成化学における有用な中間体である。

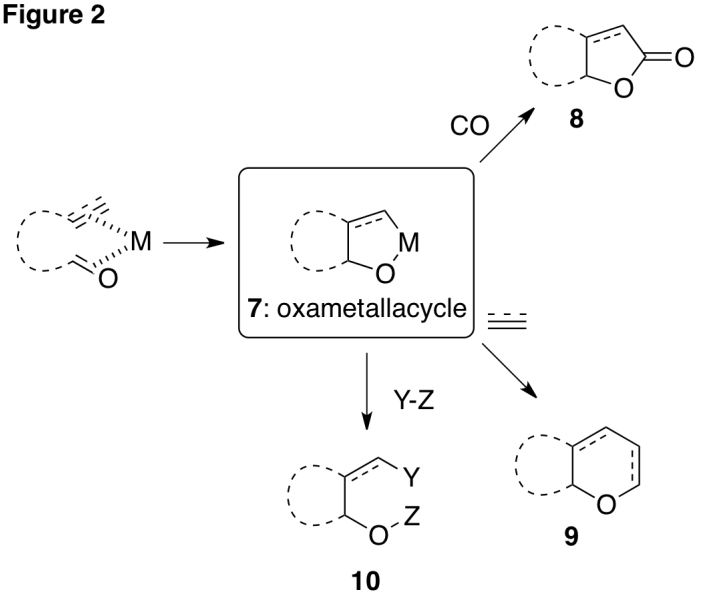
Figure 1



例えば、メタラサイクル中間体 **1** から還元的脱離が進行すれば 4 員環化合物 **2** が得られる。一方、一酸化炭素が挿入すれば 5 員環ケトン **3** が得られ、硫黄やセレンと反応させるとチオフェンやセレノフェンといった複素環 **4** が得られる。また、さらなる多重結合の挿入が進行すれば 6 員環化合物 **5** が得られ、求核剤および求電子剤と反応させることで開環体 **6** の合成も可能である [1)]。

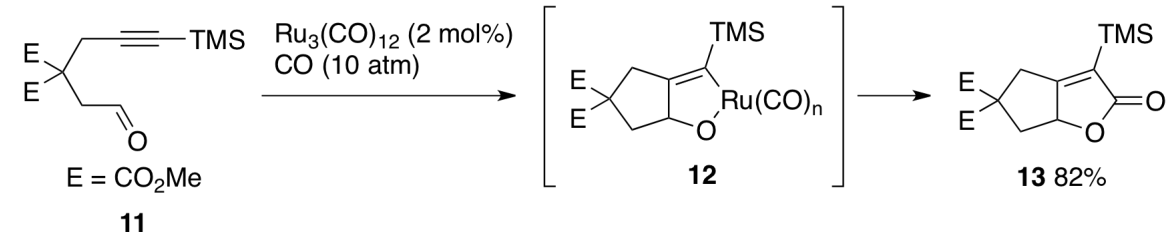
一方、カルボニル基もヘテロ元素を含む多重結合であり、反応例は少ないものの、遷移金属錯体存在下で炭素-炭素多重結合と反応し、オキサメタラサイクル中間体 **7** を与える（図 2)。この中間体からも、一酸化炭素挿入反応が進行し、ラクトン **8** が得られる反応や、さらなる多重結合の挿入により複素環 **9** が得られる反応などが報告されている。

Figure 2



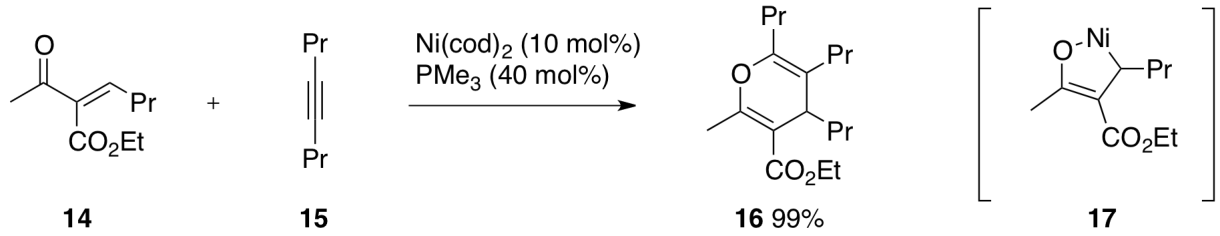
例えば 1998 年、村井らはアルキニルアルデヒド **11** に対し、一酸化炭素雰囲気下 $Ru_3(CO)_{12}$ 錯体を反応させることで、オキサルテナサイクル **12** を経由した Pauson-Khand 型反応を報告している（スキーム 1）[2)]。

Shceme 1



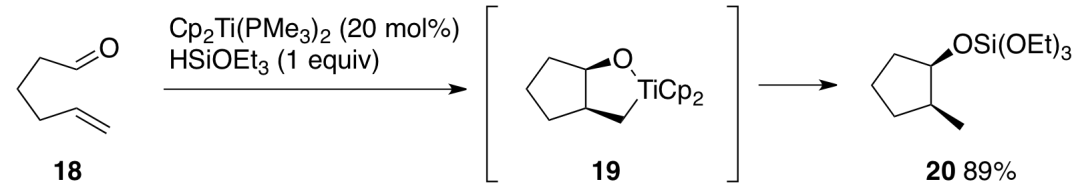
一方、2009 年に松原、倉橋らは、エノンとアルキンの [4+2]環化付加反応を報告している（スキーム 2）[3]。本反応はニッケル錯体に対しエノン **14** が酸化的環化付加したオキサニッケラサイクル中間体 **17** を経由して進行すると考えられている。

Scheme 2



また、Crowe らはオキサチタナサイクル **19** の開環を経由した 5 員環化合物 **20** の合成を報告している（スキーム 3）[4]。

Shceme 3

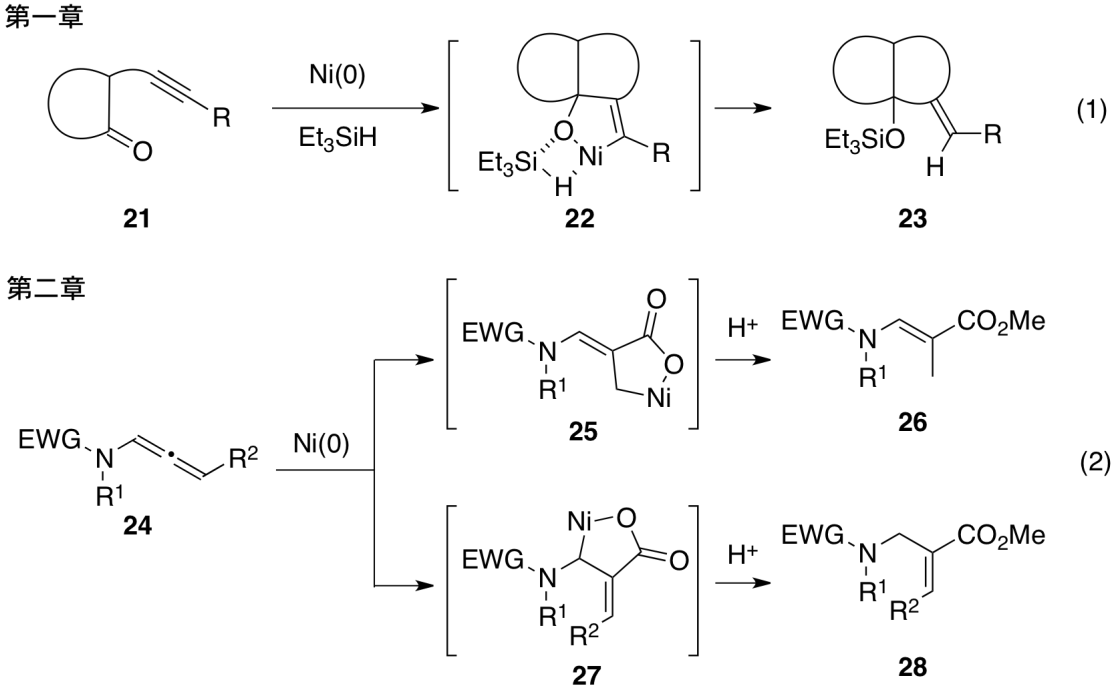


以上の反応以外にもメタラサイクル中間体を経由する反応は多岐にわたる [1]。また、当研究室でも以前から 0 価ニッケル錯体を用いた反応を開発してきた（詳細については後述する）。著者は新たな炭素-炭素結合形成反応の開発を目指し 0 価ニッケル錯体を用いた反応の検討を行った。その結果、オキサニッケラサイクル中間体の開環を経由する 2 つの新規反応の開発に成功したので以下順に記述する。

まず、第一章ではオキサニッケラサイクル **22** を経由する、0 価ニッケル触媒によるアルキンと環状ケトンとの分子内環化反応の開発の経緯について述べる（スキーム 4、式 1）。

第二章では、ニッケララクトン **25** および **27** を経由した、0 価ニッケル錯体によるアレナミド **24** への位置選択的二酸化炭素固定反応について記述する（式 2)。

Shceme 4



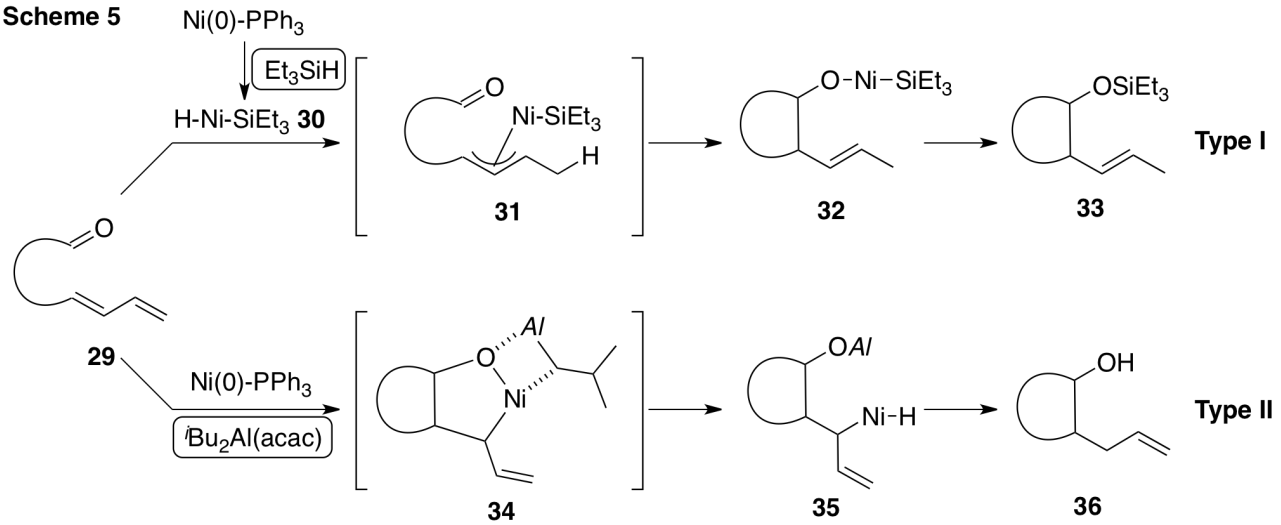
第一章

0 価ニッケル触媒を用いた環状ケトンとアルキンの分子内環化反応

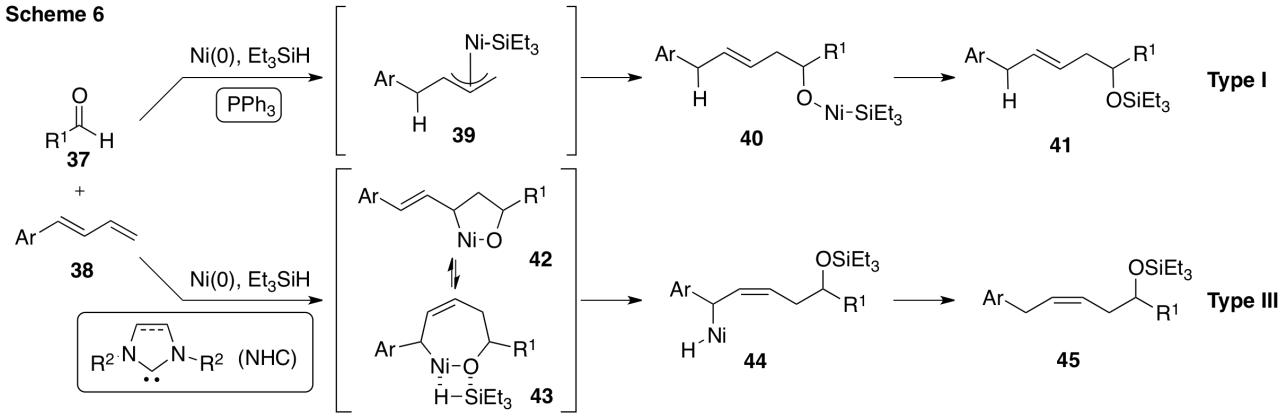
序節

当研究室ではこれまで、ニッケル触媒を用いた 1,3-ジエンと多重結合としてアルデヒドの反応を検討してきた（スキーム 5）[5]。例えば、0 価ニッケル触媒存在下、基質 **29** とトリエチルシランを反応させると *E* 配置の内部オレフィンをもつ環化体 **33** が得られる（Type I）。本反応ではまずニッケル錯体とシランから生成した 2 価ヒドリドニッケル錯体 **30** がジエンと反応し、π-アリルニッケル中間体 **31** が生成する。**31** の π-アリルニッケルとアルデヒドが反応し **32** となり、続く還元的脱離が進行して *E* オレフィンが得られる。一方、シランの代わりに $^{i}Bu_2Al(acac)$存在下反応を行うと、上記の反応とは異なり末端オレフィンをもつ環化体 **36** が得られる（Type II）。本反応ではまず 0 価ニッケル錯体に基質 **29** が酸化的環化付加によって、5 員環オキサニッケラサイクル **34** が生成する。その後 **34** とアルミニウム試薬とのトランスメタル化及び β 水素脱離を経て **35** が生成する。**35** からの還元的脱離と後処理による加水分解により末端アルケンをもつ閉環体 **36** が生成したと考えられる。この 2 つの反応はニッケルホスフィン錯体存在下ほぼ同様の条件で進行するが、用いる還元剤の違いのみで異なった反応経路で進行する興味深い反応である。

Scheme 5

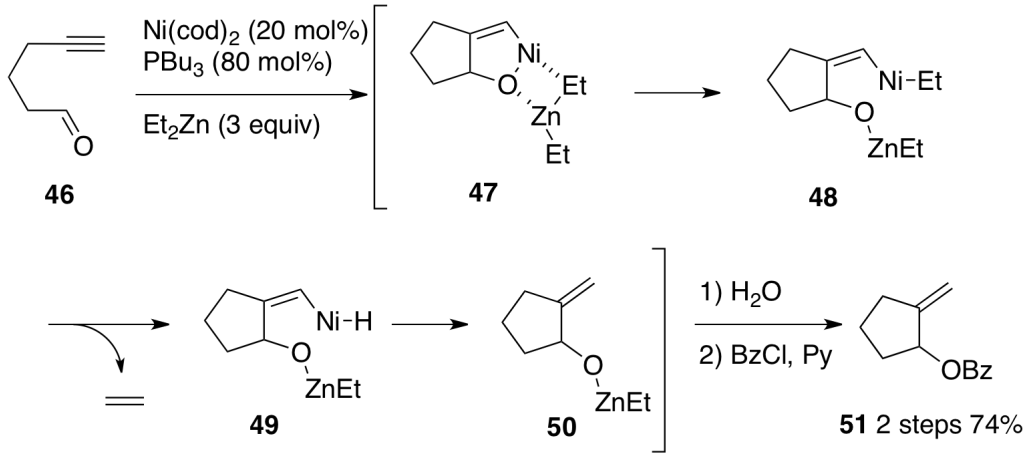


さらに本反応は分子間反応へと展開されている（スキーム 6)。ホスフィン配位子存在下で **37** と **38** をニッケル錯体と反応させると分子内反応の時と同様に π-アリル中間体を経由してカップリング体 **41** が得られるのに対し、配位子に含窒素ヘテロ環カルベン（NHC）を用いた場合には高立体選択的に *Z* 配置のオレフィンを持つカップリング体 **45** が得られる。後者の反応の機構は以下のように考えられる。まずニッケル NHC 錯体がアルデヒド **37** 及びジエン **38** と反応し 5 員環オキサニッケラサイクル **42** が生成する。この **42** は 7 員環オキサニッケラサイクル **43** と平衡状態にあり、この **43** とシランとの σ 結合メタセシスが進行し *Z* 配置のオレフィンを持つヒドリドニッケル中間体 **44** となる。最後に還元的脱離により **45** が立体選択的に得られると考えられる。この 2 つの反応はニッケルの配位子の違いのみによって異なる生成物が得られる点で興味深い [6,7]。



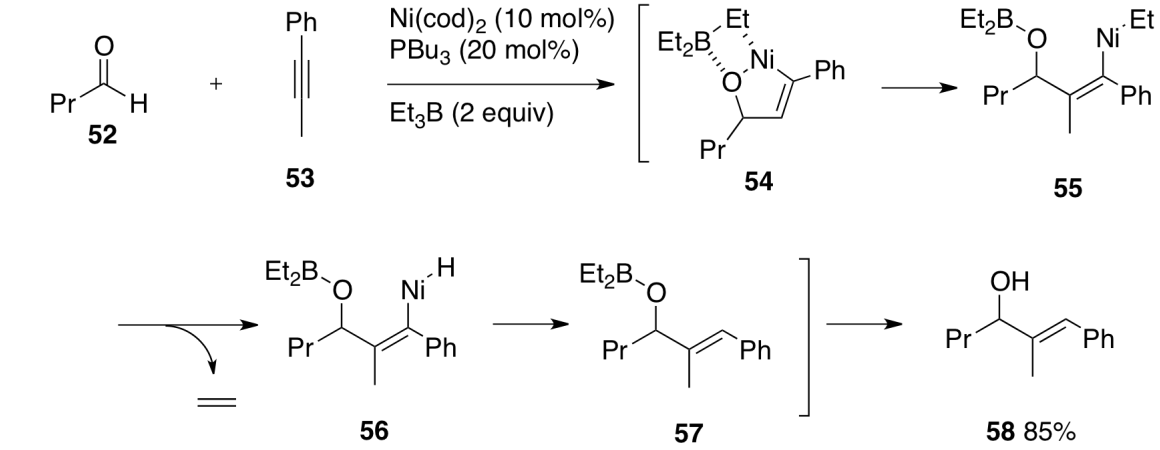
一方、アルデヒドと 1,3-ジエン以外の多重結合を用いた反応として、Montgomery らによるニッケル触媒を用いたアルデヒドとアルキンとの分子内還元的カップリング反応の報告がある [8]。この反応の反応機構は以下のように考えられる。まず基質 **46** とニッケル錯体が反応し、5 員環オキサニッケラサイクル **47** を形成した後、ジエチル亜鉛とのトランスメタル化、続く β 水素脱離によってヒドリドニッケル中間体 **49** が生成する。**49** は還元的脱離によって環化体 **50** となり、後処理による加水分解とベンゾイル化によって生成物のエステル **51** が得られる（スキーム 7)。

Scheme 7



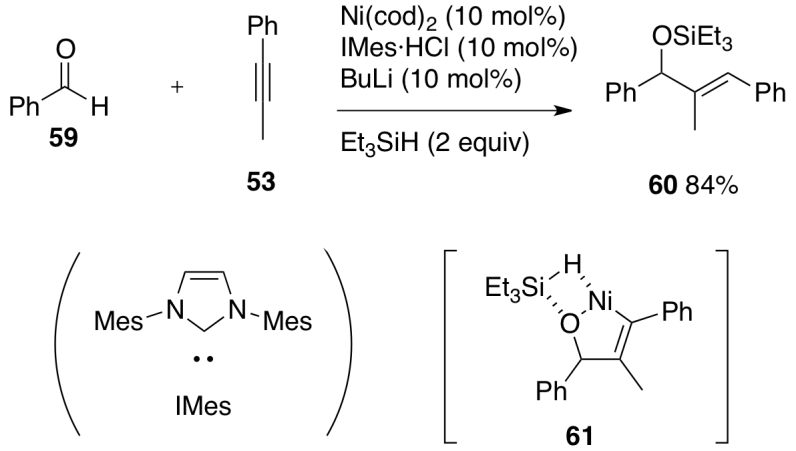
また、Jamison らはトランスメタル化剤としてトリエチルボランを用いたアルデヒドとアルキンの分子間反応を報告している（スキーム 8）[9]。反応機構は分子内環化反応と同様にオキサニッケラサイクル中間体 **54** を経由し、トリエチルボランとの σ 結合メタセシスと β 水素脱離によりヒドリドニッケル中間体 **56** が生成する。**56** からの還元的脱離と後処理による加水分解によりアリルアルコール **58** が得られる。

Scheme 8



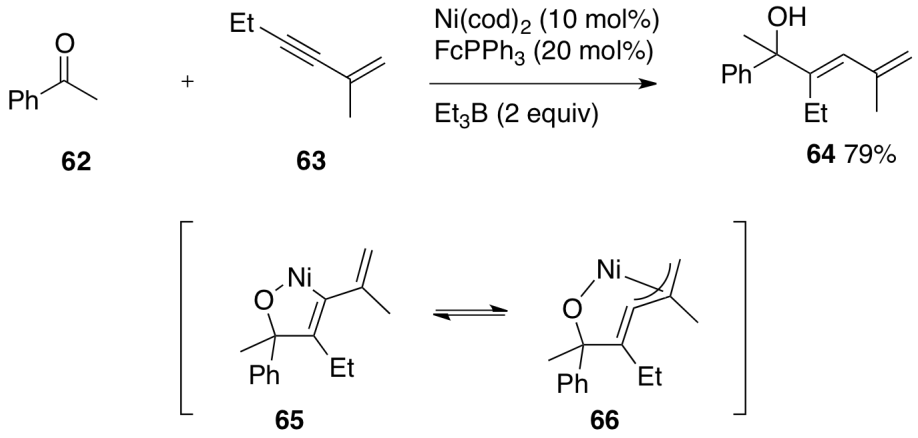
さらに、Montgomery らは本アルキンとアルデヒドとの反応にトリエチルシランを用いることで、三成分連結反応へと展開している（スキーム 9）[10]。本反応はオキサニッケラサイクル **61** とシランとの σ 結合メタセシスを経由して進行し、カップリング体 **60** が生成する。

Scheme 9



一方、ケトンとアルキンとのカップリング反応の例は少なく、例えば Jamison らによって活性の高い 1,3-エニン [11]を用いた分子間カップリングが報告されている。この反応ではアルデヒドを用いた時と同様に、まずニッケル錯体とケトン **62** 及び 1,3-エニン **63** からオキサニッケラサイクル中間体 **65** が生成する。**65** はπ-アリル錯体 **66** との間に平衡があり、反応性の乏しいケトンとも安定なニッケラサイクル中間体を形成するため高い反応性を示すものと考えられる（スキーム 10）[12]。

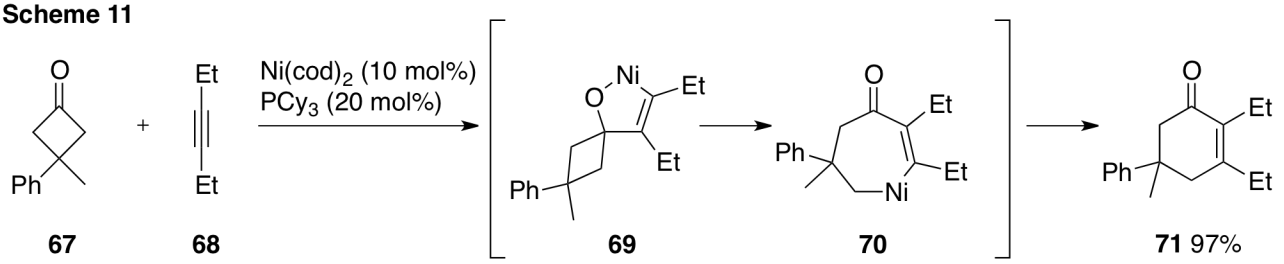
Scheme 10



また村上らはシクロブタノン **67** を用いた環拡大反応を報告している（スキーム 11）[13]。本反応の反応機構は以下のように考えられている。まず 0 価ニッケル錯体とシクロブタノン **67** 及びアルキン **68** からオキサニッケラサイクル中間体 **69** が形成する。続いてβ炭素脱離により 7 員環ニッケラサイクル中間体 **70** となり、還元的脱離を経てシクロヘキセノン誘導体 **71** が得られる。本反応に用いられるケトンはひずみによる高い反応性をもつシ

クロブタノン誘導体に限られる。

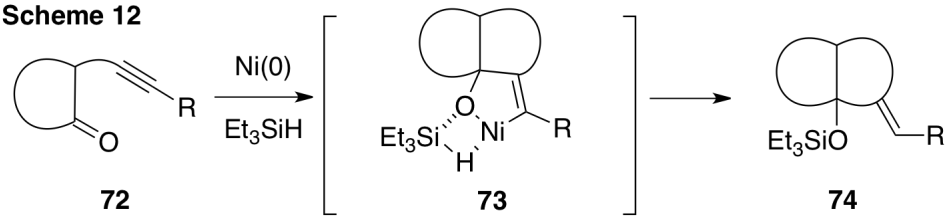
Scheme 11



67 **68** **69** **70** **71** 97%

以上のようにケトンとアルキンの反応は反応性の高い基質を用いた例に限られており、単純アルキンと単純ケトンのカップリング反応の例はほとんど無い[*1]。筆者は、ケトンとアルキンを分子内に配置することで単純ケトンも 0 価ニッケル存在下、アルキンと反応するのではないかと考えた。さらに、スキーム 12 に示すように分子内にアルキン側鎖をもつ環状ケトン **72** をシラン存在下で 0 価ニッケル錯体と反応させたならば、オキサニッケラサイクル中間体 **73** とシランとの σ 結合メタセシスを経由して、橋頭位に四置換炭素をもつ多環式化合物 **74** が合成できる。そこでケトンとアルキンとの本環化反応が多環式骨格構築の新たな方法となることを期待し検討を行うことにした。

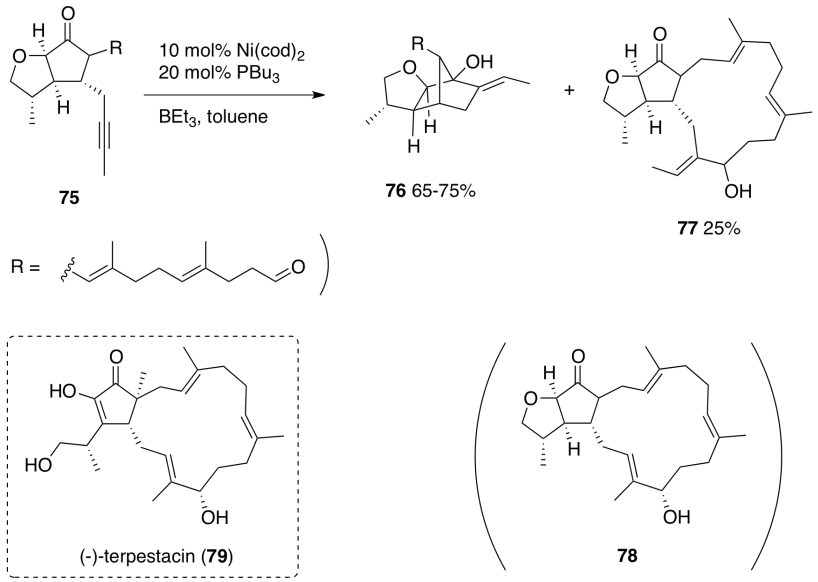
Scheme 12



72 **73** **74**

[*1] Jamison らは (-)-terpestacin (**79**)および類縁体の合成研究の途上、**75** を Ni 触媒存在下で反応させると、目的とする 15 員環化合物 **78** は全く得られず、14 員環化合物 **77** を 25%の収率で得るとともに、ケトンとアルキンが反応した **76** が得られることを報告している（スキーム 13）。[14)]

