博士論文

4-アレナールの不斉ヒドロアシル化の反応機構に関する研究及び ローダサイクル中間体を経由するアレン-アルキン-カルボニル間の 分子内環化反応の開発

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略語表

本論文中以下の略語を使用した。

Ac	: acetyl
aq.	: aqueous solution
Ar	: aryl
BAr^F	: tetrakis[3,5-bis(trifluoromethyl)phenyl]borate
BINAP	: 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
BIPHEP	: 2,2'-bis(diphenylphosphino)-1,1'-biphenyl
Bn	: benzyl
Boc	: *t*-butoxycarbonyl
BSA	: *N*,*O*-bis(trimethylsilyl)acetamide
Bu	: butyl
°C	: degrees Celsius
cat.	: catalytic or catalyst
CBS	: Corey-Bakshi-Shibata
Cbz	: carbobenzoxy
cm	: centimeter(s)
cod	: 1,5-cyclooctadiene
COSY	: correlation spectroscopy
Cp	: cyclopentadienyl
Cp*	: pentamethylcyclopentadienyl
DIAD	: diisopropyl azodicarboxylate
DIBAL-H	: diisobutylaluminium hydride
DMF	: *N,N*-dimethylformamide
DMP	: Dess-Martin periodinane
DM-SEGPHOS	: 5,5'-bis[di(3,5-xylyl)phosphino]-4,4'-bi-1,3-benzodioxole
DMSO	: dimethyl sulfoxide
DPEPHOS	: 2,2'-bis(diphenylphosphino)diphenyl ether
DPPB	: 1,4-bis(diphenylphosphino)butane
DPPBz	: 1,2-bis(diphenylphosphino)benzene

DPPE	: 1,2-bis(diphenylphosphino)ethane
DPPF	: 1,1'-bis(diphenylphosphino)ferrocene
DPPM	: 1,1-bis(diphenylphosphino)methane
DPPP	: 1,3-bis(diphenylphosphino)methane
DTBM-SEGPHOS	: 5,5'-bis[di(3,5-di-*t*-butyl-4-methoxyphenyl)phosphino]-4,4'-bi-1,3-benzodioxole
E	: electrophile
ee	: enantiomeric excess
EI	: electron ionization
equiv.	: equivalent(s)
ESI	: electrospray ionization
Et	: ethyl
h	: hour(s)
HMBC	: hetero-nuclear multiple-bond connectivity
HMQC	: hetero-nuclear multiple quantum coherence
HPLC	: high performance liquid chromatography
HRMS	: high resolution mass spectroscopy
i	: iso
I*i*Pr	: 1,3-bisisopropylimidazole-2-ylidene
IMes	: 1,3-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene
INADEQUATE	: incredible natural abundance double quantum transfer experiment
*i*Pr	: isopropyl
IR	: infrared absorption spectrometry
LHMDS	: lithium hexamethyldisilazide
Ln	: ligand
LRMS	: low resolution mass spectroscopy
M	: metal
m	: meta
*m*CPBA	: *m*-chloroperoxybenzoic acid
MOM	: methoxymethyl
Me	: methyl
Me-DuPHOS	: 1,2-bis[(2*R*,5*R*)-2,5-dimethylphospholano]benzene
min	: minute(s)

mp : melting point
MS : molecular sieves
MTPA : α-methoxy-α-(trifluoromethyl)phenylacetyl
n : normal
nbd : 2,5-norbornadiene
NBSH : 2-nitrobenzenesulfonylhydrazide
NCS : *N*-chlorosuccinimide
NHC : *N*-heterocyclic carbene
NMR : nuclear magnetic resonance
Nu : nucleophile
o : ortho
p : para
PCC : pyridinium chlorochromate
Ph : phenyl
Piv : pivaloyl
PPTS : pyridinium *p*-toluenesulfonate
Pr : propyl
quant. : quantitative yield
R : substituent
rt : room temperature
sat. : saturated
SEGPHOS : 5,5′-bis(diphenylphosphino)-4,4′-bi-1,3-benzodioxole
SIPr : 1,3-bis(2,6-diisopropylphenyl)-4,5-dihydroimidazol-2-ylidene
TBAF : tetrabutylammonium fluoride
TBDPS : *t*-butyldiphenylsilyl
TBS : *t*-butyldimethylsilyl
t : tertiary
Tf : trifluoromethanesulfonyl
THACl : tetrahexylammonium chloride
THP : tetrahydropyranyl
THF : tetrahydrofuran
TLC : thin-layer chromatography
TMS : trimethylsilyl

Tol	: tolyl
Ts	: *p*-toluenesulfonyl

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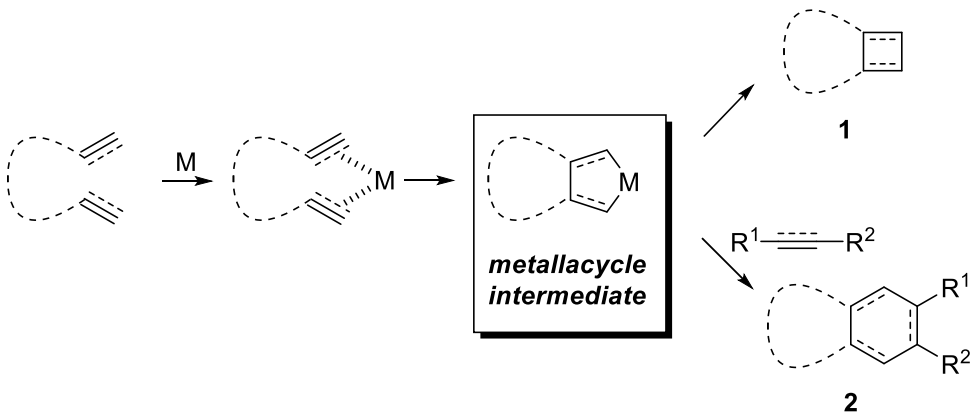
序論

有機化学は、有機化合物の製法、構造、用途、性質について研究を行なう学問である。有機化学の中でも、有機合成化学は、医薬品や機能性材料など我々の身の回りにある様々な有機化合物を簡便かつ効率的に合成するべく発展してきた研究領域である。最近になって、有機合成化学は有機金属化学を取り入れることによって、従来困難であった反応を次々と実現している。2001 年、2005 年、そして 2010 年のノーベル化学賞ではいずれも遷移金属錯体の特性を巧みに利用した有機合成反応の開発が受賞対象に選ばれており、有機金属化学が有機合成化学の発展に大きく寄与したことは言うまでもない。

遷移金属錯体を用いた反応は多岐にわたるが、金属を含む環状の中間体、いわゆるメタラサイクル中間体を経由する反応が数多く報告されている (Scheme 1)[1]。メタラサイクル中間体は一般に、二つの多重結合が金属に酸化的環化付加することによって形成される。この中間体は反応性が高く、様々な反応に利用される。例えば、この中間体から還元的脱離が進行すると 4 員環骨格 **1** を形成する。また、この中間体に多重結合が挿入すると、6 員環化合物 **2** が得られることも知られている。

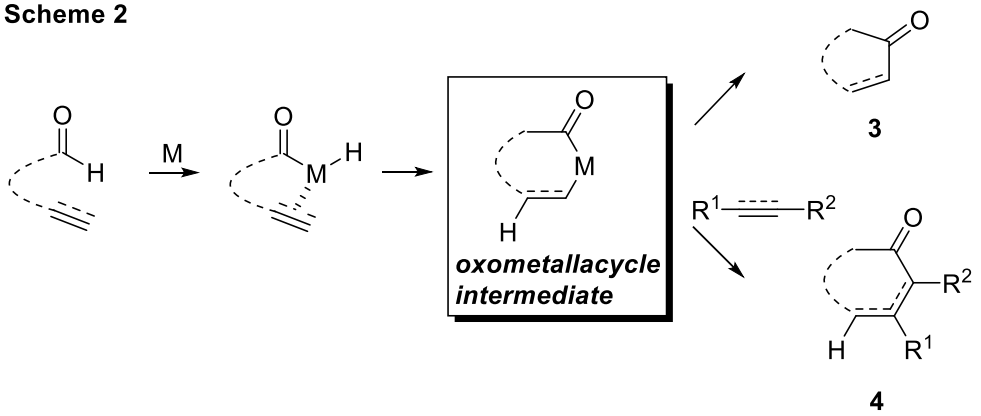
Scheme 1



ところで、メタラサイクル中間体の中には、金属原子のα位にカルボニル基を有するオキソメタラサイクル中間体も知られている。この中間体の生成法はいくつか知られており、その一つとして分子内に多重結合を有するアルデヒドと金属錯体との反応が挙げられる。この反応では、アルデヒドの C-H 結合が金属に酸化的付加し、アシル金属中間体が形成される。続いて、分子内で多重結合が挿入することによってオキソメタラサイクル中間体が形成される (Scheme 2)。この中間体からの直接還元的脱離、あるいは中間体にさらに多重結合が挿入し、環化体 **3**、**4** が生成することも報告さ

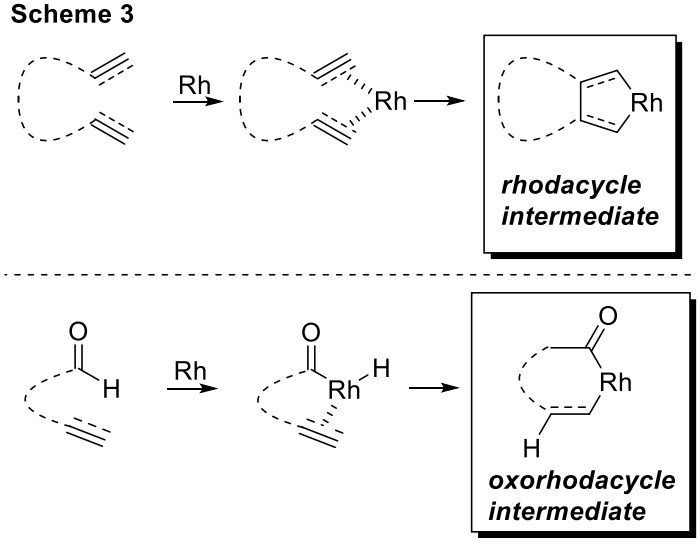
れている[23]。

Scheme 2



このような背景のもと、今回筆者は新たな環化反応の開発を目指し、Rh(I)錯体によって形成されるこれら二つのメタラサイクル中間体、すなわち 2 つの多重結合から形成されるローダサイクル中間体、及びアルデヒドと多重結合から形成されるオキソローダサイクル中間体を経由する新規分子内環化反応についての研究を行なうことにした (Scheme 3)。

Scheme 3



以下に本論文の概略を示す。

Rh(I)触媒による 4-アレナールの分子内不斉ヒドロアシル化反応について、添加剤のニトリルが反応に与える影響を調べ、反応機構に関する考察を行なった (第一章)。次に、アレンインとカルボニル基を分子内に有する基質と Rh(I)錯体との反応を検討し、5 員環と 7 員環を含む環状化合物が収率よく得られることを見出した (第二章第一節)。さらに、本環化反応の検討途上、メタラサイクル中間体の形成を引き金とする C-H 結合の切断を伴う新たな環化反応の開発に成功した (第二章第二節)。これらの研究の詳細について以下順に記載する。

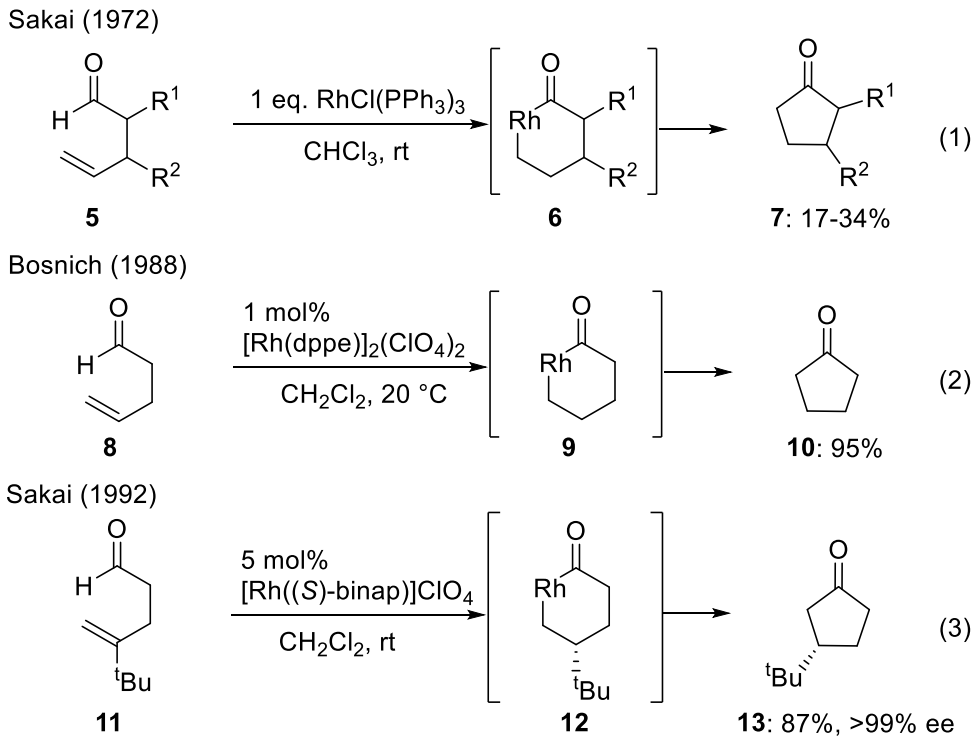
本論

第一章　Rh(I)触媒による4-アレナールの分子内不斉ヒドロアシル化反応の反応機構についての研究

第一節　研究の背景

序論で述べたように、分子内に多重結合を有するアルデヒドと金属錯体との反応では、オキソメタラサイクル中間体を経由する反応が数多く報告されている。中でも、この中間体から直接還元的脱離が進行するヒドロアシル化反応は、環状ケトンの合成法として盛んに研究されてきた。1972年酒井らは、基質**5**を当量のWilkinson錯体存在下で反応を行なうと、オキソローダサイクル中間体**6**からの還元的脱離が進行し、5員環化合物**7**が得られることを見出した(Scheme 4, eq. 1)[4a]。また、1988年Bosnichらはカチオン性Rh錯体を用いると、本反応が触媒的に進行することを見出した(Scheme 4, eq. 2)[4b]。また、光学活性なRh錯体を用いた不斉ヒドロアシル化反応も報告されている(Scheme 4, eq. 3)[4c]。

Scheme 4

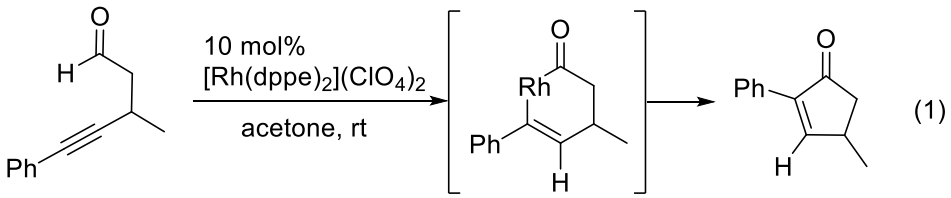


一方、多重結合として、アルケンの代わりにアルキンを用いた分子内ヒドロアシル化反応も知ら

れている。例えば2001年Fu、田中らは、4-アルキナール **14** とカチオン性Rh錯体との反応により、シクロペンテノン誘導体 **16** が高い収率で得られることを報告している (Scheme 5, eq. 1)[5a]。本反応では先の反応とは異なり、Rh-H結合がアルキンにトランス付加して反応が進行している点が興味深い。さらに、2002年同グループは、Rh-(*R*)-tol-binap錯体を用いた1,4-ジインの非対称化を伴うヒドロアシル化反応が高立体選択的に進行することも見出した (Scheme 5, eq. 2)[5b]。

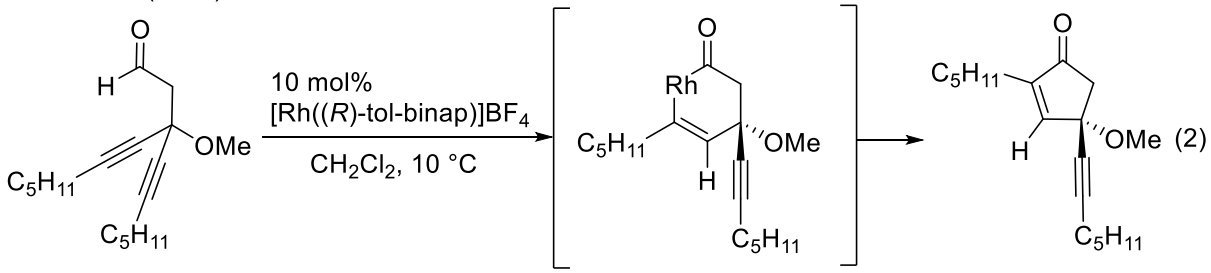
Scheme 5

Fu, Tanaka (2001)



14　　**15**　　**16**: 88%

Fu, Tanaka (2002)

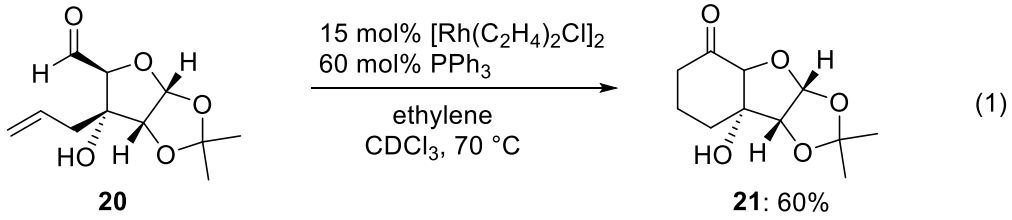


17　　**18**　　**19**: 95%, 92% ee

以上述べてきたように、分子内ヒドロアシル化反応は、5 員環骨格の効率的な合成法として盛んに研究されてきた。一方、分子内ヒドロアシル化反応を利用した6員環骨格形成反応の例は限られている。例えば、Gableらは糖誘導体である5-アルケナール **20** を用いると6員環ケトン **21** が得られることを見出している (Scheme 6, eq. 1)[6a]。また、Nicolaouらは天然物合成研究の過程で5-アルキナール **22** と化学量論量のWilkinson錯体を反応させると、6員環エノン **23** が得られることを報告している (Scheme 6, eq. 2)[6b]。さらに、2004年田中らは、6-アルキナール **24** とカチオン性Rh錯体存在下で反応させると、**25** が高収率で得られることを見出した (Scheme 6, eq. 3)[6c]。また、ごく最近Stanleyらは、アルデヒドとエキソオレフィン間のヒドロアシル化反応により、二環式化合物 **27** が良好な収率、かつ高い不斉収率で得られることを報告した (Scheme 6, eq. 4)[6d]。

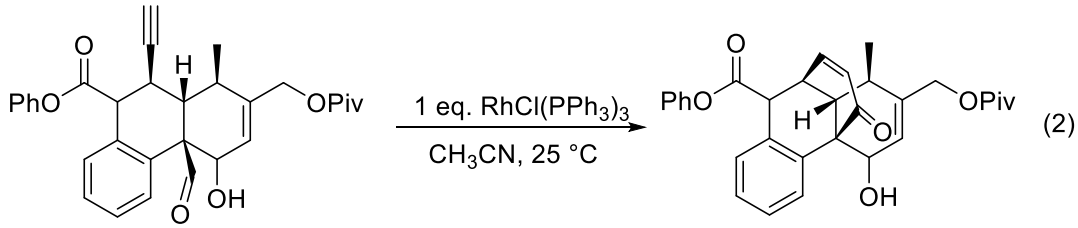
Scheme 6

Gable (1991)



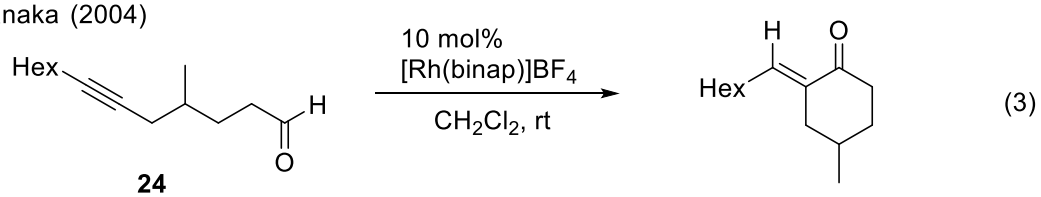
20　　**21**: 60%　(1)

Nicolaou (1996)



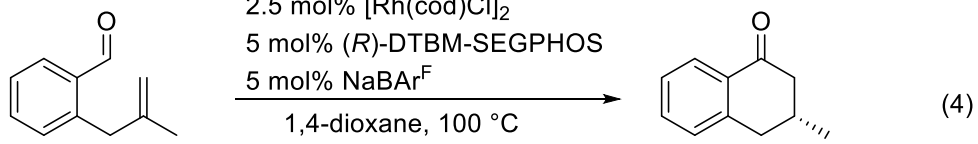
22　　**23**: 78%
(based on 50% conversion)　(2)

Tanaka (2004)



24　　**25**: 91%　(3)

Stanley (2015)

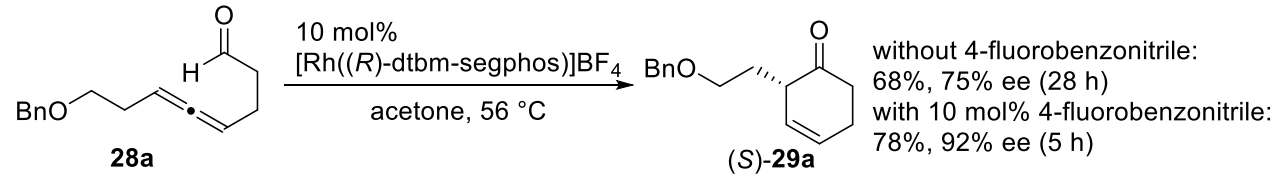


26　　**27**: 81%, 98% ee　(4)

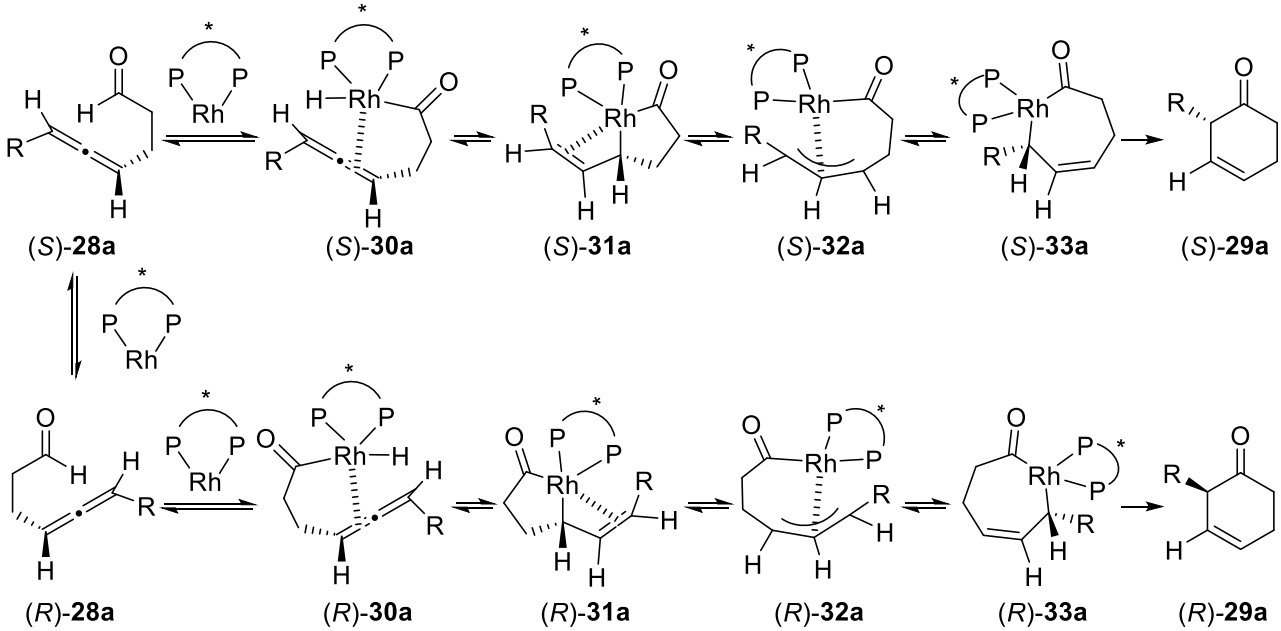
ところで、当研究室では、4-アレナール **28a** を Rh-(*R*)-dtbm-segphos 錯体存在下、アセトン中で反応を行なうと、分子内ヒドロアシル化反応が進行し、6 員環化合物 (*S*)-**29a** が高収率、かつ高い不斉収率で得られることを見出した (Scheme 7)[7]。本反応は分子内ヒドロアシル化反応において、アレンを多重結合として用いた初の例である*[1]。また、ラセミ体の 4-アレナール **28a** を用いているにも関わらず、環化体 (*S*)-**29a** が高収率かつ高い不斉収率で得られていることから、現在のところ本反応の反応機構は次のように考えている。主生成物である 6 員環ケトン (*S*)-**29a** は、(*S*)-**28a** と Rh(I)錯体から 5 員環オキソローダサイクル中間体 (*S*)-**31a** が形成され、続いて π-アリルロジウム中間体 (*S*)-**32a** を経由して 7 員環ローダサイクル中間体 (*S*)-**33a** となり、(*S*)-**33a** からの還元的脱離が進行して生成すると考えられる。一方、主生成物のエナンチオマーである (*R*)-**29a** は 4-アレナール (*R*)-**28a**

から同様の反応により生成する*[2]。ここで、得られる環化体が高収率かつ高い不斉収率であることから、本反応ではおそらく基質のアレンのラセミ化の経路が存在し*[3]、(*S*)-**28a** のみならず、(*R*)-**28a** も (*S*)-**28a** へと異性化した後、主生成物 (*S*)-**29a** へ変換されたと考えられる。さらに、本環化反応では、4-フルオロベンゾニトリルを添加剤として用いると、反応時間が短縮され、環化体の収率及び不斉収率の向上も見られることが分かっている*[4]。しかしながら、その詳細な反応機構、特にニトリルの添加効果は不明であった。そこで筆者は、反応機構の解明の一環として、ニトリルが本反応に与える影響について検討を行なうことにした。

Scheme 7



~ Reaction Mechanism ~



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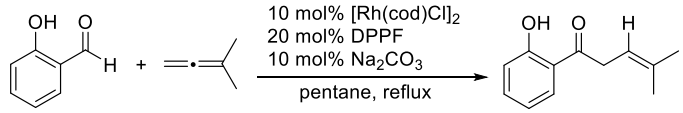
*1 多重結合としてアレンを用いた分子間ヒドロアシル化反応は、これまでに 2 例報告されている。1999 年三浦らは、Rh 触媒による、サリチルアルデヒド (**34**)と 1,1-二置換アレン **35** の分子間ヒドロアシル化反応が定量的に進行することを見出した (Scheme 8, eq. 1)[8a]。また、2008 年 Willis らは、光学活性な Rh(I)触媒によるアルデヒド **37** とアレン **38** との分子間ヒドロアシル化反応が進行することを報告している (Scheme 8, eq. 2)[8b]。本反応では、ラセミ体のアレンをアルデヒドと当量しか使用していないにもかかわらず生成物が高収率、かつ高い不斉収率で得られることから、本反応は当研究室で見出した分子内ヒドロアシル化反応と同様にアレンのラセミ化を経て進行していると考えられる。

Scheme 8

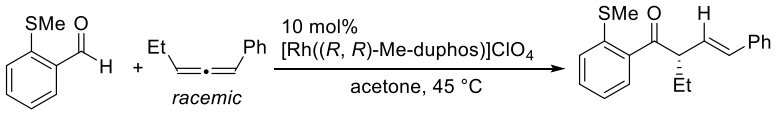
Miura (1999)



(1)

34　　**35**　　**36**: quant.

Willis (2008)

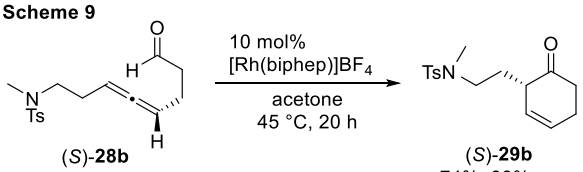


(2)

37　　**38**　　**39**: 77%, 88% ee

*2 筆者は、光学活性な基質 (*S*)-**28b** を用いてアキラルな配位子を持つ Rh(I)錯体存在下で反応を行なったところ、(*S*)体の優先絶対立体配置を持つ環化体 (*S*)-**29b** が良好な収率で得られることを確認している (Scheme 9)。この結果から、本想定反応機構において、(*S*)体の基質から (*S*)体の環化体が得られると考えている。なお、環化体の光学純度の低下が見られたのは、アキラルな配位子を持つ Rh(I)錯体存在下においても、基質のアレンのラセミ化が進行しているためであると考えられる。

Scheme 9



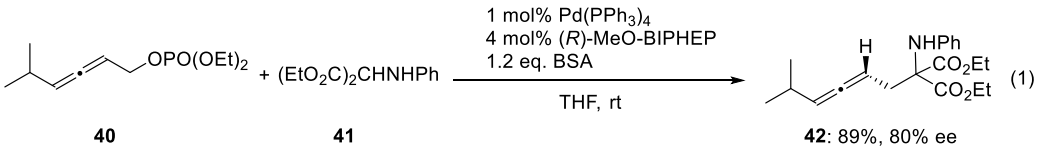
(*S*)-**28b**
>99% ee

(*S*)-**29b**
74%, 33% ee

*3 アレンのラセミ化を経由して進行する反応はいくつか報告されている。2002 年に今田及び村橋らは光学活性な Pd 錯体存在下、ラセミ体のアレン **40** とマロン酸ジエチル誘導体 **41** を反応させると、アレンのラセミ化を経由した辻-Trost 型の反応が進行することを見出している (Scheme 10, eq. 1)[9a]。その後、2005 年に Trost らは Trost 配位子を用いて本反応を行うと、カップリング体 **45** が良好な収率、かつ高い不斉収率で生成することを報告している (Scheme 10, eq. 2)[9b]。

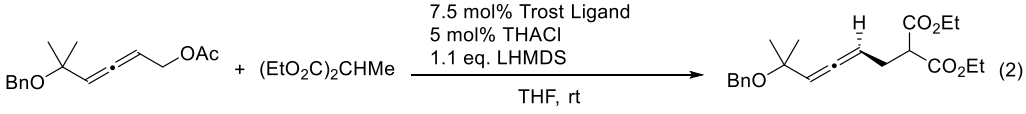
Scheme 10

Imada and Murahashi (2002)

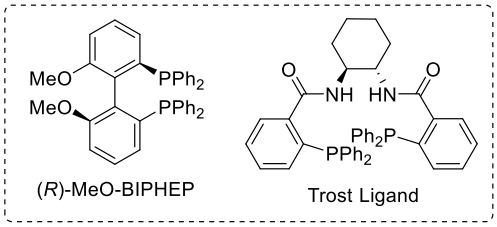


40　　**41**　　**42**: 89%, 80% ee

Trost (2005)



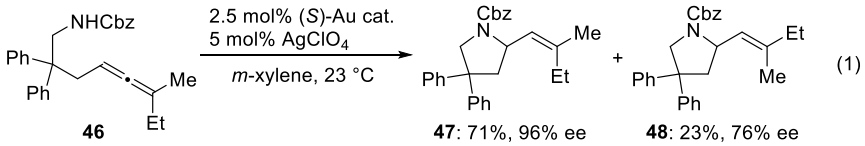
43　　**44**　　**45**: 91%, 95% ee



一方 Widenhoefer らは、光学活性な金錯体存在下でアレン **46** を用いた分子内不斉ヒドロアミノ化反応を報告している (Scheme 11, eq. 1)[10]。また、Cramer らは、Rh 錯体を用いたケトイミン **49** とアレン **50** の分子間 [3+2]環化付加反応においても、アレンのラセミ化を経由して反応が進行していることを見出している (Scheme 11, eq. 2)[11]。さらに、ごく最近 Briet らはラセミ体のアレンへのチオールの付加が立体選択的かつエナンチオ選択的に進行することを報告している (Scheme 11, eq. 3)[12]。

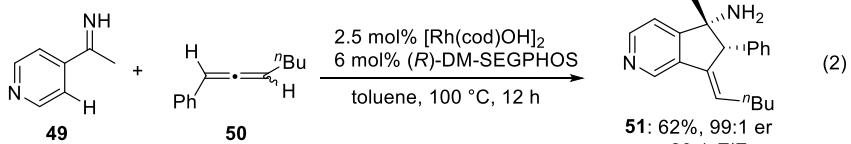
Scheme 11

Widenhoefer (2007)



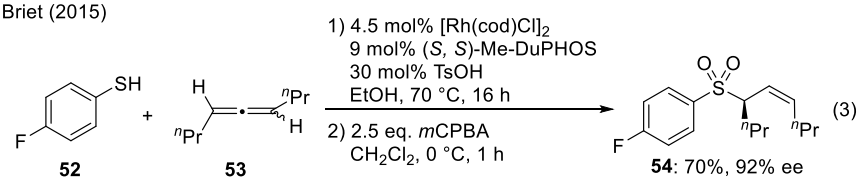
46　　**47**: 71%, 96% ee　　**48**: 23%, 76% ee

Cramer (2013)

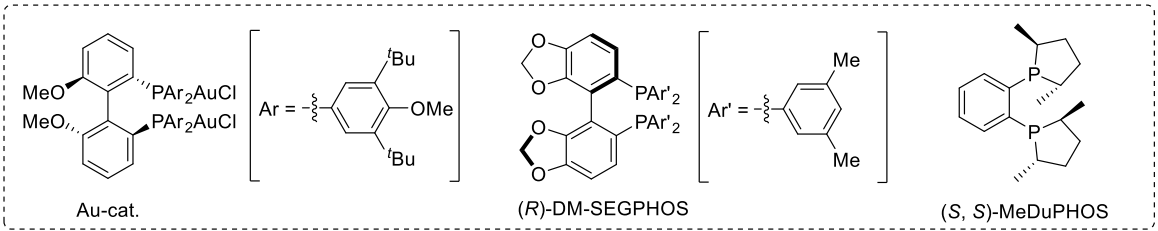


49　　**50**　　**51**: 62%, 99:1 er
>20:1 *E*/*Z*

Briet (2015)

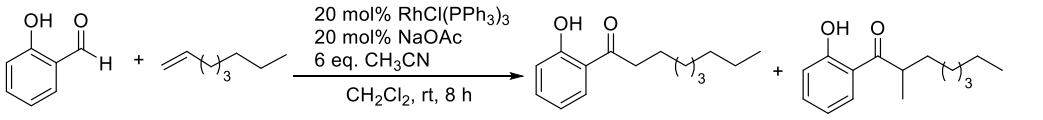


52　　**53**　　**54**: 70%, 92% ee
E/*Z* = 13/87



*[4] ニトリルの添加によりヒドロアシル化反応が促進されることは、末宗らによっても報告されている (Scheme 12)[13]。彼らは、サリチルアルデヒド (**34**)と 1-オクテン(**55**)との分子間ヒドロアシル化反応において、アセトニトリルを添加剤として用いると反応が効率的に進行し、ヒドロアシル化生成物 **56** が高収率かつ高立体選択的に得られることを見出した。また彼らは、反応系中でニトリルが Rh 錯体に配位していることを IR により観測しており、ニトリルが Rh 錯体に配位することにより、Rh 錯体の活性が向上しているのではないかと考えている。

Scheme 12
Suemune (2004)



34　　**55**

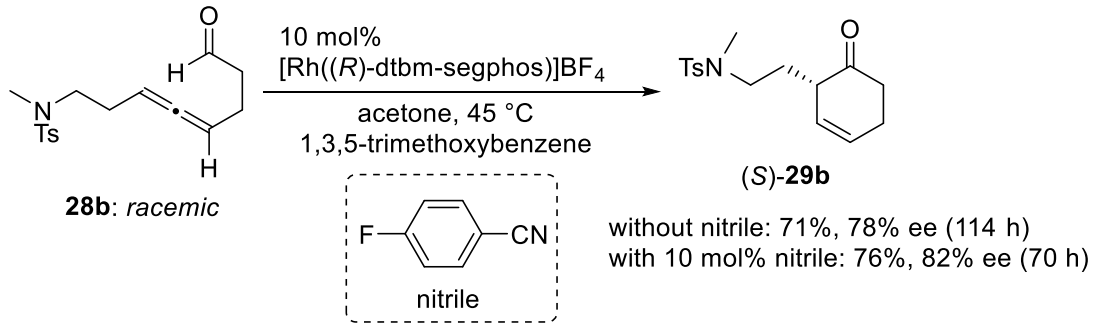
56: 86% yield (>20/1)
4% yield (in the absence of CH_3CN)

****

第二節　4-アレナールの分子内不斉ヒドロアシル化におけるニトリルの効果の検討

前節で述べたように、当研究室で見出した4-アレナールの分子内不斉ヒドロアシル化反応におけるニトリルの効果を解明すべく、反応の経時変化を調べることにした。反応の進行をHPLCで分析するため、原料及び生成物の検出が容易である基質**28b**を用いて反応を行なうことにした。ラセミ体の基質**28b**を用いて、Rh-(*R*)-dtbm-segphos錯体存在下、アセトン中、45 ℃で4-フルオロベンゾニトリルの添加及び非添加の状態で反応を行なったところ、Scheme 7に示した先の反応とは異なり、環化体 (*S*)-**29b** の収率、不斉収率に変化は見られなかったものの、ニトリル存在下において反応時間の短縮が観測された (Scheme 13)。この結果から、ニトリルの添加効果は基質によって多少異なるものの、反応時間の短縮に関与していることが示唆された。実際に反応の初期段階を比較しても、ニトリル存在下ではより速やかに基質**28b**が消失し (Figure 1, [a])、環化体が生成していることが確認された (Figure 1, [b])。一方、基質**28b**を用いた場合にはやはり環化体の不斉収率の経時変化には、ほとんど差が見られなかった (Figure 1, [d])。

Scheme 13

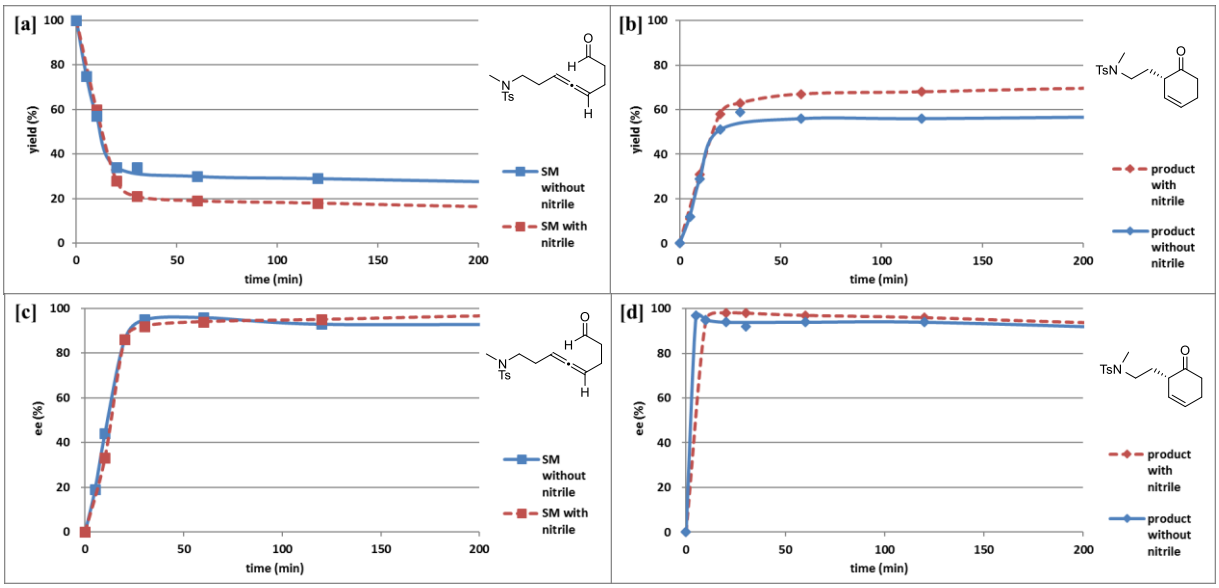


28b: *racemic*

(*S*)-**29b**

without nitrile: 71%, 78% ee (114 h)
with 10 mol% nitrile: 76%, 82% ee (70 h)