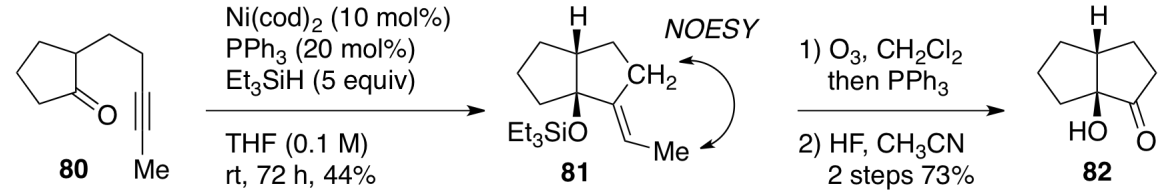
Scheme 13


10 mol% Ni(cod)2
20 mol% PBu3
BEt3, toluene
75
76 65-75%
77 25%
R =
(-)-terpestacin (79)
78

第一節　環化反応の条件検討

α 位に 3-ペンチニル基をもつシクロペンタノン誘導体 **80**[15]を基質とし、まず PPh_3 を配位子として環化反応を検討した（スキーム 14）。当研究室で開発されたジエンとアルデヒドの還元的縮合反応の条件に倣い[5,6]、10 mol%の $Ni(cod)_2$ 及び 20 mol%の PPh_3 を用いて調製した Ni(0)-PPh_3 錯体に、5 当量の Et_3SiH 及び基質 **80** を加え、THF 中室温で 72 時間撹拌した。その結果、ビシクロ [3.3.0]オクタン骨格をもつ環化体 **81** が 44%と中程度の収率ながら単一の立体異性体として生成した。この環化体 **81** の立体化学は以下のように決定した。オレフィンの幾何異性はメチル基と環上の水素間に NOESY 相関が観測されたことから *E* 体であると決定した。また核間の立体化学については **81** のオレフィンをオゾン分解により切断した後、トリエチルシリル基をアセトニトリル中、フッ化水素により脱保護することで文献既知化合物 **82**[16]に誘導し、^1H 及び ^{13}C NMR スペクトルを比較し、*cis* であると決定した。

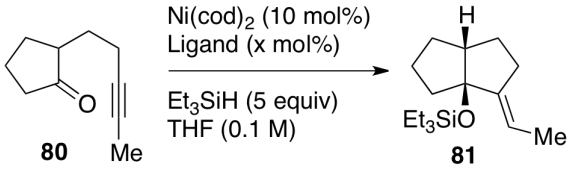
Scheme 14



次に配位子の効果について検討を行った（表 1）。まず PBu_3 を用い同様の条件下 **80** を反応させたところ、反応時間は 48 時間に短縮し、環化体 **81** の収率も 72%に向上した（run 1）。本結果より電子豊富な配位子が本反応に良好な結果を与えることが示唆された。そこで電子供与能が高いことが知られている NHC 配位子を用いて検討を続けることとした。10 mol%の $Ni(cod)_2$、10 mol%の IMes·HCl 及び 12 mol%の ^{t}BuOK より調製した Ni(0)-IMes 錯体に、5 等量の Et_3SiH 及び基質 **80** を加え、THF 中室温で 8 時間撹拌した。その結果、ホスフィン配位子を用いたときと同様に環化体 **81** が単一の立体異性体として得られ収率は 84%に向上した（run 2）。予想通り本環化反応において NHC 配位子が有効であることがわかったため NHC 配位子の検討を続けることとした。SIMes·HBF_4、IPr·HCl、SIPr·HCl を用い、先ほどと同様の条件下反応を行ったところ、いずれも良好な結果が得られた（runs 3-5）。イミダゾール環窒素上にかさ高い置換基を持つ IPr·HCl や SIPr·HCl が本反応に効果

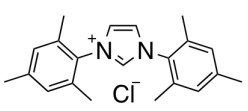
的であり（runs 4 and 5）、特に IPr を配位子として用いた場合、環化体 **81** が定量的に得られた（run 4）。

Table 1 Optimization of reaction conditions of intramolecular cycloaddition of alkynylcyclopentane **80**

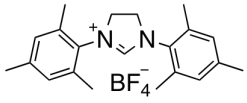


*NHC ligands were prepared in situ from the corresponding imidazolium salts (10 mol%) and ^{t}BuOK (12 mol%).

run	ligand (x)	time (h)	yield
1	PBu_3 (20)	48	72%
2*	IMes (10)	8	84%
3*	SIMes (10)	9	79%
4*	IPr (10)	1	quant
5*	SIPr (10)	1	93%

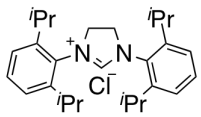


83 IMes·HCl



84 SIMes·HBF_4

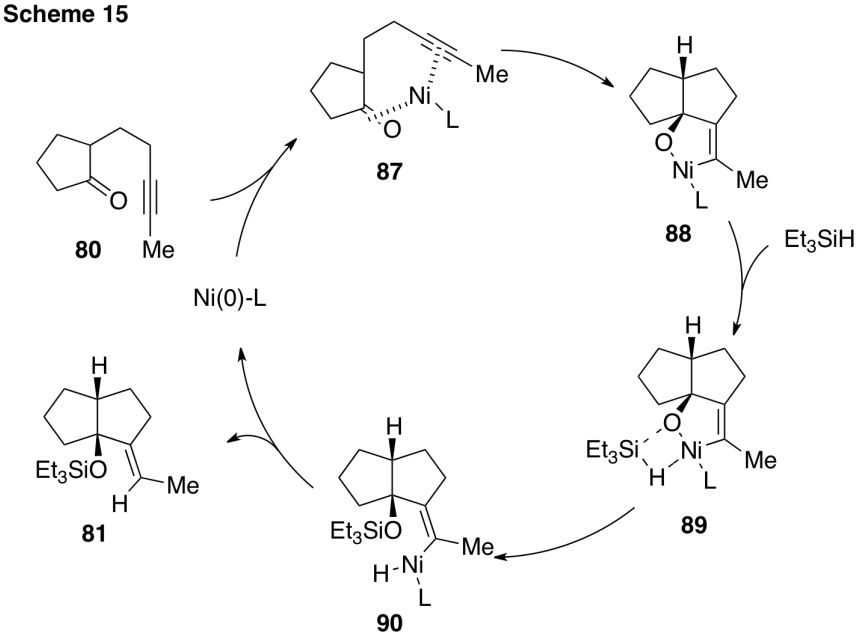
85 IPr·HCl



86 IPr·HCl

本反応の反応機構はアルデヒドを用いたときと同様、以下のように考えられる（スキーム 15）[8]。まずニッケル錯体が基質 **80** に配位後、酸化的環化付加しオキサニッケラサイクル中間体 **88** となる。次にシランとの σ 結合メタセシスによりヒドリドニッケル中間体 **90** となり続く還元的脱離により生成物 **81** を得るとともにニッケル錯体が再生する[*1]。

Scheme 15

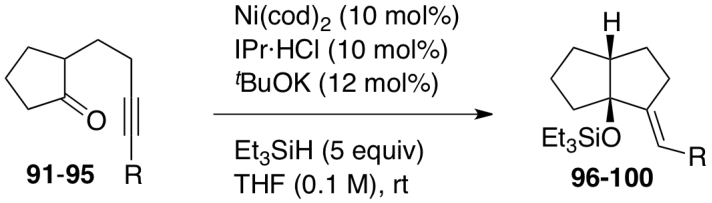


[*1] NHC 配位子は高い σ 電子供与能を持つことから、ホスフィン配位子にくらべニッケル中心の電子密度が上がり、酸化的環化付加の過程が促進されるため、良い結果を与えたと考えられる。

第二節　置換基効果の検討

次にアルキン上の置換基効果の検討を行った（表 2)。末端アルキン **91**[*1] や、アルキン上にフェニル基やシロキシメチル基を持つ基質 **92** 及び **93** を用いると反応は速やかに進行し、目的の環化体 **96-98** が立体選択的かつ高収率で得られた（runs 1-3)。一方、エステル基やシリル基を有する基質 **94** 及び **95** では反応は遅く、目的の環化体 **99** 及び **100** は低収率でしか得られなかった（runs 4 and 5)。最近 Jamison 及び Houk はニッケル触媒によるアルデヒドとアルキンの還元的カップリングにおいて、電子求引性アルキンを用いるとニッケル錯体がアルキンに強固に配位し、オキサニッケラサイクル中間体が生成しにくくなることを報告している [12)]。筆者の反応においても同様にオキサニッケラサイクル中間体が生成しにくいため、基質 **94** を用いると収率が低下したものと考えられる。基質 **95** については、アルキンとアルデヒドの還元的カップリング反応においてアルキン上にかさ高い ^{t}Bu 基がある場合に反応が進行しにくいため [12)]、アルキン上に TMS 基が存在すると立体障害により反応の進行が妨げられたと考えられる。

Table 2 Scope of alkyne structure

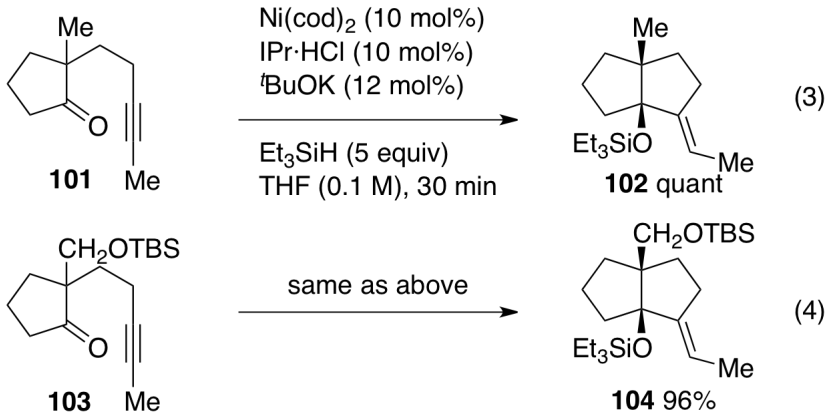


91-95　　**96-100**

run	substrate	product	time (h)	yield (%)
1	**91** (R = H)	**96**	0.5	83
2	**92** (R = CH_2OTBS)	**97**	0.5	99
3	**93** (R = Ph)	**98**	0.5	97
4	**94** (R = COOMe)	**99**	48	26
5	**95** (R = TMS)	**100**	40	26

次に、核間に二つの四置換炭素を有する環化体を合成すべくα位にメチル基を有する基質 **101** を用いたところ、環化体 **102** が定量的に得られることが分かった（スキーム 16、式 3)。またシロキシメチル基を有する基質 **103** を用いても、やはり目的とする環化体 **104** が高収率で生成した（式 4)。以上の結果よりケトンα位に置換基が導入された場合においても本反応は問題なく進行することがわかった。

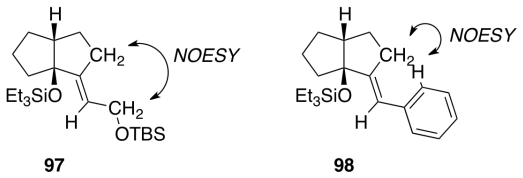
Scheme 16



以上筆者は 0 価ニッケル錯体存在下、ケトンとアルキンの還元的カップリング反応を検討した。その結果 NHC 配位子を用いることでアルキン上の置換基による制約はあるものの、ビシクロ [3.3.0]骨格を有する化合物が穏和な条件下で合成できることが明らかとなった。

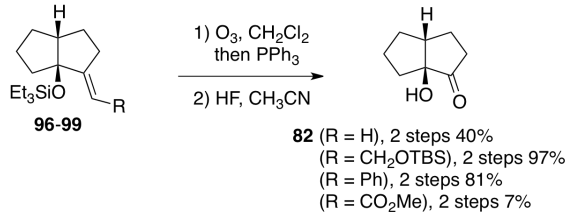
[*1] これら環化体のうち化合物 **97**、**98** の立体化学は以下のように決定した。オレフィンの幾何異性については図 3 に示す位置に NOESY 相関が観測されたことから、*E* 体であると決定した。

Figure 3



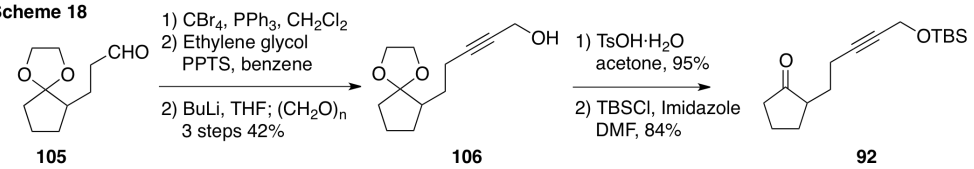
核間の立体化学については化合物 **96** も含めオゾン分解後、トリエチルシリル基をアセトニトリル中、フッ化水素により脱保護することで文献既知化合物 **83** へと誘導し、^{1}H NMR を比較することで立体構造を決定している（スキーム 17)。なお、環化体 **100** の立体化学については検討を行っていないものの同様に *E-cis* の立体構造であると考えている。

Scheme 17



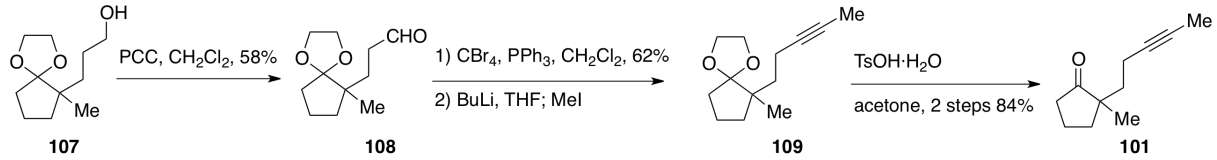
本節で用いた環化反応の基質のうち基質 **91**[15]、**93-95**[17]は文献記載の方法に従い合成し、**92** については以下のように合成した（スキーム 18）。文献既知化合物 **105**[18]を Corey-Fuchs 法によりリチウムアセチリドへと変換した後、後処理にパラホルムアルデヒドを用い **106** へと誘導化した。続いてアセタールを脱保護後、水酸基を TBS 保護することでシクロペンタノン誘導体 **92** を得た。

Scheme 18



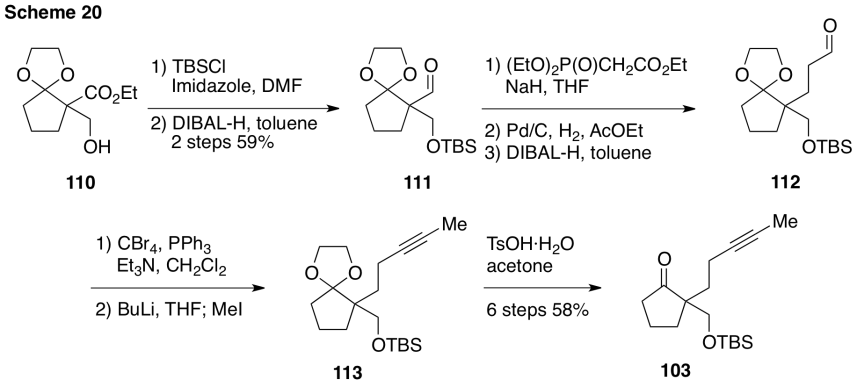
基質 **101** は以下のように合成した（スキーム 19）。文献既知化合物 **107**[19]のアルコールを酸化し、Corey-Fuchs 法によりリチウムアセチリドへと変換した後、後処理にヨウ化メチルを用い **109** へと誘導化した。**109** のアセタールをトシル酸により脱保護することでシクロペンタノン誘導体 **101** を得た。

Scheme 19



基質 **103** は以下のように合成した（スキーム 20）。文献既知のアルコール **110**[20]を TBS 保護した後、DIBAL 還元によりアルデヒド **111** とした。アルデヒド **111** を Horner-Wadsworth-Emmons 反応を用いて増炭後、オレフィンを接触水素化し、再び DIBAL 還元によりアルデヒド **112** へと変換した。続いて Corey-Fuchs 法によりリチウムアセチリドへと変換した後、後処理にヨウ化メチルを用い **113** へと誘導化した。**113** のアセタールをトシル酸により脱保護することでシクロペンタノン誘導体 **103** を得た。

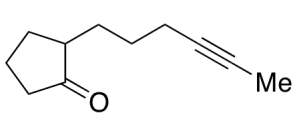
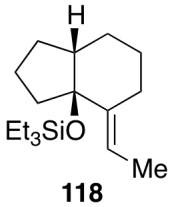
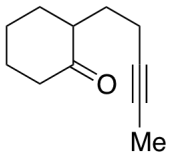
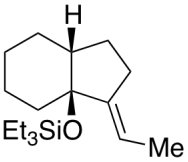
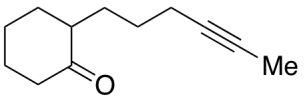
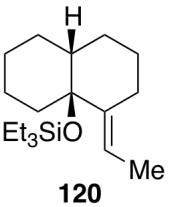
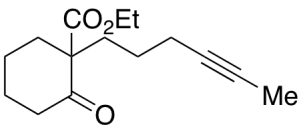
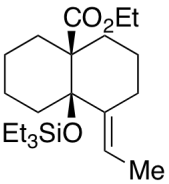
Scheme 20



第三節　多様な骨格形成への応用

様々な骨格を有する環化体を合成すべく検討した（表 3)。まずアルキン側鎖の長さを 1 炭素伸張したシクロペンタノン **114** を基質とし反応を行うこととした。最適条件下で基質 **114** を THF 中室温で反応させたところ、 反応は 30 分で終了し、ヒドリンダン誘導体 **118**[*1] が得られた。この結果より本反応が 6 員環形成にも利用可能であることがわかった（run 1)。一方、シクロヘキサノン誘導体 **115** を用いても環化反応は円滑に進行しヒドリンダン誘導体 **119**[*1] が定量的に得られた（run 2)。さらに基質 **116** 及び **117**[*2] を用い反応を行うと、対応するデカリン誘導体 **120**[*1] 及び **121**[*3] がともに良好な収率で得られた（runs 3 and 4)。

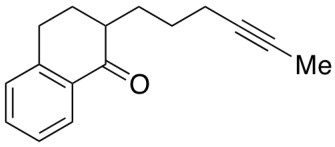
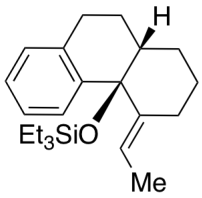
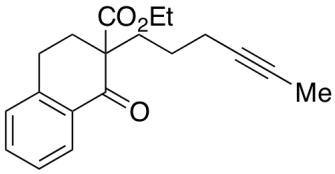
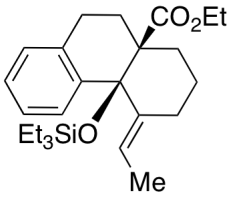
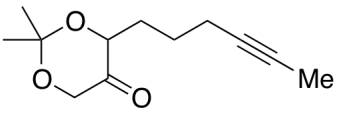
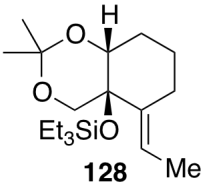
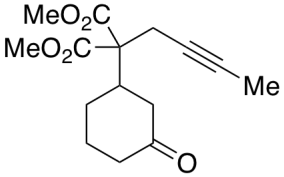
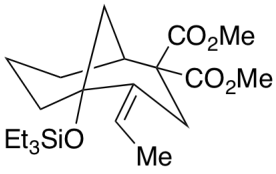
Table 3 Synthesis of hydrindan and decalin derivatives[a]

run	substrate	product	time (h)	yield (%)
1	 **114**	 **118**	0.5	quant
2	 **115**	 **119**	0.5	quant
3	 **116**	 **120**	0.5	quant
4	 **117**	 **121**	25	76

[a] Reaction procedure: A solution of substrates in THF was added to a solution of $Ni(cod)_2$ (10 mol%), IPr·HCl (10 mol%), ^{t}BuOK (12 mol%) and Et_3SiH (5 equiv) in THF.

また、芳香族ケトンも本反応に適用可能であり、α テトラロン誘導体 **122**[*4] 及び **123**[*4] を基質として用いた場合にも、目的とする三環式化合物 **126**[*5] 及び **127**[*3] がいずれも良好な収率で得られた（表 4、runs 1 and 2）。さらに環状アセタール構造を持つ基質 **124**[*6] を用いた場合も、目的とする環化体 **128** が定量的に得られた（run 3）。また、ケトンの β 位にアルキン側鎖を持つ基質 **125**[*7] を用いても反応は問題なく進行し、ビシクロ [3.3.1]ノナン骨格をもつ **129** が 99%の収率で生成した（run 4）。

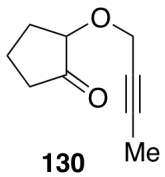
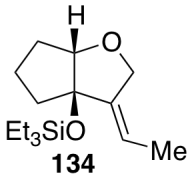
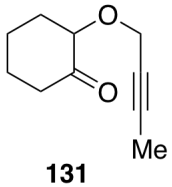
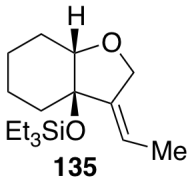
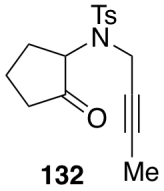
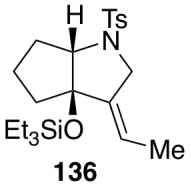
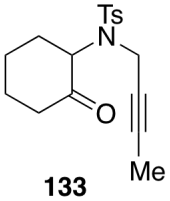
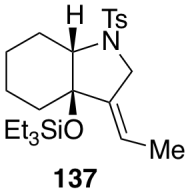
Table 4 Reactions of various alkynylcyclohexanones[a]

run	substrate	product	time (h)	yield (%)
1	 **122**	 **126**	0.5	73%[b] (quant)[c]
2	 **123**	 **127**	3	79
3	 **124**	 **128**	0.5	99
4	 **125**	 **129**	0.5	99

[a] Reaction procedure: A solution of substrates in THF was added to a solution of $Ni(cod)_2$ (10 mol%), IPr·HCl (10 mol%), ^{t}BuOK (12 mol%) and Et_3SiH (5 equiv) in THF. [b] Isorated yield. [c] Yield in parenthesis is NMR yield.

次にヘテロ環の構築を目指し、側鎖にヘテロ原子を導入した基質を用いて反応を行うこととした（表 5)。まず側鎖に酸素原子をもつ基質 **130**[*1] を用いて反応を行ったところ、フラン骨格を有する環化体 **134** が高収率で得られた（run 1)。基質 **131**[*1] を用い同様に反応を行った場合も、オクタヒドロベンゾフラン誘導体 **135** が高収率で得られることがわかった（run 2)。また、側鎖にトシルアミドを導入した基質 **132**[*1] を用い同様の条件下反応を行ったところ、対応する二環式化合物 **136** が高収率で得られた（run 3)。さらに、基質 **133** を用いたところインドリン骨格をもつ環化体 **137** が高収率で得られることがわかった（run 4)。

Table 5 Reactions of various alkenylcyclohexanones with heteroatom[a]

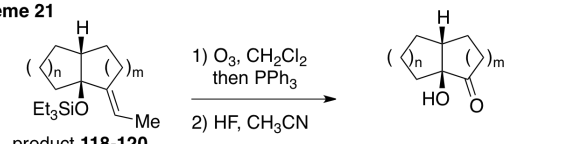
run	substrate	product	yield
1	 **130**	 **134**	90%
2	 **131**	 **135**	87%
3	 **132**	 **136**	91%
4	 **133**	 **137**	95%

[a] Reaction procedure: A solution of substrates in THF was added to a solution of $Ni(cod)_2$ (10 mol%), IPr·HCl (10 mol%), ^{t}BuOK (12 mol%) and Et_3SiH (5 equiv) in THF.

以上、筆者は様々な炭化水素骨格やヘテロ環骨格の合成を行い、本環化反応が広く二環式化合物の合成に適用可能であることを明らかとした。

[*1] 環化体 **118-120** の核間の立体化学は以下のようにして決定した（スキーム 21)。環化体 **118-120** をオゾン分解によりケトンとした後、トリエチルシリル基をアセトニトリル中、フッ化水素により脱保護し、文献既知のヒドロキシケトン **138-140**[16]へと誘導化し、^{1}H 及び ^{13}C NMR を比較することで *cis* であると決定した。その他の環化体については立体構造の決定は行っていないが、環化体 **118-120** 同様 *cis* であると考えている。

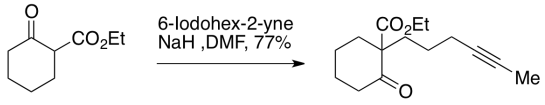
Scheme 21



138 (n = 1, m = 2), 2 steps 69%
139 (n = 2, m = 1), 2 steps 73%
140 (n = 2, m = 2), 2 steps 50%

[*2] 表 3 に用いた基質のうち **114-116**[21]は文献記載の方法に従い合成した。基質 **117** は 2-オキソシクロヘキサンカルボン酸エチルエステル **141** と 6-ヨード-2-ヘキシンをカップリングさせて合成した（スキーム 22)。

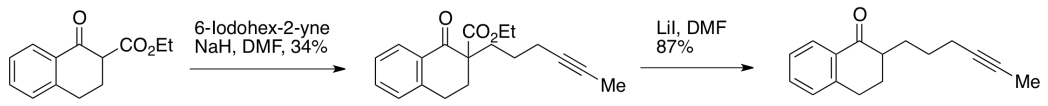
Scheme 22



141　　**117**

[*3] 環化体 **121** の IR スペクトルにおいてカルボニル伸縮のピークが二本観測さており、また ^{1}H NMR スペクトルを室温で測定を行うとピークがブロードニングしていた。また、昇温測定することでブロードニングが解消された。この結果から化合物 **121** のエステル基の自由回転が遅いことがわかり、立体障害により環化体 **121** の収率が若干低下したと考えられる。また環化体 **127** についても同様の理由で収率が低下したと考えている。
[*4] 表 4 で用いた基質は以下のように合成した。基質 **123** は β ケトエステル **142**[22] と 6-ヨード-2-ヘキシンをカップリングさせて合成し、また、基質 **123** を DMF 中、ヨウ化リチウムにより脱炭酸することで基質 **122** を合成した（スキーム 23)。

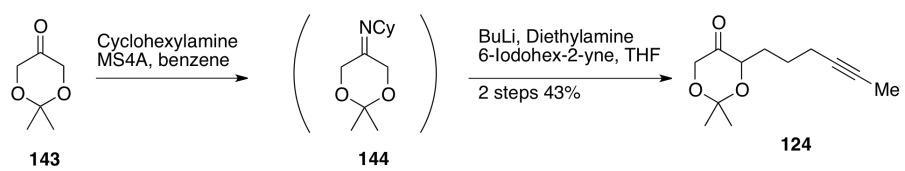
Scheme 23



142　　**123**　　**122**

[*5] 環化体 **126** はシリカゲルカラム中に容易に分解されるため単離が困難であった。このため 1,1,2,2-テトラクロロエタンを内部標準物質として用い、積分値の比較により NMR から収率を計算した。
[*6] 基質 **124** はアセトナイド **143**[23]のケトンをシクロヘキシルアミンによりイミン **144** とした後、リチウムジイソプロピルアミド及び 6-ヨード-2-ヘキシンを用い、リチオエナミンをアルキル化することで合成した（スキーム 24)。

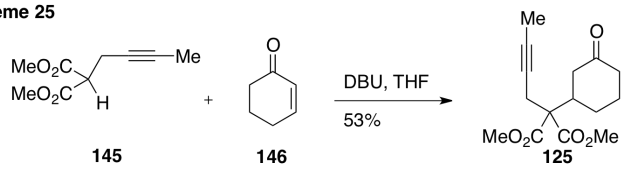
Scheme 24



143　　**144**　　**124**

[*7] 基質 **125** は DBU を用いマロン酸エステル **145**[24]とシクロヘキセノン **146** との Michael 付加により合成した （スキーム 25)。