Figure 1



そこで、より詳細に本反応におけるニトリルの効果を検討すべく、光学活性な基質 (*S*)-**28b** を用いて先と同様に経時変化を観測することにした*[1]。(*R*)-DTBM-SEGPHOS を配位子として用い反応を行なったところ、この場合はニトリル存在下、非存在下にかかわらず反応は速やかに進行し、目的のヒドロアシル化体 (*S*)-**29b** がそれぞれ良好な収率、高い不斉収率で得られた (Scheme 14, eq. 1)。一方、(*S*)-DTBM-SEGPHOS を配位子として用い反応を行なったところ、先の反応とは逆の優先絶対立体配置を持つ環化体 (*R*)-**29b** が良好な収率及び不斉収率で得られた (Scheme 14, eq. 2)。また、この際ニトリル存在下、非存在下に関わらず、反応時間の延長が観察された。Scheme 9 で述べたように、筆者はアキラルな配位子を有する Rh(I)錯体と (*S*)-**28b** との反応で (*S*)-**29b** が優先して得られることを確認しており、Scheme 14 の結果から、Rh-(*R*)-dtbm-segphos 錯体を用い、(*S*)-**28b** から (*S*)-**29b** が得られる反応は matched pair であり、環化反応が速やかに進行したと考えられる。一方、(*S*)-**28b** と Rh-(*S*)-dtbm-segphos 錯体との反応は mismatched pair であり、Scheme 7 でも述べたように、基質である (*S*)体のアレンが (*R*)体へと異性化した後に環化反応が進行する経路が優先するため、基質の異性化が律速となり反応時間が延長したものと考えられる。(*S*)-DTBM-SEGPHOS を配位子として用いた際のニトリル存在下、非存在下の 2 つの反応に関して、反応初期段階の経時変化を Figure 2 に示す。ニトリル存在下では、やはり速やかに基質の (*S*)-**28b** が消費され (Figure 2, [a])、環化体 (*R*)-**29b** が生成していることがわかった (Figure 2, [b])。また、反応開始直後に基質の鏡像異性体過剰率が低下しており、このことはニトリル存在下において、速やかに (*S*)体のアレンが (*R*)体へと異性化して

いることを示している (Figure 2, [c])。しかしながら、先にも述べたように、ニトリル存在下、非存在下にかかわらず、いずれの反応も反応の完結には同様の時間を必要とした。このことは、Rh(I)触媒の活性が高い反応の初期段階では、ニトリルの効果が顕著に観察されるものの、徐々に Rh(I)触媒の活性が低下してしまうため、反応の完結に要する見た目の時間が同じなってしまったのではないかと考えられる。以上の結果から、おそらく添加剤として用いられるニトリルは環化反応の過程ではなく、主として基質の異性化を促進しているのではないかと考えられる。

Scheme 14

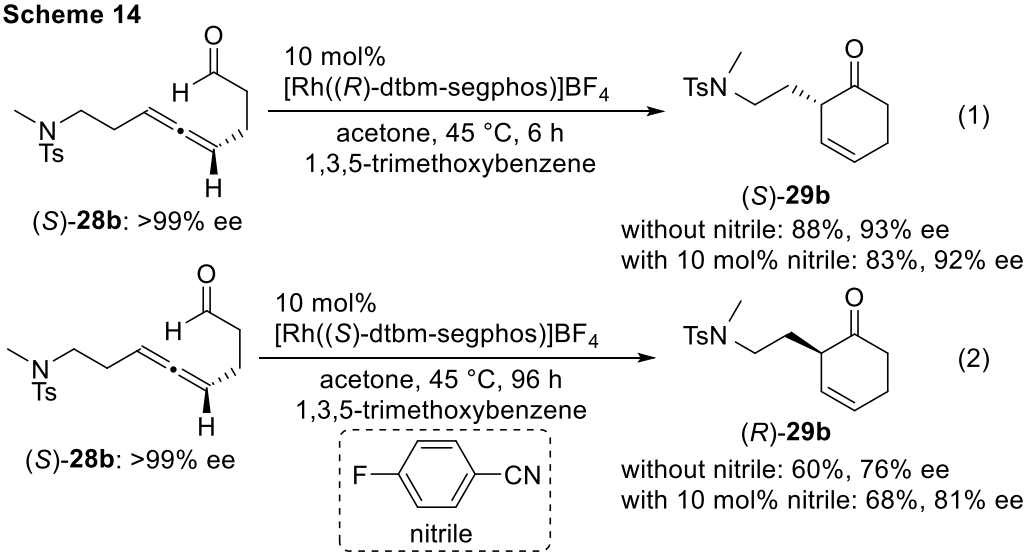
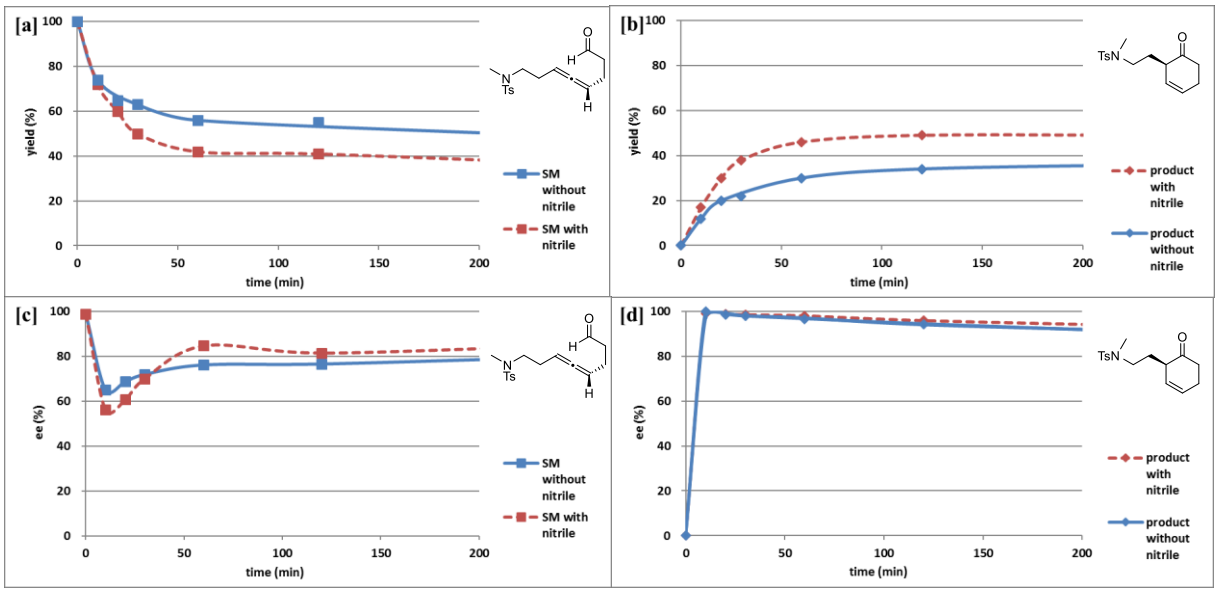


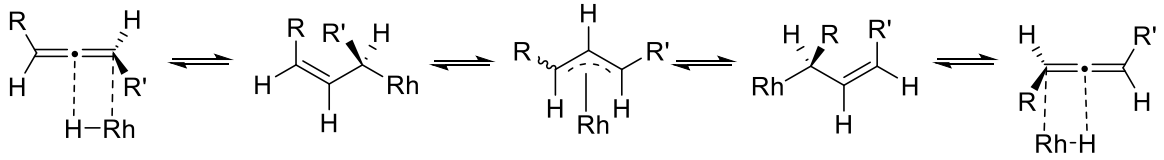
Figure 2



ところで、Rh 触媒によるアレンのラセミ化の機構については、Cramer らによって提唱されてい

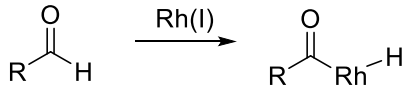
る[11]。彼らは、アレンのラセミ化に Rh-H 種が関与していると報告している (Scheme 15)。すなわち、Rh-H 錯体にアレンの二重結合が挿入し、中間体 **57** となり、π-アリル-ロジウム中間体 **58** を経由し、β-水素脱離により、アレンがラセミ化したものと考えられる。当研究室で見出したアレンの分子内ヒドロアシル化反応においても、基質のアルデヒド **28** の C-H 結合が Rh 錯体に酸化的付加する際に Rh-H 種 **60** が形成されており、Cramer らと同様の機構でアレンのラセミ化について説明することができる (Scheme 16)。また、先に述べたニトリル存在下、非存在下の経時変化の分析から、ニトリルはアレンのラセミ化を促進しているものと考えられる。その詳細は不明だが、おそらく Scheme 15 に示すラセミ化の機構において、ニトリルが Rh(I)錯体に配位し、逆供与によって Rh(I)錯体上の電子密度を低下させることで、還元的脱離による Rh-H 種とアレンの再形成を促進しているものと考えている*[2]。

Scheme 15



(*S*)-**28**　　**57**　　**58**　　**59**　　(*R*)-**28**

Scheme 16

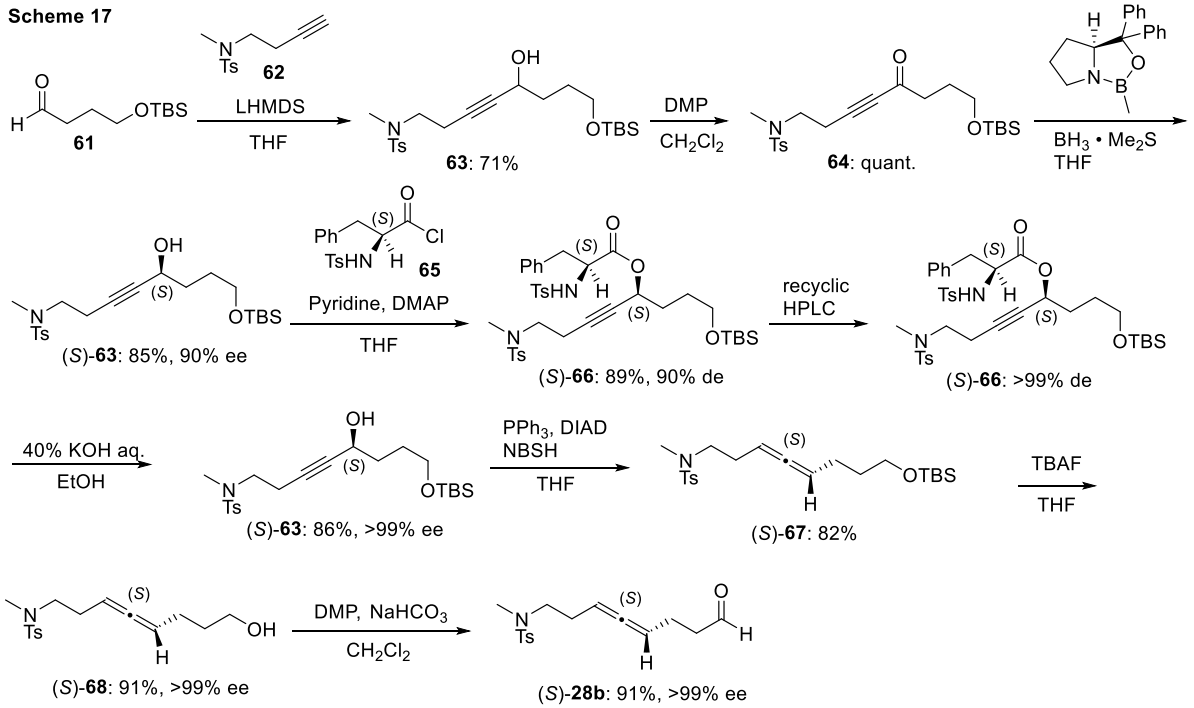


28　　**60**

以上より、筆者は当研究室で見出した Rh 触媒による 4-アレナールの分子内不斉ヒドロアシル化反応における、添加剤であるニトリルの環化反応に与える影響について、検討を行った。光学活性なアレンを有する基質を用いて反応の経時変化を測定した結果、ニトリルは基質のアレンの異性化の経路を促進していることが示唆された。

****

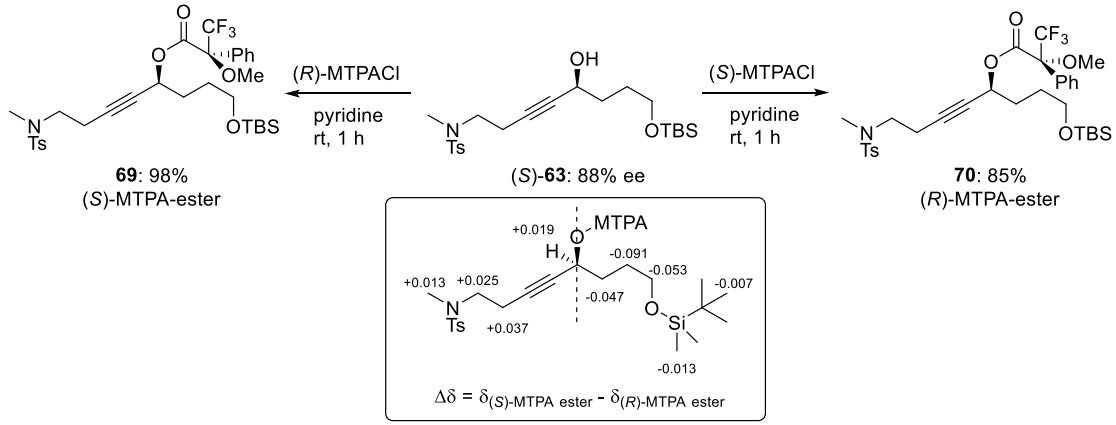
*1 基質 (*S*)-**28b** は以下のようにして合成した (Scheme 17)。文献既知のアルデヒド **61**[14] をアルキン **62**[15] とカップリングし、生成したアルコール **63** を DMP 酸化、続く CBS 還元により (*S*)-**63** を 90% ee で得た。続いて池上、橋本らの方法[16] によってジアステレオマー (*S*)-**66** とし、リサイクル型分取装置で >99% de の (*S*)-**66** を得た。続いて、エステルの加水分解でアルキニルアルコール (*S*)-**63** を得たのち、Myers の方法[17] によってアレン (*S*)-**67** へと変換した。(*S*)-**67** の TBS 基の脱保護をしたのち、生じたアルコールの Dess-Martin 酸化により (*S*)-**28b** を合成した。



なお、Myers の方法において、光学活性なアルコール体を基質とした場合、反応は光延反転と続くシグマトロピー転位により立体特異的に進行するため、本反応でも同様に (*S*)-**63** から立体選択的に (*S*)-**67** が得られたと推測した。また、アレン誘導体の絶対配置とその旋光性に関する経験則として Lowe-Brewster 則が知られている。この法則ではアレンの同一軸の 2 つの置換基の分極性の順序と、旋光度の正負からの絶対立体配置を推定することができる。例えば、(*S*)-**67** のような二置換アレンの場合には、旋光度の値が正の符号を示せば、その絶対立体配置は *S*、負の符号を示せば *R* となる。したがって (*S*)-**67** の旋光度は正の符号を示したことから、Lowe-Brewster 則を適用してもその優先絶対立体配置は *S* 配置であると推定でき、その反応機構から推測した (*S*)-**63** の絶対配置と一致する。また、(*S*)-**67** 以降の反応において軸不斉が反転することは考えられないこと、さらに (*S*)-**68**、および (*S*)-**28b** の旋光度がいずれも正の符号を示したことから、*S* 配置であると推定した。

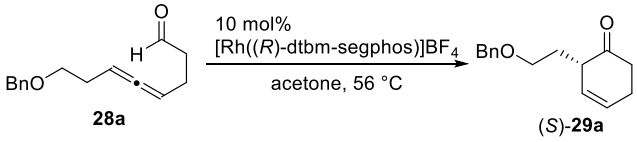
(*S*)-**63** の優先絶対配置は、(*S*)-**63** をそれぞれの MTPA エステル **69**、**70** へと導き、改良 Mosher 法[18] を適用して、得られた Δδ 値から優先絶対配置を *S* 配置と決定した (Scheme 18)。

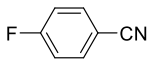
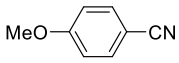
Scheme 18



*2 ニトリルが金属錯体に配位し、逆供与によって金属錯体上の電子密度を低下させる例はあまり知られていない。しかし、当研究室では、4-アレナールの分子内ヒドロアシル化反応の初期検討でニトリルの検討を行なった際、ニトリル上の置換基が反応性に影響を与えることを見出している[7]。すなわち、添加剤として 4-フルオロベンゾニトリルを用いたところ、本環化反応が良好な収率、かつ高い不斉収率で進行するのに対し、4-メトキシベンゾニトリルを添加すると、反応は完結せず、原料を回収する結果となった (Table 1, runs 1 and 2)。これはおそらく、芳香環上に電子供与基を有するため、ニトリルが Rh 錯体に配位した際、逆供与による Rh 上の電子密度の低下が十分に起こらず、アレンのラセミ化が速やかに進行しなかったためと考えられる。

Table 1. Effect of Nitrile

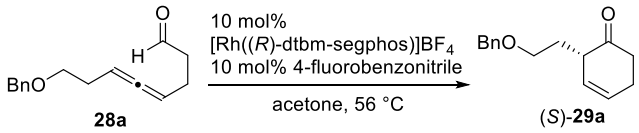


run	additive (3 eq.)	time (h)	yield (%)	ee (%)
1		13	79	90
2[a]		43	30	80

[a] 4-allenal **28a** was recovered in 24% yield.

なお、Table 1、run 1 に示した反応においてニトリルの添加量を 3 当量から触媒量に減らしたところ、環化体の収率及び不斉収率はほぼ変化せず、反応時間が短縮することが分かっている (Table 2)[7]。反応時間の短縮が見られたのは、ニトリルの Rh(I)錯体への過剰な配位がなくなったためであると考えられる。

Table 2. Effect of the Amount of 4-Fluorobenzonitrile



28a (*S*)-**29a**

run	nitrile	time (h)	yield (%)	ee (%)
1	3 eq.	13	79	90
2	30 mol%	6	79	89
3	10 mol%	5	78	92

****

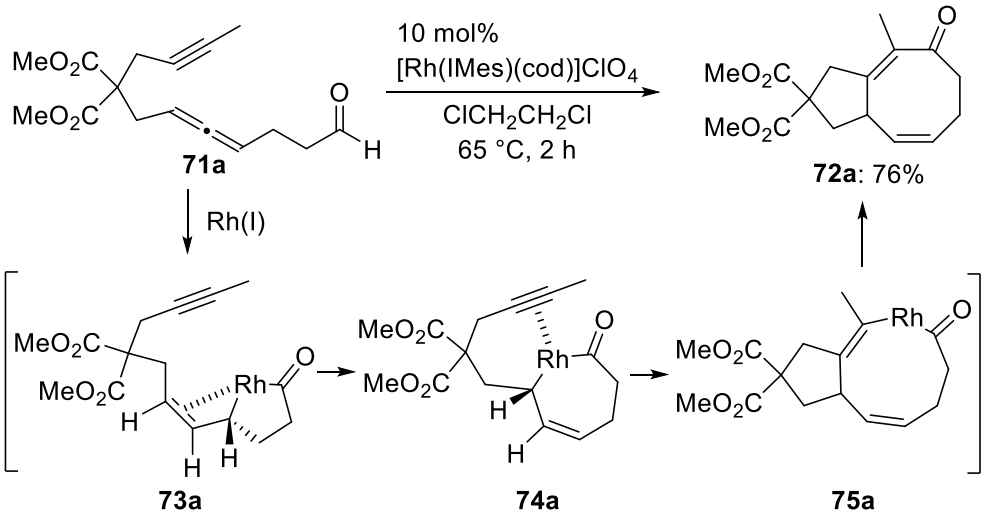
第二章　Rh(I)触媒によるアレン、アルキン、カルボニル間の分子内環化反応の開発

第一節　ローダサイクル中間体へのカルボニル基の挿入を経由する環化反応[19]

第一項　研究の背景

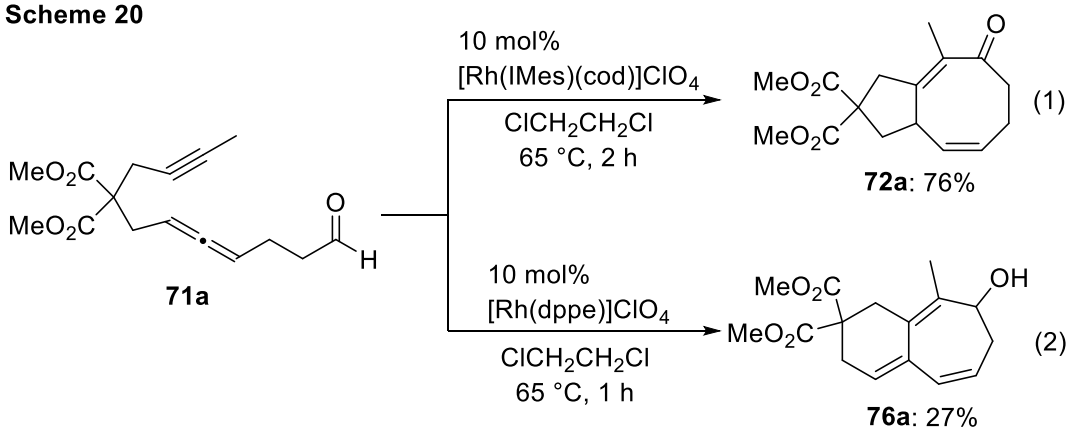
当研究室では、IMes を配位子に持つ Rh 錯体と側鎖にアルデヒドを持つアレンイン **71a** を反応させると、[6+2]環化付加反応が進行し、8 員環を含む二環式化合物 **72a** が収率よく得られることを見出し報告している (Scheme 19)[20]。この反応ではまず、基質のアルデヒドの C-H 結合が Rh 錯体に酸化的付加し、生成した Rh-H 結合へのアレンの二重結合の挿入を経て、5 員環ローダサイクル中間体 **73a** を生成する。続いて π-アリルロジウム中間体を経由して 7 員環ローダサイクル中間体 **74a** となり、この中間体 **74a** に側鎖のアルキンが挿入し、二環式化合物 **72a** が生成すると考えられる。

Scheme 19



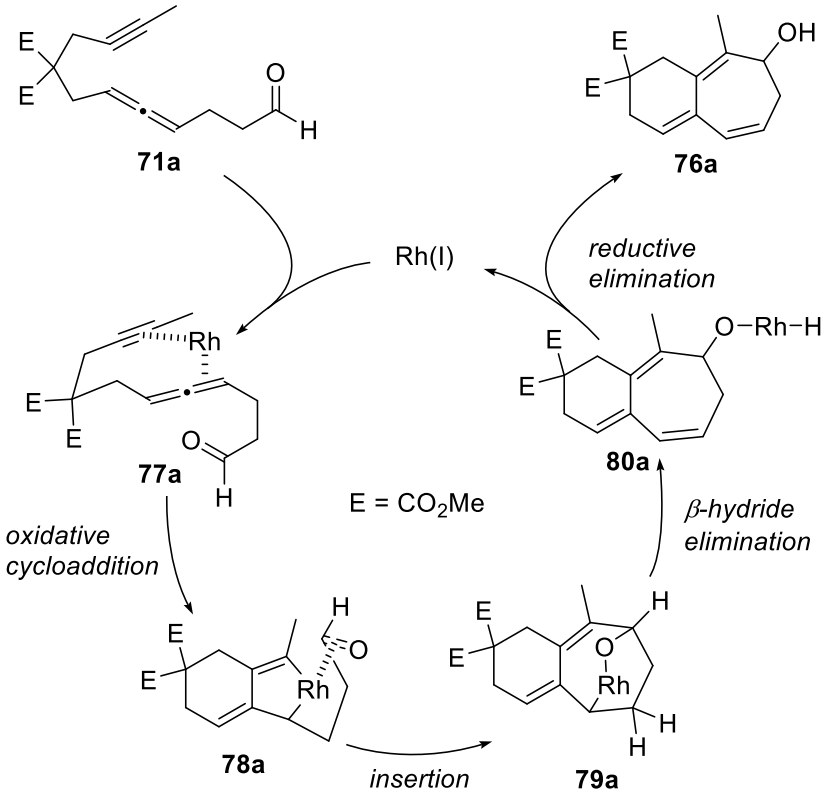
この反応の研究途上、IMes の代わりに dppe を配位子に持つ Rh 錯体を用いて反応を行なったところ、二環式化合物 **72a** は全く得られず、環サイズの異なる 6 員環と 7 員環の縮環した二環式アルコール **76a** が生成することがわかった (Scheme 20, eq. 2)。この環化体の生成は、Scheme 19 に示した[6+2]環化付加反応による機構では説明ができず、次のように考えられる (Scheme 21)。

Scheme 20



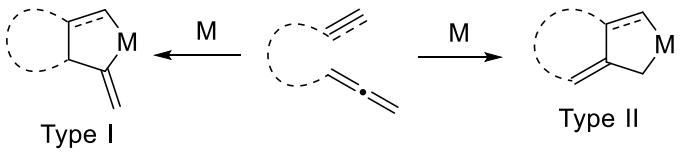
まず基質 **71a** のアレンの distal 位の二重結合*[1] とアルキンが Rh 錯体に酸化的環化付加し、ローダサイクル中間体 **78a** を生成する。次にこの中間体の C(sp^2)-Rh 結合にカルボニル基が挿入することにより、オキサローダサイクル中間体 **79a** を形成し、続いてβ-水素脱離、還元的脱離を経て反応が進行していると考えると、二環式化合物 **76a** の生成を説明することができる。本想定反応機構においては、アレンの distal 位の二重結合が Rh 触媒に選択的に酸化的環化付加し、5 員環ローダサイクル中間体 **78a** が生成する。また、ローダサイクル中間体 **78a** にカルボニル基が挿入し、非常に歪んだオキサローダサイクル中間体 **79a** を形成するという特徴をもつ。以下に、この反応機構の鍵となる 1) アレンと多重結合、金属錯体から形成されるメタラサイクル中間体を経由する環化反応及び 2) メタラサイクル中間体へのカルボニル基の挿入を伴う反応について概説する。

Scheme 21



アレンと多重結合、金属錯体から形成されるメタラサイクル中間体を経由する環化反応は数多く報告されている。アレンは二つの二重結合が連結した化合物であり、アレンと多重結合が金属錯体に酸化的環化付加して形成されるメタラサイクル中間体は、アレンの二つの二重結合のどちらが反応するかによって 2 つのメタラサイクル中間体を与える。すなわち、アレンの proximal 位の二重結合と多重結合が金属錯体と反応すれば、Scheme 22、Type I に示したメタラサイクルが生成する。一方、distal 位の二重結合と反応すれば、Scheme 22、Type II に示した環サイズの異なるメタラサイクル中間体を与える。

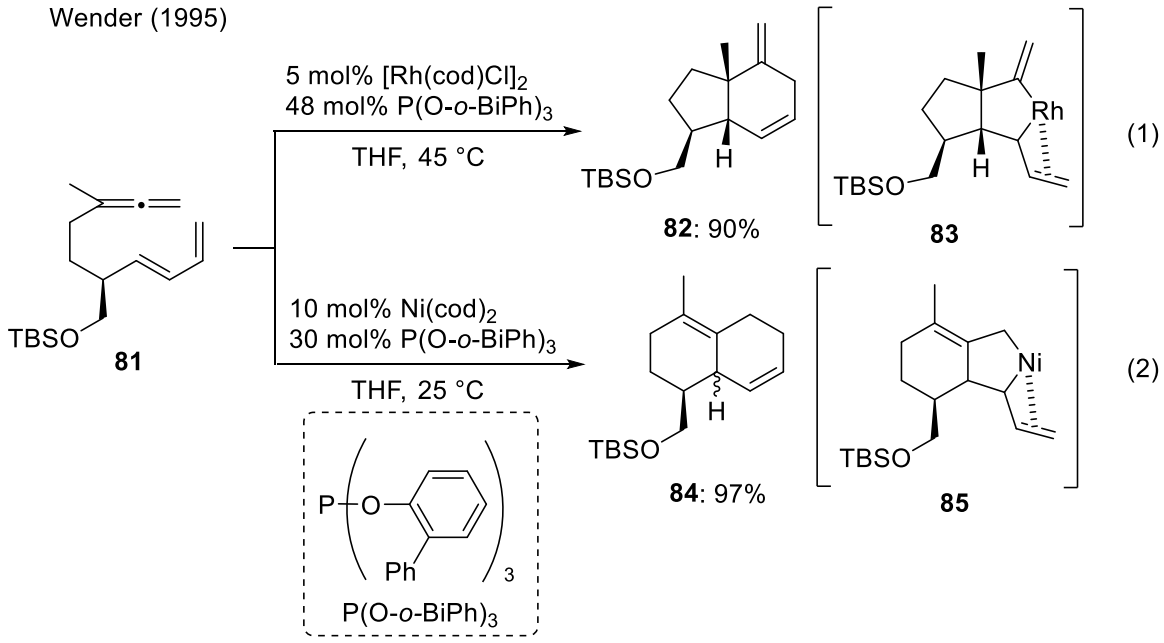
Scheme 22



例えば、Wender らは分子内にアレン、ジエンを有する基質 **81** と Rh 触媒との反応を行なうと、5 員環と 6 員環が縮環した二環式化合物 **82** が生成することを見出している (Scheme 23, eq. 1)[21]。一方、同一の基質と Ni 触媒との反応では、2 つの 6 員環が縮環した二環式化合物 **84** を与えることも見出し併せて報告している (Scheme 23, eq. 2)。この結果は、用いる金属錯体の種類によって、アレンから形成されるメタラサイクル中間体を制御していることを意味している。すなわち、Rh 触媒との反応ではアレンの proximal 位の二重結合との反応により生じたローダサイクル中間体 **83** を経由し反応が進行し、Ni 触媒を用いた場合には、アレンの distal 位の二重結合が酸化的環化付加してニッケラサイクル中間体 **85** を形成していることを示している。

Scheme 23

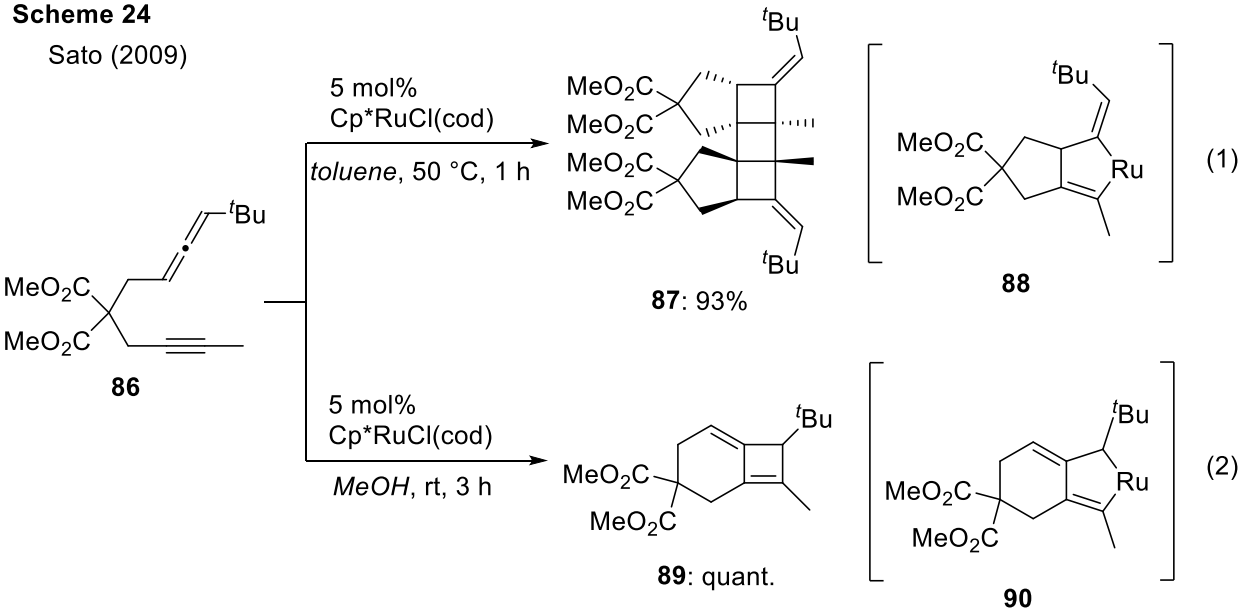
Wender (1995)



また、当研究室では、同一の基質、同一の Ru 触媒を用いて、溶媒を変えるだけで、アレンから生成するメタラサイクルを制御することに成功している。すなわち、トルエン中でアレンイン **86** と Ru 触媒との反応を行なうと、5 員環と 4 員環を含む多環式化合物 **87** が生成する (Scheme 24, eq. 1)[22a]。一方、メタノール中で反応を行なうと、6 員環と 4 員環が縮環した二環式化合物 **89** が得られることをそれぞれ見出している (Scheme 24, eq. 2)[22b]。この結果から、トルエン中ではルテナサイクル **88** を経由して反応が進行し、生成した環状化合物の二量化によって **87** を与え、一方メタノール中では、ルテナサイクル **90** の形成を経て環化反応が進行するものと考えられる。

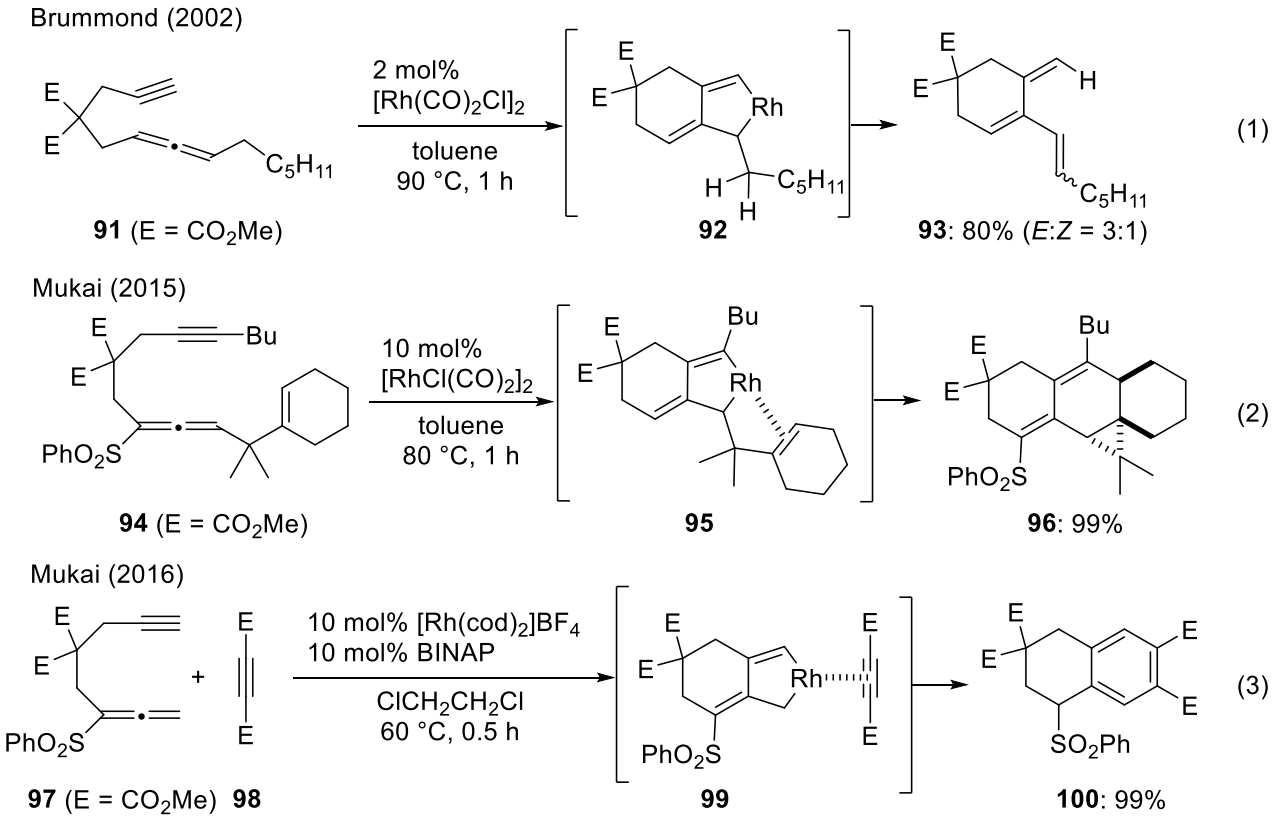
Scheme 24

Sato (2009)



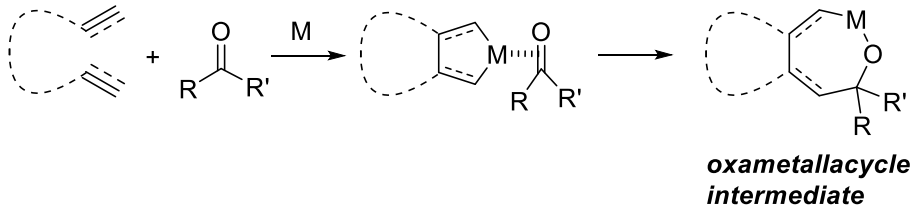
ところで、アレンとアルキンが Rh 錯体に酸化的環化付加する際には一般に、アレンの distal 位の二重結合が反応してローダサイクル中間体を形成することが知られている (Scheme 22, Type II)。例えば、2002 年 Brummond らは、分子内にアルキン、アレンを有する基質 **91** と Rh 錯体を反応させると、5 員環ローダサイクル中間体 **92** を経由し、β-水素脱離、続く還元的脱離により、環化異性化反応が進行し、トリエン **93** が得られることを報告した (Scheme 25, eq. 1)[23]。また、向らは、アレン、アルキン、アルケンを分子内に有する基質 **94** を Rh 触媒存在下で反応を行なうと、分子内[2+2+2]環化反応が速やかに進行し、3 員環を含む多環式骨格 **96** が構築されることを見出した (Scheme 25, eq. 2)[24]。また、最近彼らは、Rh 触媒によるアレンイン **97** とアルキン **98** の分子間[2+2+2]環化反応、続くオレフィンの異性化により、芳香環を含む二環式化合物 **100** がほぼ定量的に得られることも報告している (Scheme 25, eq. 3)[25]。

Scheme 25



次に、メタラサイクル中間体へのカルボニル基の挿入を伴う反応について概説する。2 つの炭素–炭素多重結合と遷移金属錯体との反応で形成されるメタラサイクル中間体へカルボニル基の挿入が進行すると、7 員環オキサメタラサイクル中間体を生成すると考えられる (Scheme 26)。しかしながら、この形式の環化反応の報告は極めて限られている。

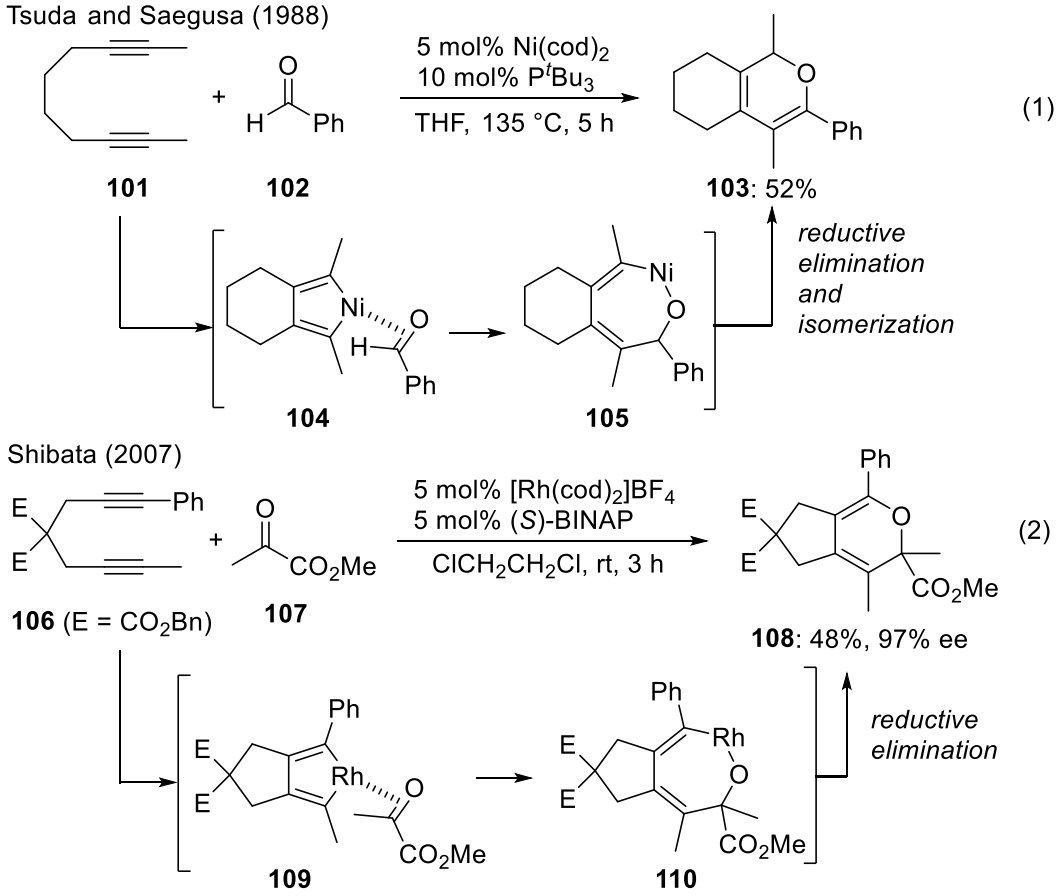
Scheme 26



例えば、1988 年津田及び三枝らは Ni 触媒存在下、ジイン **101** とベンズアルデヒド (**102**)を反応させると、ピラン環を含む二環式化合物 **103** が生成することを見出している (Scheme 27, eq. 1)[26]。また、2007 年柴田らは、ジイン **106** とピルビン酸メチル (**107**)とを Rh 触媒存在下で反応させると、

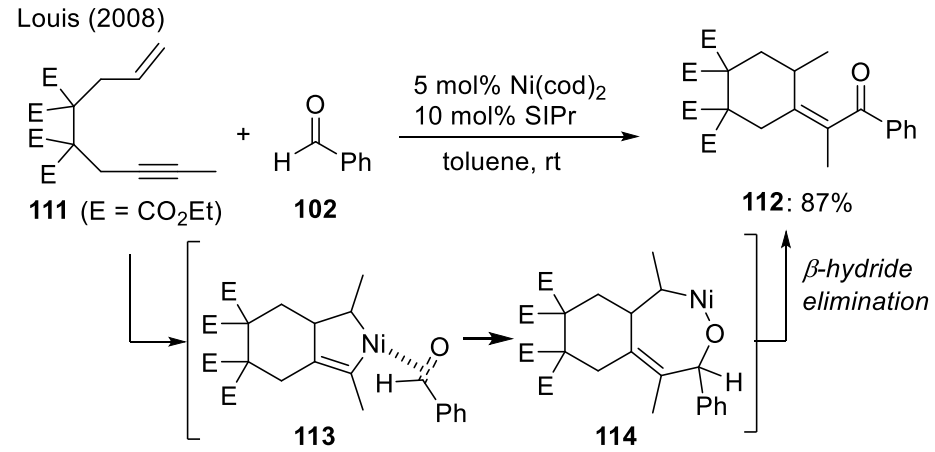
ピラン環を含む二環式化合物 **108** が得られることを報告している (Scheme 27, eq. 2)[27]。これらの反応では、ジイン **101**、**106** と金属錯体からメタラサイクル中間体 **104**、**109** を形成し、さらにカルボニル基が挿入し、オキサメタラサイクル中間体 **105**、**110** となり、このものからの還元的脱離が進行し、環化体を与える。

Scheme 27



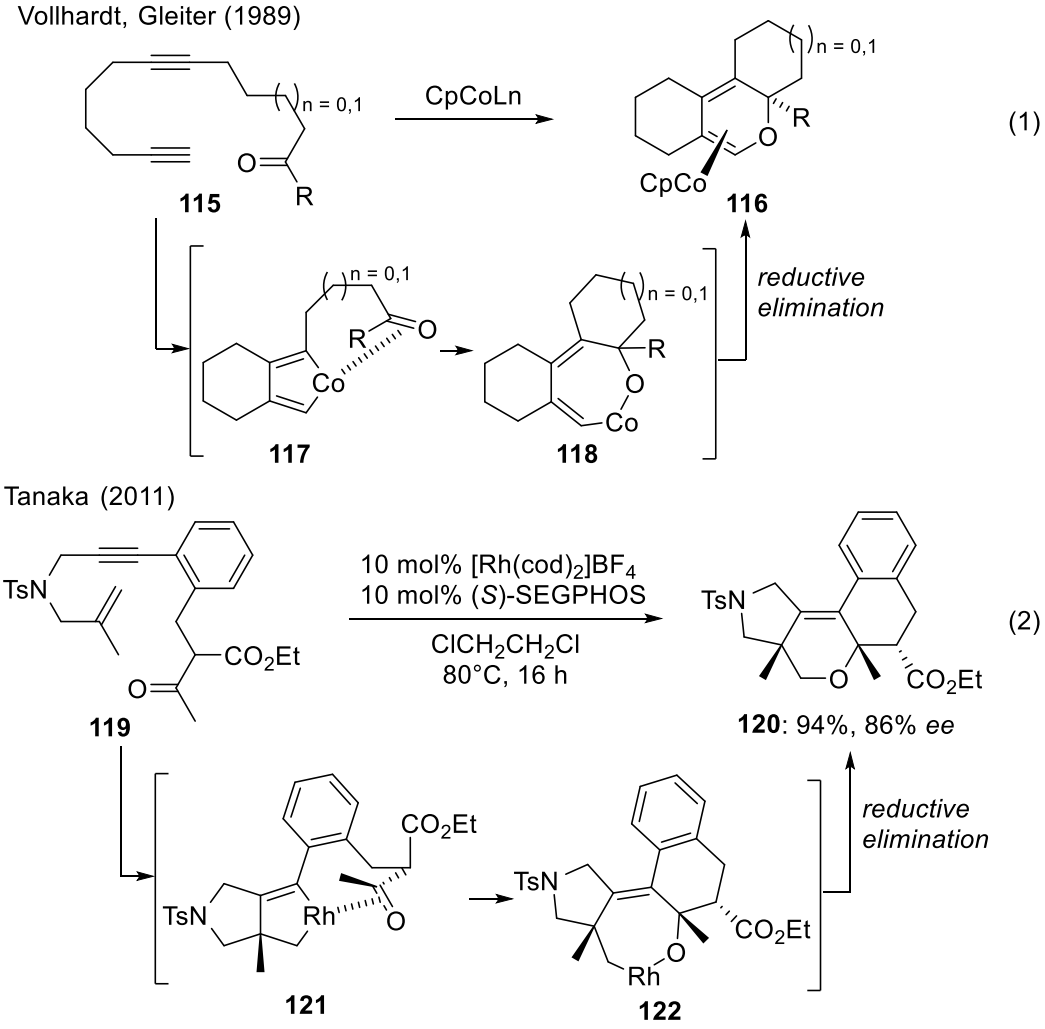
また、2008 年 Louis らは、Ni 触媒存在下、エニン **111** とベンズアルデヒド (**102**)を反応させると、エノン **112** が得られることを報告した。この反応は、先と同様に生成したオキサニッケラサイクル中間体 **114** からのβ-水素脱離が進行していると考えられる (Scheme 28)[28]。

Scheme 28



一方、メタラサイクル中間体へのカルボニル基の挿入を経由する分子内環化反応については、反応例が極めて少ない。1998 年 Vollhardt ら、および Gleiter らはそれぞれ独立に、ジインとカルボニル基を有する基質 **115** と化学量論量の Co 錯体とを反応させると、分子内[2+2+2]環化反応が進行し、ピラン環を含む三環式化合物を配位子に持つ Co 錯体 **116** が得られることを報告した (Scheme 29, eq. 1)[29]。また、2011 年に田中らは、アルケン、アルキン、カルボニル基を分子内に有する基質 **119** と光学活性な Rh 錯体との反応により、ピラン環を含む多環式化合物 **120** が良好な収率、かつ高い不斉収率で生成することを見出した (Scheme 29, eq. 2)[30]。

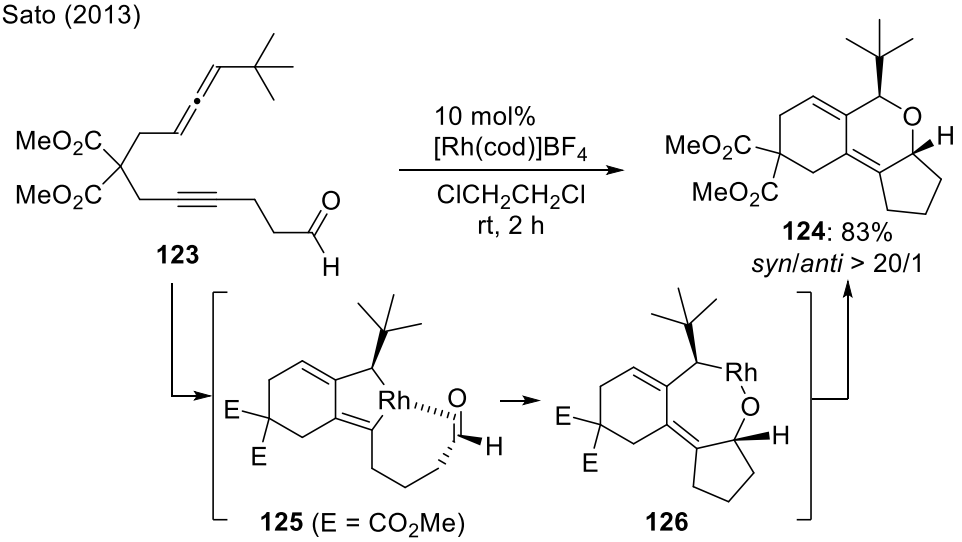
Scheme 29



また、当研究室では、分子内にアレン、アルキン、アルデヒドを有する基質 **123** と Rh 触媒との反応により、3 環式化合物 **124** が良好な収率、かつ高い立体選択性で得られることを見出した (Scheme 30)[31]。本反応は、分子内[2+2+2]環化反応において、アレンと多重結合から形成されたメタラサイクル中間体にカルボニル基が挿入する初の例である。

Scheme 30

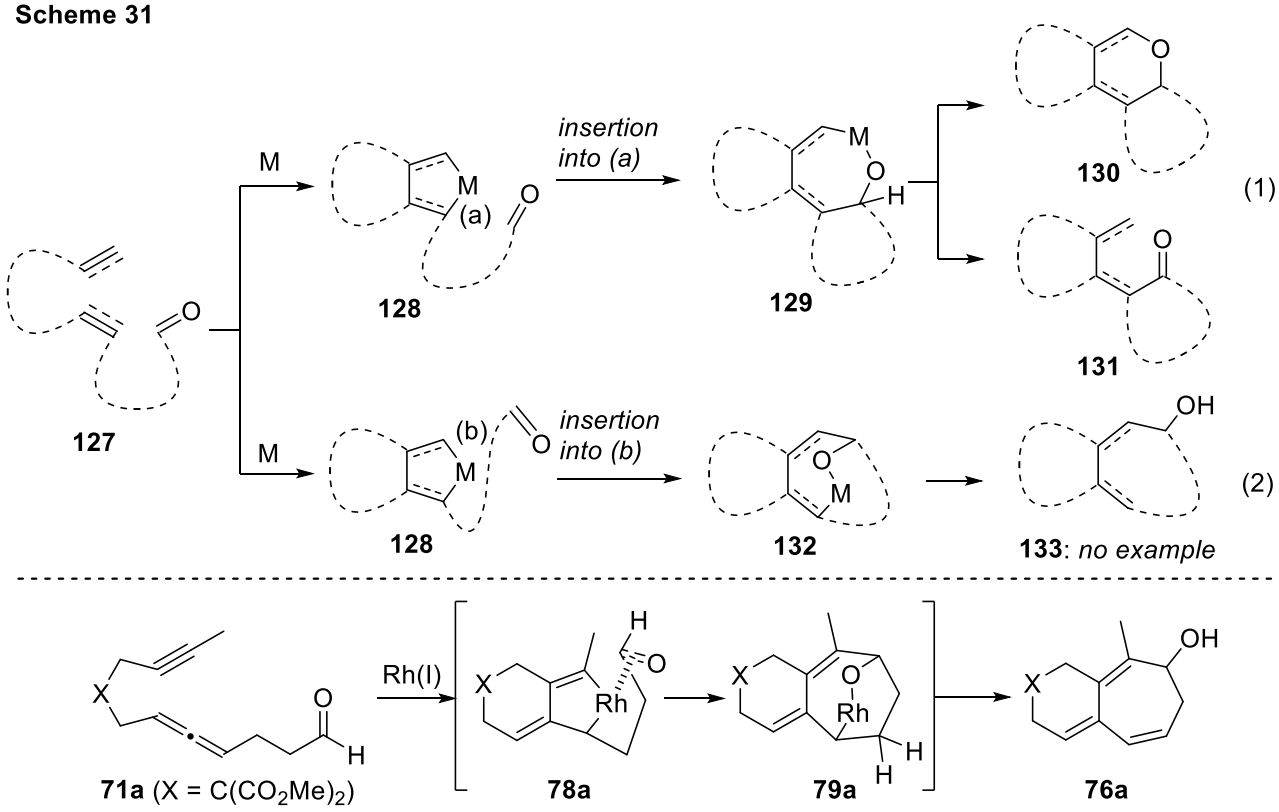
Sato (2013)



これまで述べてきたメタラサイクル中間体へのカルボニル基の挿入を経由する環化反応をまとめると、Scheme 31 のように表すことができる。すなわち、二つの炭素-炭素多重結合と遷移金属錯体から形成されたメタラサイクル中間体**128** のa で示した炭素–金属結合でカルボニル基の挿入反応が起こると、7 員環オキサメタラサイクル中間体 **129** が形成される。続いてこのものから還元的脱離が進行するとピラン環を含む環状化合物 **130** を与え、また **129** からのβ-水素脱離が進行すると開環体 **131** が生成する (Scheme 31, eq. 1)。

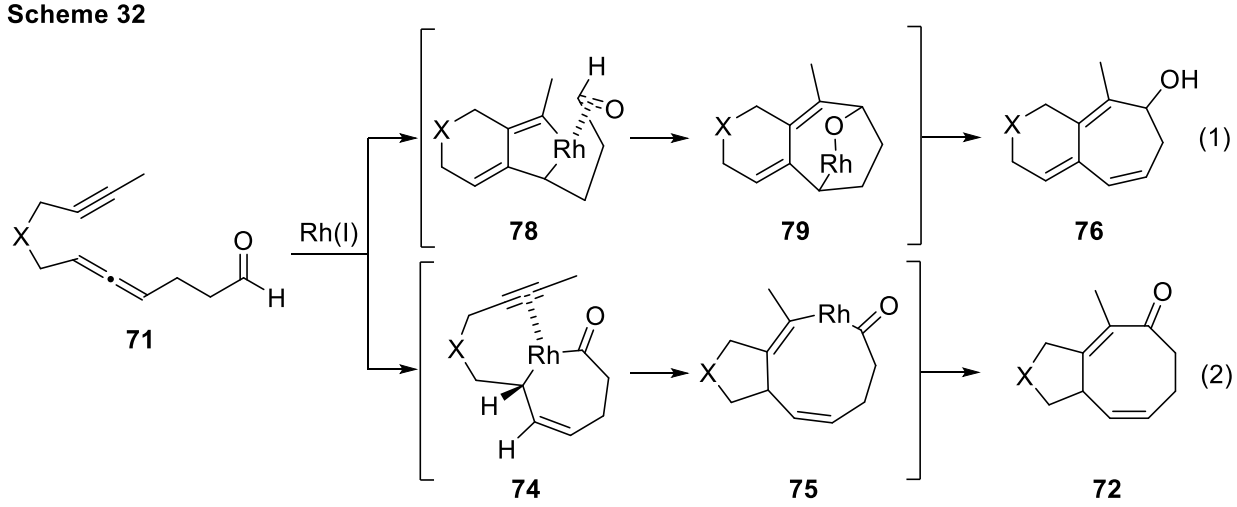
一方、Scheme 20 の eq. 2 で示した当研究室で見出した反応では、反応途中で形成されるメタラサイクル中間体 **128** の b で示す炭素-金属結合にカルボニル基が挿入し、歪んだオキサメタラサイクル中間体 **132** が生成したと考えられる (Scheme 21, Scheme 31, eq. 2)。しかしながら、これまでこのように高度に歪んだメタラサイクル中間体を経由したと考えられる反応やそのメタラサイクル自体の存在を示唆する結果は報告されていない。そこで、本反応の反応機構に興味を持ち、検討を行なうことにした。

Scheme 31



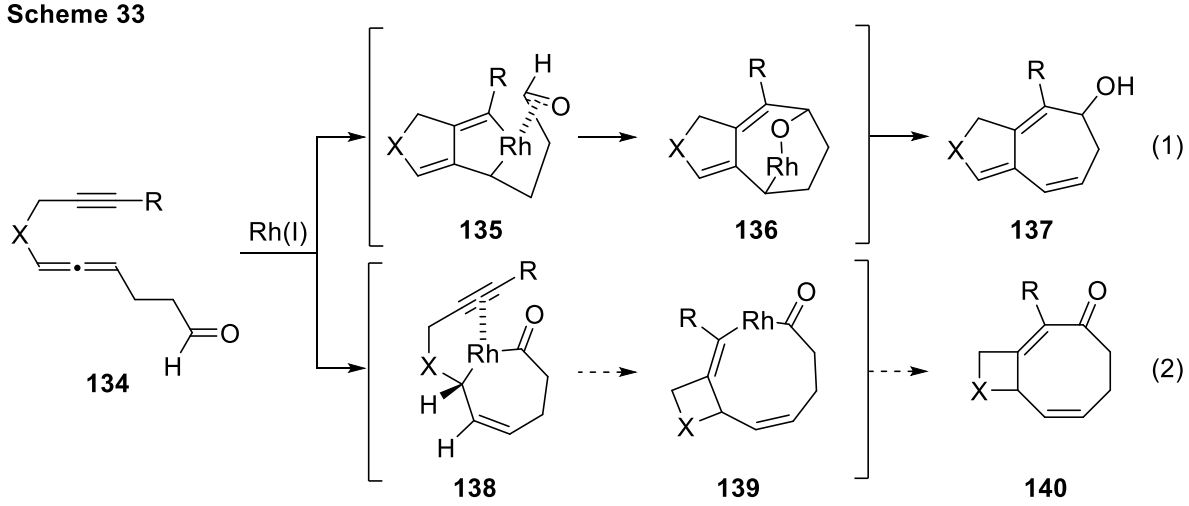
本検討を行なう際、基質 **71** を用いた場合、Scheme 32, eq. 1 に示した環化反応だけではなく、先に述べたアルデヒドとアレンとの反応で進行する[6+2]環化反応が競争反応となってしまう可能性が考えられた (Scheme 19, Scheme 32, eq. 2)。

Scheme 32



そこで筆者は、アルキンとアレンをつなぐ炭素鎖を 2 原子にした基質 **134** を新たに設計し、Rh 錯体との反応を検討することにした。この基質を用いても目的の反応が進行するならば、5 員環と 7 員環の縮環した二環式アルコール **137** が生成するものと期待される (Scheme 33, eq. 1)。一方、この基質で Scheme 33, eq. 2 に示した[6+2]環化付加反応が進行した場合は、反応の途中で 4 員環を含む非常に歪んだローダサイクル中間体 **139** を形成することになるため、この反応経路は不利になると予想される。したがって、Scheme 33, eq. 1 に示した反応が選択的に進行すると考えられ、メタラサイクル中間体 **136** の形成や想定反応機構の検証に適していると考え、研究に着手した。

Scheme 33



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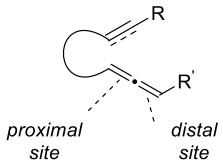
*[1] 本博士論文では、アレンの 2 つの二重結合のうち、炭素-炭素多重結合側の二重結合を proximal 位、もう一方を distal 位と定義する (Figure 3)。

Figure 3



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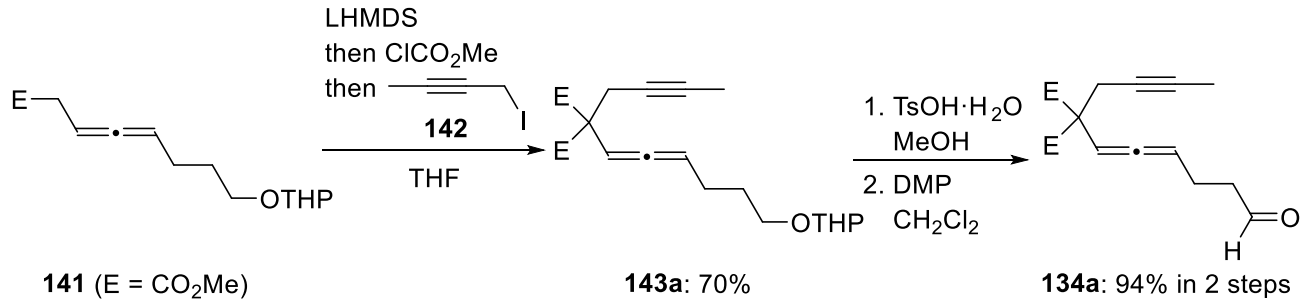
第二項　ビシクロ[5.3.0]デカトリエン骨格の構築

まず、アルキン上にメチル基を有する基質 **134a** を以下に示す方法で合成した。文献既知のアレン **141**[32] を、LHMDS で処理した後、クロロギ酸メチル、1-ヨード-2-ブチン **142**[33] と順次カップリングさせ、マロン酸エステル誘導体 **143a** を得た。続いて、THP 基の脱保護、生じたアルコールの Dess-Martin 酸化により、基質 **134a** を合成した。(Scheme 34)。

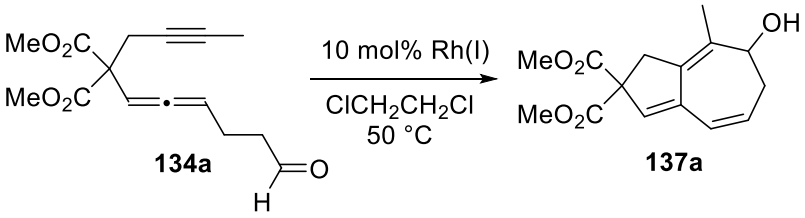
Scheme 34



141 (E = CO_2Me)　　**143a**: 70%　　**134a**: 94% in 2 steps

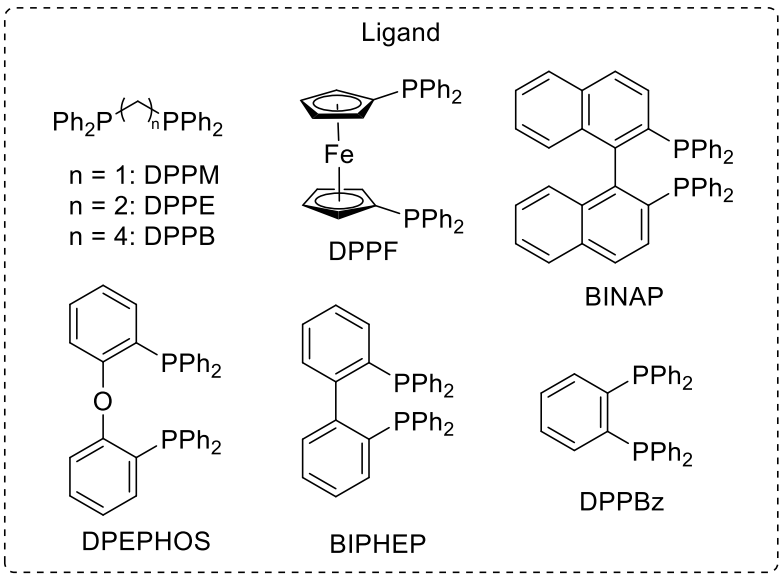
合成した基質 **134a** を用いて、種々の Rh 錯体との環化反応を検討した (Table 3)。まず、10 mol% [Rh(dppe)]ClO_4 錯体存在下、ジクロロエタン中、50 °Cにて反応を行なった。その結果、予想通り反応は円滑に進行し、目的とする 5 員環と 7 員環の縮環した二環式アルコール **137a** が 80%の収率で得られた (run 1)*[1]。次に、DPPM、DPPB を配位子に用いて反応を行なったが、いずれも目的物は得られず、原料を回収する結果となった (runs 2 and 3)。また、DPPF、DPEPHOS、BINAP、BIPHEP を用いて反応を行なったが、これらの配位子を用いても反応は完結しなかった (runs 4-7)。一方、[Rh(dppbz)]ClO_4 錯体を用いて反応を行なうと、環化体 **137a** の収率が 91%まで向上することが分かった (run 8)*[2,3]。また、中性錯体である Wilkinson 錯体を用いて反応を行なっても、原料を回収する結果となった (run 9)。以上の結果より、本反応は触媒として[Rh(dppbz)]ClO_4 を用いると、最も良い収率で目的の環化体 **137a** を与えることが明らかとなった。

Table 3. Examination of Rh(I) Catalysts



run	Rh(I)	time (h)	yields (%)[c]	
			137a	**134a**
1[a]	[Rh(dppe)]ClO_4	1	80[d]	-
2[b]	[Rh(dppm)]ClO_4	19	-	55
3[a]	[Rh(dppb)]ClO_4	24	-	75
4[b]	[Rh(dppf)]ClO_4	18	15	21
5[a]	[Rh(dpephos)]ClO_4	26	-	56
6[a]	[Rh(binap)]ClO_4	22	11	45
7[b]	[Rh(biphep)]ClO_4	24	15	31
8[a]	[Rh(dppbz)]ClO_4	1	91[d]	-
9	$Rh(PPh_3)_3Cl$	18	5	66

[a] [Rh(ligand)]ClO_4 was generated in situ from [Rh(ligand)(nbd)]ClO_4 under an atmosphere of hydrogen.
[b] [Rh(ligand)]ClO_4 was generated in situ from $[Rh(nbd)_2]ClO_4$ and ligand under an atmosphere of hydrogen.
[c] Yields were determined by ^1H NMR yields using 1,3,5-trimethoxybenzene as an internal standard.
[d] Isolated yields were given.



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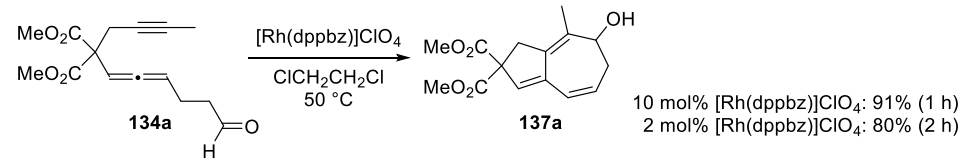
*1 環化体 **137a** の構造は、各種 2 次元 NMR スペクトル (COSY, HMQC, HMBC)の詳細な解析により決定した。

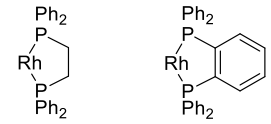
*2 本環化反応において、触媒量の低減を目指し 2 mol%の [Rh(dppbz)]ClO_4 を用いて反応を行なったところ、反応時間の延長が観察されるものの、目的物である **137a** を良好な収率で与えることが分かった (Scheme 35)。

Scheme 35



*3 Table 3 で示したように、本環化反応は配位子として DPPE あるいは DPPBz を有する Rh 錯体を用いると、速やかに進行することが分かった。これらの錯体はどちらも 5 員環のキレート環を形成しており、このことが本反応の進行を促進していると考えられるが、その詳細はよく分かっていない (Figure 4)。

Figure 4



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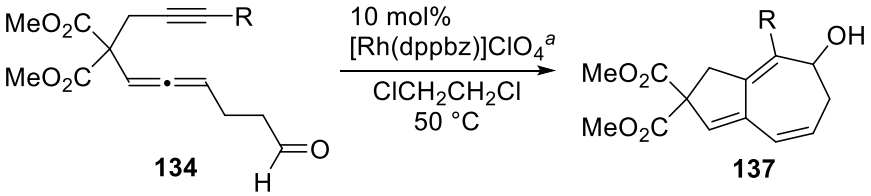
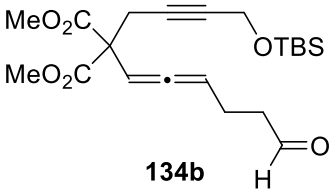
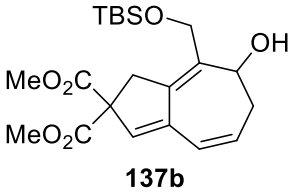
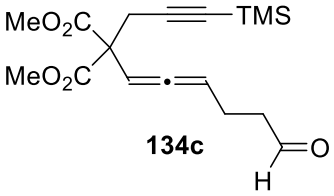
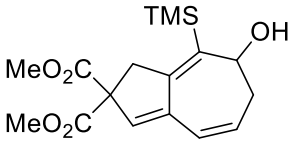
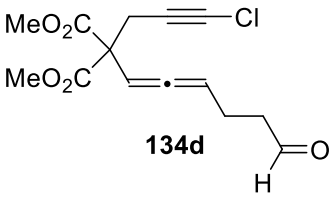
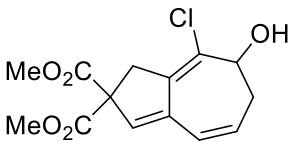
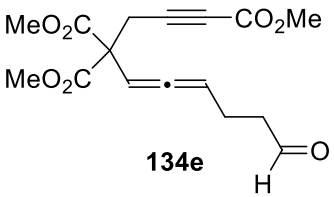
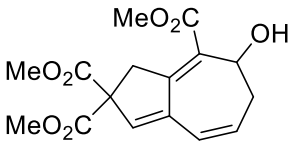
第三項　様々な置換基を有する基質を用いた検討

本反応の適用範囲を探るべく、種々の基質を用いて反応を行なった。まず、アルキン上の置換基について検討した (Table 4)*[1]。シロキシメチル基や TMS 基を有する基質 **134b** および **134c** を用いて反応を行なうと、反応は速やかに進行し良好な収率で環化体 **137b** および **137c** を与えた (runs 1 and 2)。また、クロル基やエステル基といった電子求引基を有する基質 **134d** および **134e** を用いても、二環式アルコール **137d** および **137e** が収率よく得られることが分かった (runs 3 and 4)。

Table 4. Examination of Substrates Having Substituents on the Alkyne Moiety

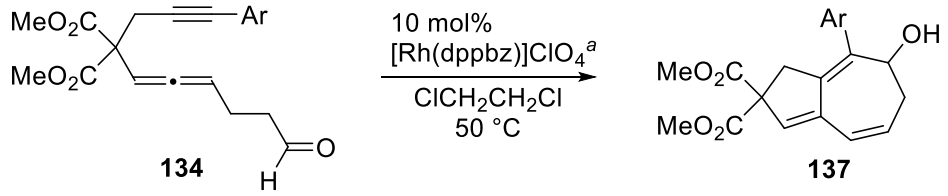


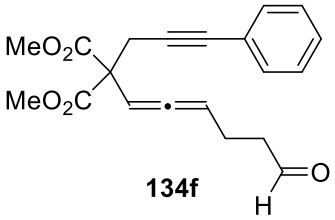
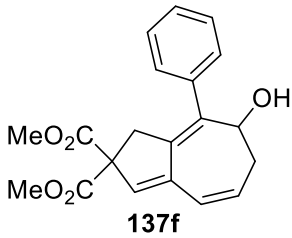
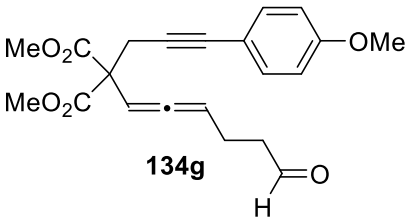
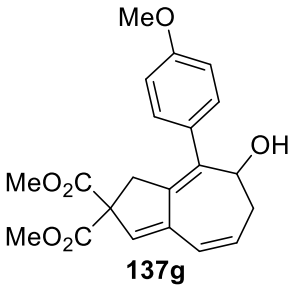
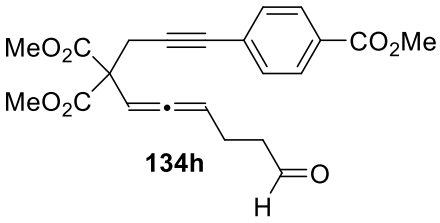
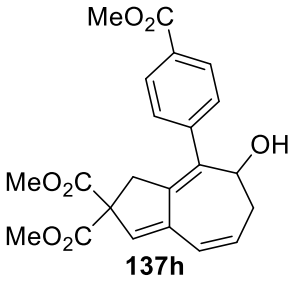
run	substrate	time (h)	product	yield (%)
1	 **134b**	2	 **137b**	72
2[b]	 **134c**	1	 **137c**	91
3	 **134d**	1	 **137d**	75
4	 **134e**	1	 **137e**	88

[a] $[Rh(dppbz)]ClO_4$ was generated in situ from $[Rh(dppbz)(nbd)]ClO_4$ under an atmosphere of hydrogen.[b] in the presence of MS4A

続いて、アルキン上に芳香環を有する基質について検討を行なった (Table 5)*[2]。その結果、芳香環上の置換基の種類によらず、良好な収率で対応する二環式アルコール **137f-137h** が得られた (runs 1-3)。

Table 5. Examination of Substrates Having Aromatic Groups on the Alkyne Moiety

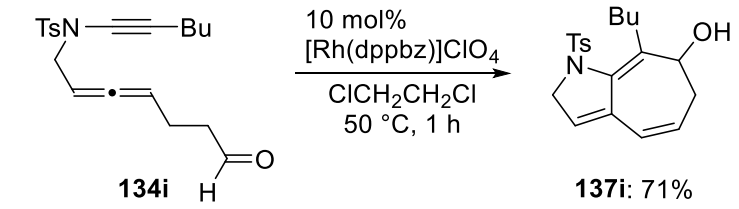


run	substrate	time (h)	product	yield (%)
1		1		83
2		2		82
3		1		76

[a] $[Rh(dppbz)]ClO_4$ was generated in situ from $[Rh(dppbz)(nbd)]ClO_4$ under an atmosphere of hydrogen.

さらに、イナミド部位を持つ基質 **134i** も本反応には適用可能であり、良好な収率で含窒素複素環を含む二環式化合物 **137i** を与えた (Scheme 36)*[3]。この結果は、本反応が複素環骨格の構築にも利用可能であることを示唆するものである*[4]。

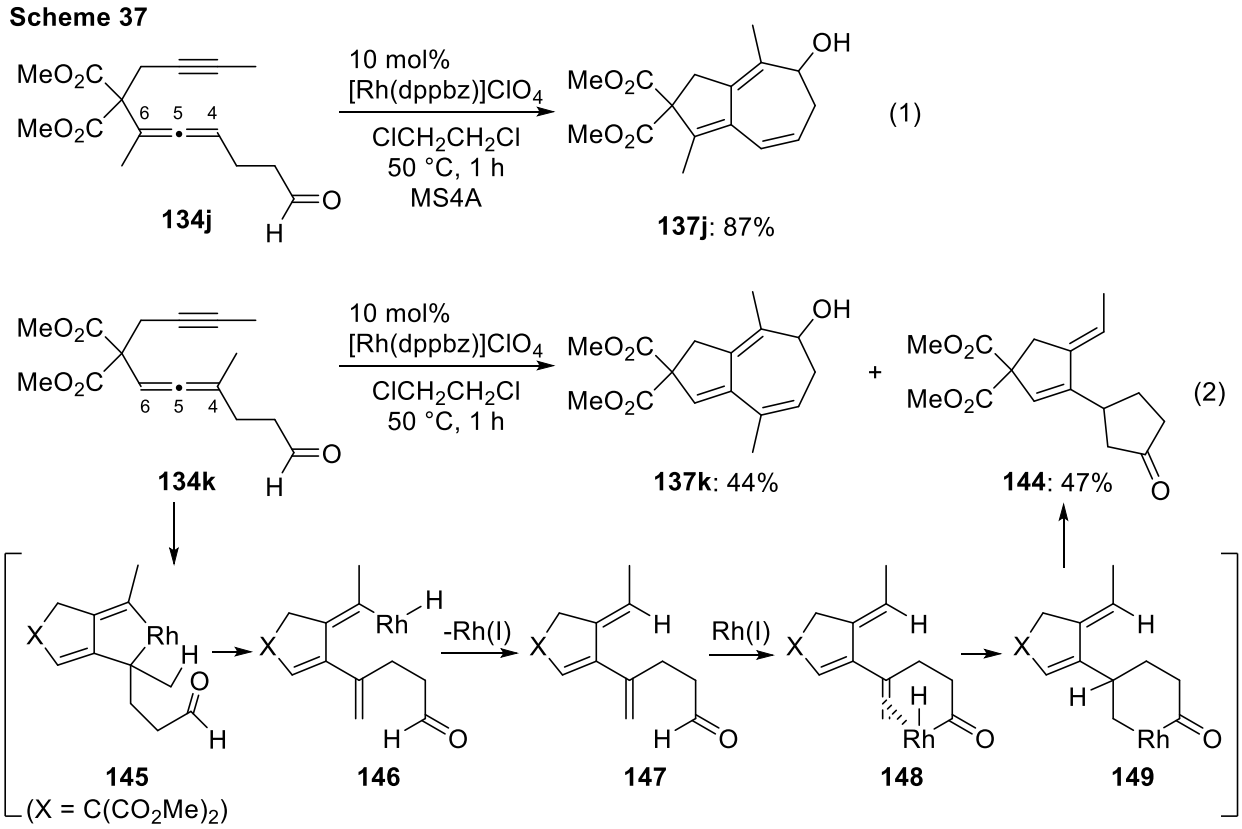
Scheme 36



134i　　**137i**: 71%

次に、アレンの置換基について検討した。6 位にメチル基を有する基質 **134j** では、二環式アルコール **137j** が良好な収率で得られることが分かった (Scheme 37, eq. 1)。一方、4 位にメチル基を有する基質 **134k** の場合、目的の環化体 **137k** とともに、2 つの 5 員環が連結した化合物 **144** も同程度の収率で得られることが分かった (Scheme 37, eq. 2)*[5,6]。環化体 **144** が得られる機構は次のように考えられる。まず、基質 **134k** のアレンとアルキンが Rh 錯体に酸化的環化付加し、ローダサイクル中間体 **145** を形成する。続いて中間体 **145** のメチル基からのβ-水素脱離、還元的脱離を経て環化体 **147** を与え、Rh 錯体が再生する。次に、環化体 **147** のアルデヒド部位の C-H 結合が再び Rh 錯体へ酸化的付加し、生成した Rh-H 結合にオレフィンが挿入し、6 員環ローダサイクル中間体 **149** となり、**149** からの還元的脱離により、環化体 **144** が生成していると考えられる*[7]。

Scheme 37



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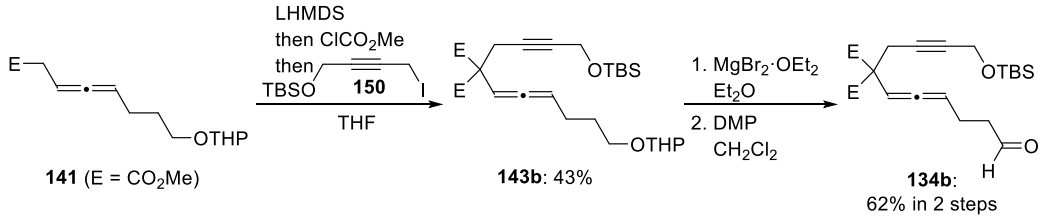
*1 基質 **134b** は以下に示す方法で合成した (Scheme 38)。アレン **141** を LHMDS で処理した後、クロロギ酸メチル、ヨウ素化物 **150**[34] と順次カップリングさせ、アレンイン **143b** を得た。その後、THP 基の選択的な脱保護、生じたアルコールの Dess-Martin 酸化により **134b** を合成した。

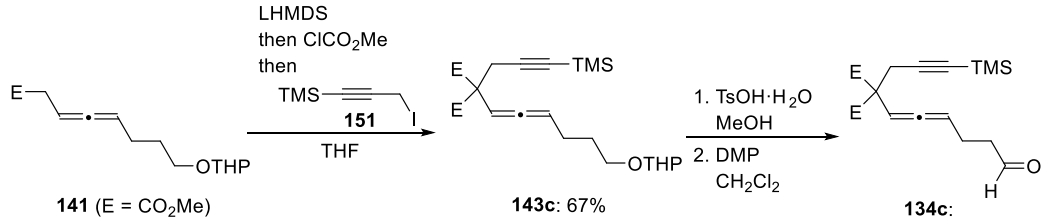
Scheme 38



141 (E = CO_2Me)　　**143b**: 43%　　**134b**: 62% in 2 steps

基質 **134c** は以下に示す方法で合成した (Scheme 39)。アレン **141** を LHMDS で処理した後、クロロギ酸メチル、ヨウ素化物 **151**[35] と順次カップリングさせ、アレンイン **143c** を得た。その後、THP 基の脱保護、生じたアルコールの Dess-Martin 酸化により **134c** を合成した。

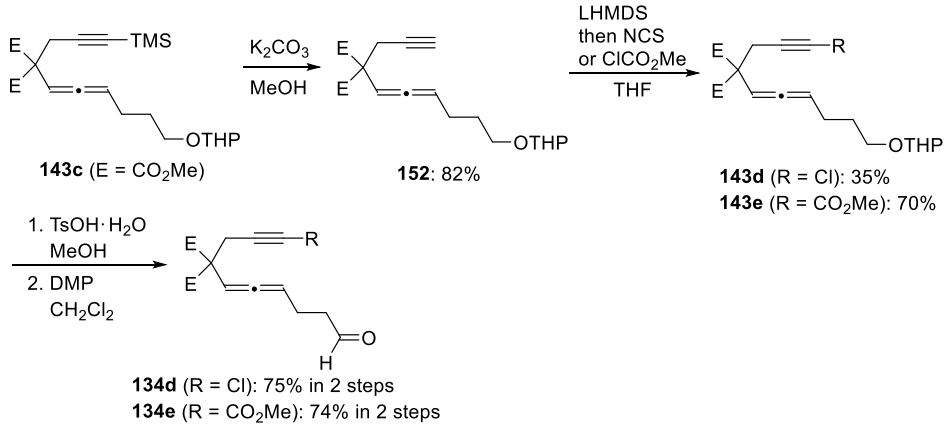
Scheme 39



141 (E = CO_2Me)　　**143c**: 67%　　**134c**: 70% in 2 steps

基質 **134d** および **134e** は以下に示す方法で合成した (Scheme 40)。アレンイン **143c** の TMS 基を脱保護して末端アルキン **152** を得た。続いて **152** を LHMDS で処理した後 *N*-クロロスクシンイミドあるいはクロロギ酸メチルを反応させて **143d** あるいは **143e** へと導いた。その後、THP 基の脱保護、生じたアルコールの Dess-Martin 酸化により **134d** および **134e** を合成した。