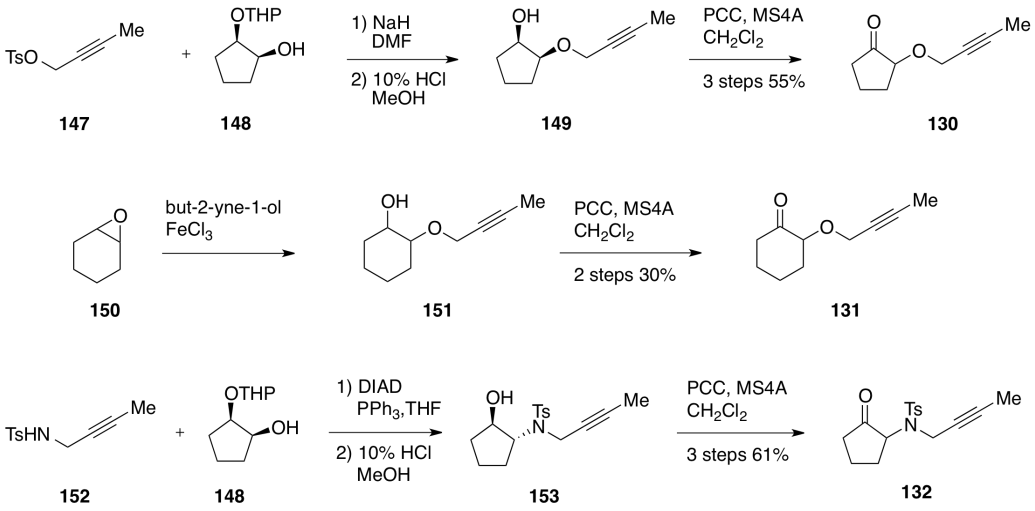
Scheme 25



145 **146** **125**

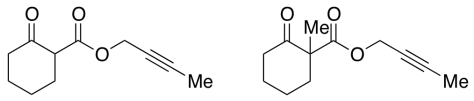
*1 表 5 に用いた基質 **133**[25]は文献記載の方法に従い合成した。その他の基質については以下の方法により合成した。基質 **130** の合成はまずアルキン **147** にシクロペンタノール **148** を求核付加させた後、THP を脱保護し、アルコール **149** を得た。得られたアルコールを PCC 酸化することで基質 **130** を合成した（スキーム 26）。基質 **131** はシクロヘキセンオキシド **150** と 2-ブチン-1-オールを塩化第二鉄触媒存在下求核付加させた後、PCC により酸化することで合成した。基質 **132** はトシルアミド **152**[26]とシクロペンタノール **148** を光延反応によりカップリングさせた後、THP を脱保護しアルコール体 **153** とした。得られたアルコールを PCC 酸化することで基質 **132** を合成した。

Scheme 26



この他にもアルキン側鎖中にエステル構造を有する化合物 **154** 及び **155** を合成し同様の条件下検討を行ったがそれぞれ 70%及び 78%の原料を回収するのみであった（図 4）。プロパルギルエステルの活性化は Pd 触媒による報告例が知られているため[27]、側鎖がニッケル触媒により切断されるとともにニッケルが失活している可能性や、エステル基の平面性によって側鎖の自由度が低く、アルキンがケトン部位に近付きにくくなっている可能性が考えられる。

Figure 4



154 SM rec. 70%　　**155** SM rec. 78%

結語

以上第一章をまとめると、著者はシラン存在下 0 価ニッケル触媒によるアルキンと環状ケトンとの分子内環化反応の開発を目指し検討した。その結果、本反応において電子豊富な配位子である NHC が有効な配位子であることを見いだし、ヒドリンダン骨格やデカリン骨格を始めとする様々な縮合多環性骨格が立体選択的かつ高収率で構築できることが明らかになった。[28)]

本環化反応は温和な条件下進行し、環サイズやヘテロ原子による影響を受けにくいことから複雑な二環式化合物を合成するための新たな方法になり得ると期待される。

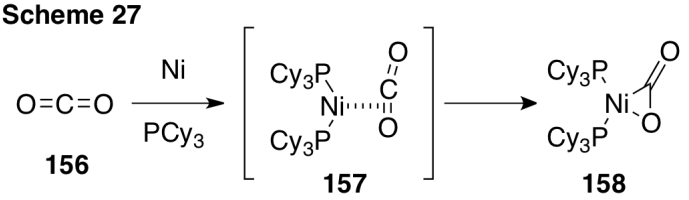
第二章

0 価ニッケル錯体を用いたアレナミドへの二酸化炭素固定反応

序節

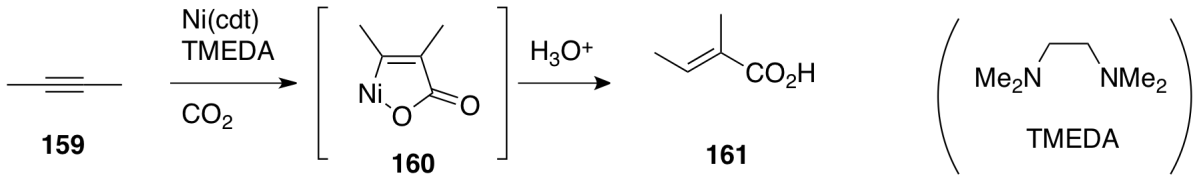
二酸化炭素は地球上に膨大に存在し、安価で毒性が低いことから有機合成化学において魅力的な 1 炭素源と考えられる。しかしながら比較的反応性に乏しく、その利用は限られている。1975 年に Aresta らは、炭素-炭素多重結合に対して高い反応性を示す低原子価ニッケルが、炭素−酸素二重結合を有する二酸化炭素とも容易に反応し、二酸化炭素-ニッケル錯体 **158** が生成することを見出した（スキーム 27）[29]。

Scheme 27



その後、ニッケル錯体を用いた二酸化炭素固定反応について様々な検討がなされてきた。1982 年、Hoberg らは 0 価ニッケル錯体にアルキンと二酸化炭素が酸化的環化付加し、ニッケララクトン **160** が生成することを初めて報告している。ニッケララクトン **160** の加水分解によりチグリン酸（**161**）が得られる（スキーム 28）[30]。

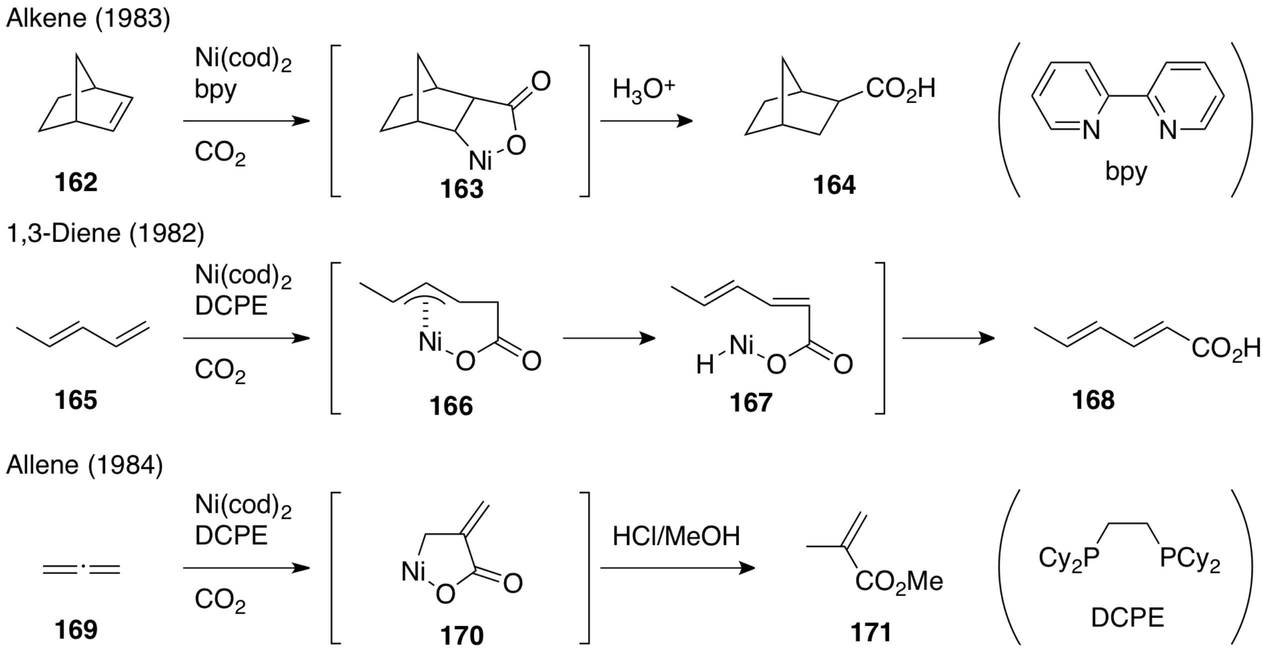
Scheme 28



その後、アルケン **162**[31]、1,3−ジエン **165**[32]、アレン **169**[33]が同様に二酸化炭素及び 0 価ニッケル触媒と反応し、ニッケラサイクル **163**、**166** 並びに **170** を生成することが報告されている。これらの中間体からも対応するカルボン酸 **164**、ソルビン酸（**168**）又はメタクリル酸メチル（**171**）への変換が可能である（スキーム 29）。以上のようにニッケララクトンは加水分解によって容易にカルボン酸へと変換できることから、有機合成において

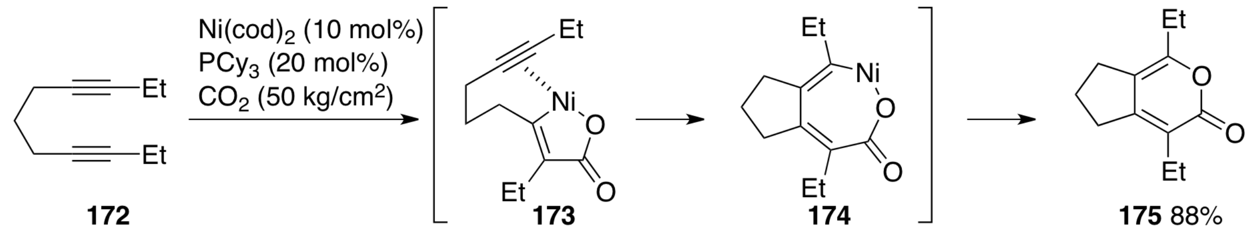
様々なカルボン酸誘導体合成の有用な中間体と考えることができる。

Scheme 29



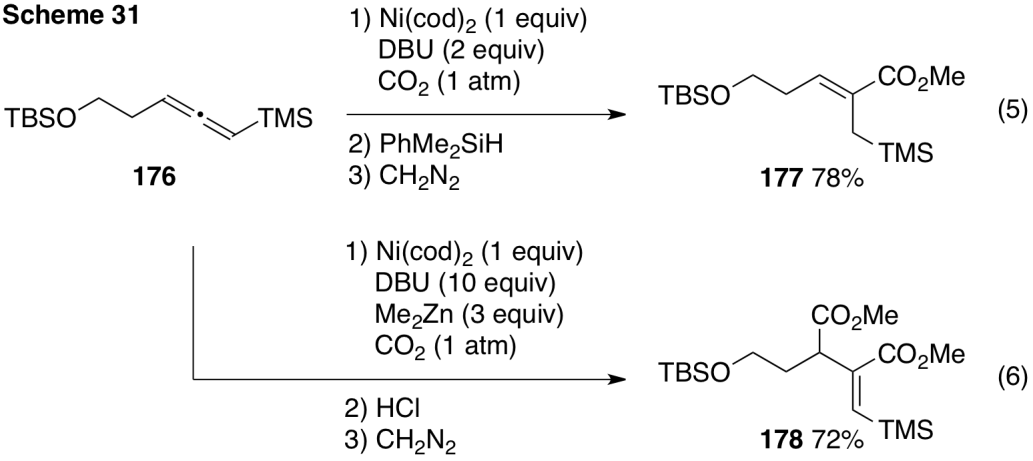
一方、津田らはジイン **172** を基質とした触媒的二酸化炭素固定反応を報告している。この反応ではまずジイン **172** の片方のアルキンと二酸化炭素がニッケル触媒に酸化的環化付加し、ニッケララクトン中間体 **173** が生成する。続いてもう片方のアルキンが挿入し 7 員環ニッケラサイクル **174** となった後、還元的脱離によりピロン誘導体 **175** が得られるとともにニッケル触媒が再生すると考えられる（スキーム 30）[34)]。

Shceme 30



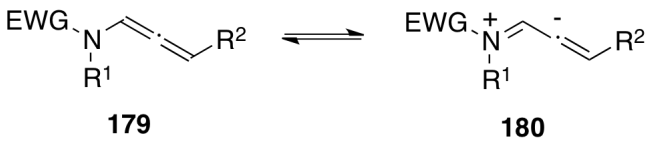
また 2004 年に、森らは、トリメチルシリルアレン **176** を基質とした位置選択的な二酸化炭素固定反応を報告した（スキーム 31、式 5）[35)]。さらに、トランスメタル化剤としてジメチル亜鉛存在下で本反応を行った場合、二酸化炭素が 2 分子取り込まれた、ジエステル **178** が得られる（式 6）[36)]。

Scheme 31



ところで、アレンに窒素原子が直結した構造を持つアレナミド **179** は、窒素原子上の非共有電子対を二重結合に非局在化できることから、分極したアレンとしてその反応性に興味が持たれる化合物であり、近年、有機合成への利用が盛んに研究されている（図 5）[37]。

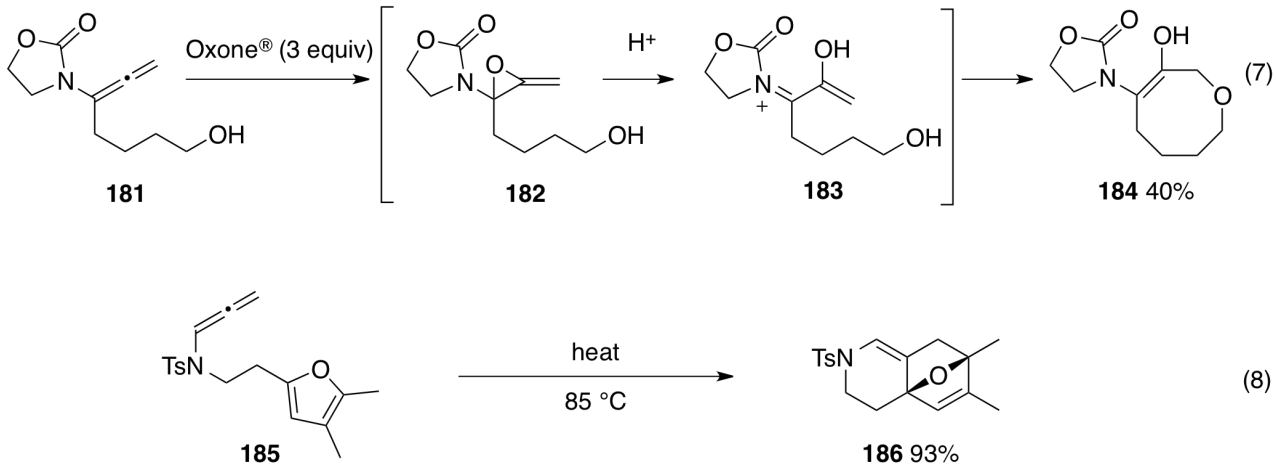
Figure 5



2002 年に Hsung らは、アレナミド **181** と Oxone®の反応を報告している。この反応では、窒素が結合した二重結合へのエポキシ化が進行し、エポキシド **182** の開環と、分子内 1,4 付加反応により、8 員環化合物 **184** が得られる（スキーム 32、式 7）[38]。

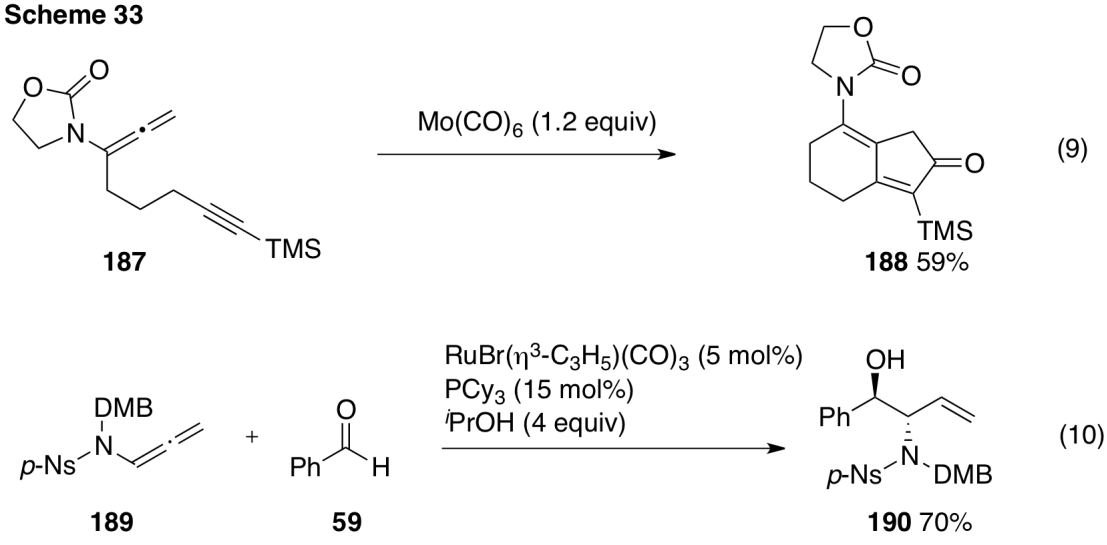
一方、アレナミド **185** を用いた分子内 Deals-Alder 反応では、アレナミドの末端側二重結合が選択的に反応し、対応する三環式化合物 **186** を高い収率で与える（式 8）[39]。

Scheme 32



一方、遷移金属錯体を用いたアレナミドの変換反応は少なく、Hsung らによるモリブデン錯体を用いたアレナミド **187** への Pauson-Khand 型反応や（スキーム 33、式 9）[40]、Kriche らによるルテニウム触媒を用いたアレナミド **189** へのアルデヒド **59** の付加反応（式 10）[41]など、数例が報告されているのみである。従って、アレナミドを基質とした遷移金属錯体との反応について、さらなる検討を加えることにより、新しい変換反応を開発できることが期待される。

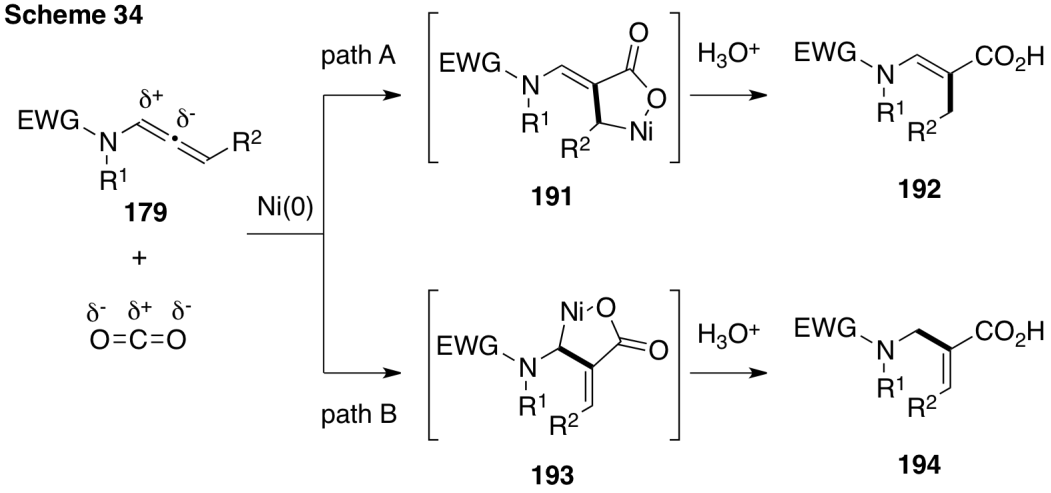
Scheme 33



このような背景から著者はアレナミドの興味深い電子的性質に着目し、ニッケル錯体を用いたアレナミドへの二酸化炭素固定化反応について検討することにした（スキーム 34）。すなわち、二酸化炭素雰囲気下、0 価ニッケル錯体とアレナミド **179** との反応が進行する

ならば、負の部分電荷を持つアレナミドの sp 炭素が二酸化炭素の sp 炭素原子と新たな炭素-炭素結合を形成するように酸化的環化付加が進行し、ニッケララクトン **191** または **193** のいずれかが形成されると予想される。続いて酸性条件下ニッケララクトンを切断することで、対応する β アミノ酸誘導体 **192** もしくは **194** が合成できるのではないかと考え、研究に着手した。

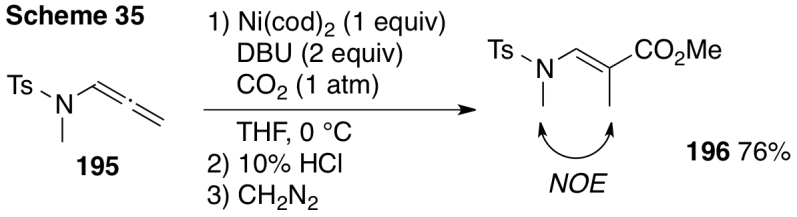
Scheme 34



第一節　二酸化炭素固定反応の条件検討

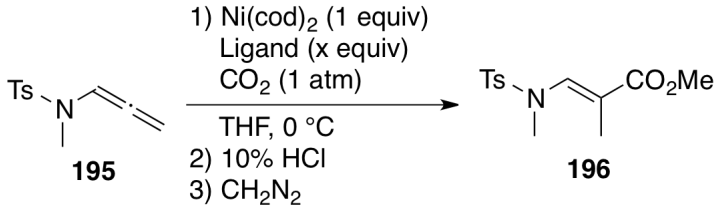
まず､森らのトリメチルシリルアレンを基質とした二酸化炭素固定反応の条件に従い[35]、1 気圧の二酸化炭素雰囲気下、1 当量の $Ni(cod)_2$ 及び 2 当量の DBU と、窒素原子上にトシル基をもつアレナミド **195**[42]を THF 中、0 °C にて反応させた。反応終了後、10%塩酸を用いた後処理とジアゾメタン処理によるメチル化を行ったところ、二酸化炭素付加体 **196** が 76%の収率で単一の立体異性体として生成した（スキーム 35)。オレフィンの幾何異性については 2 つのメチル基の間に NOE 相関が観測されたことから *E* 体であると決定した。

Scheme 35

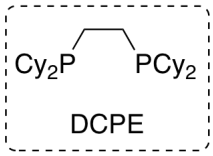


続いて収率の向上を目指し、配位子の検討を行った（表 6)。まず、DBU を 4 当量に増やしたところ、目的とする二酸化炭素付加体 **196** の収率は 89%に向上した（run 2)。一方、1,10-phenanthroline や DCPE を用いた場合、目的物の収率は大きく低下した（runs 3 and 4)。

Table 6 Ligand screening



run	ligand (x)	time (h)	yield
1	DBU (2)	2	76%
2	DBU (4)	1	89%
3	1,10-phenanthroline (1)	1	4%
4	DCPE (1)	1	trace
5	TMEDA (1)	1	82%
6	TMEDA (2)	1	88%



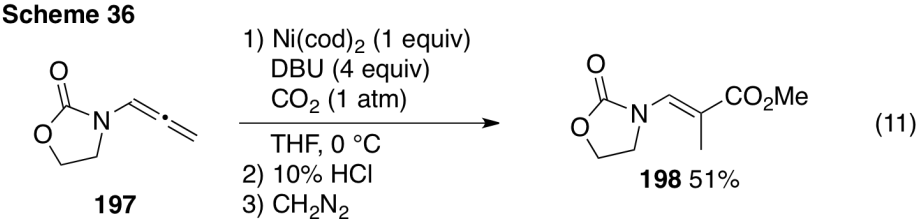
また、1 当量の TMEDA を用いた場合、目的物は 82%の収率で得られた（run 5)。さらに TMEDA を 2 当量に増やしたところ、収率は 88%まで向上した (run 6)。以上の結果より、4 等量の DBU を用いた条件を最適条件とし、以降の検討を続けることにした[*1]。

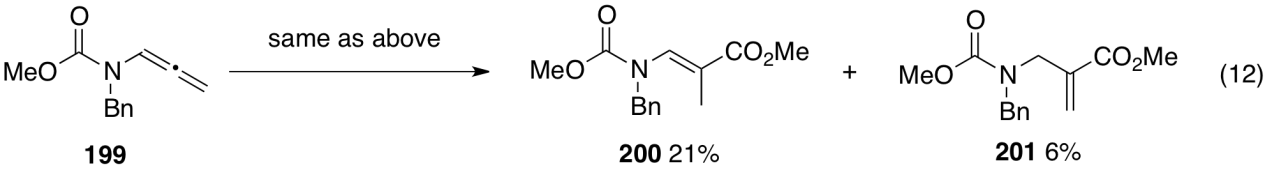
[*1] この他にも DBU と TMEDA の比較を行ったが、いずれも DBU を用いた場合の方が高い収率で目的物が得られたため、4 当量の DBU を用いた条件を最適条件とし、以降の検討を行っている。

第二節　置換基効果の検討

続いて窒素原子の保護基の効果について検討を行った（スキーム 36)。オキサゾリジノン由来のアレナミド **197**[*1] を用い最適条件下でカルボキシル化を行ったところ、目的の二酸化炭素付加体 **198**[*2] が 51%の収率で得られた（式 11)。一方、メチルカルバメート体 **199** を用いたところ、予想された β アミノ酸誘導体 **200**[*2] が 21% 得られるとともに、二重結合の位置異性体 **201** も 6%の収率で得られることが分かった（式 12)。

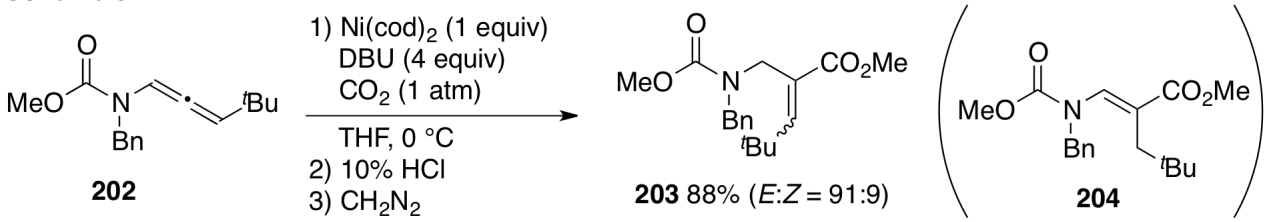
Scheme 36





次に置換基をもつアレナミドを用いて二酸化炭素固定化の検討を行った（スキーム 37)。最適条件下、^{t}Bu 基を有する基質 **202**[*3] と二酸化炭素を反応させたところ、末端アレンの場合と異なり、予想された生成物 **204** は全く得られず、二重結合の位置異性体 **203** のみが *E*:*Z* = 91:9 の幾何異性体混合物として、88%の収率で得られた[*4]。この結果より、アレン部位の置換基が、酸化的環化付加の位置選択性に大きく影響すると考えられた。

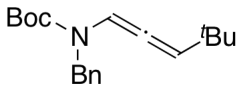
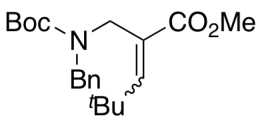
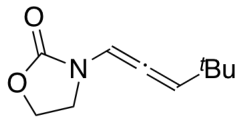
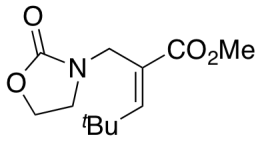
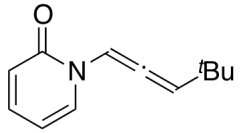
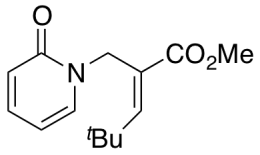
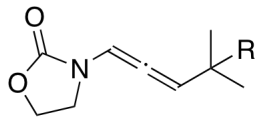
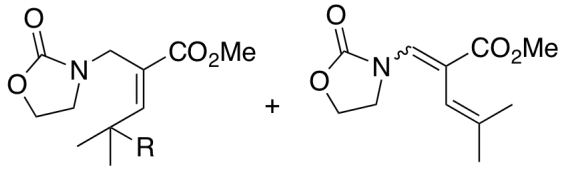
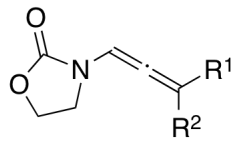
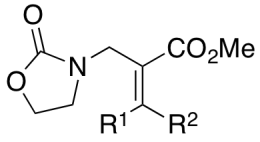
Scheme 37



次に様々な基質を用いて二酸化炭素固定化の検討を行った（表 7)。Boc 保護されたアレナミド **205**[*5] を用いカルボキシル化を行うと、対応する β アミノ酸誘導体 **213**[*6] が *E*:*Z* =

89:11 の幾何異性体混合物として、91%の収率で得られた（run 1）。オキサゾリジノン由来の基質 **206** を用い同条件下反応させたところ、*E* 体のみが単一立体異性体として 88%の収率で得られた（run 2）。ピリドン誘導体 **207** を用いても反応は円滑に進行し、対応する β アミノ酸誘導体 **215** が 60%の収率で得られた（run 3）。^{t}Bu 基の代わりにシロキシエチル基

Table 7 Reactions of various allenamides[a]

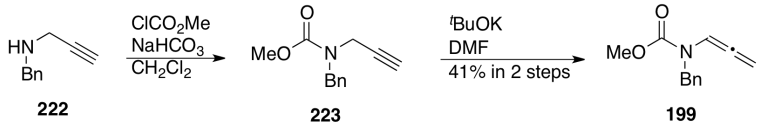
run	substrate	time (h)	product	
1	 **205**	15	 **213** 91% (*E*:*Z* = 89:11)	
2	 **206**	16	 **214** 88%	
3	 **207**	17	 **215** 60%	
				
4	**208** (R = $CH_2CH_2OTBDPS$)	16	**216** 68%	-
5	**209** (R = OBn)	15	**217** 27%	**221** 41% (*E*:*Z* = 85:15)
6	**210** (R = OTBS)	18	**218** 29%	**221** 13% (*E*:*Z* = >95:5)
				
7	**211** (R^1 = Me, R^2 = H)	1	**219** 44%	
8	**212** (R^1 = R^2 = Me)	1	**220** 59%	

[a] The reaction was carried out in the presence of $Ni(cod)_2$ (1 equiv) and DBU (4 equiv) in THF at 0 °C under CO_2 (1 atm). After acidic work-up with 10% HCl, the crude product was treated with CH_2N_2 generated from *N*-methyl-*N*-nitro-*N*′-nitrosoguanidine and aqueous KOH.

を持つ基質 **208** を用い、最適条件下反応を行ったところ、対応するβアミノ酸誘導体 **216** が 68%の収率で得られた（run 4）。一方、置換基としてベンジロキシ基やシロキシ基を持つ基質 **209** および **210** を用いた場合、目的とする二酸化炭素付加体とともに、アルコキシ基が脱離したジエン体 **221**[*7] が得られた（runs 5 and 6）。メチル基を有するアレナミド **211** を用いた場合にも ᵗBu 基の場合と同様の位置選択性で、対応する二酸化炭素固定体 **219** が 44%の収率で得られた（run 7）。三置換アレナミド **212** も本反応に適用可能であり、四置換オレフィン **220** が 59%の収率で得られた（run 8）。

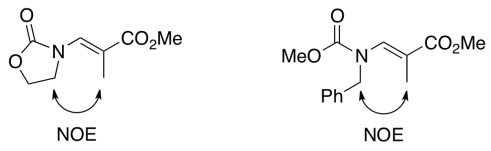
[*1] スキーム 40 に用いた基質のうち **197**[43]は文献記載の方法に従い合成した。基質 **199** はプロパルギルアミン **222** をメチルカルバメート保護した後、塩基性条件下異性化させて合成した（スキーム 38）。

Scheme 38



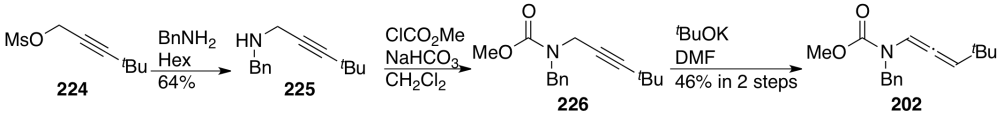
[*2] 化合物 **198**、**200** の立体化学は図 5 に示す位置に NOE 相関が観測されたことから、*E* 体であると決定した。

Figure 5



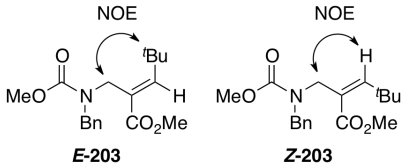
[*3] 基質 **202** は文献記載のメシル酸エステル **224**[44]にベンジルアミンを求核付加させた後、カルバメート保護、塩基性条件下異性化により合成した（スキーム 39）。

Scheme 39

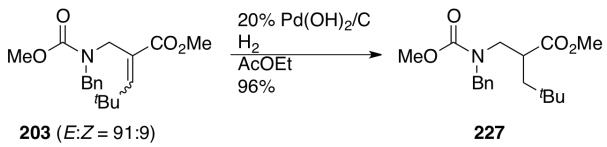


[*4] 化合物 **203** の立体化学は図 6 に示す位置に NOE 相関が観測されたことから主生成物を *E* 体と決定した。また、幾何異性体混合物を還元することで、単一の還元体 **227** を与えることを確認している（スキーム 40）。

Figure 6

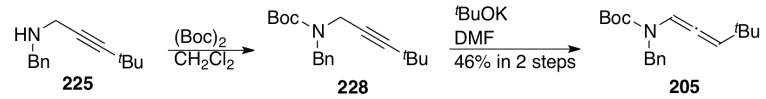


Scheme 40



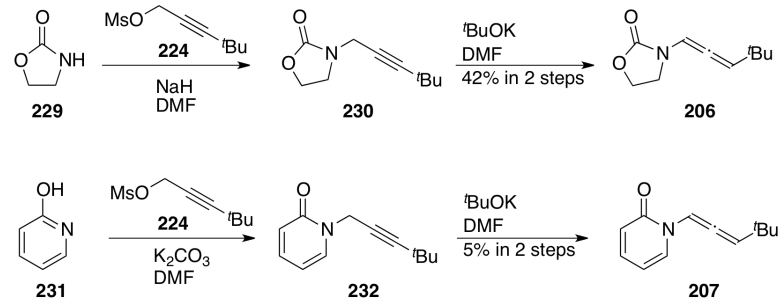
[*5] 表 7 に用いた基質 **211** および **212**[45]は文献記載の方法に従い合成した。その他の基質については以下の方法により合成した。基質 **205** はプロパルギルアミン **225** を Boc 保護した後、塩基性条件下異性化させて合成した（スキーム 41）。

Scheme 41



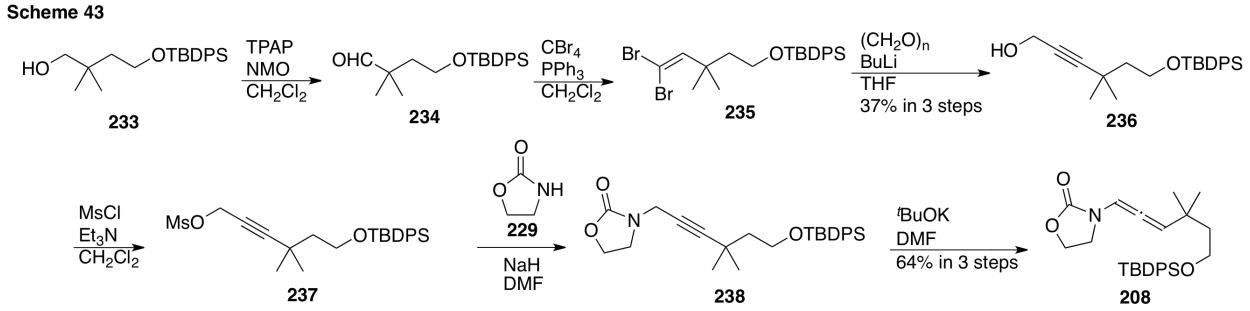
基質 **206** および **207** はメシル酸エステル **224** に対し 2-オキサゾリドン **229** 又は 2-ヒドロキシルピリジン **231** を求核付加させた後、塩基性条件下異性化させて合成した（スキーム 42）。

Scheme 42



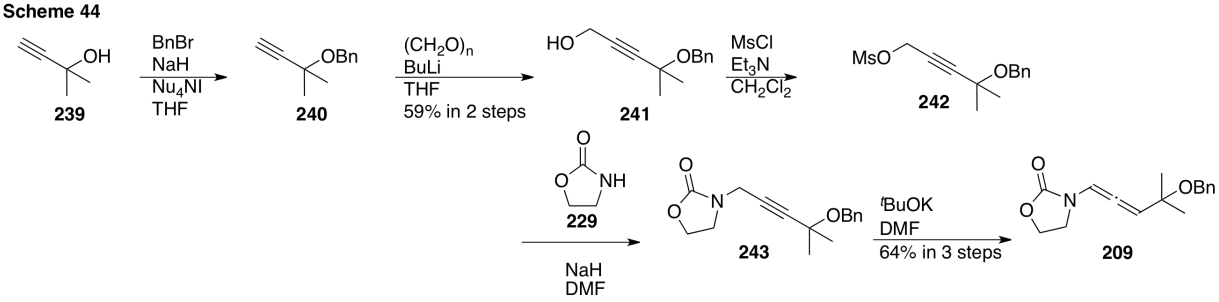
基質 **208** の合成は、まず文献記載のアルコール **233**[46]を酸化し、Corey-Fuchs 法によりリチウムアセチリドへと変換した後、後処理にパラホルムアルデヒドを用いアルコール **236** へと誘導化した。得られたアルコール **236** をメシル化し、2-オキサゾリドン **229** を求核付加させた後、塩基性条件下異性化させて基質 **208** を合成した（スキーム 43）。

Scheme 43



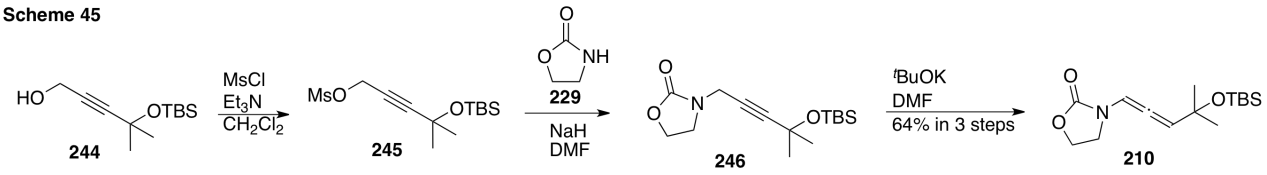
基質 **209** の合成はまず、プロパルギルアルコール **239** をベンジル保護し、BuLi とパラホルムアルデヒドを用いてアルコール **241** を合成した。アルコール **241** をメシル化し、2-オキサゾリドン **229** を求核付加させた後、塩基性条件下異性化させて基質 **209** を合成した（スキーム 44）。

Scheme 44



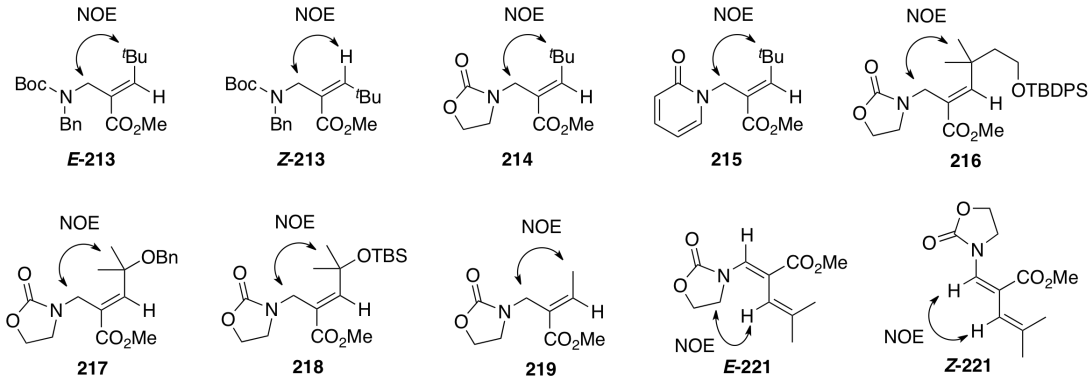
基質 **210** は文献記載のアルコール **244**[47]をメシル化し、2-オキサゾリドン **229** を求核付加させた後、塩基性条件下異性化させて基質 **210** を合成した（スキーム 45）。

Scheme 45



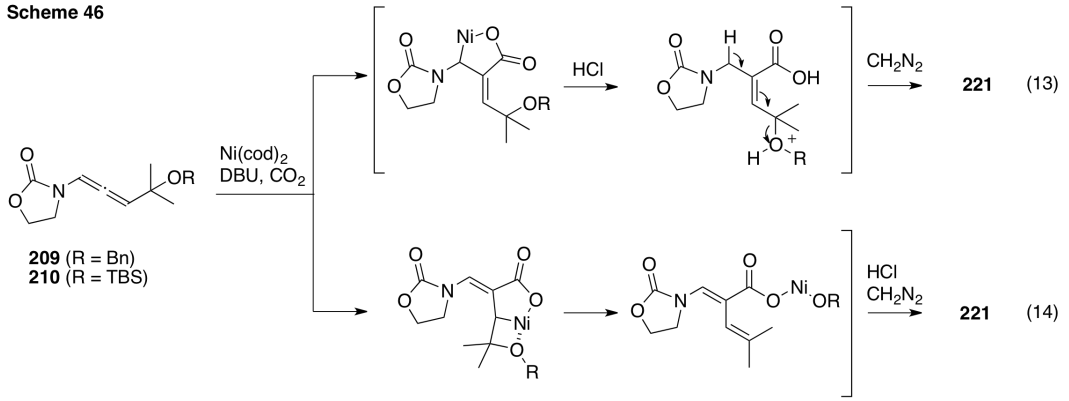
*6 表 7で得られた二酸化炭素付加体の立体化学は図 7に示す位置にそれぞれ NOE相関が観測されたことから決定した。

Figure 7



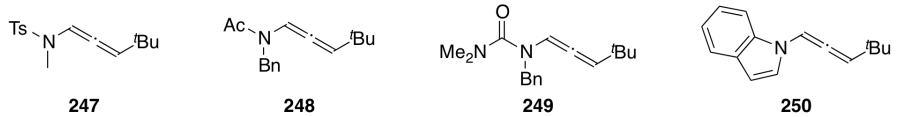
*7 ジエン **221** が得られた理由としては､酸加水分解を行った際に酸素原子が脱離した可能性や(スキーム 46、式 13)、酸素原子が配向性置換基として働き、ニッケラサイクルの生成位置が制御できなかった可能性が考えられる（式 14)。

Scheme 46



この他にも窒素上の保護基が異なる基質 **247-250** を合成し類似の条件下検討を行ったが、いずれも複雑な混合物が得られ、目的物を単離するには至らなかった（図 8)。

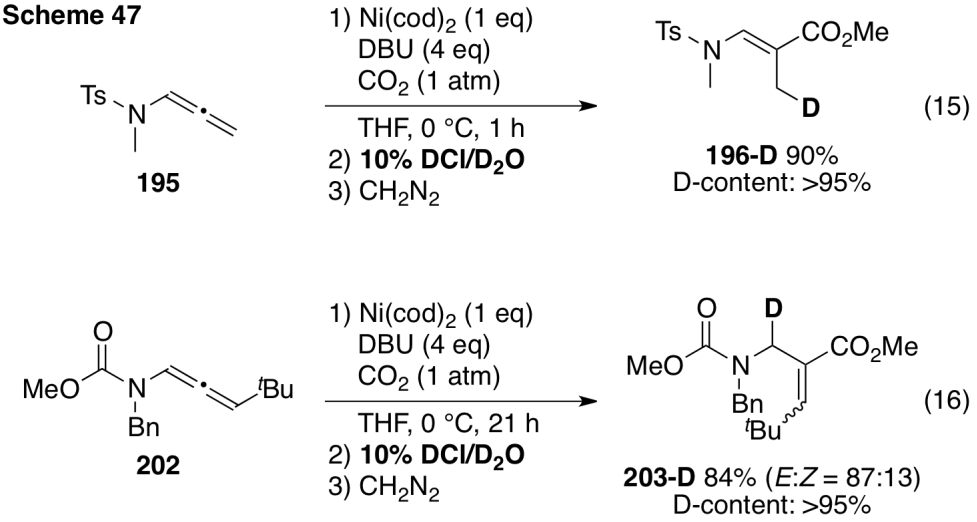
Figure 8



第三節　位置および立体選択性の考察

本反応の反応機構に関する知見を得るべく、重水素化実験を行った（スキーム 47）。トシル基を有する末端型アレナミド **195** と二酸化炭素を最適条件下反応させた後、重塩酸による後処理と引き続くジアゾメタン処理を行った。その結果、メチル基にのみ重水素が導入された目的物 **196-D** が 90%の収率で得られた（式 15）。また、^{t}Bu 基を有するメチルカルバメート由来のアレナミド **202** を用いて同様に二酸化炭素と反応させた後、重塩酸で加水分解を行ったところ、アリル位に重水素が導入された目的物 **203-D** が *E*:*Z* = 87:13 の幾何異性体混合物として、84%の収率で得られた（式 16）。

Scheme 47

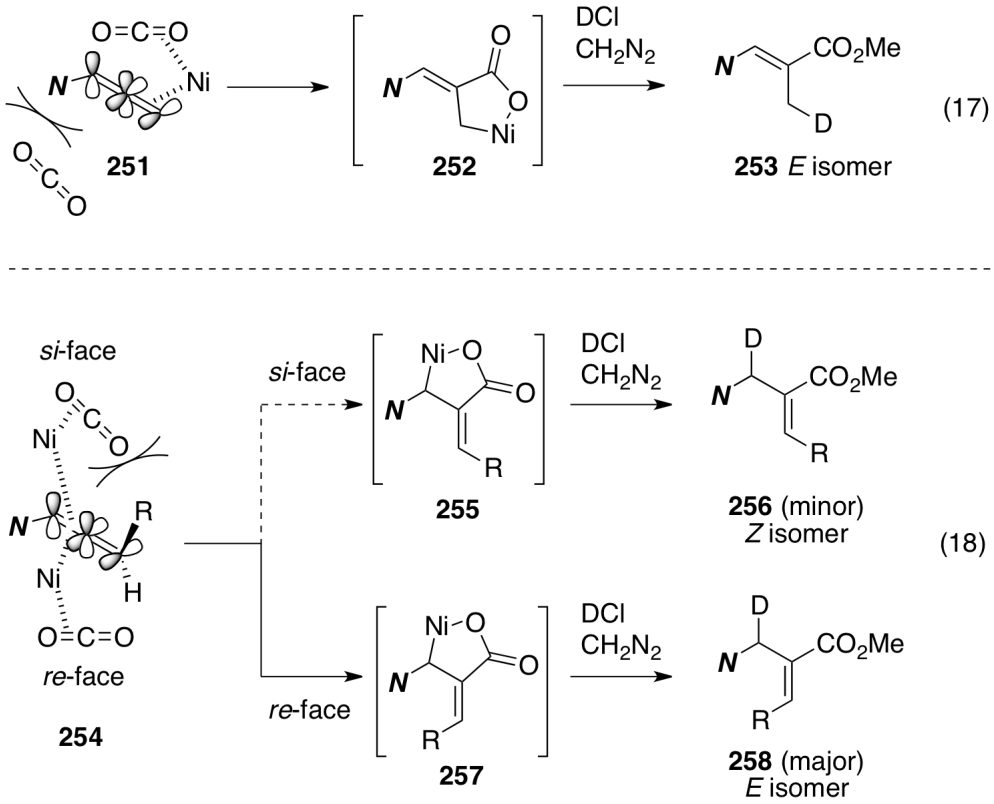


以上の結果をもとに、本反応の位置選択性の発現について考察した（スキーム 48）。まず、末端アレナミド **251** を基質とした場合、立体的により空いている末端の二重結合と二酸化炭素が反応すると考えられる。またこのとき、二酸化炭素は窒素原子との立体障害を避ける方向から反応し、ニッケララクトン中間体 **252** を形成するため、*E* 体のみが選択的に得られると考えられる（式 17）。

次に、置換基をもつアレナミド **254** を用いた場合、まずニッケルへの配位は、かさ高いアルキル基との立体反発を避けるように、より立体障害の小さいアミド基側の二重結合で起きると考えられる。またこのとき、二重結合のどちらの面と配位するかによって 2 種類の配位錯体が考えられる。すなわち、窒素原子が結合した二重結合の *si* 面と二酸化炭素が配位した後に酸化的環化付加が進行すれば、ニッケララクトン **255** が、一方二重結合の *re*

面と反応すればニッケララクトン **257** が生成すると予想される。この際、*si* 面と反応する経路ではアルキル基と二酸化炭素との立体反発が生じ、*re* 面との反応が有利となると考えられる。従ってニッケララクトン中間体 **257** が選択的に形成され、*E* 体が優先的に得られたと考えられる（式 18)。

Scheme 48



結語

第二章をまとめると、著者はアレナミドへの二酸化炭素の位置選択的固定反応の開発を目指し検討を行った。その結果、反応は１気圧の二酸化炭素雰囲気下にて進行し、目的とするβアミノ酸エステルが良好な収率かつ立体選択的に得られることわかった。また、反応の位置選択性はアレン上の置換基効果によって制御されることが明らかになった[48)]。

遷移金属錯体を用いたアレナミドの反応は、ほとんどが末端アレナミドを用いた検討に留まっており、未だに報告数も少ない。本研究により、アレナミドの窒素側二重結合もまた遷移金属錯体に対し十分な反応性をもつことが明らかとなったことから、遷移金属錯体を用いたアレナミドの利用が進展することに期待したい。

総括

本研究は以下のように要約できる。

第一章：シラン存在下 0 価ニッケル触媒によるアルキンと環状ケトンとの分子内環化反応の開発を目指し検討した。その結果、温和な条件下ヒドリンダン骨格やデカリン骨格を始めとする様々な骨格が立体選択的かつ高収率で構築できることを明らかにした。

第二章： 0 価ニッケル錯体によるアレナミドへの二酸化炭素固定反応の開発を行った。その結果、反応は温和な条件下で進行し、目的とする二酸化炭素付加体が良好な収率で位置選択的に得られることを見出した。また、反応の位置選択性はアレン上の置換基によって大きく影響を受けることが明らかとなった。

Experimental Section

All manipulations were performed under an argon atmosphere unless stated otherwise. Solvents were purified under argon using The Ultimate Solvent System (Glass Counter Inc.) (THF, Et_2O, toluene, DMF, and CH_3CN). All other solvents and reagents were purified when necessary by standard procedures. Column chromatography was performed on silica gel 60 N (Kanto, 40–50 μm) with the indicated solvent as eluent. IR spectra were obtained on a JASCO FT/IR 460 Plus spectrometer, and ^{1}H NMR (500 MHz or 400 MHz) and ^{13}C NMR (125 MHz or 100 MHz) spectroscopy were carried out on a Jeol ECA500 or a ECX400P NMR spectrometer. Mass spectra were obtained on a Jeol JMS-700TZ or a Jeol JMS-FAB mate mass spectrometer for LRMS and HRMS.

- Chapter 1 -

General Procedure for Ni(0)-Catalyzed Cyclization Using NHC Ligand

$Ni(cod)_2$ (10 mol% to a substrate), imidazolium salt (10 mol% to the substrate), and ^tBuOK (12 mol% to the substrate) were weighed into a flame-dried flask, and THF (5 mL/mmol) was added to the flask at 0 °C for 10 min. After the mixture was stirred at the same temperature for 10 min, Et_3SiH (5.0 equiv to the substrate) was added to the mixture. After stirring for 10 min, to the mixture was added a solution of the substrate in THF (5 mL/mmol) at the same temperature, and the mixture was stirred at room temperature. The mixture was concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel to give the cyclized product.

Chapter 1, Section 1

<Scheme 14>

(3a*R,6a*S**,*E*)-1-Ethylidene-6a-triethylsiloxyoctahydropentalene (81).** $Ni(cod)_2$ (13.7 mg, 0.0498 mmol) and PPh_3 (27.0 mg, 0.103 mmol) were weighed into a flame-dried flask, and THF (2.5 mL) was added to the flask at 0 °C for 10 min. After the mixture was stirred at the same temperature for 10 min, Et_3SiH (0.4 mL, 2.5 mmol) was added to the mixture. After stirring for 10 min, a solution of **80**[25] (74.3 mg, 0.495 mmol) in THF (2.5 mL) was added to the mixture at the same temperature, and the mixture was stirred at room temperature for 72 h. The mixture was concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **81** (58.5 mg, 44%) as a colorless oil. IR (neat) 1681, 1175, 1093, 1060, 1012 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.53 (q, *J* = 8.0 Hz, 6 H), 0.91 (t, *J* = 8.0 Hz, 9 H), 1.17-1.30 (m, 2 H), 1.54 (m, 1 H), 1.58-1.62 (m, 3 H), 1.67-1.78 (m, 3 H), 1.87-1.96 (m, 2 H), 2.24-2.36 (m, 3 H), 5.48 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.3, 7.1, 14.5, 24.7, 28.0, 29.5, 31.0, 41.2, 52.0, 91.9, 116.3, 148.3; EI-LRMS *m/z* 266 (M^+), 251 [$(M\text{-}Me)^+$], 237 [$(M\text{-}^tBu)^+$]; EI-HRMS calcd for $C_{17}H_{27}O_3Si$ 266.2069, found 266.2065.

(3a*R,6a*S**)-6a-Hydroxyhexahydropentalen-1(2*H*)-one (82)**[16]**.** A solution of **81** (43.9 mg, 0.165 mmol) in CH_2Cl_2 (2 mL) was cooled to -78 °C. Ozone gas was bubbled into the reaction mixture until color of the solution turned to blue. After argon gas was bubbled into the reaction mixture until the blue color disappeared, PPh_3 (50.7 mg, 0.193 mmol) was added to the mixture. The

reaction mixture was slowly allowed to warm to room temperature. The mixture was concentrated in vacuo, and the residue was roughly purified by short column chromatography on silica gel (AcOEt) to give the crude ketone. To a solution of the ketone in CH_3CN (1 mL) was added a 10% solution of HF (46% aqueous solution, commercially available) in CH_3CN (1 mL) at room temperature, and the resulting mixture was stirred 2 h the same temperature. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 1/1) to give **82** (16.9 mg, 73%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45 (m, 1 H), 1.63 (m, 1 H), 1.70 (m, 1 H), 1.75-2.00 (m, 3 H), 2.06-2.21 (m, 2 H), 2.34 (m, 1 H), 2.47-2.56 (m, 2 H), 2.55 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.0, 24.4, 32.0, 35.0, 37.4, 48.2, 88.2, 220.0.

<Table 1>

<run 1>

$Ni(cod)_2$ (13.5 mg, 0.0491 mmol) was weighed into a flame-dried flask, and THF (2.5 mL) and PBu_3 (25 mL, 0.100 mmol) were added to the flask at 0 °C for 10 min. After the mixture was stirred at the same temperature for 10 min, Et_3SiH (0.4 mL, 2.5 mmol) was added to the mixture. After stirring for 10 min, to the mixture was added a solution of **80** (74.8 mg, 0.498 mmol) in THF (2.5 mL) at the same temperature, and the mixture was stirred at the room temperature for 48 h. The mixture was concentrated in vacuo, and the residue was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **81** (95.6 mg, 72%) as a colorless oil.

<run 2>

According to the general procedure, a crude product, which was obtained from **80** (74.7 mg, 0.497 mmol), $Ni(cod)_2$ (13.8 mg, 0.0502 mmol), IMes·HCl (16.8 mg, 0.0493 mmol), ^{t}BuOK (6.4 mg, 0.0570 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **81** (111.2 mg, 84%) as a colorless oil.

<run 3>

According to the general procedure, a crude product, which was obtained from **80** (74.6 mg, 0.497 mmol), $Ni(cod)_2$ (13.7 mg, 0.0498 mmol), SIMes·HBF_4 (20.0 mg, 0.0506 mmol), ^{t}BuOK (6.8 mg,

0.0606 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **81** (104.2 mg, 79%) as a colorless oil.

<run 4>

According to the general procedure, a crude product, which was obtained from **80** (75.4 mg, 0.502 mmol), $Ni(cod)_2$ (13.7 mg, 0.0498 mmol), IPr·HCl (21.8 mg, 0.0513 mmol), ^{t}BuOK (6.9 mg, 0.0615 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **81** (135.1 mg, quant) as a colorless oil.

<run 5>

According to the general procedure, a crude product, which was obtained from **80** (74.8 mg, 0.498 mmol), $Ni(cod)_2$ (13.9 mg, 0.0505 mmol), SIPr·HCl (21.7 mg, 0.0508 mmol), ^{t}BuOK (6.6 mg, 0.0588 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **81** (123.2 mg, 93%) as a colorless oil.

Chapter 1, Section 2

<Table 2>

<run 1>

(3a*R,6a*S**)-1-Methylene-6a-triethylsiloxyoctahydropentalene (96).** According to the general procedure, a crude product, which was obtained from **91** (67.5 mg, 0.496 mmol), $Ni(cod)_2$ (13.5 mg, 0.0491 mmol), IPr·HCl (21.2 mg, 0.0499 mmol), ^{t}BuOK (6.7 mg, 0.0597 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **96** (103.8 mg, 83%) as a colorless oil. IR (neat) 3075, 2359, 1659, 1458, 1098 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.57 (q, *J* = 8.3 Hz, 6 H), 0.93 (t, *J* = 8.3 Hz, 9 H), 1.18 (m, 1 H), 1.30 (m, 1 H), 1.56 (m, 1 H), 1.67-1.73 (m, 3 H), 1.88-2.01 (m, 2 H), 2.27-2.39 (m, 2 H), 2.45 (m, 1 H), 4.88 (d, *J* = 1.7 Hz, 1 H), 5.02 (d, *J* = 1.7 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.3, 7.1, 25.2, 29.8, 32.2, 32.4, 41.8, 51.7, 91.4, 105.6, 157.9; EI-LRMS *m/z* 252 (M^+), 237 [$(M\text{-}Me)^+$], 223 [$(M\text{-}Et)^+$]; EI-HRMS calcd for $C_{15}H_{28}OSi$ 252.1916, found 252.1908.