Scheme 40

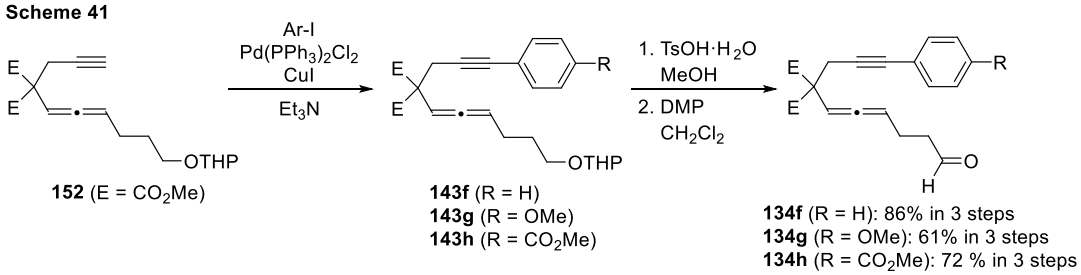


143c (E = CO_2Me)　　**152**: 82%　　**143d** (R = Cl): 35%
143e (R = CO_2Me): 70%

134d (R = Cl): 75% in 2 steps
134e (R = CO_2Me): 74% in 2 steps

*2 基質 **134f-134h** は以下のようにして合成した (Scheme 41)。末端アルキン **152** とヨウ化アリールとの薗頭カップリングによりアリール基を導入後、THP 基の脱保護、生じたアルコールの Dess-Martin 酸化により **134f-134h** を合成した。

Scheme 41



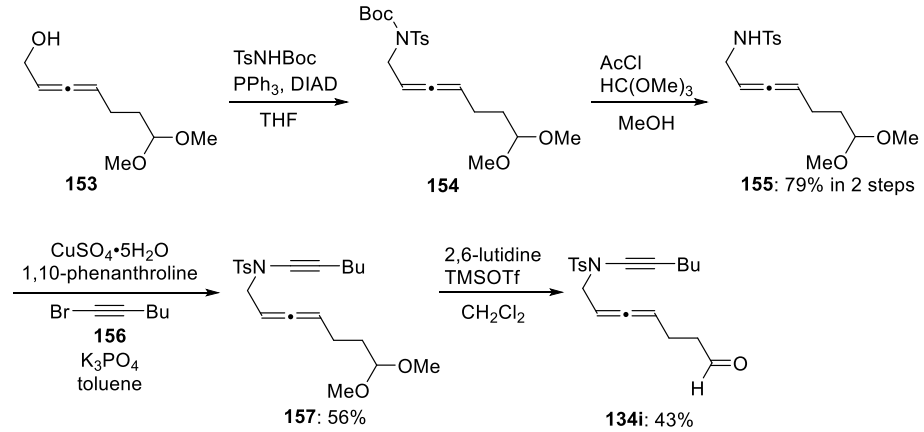
152 (E = CO_2Me)

143f (R = H)
143g (R = OMe)
143h (R = CO_2Me)

134f (R = H): 86% in 3 steps
134g (R = OMe): 61% in 3 steps
134h (R = CO_2Me): 72 % in 3 steps

*[3] 基質 **134i** は以下のようにして合成した (Scheme 42)。文献既知のアルコール **153**[20] を光延反応によりトシルアミド **154** へと変換後、Boc 基の脱保護を行った。$CuSO_4$ による *N*-アルキニル化によりイナミド **157** とし、アセタールの脱保護により **134i** を合成した。

Scheme 42



153

154

155: 79% in 2 steps

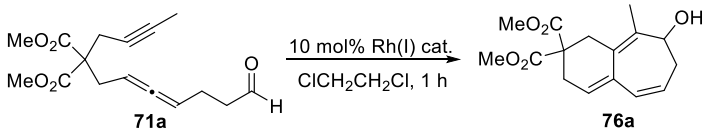
156

157: 56%

134i: 43%

*[4] [Rh(dppbz)]ClO_4 錯体を用いて、Scheme 20 で示した基質 **71a** との反応を再度検討した。その結果、[Rh(dppe)]ClO_4 錯体を用いた場合と比較して二環式アルコール **76a** の収率の向上が見られた (Scheme 43)。

Scheme 43



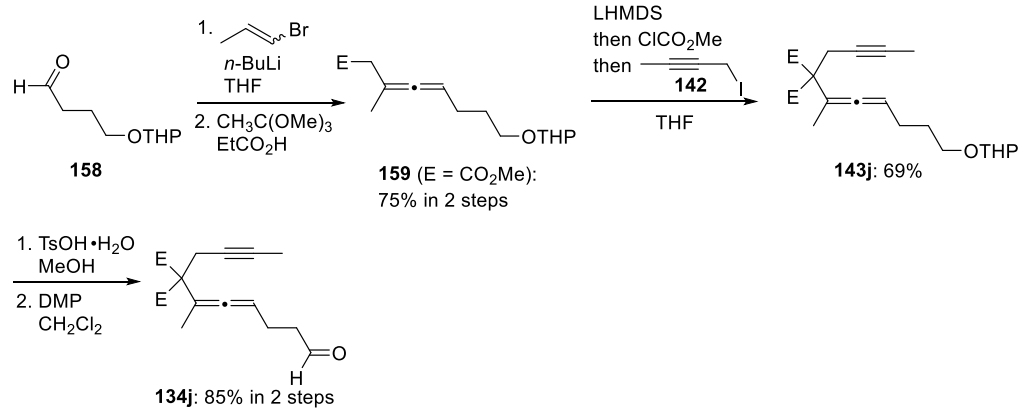
71a

76a

[Rh(dppe)]ClO_4 (65 °C): 27%
[Rh(dppbz)]ClO_4 (50 °C): 40%

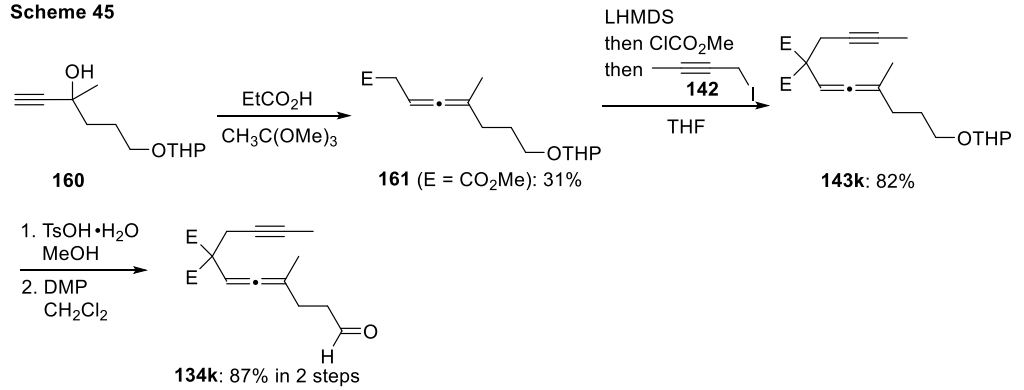
*[5] 基質 **134j** は以下のようにして合成した (Scheme 44)。文献既知のアルデヒド **158**[36] を 1-ブロモプロペンと *n*-ブチルリチウムから調製したアルキニルリチウムと反応させ、生成したアルキニルアルコールの Johnson-Claisen 転位によりアレン **159** を合成した。続いてアレン **159** を LHMDS で処理した後、クロロギ酸メチル、ヨウ素化物 **142** と順次カップリングさせ、アレンイン **143j** を得た。その後、THP 基の脱保護、生じたアルコールの Dess-Martin 酸化により **134j** を合成した。

Scheme 44



基質 **134k** は以下のようにして合成した (Scheme 45)。文献既知のアルキニルアルコール **160**[37] を Johnson-Claisen 転位によりアレン **161** とし、次にアレン **161** を LHMDS で処理した後、クロロギ酸メチル、ヨウ素化物 **142** と順次カップリングさせ、アレンイン **143k** を得た。その後、THP 基の脱保護、生じたアルコールの Dess-Martin 酸化により **134k** を合成した。

Scheme 45

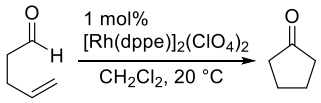


*[6] 環化体 **144** の構造は、各種 2 次元 NMR スペクトル (COSY, HMQC, HMBC)の詳細な解析により決定した。

*[7] DPPBz と同じ二座配位子である DPPE を配位子に持つ Rh 錯体によるアルケンとアルデヒドの分子内ヒドロアシル化反応は、Scheme 4 でも述べたように、Bosnich らによってすでに報告されている (Scheme 46)[4b]。なお、Rh-dppbz 錯体を用いた同様の反応は現在のところ報告されていない。

Scheme 46

Bosnich (1988)



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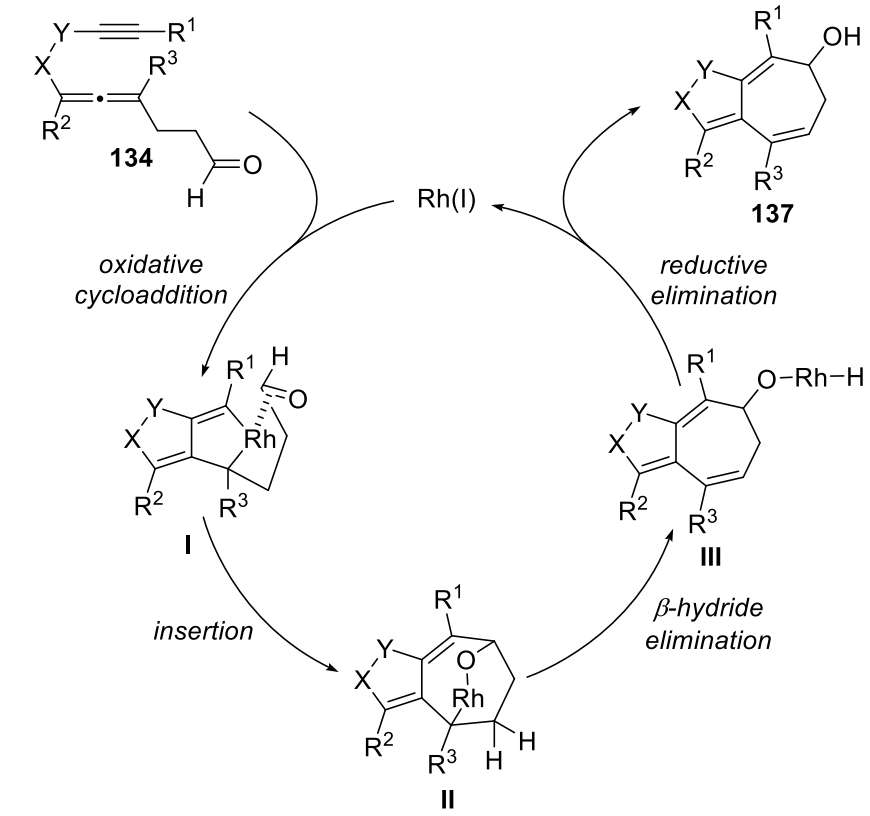
第四項　反応機構の考察

前項の検討結果から、Rh-dppbz 錯体と基質 **134** との反応により良好な収率で様々な二環式アルコール **137** が生成することを見出した。第二章第一節第一項でも述べたが、この二環式アルコール **137** が生成する反応機構は次のように考えられる (Scheme 47)。まず、**134** のアレンとアルキンが Rh 錯体に酸化的環化付加し、ローダサイクル中間体 **I** を形成する。続いて、カルボニル基が C(sp^2)-Rh 結合に挿入し、オキサローダサイクル中間体 **II** となり、β-水素脱離、還元的脱離を経て二環式アルコール **137** が生成したと考えられる。

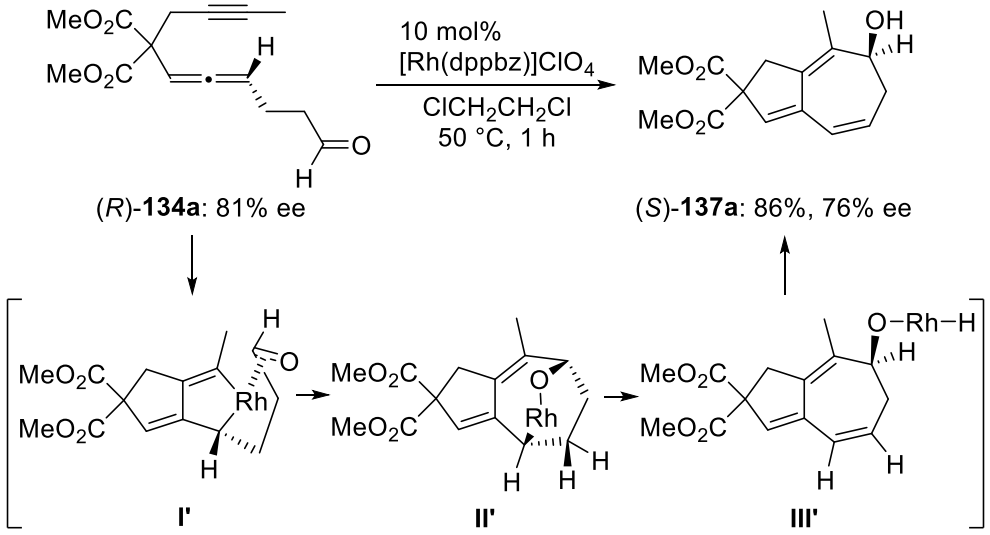
Scheme 47



そこで筆者は反応機構に関する知見を得るために、光学活性なアレン部位を有する基質 (*R*)-**134a** (81% ee)を用いて環化反応を行なった*[1]。その結果、若干の光学純度の低下が見られたものの、アレンの軸不斉が生成物に転写されて環化体 (*S*)-**137a** が良好な収率で得られた (Scheme 48)。この結果は、本反応が立体特異的に進行していることを示唆している。すなわち、基質のアレンインと Rh 錯体との酸化的環化付加、続く C(sp^2)-Rh 結合へのカルボニル基の挿入が立体特異的に進行し、中

間体 **II'**が形成される。続いてβ-水素脱離が進行するため、(*S*)-**137a** が光学活性体として生成したと考えられる。なお、反応前後で光学純度の低下が見られており、反応系中で光学活性なアレンのラセミ化が一部進行していると考えられる*[2]。

Scheme 48



次に本反応の鍵中間体と考えられるオキサローダサイクル中間体 **II** の生成を確認するために、カルボニル基のβ位に水素原子を持たない基質 **162a** を別途合成し、Rh-dppbz 錯体との反応を行なった*[3]。その結果、ジクロロエタン中、還流条件下反応を行うと、酸素原子で渡環された構造を有する環化体 **163a** が良好な収率で得られることが分かった (Scheme 49, eq. 1)*[4]。また、本反応を一酸化炭素雰囲気下で行なうと、**163a** とともに、ラクトンを含む多環式化合物 **164** が主生成物として生成した (Scheme 49, eq. 2)。Rh-dppbz 錯体と基質 **162a** との反応では、オキサローダサイクル中間体 **II"**が形成される。この中間体 **II"**はβ位に水素原子が存在しないため、β-水素脱離が起こらず、**II"**からの直接的な還元的脱離、あるいは一酸化炭素挿入反応を経て環化体 **163a** もしくは **164** を与えたと考えられる。これらの結果は、オキサローダサイクル中間体 **II** を経由する Scheme 47 に示した反応機構をよく支持するものである。なお、環化体 **164** の構造は、X 線結晶構造解析により確認している (Figure 5)。

Scheme 49

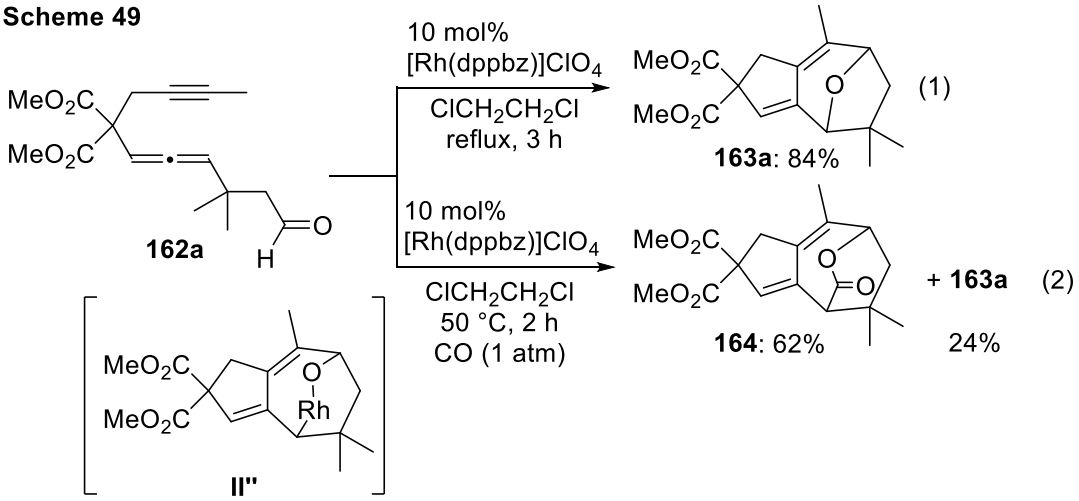
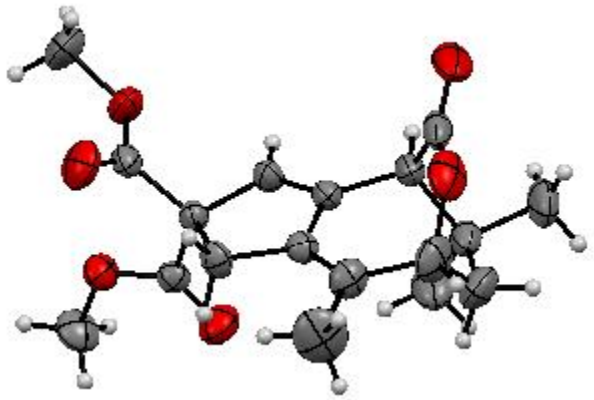


Figure 5



164

<Crystal Data>

Crystal System	monoclinic
Space Group	$P2_1/c$
Lattice Parameters	a = 13.3277 (13) Å
	b = 9.557 (2) Å
	c = 13.5981 (12) Å
	β = 102.477 (8) °
	V = 1690.5 (5) $Å^3$
R	0.0460
Rw	0.1444
GOF	1.047

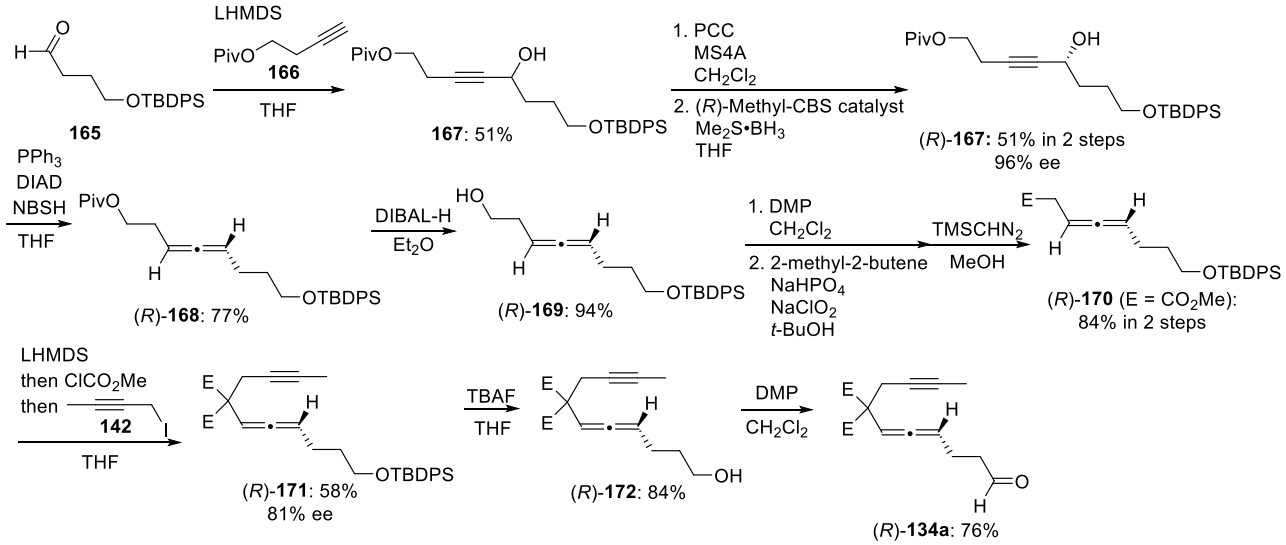
****

*1 基質 (*R*)-**134a** は以下のようにして合成した (Scheme 50)。文献既知のアルデヒド **165**[38] をアルキン **166**[39] とカップリングし、生成したアルコールを PCC 酸化、続く CBS 還元により (*R*)-**167** を 96% ee で得た。続いて Myers の方法[17] によってアレン (*R*)-**168** へと変換した。(*R*)-**168** の Piv 基の脱保護をしたのち、生じたアルコールを Dess-Martin 酸化、続く Lindgren-Kraus 酸化によりカルボン酸へと導き、さらにエステル化を行ない (*R*)-**170** を合成した。続いてアレン (*R*)-**170** を LHMDS で処理した後、クロロギ酸メチル、ヨウ素化物 **142** と順次カップリングさせ、アレンイン (*R*)-**171** を 81% ee で得た。その後、TBDPS 基の脱保護、生じたアルコールの Dess-Martin 酸化により (*R*)-**134a** を合成した。

なお、Myers の方法において、光学活性なアルコール体を基質とした場合、反応は光延反転と続くシグマトロピー転位により立体特異的に進行するため、本反応でも同様に (*R*)-**167** から立体選択的に (*R*)-**168** が得られたと推測した。また、アレン誘導体の絶対配置とその旋光性に関する経験則として Lowe-Brewster 則が知られている。この法則ではアレンの同一軸の 2 つの置換基の分極性の順序と、旋光度の正負からの絶対立体配置を推定することができる。例えば、(*R*)-**168** のような二置換アレンの場合には、旋光度の値が正の符号を示せば、その絶対立体配置は *S*、負の符号を示せば *R* となる。したがって (*R*)-**168** の旋光度は負の符号を示したことから、Lowe-Brewster 則を適用してもその優先絶対立体配置は *R* 配置であると推定でき、その反応機構から推測した (*R*)-**168** の絶対配置と一致する。また、(*R*)-**168** 以降の反応において軸不斉が反転することは考えられないこと、さらに (*R*)-**169**-**172** および (*R*)-**134a** の旋光度がいずれも正の符号を示したことから、*R* 配置であると推定した。

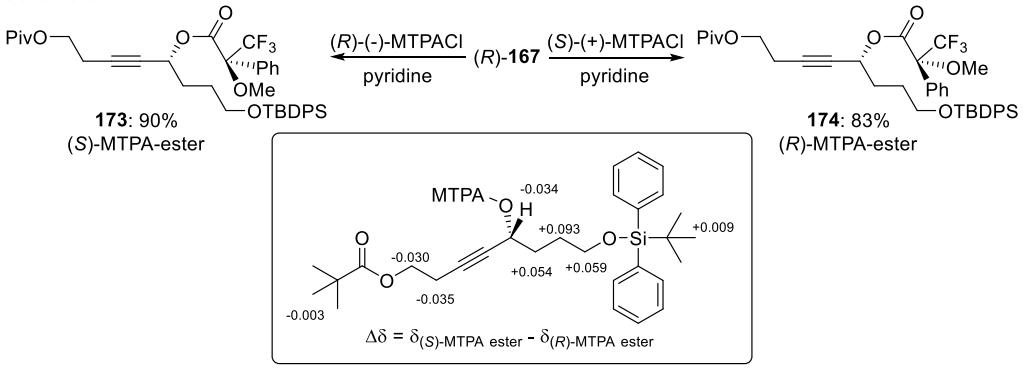
(*R*)-**171** のエナンチオマー過剰率は、HPLC 分析により 81% ee と決定した。また、(*R*)-**171** から (*R*)-**134a** への変換過程ではアレンのラセミ化が起こりにくいと考えられるため、(*R*)-**134a** の不斉収率も同様に 81% ee と推定した。

Scheme 50



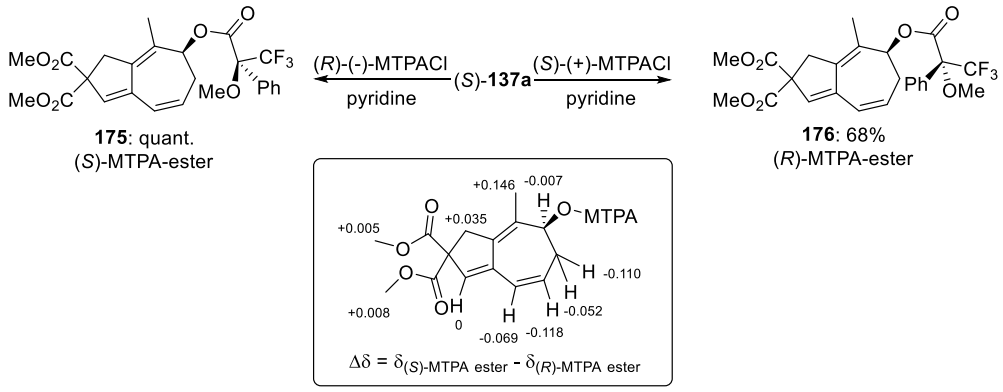
(*R*)-**167** のエナンチオマー過剰率は、HPLC 分析により 96% ee と決定した。また、その優先絶対配置は、(*R*)-**167** をそれぞれの MTPA エステル **173**、**174** へと導き、改良 Mosher 法[18] を適用して、得られたΔδ値から優先絶対配置を *R* 配置と決定した (Scheme 51)。

Scheme 51



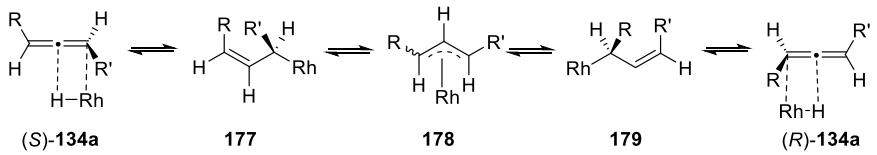
(*S*)-**137a** のエナンチオマー過剰率は、HPLC 分析により 76% ee と決定した。また、その優先絶対配置は、(*S*)-**137a** をそれぞれの MTPA エステル **175**、**176** へと導き、改良 Mosher 法を適用して、得られたΔδ値から優先絶対配置を *S* 配置と決定した (Scheme 52)。

Scheme 52



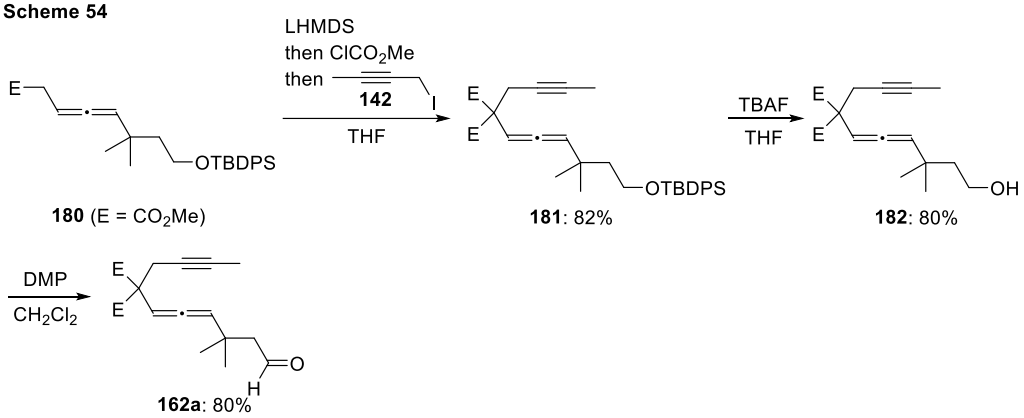
*[2] アレンがラセミ化する機構については、本反応においても第一章で述べたような機構で進行していると考えられる。すなわち、基質のアルデヒドの C-H 結合が Rh 錯体に酸化的付加することで生じる Rh-ヒドリド種が関与していると考えられる (Scheme 53)[11]。この Rh-H 錯体にアレンの二重結合が挿入し、中間体 **177** となり、π-アリル-ロジウム中間体 **178** を経由し、β-水素脱離により、アレンがラセミ化したものと考えられる。

Scheme 53



*[3] 基質 **162a** は以下に示す方法で合成した (Scheme 54)。文献既知のアレン **180**[32] を LHMDS で処理し、クロロギ酸メチル、ヨウ素化物 **142** と順次カップリングさせ、アレンイン **181** を得た。その後、TBDPS 基の脱保護、生じたアルコールの Dess-Martin 酸化により **162a** を合成した。

Scheme 54



180 (E = CO_2Me)　　**181**: 82%　　**182**: 80%

162a: 80%

*4 環化体 **163a** の構造は、各種 2 次元 NMR スペクトル (HMBC, INADEQUATE)の詳細な解析により決定した。

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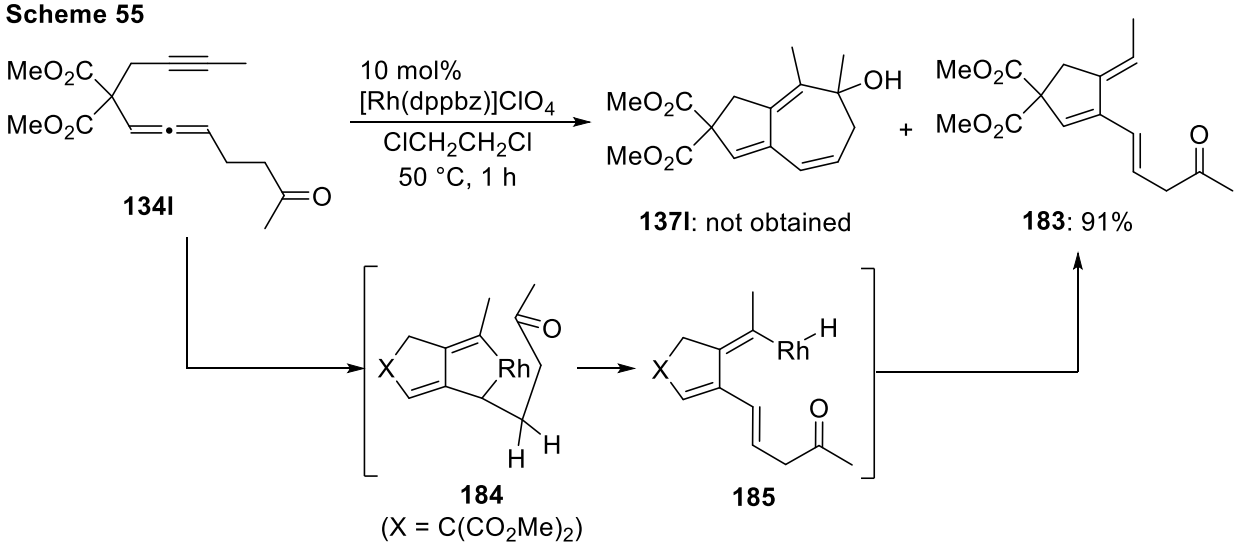
第五項　アレン、アルキン、ケトン間の分子内環化反応への展開：8-オキサビシクロ[3.2.1]オクタン骨格の構築

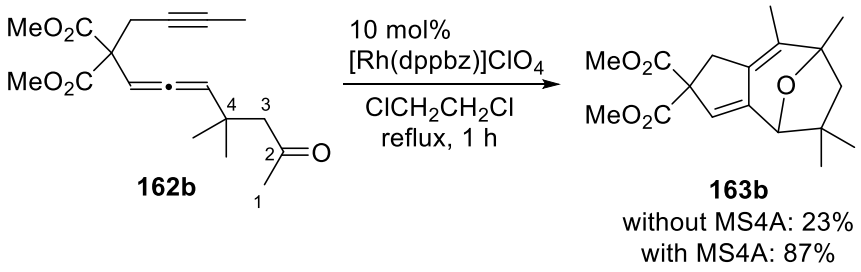
前項までに述べてきた環化反応では、カルボニル基としてアルデヒドを有する基質を用いていた。そこで、本反応の基質の適用範囲の拡大を目指し、アルデヒドの代わりにケトンを側鎖に持つ基質で反応を行なうことにした (Scheme 55)。その結果、基質 **134l** と Rh 触媒との反応では、目的とする環化体 **137l** は全く生成せず、環状トリエン **183** のみが生成することが分かった*[1]。本結果は、ロー-ダサイクル中間体 **184** において、カルボニル基の挿入よりもβ-水素脱離が優先的に進行し、環化体 **183** を与えたものと考えられ、ケトンがアルデヒドよりも 5 員環ローダサイクル中間体 **184** に挿入しにくいことを示している*[2]。

Scheme 55



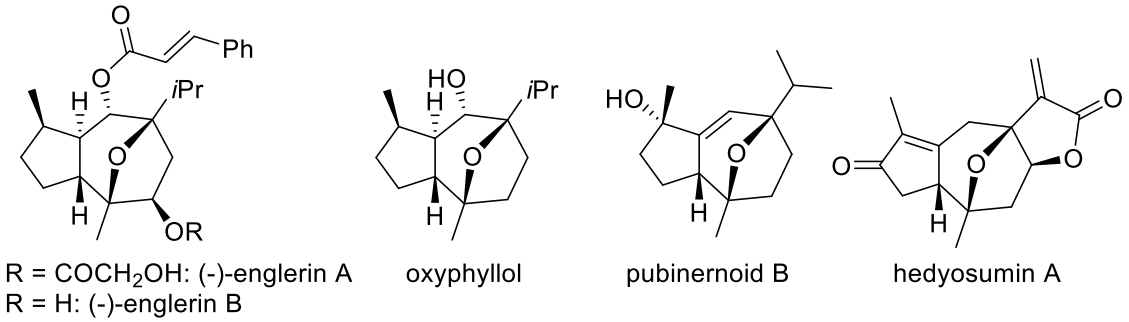
そこで、中間体 **184** からのβ-水素脱離を抑制すべく、基質の 4 位に 2 つの置換基を導入した **162b** を用いて反応を行なった (Scheme 56)*[3]。その結果、予想通りケトンのカルボニル基の挿入を経由する環化反応が進行することが分かった。反応後に **162b** が回収されなかったことから、環化体 **163b** の収率が低収率なのは、反応系内に微量に存在している水により Rh-H 種が生成し、**162b**、あるいは反応中間体の重合が進行してしまったためであると考えた。そこで、水を除く目的で MS4A を添加して反応を行なったところ、目的の環化体 **163b** の収率が 87%に向上した。

Scheme 56



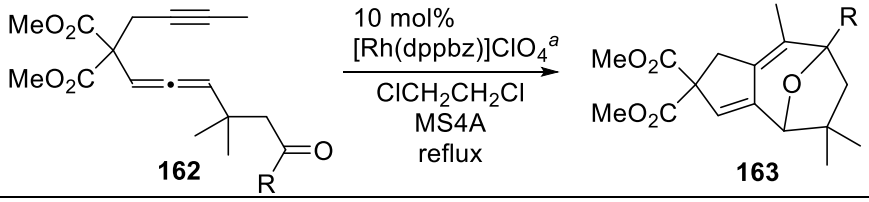
本反応で構築される 8-オキサビシクロ[3.2.1]オクタン骨格は、腎臓がん細胞に対し成長阻害活性を示す englerin 類などの多くのセスキテルペン系天然物に見られる骨格であり、本環化反応はこの骨格の新たな形成法となることが期待される (Figure 6)[40,41]。そこで、本環化反応について、さらに検討を行なうことにした。

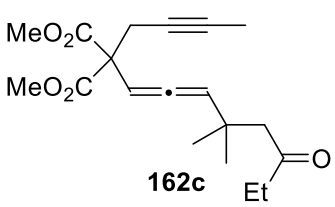
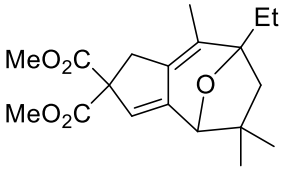
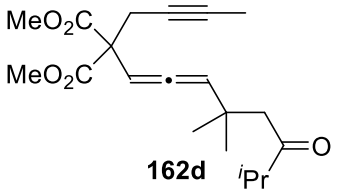
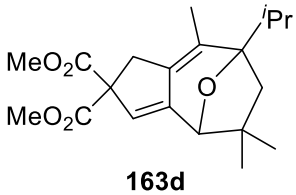
Figure 6



様々なケトンを有する基質を用いて、本反応を検討した (Table 6)*[4]。メチルケトンをエチルケトンに代えた基質 **162c** を用いて反応を行なったところ、目的とする環化体 **163c** が良好な収率で得られた (run 1)。一方で、よりかさ高いイソブタノイル基を有する基質 **162d** では反応は完結せず、原料を回収する結果となった (run 2)。

Table 6. Examination of Substrates Having Aliphatic Ketone

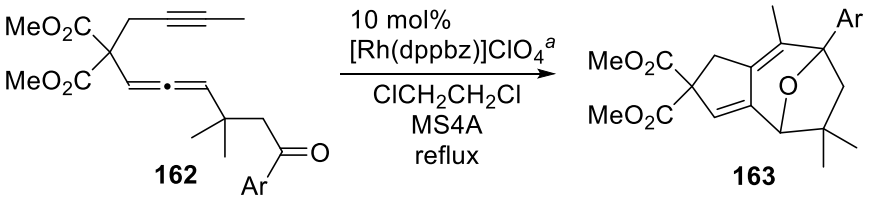


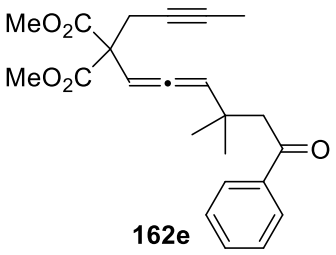
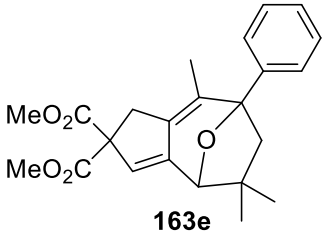
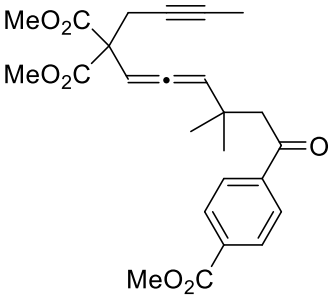
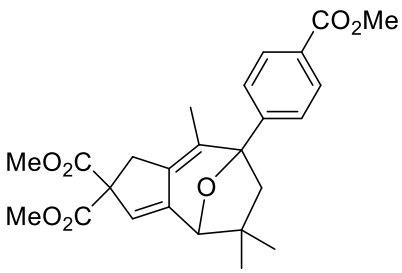
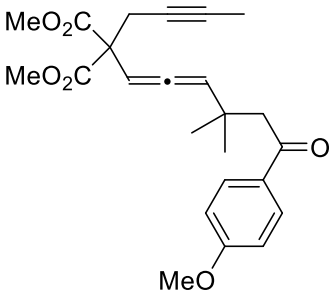
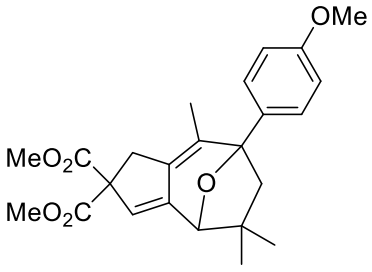
run	substrate	time (h)	product	yield (%)
1	 **162c**	24	 **163c**	90
2[b]	 **162d**	24	 **163d**	22

[a] [Rh(dppbz)]ClO_4 was generated in situ from [Rh(dppbz)(nbd)]ClO_4 under an atmosphere of hydrogen.[b] **162d** was recovered in 10% yield.