<run 2>

(3a*R,6a*S**,*E*)-1-(2-*tert*-Buthyldimethylsilyoxyethylidene)-6a-triethylsiloxyoctahydropentalene (97).** According to the general procedure, a crude product, which was obtained from **114** (136.3 mg, 0.486 mmol), $Ni(cod)_2$ (13.5 mg, 0.0491 mmol), IPr·HCl (21.3 mg, 0.0501 mmol), ^{t}BuOK (6.7 mg, 0.0597 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **92** (190.9 mg, 99%) as a colorless oil. IR (neat) 1462, 1254, 1097 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.06 (s, 6 H), 0.55 (q, *J* = 7.9 Hz, 6 H), 0.90 (s, 9 H), 0.92 (t, *J* = 7.9 Hz, 9 H), 1.15-1.32 (m, 2 H), 1.57 (m, 1 H), 1.69-1.71 (m, 3 H), 1.88-1.97 (m, 2 H), 2.23-2.40 (m, 3 H), 4.13-4.24 (m, 2 H), 5.56 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.2, -5.1, 6.3, 7.1, 18.3, 24.7, 25.9, 28.1, 29.7, 31.1, 41.2, 51.4, 61.5, 92.0, 121.7, 148.4; EI-LRMS *m/z* 396 $(M)^+$, 381 $[(M\text{-}Me)^+]$, 367 $[(M\text{-}Et)^+]$, 339 $[(M\text{-}^t Bu)^+]$; EI-HRMS calcd for $C_{22}H_{44}O_2Si_2$ 396.28799 found 396.28752.

<run 3>

(3a*R,6a*S**,*E*)-1-Benzylidene-6a-triethylsiloxyoctahydropentalene (98).** According to the general procedure, a crude product, which was obtained from **93** (108.1 mg, 0.510 mmol), $Ni(cod)_2$ (13.5 mg, 0.0491 mmol), IPr·HCl (21.2 mg, 0.0499 mmol), ^{t}BuOK (6.5 mg, 0.0579 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **98** (162.5 mg, 97%) as a colorless oil. IR (neat) 1457, 1237, 1094 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.59 (q, *J* = 7.9 Hz, 6 H), 0.95 (t, *J* = 7.9 Hz, 9 H), 1.30 (m, 1 H), 1.38 (m, 1 H), 1.66 (m, 1 H), 1.73-1.83 (m, 3 H), 1.97-2.06 (m, 2 H), 2.37 (m, 1 H), 2.65-2.79 (m, 2 H), 6.50 (m, 1 H), 7.20 (m, 1 H), 7.30-7.37 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.4, 7.1, 25.0, 30.4, 30.5, 31.3, 42.1, 50.8, 93.6, 121.8, 126.1, 128.2, 128.4, 138.4, 150.8; EI-LRMS *m/z* 328 $(M)^+$, 313 $[(M\text{-}Me)^+]$, 299 $[(M\text{-}Et)^+]$; EI-HRMS calcd for $C_{21}H_{32}OSi$ 328.22225 found 328.22239.

<run 4>

(3a*R,6a*S**,*E*)-1-(2-Methoxy-2-oxoethylidene)-6a-tryethylsiloxyoctahydropentalene (99).** According to the general procedure, a crude product, which was obtained from **94** (97.6 mg, 0.502 mmol), $Ni(cod)_2$ (14.1 mg, 0.0513 mmol), IPr·HCl (20.9 mg, 0.0492 mmol), ^{t}BuOK (6.4 mg, 0.0570 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 48 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 20/1) to give **99** (41.1 mg, 0.132 mmol) as a colorless oil. IR (neat) 1719, 1661, 1434, 1353, 1099 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.56 (q, *J*

= 8.0 Hz, 6 H), 0.92 (t, *J* = 8.0 Hz, 9 H), 1.28 (m, 1 H), 1.46 (m, 1 H), 1.76-1.93 (m, 4 H), 1.96-2.05 (m, 2 H), 2.36 (m, 1 H), 2.89-2.95 (m, 2 H), 3.71 (s, 3 H), 5.91 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.3, 7.0, 24.6, 30.0, 30.6, 30.9, 42.0, 50.5, 51.0, 93.4, 111.6, 167.8, 172.3; ESI-LRMS *m/z* 333 [$(M+Na)^+$]; ESI-HRMS calcd for $C_{17}H_{30}O_3NaSi$ 333.18564 found 333.18594.

<Run 5>

(3a*R,6a*S**,*E*)-1-(Trimethylsilylmethylidene)-6a-triethylsiloxyoctahydropentalene (100).** According to the general procedure, a crude product, which was obtained from **95** (105.7 mg, 0.507 mmol), $Ni(cod)_2$ (13.7 mg, 0.0498 mmol), IPr·HCl (20.3 mg, 0.0478 mmol), ^{t}BuOK (6.7 mg, 0.0597 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **100** (42.7 mg, 26%) as a colorless oil. IR (neat), 1630, 1458, 1247, 1060 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.09 (s, 9 H), 0.54 (q, *J* = 7.9 Hz, 6 H), 0.92 (t, *J* = 7.9 Hz, 9 H), 1.19 (m, 1 H), 1.33 (m, 1 H), 1.53-1.80 (m, 5 H), 1.85-2.01 (m, 2 H), 2.25 (m, 1 H), 2.35-2.50 (m, 2 H), 5.55 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -0.4, 6.4, 7.1, 24.9, 29.8, 31.4, 31.7, 42.0, 50.6, 91.4, 118.2, 166.4; ESI-LRMS *m/z* 347 [$(M+Na)^+$], 193 [$(M-OTBS)^+$]; ESI-HRMS calcd for $C_{18}H_{36}ONaSi_2$ 347.22024 found 347.21971.

<Scheme 16>

(Eq 1)

(3a*R,6a*S**,*E*)-1-Ethylidene-6a-triethylsiloxy-3a-methyloctahydropentalene (102).** According to the general procedure, a crude product, which was obtained from **101** (80.3 mg, 0.489 mmol), $Ni(cod)_2$ (13.5 mg, 0.0491 mmol), IPr·HCl (21.0 mg, 0.0494 mmol), ^{t}BuOK (6.4 mg, 0.0570 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **102** (138.6 mg, quant) as a colorless oil. IR (neat) 1676, 1458, 1237, 1069 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.51 (q, *J* = 7.1 Hz, 6 H), 0.90 (t, *J* = 7.1 Hz, 9 H), 0.95 (s, 3 H), 1.24-1.40 (m, 3 H), 1.47-1.63 (m, 6 H), 1.72 (m, 1 H), 2.01 (m, 1 H), 2.20-2.34 (m, 2 H), 5.50 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.3, 7.1, 14.4, 19.8, 21.1, 25.9, 34.1, 35.26, 35.30, 52.7, 89.7, 117.7, 147.9; EI-LRMS *m/z* 280 $(M)^+$, 265 $[(M-Me)^+]$, 251 $[(M-Et)^+]$; EI-HRMS calcd for $C_{17}H_{32}OSi$ 280.22225 found 280.22252.

(Eq 2)

(3a*R,6a*R**,*E*)-3a-*tert*-Butyldimethylsilyloxymethyl-1-ethylidene-6a-triethylsilyloxyoctahydro**

pentalene (104). According to the general procedure, a crude product, which was obtained from **103** (108.1 mg, 0.510 mmol), $Ni(cod)_2$ (5.4 mg, 0.0196 mmol), IPr·HCl (8.7 mg, 0.0205 mmol), ^{t}BuOK (2.8 mg, 0.0250 mmol), and Et_3SiH (0.17 mL, 1.06 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **104** (82.5 mg, 96%) as a colorless oil. IR (neat) 1676, 1462, 1254, 1105, 1089 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.03 (s, 6 H), 0.50 (q, *J* = 7.8 Hz, 6 H), 0.89 (s, 9 H), 0.90 (t, *J* = 7.8 Hz, 9 H), 1.19 (m, 1 H), 1.55-1.67 (m, 5 H), 1.75-1.85 (m, 2 H), 2.01 (m, 1 H), 2.24-2.35 (m, 2 H), 3.47 (d, *J* = 9.5 Hz, 1 H), 3.61 (d, *J* = 9.5 Hz, 1 H), 5.49 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.5, -5.4, 6.3, 7.1, 14.4, 18.3, 20.7, 26.0, 26.1, 30.9, 31.3, 36.9, 52.6, 66.9, 90.0, 117.3, 148.2; EI-LRMS *m/z* 410 (M^+), 395 [$(M\text{-}Me)^+$], 381 [$(M\text{-}Et)^+$], 353 [$(M\text{-}t\text{-}Bu)^+$], 265 [$(M\text{-}CH_2OTBS)^+$]; EI-HRMS calcd for $C_{23}H_{46}O_2Si_2$ 410.30363 found 410.30397.

<Scheme 17>

Synthesis of **82** from **96**

Similar to synthesis of **82** from **81**, a crude product, which was obtained from ozonization of **96** (34.2 mg, 0.135 mmol) in CH_2Cl_2 (2 mL) followed by reduction using PPh_3 (40.4 mg, 0.154 mmol), was treated with a 5% solution of HF in CH_3CN (4 mL). After usual work up, a crude product was purified by column chromatography on silica gel (hexane/AcOEt = 1/1) to give **82** (7.6 mg, 2 steps 40%) as a colorless oil.

Synthesis of **82** from **97**

Similar to synthesis of **82** from **81**, a crude product, which was obtained from ozonization of **97** (59.0 mg, 0.149 mmol) in CH_2Cl_2 (2 mL) followed by reduction using PPh_3 (60.1 mg, 0.229 mmol), was treated with a 5% solution of HF in CH_3CN (4 mL). After usual work up, a crude product was purified by column chromatography on silica gel (hexane/AcOEt = 3/2) to give **82** (20.2 mg, 2 steps 97%) as a colorless oil.

Synthesis of **82** from **98**

Similar to synthesis of **82** from **81**, a crude product, which was obtained from ozonization of **98** (57.4 mg, 0.175 mmol) in CH_2Cl_2 (4 mL) followed by reduction using PPh_3 (53.2 mg, 0.203 mmol), was treated with a 5% solution of HF in CH_3CN (4 mL). After usual work up, a crude product purified by column chromatography on silica gel (hexane/AcOEt = 1/1) to give **82** (19.8 mg, 2 steps

81%) as a colorless oil.

Synthesis of **82** from **99**

Similar to synthesis of **82** from **81**, a crude product, which was obtained from ozonization of **99** (26.7 mg, 0.0860 mmol) in CH_2Cl_2 (8 mL) followed by reduction using PPh_3 (33.5 mg, 0.128 mmol), was treated with a 5% solution of HF in CH_3CN (4 mL). After usual work up, a crude product was purified by column chromatography on silica gel (hexane/AcOEt = 1/1) to give **82** (0.8 mg, 2 steps 7%) as a colorless oil.

<Scheme 18>

2-(4,4-Dibromobut-3-enyl)cyclopentanone. To a solution of PPh_3 (152 g, 597 mmol) in CH_2Cl_2 (120 mL) was added a solution of CBr_4 (94.8 g, 286 mmol) in CH_2Cl_2 (120 mL) over a period of 15 min at 0 °C, and the mixture was stirred at the same temperature for 30 min. To the mixture was added a solution of **105**[18] (26.4 g, 143 mmol) in CH_2Cl_2 (60 mL) at 0 °C, and the mixture was stirred at the same temperature for 1.5 h. To the mixture was added hexane at room temperature. The mixture was filtered through Celite® pad, and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) to give dibromoolefin (27.2 g, 64%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.39 (m, 1 H), 1.52 (m, 1 H), 1.79 (m, 1 H), 1.90 (m, 1 H), 1.99-2.21 (m, 5 H), 2.23-2.36 (m, 2 H), 6.37 (m, 1 H).

6-(4,4-Dibromobut-3-enyl)-1,4-dioxaspiro[4.4]nonane. To a suspension of ethylene glycol (54 mL, 968 mmol) in benzene (180 mL) was added the above dibromoolefin (27.2 g, 91.8 mmol) and PPTS (2.25 g, 8.95 mmol) at room temperature, and the mixture was refluxed with a Dean-Stark system for 5 h. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 20/1) to give acetal (29.0 g, 93%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28-1.40 (m, 2 H), 1.57-1.80 (m, 5 H), 1.86-1.95 (m, 2 H), 2.03-2.18 (m, 2 H), 3.84-3.96 (m, 4 H), 6.39 (m, 1 H).

5-(1,4-Dioxaspiro[4.4]nonan-6-yl)pent-2-yn-1-ol (106). To a solution of the above acetal (1.71g, 5.04 mmol) in THF (15 mL) was added a solution of BuLi in hexane (1.61 M, 7 mL, 11.3 mmol) at

-78 °C, and the mixture was stirred at the same temperature for 1 h. After additional stirring for 1 h at room temperature, the reaction mixture was recooled to -78 °C. To the mixture was added paraformaldehyde (1.48 g, 49.3 mmol), and the reaction mixture was slowly warmed to room temperature overnight. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 4/1) to give **106** (746 mg, 70%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.32 (m, 1 H), 1.45 (m, 1 H), 1.52-1.81 (m, 6 H), 1.92 (m, 1 H), 2.03 (m, 1 H), 2.19 (m, 1 H), 2.31 (m, 1 H), 3.85-3.96 (m, 4 H), 4.23-4.27 (m, 2 H).

2-(5-Hydroxypent-3-ynyl)cyclopentanone. To a solution of **106** (679 mg, 3.23 mmol) in acetone (65 mL) was added *p*-TsOH·H_2O (1.26 g, 6.62 mmol) at room temperature, and the mixture was stirred at the same temperature for 12.5 h. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 1/1) to ketone (521 mg, 95%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.43-1.62 (m, 3 H), 1.80 (m, 1 H), 1.96-2.43 (m, 8 H), 4.21-4.26 (m, 2 H).

2-[5-(*tert*-Butyldimethylsilyloxy)pent-3-ynyl]cyclopentanone (92). To a solution of the above ketone (476 mg, 2.86 mmol) and imidazole (598 mg, 8.78 mmol) in DMF (2.8 mL) was added TBSCl (655 mg, 4.34 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 20/1) to give **92** (675 mg, 84%) as a colorless oil. IR (neat) 1739, 1463, 1078 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.10 (s, 6 H), 0.90 (s, 9 H), 1.49-1.55 (m, 2 H), 1.73-1.83 (m, 1 H), 1.95-2.05 (m, 2 H), 2.07-2.16 (m, 1 H), 2.18-2.40 (m, 5 H), 4.26-4.28 (m, 2 H); ^{13}C NMR (125 MHz, CDCl3) δ -5.1, 17.1, 18.3, 20.7, 25.8, 28.5, 29.5, 38.0, 48.1, 51.9, 79.4, 84.3, 220.8; EI-LRMS *m/z* 223 [(M-^{t}Bu)$^+$], 181, 167, 143; EI-HRMS calcd for $C_{12}H_{19}O_2Si$ 223.11543 found 223.11493.

<Scheme 19>

3-(6-Methyl-1,4-dioxaspiro[4.4]nonan-6-yl)propanal (108). To a solution of **107**[19] (685 mg, 3.42

mmol) in CH_2Cl_2 (17 mL) was added PCC (1.21 g, 5.14 mmol) at 0 °C, and the mixture was stirred at room temperature for 4 h. To the mixture was added hexane at room temperature. The reaction mixture was filtered through Florisil® column (hexane), and the filtrate was concentrated. The residue was purified by short column chromatography on silica gel (AcOEt) to give **108** (390 mg) as a yellow oil. IR (neat) 1725, 1465, 1417, 1313, 950 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.96 (s, 3 H), 1.49 (m, 1 H), 1.56-1.88 (m, 7 H), 2.35-2.52 (m, 2 H), 3.87-3.93 (m, 4 H), 9.77 (t, *J* = 1.9, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.8, 20.2, 27.2, 33.3, 35.7, 40.0, 45.1, 64.4, 64.7, 119.3, 203.3; EI-LRMS *m/z* 198 $(M)^+$, 169 $[(M\text{-}CHO)^+]$, 155 $[(M\text{-}CH_2CHO)^+]$, 141 $[(M\text{-}CH_2CH_2CHO)^+]$; EI-HRMS calcd for $C_{11}H_{18}O_3$ 198.1255 found 198.1250.

6-(4,4-Dibromobut-3-enyl)-6-methyl-1,4-dioxaspiro[4.4]nonane. To a solution of PPh_3 (1.06 g, 4.04 mmol) in CH_2Cl_2 (4 mL) was added a solution of CBr_4 (993 mg, 2.99 mmol) in CH_2Cl_2 (4 mL) at 0 °C, and the mixture was stirred at the same temperature for 30 min. To the mixture was added a solution of **108** (26.4 g, 143 mmol) in CH_2Cl_2 (2 mL) at 0 °C, and the mixture was stirred at same temperature for 10 min. To the mixture was added hexane at room temperature. The mixture was filtered through Celite® pad, and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) and purified by flash column chromatography on silica gel (toluene) to dibromoolefin (436 mg, 2 steps 36%) as a yellow oil. IR (neat) 1627, 1463, 1376, 1313, 948 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.98 (s, 3 H), 1.43-1.54 (m, 3 H), 1.59-1.62 (m, 3 H), 1.75-1.90 (m, 2 H), 1.99-2.17 (m, 2 H), 3.87-3.93 (m, 4 H), 6.39 (t, *J* = 7.3, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.9, 20.0, 28.9, 32.9, 33.3, 35.3, 45.6, 64.5, 64.8, 88.2, 119.4, 139.5; EI-LRMS *m/z* 354 $(M)^+$, 273 $[(M\text{-}Br)^+]$; EI-HRMS calcd for $C_{12}H_{18}Br_2O_2$ 351.96731 found 351.96710.

6-Methyl-6-(pent-3-ynyl)-1,4-dioxaspiro[4.4]nonane (109). To a solution of the above dibromoolefin (436 mg, 1.23 mmol) in THF (6 mL) was added a solution of BuLi in hexane (1.61 M, 1.6 mL, 2.58 mmol) at -78 °C, and the mixture was stirred at the same temperature for 30 min. To the mixture was added MeI (0.4 mL, 6.43 mmol) at -78 °C, the mixture was stirred at the same temperature for 1.5 h, and was slowly warmed to room temperature overnight. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by short column chromatography on silica gel (AcOEt) to give **109** (260 mg) as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$) δ 0.94 (s, 3 H), 1.49 (m, 1 H), 1.58-1.68 (m, 5 H),

1.75-1.87 (m, 5 H), 2.02-2.20 (m, 2 H), 3.86-3.95 (m, 4 H).

2-Methyl-2-(pent-3-ynyl)cyclopentanone (101). To a solution of **109** (260 mg) in acetone (12 mL) was added $TsOH \cdot H_2O$ (487 mg, 2.56 mmol) at room temperature, and the mixture was stirred at the same temperature for 12.5 h. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 20/1) to give **101** (168.7 mg, 2 steps 84%) as a yellow oil. IR (neat) 1736, 1457, 1409, 1374, 948 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.99 (s, 3 H), 1.65 (m, 1 H), 1.70-1.77 (m, 4 H), 1.80-1.97 (m, 3 H), 2.02-2.33 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.4, 14.2, 18.6, 21.5, 35.5, 35.8, 37.5, 47.9, 75.9, 78.8, 222.8; EI-LRMS *m/z* 164 $(M)^+$, 149 $[(M\text{-}Me)^+]$, 98 $[(M\text{-}CH_2CCMe)^+]$; EI-HRMS calcd for $C_{11}H_{16}O$ 164.1196 found 164.1199.

<Scheme 20>

6-(*tert*-Butyldimethylsilyloxy)methyl-1,4-dioxaspiro[4.4]nonane-6-carbaldehyde (111). To a solution of **110**[20] (172 mg, 0.747 mmol) and imidazole (157 mg, 2.31 mmol) in DMF (0.75 mL) were added TBSCl (168 mg, 1.11 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 min. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by short column chromatography on silica gel (AcOEt) to give a crude TBS ether (286 mg) as a colorless oil. To the TBS ether (286 mg) in toluene (3.7 mL) was added a solution of DIBAL-H in toluene (0.99 M, 1.6 mL, 1.58 mmol) at -78 °C, and the mixture was stirred at the same temperature for 30 min. After the mixture was diluted with Et_2O, to the mixture was added saturated potassium sodium tartrate aqueous solution at -78 °C, and the resulting mixture was stirred at room temperature overnight. The aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 4/1) to give **111** (133 mg, 2 steps 59%) as a colorless oil. IR (neat) 1731, 1472, 1254, 1092 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ -0.029 (s, 3 H), 0.032 (s, 3 H), 0.84 (s, 9 H), 1.61-1.81 (m, 5 H), 2.27 (m, 1 H), 3.63 (d, J = 10.2 Hz, 1 H), 3.80-3.94 (m, 4 H), 4.12 (d, J = 10.2 Hz, 1 H), 9.62 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.62, -5.58, 18.2, 20.0, 25.8, 27.3, 36.8, 62.6, 63.1, 64.5, 65.1, 118.7, 203.3.

(*E*)-Ethyl 3-[6-(*tert*-butyldimethylsilyloxy)methyl-1,4-dioxaspiro[4.4]nonan-6-yl]acrylate. To a suspension of NaH (60% dispersion in mineral oil, 36.4 mg, 0.910 mmol) in THF (1.5 mL) was added a solution of diethylphosphonoacetic acid ethyl ester (0.2 mL, 1.01 mmol) in THF (1 mL) at 0 °C, and the mixture was stirred at the same temperature for 10 min. To the mixture was added a solution of **111** (133 mg, 0.444 mmol) in THF (2 mL) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by column chromatography on silica gel (hexane/AcOEt = 10/1) to give acrylate (175 mg) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.01 (s, 3 H), 0.02 (s, 3 H), 0.86 (s, 9 H), 1.27 (dd, *J* = 7.0, 7.0 Hz, 3 H), 1.65-1.73 (m, 2 H), 1.79-1.87 (m, 3 H), 1.96 (m, 1 H), 3.59 (d, *J* = 10.0 Hz, 1 H), 3.66 (d, *J* = 10.0 Hz, 1 H), 3.85-3.95 (m, 4 H), 4.18 (dq, *J* = 2.9, 7.0 Hz, 1 H), 4.19 (dq, *J* = 2.9, 7.0 Hz, 1 H), 5.87 (d, *J* = 16.6 Hz, 1 H), 7.05 (d, *J* = 16.6 Hz, 1 H).

Ethyl 3-[6-(*tert*-butyldimethylsilyloxy)methyl-1,4-dioxaspiro[4.4]nonan-6-yl]propanoate. To a solution of the above acrylate (175 mg) in AcOEt (4.4 mL) was added Pd-C (10% Pd, 3.5 mg, 0.74 mmol) at room temperature, and the mixture was stirred at same temperature under H_2 atmosphere for 6 h. The mixture was roughly purified by short column chromatography on silica gel (AcOEt) to give crude ester (162 mg) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.04 (s, 6 H), 0.89 (s, 9 H), 1.24 (t, *J* = 7.2 Hz, 3 H), 1.47 (m, 1 H), 1.56-1.64 (m, 2 H), 1.70-1.92 (m, 5 H), 2.29 (m, 1 H), 2.42 (m, 1 H), 3.43 (d, *J* = 9.7 Hz, 1 H), 3.61 (d, *J* = 9.7 Hz, 1 H), 3.81-3.95 (m, 4 H), 4.11 (q, *J* = 7.2 Hz, 2 H), 5.87 (d, *J* = 16.6 Hz, 1 H), 7.05 (d, *J* = 16.6 Hz, 1 H).

3-[6-(*tert*-Butyldimethylsilyloxy)methyl-1,4-dioxaspiro[4.4]nonan-6-yl]propanal (112). To a solution of the above crude ester (162 mg) in toluene (2.2 mL) a solution of DIBAL-H in toluene (0.99 M, 0.45 mL, 0.446 mmol) at -78 °C, and the mixture was stirred at the same temperature for 30 min. After the mixture was diluted with Et_2O, saturated potassium sodium tartrate aqueous solution was added to the mixture at -78 °C, and the resulting mixture was stirred at room temperature overnight. The aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by short column chromatography on silica gel (hexane/AcOEt = 10/1) to give crude **112** (137 mg) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.036 (s, 3 H), 0.041 (s, 3 H), 0.88 (s, 9 H), 1.47 (m, 1 H), 1.57-1.65 (m, 2 H), 1.73-1.92 (m, 5 H), 2.52 (m, 1 H), 2.54 (m, 1 H), 3.44 (d, *J* = 9.7 Hz, 1 H), 3.62 (d, *J* = 9.7 Hz, 1 H), 3.81-3.93 (m, 4 H), 9.74 (m, 1 H).

6-(4,4-Dibromobut-3-enyl)-6-(*tert*-butyldimethylsiloxy)methyl-1,4-dioxaspiro[4.4]nonane. To a solution of PPh_3 (445 mg, 1.70 mmol) and CBr_4 (278 mg, 0.837 mmol) in CH_2Cl_2 (3.1 mL) was Et_3N (0.46 mL, 3.30 mmol) at room temperature, and the mixture was stirred at the same temperature for 15 min. To the mixture was added a solution of **112** (137 mg) in CH_2Cl_2 (1 mL) at -78 °C, and the mixture was stirred at room temperature for 4 h. The mixture was filtered through silica gel pad, and the filtrate was concentrated. The residue was roughly purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1) to give crude dibromoolefin (191 mg) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.05 (s, 6 H), 0.89 (s, 9 H), 1.43-1.87 (m, 8 H), 2.03-2.21 (m, 2 H), 3.43 (d, *J* = 10.0 Hz, 1 H), 3.65 (d, *J* = 10.0 Hz, 1 H), 3.82-3.95 (m, 4 H), 6.38 (m, 1 H).

6-(*tert*-Butyldimethylsiloxy)methyl-6-(pent-3-ynyl)-1,4-dioxaspiro[4.4]nonane (113). Similar to synthesis of **136** from 6-(4,4-dibromobut-3-enyl)-6-methyl-1,4-dioxaspiro[4.4]nonane, a crude product, which was obtained from above dibromoolefin (191 mg), BuLi in hexane solution (1.55 M, 0.55 mL, 0.835 mmol), MeI (0.12 mL, 1.93 mmol) in THF (4 mL) at -78 °C to 0 °C for 2 h, was roughly purified by flash column chromatography on silica gel (AcOEt) to give crude **113** (123 mg) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.04 (s, 6 H), 0.89 (s, 9 H), 1.48 (m, 1 H), 1.56-1.86 (m, 9 H), 2.04-2.25 (m, 2 H), 3.41 (d, *J* = 10.3 Hz, 1 H), 3.59 (d, *J* = 10.3 Hz, 1 H), 3.80-3.95 (m, 4 H).

2-(*tert*-Butyldimethylsilyloxy)methyl-2-(pent-3-ynyl)cyclopentanone (103). Similar to synthesis of **101** from **109**, a crude product, which was obtained from **113** (123 mg), $TsOH·H_2O$ (137 mg, 0.721 mmol) in acetone (8 mL) at room temperature for 30 min, was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) to give **103** (75.9 mg, 6 steps 58%) as a colorless oil. IR (neat) 1739, 1471, 1256, 1097, 839, 778 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.01 (s, 3 H), 0.01 (s, 3 H), 0.85 (s, 9 H), 1.53-1.68 (m, 2 H), 1.74 (t, *J* = 2.6 Hz, 3 H), 1.79-1.99 (m, 3 H), 2.01-2.27 (m, 5 H), 3.40 (d, *J* = 9.2 Hz, 1 H), 3.63 (d, *J* = 9.2 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.72, -5.68, 3.4, 14.2, 18.2, 19.3, 25.8, 30.5, 32.8, 39.3, 53.6, 67.1, 222.2; EI-LRMS *m/z* 279 [$(M\text{-}Me)^+$], 237 [$(M\text{-}t\text{-}Bu)^+$]; EI-HRMS calcd for $C_{13}H_{21}O_2Si$ 237.13108 found 237.13143.