次に、芳香族ケトン部位を有する基質について検討を行なった (Table 7)*[5]。ベンゾイル基を有する基質 **162e** では環化体 **163e** の収率は中程度にとどまったものの (run 1)、芳香環上に電子求引基を有する基質 **162f** では環化体 **163f** の収率が大きく向上した (run 2)。一方、電子供与基を芳香環上に有する基質 **162g** で反応を行なうと、目的物 **163g** を含む複雑な混合物を与えた (run 3)。しかしながら、芳香環上の置換基が本反応に与える影響については、その詳細は分かっていない*[6]。

Table 7. Examination of Substrates Having Aromatic Ketone

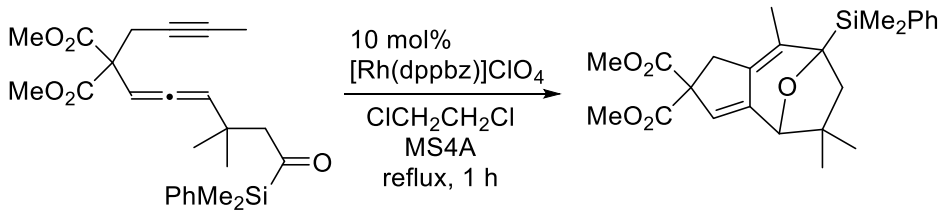


run	substrate	time (h)	product	yield (%)
1	 **162e**	24	 **163e**	42
2	 **162f**	24	 **163f**	90
3[b]	 **162g**	24	 **163g**	-

[a] [Rh(dppbz)]ClO_4 was generated in situ from [Rh(dppbz)(nbd)]ClO_4 under an atmosphere of hydrogen.[b] A complex mixture including the desired compound was obtained.

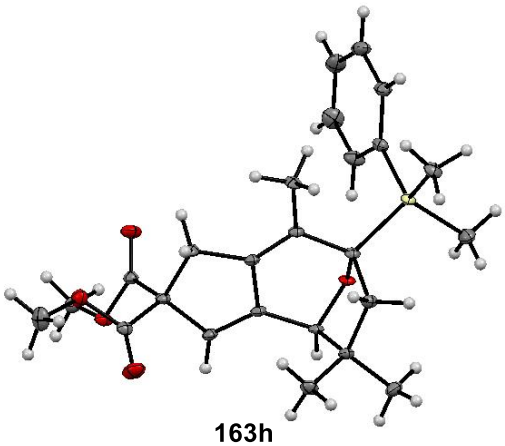
さらに、ケトン部位をアシルシラン部位に代えた基質 **162h** を用いて反応を行なった (Scheme 57)*[7]。その結果、反応は速やかに進行し、シリル基を含む環化体 **163h** が良好な収率で得られてきた。なお、環化体 **163h** は、X 線結晶構造解析により、その構造を確認している (Figure 7)。

Scheme 57



162h　　**163h**: 81%

Figure 7



163h

<Crystal Data>

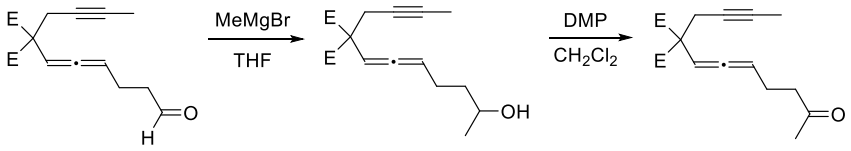
Crystal System	triclinic
Space Group	P-1
Lattice Parameters	a = 11.065 (4) Å
	b = 12.052 (4) Å
	c = 10.146 (6) Å
	β = 108.94 (4) °
	V = 1190.8 (9) Å^3
R	0.0402
Rw	0.1655
GOF	1.018

以上第二章第一節では、筆者はアレン、アルキンおよびカルボニル基を分子内に有する基質と Rh 錯体との反応を検討した。その結果、ローダサイクル中間体へのカルボニル基の挿入が C(sp^2)-Rh 結合で進行し、オキサローダサイクル中間体を経由する新たな環化反応を見出した。この反応では、5 員環と 7 員環を含む環状化合物が収率よく得られることを見出した。

****

*1 基質 **134l** は以下に示す方法で合成した (Scheme 58)。アルデヒド **134a** とグリニャール試薬を反応させ、生じたアルコールの Dess-Martin 酸化により **134l** を合成した。

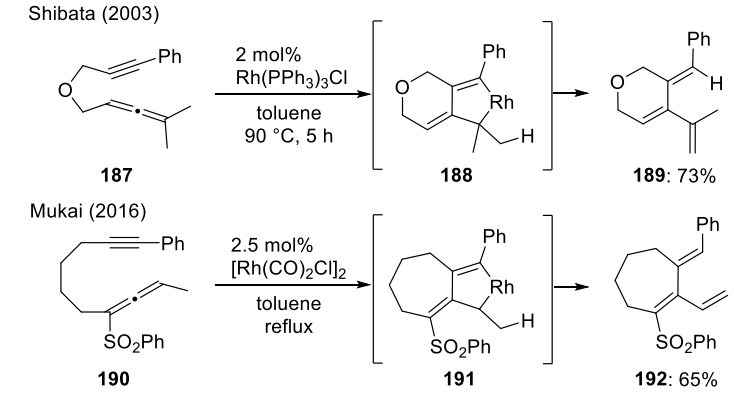
Scheme 58



134a (E = CO_2Me)　　**186**: 46%　　**134l**: 90%

*2 ローダサイクル中間体から β-水素脱離する形式の環化異性化反応は、Scheme 25 で示した Brummond らの報告[23]のほかに、以下の例が知られている (Scheme 59)[42]。

Scheme 59

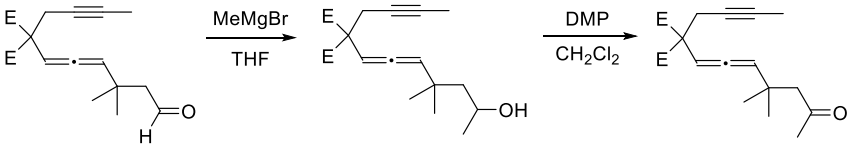


187　　**188**　　**189**: 73%

190　　**191**　　**192**: 65%

*3 基質 **162b** は以下に示す方法で合成した (Scheme 60)。アルデヒド **162a** とグリニャール試薬を反応させ、生じたアルコールの Dess-Martin 酸化により **162b** を合成した。

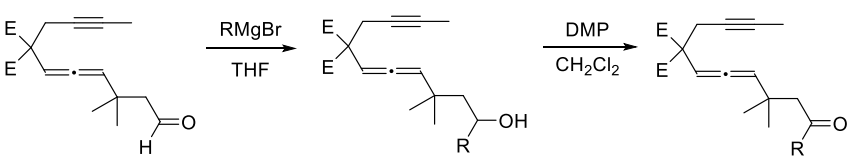
Scheme 60



162a (E = CO_2Me)　　**193b**: 64%　　**162b**: 94%

*4 基質 **162c**、**162d** は以下に示す方法で合成した (Scheme 61)。アルデヒド **162a** とグリニャール試薬を反応させ、生じたアルコールの Dess-Martin 酸化により **162c**、**162d** を合成した。

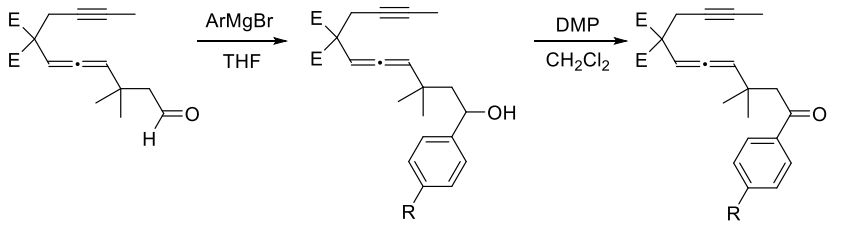
Scheme 61



162a (E = CO_2Me)　　**193c** (R = Et): 60%　　**162c** (R = Et): 82%
193d (R = ^{i}Pr): 38%　　**162d** (R = ^{i}Pr): 83%

*5 基質 **162e-162g** は以下に示す方法で合成した (Scheme 62)。アルデヒド **162a** とグリニャール試薬を反応させ、生じたアルコールの Dess-Martin 酸化により **162e-162g** を合成した。

Scheme 62



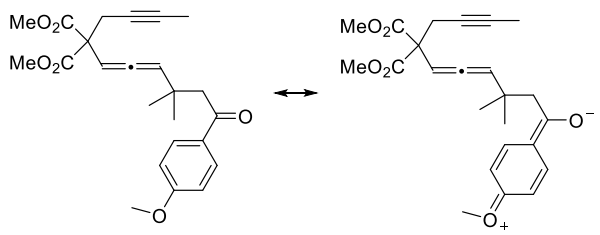
162a (E = CO_2Me)

193e (R = H)
193f (R = CO_2Me): 90%
193g (R = OMe): 76%

162e (R = H): 49% in 2 steps
162f (R = CO_2Me): 97%
162g (R = OMe): 88%

*6 基質 **162g** を用いて反応を行った場合、芳香環上のメトキシ基の電子供与能によって、カルボニル基の二重結合性が低下していると考えられる (Scheme 63)。このため、目的の環化反応が進行せず、複雑な混合物を与えたと考えられる。

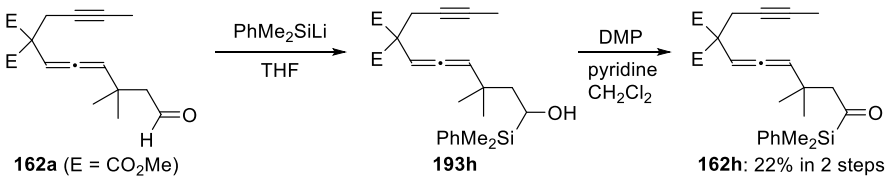
Scheme 63



162g　　**162g'**

*7 基質 **162h** は以下に示す方法で合成した (Scheme 64)。アルデヒド **162a** とシリルリチウム試薬を反応させ、生じたアルコールの Dess-Martin 酸化により **162h** を合成した。

Scheme 64



162a (E = CO_2Me)　　**193h**　　**162h**: 22% in 2 steps

****

第二節　ビシクロ[6.3.0]ウンデカジエン骨格の新規構築法の開発

第一項　8 員環化合物の生成

前節の反応の検討途上、興味深い知見が得られた。すなわち、基質 **162b** を Rh-dppbz 錯体存在下、ジクロロエタン中で反応を行なうと、7 員環を含む多環式化合物 **163b** が得られるのに対し、溶媒を DMF に代えて反応を行なうと、先の環化体 **163b** は得られず、5 員環と 8 員環の縮環した二環式化合物 **194b** が選択的に得られてくることが分かった (Scheme 65, eq. 2)。なお、二環式化合物 **194b** については、X 線結晶構造解析によりその構造を確認している (Figure 8)。

Scheme 65

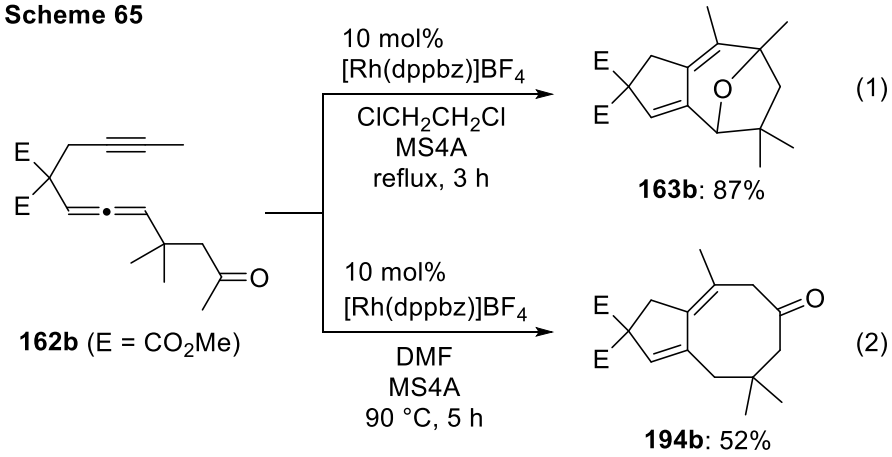
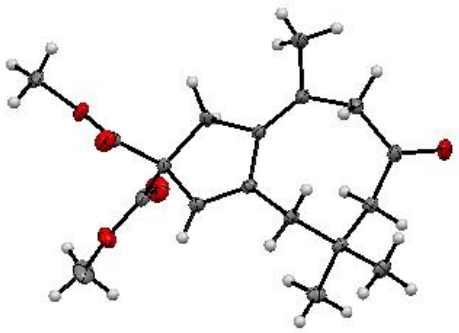


Figure 8



194b

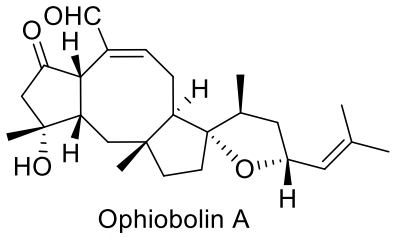
<Crystal Data>

Crystal system	triclinic
Space Group	P-1
Lattice Parameters	a = 9.446 (2) Å
	b = 10.625 (4) Å
	c = 8.741 (2) Å
	β = 93.102 (19) °
	V = 835.0 (4) Å^3
R	0.0429
Rw	0.1753
GOF	1.016

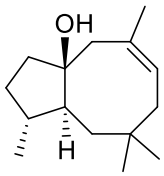
詳細は不明であるが、溶媒を変えるだけで同一の基質から異なる環化体が得られることは興味深い。また、この反応で生成する 5 員環と 8 員環が縮環した二環式化合物 **194b** も、セスキテルペン系天然物によく見られる骨格であり (Figure 9)[43,44]、本反応をこれら天然物の新たな骨格構築法とし

て確立すべく、さらに検討することにした。

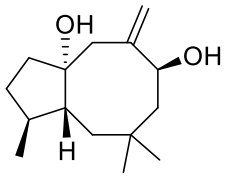
Figure 9



Ophiobolin A
cytotoxicity and
apoptosis inducing effect



Dactylol

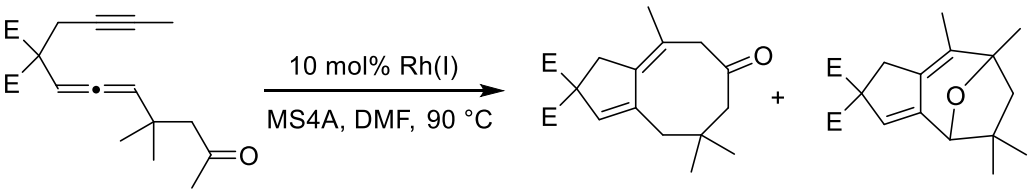


Poitediol

第二項　反応条件の検討と反応機構

まず、基質 **162b** を用いて、種々の Rh(I)錯体との環化反応を検討した (Table 8)。DPPBz と同じ二座配位子である DPPE を用いて反応を行なったところ、原料は消失するものの、目的とする二環式化合物 **194b** の収率が低下し、7 員環を含む環化体 **163b** が副生成物として得られた (run 2)。一方 DPPP を配位子として用いたところ、目的の生成物 **194b** が 63%で得られた (run 3)。次に、リン原子間の炭素数をさらに伸長した DPPB を配位子に用いて反応を行なったが、この場合は反応が完結しなかった (run 4)。また、他の二座配位子である DPPF、BIPHEP を用いて反応を行なったが、原料を回収する結果となった (runs 5 and 6)。さらに、単座配位子を有する Rh(I)錯体や、Rh(I)-NHC 錯体を用いて反応を行なっても、目的物の収率は向上しなかった (runs 7 and 8)。以上の結果より、DPPP を配位子として用い、次に反応溶媒の再検討を行なうことにした。

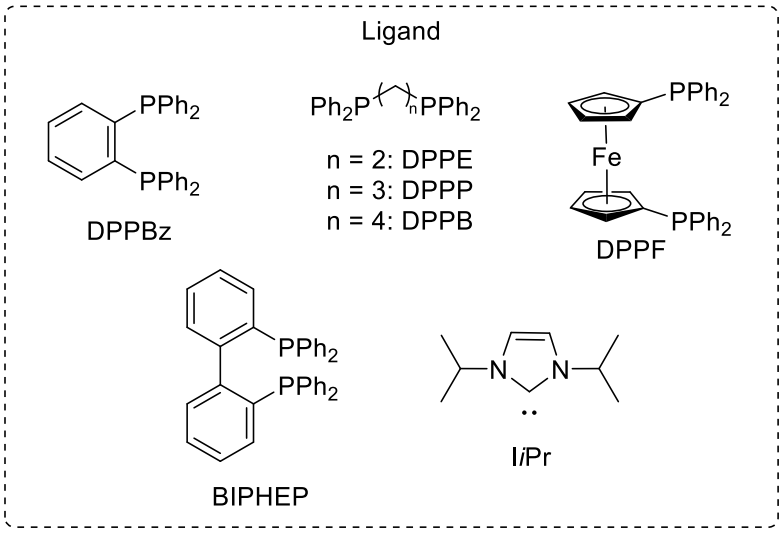
Table 8. Examination of Rh(I) Catalysts



162b (E = CO_2Me)　　**194b**　　**163b**

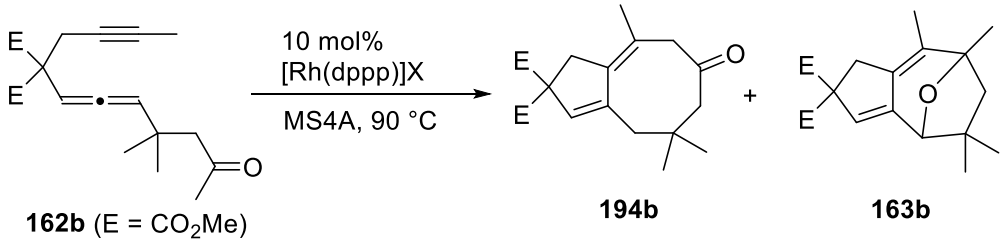
run	Rh(I) catalyst	time (h)	yields (%)[a]		
			194b	**163b**	**162b**
1	[Rh(dppbz)]BF_4	5	52	-	-
2	[Rh(dppe)]BF_4	19	43	5	-
3	[Rh(dppp)]BF_4	1	63	-	-
4	[Rh(dppb)]BF_4	19	8	6	33
5	[Rh(dppf)]BF_4	19	4	4	53
6	[Rh(biphep)]BF_4	22	-	-	47
7	[Rh(PPh_3)$_2$]BF_4	19	5	12	23
8[b]	[Rh(I*i*Pr)(cod)]BF_4	21	-	-	41

[a] ^{1}H NMR yields.
[b] The reaction was carried out at 90 °C for 9 h and 120 °C for 12 h.



反応溶媒としてジクロロエタンを用いて反応を行なったところ、二環式化合物 **194b** は得られず、多環式化合物 **163b** が良好な収率で得られてきた (Table 9, run 2)。アセトニトリルを用いた場合には反応がほとんど進行せず、原料を回収する結果となった (run 3)。また THF や DMSO 中で反応を行なうと、目的の環化体 **194b** が主生成物として得られるものの、収率の向上は見られなかった (runs 4 and 5)。そこで次に、反応溶媒として DMF を用いて、カウンターアニオンの検討をすることにした。カウンターアニオンを ClO_4 として反応を行なったところ、環化体 **194b** の収率の向上がみられた (run 6)。一方で SbF_6 や BAr^F をカウンターアニオンとして用いると、収率がやや低下した (runs 7 and 8)。以上の結果より、最も良好な結果を与えた[Rh(dppp)]ClO_4 錯体を用いて、次に、本反応における添加剤の効果を見ることにした。

Table 9. Examination of Various Solvents and Counter Anions



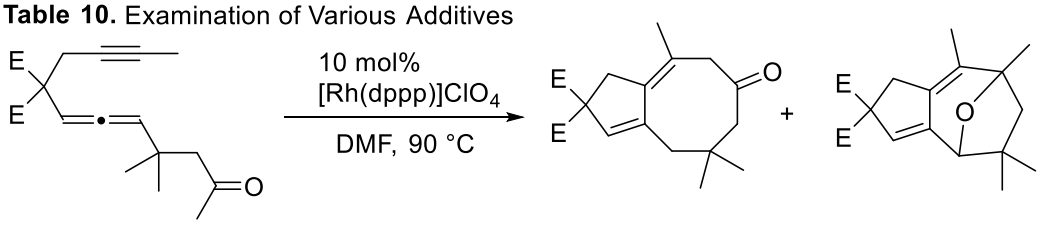
162b (E = CO_2Me)　　**194b**　　**163b**

run	solvent	X	time (h)	yields (%)[a]		
				194b	**163b**	**162b**
1	DMF	BF_4	1	63	-	-
2[b]	$ClCH_2CH_2Cl$	BF_4	20	-	87	-
3[b]	CH_3CN	BF_4	17	4	-	72
4[b]	THF	BF_4	19	60	5	-
5	DMSO	BF_4	2	41	-	-
6	DMF	ClO_4	1	66	-	-
7	DMF	SbF_6	1	59	-	-
8	DMF	BAr^F	1	56	-	-

[a] ^1H NMR yields. [b] The reactions were carried out under reflux condition.
$BArF^-$ = $[B[3,5\text{-}(CF_3)_2C_6H_3]_4]^-$

まずMS4A非存在下で反応を行なったところ、この場合には環化体は生成せず、原料を回収する結果となった (Table 10, run 2)。MS3Aを添加剤として反応を行なうと、環化体**194b**の収率が72%まで向上した (run 3)。一方、MS5Aを用いた場合には、目的とする環化体は全く得られず、多環式化合物**163b**が選択的に生成することがわかった (run 4)。この結果は、モレキュラーシーブの種類が反応経路に大きく影響していることを示している*[1]。そこで、モレキュラーシーブが酸または塩基として働いていることを想定し、さらに添加剤を検討した。その結果、塩基存在下では目的の環化体が得られることが分かったが、その収率は低く、MS3Aを超える結果は得られなかった (runs 5-10)。以上の結果から、最も良い収率を与えたMS3Aを添加剤として用いる条件を最適条件とした。

Table 10. Examination of Various Additives



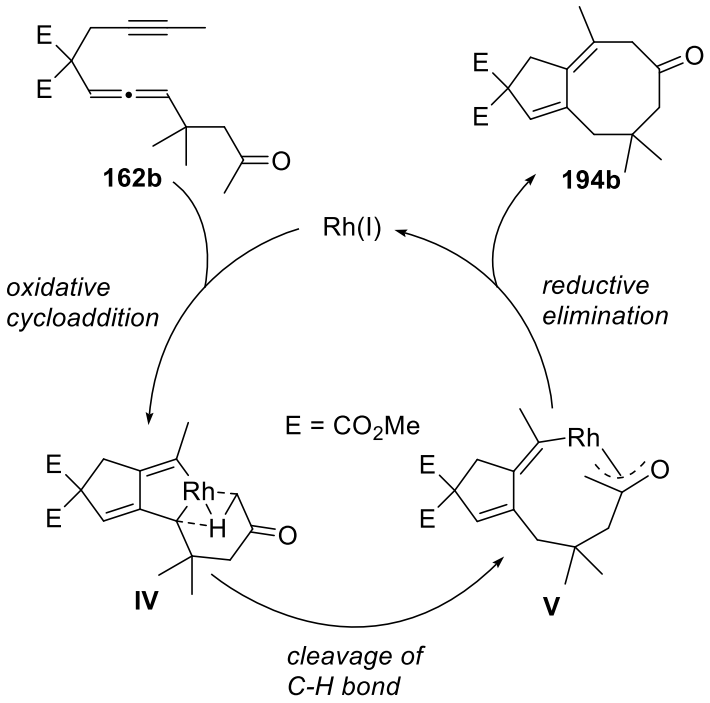
162b (E = CO_2Me) **194b** **163b**

run	additive	time (h)	yields (%)[a]		
			194b	**163b**	**162b**
1	MS4A	1	66	-	-
2	-	19	-	-	46
3	MS3A	1	72[b]	-	-
4	MS5A	19	-	55	-
5[c]	$PhCO_2H$	18	-	-	21
6[c]	$EtCO_2H$	18	-	-	22
7[c]	Na_2CO_3	18	7	4	42
8[c]	K_2CO_3	18	17	5	28
9[c]	Cs_2CO_3	18	9	-	35
10[c]	$CaCO_3$	18	-	6	64

[a] ^1H NMR yields. [b] Isolated yields.
[c] 1 eq. of additive were used.

本反応の反応機構は現在のところ次のように考えている (Scheme 66)。まずアレンの distal 位の二重結合とアルキンが Rh 錯体に酸化的環化付加し、5 員環ロータサイクル中間体 **IV** を生成する。続いて、この中間体の形成を引き金として、カルボニルメチル基の C-H 結合の切断が進行し、オキサ-π-アリルロジウム中間体 **V** を形成する。最後に還元的脱離を経て反応が進行していると現在のところ考えている。

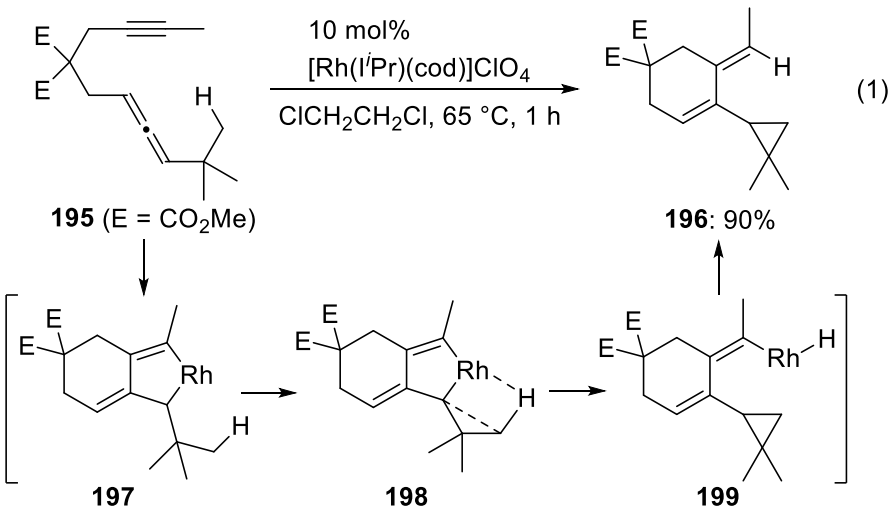
Scheme 66



ところで、このようなメタラサイクル中間体の形成を引き金とした C-H 活性化反応はすでに当研究室で報告している。すなわち、アレン上に *t*-ブチル基を有するアレンイン **195** を Rh(I)-NHC 錯体存在下で反応を行なうと、3 員環を含む環化体 **196** が得られることを見出している (Scheme 67, eq. 1)[45]。この反応では、アレンの distal 位の二重結合とアルキンがロジウム錯体に酸化的環化付加し、5 員環ローダサイクル中間体 **197** を形成する。続いて、*t*-ブチル基のメチル基の C-H 結合活性化が起こり、還元的脱離が進行していると考えられる。筆者が見出した反応でも、C-H 結合の酸性度の違いはあるものの、これと同様の経路で反応が進行していると考えられる。なお、向らもほぼ同時期に、当研究室と同様の反応を報告している (Scheme 67, eq. 2)[46,*2]。

Scheme 67

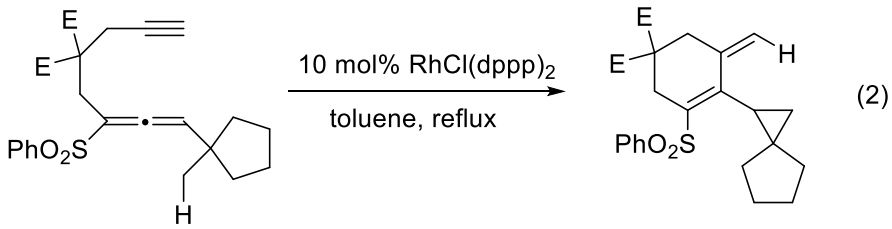
Sato (2012)



195 (E = CO_2Me)　　**196**: 90%

197　　**198**　　**199**

Mukai (2012)



200 (E = CO_2Me)　　**201**: 81%

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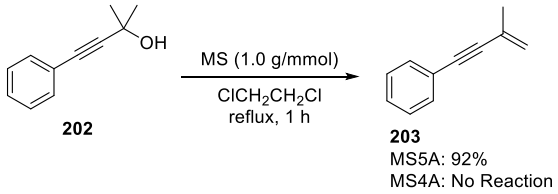
*1 添加剤としてモレキュラーシーブが良好な結果を与えた理由については、現在のところ分かっていない。しかしながら、MS3A, 4A は反応性が類似しているのに対し、MS5A は異なる反応性を示すことが知られている。例えば、2011 年山田らは、**202** を MS5A 存在下ジクロロエタン中加熱還流条件で反応を行なうと、脱水反応が進行し、共役エニン **203** が得られることを見出している (Scheme 68)[47]。この反応では、MS5A の代わりに MS4A を添加剤として用いても、反応は全く進行しない。

Scheme 68

Yamada (2011)



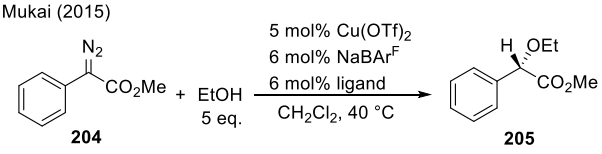
202

203
MS5A: 92%
MS4A: No Reaction

また、2015 年向、北垣らは、α-アゾエステル **204** をエタノール及び MS5A 存在下 Cu 触媒を用いて反応を行なうと、エタノールの O-H 結合の挿入が起こり、**205** が高収率かつ高い不斉収率で得られることを見出している (Table 11, run 1)[48]。興味深いことに、添加剤の MS5A を MS4A、あるいは MS3A に代えて反応を行なうと、**205** は高収率で得られるものの、その不斉収率は著しく低下することが分かっている (runs 2 and 3)。これらの反応におけるモレキュラーシーブの働きの違いについて、その詳細は不明である。以上述べてきたように、モレキュラーシーブが反応に影響を与えるという報告はいくつか知られている。

Table 11.

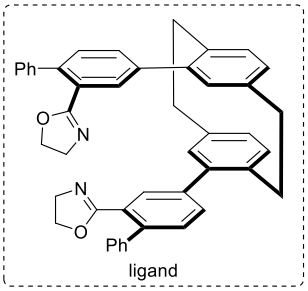
Mukai (2015)



204 **205**

run	additive	time (h)	yield (%)[a]	ee
1	MS5A	1.5	86	76
2	MS4A	3.5	83	5
3	MS3A	2	89	7

[a] Isolated yields.



ligand

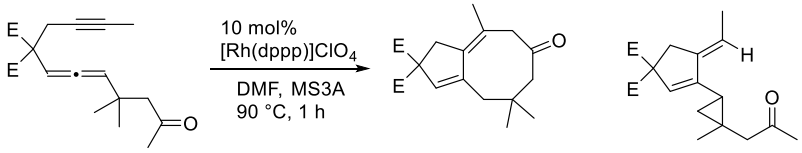
MS3A:
$K_nNa_{12-n}[(AlO_2)_{12}(SiO_2)_{12}]\cdot xH_2O$

MS4A:
$Na_{12}[(AlO_2)_{12}(SiO_2)_{12}]\cdot xH_2O$

MS5A:
$Ca_nNa_{12-2n}[(AlO_2)_{12}(SiO_2)_{12}]\cdot xH_2O$

*2 アレンイン **162b** を用いた反応では、Scheme 67 に示した反応は進行せず、3 員環を含む環化体 **196b** は得られなかった (Scheme 69)。これはおそらく、カルボニル α 位のメチル基の C-H 結合がより反応しやすいためであると考えられる。

Scheme 69



162b (E = CO_2Me)　　**194b**: 72%　　**196b**: not obtained

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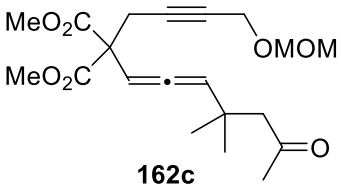
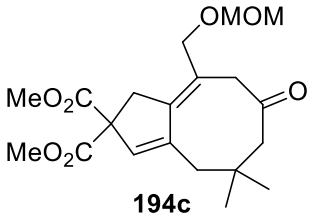
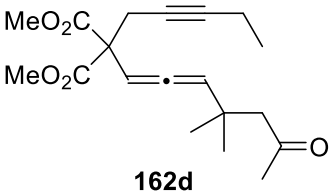
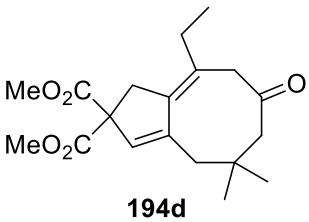
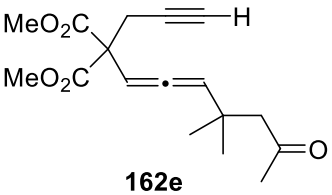
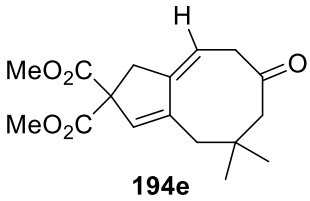
第三項　様々な置換基を有する基質を用いた検討

本反応の基質の適用範囲を探るべく、種々の基質を用いて反応を行なった。まず、アルキン上の置換基について検討した (Table 12)*[1]。水酸基を MOM 基で保護した基質 **162c** を用いて反応を行なうと、目的の環化体 **194c** が 43%の収率で得られた (run 1)。なお、**162c** を用いた場合には、THF 中で反応を行なうと、収率が飛躍的に向上した (run 2)。また、エチル基を有する基質 **162d** を用いて反応を行なうと、環化体 **194d** の収率が低下した (runs 3 and 4)。また、末端アルキンを有する基質 **162e** を用いた場合には、添加剤を MS4A とすると、低収率ながら二環式化合物 **194e** が得られることが分かった (runs 5 and 6)。MS4A が良い結果を与えた理由について、詳細は不明である。

Table 12. Examination of Substrates Having Substituents on Alkyne Moiety

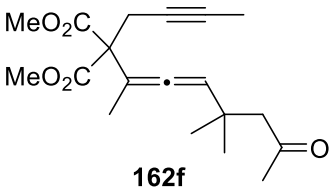
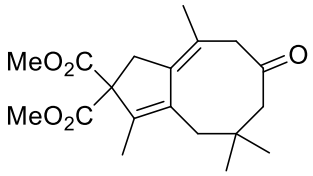
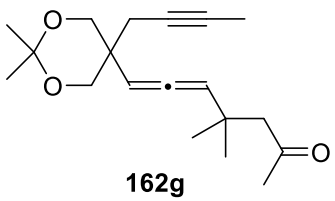
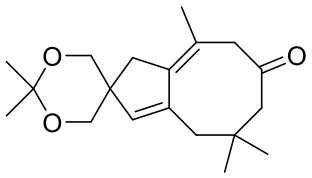
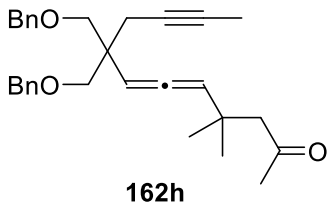
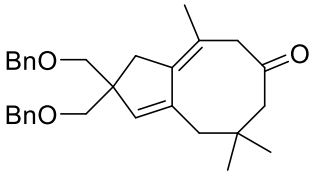
run	substrate	temperature (°C)	time (h)	product	yield (%)
1		90	19		43
2[a]		reflux	40		77
3		90	72		29
4[a]		reflux	64		32
5		90	24		-
6[b]		90	24		34

[a] THF was used as a solvent instead of DMF. [b] MS4A was used as an additive instead of MS3A.

続いて、様々な基質について検討を行なった (Table 13)*[2]。その結果、アレン上の置換基としてメチル基を有する基質 **162f** では、反応は速やかに進行した (run 1)。また、アセトニド部位を有する基質 **162g** でも、本反応は進行した (run 2)。一方ジベンジルエーテル部位を有する基質 **162h** では、環化体 **194h** の収率が低下したが、MS4A を添加剤として用いると対応する二環式化合物 **194h** の収率が向上した (runs 3 and 4)。以上述べてきたように、反応条件を適切に選択することによって、良好な収率で目的の環化体が得られることが分かった*[3]。

Table 13. Examination of Various Substrates

162 **194**

run	substrate	temperature (°C)	time (h)	product	yield (%)
1	 **162f**	90	2	 **194f**	65
2	 **162g**	50	24	 **194g**	50
3	 **162h**	50	18	 **194h**	31
4[a]		50	18		58

[a] MS4A was used as an additive instead of MS3A.

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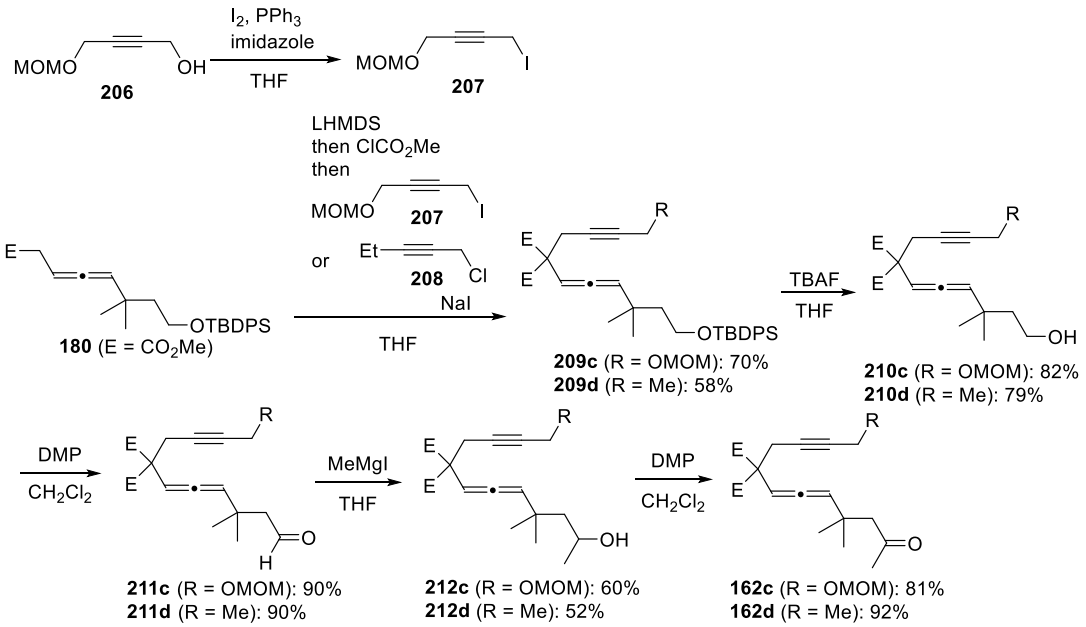
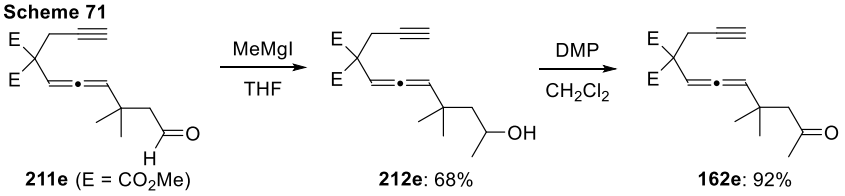
*[1] 基質 **162c** 及び **162d** は以下に示す方法で合成した (Scheme 70)。まず、文献既知のアルコール **206**[49] をヨウ素化し、**207** を合成した。アレン **180** を LHMDS で処理した後、クロロギ酸メチル、続いてヨウ素化物 **207** あるいは塩素化物 **208** とヨウ化ナトリウムから調製したヨウ素化物を順次カップリングさせ、アレンイン **209c** あるいは **209d** を得た。続いて、TBDPS 基の脱保護、生じたアルコールの Dess-Martin 酸化によりアルデヒド **211c** あるいは **211d** とした。その後、Grignard 試薬によるアルキル化、Dess-Martin 酸化により **162c** あるいは **162d** を合成した。

Scheme 70

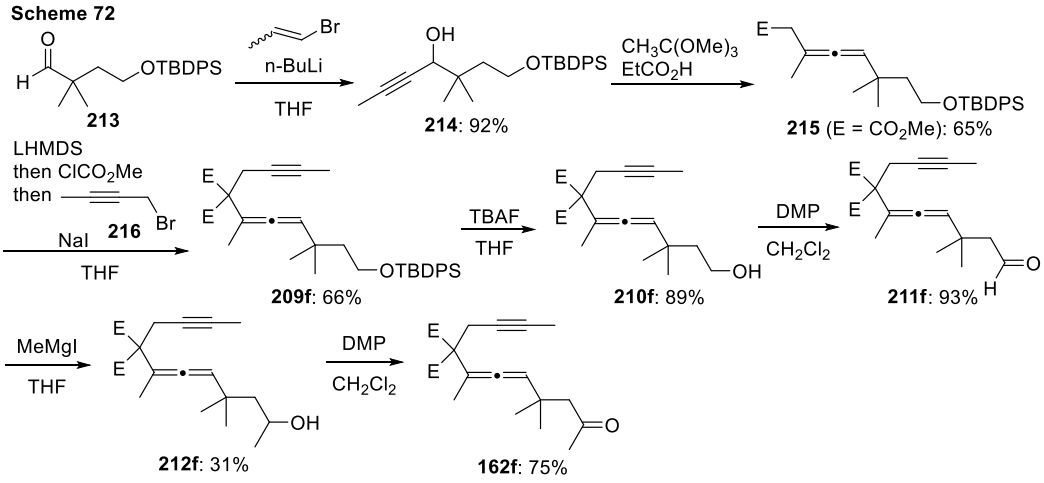


基質 **162e** は以下に示す方法で合成した (Scheme 71)。アレンイン **211e**[50] を Grignard 試薬によるアルキル化、Dess-Martin 酸化により **162e** を合成した。

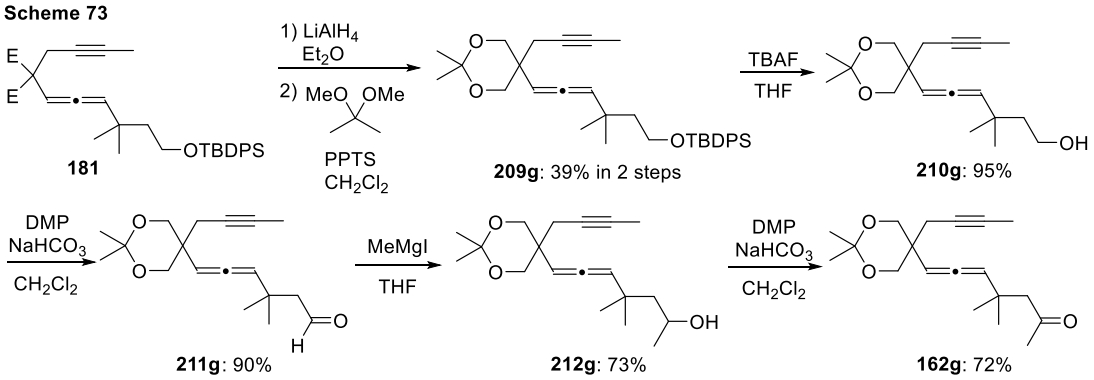
Scheme 71



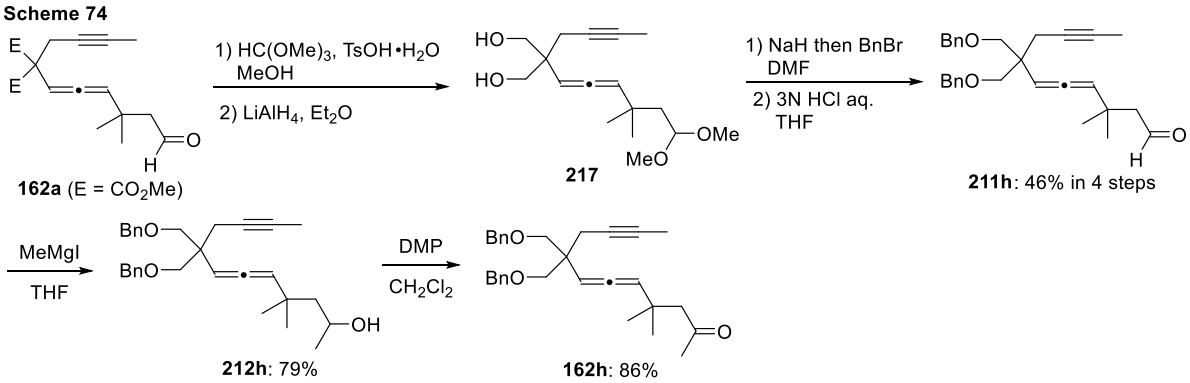
基質 **162f** は以下のようにして合成した (Scheme 72)。文献既知のアルデヒド **213**[51] を 1-ブロモ-1-プロペンと *n*-ブチルリチウムから調製したアルキニルリチウムと反応させ、生成したアルコール **214** を Johnson-Claisen 転位によりアレン **215** へと変換した。アレン **215** を LHMDS で処理した後、クロロギ酸メチル、及び、臭化物 **216** とヨウ化ナトリウムから調製したヨウ素化物と順次カップリングさせ、アレンイン **209f** を得た。続いて、TBDPS 基の脱保護、生じたアルコールの Dess-Martin 酸化によりアルデヒド **211f** とした。その後、Grignard 試薬によるアルキル化、Dess-Martin 酸化により **162f** を合成した。



*2 基質 **162g** は以下のようにして合成した (Scheme 73)。**181** のエステル部位を $LiAlH_4$ で還元してジオールへと変換した後、2,2-ジメトキシプロパンと反応させてアセトニド **209g** へと導いた。続いて、TBDPS 基の脱保護、生じたアルコールの Dess-Martin 酸化によりアルデヒド **211g** とした。その後、Grignard 試薬によるアルキル化、Dess-Martin 酸化により **162g** を合成した。



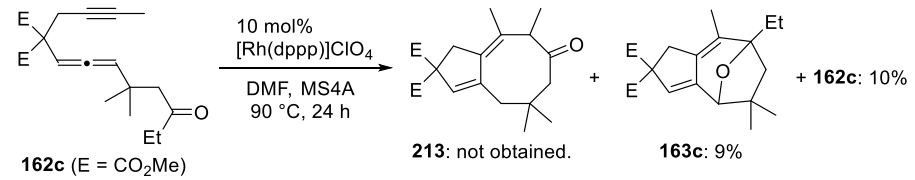
基質 **162h** は以下のようにして合成した (Scheme 74)。**162a** のアルデヒドのアセタール保護の後、ジエステル部位を $LiAlH_4$ で還元し、ジオール体 **217** へと変換した。続いて、α-ブロモトルエンと反応させてジベンジルエーテルとし、アセタールの脱保護を行い、アルデヒド **211h** を得た。その後、Grignard 試薬によるアルキル化、Dess-Martin 酸化により **162h** を合成した。



*3 エチルケトンを有する基質 **162c** を用いて本反応を行なったところ、目的の環化体 **213** は得られず、環化体 **163c** と基質 **162c** が低収率で得られるのみであった (Scheme 75)。詳細は不明であるが、立体障害によってオキサ-π-アリルロジウム中

間体の形成が妨げられている可能性が考えられる。

Scheme 75



162c (E = CO_2Me)　　**213**: not obtained.　　**163c**: 9%

****

結語

本論文は、以下に示すように要約できる。

1. 当研究室で見出したRh触媒による4-アレナールの分子内不斉ヒドロアシル化反応において、添加剤のニトリルが環化反応に与える影響について検討を行なった。光学活性なアレンを有する基質を用いて反応の経時変化を測定した結果、ニトリルは基質のアレンのラセミ化を促進していることが示唆された。

2. 分子内にアレン、アルキンおよびカルボニル基を有する基質とRh錯体との反応を検討した。その結果、ローダサイクル中間体へのカルボニル基の挿入が $C(sp^2)$-Rh結合で選択的に進行し、非常に歪んだオキサローダサイクル中間体を経由する新たな環化反応を見出した。このオキサローダサイクル中間体からβ-水素脱離が進行すると、5員環と7員環の縮環した二環式化合物が、また、直接還元的脱離が進行すると、8-オキサビシクロ[3.2.1]オクタン骨格を含む多環式化合物が収率よく得られることを見出した。

3. オキサローダサイクル中間体を経由する反応を検討中に、反応溶媒をジクロロエタンからDMFに変えると、同様の基質から5員環と8員環の縮環した二環式化合物が選択的に得られることを見出した。この反応は、ローダサイクル中間体の形成を引き金とする $C(sp^3)$-H結合の切断を伴う、オキサ-π-アリルロジウム中間体を経由して進行していると考えられる。

Experimental Section

General

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, CH_3CN, DMF), and were distilled under an argon atmosphere from CaH_2 ($ClCH_2CH_2Cl$). All other solvents and reagents were purified when necessary by standard procedures. Column chromatography was performed on silica gel 60 N (spherical, neutral; Kanto Kagaku, 45-50 μm), silica gel 60 N (spherical, neutral; Kanto Kagaku, 63-210 μm), or Wakogel® (spherical, neutral; Wako, 20-40 μm) with the indicated solvent as eluent. TLC and PTLC were performed on Silica gel 60 $PF_{254\alpha}$ (Merck). IR spectra were obtained on a JASCO FT/IR 460Plus spectrometer. ^1H NMR spectroscopy was recorded on JEOL ECX400P (400 MHz), JEOL ECS400 (400 MHz), and JEOL ECA500 (500 MHz) NMR spectrometer. Chemical shifts are reported in ppm from the solvent as the internal standard ($CDCl_3$: δ = 7.26 ppm, C_6D_6: δ = 7.16 ppm, DMSO: δ = 2.54 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, br = broad, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR spectroscopy was recorded on JEOL ECX400P (100 MHz), JEOL ECS400 (100 MHz), and JEOL ECA500 (125 MHz) NMR spectrometer. Chemical shifts are reported in ppm from the solvent as the internal standard ($CDCl_3$: δ = 77.00 ppm, C_6D_6: δ = 128.06 ppm). Mass spectra were obtained on JEOL JMS-T100LP and JMS-T100GCV and JEOL JMS-FAB mate mass spectrometer, and Thermo Scientific Exactive mass spectrometer. Optical rotations were measured on a JASCO P-1030 digital polarimeter at the sodium D line (589 nm). Chiral HPLC analyses were carried out using a JASCO PU-980 and using indicated chiral column.

Experimental Section of Chapter 1

General Procedure for Monitoring Cyclization Using [Rh(dtbm-segphos)]BF_4

A solution of $[Rh(cod)_2]BF_4$ (0.100 mmol, 10 mol% to a substrate) and (*S*)- or (*R*)-DTBM-SEGPHOS (0.100 mmol, 10 mol% to a substrate) in dehydrated acetone (3.8 mL: 0.026 M to Rh) was stirred under H_2 atmosphere at room temperature for 1 h. Then the reaction mixture was degassed, and the reaction vessel was flushed with Ar gas. To the mixture was added a solution of substrate **28b** (1.00 mmol) and 1,3,5-trimethoxybenzene (0.250 mmol, 2.5 eq. to a substrate) as an internal standard with or without 4-fluorobenzonitrile (0.100 mmol, 10 mol% to a substrate) in dehydrated acetone (6.2 mL) and the reaction mixture was stirred at 45 °C. The reaction was monitored by poured reaction solution, removed the Rh complex by short silica gel colomn chlomatograpy to give mixture of substrate and product. The yields of **28b** and **29b** were determined by ^1H NMR. The enantiomeric excesses of **28b** and **29b** were determined by HPLC analysis with a DAICEL CHIRALPAK AS-H [eluent: *n*-hexane/2-propanol = 9/1, flow rate: 1.0 mL/min, detector: UV (220 nm)]: t_R = 25.4 min for (*S*)-enantiomer of **29b**: t_R = 32.9 min for (*R*)-enantiomer of **29b**: t_R = 39.2 min for (*S*)-enantiomer of **28b**: t_R = 58.8 min for (*R*)-enantiomer of **28b**.

<Scheme 9>

A solution of $[Rh(cod)_2]BF_4$ (8.1 mg, 0.020 mmol) and BIPHEP (10.6 mg, 0.0203 mmol) in dehydrated acetone (0.80 mL: 0.026 M to Rh) was stirred under H_2 atmosphere at room temperature for 1 h. Then the reaction mixture was degassed, and the reaction vessel was flushed with Ar gas. To the mixture was added a solution of (*S*)-**28b** (61.0 mg, 0.198 mmol) in dehydrated acetone (1.20 mL) and the reaction mixture was stirred at 45 °C until the substrate disappeared on TLC. After removal of the solvent, the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 3/1) to give (*S*)-**29b** (5.86 g, 74% yield) as a pale yellow oil, whose spectral were consistent to those reported literature[7]. Spectral data of (*S*)-**29b**: $[\alpha]_D^{19}$ +9.94 (*c* 0.90, $CHCl_3$). The enantiomeric excess was determined to be 33% ee by HPLC analysis with a DAICEL CHIRALPAK AS-H [eluent: *n*-hexane/2-propanol = 9/1, flow rate: 1.0 mL/min, detector: UV (230 nm)]: t_R (major) = 25.4 min for (*S*)-enantiomer: t_R (minor) = 32.9 min for (*R*)-enantiomer.

<Scheme 13>

<without nitrile>

According to the general procedure, monitoring of cyclization which was reacted from **28b** (307 mg, 1.00 mmol), $[Rh(cod)_2]BF_4$ (40.6 mg, 0.100 mmol), (*R*)-DTBM-SEGPHOS (118 mg, 0.100 mmol) and 1,3,5-trimethoxybenzene (42.7 mg, 0.254 mmol) in acetone (10 mL) at 45 °C, was conducted. The yields and ee's were shown in Table 14.

<with nitrile>

According to the general procedure, monitoring of cyclization which was reacted from **28b** (369 mg, 1.20 mmol), $[Rh(cod)_2]BF_4$ (48.8 mg, 0.120 mmol), (*R*)-DTBM-SEGPHOS (142 mg, 0.120 mmol) and 1,3,5-trimethoxybenzene (51.4 mg, 0.306 mmol) with 4-fluorobenzonitrile (14.5 mg, 0.120 mmol) in acetone (12 mL) at 45 °C, was conducted. The yields and ee's were shown in Table 15.

Table 14

Time (min)	yield of **29b** (%)	ee of **29b** (% ee)	(*S*)-**29b** (%)	(*R*)-**29b** (%)	yield of **28b** (%)	ee of **28b** (% ee)	(*S*)-**28b** (%)	(*R*)-**28b** (%)
0	0	0	0	0	100	0	50	50
5	12	97	12	0	75	19	30	45
10	29	95	28	1	57	44	16	41
20	51	94	49	2	34	86	2	32
30	59	92	57	2	34	95	1	33
60	56	94	54	2	30	96	1	29
120	56	94	54	2	29	93	1	28
240	57	91	54	3	27	93	1	26
480	63	83	58	5	27	93	1	26
900	66	83	60	6	26	93	1	25
1440	65	80	59	7	22	90	1	21
4080	69	79	62	7	6	0	3	3
5580	69	78	61	8	2	0	1	1
6840	71	78	63	8	0	0	0	0

Table 15

Time (min)	yield of **29b** (%)	ee of **29b** (% ee)	(*S*)-**29b** (%)	(*R*)-**29b** (%)	yield of **28b** (%)	ee of **28b** (% ee)	(*S*)-**28b** (%)	(*R*)-**28b** (%)
0	0	0	0	0	100	0	50	50
10	31	95	30	1	60	33	20	40
20	58	98	57	1	28	86	2	26
30	63	98	62	1	21	92	1	20
60	67	97	66	1	19	94	1	18
120	68	96	67	1	18	95	0	18
240	70	93	68	2	16	97	0	16
480	71	90	67	4	15	98	0	15
1320	72	84	66	6	11	95	0	11
1800	76	81	69	7	10	75	1	9
2880	73	82	66	7	4	1	2	2
4200	76	83	70	6	0	0	0	0
7080	76	82	69	7	0	0	0	0

<Scheme 14>

<eq. 1, without 4-fluorobenzonitrile>

According to the general procedure, monitoring of cyclization which was reacted from (*S*)-**28b** (295 mg, 0.960 mmol), $[Rh(cod)_2]BF_4$ (39.6 mg, 0.0974 mmol), (*R*)-DTBM-SEGPHOS (113 mg, 0.0958 mmol) and 1,3,5-trimethoxybenzene (40.9 mg, 0.243 mmol) in acetone (9.6 mL) at 45 °C, was conducted. The yields and ee's were shown in Table 16.

<eq. 1, with 4-fluorobenzonitrile>

According to the general procedure, monitoring of cyclization which was reacted from (*S*)-**28b** (301 mg, 0.979 mmol), $[Rh(cod)_2]BF_4$ (40.0 mg, 0.0984 mmol), (*R*)-DTBM-SEGPHOS (117 mg, 0.0992 mmol) and 1,3,5-trimethoxybenzene (42.8 mg, 0.254 mmol) with 4-fluorobenzonitrile (12.1 mg, 0.0999 mmol) in acetone (9.8 mL) at 45 °C, was conducted. The yields and ee's were shown in Table 17.

<eq. 2, without 4-fluorobenzonitrile>

According to the general procedure, monitoring of cyclization which was reacted from (*S*)-**28b** (292 mg, 0.950 mmol), $[Rh(cod)_2]BF_4$ (38.6 mg, 0.0950 mmol), (*S*)-DTBM-SEGPHOS (113 mg, 0.0955 mmol) and 1,3,5-trimethoxybenzene (40.1 mg, 0.238 mmol) in acetone (9.5 mL) at 45 °C, was conducted. The yields and ee's were shown in Table 18.

<eq. 2, with 4-fluorobenzonitrile>

According to the general procedure, monitoring of cyclization which was reacted from (*S*)-**28b** (300 mg, 0.976 mmol), $[Rh(cod)_2]BF_4$ (40.0 mg, 0.0984 mmol), (*S*)-DTBM-SEGPHOS (116 mg, 0.0982 mmol) and 1,3,5-trimethoxybenzene (42.8 mg, 0.244 mmol) with 4-fluorobenzonitrile (11.7 mg, 0.0966 mmol) in acetone (9.8 mL) at 45 °C, was conducted. The yields and ee's were shown in Table 19.

Table 16

Time (min)	yield of **29b** (%)	ee of **29b** (% ee)	(*S*)- **29b** (%)	(*R*)-**29b** (%)	yield of **28b** (%)	ee of **28b** (% ee)	(*S*)-**28b** (%)	(*R*)-**28b** (%)
0	0	0	0	0	100	99	100	1
5	19	95	18	1	70	72	60	10
10	44	99	44	0	45	41	32	13
20	83	99	83	0	7	-89	0	7
30	86	99	86	0	3	-84	0	3
40	76	94	74	2	0	0	0	0
50	82	99	82	0	0	0	0	0
60	82	99	81	1	0	0	0	0
120	87	97	86	1	0	0	0	0
240	86	96	84	2	0	0	0	0
480	88	93	85	3	0	0	0	0
960	86	93	83	3	0	0	0	0
1440	85	91	81	4	0	0	0	0

Table 17

Time (min)	yield of **29b** (%)	ee of **29b** (% ee)	(*S*)- **29b** (%)	(*R*)-**29b** (%)	yield of **28b** (%)	ee of **28b** (% ee)	(*S*)-**28b** (%)	(*R*)-**28b** (%)
0	0	0	0	0	100	99	100	1
5	16	98	16	0	73	54	56	17
10	41	99	41	0	50	21	30	20
20	76	99	76	0	15	-78	2	13
30	80	99	80	0	9	-94	0	9
40	80	99	80	0	7	-94	0	7
50	80	99	79	1	6	-95	0	6
60	82	99	82	0	7	-96	0	7
120	83	98	82	1	5	-91	0	5
240	83	97	82	1	3	-79	0	3
480	83	92	80	3	0	0	0	0
960	83	91	79	4	0	0	0	0
1440	87	90	83	4	0	0	0	0

Table 18

Time (min)	yield of **29b** (%)	ee of **29b** (% ee)	(*S*)-**29b** (%)	(*R*)-**29b** (%)	yield of **28b** (%)	ee of **28b** (% ee)	(*S*)-**28b** (%)	(*R*)-**28b** (%)
0	0	0	0	0	100	99	100	1
10	12	100	0	12	74	65	61	13
20	20	99	0	20	65	69	55	10
30	22	98	0	22	63	72	54	9
60	30	97	0	30	56	76	49	7
120	34	94	1	33	55	77	49	6
240	36	91	2	34	49	80	44	5
480	40	86	3	37	45	82	41	4
960	44	80	4	40	40	76	35	5
1440	48	74	6	42	37	64	30	7
2880	59	76	7	52	26	5	14	12
4320	60	76	7	53	16	0	8	8
5760	60	76	7	53	10	0	5	5
7200	53	76	6	47	5	0	3	2

Table 19

Time (min)	yield of **29b** (%)	ee of **29b** (% ee)	(*S*)- **29b** (%)	(*R*)-**29b** (%)	yield of **28b** (%)	ee of **28b** (% ee)	(*S*)-**28b** (%)	(*R*)-**28b** (%)
0	0	0	0	0	100	99	100	1
10	17	99	0	17	72	56	56	16
20	30	99	0	30	60	61	48	12
30	38	99	0	38	50	70	43	7
60	46	98	0	46	42	85	39	3
120	49	96	1	48	41	82	37	4
240	49	94	2	47	37	85	34	3
480	54	89	3	51	33	67	28	5
960	59	85	5	54	31	86	29	2
1440	59	83	5	54	28	68	24	4
2880	64	83	5	59	17	-2	8	9
4320	68	82	6	62	12	1	6	6
5760	68	81	6	62	10	1	5	5
7200	61	80	6	55	7	1	4	3

<Scheme 17>

***N*-(8-((*tert*-Butyldimethylsilyl)oxy)-5-hydroxyoct-3-yn-1-yl)-*N*,4-dimethylbenzenesulfonamide (63)**

To a solution of **62** (6.64 g, 28.0 mmol) in THF (17 mL) was added LHMDS (1.30 M in THF, 21.5 mL, 28.0 mmol) at -78 °C, and the mixture was stirred at the same temperature for 1.5 h. To the mixture was added a solution of **61** (3.78 g, 18.7 mmol) in THF (20 mL) at -78 °C, and the mixture was stirred at -78 °C for 2 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. 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 (*n*-hexane/EtOAc = 3/1) to give **63** (5.86 g, 71% yield) as a yellow oil. Spectral data of **63**: IR (neat) 3512, 1598, 1342, 1162, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.1 Hz, 2 H), 7.32 (d, *J* = 8.1 Hz, 2 H), 4.44-4.33 (m, 1 H), 3.75-3.60 (m, 2 H), 3.20 (d, *J* = 5.8 Hz, 1 H), 3.18 (t, *J* = 7.6 Hz, 2 H), 2.80 (s, 3 H), 2.48 (dt, *J* = 7.6, 1.8 Hz, 2 H), 2.43 (s, 3 H), 1.85-1.58 (m, 4 H), 0.89 (s, 9 H), 0.07 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4, 134.8, 129.7 (2 C), 127.3 (2 C), 83.3, 81.2, 63.2, 62.1, 49.2, 35.5, 35.4, 28.5, 25.9 (3 C), 21.5, 19.0, 18.3, -5.4 (2 C); LRMS (EI) *m/z* 382 $[(M-C_4H_9)^+]$, 364, 155, 91; HRMS (EI) calcd for $C_{18}H_{28}NO_4SSi$ $[(M-C_4H_9)^+]$ 382.1508, found 382.1497.

***N*-(8-((*tert*-Butyldimethylsilyl)oxy)-5-oxooct-3-yn-1-yl)-*N*,4-dimethylbenzenesulfonamide (64)**

To a solution of **63** (16.4 g, 37.3 mmol) in CH_2Cl_2 (190 mL) was added Dess-Martin Periodinane (19.0 g, 44.8 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 min. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10 % $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 8/1, 5/1, 4/1) to give **64** (15.1 g, 92% yield) as a pale yellow oil. Spectral data of **64**: IR (neat) 2214, 1675, 1598, 1344, 1162, 838 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.0

Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 3.61 (t, *J* = 5.7 Hz, 2 H), 3.23 (t, *J* = 7.4 Hz, 2 H), 2.81 (s, 3 H), 2.65 (t, *J* = 6.8 Hz, 2 H), 2.60 (t, *J* = 7.4 Hz, 2 H), 2.43 (s, 3 H), 1.85 (tt, *J* = 6.8, 5.7 Hz, 2 H), 0.87 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.6, 143.6, 134.5, 129.8 (2 C), 127.3 (2 C), 89.4, 82.0, 61.8, 48.4, 42.0, 35.7, 26.9, 25.9 (3 C), 21.5, 19.5, 18.2, -5.4 (2 C); LRMS (EI) *m/z* 380 [$(M-C_4H_9)^+$], 225, 155, 91; HRMS (EI) calcd for $C_{18}H_{26}NO_4SSi$ [$(M-C_4H_9)^+$] 380.1352, found 380.1352.

(*S*)-*N*-(8-((*tert*-Butyldimethylsilyl)oxy)-5-hydroxyoct-3-yn-1-yl)-*N*,4-dimethylbenzenesulfonamide ((*S*)-63)

To a solution of (*S*)-CBS-catalyst (11.6 g, 41.9 mmol) in THF (160 mL) was added a solution of **64** (9.19 g, 21.0 mmol) in THF (50 mL) at room temperature. To the mixture was added a BH_3·Me_2S complex at -30 ℃ for 20 min and the reaction mixture was stirred at the same temperature for 30 min. To the mixture was added MeOH at -30 °C and diluted with Et_2O at room temperature. The organic layer was washed with saturated NH_4Cl aqueous solution, saturated $NaHCO_3$ aqueous solution, H_2O, and brine. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 2.5/1, 2/1, 1.5/1) to give (*S*)-**63** (7.85 g, 85% yield, 90% ee) as a pale yellow oil. Spectral data of (*S*)-**63**: $[\alpha]_D^{24}$ -3.2 (*c* 1.38, $CHCl_3$). The enantiomeric excess was determined to be 90% ee by HPLC analysis with a DAICEL CHIRALPAK OD-H [eluent: *n*-hexane/2-propanol = 95/5, flow rate: 1.0 mL/min, detector: UV (240 nm)]: t_R (minor) = 13.3 min for (*R*)-enantiomer: t_R (major) = 19.8 min for (*S*)-enantiomer.

(*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-8-((*N*,4-dimethylphenyl)sulfonamido)oct-5-yn-4-yl tosyl-*L*-phenylalaninate ((*S*)-66)

To a solution of (*S*)-**63** (2.50 g, 5.69 mmol) in THF (30 mL) were added DMAP (73.0 mg, 0.598 mmol), pyridine (600 μL, 7.43 mmol) and **65** (2.30 g, 6.81 mmol) at 0 °C, and the mixture was stirred at room temperature for 1.5 h. To the mixture was added H_2O at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with 1 N HCl aqueous solution, saturated $NaHCO_3$ aqueous solution and brine. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1) to give (*S*)-**66** (3.77 g, 89% yield, 90% de) as a yellow oil. Further purification was performed by recycling HPLC [column: SIL-P, eluent: *n*-hexane/EtOAc = 3/1, flow rate: 3.5 mL/min, detector: UV (254 nm)] to give (*S*)-**66** (>99% de) as a pale yellow oil. Spectral data of (*S*)-**66**: IR (neat) 3290, 3029, 2928, 2856, 1745 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.5 Hz, 2 H), 7.63 (d, *J* = 8.5 Hz, 2 H), 7.30 (d, *J* = 8.5 Hz, 2 H), 7.24-7.19 (m, 5 H), 7.12 (dd, *J* = 6.8, 2.8 Hz, 2 H), 5.11 (tt, *J* = 6.8, 2.0 Hz, 1 H), 5.01 (d, *J* = 9.0 Hz, 1 H), 4.19 (dt, *J* = 9.0, 5.5 Hz, 1 H), 3.57 (td, *J* = 6.8, 2.0 Hz, 2 H), 3.15 (t, *J* = 7.5 Hz, 2 H), 3.04 (d, *J* = 5.5 Hz, 2 H), 2.78 (s, 3 H), 2.49 (td, *J* = 7.5, 2.0 Hz, 2 H), 2.42 (s, 3 H), 2.39 (s, 3 H), 1.68-1.63 (m, 2 H), 1.50-1.44 (m, 2 H), 0.90 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 143.54, 143.50, 136.7, 134.7, 129.8 (4 C), 129.6 (2 C), 128.5 (2 C), 127. 3 (2 C), 127.2 (4 C), 83.4, 78.6, 65.8, 62.3, 56.2, 49.0, 39.1, 35.6, 31.3, 28.1, 25.9 (3 C), 21.53, 21.51, 19.2, 18.3, -5.3 (2 C); LRMS (EI) *m/z* 683 [$(M-C_4H_9)^+$], 585, 422, 364, 198, 155, 91; HRMS (EI) calcd for $C_{34}H_{43}N_2O_7S_2Si$ [$(M-C_4H_9)^+$] 683.2281, found 683.2312; $[\alpha]_D^{25}$ -40.7 (*c* 1.17, $CHCl_3$). The diastereomeric excess was determined to be >99% ee by HPLC analysis with a DAICEL CHIRALPAK AD-H [eluent: *n*-hexane/2-propanol = 8/2, flow rate: 1.0 mL/min, detector: UV (254 nm)]: t_R (minor) = 9.2 min for (*S*, *R*)-diastereomer: t_R (major) = 12.9 min for (*S*, *S*)-diastereomer.

(*S*)-*N*-(8-((*tert*-Butyldimethylsilyl)oxy)-5-hydroxyoct-3-yn-1-yl)-*N*,4-dimethylbenzenesulfonamide ((*S*)-63)

To a solution of (*S*)-**66** (5.18 g, 6.99 mmol, >99% de) in EtOH (15 mL) was added a solution of 40% KOH aqueous

solution (5.0 mL, 35.7 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 EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 2/1, 1/1, EtOAc) to give (*S*)-**63** (2.65 g, 86% yield) as a pale yellow oil. Spectral data of (*S*)-**63**: $[\alpha]_D^{25}$ -3.6 (*c* 1.00, $CHCl_3$). The enantiomeric excess was determined to be 99% ee by HPLC analysis with a DAICEL CHIRALPAK OD-H.

(*S*)-*N*-(8-((*tert*-Butyldimethylsilyl)oxy)octa-3,4-dien-1-yl)-*N*,4-dimethylbenzenesulfonamide ((*S*)-67)

To a solution of PPh_3 (586 mg, 2.23 mmol) in THF (6.0 mL) was added DIAD (450 μL, 2.29 mmol) at -15 °C, and the mixture was stirred at the same temperature for 15 min. To the mixture was added a solution of (*S*)-**63** (655 mg, 1.49 mmol) in THF (4.5 mL) at – 15 °C, and the mixture was stirred at the same temperature for 15 min. To the mixture was added a solution of NBSH (490 mg, 2.26 mmol) in THF (4.5 mL) at -15 °C, and the mixture was stirred at the same temperature for 1 h and warm to room temperature for 20 h. To the mixture was concentrated and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 8/1) to give (*S*)-**67** (518 mg, 82% yield) as a pale yellow oil. Spectral data of (*S*)-**67**: IR (neat) 2928, 1962, 1739, 1599, 1344, 1163, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.1 Hz, 2 H), 7.30 (d, *J* = 8.1 Hz, 2 H), 5.17-5.08 (m, 1 H), 5.08-4.98 (m, 1 H), 3.62 (t, *J* = 6.3 Hz, 2 H), 3.05 (td, *J* = 7.5, 1.3 Hz, 2 H), 2.72 (s, 3 H), 2.42 (s, 3 H), 2.27-2.15 (m, 2 H), 2.09-1.96 (m, 2 H), 1.60 (tt, *J* = 7.2 6.3 Hz, 2 H), 0.88 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.4, 143.2, 134.7, 129.6 (2 C), 127.3 (2 C), 91.4, 87.5, 62.4, 49.7, 34.8, 32.1, 27.6, 25.9 (3 C), 25.0, 21.5, 18.3, -5.3 (2 C); LRMS (EI) *m/z* 408 $[(M\text{-}CH_3)^+]$, 366, 268, 198, 155, 91; HRMS (EI) calcd for $C_{21}H_{34}NO_3SSi$ $[(M\text{-}CH_3)^+]$ 408.2029, found 408.2024; $[\alpha]_D^{24}$ +46.9 (*c* 1.06, $CHCl_3$).

(*S*)-*N*-(8-Hydroxyocta-3,4-dien-1-yl)-*N*,4-dimethylbenzenesulfonamide ((*S*)-68)

To a solution of (*S*)-**67** (2.00 g, 4.72 mmol) in THF (30 mL) was added TBAF (1.0 M in THF, 6.3 mL, 6.3 mmol) 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 EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 2/1, 1/1) to give (*S*)-**68** (1.33 g, 91% yield) as a pale yellow oil. Spectral data of (*S*)-**68**: IR (neat) 3408, 1962, 1337, 1160, 817 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.5 Hz, 2 H), 7.31 (d, *J* = 8.5 Hz, 2 H), 5.20-5.01 (m, 2 H), 3.67 (t, *J* = 6.7 Hz, 2 H), 3.16-2.97 (m, 2 H), 2.72 (s, 3 H), 2.42 (s, 3 H), 2.21 (ddt, *J* = 7.2, 7.2, 3.1 Hz, 2 H), 2.07 (ddt, *J* = 7.2, 7.2, 2.7 Hz, 2 H), 1.75-1.53 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 143.3, 134.6, 129.6 (2 C), 127.3 (2 C), 91.1, 87.7, 62.1, 49.7, 34.8, 31.7, 27.6, 24.8, 21.5; LRMS (EI) *m/z* 264 $[(M\text{-}CH_2CH_2OH)^+]$, 198, 155, 154, 91; HRMS (EI) calcd for $C_{14}H_{18}NO_2S$ $[(M\text{-}CH_2CH_2OH)^+]$ 264.1058, found 264.1055; $[\alpha]_D^{25}$ +35.8 (*c* 1.03, $CHCl_3$). The enantiomeric excess was determined to be 99% ee by HPLC analysis with a DAICEL CHIRALPAK AD-H [eluent: *n*-hexane/2-propanol = 95/5, flow rate: 1.0 mL/min, detector: UV (240 nm)]: t_R (minor) = 41.1 min for (*R*)-enantiomer: t_R (major) = 45.3 min for (*S*)-enantiomer.

(*S*)-*N*,4-Dimethyl-*N*-(8-oxoocta-3,4-dien-1-yl)benzenesulfonamide ((*S*)-28b)

To a solution of (*S*)-**68** (765 mg, 2.47 mmol) in CH_2Cl_2 (24 mL) were added $NaHCO_3$ (451 mg, 5.37 mmol) and Dess-Martin Periodinane (1.59 g, 3.75 mmol) at 0 °C, and the mixture was stirred at room temperature for 1.5 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10 % $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 2/1) to give (*S*)-**28b** (692 mg, 91% yield) as a colorless oil, whose spectral were consistent to those reported literature[7]. Spectral data of (*S*)-**28b**: $[\alpha]_D^{19}$ +55.0 (*c* 1.14, $CHCl_3$). The enantiomeric excess was determined to be 99% ee by HPLC analysis with a DAICEL CHIRALPAK AS-H [eluent: *n*-hexane/2-propanol = 9/1, flow rate: 1.0 mL/min, detector: UV (220 nm)]: t_R (major) = 39.2 min for (*S*)-enantiomer: t_R (minor) = 58.8 min for (*R*)-enantiomer.

<Scheme 18>

(*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-8-((*N*,4-dimethylphenyl)sulfonamido)oct-5-yn-4-yl (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (69)

To a solution of (*R*)-MTPACl (70.9 mg, 0.28 mmol) in pyridine (0.3 mL) was added a solution of (*S*)-**63** (22.0 mg, 0.0500 mmol) in pyridine (0.7 mL) at room temperature, and the mixture was stirred at the same temperature for 1 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 2/1) to give (*S*)-MTPA ester **69** (32.3 mg, 98% yield) as a colorless oil. Spectral data of **69**: IR (neat) 1752, 1254, 1163, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.0 Hz, 2 H), 7.57-7.49 (m, 2 H), 7.43-7.35 (m, 3 H), 7.31 (d, *J* = 8.0 Hz, 2 H), 5.55 (tt, *J* = 6.6, 1.7 Hz, 1 H), 3.57 (s, 3 H), 3.57 (t, *J* = 6.0 Hz, 2 H), 3.15 (t, *J* = 7.2 Hz, 2 H), 2.78 (s, 3 H), 2.51 (dt, *J* = 7.2, 1.7 Hz, 2 H), 2.43 (s, 3 H), 1.83 (tt, *J* = 7.2, 6.6 Hz, 2 H), 1.60-1.46 (m, 2 H), 0.87 (s, 9 H), 0.02 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7, 143.5, 134.7, 132.3, 129.7 (3 C), 129.6 (2 C), 128.3 (2 C), 127.3 (2 C), 123.2, ($J^1_{C\text{-}F}$ = 290.3 Hz), 84.3 ($J^2_{C\text{-}F}$ = 27.6 Hz), 83.8, 78.3, 66.3, 62.1, 55.4, 49.0, 35.6, 31.3, 27.9, 25.9 (3 C), 21.5, 19.2, 18.2, -5.4 (2 C); LRMS (EI) *m/z* 598 $[(M\text{-}C_4H_9)^+]$, 198, 155, 91; HRMS (EI) calcd for $C_{28}H_{35}F_3NO_6SSi$ $[(M\text{-}C_4H_9)^+]$ 598.1906, found 598.1892; $[\alpha]_D^{26}$ -32.7 (*c* 1.02, $CHCl_3$).

(*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-8-((*N*,4-dimethylphenyl)sulfonamido)oct-5-yn-4-yl (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (70)

To a solution of (*S*)-MTPACl (73.1 mg, 0.29 mmol) in pyridine (0.3 mL) was added a solution of (*S*)-**63** (22.0 mg, 0.0500 mmol) in pyridine (0.7 mL) at room temperature, and the mixture was stirred at the same temperature for 1 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 2/1) to give (*R*)-MTPA ester **70** (27.9 mg, 85% yield) as a colorless oil. Spectral data of **70**: IR (neat) 1751, 1599, 1345, 1164, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 2 H), 7.56-7.45 (m, 2 H), 7.44-7.35 (m, 3 H), 7.32 (d, *J* = 8.3 Hz, 2 H), 5.53 (tt, *J* = 6.6, 1.7 Hz, 1 H), 3.62 (t, *J* = 6.0 Hz, 2 H), 3.54 (s, 3 H), 3.19-3.07 (m, 2 H), 2.77 (s, 3 H), 2.47 (dt, *J* = 7.3, 1.7 Hz, 2 H), 2.43 (s, 3 H), 1.94-1.79 (m, 2 H), 1.71-1.56 (m, 2 H), 0.88 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 143.5, 134.7, 131.9, 129.7 (3 C), 129.6 (2 C), 128.3 (2 C), 127.4, 127,3 (2 C), 123.2 ($J^1_{C\text{-}F}$ = 289.1 Hz), 84.6 ($J^2_{C\text{-}F}$ = 27.6 Hz), 83.7, 78.1, 66.6, 62.2, 55.5, 49.0, 35.7, 31.3, 28.1, 25.9 (3 C), 21.5, 19.2, -5.4 (2 C); LRMS (EI) *m/z* 598 $[(M\text{-}C_4H_9)^+]$, 198, 155, 91; HRMS (EI) calcd for $C_{28}H_{35}F_3NO_6SSi$ $[(M\text{-}C_4H_9)^+]$ 598.1906, found 598.1890; $[\alpha]_D^{24}$ +8.3 (*c* 0.94, $CHCl_3$).

Experimental Section of Chapter 2, Section 1

General Procedure for Cyclization Using [Rh(phosphine)]ClO_4.

A solution of [Rh(ligand)(nbd)]ClO_4 (0.0150 mmol, 10 mol% to a substrate) or [$Rh(nbd)_2$]ClO_4 (0.0150 mmol, 10 mol% to a substrate) and ligand (0.0150 mmol, 10 mol% to a substrate) in degassed (Freeze-Pump up-Thaw cycle was conducted) $ClCH_2CH_2Cl$ (0.58 mL: 0.026 M to Rh) was stirred under H_2 atmosphere at room temperature for 1 h. Then the reaction mixture was degassed, and the reaction vessel was flushed with Ar gas. To the mixture was added a solution of substrate (0.150 mmol) in degassed $ClCH_2CH_2Cl$ (0.92 mL) and the reaction mixture was stirred at 50 °C or reflux until the substrate disappeared on TLC. After removal of the solvent, the residue was purified by column chromatography on silica gel to give product.

<Scheme 34>

Methyl 8-((tetrahydro-2*H*-pyran-2-yl)oxy)octa-3,4-dienoate (143a)

To a solution of **141** (1.27 g, 4.99 mmol) in THF (5.0 mL) was added LHMDS (1.3 M in THF, 8.5 mL, 11 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the solution was added methyl chloroformate (400 μL, 5.18 mmol), and the mixture was stirred at the same temperature for 10 min. Then, to the solution was added a solution of **142** (1.39 g, 7.72 mmol) in THF (2.0 mL) at -78 °C, and the mixture was stirred and warmed to room temperature for 21 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1) to give **143a** (1.28 g, 70% yield) as a pale yellow oil. Spectral data of **143a**: IR (neat) 2951, 2869, 1968, 1740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.73 (dt, *J* = 7.0, 3.1 Hz, 1 H), 5.43 (dt, *J* = 7.0, 6.7 Hz, 1 H), 4.60-4.55 (m, 1 H), 3.85 (ddd, *J* = 11.0, 8.0, 3.0 Hz, 1 H), 3.78-3.73 (m, 7 H), 3.53-3.46 (m, 1 H), 3.44-3.37 (m, 1 H), 2.85 (q, *J* = 2.5 Hz, 2 H), 2.20-2.07 (m, 2 H), 1.88-1.47 (m, 11 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2, 169.7, 169.6, 98.7*[1], 95.4, 90.3, 78.3, 73.6, 66.7*, 62.2*, 57.7, 52.8 (2 C), 30.6, 28.9, 25.4, 25.1, 24.9, 19.5*, 3.4; LRMS (EI) *m/z* 364 [M^+], 203, 177, 145, 85.