Chapter 1, Section 3

<Table 3>

<run 1>

(3a*S,7a*S**,*E*)-4-Ethylidene-3a-triethylsiloxyoctahydro-1*H*-indene (118).** According to the general procedure, a crude product, which was obtained from **114** (80.4 mg, 0.490 mmol), $Ni(cod)_2$ (13.7 mg, 0.0498 mmol), IPr·HCl (21.3 mg, 0.0501 mmol), ^{t}BuOK (6.9 mg, 0.0615 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **118** (143.3 mg, quant) as a colorless oil. IR (neat) 1665, 1457, 1237, 1114, 1075, 894 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.55 (q, *J* = 8.0 Hz, 6 H), 0.92 (t, *J* = 8.0 Hz, 9 H), 1.24-1.37 (m, 2 H), 1.38-1.57 (m, 4 H), 1.61 (m, *J* = 6.7 Hz, 3 H), 1.63-1.80 (m, 3 H), 1.94 (m, 1 H), 2.05 (m, 1 H), 2.13 (m, 1 H), 2.26 (m, 1 H), 5.46 (q, *J* = 6.7 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.4, 7.2, 12.9, 20.1, 23.7, 25.0, 26.6, 27.2, 36.9, 48.6, 84.0, 116.1, 140.3; EI-LRMS *m/z* 280 (M^+), 265, 251, 224, 209, 147, 115; EI-HRMS calcd for $C_{17}H_{32}OSi$ 280.22225, found 280.22229.

<run 2>

(3a*R,7a*S**,*E*)-1-Ethylidene-7a-methoxyoctahydro-1*H*-indene (119).** According to the general procedure, a crude product, which was obtained from **115** (81.8 mg, 0.498 mmol), $Ni(cod)_2$ (13.7 mg, 0.0498 mmol), IPr·HCl (21.1 mg, 0.0496 mmol), ^{t}BuOK (6.6 mg, 0.0588 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O/Et_3N = 500/1/5) to give **119** (140.6 mg, quant) as a colorless oil. IR (neat) 1679, 1448, 1260, 1237, 1078, 1009 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.51 (q, *J* = 7.8 Hz, 6 H), 0.90 (t, *J* = 7.8 Hz, 9 H), 1.10-1.30 (m, 3 H), 1.43-1.62 (m, 8 H), 1.83 (m, 1 H), 1.93-2.01 (m, 2 H), 2.23-2.28 (m, 2 H), 5.38 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.4, 7.1, 14.3, 23.7, 24.5, 25.7, 26.6, 28.5, 34.4, 48.5, 82.1, 116.9, 144.8; EI-LRMS *m/z* 280 (M^+), 251 [$(M\text{-}Et)^+$]; EI-HRMS calcd for $C_{17}H_{32}OSi$ 280.22225, found 280.22235.

<run 3>

(4a*R,8a*S**,*E*)-1-Ethylidene-8a-triethylsiloxydecahydronaphthalene (120).** According to the general procedure, a crude product, which was obtained from **116** (89.0 mg, 0.499 mmol), $Ni(cod)_2$ (13.9 mg, 0.0505 mmol), IPr·HCl (21.7 mg, 0.0511 mmol), ^{t}BuOK (6.9 mg, 0.0615 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column

chromatography on silica gel (hexane/Et_2O = 500/1) to give **120** (147.4 mg, quant) as a colorless oil. IR (neat) 1663, 1457, 1237, 1071 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.54 (q, *J* = 8.0 Hz, 6 H), 0.92 (t, *J* = 8.0 Hz, 9 H), 1.20-1.50 (m, 8 H), 1.57-1.68 (m, 6 H), 2.07-2.23 (m, 3 H), 2.35 (m, 1 H), 5.39 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.8, 7.3, 12.9, 21.8, 24.6, 24.9, 26.3, 27.9, 28.5, 37.7, 46.2, 77.3, 117.6, 139.6; EI-LRMS *m/z* 294 (M^+), 279, 265, 251, 237, 223, 209, 161, 103; EI-HRMS calcd for $C_{18}H_{34}OSi$ 294.2383, found 294.2377.

<run 4>

(4a*S,8a*R**,*E*)-1-Ethylidene-4a-ethoxycarbonyl-8a-triethylsiloxydecahydronaphthalene (121).** According to the general procedure, a crude product, which was obtained from **117** (131.0 mg, 0.523 mmol), $Ni(cod)_2$ (13.8 mg, 0.0502 mmol), IPr·HCl (21.2 mg, 0.0502 mmol), ^{t}BuOK (6.8 mg, 0.0606 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/AcOEt = 20/1) to give **121** (145.1 mg, 76%) as a colorless oil. IR (neat) 1737, 1723, 1458, 1239, 1181, 1131, 1074 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.55 (dq, *J* = 3.2, 7.9 Hz, 3 H), 0.55 (dq, *J* = 3.2, 7.9 Hz, 3 H), 0.91 (t, *J* = 7.9 Hz, 9 H), 1.23-1.26 (m, 3 H), 1.35-1.68 (m, 13 H), 2.02 (m, 1 H), 2.10-2.50 (m, 4 H), 4.05-4.15 (m, 2 H), 5.53 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) d 6.8, 7.1, 13.2, 14.2, 21.3, 21.9, 23.9, 24.3, 30.1, 31.5, 32.4, 53.4, 59.5, 78.3, 118.5, 139.6; EI-LRMS *m/z* 366 (M^+), 337 [$(M-Et)^+$]; EI-HRMS calcd for $C_{21}H_{38}O_3Si$ 366.25902, found 366.25902.

<Table 4>

<run 1>

(4a*S,10a*S**,*E*)-4-Ethylidene-4a-triethylsiloxy-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (126).** According to the general procedure, a crude product, which was obtained from **122** (109.6 mg, 0.484 mmol), $Ni(cod)_2$ (13.6 mg, 0.0494 mmol), IPr·HCl (21.6 mg, 0.0508 mmol), ^{t}BuOK (6.6 mg, 0.0588 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane) to give **126** (121.3 mg, 73%) as a colorless oil. IR (neat) 1920, 1603, 1578, 1455, 1235, 1087 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.12-0.33 (m, 6 H), 0.71 (t, *J* = 8.0 Hz, 9 H), 1.57-1.75 (m, 3 H), 1.60 (d, *J* = 6.9 Hz, 3 H), 1.90-2.08 (m, 3 H), 2.41 (s, 3 H), 3.65 (dd, *J* = 3.4, 7.4 Hz, 1 H), 3.78 (dt, *J* = 13.7, 2.3 Hz, 1 H), 4.18 (d, *J* = 13.2 Hz, 1 H), 5.55 (ddq, *J* = 2.3, 2.3, 6.9 Hz, 1 H), 7.32 (d, *J* = 8.3 Hz, 2 H), 7.74 (d, *J* = 8.3 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.8, 6.8, 14.6, 21.5, 24.2, 32.8, 39.4, 51.0, 73.0, 90.2, 119.0, 127.9, 129.5,

133.4, 140.3, 143.4; EI-LRMS *m/z* 342 (M^+), 313, 273, 285, 273, 259, 211; EI-HRMS calcd for $C_{22}H_{34}OSi$ 342.23789, found 342.23727.

<run 2>

(4a*S,10a*R**,*E*)-4-Ethylidene-10a-ethoxycarbonyl-4a-triethylsiloxy- 1,2,3,4,4a,9,10,10a-octa hydrophenanthrene (127).** According to the general procedure, a crude product, which was obtained from **123** (149.0 mg, 0.499 mmol), $Ni(cod)_2$ (13.5 mg, 0.0491 mmol), IPr·HCl (21.6 mg, 0.0508 mmol), ^{t}BuOK (6.3 mg, 0.0561 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 3 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 20/1) to give **127** (163.9 mg, 79%) as a colorless oil. IR (neat) 1725, 1602, 1455, 1251, 1096 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.18 (dq, *J* = 15.8, 7.7 Hz, 3 H), 0.25 (dq, *J* = 15.8, 7.7 Hz, 3 H), 0.76 (dd, *J* = 7.7, 7.7 Hz, 9 H), 1.21-1.24 (m, 3 H), 1.33-1.45 (m, 2 H), 1.58-1.68 (m, 2 H), 1.73-1.97 (m, 5 H), 2.50-2.64 (m, 2 H), 2.81-2.96 (m, 2 H), 3.98-4.15 (m, 2 H), 5.82 (m, 1 H), 7.05-7.13 (m, 2 H), 7.12 (m, 1 H), 7.31 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.1, 7.1, 12.9, 14.1, 22.7, 25.4, 25.5, 26.0, 29.2, 52.6, 59.7, 79.5, 117.6, 126.0, 127.7, 129.0, 129.4, 135.9, 138.1, 139.6, 174.7; EI-LRMS *m/z* 414 (M^+), 385 [$(M-Et)^+$]; EI-HRMS calcd for $C_{25}H_{38}O_3Si$ 414.25902, found 414.25902.

<run 3>

(4a*S,8a*R**,*E*)-5-Ethylidene-4a-triethylsiloxy-2,2-dimethylhexahydro-4*H*-benzo[*d*][1,3]dioxine (128).** According to the general procedure, a crude product, which was obtained from **124** (103.0 mg, 0.490 mmol), $Ni(cod)_2$ (13.8 mg, 0.0502 mmol), IPr·HCl (21.6 mg, 0.0508 mmol), ^{t}BuOK (7.0 mg, 0.0624 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/Et_2O = 500/1) to give **128** (158.3 mg, 99%) as a colorless oil. IR (neat) 1459, 1376, 1098, 1083 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.52 (q, *J* = 7.8 Hz, 6 H), 0.91 (t, *J* = 7.8 Hz, 9 H), 1.33 (s, 3 H), 1.45 (s, 3 H), 1.47-1.60 (m, 3 H), 1.67 (d, *J* = 6.7 Hz, 3 H), 1.93-2.08 (m, 2 H), 2.47 (m, 1 H), 3.62 (d, *J* = 11.2 Hz, 1 H), 3.84 (t, *J* = 2.3 Hz, 1 H), 4.05 (d, *J* = 11.2 Hz, 1 H), 5.66 (dq, *J* = 2.3, 6.7 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.5, 7.0, 13.1, 18.9, 21.2, 24.1, 26.9, 29.4, 66.3, 70.4, 74.3, 98.4, 120.2, 136.4; EI-LRMS *m/z* 311 [$(M-Me)^+$], 268 [$(M-C_3H_6O)^+$].

<run 4>

(*E*)-2-Ethylidene-4,4-diethoxycarbonyl-1-triethylsiloxybicyclo[3.3.1]nonane (129). According to the general procedure, a crude product, which was obtained from **125** (147.2 mg, 0.525 mmol),

$Ni(cod)_2$ (13.7 mg, 0.0498 mmol), IPr·HCl (22.0 mg, 0.0518 mmol), ^{t}BuOK (6.4 mg, 0.0570 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1) to give **129** (205.2 mg, 99%) as a colorless oil. IR (neat) 1737, 1461, 1240, 1122 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 0.65 (q, *J* = 7.9 Hz, 6 H), 1.03 (t, *J* = 7.9 Hz, 9 H), 1.35-1.50 (m, 2 H), 1.57-1.73 (m, 6 H), 1.82-1.94 (m, 2 H), 2.36 (d, *J* = 12.0 Hz, 1 H), 3.14 (s, 1 H), 3.299 (s, 3 H), 3.304 (s, 3 H), 3.33 (s, 1 H), 3.60 (d, *J* = 17.2 Hz, 1 H), 6.07 (m, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 5.46, 5.51, 10.7, 20.2, 25.5, 29.8, 34.8, 39.8, 40.1, 50.15, 50.21, 57.0, 63.9, 72.5, 115.7, 137.9, 169.2, 169.6; EI-LRMS *m/z* 396 (M^+), 353 [$(M-Et)^+$]; EI-HRMS calcd for $C_{21}H_{36}O_5Si$ 396.23320, found 396.23334.

<Table 5>

<run 1>

(3a*R,6a*S**,*E*)-3-Ethylidene-3a-triethylsiloxyhexahydro-2*H*-cyclopenta[*b*]furan (134).** According to the general procedure, a crude product, which was obtained from **130** (52.2 mg, 0.343 mmol), $Ni(cod)_2$ (9.0 mg, 0.0498 mmol), IPr·HCl (14.4 mg, 0.0339 mmol), ^{t}BuOK (4.6 mg, 0.0410 mmol), and Et_3SiH (0.28 mL, 1.75 mmol) in THF (3.4 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/AcOEt = 40/1) to give **134** (83.8 mg, 90%) as a colorless oil. IR (neat) 1692, 1460, 1241, 1106, 1058 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.55 (q, *J* = 7.9 Hz, 6 H), 0.92 (t, *J* = 7.9 Hz, 9 H), 1.59 (m, 1 H), 1.60 (dt, *J* = 6.9, 1.6 Hz, 3 H), 1.67-1.89 (m, 4 H), 1.96 (m, 1 H), 4.20 (d, *J* = 5.7 Hz, 1 H), 4.45 (dq, *J* = 2.9, 1.6 Hz, 2 H), 5.55 (td, *J* = 2.9, 6.9 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.2, 7.0, 14.6, 24.1, 32.2, 41.8, 69.5, 89.6, 90.9, 116.3, 145.6; EI-LRMS *m/z* 268 (M^+), 253, 239, 225, 197, 115; EI-HRMS calcd for $C_{15}H_{28}O_2Si$ 268.18586 found 268.18478.

<run 2>

(3a*R,7a*S**,*E*)-3-Ethylidene-3a-triethylsiloxyoctahydrobenzofuran (135).** According to the general procedure, a crude product, which was obtained from **131** (82.5 mg, 0.496 mmol), $Ni(cod)_2$ (13.8 mg, 0.0502 mmol), IPr·HCl (21.6 mg, 0.0508 mmol), ^{t}BuOK (6.9 mg, 0.0615 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/AcOEt = 40/1) to give **135** (121.7 mg, 87%) as a colorless oil. IR (neat) 1697, 1459, 1223, 1089 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.55 (q, *J* = 8.0 Hz, 6 H), 0.93 (t, *J* = 8.0 Hz, 9 H), 1.22-1.36 (m, 2 H), 1.45-1.54 (m, 3 H), 1.58 (m, 1 H), 1.57 (dt, *J* = 7.0, 1.6 Hz, 3 H), 1.71 (m, 1 H), 1.79 (m, 1 H), 3.75 (dd, *J* = 5.3, 5.3 Hz, 1 H), 4.43 (q, *J* = 6.9 Hz, 2 H),

5.41 (ddq, *J* = 5.3, 5.3, 7.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.5, 7.1, 14.1, 21.6, 22.5, 27.1, 35.4, 67.4, 78.9, 83.0, 114.7, 143.8; EI-LRMS *m/z* 282 (M^+), 253 [$(M\text{-}Et)^+$]; EI-HRMS calcd for $C_{16}H_{30}O_2Si$ 282.20151, found 282.20154.

<run 3>

(3a*R,6a*S**,*E*)-3-Ethylidene-3a-triethylsiloxy-1-tosyloctahydrocyclopenta[*b*]pyrrole (136).** According to the general procedure, a crude product, which was obtained from **132** (152.4 mg, 0.499 mmol), $Ni(cod)_2$ (14.0 mg, 0.0509 mmol), IPr·HCl (21.8 mg, 0.0513 mmol), ^{t}BuOK (6.7 mg, 0.0597 mmol), and Et_3SiH (0.40 mL, 2.50 mmol) in THF (5.0 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) to give **136** (191.7 mg, 91%) as a colorless oil. IR (neat) 1919, 1689, 1459, 1350, 1239, 1163, 1093 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.22 (dt, *J* = 14.4, 8.0 Hz, 3 H), 0.28 (dt, *J* = 14.4, 8.0 Hz, 3 H), 0.71 (dd, *J* = 8.0, 8.0 Hz, 9 H), 1.57-1.75 (m, 3 H), 1.60 (d, *J* = 6.9 Hz, 3 H), 1.90-2.08 (m, 3 H), 2.41 (s, 3 H), 3.65 (m, 1 H), 3.78 (dt, *J* = 13.7, 2.3 Hz, 1 H), 4.18 (d, *J* = 13.2 Hz, 1 H), 5.55 (dqm, *J* = 2.3, 6.9 Hz, 1 H), 7.32 (d, *J* = 8.3 Hz, 2 H), 7.74 (d, *J* = 8.3 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.8, 6.8, 14.6, 21.5, 24.2, 32.8, 39.4, 51.0, 73.0, 90.3, 119.0, 127.9, 129.5, 133.4, 140.3, 143.4; 143.4; EI-LRMS *m/z* 392 [$(M\text{-}Et)^+$], 290, 266, 237, 223, 209, 115; EI-HRMS calcd for $C_{20}H_{30}NO_3SSi$ 392.17157, found 392.17051.

<run 4>

(3a*R,7a*S**,*E*)-3-Ethylidene-3a-triethylsiloxy-1-tosyloctahydro-1*H*-indole (137).** According to the general procedure, a crude product, which was obtained from **133** (122.4 mg, 0.418 mmol), $Ni(cod)_2$ (11.4 mg, 0.0414 mmol), IPr·HCl (17.9 mg, 0.0421 mmol), ^{t}BuOK (5.9 mg, 0.0526 mmol), and Et_3SiH (0.34 mL, 2.13 mmol) in THF (4.2 mL) for 30 min, was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) to give **137** (173.2 mg, 95%) as a colorless oil. IR (neat) 1920, 1599, 1459, 1349, 1239, 1164, 1093 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.27 (qm, *J* = 7.9 Hz, 6 H), 0.74 (t, *J* = 7.9 Hz, 9 H), 1.05-1.27 (m, 3 H), 1.51-1.60 (m, 3 H), 1.61 (d, *J* = 6.9 Hz, 3 H), 2.07-2.20 (m, 2 H), 2.40 (s, 3 H), 3.59 (m, 1 H), 3.79 (dm, *J* = 13.5 Hz, 1 H), 4.06 (d, *J* = 13.5 Hz, 1 H), 5.46 (qm, *J* = 6.9 Hz, 1 H), 7.27 (d, *J* = 7.4 Hz, 2 H), 7.75 (d, *J* = 7.4 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 6.1, 7.0, 14.2, 21.4, 23.1, 23.4, 31.7, 33.4, 47.0, 68.8, 79.8, 118.2, 127.4, 129.4, 136.6, 138.1, 142.7; EI-LRMS *m/z* 406 [$(M\text{-}Et)^+$], 304, 280, 256, 148; EI-HRMS calcd for $C_{21}H_{32}NO_3SSi$ 406.18722, found 406.18662.

<Scheme 21>

(3a*S,7a*R**)-3a-Hydroxyhexahydro-1*H*-inden-4(2*H*)-one (138)**[16]**.** Similar to synthesis of **82** from **81**, a crude product, which was obtained from ozonization of **118** (55.7 mg, 0.199 mmol) in CH_2Cl_2 (5 mL) followed by reduction using PPh_3 (52.1 mg, 0.199 mmol), was treated with a 5% solution of HF in CH_3CN (4 mL). After usual work up, a crude product was purified by column chromatography on silica gel (hexane/AcOEt = 3/2) to give **138** (21.1 mg, 2 steps 69%) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (m, 1 H), 1.56 (m, 1 H), 1.62-1.77 (m, 3 H), 1.85-2.22 (m, 6 H), 2.43-2.59 (m, 2 H), 3.92 (s, 1 H): ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.4, 26.2, 30.1, 30.7, 37.3, 37.4, 52.7, 86.5, 214.5.

(3a*R,7a*S**)-7a-Hydroxyoctahydro-1*H*-inden-1-one (139)**[16]**.** Similar to synthesis of **82** from **81**, a crude product, which was obtained from ozonization of **119** (119.5 mg, 0.426 mmol) in CH_2Cl_2 (5 mL) followed by reduction using PPh_3 (112 mg, 0.427 mmol), was treated with a 5% solution of HF in CH_3CN (8 mL). After usual work up, a crude product was purified by column chromatography on silica gel (hexane/AcOEt = 1/1) to give **139** (47.8 mg, 2 steps 73%) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (m, 1 H), 1.40-1.66 (m, 6 H), 1.74-1.93 (m, 3 H), 2.10 (m, 1 H), 2.22-2.47 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.6, 20.7, 20.9, 24.3, 29.4, 33.2, 40.8, 77.8, 219.8.

(4a*R,8a*S**)-8a-Hydroxyoctahydronaphthalen-1(2*H*)-one (140)**[16]**.** Similar to synthesis of **82** from **81**, a crude product, which was obtained from ozonization of **120** (68.0 mg, 0.231 mmol) in CH_2Cl_2 (5 mL) followed by reduction using PPh_3 (60.6 mg, 0.231 mmol), was treated with a 5% solution of HF in CH_3CN (8 mL). After usual work up, a crude product was purified by column chromatography on silica gel (hexane/AcOEt = 1/1) to give **140** (19.3 mg, 2 steps 50%) as colorless needle. ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25-2.13 (m, 13 H), 2.39-2,62 (m, 2 H), 3.87 (s, 1 H): ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.1, 21.2, 26.1, 26.4, 27.5, 31.4, 37.3, 44.6, 78.1, 214.5.

<Scheme 22>

2-Ethoxycarbonyl-2-(hex-4-ynyl)cyclohexanone (117). To a suspension of NaH (60% dispersion in mineral oil, 1.96 g, 48.9 mmol) in DMF (40 mL) was added a solution of 6-iodohex-2-yne (9.10 g, 43.7 mmol) in DMF (40 mL) at 0 °C, and the mixture was stirred at the room temperature for 1 h.

To the mixture was added a solution of **141** (6.5 mL, 40.6 mmol) in DMF (40 mL) at the same temperature, and the mixture was stirred at room temperature for 13 h. To the mixture was added 10% HCl aqueous solution at 0 °C, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by column chromatography on silica gel (hexane/AcOEt = 10/1) and purified by column chromatography on silica gel (toluene) to give **117** (7.42 g, 77%) as a colorless oil. IR (neat) 1713, 1450, 1182 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.26 (t, *J* = 7.1 Hz, 3 H), 1.32-1.47 (m, 3 H), 1.60-1.78 (m, 7 H), 1.91 (m, 1 H), 1.99 (m, 1 H), 2.09-2.14 (m, 2 H), 2.40-2.54 (m, 3 H), 4.20 (d, *J* = 7.1 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.5, 14.1, 19.1, 22.5, 23.9, 27.6, 34.0, 36.0, 41.1, 60.7, 61.2, 75.8, 78.6, 171.9, 207.9; EI-LRMS *m/z* 205 [$(M-Et)^+$], 177, 159, 141; EI-HRMS calcd for $C_{13}H_{17}O_2$ 205.12285, found 205.12263.

<Scheme 23>

2-Ethoxycarbonyl-2-(hex-4-ynyl)-3,4-dihydronaphthalen-1(2*H*)-one (123). Similar to synthesis of **117** from **141**, a crude product, which was obtained from **142**[22] (1.19 g, 5.26 mmol), NaH (60% dispersion in mineral oil, 319 mg, 7.99 mmol), 6-iodohex-2-yne (1.36 g, 6.55 mmol) in DMF (26 mL) at room temperature for 2 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) to give **123** (540 mg, 34%) as a yellow oil. IR (neat) 1730, 1688, 1455, 1235, 1095 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.16 (t, *J* = 10.4 Hz, 3 H), 1.46-1.66 (m, 2 H), 1.77 (t, *J* = 2.6, 3 H), 1.91-2.20 (m, 5 H), 2.57 (dt, *J* = 13.7, 5.2, 1 H), 2.90-3.11 (m, 2 H), 4.14 (dq, *J* = 1.7, 10.4, 2 H), 7.21 (d, *J* = 7.4 Hz, 1 H), 7.30 (dd, *J* = 7.4, 7.4 Hz, 1 H), 7.46 (dd, *J* = 7.7, 7.7 Hz, 1 H), 8.04 (d, *J* = 8.0 Hz, 1 H); EI-LRMS *m/z* 298 (M^+), 252, 225; EI-HRMS calcd for $C_{19}H_{22}O_3$ 298.15689, found 298.15690.

2-(Hex-4-ynyl)-3,4-dihydronaphthalen-1(2*H*)-one (122). To a solution of **123** (347 mg, 1.16 mmol) in DMF (2.4 mL) was added LiI (806 mg, 6.02 mmol) at room temperature, and the mixture was refluxed for 2 h. After the mixture was diluted with H_2O, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 15/1) to give **122** (229 mg, 87%) as a colorless oil. IR (neat) 1946, 1683, 1455, 1290 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.55-1.67 (m, 3 H), 1.77 (t, *J* = 2.6 Hz, 3 H), 1.90 (m, 1 H), 2.12 (m, 1 H), 2.12-2.28 (m, 3 H), 2.49 (m, 1 H), 2.94-3.05 (m, 2 H), 7.23 (d, *J* = 7.4 Hz, 1 H), 7.30 (dd, *J* = 7.8, 7.8 Hz, 1 H), 7.46

(dd, *J* = 7.4, 7.4 Hz, 1 H), 8.02 (d, *J* = 8.6 Hz, 1 H); EI-LRMS *m/z* 226 (M^+), 211, 159, 145, 118; EI-HRMS calcd for $C_{16}H_{18}O$ 226.13576, found 226.13578.

<Scheme 24>

4-(Hex-4-ynyl)-2,2-dimethyl-1,3-dioxan-5-one (124). To a suspension of **143**[23] (486.3 mg, 3.74 mmol) in benzene (12.5 mL) were added MS4A (988 mg) and cyclohexylamine (0.86 mL, 7.52 mmol) at room temperature, and the mixture was stirred at the same temperature over night. The mixture was filtered, and the filtrate was concentrated to give crude **144** as a colorless oil. To a solution of diethylamine (0.46 mL, 4.45 mmol) in THF (2.5 mL) was added BuLi in hexane (1.65 M, 2.5 mL, 4.13 mmol) at -35 °C, and stirred at the same temperature for 10 min. To the mixture was added a solution of **144** in THF (2.5 mL) at -78 °C, and the reaction mixture was slowly warmed to -20 °C for 2 h. To the reaction mixture was added a solution of 6-iodo-2-hexyne (867.5 mg, 4.17 mmol) in THF (2.5 mL) at -78 °C, and the reaction mixture was warmed to room temperature over a period of 3 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 10/1) to give **124** (340 mg, 43%) as a colorless oil. IR (neat) 1748, 1436, 1225 cm-1; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.43 (s, 3 H), 1.45 (s, 3 H), 1.53-1.68 (m, 3 H), 1.77 (t, *J* = 2.6, 3 H), 1.99 (m, 1 H), 2.13-2.19 (m, 2 H), 3.99 (d, *J* = 16.2, 1 H), 4.24 (m, 1 H), 4.25 (d, *J* = 16.2 Hz, 1 H); EI-LRMS *m/z* 195 [$(M-Me)^+$], 152, 110; EI-HRMS calcd for $C_{11}H_{15}O_3$ 195.10212, found 195.10171.

<Scheme 25>

Dimethyl 2-(but-2-ynyl)-2-(3-oxocyclohexyl)malonate (125). To a solution of **145**[24] (301 mg, 1.64 mmol) in THF (3.3 mL) were added cyclohex-2-enone (**146**) (0.18 mL, 1.86 mmol) and DBU (0.28 mL, 1.87 mmol) at room temperature, and the reaction mixture was stirred over night. After the mixture was concentrated, the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 2/1) to give **125** (242.6 mg, 53%) as a colorless oil. IR (neat) 2236, 1731, 1714, 1435 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35 (m, 1 H), 1.64 (m, 1 H), 1.73 (t, *J* = 2.6 Hz, 3 H), 2.04-2.12 (m, 2 H), 2.16-2.26 (m, 2 H), 2.40 (m, 1 H), 2.54-2.68 (m, 2 H), 2.79 (m, 2 H), 3.737 (s, 3 H), 3.741 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.5, 23.3, 24.7, 27.0, 40.6, 41.1, 43.4, 52.5, 52.6, 60.2, 73.0, 79.3, 169.9, 170.0, 210.3; EI-LRMS *m/z* 249 [$(M-OMe)^+$], 221, 183; EI-HRMS

calcd for $C_{14}H_{17}O_4$ 249.11268, found 249.11259.