Dimethyl 2-(but-2-yn-1-yl)-2-(6-((tetrahydro-2*H*-pyran-2-yl)oxy)hexa-1,2-dien-1-yl)malonate (134a)

To a solution of **143a** (770 mg, 2.11 mmol) in MeOH (21 mL) was added $TsOH \cdot H_2O$ (40.3 mg, 0.212 mmol) at 0 °C, and the mixture was stirred at room temperature for 16.5 h. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C. After removal of MeOH, the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (25 mL) was added Dess-Martin Periodinane (1.55 g, 3.65 mmol) at 0 °C, and the mixture was stirred at room temperature for 1.5 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1, 4/1) to give **134a** (554 mg, 94% yield in 2 steps) as a colorless oil. Spectral data of **134a**: IR (neat) 3003, 2955, 2923, 2843, 2729, 1969, 1737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.77 (t, *J* = 1.3 Hz, 1 H), 5.77 (dt, *J* = 6.5, 3.3 Hz, 1 H),

[1] The * at ^{13}C NMR data points indicates two peaks due to the presence of the diastereomers associated with the stereocenter of THP group.

5.47 (dt, *J* = 6.5, 6.2 Hz, 1 H), 3.75 (s, 3 H), 3.73 (s, 3 H), 2.84 (dq, *J* = 17.0, 2.5 Hz, 1 H), 2.80 (dq, *J* = 17.0, 2.5 Hz, 1 H), 2.66-2.54 (m, 2 H), 2.34 (tdd, *J* = 6.4, 6.2, 3.3 Hz, 2 H), 1.72 (t, *J* =2.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.1, 201.5, 169.5, 169.5, 94.4, 91.8, 78.5, 73.6, 57.7, 52.9 (2 C), 42.2, 24.8, 20.6, 3.5; LRMS (EI) *m/z* 225 [(M-MeC≡CCH_2)$^+$], 193, 161, 115, 91; HRMS (EI) calcd for $C_{11}H_{13}O_5$ [(M-MeC≡CCH_2)$^+$] 225.0763, found 225.0764.

<Table 3>

<run 1>

Dimethyl (1*Z*, 5*Z*, 7*Z*)-3-hydroxy-2-methylbicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate (137a)

According to the general procedure for cyclization, a crude product, which was prepared from **134a** (41.6 mg, 0.149 mmol) and [Rh(dppe)(nbd)]ClO_4 (10.4 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1) to give **137a** (33.2 mg, 80% yield) as a colorless oil. The structure of **137a** was determined by 2D-NMR (COSY, HMQC, HMBC). Spectral data of **137a**: IR (neat) 3433, 3029, 3006, 2953, 2925, 2849, 1731 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.34 (dd, *J* = 10.8, 1.6 Hz, 1 H), 5.97 (s, 1 H), 5.76 (ddd, *J* = 10.8, 7.2, 4.8 Hz, 1 H), 4.21 (ddd, *J* = 9.6, 5.8, 3.0 Hz, 1 H), 3.75 (s, 6 H), 3.22 (d, *J* = 17.2 Hz, 1 H), 3.17 (d, *J* = 17.2 Hz, 1 H), 2.71-2.57 (m, 2 H), 1.93 (s, 3 H), 1.69 (d, *J* = 9.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 170.9, 143.7, 136.3, 133.5, 132.9, 128.3, 126.5, 72.2, 62.6, 53.0 (2 C), 38.6, 35.8, 21.3; LRMS (EI) *m/z* 278 [M$^+$], 219, 159, 131, 115, 91; HRMS (EI) calcd for $C_{15}H_{18}O_5$ [M$^+$] 278.1154, found 278.1148.

<run 2>

According to the general procedure for cyclization, a crude product, which was prepared from **134a** (41.8 mg, 0.150 mmol), [Rh(nbd)$_2$]ClO_4 (5.8 mg, 0.015 mmol) and DPPM (5.8 mg, 0.015 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 19 h, was obtained. Yield of **134a** was determined to be 55% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 3>

According to the general procedure for cyclization, a crude product, which was prepared from **134a** (41.5 mg, 0.149 mmol) and [Rh(dppb)(nbd)]ClO_4 (10.8 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 24 h, was obtained. Yield of **134a** was determined to be 75% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 4>

According to the general procedure for cyclization, a crude product, which was prepared from **134a** (41.8 mg, 0.150 mmol), [Rh(nbd)$_2$]ClO_4 (5.8 mg, 0.015 mmol) and DPPF (8.3 mg, 0.015 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 18 h, was obtained. Yields of **134a** and **137a** were determined to be 21% and 15% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 5>

According to the general procedure for cyclization, a crude product, which was prepared from **134a** (41.5 mg, 0.149 mmol) and [Rh(dpephos)(nbd)]ClO_4 (12.5 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 26 h, was obtained. Yield of **134a** was determined to be 56% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 6>

According to the general procedure for cyclization, a crude product, which was prepared from **134a** (41.8 mg, 0.150 mmol) and [Rh(binap)(nbd)]ClO_4 (13.8 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 22 h, was obtained. Yields of **134a** and **137a** were determined to be 45% and 11% by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 7>

According to the general procedure for cyclization, a crude product, which was prepared from **134a** (41.8 mg, 0.150 mmol), [Rh(nbd)$_2$]ClO_4 (5.8 mg, 0.015 mmol) and BIPHEP (7.8 mg, 0.015 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 24 h, was obtained. Yields of **134a** and **137a** were determined to be 31% and 15% by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 8>

According to the general procedure for cyclization, a crude product, which was prepared from **134a** (41.8 mg, 0.150 mmol) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 2/1) to give **137a** (38.2 mg, 91% yield) as a colorless oil.

<run 9>

A solution of $Rh(PPh_3)_3Cl$ (13.7 mg, 0.0148 mmol) in $ClCH_2CH_2Cl$ (0.58 mL) was stirred at room temperature for 10 min. Then to the solution was added a solution of **134a** (41.5 mg, 0.149 mmol) in $ClCH_2CH_2Cl$ (0.92 mL) and the reaction mixture was stirred at 50 °C for 18 h. After removal of the solvent, the residue was obtained. Yields of **134a** and **137a** were determined to be 66% and 5% by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<Scheme 35>

According to the general procedure for cyclization, a crude product, which was prepared from **134a** (104 mg, 0.374 mmol) and [Rh(dppbz)(nbd)]ClO_4 (5.6 mg, 0.0075 mmol) in $ClCH_2CH_2Cl$ (0.75 mL) at 50 °C for 2 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1) to give **137a** (83.0 mg, 80% yield) as a colorless oil.

<Table 4>

<run 1>

Dimethyl (1*Z*, 5*Z*, 7*Z*)-2-(*tert*-butyl-dimethylsilyl)methyl
-3-hydroxybicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate (137b)

According to the general procedure for cyclization, a crude product, which was prepared from **134b** (61.3 mg, 0.150 mmol) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 2 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1) to give **137b** (44.0 mg, 72% yield) as a colorless oil. Spectral data of **137b**: IR (neat) 3479, 3030, 3000, 2953, 2926, 2893, 2856, 1737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.29 (d, *J* = 11.5 Hz, 1 H), 6.05 (s, 1 H), 5.84 (ddd, *J* = 11.5, 5.8, 5.8 Hz, 1 H), 4.55 (dd, *J* = 5.5, 5.5 Hz, 1 H), 4.41 (d, *J* = 12.5 Hz, 1 H), 4.29 (d, *J* = 12.5 Hz, 1 H), 3.74 (s, 3 H), 3.74 (s, 3 H), 3.26 (d, *J* = 17.0 Hz, 1 H), 3.21 (d, *J* = 17.0 Hz, 1 H), 3.04 (d, *J* = 5.5 Hz, 1 H), 2.66 (ddd, *J* = 16.0, 5.8, 5.5 Hz, 1 H), 2.61-2.53 (m, 1 H), 0.90 (s, 9 H), 0.11 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.6, 144.1, 136.7, 134.94, 134.85, 129.5, 125.6, 69.1, 64.6,

62.8, 53.1, 53.0, 37.5, 35.8, 25.8 (3 C), 18.1, -5.4 (2 C); LRMS (EI) *m/z* 351 [(M-$(CH_3)_3C)^+$], 259, 227, 199, 75; HRMS (EI) calcd for $C_{17}H_{23}O_6Si$ [(M-$(CH_3)_3C)^+$] 351.1264, found 351.1264.

<run 2>

Dimethyl (1*E*, 5*Z*, 7*Z*)-3-hydroxy-2-trimethylsilylbicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate (137c)

According to the general procedure for cyclization, a crude product, which was prepared from **134c** (50.5 mg, 0.150 mmol), MS4A (100 mg) and [Rh(dppbz)(nbd)]ClO_4 (11.1 mg, 0.0149 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 1/1) to give **137c** (46.1 mg, 91% yield) as a colorless oil. Spectral data of **137c**: IR (neat) 3454, 3029, 3003, 2953, 2896, 2843, 1737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.32 (dd, *J* = 11.5, 3.0 Hz, 1 H), 6.02 (s, 1 H), 5.75 (ddd, *J* = 11.5, 6.5, 3.0 Hz, 1 H), 4.50 (dd, *J* = 6.8, 6.5 Hz, 1 H), 3.75 (s, 3 H), 3.73 (s, 3 H), 3.34 (d, *J* = 16.5 Hz, 1 H), 3.17 (d, *J* = 16.5 Hz, 1 H), 2.70 (ddd, *J* = 16.5, 6.8, 6.5 Hz, 1 H), 2.58-2.49 (m, 1 H), 1.67 (d, *J* = 6.5 Hz, 1 H), 0.23 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.3, 151.0, 145.8, 137.4, 136.1, 129.1, 125.6, 67.9, 63.0, 53.0 (2 C), 40.8, 36.3, -0.09 (3 C); LRMS (EI) *m/z* 336 [M^+], 277, 187, 173, 73; HRMS (EI) calcd for $C_{17}H_{24}O_5Si$ [M^+] 336.1393, found 336.1381.

<run 3>

Dimethyl (1*E*, 5*Z*, 7*Z*)-2-chloro-3-hydroxybicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate (137d)

According to the general procedure for cyclization, a crude product, which was prepared from **134d** (44.8 mg, 0.150 mmol) and [Rh(dppbz)(nbd)]ClO_4 (11.1 mg, 0.0149 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 2/1) to give **137d** (33.6 mg, 75% yield) as a pale yellow oil. Spectral data of **137d**: IR (neat) 3478, 3075, 3032, 3006, 2954, 2900, 1733 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.34 (d, *J* = 11.5 Hz, 1 H), 6.12 (s, 1 H), 5.81 (ddd, *J* = 11.5, 7.4, 4.4 Hz, 1 H), 4.53-4.48 (m, 1 H), 3.76 (s, 6 H), 3.38 (d, *J* = 18.5 Hz, 1 H), 3.33 (d, *J* = 18.5 Hz, 1 H), 2.77-2.70 (m, 1 H), 2.66 (ddd, *J* = 16.0, 7.4, 7.4 Hz, 1 H), 2.38-2.08 (brs, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 170.1, 141.3, 139.6, 136.5, 129.6, 128.1, 126.0, 73.2, 62.5, 53.20, 53.18, 40.3, 34.7; LRMS (EI) *m/z* 298 [M^+], 239, 203, 115, 59; HRMS (EI) calcd for $C_{14}H_{15}ClO_5$ [M^+] 298.0608, found 298.0608.

<run 4>

Trimethyl (1*Z*, 5*Z*, 7*Z*)-3-hydroxybicyclo[5.3.0]deca-1,5,7-triene-2,9,9-tricarboxylate (137e)

According to the general procedure for cyclization, a crude product, which was prepared from **134e** (48.3 mg, 0.150 mmol) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 4/1, 2/1) to give **137e** (42.6 mg, 88% yield) as a pale yellow oil. Spectral data of **137e**: IR (neat) 3508, 3074, 3033, 3004, 2954, 2846, 1732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.41 (s, 1 H), 6.39 (dd, *J* = 11.5, 2.0 Hz, 1 H), 5.86 (ddd, *J* = 11.5, 7.9, 3.4 Hz, 1 H), 5.01 (d, *J* = 7.9 Hz, 1 H), 3.81 (s, 3 H), 3.76 (s, 3 H), 3.74 (s, 3 H), 3.65 (s, 2 H), 2.75 (ddd, *J* = 16.5, 7.9, 7.2 Hz, 1 H), 2.63-2.55 (m, 1 H), 2.40-2.20 (brs, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0, 169.8, 168.4, 153.8, 144.0, 142.0, 129.2, 128.2, 125.2, 66.3, 63.3, 53.2 (2 C), 52.0, 41.2, 34.8; LRMS (EI) *m/z* 322 [M^+], 290, 231, 203, 115, 59; HRMS (EI) calcd for $C_{16}H_{18}O_7$ [M^+] 322.1053, found 322.1045.

<Table 5>

<run 1>

Dimethyl (1*Z*, 5*Z*, 7*Z*)-3-hydroxy-2-phenylbicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate (137f)

According to the general procedure for cyclization, a crude product, which was prepared from **134f** (51.1 mg, 0.150 mmol) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1) to give **137f** (42.5 mg, 83% yield) as a pale yellow oil. Spectral data of **137f**: IR (neat) 3472, 3056, 3028, 2953, 2844, 2250, 1731 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41-7.27 (m, 5 H), 6.42 (d, *J* = 11.0 Hz, 1 H), 6.12 (s, 1 H), 5.86 (dt, *J* = 11.0, 5.6 Hz, 1 H), 4.56-4.50 (m, 1 H), 3.73 (s, 3 H), 3.69 (s, 3 H), 3.20 (d, *J* = 17.5 Hz, 1 H), 3.03 (d, *J* = 17.5 Hz, 1 H), 2.77 (t, *J* = 5.6 Hz, 2 H), 1.98 (d, *J* = 8.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 170.4, 143.9, 142.5, 138.6, 138.4, 135.3, 128.7, 128.5 (2 C), 127.7 (2 C), 127.0, 125.8, 71.9, 62.7, 52.97, 52.95, 39.7, 36.2; LRMS (EI) *m/z* 340 [M^+], 281, 252, 221, 178, 91; HRMS (EI) calcd for $C_{20}H_{20}O_5$ [M^+] 340.1311, found 340.1319.

<run 2>

Dimethyl (1*Z*, 5*Z*, 7*Z*)-3-hydroxy-2-(4-methoxyphenyl)bicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate (137g)

According to the general procedure for cyclization, a crude product, which was prepared from **134g** (55.3 mg, 0.149 mmol) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 2 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 2/1) to give **137g** (45.2 mg, 82% yield) as a pale yellow oil. Spectral data of **137g**: IR (neat) 3501, 3031, 3003, 2953, 2839, 1732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.27-7.24 (m, 2 H), 6.92-6.89 (m, 2 H), 6.40 (d, *J* = 11.0 Hz, 1 H), 6.10 (s, 1 H), 5.84 (dt, *J* = 11.0, 5.8 Hz, 1 H), 4.56-4.49 (m, 1 H), 3.82 (s, 3 H), 3.73 (s, 3 H), 3.69 (s, 3 H), 3.21 (d, *J* = 17.5 Hz, 1 H), 3.04 (d, *J* = 17.5 Hz, 1 H), 2.75 (t, *J* = 5.8 Hz, 2 H), 1.98 (d, *J* = 8.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.5, 158.5, 144.0, 138.3, 138.1, 135.0, 134.8, 129.0 (2 C), 128.7, 125.9, 113.9 (2 C), 72.1, 62.6, 55.2, 52.98, 52.95, 39.8, 36.2; LRMS (EI) *m/z* 370 [M^+], 311, 203, 135, 121; HRMS (EI) calcd for $C_{21}H_{22}O_6$ [M^+] 370.1416, found 370.1416.

<run 3>

Dimethyl (1*Z*, 5*Z*, 7*Z*)-3-hydroxy-2-(4-methoxycarbonylphenyl)bicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate (137h)

According to the general procedure for cyclization, a crude product, which was prepared from **134h** (59.8 mg, 0.150 mmol) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 2/1) to give **137h** (45.6 mg, 76% yield) as a pale yellow oil. Spectral data of **137h**: IR (neat) 3500, 3030, 3002, 2953, 2846, 1731, 1606 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.06-8.03 (m, 2 H), 7.43-7.40 (m, 2 H), 6.43 (d, *J* = 11.5 Hz, 1 H), 6.17 (s, 1 H), 5.86 (dt, *J* = 11.5, 5.6 Hz, 1 H), 4.55-4.49 (m, 1 H), 3.93 (s, 3 H), 3.74 (s, 3 H), 3.69 (s, 3 H), 3.20 (d, *J* = 17.0 Hz, 1 H), 2.98 (d, *J* = 17.0 Hz, 1 H), 2.78 (t, *J* = 5.6 Hz, 2 H), 2.01 (d, *J* = 9.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 170.2, 166.8, 147.3, 143.7, 139.7, 137.5, 136.1, 129.8 (2 C), 128.7, 128.6, 127.8 (2 C), 125.9, 71.6, 62.7, 53.1, 53.0, 52.1, 39.6, 36.2; LRMS (EI) *m/z* 398 [M^+], 339, 307, 279, 191, 59; HRMS (EI) calcd for $C_{22}H_{22}O_7$ [M^+] 398.1366, found 398.1363.

<Scheme 36>

Dimethyl (1*E*, 5*Z*, 7*Z*)-2-butyl-3-hydroxy-*N*-tosyl-10-azabicyclo[5.3.0]deca-1,5,7-triene (137i)

According to the general procedure for cyclization, a crude product, which was prepared from **134i** (55.1 mg, 0.153 mmol) and [Rh(dppbz)(nbd)]ClO_4 (10.8 mg, 0.0145 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 4/1) to give **137i** (39.0 mg, 71% yield) as a pale yellow oil.

Spectral data of **137i**: IR (neat) 3408, 3030, 2956, 2928, 2871, 1597 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.0 Hz, 2 H), 7.18 (d, *J* = 8.0 Hz, 2 H), 5.98 (dd, *J* = 11.0, 2.3 Hz, 1 H), 5.62 (ddd, *J* = 11.0, 7.4, 3.9 Hz, 1 H), 5.42 (s, 1 H), 4.50 (dd, *J* = 7.0, 7.0 Hz, 1 H), 4.18 (d, *J* = 17.5 Hz, 1 H), 4.06 (d, *J* = 17.5 Hz, 1 H), 2.87 (ddd, *J* = 14.0, 9.8, 5.8 Hz, 1 H), 2.74 (ddd, *J* = 16.5, 7.4, 7.0 Hz, 1 H), 2.70-2.63 (m, 1 H), 2.58 (ddd, *J* = 14.0, 9.6, 4.6 Hz, 1 H), 1.94 (s, 3 H), 1.93 (d, *J* = 7.0 Hz, 1 H), 1.70-1.61 (m, 1 H), 1.56-1.46 (m, 1 H), 1.39 (tq, *J* = 7.5, 7.5 Hz, 2 H), 0.94 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 138.9, 138.8, 138.7, 133.3, 129.1 (2 C), 127.9 (2 C), 127.8, 126.9, 123.8, 69.7, 54.4, 35.4, 35.1, 30.1, 22.9, 21.5, 14.1; LRMS (ESI) *m/z* 382 [$(M+Na)^+$], 358, 340, 293, 218; HRMS (ESI) calcd for $C_{20}H_{25}O_3NNaS$ [$(M+Na)^+$] 382.1447, found 382.1450.

<Scheme 37>

<eq. 1>

Dimethyl (1*Z*, 5*Z*, 7*Z*)-3-hydroxy-2,8-dimethylbicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate (137j)

According to the general procedure for cyclization, a crude product, which was prepared from **134j** (43.8 mg, 0.150 mmol), MS4A (87.4 mg) and $[Rh(dppbz)(nbd)]ClO_4$ (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 1/1) to give **137j** (38.1 mg, 87% yield). Spectral data of **137j**: IR (neat) 3409, 3034, 2998, 2952, 2916, 2848, 1732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.37 (d, *J* = 12.0 Hz, 1 H), 5.79 (ddd, *J* = 12.0, 7.0, 4.8 Hz, 1 H), 4.22-4.13 (m, 1 H), 3.74 (s, 3 H), 3.73 (s, 3 H), 3.12 (d, *J* = 16.5 Hz, 1 H), 3.06 (d, *J* = 16.5 Hz, 1 H), 2.66-2.53 (m, 2 H), 1.96 (s, 3 H), 1.88 (s, 3 H), 1.84-1.71 (brs, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 171.0, 141.0, 138.5, 136.7, 129.8, 127.5, 124.9, 72.1, 65.7, 52.7 (2 C), 38.7, 35.5, 21.2, 13.3; LRMS (EI) *m/z* 292 [M^+], 274, 215, 156, 115, 59; HRMS (EI) calcd for $C_{16}H_{20}O_5$ [M^+] 292.1311, found 292.1310.

<eq. 2>

Dimethyl (1*Z*, 5*Z*, 7*Z*)-3-hydroxy-2,6-dimethylbicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate (137k)

Dimethyl (*E*)-5-ethylidene-2'-oxo-[1,1'-bi(cyclopentan)]-1-ene-3,3-dicarboxylate (144)

According to the general procedure for cyclization, a crude product, which was prepared from **134k** (43.8 mg, 0.150 mmol) and $[Rh(dppbz)(nbd)]ClO_4$ (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1, 5/1, 1/1) to give **137k** (19.1 mg, 44% yield) and **144** (20.8 mg, 47% yield). Spectral data of **137k**: IR (neat) 3515, 3002, 2953, 2922, 2852, 1735 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.10 (s, 1 H), 5.66 (t, *J* = 6.0 Hz, 1 H), 4.15-4.05 (m, 1 H), 3.76 (s, 3 H), 3.75 (s, 3 H), 3.20 (d, *J* = 17.0 Hz, 1 H), 3.14 (d, *J* = 17.0 Hz, 1 H), 2.60-2.49 (m, 2 H), 1.97 (s, 3 H), 1.90 (s, 3 H), 1.75-1.60 (brs, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 171.0, 145.6, 136.4, 133.0, 132.5, 131.7, 125.5, 72.6, 62.1, 53.04, 53.01, 38.6, 34.7, 23.1, 21.2; LRMS (EI) *m/z* 292 [M^+], 233, 204, 173, 145, 129, 59; HRMS (EI) calcd for $C_{16}H_{20}O_5$ [M^+] 292.1311, found 292.1304.

Spectral data of **144**: IR (neat) 3078, 3029, 2954, 2920, 2857, 1739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.78 (s, 1 H), 5.47 (qt, *J* = 7.2, 2.5 Hz, 1 H), 3.73 (s, 6 H), 3.13 (s, 2 H), 3.09-2.99 (m, 1 H), 2.52 (dd, *J* = 18.4, 7.4 Hz, 1 H), 2.39-2.13 (m, 4 H), 1.96-1.85 (m, 1 H), 1.72 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.2, 171.2, 171.1, 149.8, 142.1, 126.1, 115.6, 63.1, 52.9 (2 C), 44.1, 37.7, 35.7, 34.1, 28.2, 14.7; LRMS (EI) *m/z* 292 [M^+], 233, 201, 173, 117, 91, 59; HRMS (EI) calcd for $C_{16}H_{20}O_5$ [M^+] 292.1311, found 292.1303.

<Scheme 38>

Dimethyl 2-(4-((*tert*-butyldimethylsilyl)oxy)but-2-yn-1-yl)
-2-(6-((tetrahydro-2*H*-pyran-2-yl)oxy)hexa-1,2-dien-1-yl)malonate (143b)

To a solution of **141** (1.00 g, 3.93 mmol) in THF (2.0 mL) was added LHMDS (1.6 M in THF, 5.5 mL, 8.8 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the solution was added methyl chloroformate (310 μL, 4.01 mmol), and the mixture was stirred at the same temperature for 15 min. Then, to the solution was added a solution of **150** (2.25 g, 7.25 mmol) in THF (2.0 mL) at -78 °C, and the mixture was stirred and warmed to room temperature for 34 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1) to give **143b** (842 mg, 43% yield) as a pale yellow oil. Spectral data of **143b**: IR (neat) 2952, 2857, 1969, 1742 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.74 (dt, *J* = 6.5, 3.3 Hz, 1 H), 5.43 (dt, *J* = 6.5, 6.2 Hz, 1 H), 4.60-4.55 (m, 1 H), 4.25 (t, *J* = 2.0 Hz, 2 H), 3.85 (ddd, *J* = 11.0, 7.9, 3.1 Hz, 1 H), 3.78-3.72 (m, 7 H), 3.53-3.47 (m, 1 H), 3.43-3.37 (m, 1 H), 2.94 (t, *J* = 2.0 Hz, 2 H), 2.20-2.05 (m, 2 H), 1.85-1.48 (m, 8 H), 0.89 (s, 9 H), 0.09 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2, 169.5, 169.4, 98.8*[1], 95.6, 90.3, 81.4, 79.7, 66.7*, 62.2*, 57.5, 52.9 (2 C), 51.7, 30.7, 28.9, 25.8 (3 C), 25.4, 25.1, 25.0, 19.6*, 18.2, -5.2 (2 C); LRMS (EI) *m/z* 437 [$(M-(CH_3)_3C)^+$], 201, 85.

Dimethyl 2-(4-((*tert*-butyldimethylsilyl)oxy)but-2-yn-1-yl)-2-(6-oxohexa-1,2-dien-1-yl)malonate (134b)

To a solution of **143b** (184 mg, 0.372 mmol) in Et_2O (1.3 mL) was added $MgBr_2 \cdot OEt_2$ (290 mg, 1.12 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 to give a crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (4.0 mL) was added Dess-Martin Periodinane (239 mg, 0.563 mmol) at 0 °C, and the mixture was stirred at room temperature for 1.5 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1, 5/1) to give **134b** (93.7 mg, 62% yield in 2 steps) as a colorless oil. Spectral data of **134b**: IR (neat) 2954, 2930, 2897, 2857, 2723, 1969, 1740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.77 (s, 1 H), 5.78 (dt, *J* = 6.5, 3.4 Hz, 1 H), 5.47 (dt, *J* = 6.5, 6.2 Hz, 1 H), 4.23 (t, *J* = 2.0 Hz, 2 H), 3.74 (s, 3 H), 3.73 (s, 3 H), 2.93 (dt, *J* = 17.0, 2.0 Hz, 1 H), 2.90 (dt, *J* = 17.0, 2.0 Hz, 1 H), 2.64-2.52 (m, 2 H), 2.38-2.31 (m, 2 H), 0.87 (s, 9 H), 0.07 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.1, 201.4, 169.3, 169.2, 94.6, 91.7, 81.5, 79.5, 57.5, 53.0 (2 C), 51.7, 42.2, 25.7 (3 C), 24.9, 20.6, 18.2, -5.3 (2 C); LRMS (EI) *m/z* 408 [M^+], 351, 213, 143, 115, 89; HRMS (EI) calcd for $C_{21}H_2O_6Si$ [M^+] 408.1968, found 408.1968.

<Scheme 39>

Dimethyl 2-(6-((tetrahydro-2*H*-pyran-2-yl)oxy)hexa-1,2-dien-1-yl)-2-(3-(trimethylsilyl)prop-2-yn-1-yl)malonate (143c)

To a solution of **141** (590 mg, 2.32 mmol) in THF (0.60 mL) was added LHMDS (1.6 M in THF, 3.1 mL, 5.0 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the solution was added methyl chloroformate (200 μL, 2.59 mmol), and the mixture was stirred at the same temperature for 20 min. Then, to the solution was added a solution of **151** (806 mg, 3.38 mmol) in THF (1.8 mL) at -78 °C, and the mixture was stirred and warmed to room temperature for 15.5 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and

concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 15/1) to give **143c** (653 mg, 67% yield) as a pale yellow oil. Spectral data of **143c**: IR (neat) 2952, 2871, 2180, 1969, 1742 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.72 (dt, *J* = 6.5, 3.0 Hz, 1 H), 5.41 (dt, *J* = 6.5, 6.5 Hz, 1 H), 4.59-4.54 (m, 1 H), 3.84 (ddd, *J* = 11.5, 8.1, 3.1 Hz, 1 H), 3.78-3.73 (m, 7 H), 3.53-3.47 (m, 1 H), 3.43-3.37 (m, 1 H), 2.91 (s, 2 H), 2.21-2.05 (m, 2 H), 1.90-1.43 (m, 8 H), 0.11 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.1, 169.4 (2 C), 101.5, 98.8*[1], 95.7, 90.3*, 87.6, 66.7*, 62.2*, 57.8, 52.9 (2 C), 30.7*, 29.0, 25.9, 25.4, 25.2, 19.6*, -0.06 (3 C); LRMS (EI) *m/z* 422 [M^+], 263, 157, 131, 85.

Dimethyl 2-(6-oxohexa-1,2-dien-1-yl)-2-(3-(trimethylsilyl)prop-2-yn-1-yl)malonate (134c)

To a solution of **143c** (390 mg, 0.923 mmol) in MeOH (9.3 mL) was added $TsOH·H_2O$ (18.2 mg, 0.0957 mmol) at 0 °C, and the mixture was stirred at room temperature for 4 h. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C. After removal of MeOH, the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (9.3 mL) was added Dess-Martin Periodinane (622 mg, 1.47 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **134c** (216 mg, 70% yield in 2 steps) as a colorless oil. Spectral data of **134c**: IR (neat) 2956, 2842, 2726, 2180, 1970, 1740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.78 (t, *J* = 1.0 Hz, 1 H), 5.78 (dt, *J* = 7.0, 3.3 Hz, 1 H), 5.46 (dt, *J* = 7.0, 6.2 Hz, 1 H), 3.74 (s, 3 H), 3.73 (s, 3 H), 2.92 (d, *J* = 17.0 Hz, 1 H), 2.87 (d, *J* = 17.0 Hz, 1 H), 2.66-2.53 (m, 2 H), 2.39-2.32 (m, 2 H), 0.10 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.1, 201.4, 169.2 (2 C), 101.4, 94.7, 91.7, 87.8, 57.7, 53.0, 52.9, 42.2, 25.8, 20.7, -0.1 (3 C); LRMS (EI) *m/z* 277 [$(M-CO_2Me)^+$], 225, 193, 161, 89, 73; HRMS (EI) calcd for $C_{15}H_{21}O_3Si$ [$(M-CO_2Me)^+$] 277.1260, found 277.1255.

<Scheme 40>

Dimethyl 2-(prop-2-yn-1-yl)-2-(6-((tetrahydro-2*H*-pyran-2-yl)oxy)hexa-1,2-dien-1-yl)malonate (152)

To a solution of **143c** (3.86 g, 9.13 mmol) in MeOH (91 mL) was added K_2CO_3 (1.94 g, 14.0 mmol) at 0 °C, and the mixture was stirred at room temperature for 1.5 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C. After removal of MeOH, the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 3/1) to give **152** (2.61 g, 82% yield) as a pale yellow oil. Spectral data of **152**: IR (neat) 3288, 2951, 2869, 1968, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.72 (dt, *J* = 6.5, 3.0 Hz, 1 H), 5.43 (dt, *J* = 6.5, 6.5 Hz, 1 H), 4.57-4.53 (m, 1 H), 3.83 (ddd, *J* = 11.5, 7.9, 3.4 Hz, 1 H), 3.77-3.70 (m, 7 H), 3.51-3.44 (m, 1 H), 3.41-3.35 (m, 1 H), 2.89 (d, *J* = 3.0 Hz, 2 H), 2.20-2.05 (m, 2 H), 1.97 (t, *J* = 3.0 Hz, 1 H), 1.86-1.43 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.3, 169.4, 169.3, 98.8*[1], 95.8, 90.0, 79.1, 70.9, 66.7*, 62.2*, 57.3, 53.0 (2 C), 30.6, 28.9, 25.4, 25.1, 24.4, 19.5*; LRMS (EI) *m/z* 350 [M^+], 190, 129, 85.

Dimethyl 2-(3-chloroprop-2-yn-1-yl)-2-(6-((tetrahydro-2*H*-pyran-2-yl)oxy)hexa-1,2-dien-1-yl)malonate (143d)

To a solution of **152** (359 mg, 1.02 mmol) in THF (5.0 mL) was added LHMDS (1.6 M in THF, 0.80 mL, 1.3 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the solution was added *N*-chlorosuccinimide (299 mg, 2.24 mmol), and the mixture was stirred and warmed to room temperature for 15 h. To

the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1) to give **143d** (138 mg, 35% yield) as a pale yellow oil. Spectral data of **143d**: IR (neat) 2952, 2871, 1968, 1741 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.70 (dt, *J* = 7.0, 3.1 Hz, 1 H), 5.45 (dt, *J* = 7.0, 6.5 Hz, 1 H), 4.59-4.55 (m, 1 H), 3.84 (ddd, *J* = 10.5, 8.3, 3.0 Hz, 1 H), 3.78-3.73 (m, 7 H), 3.52-3.46 (m, 1 H), 3.44-3.37 (m, 1 H), 2.89 (s, 2 H), 2.18-2.10 (m, 2 H), 1.86-1.46 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.3, 169.32, 169.26, 98.8*[1], 96.0*, 90.0, 66.7*, 64.6, 62.2*, 60.0, 57.2, 53.1 (2 C), 30.6, 28.9, 25.4, 25.2, 24.6, 19.6*; LRMS (EI) *m/z* 384 [M^+], 349, 207, 129, 115, 85.

Dimethyl 2-(3-chloroprop-2-yn-1-yl)-2-(6-oxohexa-1,2-dien-1-yl)malonate (134d)

To a solution of **143d** (138 mg, 0.358 mmol) in MeOH (3.6 mL) was added $TsOH \cdot H_2O$ (12.4 mg, 0.0652 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C. After removal of MeOH, the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (3.6 mL) was added Dess-Martin Periodinane (233 mg, 0.549 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 4/1) to give **134d** (80.4 mg, 75% yield in 2 steps) as a colorless oil. Spectral data of **134d**: IR (neat) 3013, 2955, 2844, 2727, 2247, 1969, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.78 (t, *J* = 1.5 Hz, 1 H), 5.75 (dt, *J* = 6.5, 3.4 Hz, 1 H), 5.54 (dt, *J* = 6.5, 6.2 Hz, 1 H), 3.77 (s, 3 H), 3.75 (s, 3 H), 2.90 (d, *J* = 16.5 Hz, 1 H), 2.86 (d, *J* = 16.5 Hz, 1 H), 2.63-2.57 (m, 2 H), 2.40-2.33 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2, 201.4, 169.2, 169.1, 94.9, 91.4, 64.6, 60.2, 57.2, 53.2 (2 C), 42.2, 24.5, 20.6; LRMS (EI) *m/z* 239 [$(M\text{-}CO_2Me)^+$], 225, 193, 161, 115, 59; HRMS (EI) calcd for $C_{12}H_{15}O_3$ [$(M\text{-}CO_2Me)^+$] 239.0475, found 239.0475.

Trimethyl 10-((tetrahydro-2*H*-pyran-2-yl)oxy)deca-5,6-dien-1-yne-1,4,4-tricarboxylate (143e)

To a solution of **152** (350 mg, 0.999 mmol) in THF (5.0 mL) was added LHMDS (1.6 M in THF, 1.3 mL, 1.9 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 1 h. To the solution was added methyl chloroformate (150 μL, 1.94 mmol), and the mixture was stirred and warmed to room temperature for 19 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1, 3/1) to give **143e** (284 mg, 70% yield) as a pale yellow oil. Spectral data of **143e**: IR (neat) 2952, 2871, 2242, 1968, 1740, 1714 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.71 (dt, *J* = 6.5, 3.1 Hz, 1 H), 5.45 (dt, *J* = 6.5, 6.5 Hz, 1 H), 4.57-4.54 (m, 1 H), 3.84 (ddd, *J* = 11.5, 7.8, 3.3 Hz, 1 H), 3.79-3.70 (m, 10 H), 3.52-3.45 (m, 1 H), 3.41-3.36 (m, 1 H), 3.04 (s, 2 H), 2.19-2.10 (m, 2 H), 1.86-1.46 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.3, 168.9 (2 C), 153.6, 98.8*[1], 96.5, 89.8*, 84.1, 74.8, 66.6*, 62.2*, 56.8, 53.2 (2 C), 52.6, 30.6, 28.9, 25.4, 25.1, 24.4, 19.6*; LRMS (EI) *m/z* 277 [$(M\text{-}2CO_2Me\text{-}Me)^+$], 199, 183, 77.

Trimethyl 10-oxodeca-5,6-dien-1-yne-1,4,4-tricarboxylate (134e)

To a solution of **143e** (155 mg, 0.379 mmol) in MeOH (3.8 mL) was added $TsOH \cdot H_2O$ (7.9 mg, 0.042 mmol) at 0 °C, and the mixture was stirred at room temperature for 14 h. To the mixture was added saturated $NaHCO_3$ aqueous

solution at 0 °C. After removal of MeOH, the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (3.8 mL) was added Dess-Martin Periodinane (254 mg, 0.599 mmol) at 0 °C, and the mixture was stirred at room temperature for 2.5 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 4/1) to give **134e** (90.1 mg, 74% yield in 2 steps) as a colorless oil. Spectral data of **134e**: IR (neat) 3010, 2956, 2844, 2729, 2243, 1969, 1739, 1714 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.77 (t, *J* = 1.2 Hz, 1 H), 5.76 (dt, *J* = 6.4, 3.2 Hz, 1 H), 5.54 (dt, *J* = 6.4, 6.3 Hz, 1 H), 3.78 (s, 3 H), 3.76 (s, 3 H), 3.72 (s, 3 H), 3.06 (d, *J* = 17.6 Hz, 1 H), 3.00 (d, *J* = 17.6 Hz, 1 H), 2.65-2.57 (m, 2 H), 2.41-2.33 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 201.4, 168.8, 168.7, 153.6, 95.4, 91.1, 83.9, 74.9, 56.8, 53.3 (2 C), 52.7, 42.2, 24.1, 20.5; LRMS (EI) *m/z* 263 [$(M\text{-}CO_2Me)^+$], 225, 193, 161, 115, 59; HRMS (EI) calcd for $C_{14}H_{15}O_5$ [$(M\text{-}CO_2Me)^+$] 263.0920, found 263.0921.

<Scheme 41>

Dimethyl 2-(6-oxohexa-1,2-dien-1-yl)-2-(3-phenylprop-2-yn-1-yl)malonate (134f)

To a solution of **152** (170 mg, 0.485 mmol) in Et_3N (5.0 mL) were added iodobenzene (100 μL, 0.894 mmol), $PdCl_2(PPh_3)_2$ (13.8 mg, 0.0197 mmol) and CuI (31.0 mg, 0.163 mmol) at 0 °C, and the mixture was stirred at 40 °C for 1.5 h. To the mixture were added EtOAc and saturated NH_4Cl aqueous solution at 0 °C and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude aromatic alkyne **143f**. To a solution of **143f** in MeOH (5.0 mL) was added $TsOH\cdot H_2O$ (18.3 mg, 0.0962 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C. After removal of MeOH, the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (5.0 mL) was added Dess-Martin Periodinane (344 mg, 0.811 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **134f** (142 mg, 86% yield in 3 steps) as a colorless oil. Spectral data of **134f**: IR (neat) 2954, 2841, 2727, 1969, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.66 (t, *J* = 1.3 Hz, 1 H), 7.34-7.22 (m, 5 H), 5.84 (dt, *J* = 6.5, 3.3 Hz, 1 H), 5.51 (dt, *J* = 6.5, 6.0 Hz, 1 H), 3.78 (s, 3 H), 3.76 (s, 3 H), 3.13 (d, *J* = 17.0 Hz, 1 H), 3.09 (d, *J* = 17.0 Hz, 1 H), 2.60-2.56 (m, 2 H), 2.34 (tdd, *J* = 6.8, 6.0, 3.3 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2, 201.4, 169.4, 169.3, 131.5 (2 C), 128.2 (2 C), 128.0, 123.0, 94.7, 91.8, 84.6, 83.2, 57.7, 53.1 (2 C), 42.1, 25.3, 20.6; LRMS (EI) *m/z* 340 [M^+], 281, 253, 193, 178, 115, 91 ; HRMS (EI) calcd for $C_{18}H_{17}O_3$ [$(M\text{-}CO_2Me)^+$] 281.1178, found 281.1174.