<Scheme 26>

2-(But-2-ynyloxy)cyclopentanone (130). To a suspension of NaH (60% dispersion in mineral oil, 186 mg, 4.66 mmol) in THF (3 mL) was added a solution of compound **148** (579 mg, 3.11 mmol, prepared from cis-cyclopentane-1,2-diol and 3,4-dihydoro-2*H*-pyrane by using standard procedure) in THF (3 mL) at 0 °C, and the mixture was stirred at the room temperature for 30 min. To the mixture were added a solution of **147** (668 mg, 2.98 mmol, prepared by standard tosylation of but-2-yn-1-ol with TsCl) in THF (3 mL) and NaI (35.4 mg, 0.236 mmol) at 0 °C, and the mixture was stirred at the room temperature for 13 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by column chromatography on silica gel to give crude THP ester (735 mg) as a colorless oil. To a solution of the above crude THP ester (735 mg) in MeOH (3 mL) was added a 10% aqueous solution of hydrochloric acid (3 mL) at 0 °C, and stirred at room temperature for 30 min. To the mixture was added saturated Na_2CO_3 aqueous solution, at 0°C, and the aqueous layer was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by column chromatography on silica gel to give an alcohol **149** (339 mg) as a colorless oil. To a solution of the crude the alcohol **149** (339 mg) in CH_2Cl_2 (11 mL) were added PCC (983 mg, 4.56 mmol) and MS4A (2.13 g) at 0 °C, and the mixture was stirred at room temperature for 13 h. The mixture was diluted with AcOEt and filtered through silica gel pad. After the filtrate was concentrated, the residue was purified by column chromatography on silica gel (hexane/AcOEt = 10/1) to give **130** (261 mg, 3 steps 55%) as a colorless oil. IR (neat) 1749, 1451, 1050 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.75-1.86 (m, 2 H), 1.85 (t, *J* = 2.2 Hz, 3 H), 2.05 (m, 1 H), 2.18-2.39 (m, 3 H), 3.97 (m, 1 H), 4.59 (q, *J* = 2.2 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.6, 17.2, 29.3, 35.3, 57.9, 74.5, 79.3, 83.0, 216.1; EI-LRMS *m/z* 124, 99, 84; EI-HRMS calcd for $C_8H_{12}O$ 124.08881 found 128.08824.

2-(But-2-ynyloxy)cyclohexanone (131). To a solution of $FeCl_3$ (82.4 mg, 0.508 mmol) in but-2-yn-1-ol (0.75 mL) was added cyclohexene oxide (0.50 mL, 5.04 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture was added H_2O, at same temperature, and the aqueous layer was extracted with Et_2O. The organic layer was washed with

brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by column chromatography on silica gel (hexane/AcOEt 4/1) to give crude **151** (500 mg) as a colorless oil. To a solution of the above **151** (500 mg) in CH_2Cl_2 (25 mL) were added PCC (3.26 g, 1.51 mmol) and MS4A (6.60 g) at 0 °C, and stirred at same temperature over night. The mixture was diluted with AcOEt, filtered, and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (hexane/AcOEt = 10/1) to give **131** (255 mg, 2 steps 30%) as a colorless oil. IR (neat) 2296, 2240, 1721, 1052, 1143, 1110 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.62-1.77 (m, 3 H), 1.85 (dd, *J* = 2.2, 2.2 Hz, 3 H), 1.90-2.02 (m, 2 H), 2.20-2.35 (m, 2 H), 2.53 (m, 1 H), 4.07 (m, 1H), 4.18 (dq, *J* = 15.4, 2.2 Hz, 2 H), 4.32 (dq, *J* = 15.4, 2.2 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.6, 23.3, 27.6, 34.4, 40.7, 57.5, 74.7, 80.7, 82.8, 209.7; EI-LRMS *m/z* 166 (M^+), 122, 98; EI-HRMS calcd for $C_{10}H_{14}O_2$ 166.09938, found 166.09979.

***N*-(But-2-ynyl)-4-methyl-*N*-(2-oxocyclopentyl)benzenesulfonamide (132).** To a solution of **152**[26] (742.6 mg, 3.99 mmol), **148** (228.1 mg, 1.02 mmol) and PPh_3 (1.34 g, 5.13 mmol) in THF (5 mL) was added DIAD (1 mL, 5.08 mmol) at 0 °C. The resulting reaction mixture was stirred at 50 °C for 20 h and concentrated. The residue was roughly purified by column chromatography on silica gel (hexane/AcOEt = 5/1) to give crude tosylamide (480 mg) as a yellow oil. To a solution of the above crude tosylamide (480 mg) in MeOH (5 mL) were added 10% HCl aqueous solution at room temperature, and stirred at same temperature for 30 min. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by short column chromatography on silica gel (AcOEt) to give crude **153** (400 mg) as a yellow oil. To a solution of the above **153** (400 mg) in CH_2Cl_2 (10 mL) were added PCC (334 mg, 1.55 mmol) and MS4A (702 mg) at 0 °C, and stirred at same temperature over night. After usual work up, a crude product was purified by column chromatography on silica gel (toluene/AcOEt = 10/1) to give **132** (190 mg, 3 steps 61%) as a colorless oil. IR (neat) 1923, 1754, 1598, 1451, 1092 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.71 (dd, *J* = 2.3, 2.3 Hz, 3 H), 1.82 (m, 1 H), 2.07 (m, 1 H), 2.17-2.35 (m, 4 H), 2.42 (s, 3 H), 3.81 (dq, *J* = 18.3, 2.3 Hz, 1 H), 4.07 (dq, *J* = 18.3, 2.3 Hz, 1 H), 4.21 (m, 1 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 7.81 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.5, 18.4, 21.5, 27.7, 35.6, 35.8, 64.2, 73.8, 81.9, 127.6, 129.5, 136.8, 143.5, 213.2; ESI-LRMS *m/z* 633 [$(2M+Na)^+$], 328 [$(M-Na)^+$]; ESI-HRMS calcd for $C_{16}H_{19}NO_3NaS$ 328.09779, found 328.09720.

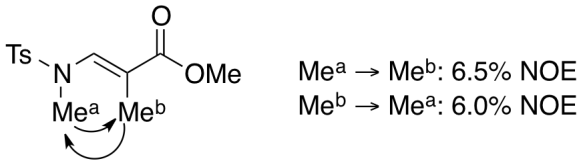
- Chapter 2 -

General Procedure for the Carboxylation of Allenamide

$Ni(cod)_2$ (1 eq to a substrate) was weighed into a flame-dried flask. To this were added THF (8 mL/mmol) and ligand at 0 °C, and the flask was immersed in a liquid nitrogen bath. After the mixture had been frozen, the flask was evacuated to 0.05 mmHg. The flask was backfilled with CO_2 in a plastic balloon and the frozen mixture was slowly thawed at 0 °C. To this suspension was added a solution of the substrate in THF (8 mL/mmol) at 0 °C, and the resulting mixture was stirred at the same temperature. To the mixture wad added 10% aqueous HCl at 0 °C, and the aqueous layer was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was treated with diazomethane in Et_2O or MeOH according to the standard procedure. After the usual work-up, the crude product was purified by flash column chromatography on silica gel to give the corresponding ester.

Chapter 2, Section 1

<Scheme 35>



(*E*)-Methyl 2-methyl-3-(*N*-methyl-*N*-tosylamino)acrylate (196). According to the general procedure, a crude product, which was obtained from **195**[42] (80.8 mg, 0.362 mmol), $Ni(cod)_2$ (99.8 mg, 0.363 mmol), and DBU (0.11 mL, 0.736 mmol) in THF (5.8 mL) for 2 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1) to give **196** (78.1 mg, 76%) as a colorless oil. IR (film, CH_2Cl_2) 2952, 2361, 2342, 1710, 1637, 1356, 1164 cm-1; ^{1}H NMR (500 MHz, CDCl3) δ 1.91 (d, *J* = 1.3 Hz, 3 H), 2.42 (s, 3 H), 3.08 (s, 3 H), 3.72 (s, 3 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 7.53 (d, *J* = 1.3 Hz, 1 H), 7.69 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.5, 21.5, 36.0, 51.9, 115.4, 127.2, 129.9, 134.2, 137.9, 144.4, 168.6; EI-LRMS *m/z* 283 (M^+), 252, 178, 155, 146, 128, 96, 91; EI-HRMS calcd for $C_{13}H_{17}NO_4S$ 283.08783, found 283.08826.

<Table 6>

<run 2>

According to the general procedure, a crude product, which was obtained from **195** (81.2 mg, 0.364 mmol), $Ni(cod)_2$ (99.7 mg, 0.362 mmol), and DBU (0.22 mL, 1.47 mmol) in THF (5.8 mL) for 1 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1) to give **196** (90.8 mg, 89%) as a colorless oil.

<run 3>

$Ni(cod)_2$ (99.2 mg, 0.361 mmol) and 1,10-phenanthlorine (65.7 mg, 0.363 mmol) were weighed into a flame-dried flask. To this was added THF (2.9 mL) at 0 °C, and the flask was immersed in a liquid nitrogen bath. After the mixture had been frozen, the flask was evacuated to 0.05 mmHg. The flask was backfilled with CO_2 in a plastic balloon and the frozen mixture was slowly thawed at 0 °C. To this suspension was added a solution of **195** (81.3 mg, 0.364 mmol) in THF (2.9 mL) at 0 °C, and the resulting mixture was stirred at the same temperature. To the mixture wad added 10% aqueous HCl at 0 °C, and the aqueous layer was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was treated with diazomethane in MeOH according to the standard procedure. After the usual work-up, the crude product was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1) to give **196** (4.6 mg, 4%) as a colorless oil.

<run 4>

$Ni(cod)_2$ (99.7 mg, 0.365 mmol) and DCPE (154.5 mg, 0.366 mmol) were weighed into a flame-dried flask. To this was added THF (2.9 mL) at 0 °C, and the flask was immersed in a liquid nitrogen bath. After the mixture had been frozen, the flask was evacuated to 0.05 mmHg. The flask was backfilled with CO_2 in a plastic balloon and the frozen mixture was slowly thawed at 0 °C. To this suspension was added a solution of **195** (81.4 mg, 0.365 mmol) in THF (2.9 mL) at 0 °C, and the resulting mixture was stirred at the same temperature. To the mixture wad added 10% aqueous HCl at 0 °C, and the aqueous layer was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was treated with diazomethane in MeOH according to the standard procedure. After the usual work-up, the crude product was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1) to give only trace amount of **196**.

<run 5>

According to the general procedure, a crude product, which was obtained from **195** (79.3 mg, 0.355 mmol), $Ni(cod)_2$ (99.6 mg, 0.362 mmol), and TMEDA (55 μL, 0364. mmol) in THF (5.8 mL) for 1 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1) to give **196** (83.8 mg, 82%) as a colorless oil.

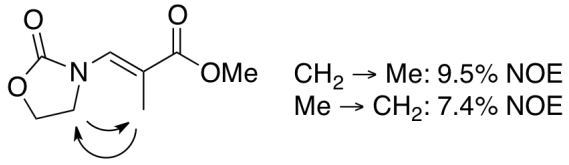
<run 6>

According to the general procedure, a crude product, which was obtained from **195** (81.1 mg, 0.363 mmol), $Ni(cod)_2$ (99.9 mg, 0.363 mmol), and TMEDA (0.11 mL, 0.729 mmol) in THF (5.8 mL) for 1 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1) to give **196** (90.4 mg, 88%) as a colorless oil.

Chapter 2, Section 2

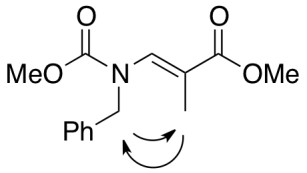
<Scheme 36>

<Eq. 11>



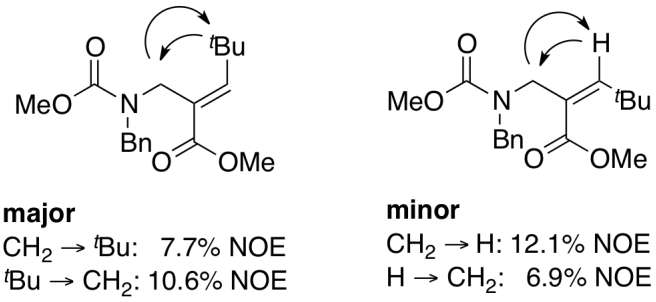
(*E*)-Methyl 2-methyl-3-(2-oxazolidon-3-yl)acrylate (198). According to the general procedure, a crude product, which was obtained from **197**[43] (45.5 mg, 0.364 mmol), $Ni(cod)_2$ (99.3 mg, 0.361 mmol), and DBU (0.22 mL, 1.47 mmol) in THF (5.8 mL) for 1 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 1/1 ~ AcOEt) to give **198** (33.9 mg, 51%) as a colorless solid. mp 139-140 °C (recrystallized from CH_2Cl_2/hexane); IR (film CH_2Cl_2) 2954, 1772, 1703, 1657, 1408, 1203, 748 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.02 (s, 3 H), 3.75 (s, 3 H), 4.18 (t, *J* = 8.0 Hz, 2 H), 4.47 (t, *J* = 8.0 Hz, 2 H), 7.80 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.2, 44.3, 51.7, 62.2, 108.5, 133.4, 155.9, 168.7; EI-LRMS *m/z* 185 (M^+), 154, 153, 125, 109, 81; EI-HRMS calcd for $C_8H_{11}NO_4$ 185.06881, found 185.06883.

<Eq. 12>



According to the general procedure, a crude product, which was obtained from **199** (73.7 mg, 0.363 mmol), $Ni(cod)_2$ (98.8 mg, 0.359 mmol), and DBU (0.11 mL, 0. mmol) in THF (5.8 mL) for 1 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1~2/1) to give **200** (20.2 mg, 21%) and **201** (5.7 mg, 6%). **(*E*)-Methyl 3-{*N*-benzyl-*N*-(methoxycarbonyl)amino}-2-methylacrylate (200).** colorless oil; IR (film CH_2Cl_2) 2952, 2361, 2342, 1710, 1637, 1356, 1164 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.78-1.80 (m, 3 H), 3.73 (s, 3 H), 3.79 (s, 1 H), 4.12 (s, 1 H), 7.16-7.35 (m, 5 H), 7.69 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.7, 51.1, 51.9, 53.7, 115.7, 126.5, 127.4, 128.6, 137.3, 137.9, 155.3, 168.9; EI-LRMS *m/z* 263 (M^+), 231, 204, 172, 91; EI-HRMS calcd for $C_{14}H_{17}NO_4$ 263.11576, found 263.11511. **Methyl 2-[{*N*-benzyl-*N*-(methoxycarbonyl)amino}methyl]acrylate (201).** colorless oil; IR (film, CH_2Cl_2) 2953, 1707, 1472, 1246, 1141, 956, 737 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, at 100 °C) δ 3.66 (s, 3 H), 3.69 (s, 3 H), 4.05 (s, 2 H), 4.45 (s, 2 H), 5.61 (s, 1 H), 6.16 (m, 1 H), 7.21-7.36 (m, 5 H); ^{13}C NMR (125 MHz, DMSO-d_6, at 100 °C) δ 46.5, 49.7, 51.1, 51.9, 124.8, 126.6, 126.9, 127.9, 135.7, 137.3, 155.9, 165.4; EI-LRMS *m/z* 263 (M^+), 232, 204, 172, 164, 91; EI-HRMS calcd for $C_{14}H_{17}NO_4$ 263.11576, found 263.11518.

<Scheme 37>

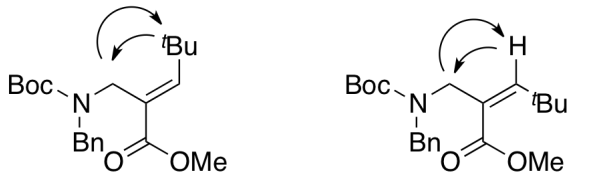


Methyl 2-[{*N*-benzyl-*N*-(methoxycarbonyl)amino}methyl]-4,4-dimethylpent-2-enoate (203). According to the general procedure, a crude product, which was obtained from **202** (94.5 mg, 0.364 mmol), $Ni(cod)_2$ (98.4 mg, 0.358 mmol), and DBU (0.22 mL, 1.47 mmol) in THF (5.8 mL) for 13 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) to give **203**

(100.5 mg, 88%, *E*:*Z* = 91:9) as a colorless oil. ***E*-203**. ^{1}H NMR (500 MHz, DMSO-d_6, at 100 °C) δ 1.09 (s, 9 H), 3.60 (s, 3 H), 3.64 (s, 3 H), 4.35 (s, 2 H), 4.41 (s, 2 H), 6.63 (s, 1 H), 7.14-7.35 (m, 5 H). ***Z*-203**. ^{1}H NMR (500 MHz, DMSO-d_6, at 100 °C) δ 1.04 (s, 9 H), 3.64 (s, 3 H), 3.66 (s, 3 H), 3.93 (s, 2 H), 4.39 (s, 2 H), 5.49 (s, 1 H), 7.14-7.35 (m, 5 H).

<Table 7>

<run 1>

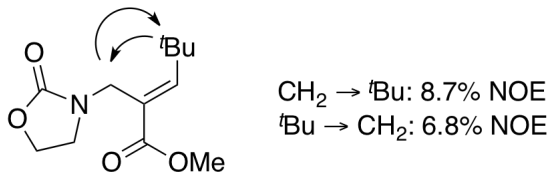


major
CH_2 → ^{t}Bu: 8.7% NOE
^{t}Bu → CH_2: 5.0% NOE

minor
CH_2 → H: 12.7% NOE
H → CH_2: 5.7% NOE

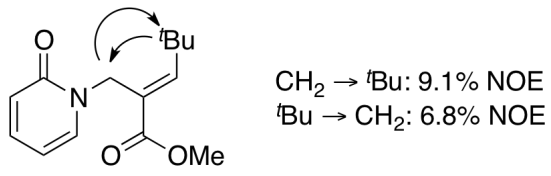
Methyl 2-[{*N*-benzyl-*N*-(*tert*-butoxycarbonyl)amino}methyl]-4,4-dimethylpent-2-enoate (213). According to the general procedure, a crude product, which was obtained from **205** (109.1 mg, 0.362 mmol), Ni(cod)$_2$ (99.0 mg, 0.360 mmol), and DBU (0.22 mL, 1.47 mmol) in THF (5.8 mL) for 15 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) to give **213** (118.3 mg, 91%, *E*:*Z* = 89:11) as a colorless oil. ***E*-213**. colorless oil; IR (neat) 2959, 1721, 1698, 1454, 1249, 1168, 881, 699 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, at 100 °C) δ 1.09 (s, 9 H), 1.40 (s, 9 H), 3.60 (s, 3 H), 4.33 (s, 2 H), 4.35 (s, 2 H), 6.63 (s, 1 H), 7.13-7.34 (m, 5 H); ^{13}C NMR (125 MHz, DMSO-*d*6, at 100 °C) δ 27.6, 29.5, 32.9, 41.8, 48.4, 50.9, 78.7, 126.10, 126.13, 126.9, 127.8, 138.2, 152.3, 154.5, 167.6; EI-LRMS *m/z* 305 [(M-^{t}Bu+H)$^+$], 260, 237, 228, 214, 204, 170, 138, 106, 91; EI-HRMS calcd for $C_{17}H_{23}NO_4$ 305.16271, found 305.16200. ***Z*-213**. colorless oil; IR (film, CH_2Cl_2) 2956, 1733, 1698, 1454, 1244, 1167, 873, 700 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 100 °C) δ 1.05 (s, 9 H), 1.41 (s, 9 H), 3.67 (s, 3 H), 3.90 (s, 2 H), 4.34 (s, 2 H), 5.48 (s, 1 H), 7.20-7.35 (m, 5 H); ^{13}C NMR (125 MHz, DMSO-d_6 at 100 °C) δ 27.5, 29.0, 32.3, 48.5, 50.3, 50.7, 78.8, 126.2, 126.4, 126.9, 127.8, 137.6, 143.2, 154.2, 168.4; EI-LRMS *m/z* 305 [(M-^{t}Bu+H)$^+$], 274, 260, 248, 214, 204, 182, 170, 150, 138, 106, 91; EI-HRMS calcd for $C_{17}H_{23}NO_4$ 305.16271, found 305.16224.

<run 2>



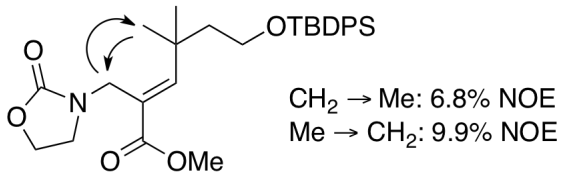
(*E*)-Methyl 4,4-dimethyl-2-{(2-oxazolidon-3-yl)methyl}pent-2-enoate (214). According to the general procedure, a crude product, which was obtained from **206** (64.8 mg, 0.358 mmol), $Ni(cod)_2$ (99.4 mg, 0.361 mmol), and DBU (0.22 mL, 1.47 mmol) in THF (5.8 mL) for 16 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1~1/1) to give **214** (76.7 mg, 88%) as a colorless oil. IR (film, CH_2Cl_2) 2964, 1752, 1714, 1435, 1266, 739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.23 (s, 9 H), 3.47-3.52 (m, 2 H), 3.76 (s, 3 H), 4.24-4.28 (m, 2 H), 4.32 (s, 2 H), 7.07 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.5, 34.0, 39.8, 44.4, 52.2, 61.9, 124.7, 157.4, 158.1, 168.5; EI-LRMS *m/z* 241 (M^+), 209, 184, 166, 140, 122, 100; EI-HRMS calcd for $C_{12}H_{19}NO_4$ 241.13141, found 241.13139.

<run 3>



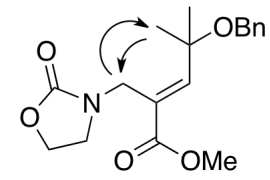
(*E*)-Methyl 4,4-dimethyl-2-{(2-pyridon-1-yl)methyl}pent-2-enoate (215). According to the general procedure, a crude product, which was obtained from **207** (38.7 mg, 0.204 mmol), $Ni(cod)_2$ (53.6 mg, 0.195 mmol), and DBU (0.12 mL, 0.802 mmol) in THF (3.2 mL) for 17 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1~1/1) to give **215** (29.3 mg, 60%) as a brown oil. IR (neat) 3429, 2958, 1714, 1662, 1588, 1537, 1436, 1235, 767 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.19 (s, 9 H), 3.67 (s, 3 H), 4.91 (s, 2 H), 6.11 (m, 1 H), 6.53 (m, 1 H), 7.20 (s, 1 H), 7.22 (m, 1 H), 7.28 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.0, 34.3, 44.0, 52.2, 105.6, 120.4, 123.9, 135.6, 139.1, 159.0, 162.8, 167.7; EI-LRMS *m/z* 249 (M^+), 218, 202, 192, 139, 96; EI-HRMS calcd for $C_{14}H_{19}NO_3$ 249.13649, found 249.13616

<run 4>

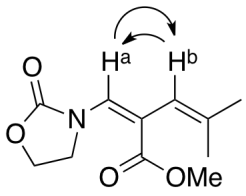


(*E*)-Methyl 6-*tert*-butyldiphenylsilyloxy-4,4-dimethyl-2-{(2-oxazolidon-3-yl)methyl}hex-2-enoate (216). According to the general procedure, a crude product, which was obtained from **208** (162.8 mg, 0.362 mmol), $Ni(cod)_2$ (100.0 mg, 0.364 mmol), and DBU (0.22 mL, 1.47 mmol) in THF (5.8 mL) for 16 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 2/1) to give **216** (126.1 mg, 68%) as a colorless oil. IR (neat) 2954, 2248, 1760, 1719, 1422, 1256, 1038, 775 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.13 (s, 6 H), 0.87 (s, 9 H), 1.47 (s, 6 H), 3.47-3.51 (m, 2 H), 3.74 (s, 3 H), 4.22-4.26 (m, 2 H), 4.51 (s, 2 H), 6.93 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -1.9, 18.1, 25.9, 30.9, 39.4, 44.4, 52.2, 61.7, 74.4, 125.2, 153.7, 158.0, 168.0; EI-LRMS *m/z* 342 [$(M-Me)^+$], 300, 225, 213, 144, 100; EI-HRMS calcd for $C_{16}H_{28}NO_5Si$ 342.17367, found 342.17322.

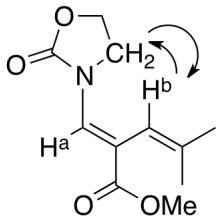
<run 5>



CH_2 → Me: 3.6% NOE
Me → CH_2: 12.4% NOE



minor
H^a → H^b: 2.5% NOE
H^b → H^a: 2.6% NOE

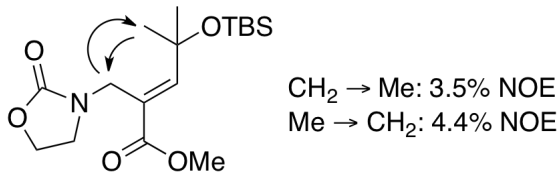


major
CH_2 → H^b: 3.4% NOE
H^b → CH_2: 1.9% NOE

According to the general procedure, a crude product, which was obtained from **209** (99.5 mg, 0.361 mmol), $Ni(cod)_2$ (98.1 mg, 0.357 mmol), and DBU (0.22 mL, 1.47 mmol) in THF (5.8 mL) for 15 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1~1/1) to give **217** (32.0 mg, 27%), ***E*-221** (28.4 mg, 35%), and ***Z*-221** (4.8 mg, 6%). **(*E*)-Methyl 4-benzyloxy-4-methyl-2-{(2-oxazolidon-3-yl)methyl}pent-2-enoate (217).** colorless oil. IR (neat) 2978, 2248, 1754, 1719, 1435, 1266, 916, 767 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.52 (s, 6 H), 3.27-3.32 (m, 2 H), 3.76 (s, 3 H), 4.07-4.11 (m, 2 H), 4.45 (s, 2 H), 4.47 (s, 2 H), 6.95 (s, 1 H), 7.24-7.36 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.0, 40.0, 44.4, 52.2, 61.7, 65.0, 75.8, 127.5, 127.7, 128.4, 138.4, 150.6, 158.0, 167.7; EI-LRMS *m/z* 318 [$(M-Me)^+$], 225, 195, 140, 108, 91;

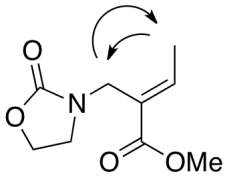
EI-HRMS calcd for $C_{17}H_{20}NO_5$ 318.13415, found 318.13436. **(*E*)-Methyl 4-methyl-2-{(2-oxazolidon-3-yl)methylidene}pent-3-enoate (*E*-221)**. colorless solid; mp. 107-109 °C (recrystallized from CH_2Cl_2/hexane); IR (film, CH_2Cl_2) 2985, 1775, 1704, 1627, 1400, 1201, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.52 (m, 3 H), 1.86 (m, 3 H), 3.72-3.77 (m, 2 H), 3.74 (s, 3 H), 4.37-4.43 (m, 2 H), 5.81 (s, 1 H), 7.88 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.7, 25.2, 43.9, 51.9, 63.0, 111.1, 117.1, 134.0, 140.0, 156.2, 168.1; EI-LRMS *m/z* 225 (M^+), 225, 193, 166, 149, 138, 120, 106; EI-HRMS calcd for $C_{11}H_{15}NO_4$ 225.10011, found 225.10009. **(*Z*)-Methyl 4-methyl-2-{(2-oxazolidon-3-yl)methylidene}pent-3-enoate (*Z*-221).** colorless oil; IR (film, CH_2Cl_2) 2917, 1767, 1712, 1624, 1401, 1158, 738 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.72 (m, 3 H), 1.82 (m, 3 H), 3.75 (s, 3 H), 3.94-3.98 (m, 2 H), 4.40-4.46 (m, 2 H), 5.78 (m, 1 H), 6.84 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.1, 26.4, 44.5, 51.9, 62.8, 111.6, 120.5, 131.9, 136.7, 156.5, 167.5; EI-LRMS *m/z* 225 $(M)^+$, 225, 193, 166, 149, 138, 120, 106; EI-HRMS calcd for $C_{11}H_{15}NO_4$ 225.10011, found 225.09994.

<run 6>



According to the general procedure, a crude product, which was obtained from **210** (107.5 mg, 0.361 mmol), $Ni(cod)_2$ (99.5 mg, 0.362 mmol), and DBU (0.22 mL, 1.47 mmol) in THF (5.8 mL) for 18 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1~1/1) to give **218** (37.6 mg, 27%) and ***E*-221** (11.0 mg, 13%). **(*E*)-Methyl 4-*tert*-butyldimethylsilyloxy-4-methyl-2-{(2-oxazolidon-3-yl)methyl}pent-2-enoate (218).** colorless oil; IR (neat) 2956, 1755, 1714, 1428, 1258, 1109, 704 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.02 (s, 9 H), 1.21 (s, 9 H), 1.78 (t, *J* = 6.9 Hz, 2 H), 3.35-3.40 (m, 2 H), 3.67 (t, *J* = 6.9 Hz, 2 H), 3.72 (s, 3 H), 4.13-4.17 (m, 2 H), 4.23 (s, 2 H), 7.05 (s, 1 H), 7.36-7.45 (m, 6 H), 7.62-7.66 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.0, 26.7, 28.5, 36.3, 39.9, 44.4, 46.2, 52.1, 60.9, 61.8, 124.9, 127.6, 129.6, 133.6, 135.5, 156.6, 158.1, 168.3; EI-LRMS *m/z* 494 $[(M\text{-}Me)^+]$, 452, 365, 268, 213, 183, 135, 107; EI-HRMS calcd for $C_{28}H_{36}NO_5Si$ 494.23627, found 464.23636.

<run 7>



CH_2 → Me: 4.9% NOE
Me → CH_2: 3.4% NOE

(*E*)-Methyl 2-{(2-oxazolidon-3-yl)methyl}but-2-enoate (219). According to the general procedure, a crude product, which was obtained from **211** (50.2 mg, 0.361 mmol), $Ni(cod)_2$ (99.4 mg, 0.361 mmol), and DBU (0.22 mL, 1.47 mmol) in THF (5.8 mL) for 1 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 1/1) to give **219** (32.0 mg, 44%) as a colorless oil. IR (neat) 2952, 1752, 1714, 1650, 1436, 1273, 1053, 761 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.99 (d, *J* = 7.3 Hz, 3 H), 3.53-3.57 (m, 2 H), 3.76 (s, 3 H), 4.17 (s, 2 H), 4.25-4.30 (m, 2 H), 7.17 (q, *J* = 7.3 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.8, 39.3, 44.8, 52.0, 61.9, 127.7, 144.5, 158.1, 167.5; EI-LRMS *m/z* 200, 199 $(M)^+$, 184 $[(M\text{-}Me)^+]$, 167, 155, 140, 123, 111, 100, 96; EI-HRMS calcd for $C_9H_{13}NO_4$ 199.08446, found 199.08402.

<run 8>

Methyl 3-methyl-2-{(2-oxazolidon-3-yl)methyl}but-2-enoate (220). According to the general procedure, a crude product, which was obtained from **212** (55.0 mg, 0.359 mmol), $Ni(cod)_2$ (99.4 mg, 0.361 mmol), and DBU (0.22 mL, 1.47 mmol) in THF (5.8 mL) for 1 h, was purified by flash column chromatography on silica gel (hexane/AcOEt = 1/1) to give **220** (45.3 mg, 59%) as a colorless oil. IR (neat) 2951, 1753, 1716, 1635, 1432, 1222, 1093, 1060, 762 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.97 (s, 3 H), 2.08 (s, 3 H), 3.47-3.51 (m, 2 H), 3.75 (s, 3 H), 4.17 (s, 2 H), 4.25-4.30 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.7, 23.5, 42.7, 44.2, 51.6, 61.8, 122.3, 151.6, 158.1, 167.5; EI-LRMS *m/z* 213 $(M)^+$, 181 $[(M\text{-}MeO\text{-}H)^+]$, 153, 125, 110, 100, 95; EI-HRMS calcd for $C_{10}H_{15}NO_4$ 213.10011, found 213.10018.

<Scheme 38>

Methyl *N*-benzyl-*N*-(propa-1,2-dien-1-yl)carbamate (199). To a solution of **222** (1.44 g, 9.91 mmol) in CH_2Cl_2 (40 mL) were added $NaHCO_3$ (2.54 g, 30.2 mmol) and $ClCO_2Me$ (1.15 mL, 14.9 mmol), and the mixture was stirred at room temperature for 24 h. To the mixture was added H_2O, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was roughly purified by short column chromatography on silica gel (CH_2Cl_2) to give crude 16 (1.92 g), which was dissolved in DMF (40 mL). To the DMF solution

was added ^{t}BuOK (339.3 mg, 3.02 mmol) at room temperature, and the mixture was stirred at the same temperature for 30 min. To the mixture was added saturated NH_4Cl aqueous solution, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified flash column chromatography on silica gel (hexane/AcOEt = 20/1) to give **199** (832.3 mg, 2 steps 41%) as a colorless oil. IR (neat) 2955, 1962, 1711, 1465, 1311, 1228 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, 100 °C) δ 3.73 (s, 3 H), 4.56 (s, 2 H), 5.35 (d, J = 6.3 Hz, 2 H), 7.09 (t, J = 6.3 Hz, 1 H), 7.20-7.26 (m, 3 H), 7.29-7.34 (m, 2 H); ^{13}C NMR (125 MHz, DMSO-d_6, 100 °C) δ 47.8, 52.5, 87.1, 99.7, 126.6, 126.7, 127.8, 137.1, 153.4, 200.6; EI-LRMS *m/z* 203 $(M)^+$, 202, 188, 158, 144, 115, 91; EI-HRMS calcd for $C_{12}H_{12}NO_2$ 202.08680, found 202.08649.

<Scheme 39>

***N*-Benzyl-4,4-dimethylpent-2-yn-1-amine (225).** A solution of **224**[57] (7.00 g, 36.8 mmol) in hexane (6 mL) was added to neat $BnNH_2$ (24 mL, 220 mmol) at 0 °C, and mixture was stirred at room temperature for 18 h. After the mixture was concentrated in vacuo, the residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1) to give **225** (4.65 g, 63%) as a colorless oil. IR (neat) 3322, 2968, 2226, 1742, 1455, 1362, 1263, 737, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (s, 9 H), 3.40 (s, 2 H), 3.86 (s, 2 H), 7.24-7.36 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.4, 31.2, 37.8, 52.3, 76.2, 92.5, 127.0, 128.36, 128.42, 139.7; EI-LRMS *m/z* 200 $[(M-H)^+]$, 186, 158, 144, 110, 91; EI-HRMS calcd for $C_{14}H_{18}N$ 200.14392, found 200.14332.

Methyl *N*-benzyl-*N*-(4,4-dimethylpenta-1,2-dien-1-yl)carbamate (202). Similar to the synthesis of **199** from **222**, a crude product, which was obtained from **225** (5.20 g, 25.8 mmol), $ClCO_2Me$ (3 mL, 38.9 mmol), $NaHCO_3$ (6.51g, 77.5 mmol), CH_2Cl_2 (50 mL) for 14 h, was roughly purified by short column chromatography on silica gel (CH_2Cl_2) to give crude **226** (6.55 g), which was dissolved in DMF (50 mL). To the DMF solution was added ^{t}BuOK (2.13 g, 19.0 mmol) at room temperature, and the mixture was stirred at the same temperature for 3 h. After the usual work-up, a crude product was purified flash column chromatography on silica gel (hexane/AcOEt = 20/1) to give **202** (3.09 g, 2 steps 46%) as a colorless solid. mp. 49-50 °C (recrystallized from hexane); IR (neat) 2960, 1963, 1704, 1340, 1265, 739 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6, at 100 °C) δ 0.88 (s, 9 H), 3.74 (s, 3 H), 4.57 (s, 2 H), 5.68 (d, J = 5.7 Hz, 1 H), 7.08 (d, J = 5.7 Hz, 1 H), 7.15-7.25 (m, 3 H), 7.27-7.33 (m, 2 H); ^{13}C NMR (125 MHz, DMSO-d_6, at 100 °C) δ 28.6, 31.9, 47.6, 52.5, 100.9,

114.2, 126.0, 126.3, 127.7, 137.1, 153.6, 190.4; EI-LRMS *m/z* 259 (M^+), 244, 216, 202, 170, 144, 91; EI-HRMS calcd for $C_{16}H_{21}NO_2$ 259.15723, found 259.15748.

<Scheme 40>

Methyl 2-[{*N*-benzyl-*N*-(methoxycarbonyl)amino}methyl]-4,4-dimethylpentanoate (227). To a solution of **203** (*E*:*Z* = 91:9, 31.9 mg, 99.9 μmol) in AcOEt (2 mL) was added $Pd(OH)_2$/C (20 w/w% on charcoal, 10.0 g, 7.12 mmol), and the mixture was stirred at room temperature for 8 h. After the Pd catalyst was removed by filtration through silica gel pad, the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1~4/1) to give **227** (30.8 mg, 96%) as colorless oil. IR (neat) 2953, 1736, 1708, 1475, 1237, 1119, 701 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, at 100 °C) δ 0.83 (s, 9 H), 1.16 (dd, *J* = 3.0, 14.3 Hz, 1 H), 1.62 (dd, *J* = 9.1, 14.3 Hz, 1 H), 2.77 (dddd, *J* = 3.0, 5.8, 9.1, 9.1 Hz, 1 H), 3.25 (dd, *J* = 5.8, 14.0 Hz, 1 H), 3.26 (dd, *J* = 9.1, 14.0 Hz, 1 H), 3.60 (s, 3 H), 3.65 (s, 3 H), 4.31 (d, *J* = 15.5 Hz, 1 H), 4.53 (d, *J* = 15.5, 1 H), 7.20-7.36 (m, 5 H); ^{13}C NMR (125 MHz, DMSO-d_6, at 100 °C) δ 28.5, 29.7, 40.4, 42.6, 50.1, 50.2, 50.8, 51.8, 126.6, 126.8, 127.9, 137.3, 155.9, 174.6; EI-LRMS *m/z* 321 $(M)^+$, 290, 274, 262, 230, 178, 91; EI-HRMS calcd for $C_{18}H_{27}NO_2$ 321.19401, found 321.19357.

<Scheme 41>

***tert*-Butyl *N*-benzyl-*N*-(4,4-dimethylpenta-1,2-dien-1-yl)carbamate (205).** To a solution of **225** (780 mg, 3.88 mmol) in CH_2Cl_2 (16 mL) was added $(Boc)_2O$ (1.27 g, 5.82 mmol), and the mixture was stirred at room temperature for 22 h. To the mixture was added saturated Na_2CO_3 aqueous solution was added, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by short column chromatography on silica gel (hexane/AcOEt = 10/1) to give crude **228** (1.29 g), which was dissolved in DMF (20 mL). To the DMF solution was added ^{t}BuOK (646.0 mg, 5.76 mmol) at room temperature, and the mixture was stirred at the same temperature for 7 h. After the usual work-up, a crude product was purified flash column chromatography on silica gel (hexane/AcOEt = 20/1) to give **205** (767.1 mg, 2 steps 65%) as a colorless oil. IR (neat) 2961, 1962, 1704, 1445, 1165, 894 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6, at 100 °C) δ 0.89 (s, 9 H), 1.44 (s, 9 H), 4.52 (s, 2 H), 5.67 (d, *J* = 6.0 Hz, 1 H), 7.09 (d, *J* = 6.0 Hz, 1 H), 7.15-7.25 (m, 3 H), 7.27-7.33 (m, 2 H); ^{13}C NMR (125 MHz, DMSO-d_6, at 100 °C) δ 27.4, 28.6, 31.9, 47.4, 80.2, 101.2,

114.0, 125.9, 126.1, 127.6, 137.5, 152.0, 190.2; EI-LRMS *m/z* 301 (M^+), 245, 230, 200, 188, 144, 91; EI-HRMS calcd for $C_{19}H_{27}NO_2$ 301.20418, found 301.20405.

<Scheme 42>

3-(4,4-Dimethylpenta-1,2-dien-1-yl)oxazolidin-2-one (206). To a suspension of NaH (60% in mineral oil, 358.7 mg, 8.97 mmol) in DMF (30 mL) was added **229** (764 mg, 8.77 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 min. To the mixture was added a solution of **224** (1.51g, 7.96 mmol) in DMF (10 mL) at 0 °C, and the resulting mixture was stirred at room temperature for 16 h. To the mixture was added saturated NH_4Cl aqueous solution, and the organic layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4 dry, and concentrated. The residue was roughly purified by short column chromatography on silica gel (AcOEt) to give crude **230** (1.52 g), which was dissolved in DMF (15 mL). To the DMF solution was added ^{t}BuOK (499.4 mg, 4.45 mmo) at room temperature, and the mixture was stirred at the same temperature for 41 h. After the usual work-up, a crude product was purified flash column chromatography on silica gel (hexane/AcOEt = 4/1) to give **206** (609 mg, 2 steps 42%) as a colorless solid. mp 51-52 °C (recrystallized from hexane); IR (film, CH_2Cl_2) 2962, 1966, 1753, 1450, 1236, 1056, 738 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9 H), 3.50-3.62 (m, 2 H), 4.37-4.46 (m, 2 H), 5.82 (d, *J* = 5.7 Hz, 1 H), 6.86 (d, *J* = 5.7 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 29.7, 32.9, 43.1, 62.1, 98.1, 115.5, 155.3, 191.5; EI-LRMS *m/z* 181 (M^+), 166, 122, 94, 81; EI-HRMS calcd for $C_{10}H_{15}NO_2$ 181.11028, found 181.10978.

1-(4,4-Dimethylpenta-1,2-dien-1-yl)-2-pyridone (207). To a solution of **231** (1.05 g, 5.53 mmol) in DMF (25 mL) were added **224** (491.3 mg, 5.17 mmol) and K_2CO_3 (1.38 g, 9.99 mmol) at room temperature, and the mixture was stirred at 60 °C for 4 days. To the mixture was added saturated NH_4Cl aqueous solution, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine dried over Na_2SO_4, and concentrated. The residue was roughly purified by short column chromatography on silica gel (hexane/AcOEt = 2/1~1/1) to give crude **232** (400 mg), which was dissolved in DMF (8 mL). To the DMF solution was added ^{t}BuOK (150 mg, 1.36 mmol), and the mixture was stirred at room temperature for 5 h. After the usual work-up, a crude product was purified flash column chromatography on silica gel (hexane/AcOEt = 2/1~1/1) to give **207** (49.9 mg, 2 steps 5% yield) as a black oil. IR (neat) 3476, 2961, 1962, 1666, 1591, 1537, 1260, 1067 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (s, 9 H), 6.01 (d, *J* = 6.3 Hz, 1 H), 6.19 (m, 1 H),

6.59 (m, 1 H), 7.26 (m, 1 H), 7.46 (m, 1 H) 7.71 (d, J = 6.3 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 29.8, 33.6, 47.6, 98.9, 106.6, 117.0, 121.2, 132.7, 138.9, 160.9, 193.2; EI-LRMS *m/z* 189 (M^+), 174, 130, 96; EI-HRMS calcd for $C_{12}H_{15}NO$ 189.11536, found 189.11552.

<Scheme 43>

6-*tert*-Butyldiphenylsilyloxy-4,4-dimethylhex-2-yn-1-ol (236). To a solution of **233** (6.69 g, 18.8 mmol) in CH_2Cl_2 (40 mL) were added MS4A (10.6 g) and NMO (3.21 g, 27.4 mmol), and the mixture was stirred at room temperature for 10 min. To the suspension were added TPAP (202.2 mg, 0.573 mmol), and the mixture was stirred at same temperature for 1.5 h. After filtration through Celite® pad, and the filtrate was concentrated. The residue was roughly purified by short column chromatography on silica gel (CH_2Cl_2) to give crude **234** (6.63 g). To a solution of PPh_3 (19.4 g, 74.9 mmol) in CH_2Cl_2 (36 mL) was added a solution of CBr_4 (12.2 g, 36.8 mmol) in CH_2Cl_2 (20 mL) at 0 °C, and the mixture was stirred at the same temperature for 15 min. To the mixture was added a solution of **234** (6.63 g) in CH_2Cl_2 (20 mL) at 0 °C, and the mixture was stirred at the same temperature for 30 min. After additional stirring at room temperature for 2 h, the mixture was diluted with AcOEt. After the mixture was filtered through short column packed with a mixture of Celite® and silica gel (1/1), and the filtrate was concentrated. The residue was purified by short column chromatography on silica (hexane/AcOEt = 10/1) to give **235** (8.18 g), which was dissolved in THF (80 mL). To the THF solution was added a solution of BuLi (1.58 M, 22.5 mL, 35.6 mmol) in hexane at -78 °C, and the mixture was stirred at the same temperature for 1 h, then warmed to room temperature over 30 min. To the mixture was added paraformaldehyde (4.74 g, 158 mmol) at -78 °C, and the mixture was stirred at an ambient temperature for 15 h. To the mixture was added saturated NH_4Cl aqueous solution, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1) to give **236** (2.65 g, 3 steps 37%) as colorless oil. IR (neat) 3343, 2931, 1960, 1890, 1824, 1589, 1428, 1110, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04 (s, 9 H), 1.17 (s, 6 H), 1.72 (t, J = 7.3 Hz, 2 H), 3.85 (t, J = 7.3 Hz, 2 H), 4.12-4.15 (m, 2 H), 7.36-7.45 (m, 6 H), 7.66-7.70 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.1, 26.8, 29.6, 29.8, 45.1, 51.3, 61.6, 92.8, 127.6, 129.5 133.9, 135.6; EI-LRMS *m/z* 323 [(M-^{t}Bu)$^+$], 305, 237, 199, 139, 91; EI-HRMS calcd for $C_{20}H_{23}O_2Si$ 323.14673, found 323.14659.

3-(6-*tert*-Butyldiphenylsilyloxy-4,4-dimethylhexa-1,2-dien-1-yl)oxazolidin-2-one (208).
To a solution of **236** (1.45 g, 3.80 mmol) in CH_2Cl_2 (19 mL) were successively added Et_3N (0.64 mL, 4.59 mmol) and MsCl (0.35 mL, 4.52 mmol), and the mixture was stirred at 0 °C for 30 min. To the mixture was added H_2O, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was roughly purified by short column chromatography on silica gel (CH_2Cl_2) to give crude **237** (1.80 g). To a suspension of NaH (60% dispersion in mineral oil, 206.9 mg, 5.17 mmol) in DMF (7.5 mL) was added **229** (340.3 mg, 3.91 mmol), and the mixture was stirred at 1 h. To the mixture was added a solution of **237** (1.80 g) in DMF (7.5 mL), and the mixture was stirred at room temperature for 3 h. To the mixture was added saturated NH_4Cl aqueous solution, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by short column chromatography on silica gel to give crude **238** (1.70 g), which was dissolved in DMF (19 mL). To the DMF solution was added ^{t}BuOK (120.4 mg, 1.07 mmol) at room temperature, and the mixture was stirred at room temperature for 1 min. After the usual work-up, a crude product was purified by flash column chromatography on silica gel (hexane/AcOEt= 2/1) to give **208** (1.04 g, 3 steps 61% yield) as a colorless oil. IR (film CH_2Cl_2) 2960, 1965, 1760, 1446, 1112, 704 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.97 (s, 3 H), 1.00 (s, 3 H), 1.03 (s, 9 H), 1.58-1.61 (m, 2 H), 3.20-3.33 (m, 2 H), 3.63-3.73 (m, 2 H), 4.20-4.30 (m, 2 H), 5.70 (d, J = 6.0 Hz, 1 H), 6.78 (d, J = 6.0 Hz, 1 H), 7.36-7.46 (m, 6 H), 7.62-7.69 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.0, 26.7, 27.3, 28.3, 34.9, 43.0, 44.7, 61.1, 62.1, 98.2, 114.1, 127.61, 127.63, 129.6, 133.8, 135.50, 135.53, 155.2, 192.1; EI-LRMS *m/z* 434 [$(M-Me)^+$], 392, 362, 314, 268, 224, 199, 167; EI-HRMS calcd for $C_{26}H_{32}NO_3Si$ 434.21514, found 434.21429.

<Scheme 44>

4-Benzyloxy-4-methylpent-2-yn-1-ol (241). To a suspension of NaH (2.02 g, 50.5 mmol) in THF (100 mL) was added **239** (4 mL, 41.3 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 min. To the mixture were successively added Bu_4NI (760.3 mg, 2.06 mmol) and BnBr (6 mL, 50.4 mmol) at room temperature, and the resulting mixture was stirred at the same temperature for 4 h. To the mixture was added saturated NH_4Cl aqueous solution, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by short column chromatography on silica gel (hexane/AcOEt = 20/1) to give crude **240** (7.87 g), which was dissolved in THF (80 mL). To the

THF solution was added a solution of BuLi (1.64 M, 28 mL, 45.9 mmol) at -78 °C, and the mixture was stirred at the same temperature for 30 min. To the mixture was added paraformaldehyde (1.47 g, 49.0 mmol) at -78 °C, and the mixture was stirred at an room temperature for 19 h. To the mixture was added saturated NH_4Cl aqueous solution, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by flash column (hexane/AcOEt = 4/1) to give **241** (5.01 g, 2 steps 59%) as colorless oil. IR (neat) 3390, 2984, 1953, 1246, 1156, 1058, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.55 (s, 3 H), 4.28-4.31 (m, 2 H), 4.63 (s, 2 H), 7.24-7.39 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.8, 51.1, 66.4, 70.5, 82.4, 88.0, 127.3, 127.6 128.3, 139.0; EI-LRMS *m/z* 189 $[(M-Me)^+]$, 173, 159, 145, 91; EI-HRMS calcd for $C_{12}H_{13}O_2$ 189.09155, found 189.09148.

3-(4-Benzyloxy-4-methylpenta-1,2-dien-1-yl)oxazolidin-2-one (209). To a solution of **241** (1.02 g, 4.99 mmol) in CH_2Cl_2 (20 mL) were successively added Et_3N (0.8 mL, 5.74 mmol) and MsCl (0.45 mL, 5.81 mmol), and the mixture was stirred at 0 °C for 30 min. To the mixture was added H_2O, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was roughly purified by short column chromatography on silica gel (CH_2Cl_2) to give crude **242** (1.50 g). To a suspension of NaH (60% dispersion in mineral oil, 246.7 mg, 6.17 mmol) in DMF (10 mL) was added **229** (431 mg, 4.95 mmol), and the mixture was stirred at 30 min. To the mixture was added a solution of **242** (1.50 g) in DMF (10 mL), and the mixture was stirred at room temperature for 15 h. To the mixture was added saturated NH_4Cl aqueous solution, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by short column chromatography on silica gel to give crude **243** (1.75 g), which was dissolved in DMF (20 mL). To the DMF solution was added ^{t}BuOK (153 mg, 1.36 mmol) at room temperature, and the mixture was stirred at room temperature for 30 min. After the usual work-up, a crude product was purified by flash column chromatography on silica gel (hexane/AcOEt= 2/1) to give **209** (877 mg, 3 steps 64% yield) as a colorless solid. mp 73-75 °C (recrystallized from CH_2Cl_2/Hex); IR (film, CH_2Cl_2) 2979, 1968, 1758, 1449, 1230, 1056, 737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.40 (s, 3 H), 1.41 (s, 3 H), 3.52-3.65 (m, 2 H), 4.39-4.48 (m, 4 H), 5.97 (d, J = 5.7 Hz, 1 H), 6.99 (d, J = 5.7 Hz, 1 H), 7.24-7.36 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.5, 26.7, 43.1, 62.2, 65.4, 98.9, 110.8, 127.4 (2 C), 128.4, 139.0, 155.2, 193.9; ESI-LRMS *m/z* 296 $[(M+Na)^+]$, 166; ESI-HRMS calcd for $C_{16}H_{19}NNaO_3$ 269.12571, found 296.12558.

<Scheme 45>

3-(4-*tert*-Butyldimethylsilyloxy-4-methylpenta-1,2-dien-1-yl)oxazolidin-2-one (210). Similar to that of the synthesis of **241** to **209**, a crude product, which was obtained from **244**[47] (1.27 g, 5.56 mmol), MsCl (0.52 mL, 6.72 mmol), and Et_3N (0.95 mL, 6.82 mmol) in CH_2Cl_2 (11 mL), was roughly purified by short column chromatography on silica gel (CH_2Cl_2) to give crude **245** (1.78 g). To a suspension of NaH (283.8 mg, 7.10 mmol) in DMF (11 mL) was added **229** (493 mg, 5.67 mmol), and the mixture was stirred at room temperature for 30 min. To the mixture was added a solution of **245** (1.78 g) in DMF (22 mL), and the mixture was stirred at room temperature for 3 h. To the mixture was added saturated NH_4Cl aqueous solution, and the aqueous layer was extracted with Et_2O. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was roughly purified by short column chromatography on silica gel (AcOEt) to give crude **246** (2.02 g), which was dissolved in DMF (22 mL). To the DMF solution was added ^{t}BuOK (172.7 mg, 1.54 mmol), and the mixture was stirred at room temperature for 3 h. After the usual work-up, a crude product was purified by flash column chromatography on silica gel (hexane/AcOEt = 4/1) to give **210** (908 mg, 3 steps 55% yield) as a colorless solid. mp 49-50 °C (recrystallized from heane); IR (film, CH_2Cl_2) 2929, 1970, 1761, 1450, 1229, 1055, 835, 739 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.06 (s, 6 H), 0.84 (s, 9 H), 1.31 (s, 3 H), 1.32 (s, 3 H), 3.48-3.61 (m, 2 H), 4.37-4.45 (m, 2 H), 5.93 (d, J = 6.3 Hz, 1 H), 6.88 (d, J = 6.3 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -2.27, -2.25, 17.9, 25.6, 30.3, 30.5, 43.2, 62.1, 72.5, 98.6, 113.9, 155.2, 191.2; ESI-LRMS *m/z* 320 [(M+Na)$^+$], 298, 173; ESI-HRMS calcd for $C_{15}H_{27}NNaO_3Si$ 320.16524, found 320.16538.

Chapter 2, Section 3

<Scheme 47>

<Eq. 15>

$Ni(cod)_2$ (98.7 mg, 0.359 mmol) was weighed into a flame-dried flask. To this was added THF (2.9 mL) and DBU (0.22 mL, 1.47 mmol) at 0 °C, and the flask was immersed in a liquid nitrogen bath. After the mixture had been frozen, the flask was evacuated to 0.05 mmHg. The flask was backfilled with CO_2 in a plastic balloon and the frozen mixture was slowly thawed at 0 °C. To this suspension was added a solution of **195** (81.4 mg, 0.365 mmol) in THF (2.9 mL) at 0 °C, and the resulting mixture was stirred for 1 h at the same temperature. To the mixture wad added 10% DCl/D_2O at 0 °C, and the aqueous layer was extracted with AcOEt. The organic layer was washed

with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was treated with diazomethane in MeOH according to the standard procedure. After the usual work-up, the crude product was purified by flash column chromatography on silica gel (hexane/AcOEt = 10/1~4/1) to give **196-D** (91.5 mg, 90%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.89-1.92 (m, 2 H), 2.42 (s, 3 H), 3.07 (s, 3 H), 3.71 (s, 3 H), 7.27 (d, *J* = 8.2 Hz, 2 H), 7.46 (m, 1 H), 7.63 (d, *J* = 8.2 Hz, 2 H).

<Eq. 16>

$Ni(cod)_2$ (99.6 mg, 0.362 mmol) was weighed into a flame-dried flask. To this was added THF (2.9 mL) and DBU (0.22 mL, 1.47 mmol) at 0 °C, and the flask was immersed in a liquid nitrogen bath. After the mixture had been frozen, the flask was evacuated to 0.05 mmHg. The flask was backfilled with CO_2 in a plastic balloon and the frozen mixture was slowly thawed at 0 °C. To this suspension was added a solution of **202** (93.3 mg, 0.360 mmol) in THF (2.9 mL) at 0 °C, and the resulting mixture was stirred for 21 h at the same temperature. To the mixture wad added 10% DCl/D_2O at 0 °C, and the aqueous layer was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was treated with diazomethane in MeOH according to the standard procedure. After the usual work-up, the crude product was purified by flash column chromatography on silica gel (hexane/AcOEt = 20/1~4/1) to give **203-D** (111.2 mg, 84%, *E*:*Z* = 87:13). ***E*-203-D**: ^{1}H NMR (500 MHz, DMSO-d_6, at 100 °C) δ 1.09 (s, 9 H), 3.60 (s, 3 H), 3.64 (s, 3 H), 4.33 (s, 1 H), 4.41 (s, 2 H), 6.63 (s, 1 H), 7.14-7.35 (m, 5 H). ***Z*-203-D**: ^{1}H NMR (500 MHz, DMSO-d_6, at 100 °C) δ 1.04 (s, 9 H), 3.64 (s, 3 H), 3.66 (s, 3 H), 3.91 (s, 1 H), 4.39 (s, 2 H), 5.49 (s, 1 H), 7.14-7.35 (m, 5 H).

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