Dimethyl 2-(3-(4-methoxyphenyl)prop-2-yn-1-yl)-2-(6-oxohexa-1,2-dien-1-yl)malonate (134g)

To a solution of **152** (511 mg, 1.46 mmol) in Et_3N (15 mL) were added *p*-iodoanisole (440 mg, 1.88 mmol), $PdCl_2(PPh_3)_2$ (45.8 mg, 0.0653 mmol) and CuI (44.5 mg, 0.234 mmol) at 0 °C, and the mixture was stirred at 40 °C for 2 h. To the mixture was added EtOAc and saturated NH_4Cl aqueous solution at 0 °C and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude aromatic alkyne **143g**. To a solution of **143g** in MeOH (15 mL) was added $TsOH\cdot H_2O$ (26.5 mg, 0.139 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. To the mixture were added saturated $NaHCO_3$ aqueous solution

at 0 °C. After removal of MeOH, the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (15 mL) was added Dess-Martin Periodinane (980 mg, 2.31 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1, 3/1) to give **134g** (329 mg, 61% yield in 3 steps) as a colorless oil. Spectral data of **134g**: IR (neat) 3005, 2954, 2839, 2727, 1970, 1739, 1738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.78 (t, *J* = 1.5 Hz, 1 H), 7.29-7.23 (m, 2 H), 6.82-6.74 (m, 2 H), 5.84 (dt, *J* = 6.4, 3.3 Hz, 1 H), 5.51 (dt, *J* = 6.4, 6.0 Hz, 1 H), 3.78 (s, 6 H), 3.77 (s, 3 H), 3.12 (d, *J* = 16.8 Hz, 1 H), 3.06 (d, *J* = 16.8 Hz, 1 H), 2.63-2.55 (m, 2 H), 2.40-2.30 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 201.5, 169.5, 169.4, 159.3, 132.9 (2 C), 115.2, 113.8 (2 C), 94.6, 91.8, 83.0 (2 C), 57.8, 55.2, 53.1, 53.0, 42.2, 25.3, 20.6; LRMS (EI) *m/z* 370 [M^+], 311, 251, 223, 145, 135, 121, 91; HRMS (EI) calcd for $C_{21}H_{22}O_6$ [M^+] 370.1416, found 370.1412.

Dimethyl 2-(3-(4-(methoxycarbonyl)phenyl)prop-2-yn-1-yl)-2-(6-oxohexa-1,2-dien-1-yl)malonate (134h)

To a solution of **152** (346 mg, 0.987 mmol) in Et_3N (10 mL) were added methyl 4-iodobenzoate (384 mg, 1.47 mmol), $PdCl_2(PPh_3)_2$ (26.8 mg, 0.0382 mmol) and CuI (39.3 mg, 0.206 mmol) at 0 °C, and the mixture was stirred at 40 °C for 1 h. To the mixture were added EtOAc and saturated NH_4Cl aqueous solution at 0 °C and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude aromatic alkyne **143h**. To a solution of **143h** in MeOH (10 mL) was added $TsOH·H_2O$ (22.3 mg, 0.117 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C. After removal of MeOH, the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (10 mL) was added Dess-Martin Periodinane (699 mg, 1.65 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 4/1) to give **134h** (282 mg, 72% yield in 3 steps) as a colorless oil. Spectral data of **134h**: IR (neat) 3005, 2954, 2844, 2727, 2226, 1969, 1731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1 H), 8.00-7.87 (m, 2 H), 7.44-7.32 (m, 2 H), 5.83 (dt, *J* = 6.4, 3.5 Hz, 1 H), 5.52 (dt, *J* = 6.4, 6.1 Hz, 1 H), 3.90 (s, 3 H), 3.79 (s, 3 H), 3.77 (s, 3 H), 3.16 (d, *J* = 17.2 Hz, 1 H), 3.10 (d, *J* = 17.2 Hz, 1 H), 2.62-2.56 (m, 2 H), 2.40-2.29 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 201.2, 169.3, 169.2, 166.5, 131.4 (2 C), 129.4 (2 C), 129.3, 127.7, 94.6, 91.7, 88.0, 82.6, 57.6, 53.1 (2 C), 52.2, 42.2, 25.3, 20.6; LRMS (EI) *m/z* 398 [M^+], 339, 307, 191, 173, 163, 149, 91; HRMS (EI) calcd for $C_{22}H_{22}O_7$ [M^+] 398.1366, found 398.1360.

<Scheme 42>

***N*-(7,7-Dimethoxyhepta-2,3-dien-1-yl)-4-methylbenzenesulfonamide (155)**

To a solution of TsNHBoc (1.64 g, 6.04 mmol) in THF (6.0 mL) were added PPh_3 (1.60 g, 6.10 mmol), a solution of **153** (693 mg, 4.02 mmol) in THF (2.0 mL) and DIAD (1.20 mL, 5.82 mmol) at 0 °C. The mixture was stirred at room temperature for 16 h, and the mixture was concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1, 4/1) to give a mixture of **154** and TsNHBoc (2.03 g, ca. **154**/TsNHBoc = 2/1) as a colorless oil. To a solution of a part of this mixture (951 mg, ca. 1.92 mmol of **154**) in MeOH (10 mL) were added trimethyl orthoformate (6.00 mL, 54.8 mmol) and acetyl chloride (2.50 mL, 35.2 mmol) at 0 °C. The mixture was stirred under

reflux for 22 h, and the mixture was added acetyl chloride (2.50 mL, 35.2 mmol) at 0 °C. The mixture was stirred under reflux for 1 h, and the mixture was added trimethyl orthoformate (6.00 mL, 54.8 mmol) at 0 °C. The mixture was stirred under reflux for 1 h. To the mixture were added $NaHCO_3$ and then added H_2O at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 6/1, 2/1) to give **155** (493 mg, 79% yield in 2 steps) as a colorless oil. Spectral data of **155**: IR (neat) 3276, 2984, 2935, 2832, 1965, 1736, 1599 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 5.23 (dtt, *J* = 6.5, 6.3, 3.1 Hz, 1 H), 5.10 (dtt, *J* = 6.5, 5.8, 3.0 Hz, 1 H), 4.96-4.90 (m, 1 H), 4.42 (t, *J* = 5.8 Hz, 1 H), 3.55 (ddd, *J* = 9.0, 6.3, 3.0 Hz, 2 H), 3.34 (s, 3 H), 3.32 (s, 3 H), 2.44 (s, 3 H), 2.26 (tdd, *J* = 7.3, 5.8, 3.1 Hz, 2 H), 1.72-1.66 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.4, 143.3, 137.0, 129.6 (2 C), 127.1 (2 C), 103.5, 93.9, 88.4, 53.2, 52.2, 41.8, 31.0, 23.6, 21.5; LRMS (EI) *m/z* 294 [$(M\text{-}OMe)^+$], 222, 155, 138, 91.

_N_-(7,7-Dimethoxyhepta-2,3-dien-1-yl)-_N_-(hex-1-yn-1-yl)-4-methylbenzenesulfonamide (157)

To a solution of **156** (399 mg, 2.48 mmol) in toluene (1.5 mL) were added 1,10-phenanethroline (76.2 mg, 0.384 mmol), $CuSO_4 \cdot 5H_2O$ (94.5 mg, 0.378 mmol), K_3PO_4 (483 mg, 2.23 mmol) and a solution of **155** (492 mg, 1.51 mmol) in toluene (1.5 mL) at 0 °C. The mixture was stirred at 60 °C for 18 h. The mixture was filtered through Celite® with Et_2O and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1) to give **157** (343 mg, 56% yield) as a colorless oil. Spectral data of **157**: IR (neat) 2955, 2931, 2872, 2828, 2254, 1966 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 5.19 (dtt, *J* = 6.5, 6.5, 2.3 Hz, 1 H), 5.04 (dtt, *J* = 6.5, 6.5, 3.3 Hz, 1 H), 4.36 (t, *J* = 5.9 Hz, 1 H), 3.96-3.87 (m, 2 H), 3.30 (s, 6 H), 2.44 (s, 3 H), 2.26 (t, *J* = 6.8 Hz, 2 H), 2.06-1.98 (m, 2 H), 1.71-1.64 (m, 2 H), 1.49-1.41 (m, 2 H), 1.40-1.32 (m, 2 H), 0.89 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.4, 144.3, 134.8, 129.5 (2 C), 127.7 (2 C), 103.9, 92.3, 86.4, 72.8, 70.7, 52.9 (2 C), 51.4, 31.6, 30.9, 23.4, 21.8, 21.6, 18.1, 13.6; LRMS (EI) *m/z* 374 [$(M\text{-}OMe)^+$], 302, 218, 91.

_N_-(Hex-1-yn-1-yl)-4-methyl-_N_-(7-oxohepta-2,3-dien-1-yl)benzenesulfonamide (134i)

To a solution of **157** (278 mg, 0.685 mmol) in CH_2Cl_2 (7.0 mL) were added 2,6-lutidine (250 μL, 2.16 mmol) and TMSOTf (250 μL, 1.38 mmol) at 0 °C and the reaction mixture was stirred at the same temperature for 2 h. To the mixture was added H_2O at 0 °C, and the mixture was stirred at the same temperature for 1 h. Then aqueous layer was extracted with CH_2Cl_2, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1, 4/1) to give **134i** (106 mg, 43% yield) as a colorless oil. Spectral data of **134i**: IR (neat) 2957, 2930, 2871, 2724, 2253, 1967, 1725 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.40 (t, *J* = 1.5 Hz, 1 H), 7.76 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 5.25 (dtt, *J* = 7.0, 7.0, 2.5 Hz, 1 H), 5.11 (dtt, *J* = 7.0, 7.0, 3.5 Hz, 1 H), 3.92 (ddd, *J* = 14.0, 7.0, 2.5 Hz, 1 H), 3.88 (ddd, *J* = 14.0, 7.0, 2.5 Hz, 1 H), 2.57-2.53 (m, 2 H), 2.44 (s, 3 H), 2.29 (dtd, *J* = 7.0, 6.7, 3.5 Hz, 2 H), 2.24 (t, *J* = 6.8 Hz, 2 H), 1.48-1.41 (m, 2 H), 1.39-1.31 (m, 2 H), 0.88 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.3, 201.5, 144.4, 134.7, 129.6 (2 C), 127.6 (2 C), 91.7, 87.7, 72.9, 70.6, 51.1, 42.2, 30.9, 21.8, 21.6, 20.7, 18.1, 13.6; LRMS (EI) *m/z* 359 [M^+], 204, 91; HRMS (EI) calcd for $C_{20}H_{25}NO_3S$ [M^+] 359.1555, found 359.1556.

<Scheme 43>

According to the general procedure for cyclization, a crude product, which was prepared from **71a** (43.8 mg, 0.150 mmol), [Rh(dppbz)(cod)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by

column chromatography on silica gel (*n*-hexane/EtOAc = 4/1) to give **76a** (17.4 mg, 40% yield) as a pale yellow oil, whose spectral were consistent to those reported literature[20].

<Scheme 44>

Methyl 3-methyl-8-((tetrahydro-2*H*-pyran-2-yl)oxy)octa-3,4-dienoate (159)

To a solution of 1-bromo-1-propene (3.80 mL, 44.6 mmol) in THF (140 mL) was added *n*-BuLi (1.65 M in hexane, 45.0 mL, 74.3 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 1 h. To the solution was added a solution of **158** (5.17 g, 30.0 mmol) in THF (10 mL), and the mixture was stirred and warmed to room temperature for 14 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated to give a crude alkynyl alcohol. To a solution of the crude alcohol (5.58 g, 26.3 mmol) in trimethylorthoacetate (20.0 mL, 160 mmol) was added propionic acid (400 μL, 5.36 mmol) at 0 °C, and the mixture was stirred at 115 °C for 14 h and 130 °C for 21 h with azeotropic removal of methanol. After concentration of the reaction mixture by vaccum distillation, the redisue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1) to give **159** (6.06 g, 75% yield in 2 steps) as a colorless oil. Spectral data of **159**: IR (neat) 2943, 2870, 1741 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.14-5.08 (m, 1 H), 4.56 (t, *J* = 3.8 Hz, 1 H), 3.84 (ddd, *J* = 10.5, 8.0, 3.0 Hz, 1 H), 3.78-3.70 (m, 1 H), 3.67 (s, 3 H), 3.51-3.44 (m, 1 H), 3.43-3.35 (m, 1 H), 2.96 (d, *J* = 2.5 Hz, 2 H), 2.10-1.96 (m, 2 H), 1.85-1.43 (m, 11 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.8, 171.7, 98.8*[1], 93.5, 90.4, 66.8*, 62.2*, 51.7, 40.2, 30.7, 28.9*, 26.5, 25.4*, 19.6*, 19.0 ; LRMS (EI) *m/z* 183 $[(M-(CH_2)_5O)^+]$, 85.

Dimethyl 2-(but-2-yn-1-yl)-2-(7-((tetrahydro-2*H*-pyran-2-yl)oxy)hepta-2,3-dien-2-yl)malonate (143j)

To a solution of **159** (1.34 g, 4.99 mmol) in THF (5 mL) was added LHMDS (1.3 M in THF, 8.0 mL, 10 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the solution was added methyl chloroformate (400 μL, 5.18 mmol), and the mixture was stirred at the same temperature for 10 min. Then, to the solution was added a solution of **142** (1.29 g, 7.17 mmol) in THF (2 mL) at -78 °C, and the mixture was stirred and warmed to room temperature for 12 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1) to give **143j** (1.31 g, 69% yield) as a colorless oil. Spectral data of **143j**: IR (neat) 2950, 2869, 1737 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.30 (tq, *J* = 6.3, 3.0 Hz, 1 H), 4.56 (t, *J* = 3.5 Hz, 1 H), 3.84 (ddd, *J* = 11.0, 7.9, 2.9 Hz, 1 H), 3.78-3.71 (m, 7 H), 3.52-3.45 (m, 1 H), 3.43-3.36 (m, 1 H), 2.82-2.79 (m, 2 H), 2.16-2.02 (m, 2 H), 1.87-1.46 (m, 14 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.0*[1], 169.7 (2 C), 98.8, 98.4, 93.7*, 78.0, 74.4, 66.9*, 62.2, 60.9, 52.6 (2 C), 30.7, 28.8*, 25.5, 25.44, 25.40*, 19.6, 16.9, 3.6; LRMS (EI) *m/z* 378 $[M^+]$, 85.

Dimethyl 2-(but-2-yn-1-yl)-2-(7-oxohepta-2,3-dien-2-yl)malonate (134j)

To a solution of **143j** (1.31 g, 3.46 mmol) in MeOH (34 mL) was added $TsOH·H_2O$ (66.0 mg, 0.347 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture was added $TsOH·H_2O$ (60.0 mg, 0.315 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C. After removal of MeOH, the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (34 mL) was added Dess-Martin Periodinane (2.24 g, 5.28 mmol) at 0 °C, and the mixture was stirred at room

temperature for 2 h. To the mixture was added Dess-Martin Periodinane (1.95 g, 4.60 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. To the mixture was added Dess-Martin Periodinane (1.83 g, 4.31 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **134j** (857 mg, 85% yield in 2 steps) as a colorless oil. Spectral data of **134j**: IR (neat) 2953, 2923, 2844, 2731, 2359, 2341, 1733 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.76 (s, 1 H), 5.35 (tq, *J* = 5.8, 2.5 Hz, 1 H), 3.74 (s, 3 H), 3.73 (s, 3 H), 2.79 (q, *J* = 2.5 Hz, 2 H), 2.65-2.51 (m, 2 H), 2.39-2.26 (m, 2 H), 1.80 (d, *J* = 2.5 Hz, 3 H), 1.71 (t, *J* = 2.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.0, 201.9, 169.5 (2 C), 100.0, 92.5, 78.1, 74.3, 60.9, 52.6 (2 C), 41.8, 25.3, 21.0, 16.7, 3.5; LRMS (EI) *m/z* 292 [M^+], 233, 173, 145; HRMS (EI) calcd for $C_{16}H_{20}O_5$ [M^+] 292.1311, found 292.1311.

<Scheme 45>

Methyl 5-methyl-8-((tetrahydro-2*H*-pyran-2-yl)oxy)octa-3,4-dienoate (161)

To a solution of **160** (2.53 g, 11.9 mmol) in trimethylorthoacetate (9.00 mL, 71.9 mmol) was added propionic acid (200 μL, 2.68 mmol) at 0 °C, and the mixture was stirred at 130 °C for 24 h with azeotropic removal of methanol. After concentration of the reaction mixture by vaccum distillation, the redisue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **161** (978 mg, 31% yield) as a colorless oil. Spectral data of **161**: IR (neat) 2943, 2868, 1742 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.17-5.11 (m, 1 H), 4.57-4.51 (m, 1 H), 3.84 (ddd, *J* = 11.5, 7.8, 3.3 Hz, 1 H), 3.75-3.69 (m, 1 H), 3.67 (s, 3 H), 3.50-3.44 (m, 1 H), 3.40-3.34 (m, 1 H), 2.98 (d, *J* = 7.5 Hz, 2 H), 2.05-1.94 (m, 2 H), 1.85-1.43 (m, 11 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.3, 172.3, 100.5, 98.8*[1], 83.6, 67.0*, 62.3*, 51.8*, 35.1*, 30.7*, 30.3*, 27.5*, 25.6*, 19.6*, 19.0 ; LRMS (EI) *m/z* 183 [$(M-(CH_2)_5O)^+$], 85.

Dimethyl 2-(but-2-yn-1-yl)-2-(3-methyl-6-((tetrahydro-2*H*-pyran-2-yl)oxy)hexa-1,2-dien-1-yl)malonate (143k)

To a solution of **161** (795 mg, 2.96 mmol) in THF (3 mL) was added LHMDS (1.3 M in THF, 5.1 mL, 6.6 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the solution was added methyl chloroformate (240 μL, 3.11 mmol), and the mixture was stirred at the same temperature for 10 min. Then, to the solution was added a solution of **142** (2.16 g, 12.0 mmol) in THF (3 mL) at -78 °C, and the mixture was stirred and warmed to 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 EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1) to give **143k** (915 mg, 82% yield) as a colorless oil. Spectral data of **143k**: IR (neat) 2951, 2859, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.64 (qt, *J* = 3.0, 2.9 Hz, 1 H), 4.58-4.53 (m, 1 H), 3.84 (ddd, *J* = 11.0, 7.9, 2.9 Hz, 1 H), 3.75-3.70 (m, 7 H), 3.51-3.46 (m, 1 H), 3.41-3.35 (m, 1 H), 2.81 (q, *J* = 2.5 Hz, 2 H), 2.13-1.97 (m, 2 H), 1.86-1.45 (m, 14 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9, 170.0, 169.9, 104.8, 98.8*[1], 89.6, 78.1, 73.9, 67.0*, 62.3*, 58.0, 52.8 (2 C), 30.7, 30.4, 27.5, 25.5, 24.9, 19.6*, 18.7, 3.5; LRMS (EI) *m/z* 377 [$(M-H)^+$], 85.

Dimethyl 2-(but-2-yn-1-yl)-2-(3-methyl-6-oxohexa-1,2-dien-1-yl)malonate (134k)

To a solution of **143k** (544 mg, 1.44 mmol) in MeOH (15 mL) was added $TsOH·H_2O$ (30.2 mg, 0.159 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C. After removal of MeOH, the aqueous layer was extracted with EtOAc. The organic layer was washed with

brine, dried over Na_2SO_4, and concentrated to give a crude alcohol. To a solution of the crude alcohol in CH_2Cl_2 (15 mL) was added Dess-Martin Periodinane (1.01 g, 2.38 mmol) at 0 °C, and the mixture was stirred at room temperature for 2.5 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **134k** (365 mg, 87% yield in 2 steps) as a colorless oil. Spectral data of **134k**: IR (neat) 2953, 2921, 2845, 2726, 1737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1 H), 5.35 (qt, *J* = 4.0, 3.5 Hz, 1 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 2.83-2.74 (m, 2 H), 2.64-2.50 (m, 2 H), 2.36-2.18 (m, 2 H), 1.73 (d, *J* = 3.5 Hz, 3 H), 1.71 (t, *J* = 2.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.7, 200.5, 169.7 (2 C), 104.2, 91.2, 78.3, 73.8, 58.0, 52.9, 52.8, 41.3, 25.8, 24.7, 18.9, 3.5; LRMS (EI) *m/z* 239 [(M-MeC≡CCH_2)$^+$], 175, 91, 53; HRMS (EI) calcd for $C_{12}H_{15}O_5$ [(M-MeC≡CCH_2)$^+$] 239.0920, found 239.0926.

<Scheme 48>

Dimethyl (*S*, 1*Z*, 5*Z*, 7*Z*)-3-hydroxy-2-methylbicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate ((*S*)-137a)

According to the general procedure for cyclization, a crude product, which was prepared from (*R*)-**134a** (41.8 mg, 0.150 mmol) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 2/1) to give (*S*)-**137a** (35.8 mg, 86% yield) as a colorless oil. Spectral data of (*S*)-**137a**: $[\alpha]_D^{22}$ +0.3 (*c* 1.25, $CHCl_3$). The enantiomeric excess was determined to be 76% ee by HPLC analysis with a DAICEL CHIRALPAK OJ-H (eluent: *n*-hexane/*i*-PrOH = 98/2, flow rate: 1.0 mL/min, detecter: UV (254 nm)): t_R (minor) = 36.3 min for (*R*)-enantiomer: t_R (major) = 40.3 min for (*S*)-enantiomer.

<Scheme 49>

<eq. 1>

Dimethyl (2*E*, 6*Z*)-7,10,10-trimethyl-11-oxatricyclo[6.2.1.$0^{2,6}$]undeca-2,6-diene-4,4-dicarboxylate (163a)

According to the general procedure for cyclization, a crude product, which was prepared from **162a** (46.0 mg, 0.150 mmol) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) under reflux for 3 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **163a** (38.7 mg, 84% yield) as a pale yellow oil. The structure of **163a** was determined by 2D-NMR (HMBC, INADEQUATE). Spectral data of **163a**: IR (neat) 3076, 3002, 2954, 2907, 2869, 1736, 1632 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.58 (s, 1 H), 4.38 (s, 1 H), 4.27 (d, *J* = 7.5 Hz, 1 H), 3.74 (s, 3 H), 3.72 (s, 3 H), 3.06 (s, 2 H), 1.87 (dd, *J* = 12.0, 7.5 Hz, 1 H), 1.71 (s, 3 H), 1.57 (d, *J* = 12.0 Hz, 1 H), 1.23 (s, 3 H), 0.95 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 171.0, 145.0, 133.5, 132.0, 121.3, 83.6, 78.2, 64.8, 52.7 (2 C), 46.4, 42.5, 33.4, 31.7, 25.4, 15.8; LRMS (EI) *m/z* 306 [M^+], 250, 191, 159, 132, 59; HRMS (EI) calcd for $C_{17}H_{22}O_5$ [M^+] 306.1467, found 306.1465.

<eq. 2>

Dimethyl (2*Z*, 6*Z*)-7,11,11-trimethyl-10-oxo-9-oxatricyclo[6,2,2,$0^{2,6}$]dodeca-2,6-diene-4,4-dicarboxylate (164)

A solution of [Rh(dppbz)(nbd)]ClO_4 (0.0150 mmol, 10 mol% to a substrate) in degassed $ClCH_2CH_2Cl$ (0.58 mL: 0.026 M to Rh) was stirred under H_2 atmosphere at room temperature for 1 h. Then the reaction mixture was degassed, and the reaction vessel was flushed with CO gas. The mixture was added a solution of **162a** (46.0 mg, 0.150 mmol) in degassed $ClCH_2CH_2Cl$ (0.92 mL) and the reaction mixture was stirred at 50 °C for 2 h. After removal of the solvent, the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1, 2/1) to give **164** (31.2 mg, 62% yield) as

a white solid and **163a** (11.1 mg, 24% yield) as a pale yellow oil. The structure of **164** was determined by X-ray analysis. Spectral data of **164**: mp 143.5 °C (recrystallized from *n*-hexane-EtOAc at room temperature.)

<Scheme 50>

8-((*tert*-Butyldiphenylsilyl)oxy)-5-hydroxyoct-3-yn-1-yl pivalate (167)

To a solution of **166** (2.33 g, 15.1 mmol) in THF (20 mL) was added LHMDS (1.3 M in THF, 11 mL, 14 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 1 h. To the solution was added a solution of **165** (3.04 g, 9.31 mmol) in THF (5.0 mL), and the mixture was stirred and warmed to room temperature for 23 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1) to give **167** (2.27 g, 51% yield) as a pale yellow oil. Spectral data of **167**: IR (neat) 3452, 3071, 3050, 2958, 2931, 2859, 1731, 1589 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70-7.65 (m, 4 H), 7.45-7.36 (m, 6 H), 4.41 (dtt, *J* = 5.5, 5.5, 2.4 Hz, 1 H), 4.19-4.10 (m, 2 H), 3.74-3.64 (m, 2 H), 2.64 (d, *J* = 5.5 Hz, 1 H), 2.55 (td, *J* = 6.6, 2.4 Hz, 2 H), 1.87-1.62 (m, 4 H), 1.20 (s, 9 H), 1.05 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3, 135.5 (4 C), 133.48, 133.46, 123.0 (2 C), 127.6 (4 C), 82.7, 80.8, 63.8, 62.3, 62.1, 38.7, 35.1, 28.2, 27.1 (3 C), 26.8 (3 C), 19.2, 19.1; LRMS (EI) *m/z* 269 [(M-2Ph-$(CH_3)_3C)^+$], 199, 139 , 77, 43.

(*R*)-8-((*tert*-Butyldiphenylsilyl)oxy)-5-hydroxyoct-3-yn-1-yl pivalate ((*R*)-167)

To a solution of **167** (2.27 g, 4.72 mmol) in CH_2Cl_2 (20 mL) were added MS4A (5.02 g) and PCC (2.09 g, 9.70 mmol) at 0 °C, and the mixture was stirred at the same temperature for 2 h. After removal of CH_2Cl_2, the residue was filtered through column chromatography on silica gel (Et_2O) to give a crude ketone. To a solution of the crude ketone in THF (19 mL) was added (*R*)-(+)-2-methyl-CBS-oxaborolidine (2.13 g, 7.69 mmol) at 0 °C. To the solution was added $Me_2S{\cdot}BH_3$ (1.80 mL, 19.0 mmol) at -30 °C, and the mixture was stirred at the same temperature for 30 min. To the mixture were added MeOH, saturated NH_4Cl aqueous solution and 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 (*n*-hexane/EtOAc = 5/1, 3/1) to give (*R*)-**167** (1.17 g, 51% yield in 2 steps) as a pale yellow oil. Spectral data of (*R*)-**167**: $[\alpha]_D^{23}$ -2.3 (*c* 1.07, $CHCl_3$). The enantiomeric excess was determined to be 96% ee by HPLC analysis with a DAICEL CHIRALPAK OD-H (eluent: *n*-hexane/*i*-PrOH = 99/1, flow rate: 1.0 mL/min, detecter: UV (254 nm)): t_R (major) = 18.2 min for (*R*)-enantiomer: t_R (minor) = 22.7 min for (*S*)-enantiomer.

(*R*)-8-((*tert*-Butyldiphenylsilyl)oxy)octa-3,4-dien-1-yl pivalate ((*R*)-168)

To a solution of PPh_3 (870 mg, 3.32 mmol) in THF (14 mL) were added DIAD (660 μL, 3.33 mmol), a solution of (*R*)-**167** (1.07 g, 2.23 mmol) in THF (5.0 mL) and a solution of NBSH (733 mg, 3.37 mmol) in THF (5.0 mL) at -15 °C. The mixture was stirred at the same temperature for 1 h and warmed to room temperature for 19 h. After concentration of the reaction mixture the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1) to give (*R*)-**168** (797 mg, 77% yield) as a pale yellow oil. Spectral data of (*R*)-**168**: IR (neat) 3070, 3051, 2957, 2931, 2858, 1963, 1730, 1479 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.69-7.65 (m, 4 H), 7.45-7.36 (m, 6 H), 5.13 (dtt, *J* = 6.5, 6.5, 3.2 Hz, 1 H), 5.05 (dtt, *J* = 6.5, 6.5, 3.3 Hz, 1 H), 4.09 (t, *J* = 6.5 Hz, 2 H), 3.69 (t, *J* = 6.3 Hz, 2 H), 2.28 (tdd, *J* = 6.5, 6.5, 3.3 Hz, 2 H), 2.13-2.07 (m, 2 H), 1.72-1.64 (m, 2 H), 1.19 (s, 9 H), 1.05 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.5, 178.5, 135.5 (4 C), 134.0 (2 C), 129.5 (2 C), 127.6 (4 C), 91.3, 87.0, 63.6, 63.1, 38.7, 31.9, 28.5, 27.2 (3 C), 26.8 (3 C),

25.0, 19.2; LRMS (EI) *m/z* 283 [(M-(*t*-BuPh$_2$Si)OCH$_2$CH$_2$)$^+$], 223, 199, 181, 107, 79, 57; $[\alpha]_D^{24}$ -29.7 (*c* 1.18, $CHCl_3$).

(*R*)-8-((*tert*-Butyldiphenylsilyl)oxy)octa-3,4-dien-1-ol ((*R*)-169)

To a solution of (*R*)-**168** (741 mg, 1.59 mmol) in Et_2O (16 mL) was added DIBAL-H (1.03 M in hexane, 6.20 mL, 6.39 mmol) at -78 °C and the reaction mixture was stirred at the same temperature for 1 h. To the mixture was added saturated Rochelle salt aqueous solution at 0 °C, and the reaction mixture was stirred at room temperature for 2 h. 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 (*n*-hexane/EtOAc = 5/1) to give (*R*)-**169** (568 mg, 94% yield) as a pale yellow oil. Spectral data of (*R*)-**169**: IR (neat) 3348, 3071, 3048, 2931, 2894, 2858, 1962, 1589 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.65 (m, 4 H), 7.45-7.36 (m, 6 H), 5.16 (dtt, *J* = 7.0, 6.5, 3.1 Hz, 1 H), 5.08 (dtt, *J* = 7.0, 6.5, 3.2 Hz, 1 H), 3.70 (t, *J* = 6.3 Hz, 2 H), 3.66 (t, *J* = 7.0 Hz, 2 H), 2.22 (tdd, *J* = 6.3, 6.5, 3.2 Hz, 2 H), 2.13 (tdd, *J* = 7.3, 6.5, 3.1 Hz, 2 H), 1.69 (tt, *J* = 7.3, 7.0 Hz, 2 H), 1.58-1.50 (brs, 1 H), 1.06 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.6, 135.5 (4 C), 134.0 (2 C), 129.5 (2 C), 127.6 (4 C), 91.2, 87.5, 63.1, 62.0, 32.2, 31.8, 26.8 (3 C), 25.1, 19.2; LRMS (EI) *m/z* 305 [(M-(CH$_3$)$_3$C-H$_2$O)$^+$], 283, 223, 199, 107, 79, 57; $[\alpha]_D^{24}$ -33.2 (*c* 1.08, $CHCl_3$).

Methyl (*R*)-8-((*tert*-butyldiphenylsilyl)oxy)octa-3,4-dienoate ((*R*)-170)

To a solution of (*R*)-**169** (517 mg, 1.36 mmol) in CH_2Cl_2 (14 mL) was added Dess-Martin Periodinane (871 mg, 2.05 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture was added Dess-Martin Periodinane (559 mg, 1.32 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated to give a crude aldehyde. To a solution of the crude aldehyde in *t*-BuOH (6.8 mL) were added 2-methyl-2-butene (1.10 g, 15.7 mmol), 0.50 M $NaHPO_4$ aqueous solution (13.4 mL, 6.73 mmol), and 0.31 M $NaClO_2$ aqueous solution (13.4 mL, 4.12 mmol) at 0 °C, and the mixture was stirred at room temperature for 30 min. To the mixture was added brine at 0 °C, and the aqueous layer was extracted with $CHCl_3$. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude carboxylic acid. To a solution of the crude carboxylic acid in MeOH (6.8 mL) was added $TMSCHN_2$ (2.0 M in Et_2O, 4.5 mL, 9.0 mmol) at 0 °C, and the mixture was stirred 20 min at the same temperature. To the mixture was added AcOH at 0 °C, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1) to give (*R*)-**170** (468 mg, 84% yield in 3 steps) as a pale yellow oil. Spectral data of (*R*)-**170**: IR (neat) 3070, 3051, 2951, 2931, 2894, 2857, 1967, 1742 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70-7.65 (m, 4 H), 7.45-7.36 (m, 6 H), 5.25-5.17 (m, 2 H), 3.71-3.67 (m, 5 H), 3.00 (dd, *J* = 6.8, 3.3 Hz, 2 H), 2.16-2.07 (m, 2 H), 1.68 (tt, *J* = 7.0, 6.5 Hz, 2 H), 1.06 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.9, 170.0, 135.5 (4 C), 133.9 (2 C), 129.5 (2 C), 127.6 (4 C), 91.8, 84.3, 63.1, 51.8, 34.7, 31.7, 26.8 (3 C), 24.7, 19.2; LRMS (EI) *m/z* 351 [(M-(CH$_3$)$_3$C)$^+$], 213, 183, 121, 93, 77; $[\alpha]_D^{24}$ -27.6 (*c* 1.02, $CHCl_3$).

Dimethyl (*R*)-2-(but-2-yn-1-yl)-2-(6-((*tert*-butyldiphenylsilyl)oxy)hexa-1,2-dien-1-yl)malonate ((*R*)-171)

To a solution of (*R*)-**170** (416 mg, 1.02 mmol) in THF (1.0 mL) was added LHMDS (1.3 M in THF, 1.7 mL, 2.2 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the solution was added methyl chloroformate (80.0 μL, 1.04 mmol), and the mixture was stirred at the same temperature for 10 min. Then, to the solution was added a solution of **142** (1.81 g, 10.1 mmol) in THF (1.0 mL) at -78 °C, and the mixture was stirred and warmed to room temperature for 5 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the

aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1) to give (*R*)-**171** (305 mg, 58% yield) as a pale yellow oil. Spectral data of (*R*)-**171**: IR (neat) 3072, 3049, 2999, 2952, 2931, 2894, 2858, 1967, 1740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.68-7.64 (m, 4 H), 7.44-7.36 (m, 6 H), 5.72 (dt, *J* = 7.0, 3.3 Hz, 1 H), 5.72 (dt, *J* = 7.0, 6.5 Hz, 1 H), 3.74 (s, 3 H), 3.73 (s, 3 H), 3.68 (t, *J* = 6.3 Hz, 2 H), 2.83 (q, *J* = 2.5 Hz, 2 H), 2.20-2.08 (m, 2 H), 1.72-1.64 (m, 5 H), 1.04 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2, 169.8, 169.7, 135.5 (4 C), 133.9 (2 C), 129.5 (2 C), 127.6 (4 C), 95.6, 90.3, 78.4, 73.7, 63.2, 57.8, 52.91, 52.89, 31.7, 26.8 (3 C), 25.0, 24.8, 19.2, 3.5; LRMS (EI) *m/z* 351 [(M-$(CH_3)_3C$-CO_2Me-MeC≡CCH_2)$^+$], 213, 199, 183, 121, 93, 77, 43; $[\alpha]_D^{24}$ -28.2 (*c* 1.15, $CHCl_3$). The enantiomeric excess was determined to be 81% ee by HPLC analysis with a DAICEL CHIRALPAK OD-H (eluent: *n*-hexane/*i*-PrOH = 99/1, flow rate: 0.3 mL/min, detecter: UV (254 nm)): t_R (minor) = 15.7 min for (*S*)-enantiomer: t_R (major) = 16.9 min for (*R*)-enantiomer.

Dimethyl (*R*)-2-(but-2-yn-1-yl)-2-(6-hydroxyhexa-1,2-dien-1-yl)malonate ((*R*)-172)

To a solution of (*R*)-**171** (269 mg, 0.519 mmol) in THF (1.7 mL) was added TBAF (1.0 M in THF, 700 μL, 0.70 mmol) 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 EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 1/2) to give (*R*)-**172** (122 mg, 84% yield) as a pale yellow oil. Spectral data of (*R*)-**172**: IR (neat) 3418, 3004, 2953, 2924, 2865, 1968, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.72 (dt, *J* = 6.5, 3.1 Hz, 1 H), 5.39 (td, *J* = 6.7, 6.5 Hz, 1 H), 3.74 (s, 3 H), 3.73 (s, 3 H), 3.65 (t, *J* = 6.5 Hz, 2 H), 2.83 (q, *J* = 2.5 Hz, 2 H), 2.12 (tdd, *J* = 7.3, 6.7, 3.1 Hz, 2 H), 1.76-1.63 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2, 169.8, 169.7, 95.3, 90.4, 78.5, 73.6, 61.9, 57.7, 52.9 (2 C), 31.5, 25.0, 24.5, 3.5; LRMS (EI) *m/z* 280 [M^+], 221, 189, 143, 115, 91, 77, 59, 43; $[\alpha]_D^{22}$ -40.0 (*c* 1.24, $CHCl_3$).

Dimethyl (*R*)-2-(but-2-yn-1-yl)-2-(6-oxohexa-1,2-dien-1-yl)malonate ((*R*)-134a)

To a solution of (*R*)-**172** (102 mg, 0.364 mmol) in CH_2Cl_2 (4.0 mL) was added Dess-Martin Periodinane (310 mg, 0.731 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give (*R*)-**134a** (76.7 mg, 76% yield) as a colorless oil. Spectral data of (*R*)-**134a**: $[\alpha]_D^{22}$ -71.2 (*c* 0.93, $CHCl_3$).

<Scheme 51>

(*R*)-1-((*tert*-Butyldiphenylsilyl)oxy)-8-(pivaloyloxy)oct-5-yn-4-yl (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (173)

To a solution of (*R*)-MTPACl (37.0 mg, 0.146 mmol) in pyridine (0.20 mL) was added a solution of (*R*)-**167** (8.2 mg, 0.017 mmol) in pyridine (0.80 mL) at 0 °C, and the mixture was stirred at room temperature for 4 h. To the mixture was added 1 N 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 purified by PTLC (*n*-hexane/EtOAc = 8/1, twice) to give **173** (10.7 mg, 90% yield) as a pale yellow oil. Spectral data of **173**: IR (neat) 3073, 2958, 2931, 2857, 1752, 1732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.66-7.62 (m, 4 H), 7.54-7.51 (m, 2 H), 7.45-7.35 (m, 9 H), 5.56 (tt, *J* = 6.5, 2.0 Hz, 1 H), 4.10 (t, *J* = 6.8 Hz, 2 H), 3.67 (t, *J* = 6.0 Hz, 2 H), 3.53 (s, 3 H), 2.52 (td, *J* = 6.8, 2.0 Hz, 2 H), 1.94 (dt, *J* = 6.5,

7.7 Hz, 2 H), 1.75-1.64 (m, 2 H), 1.18 (s, 9 H), 1.04 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3, 165.6, 135.5 (4 C), 133.7 (2 C), 132.0, 129.6 (3 C), 128.3 (2 C), 127.6 (4 C), 127.4 (2 C), 123.2 ($J^1_{C\text{-}F}$ = 287.0 Hz), 84.6 ($J^2_{C\text{-}F}$ = 27.4 Hz), 83.0, 77.6, 66.6, 63.0, 61.8, 55.5, 38.7, 31.4, 28.0, 27.1 (3 C), 26.8 (3 C), 19.2, 19.1; LRMS (EI) *m/z* 405 [(M-OMTPA-C$(CH_3)_3$-2H)$^+$], 283, 207, 105, 79, 57, 44; $[\alpha]_D^{23}$ -2.7 (*c* 1.08, $CHCl_3$).

(*R*)-1-((*tert*-Butyldiphenylsilyl)oxy)-8-(pivaloyloxy)oct-5-yn-4-yl
(*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (174)

To a solution of (*S*)-MTPACl (37.0 mg, 0.146 mmol) in pyridine (0.20 mL) was added a solution of (*R*)-**167** (8.3 mg, 0.017 mmol) in pyridine (0.80 mL) at 0 °C, and the mixture was stirred at room temperature for 4 h. To the mixture was added 1 N 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 purified by PTLC (*n*-hexane/EtOAc = 8/1, twice) to give **174** (10.0 mg, 83% yield) as a pale yellow oil. Spectral data of **174**: IR (neat) 3072, 2958, 2930, 2857, 1753, 1732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66-7.60 (m, 4 H), 7.56-7.51 (m, 2 H), 7.45-7.34 (m, 9 H), 5.59 (tt, *J* = 6.3, 1.9 Hz, 1 H), 4.13 (t, *J* = 7.0 Hz, 2 H), 3.63-3.58 (m, 2 H), 3.58 (s, 3 H), 2.56 (td, *J* = 7.0, 1.9 Hz, 2 H), 1.88 (dt, *J* = 6.3, 7.3 Hz, 2 H), 1.65-1.52 (m, 2 H), 1.18 (s, 9 H), 1.03 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3, 165.6, 135.5 (4 C), 133.69, 133.67, 132.3, 129.62, 129.60 (2 C), 128.3 (2 C), 127.6 (4 C), 127.3 (2 C), 123.2 ($J^1_{C\text{-}F}$ = 286.5 Hz), 84.3 ($J^2_{C\text{-}F}$ = 27.8 Hz), 83.1, 77.8, 66.2, 62.9, 61.8, 55.4, 38.7, 31.4, 27.7, 27.1 (3 C), 26.8 (3 C), 19.2 (2 C); LRMS (EI) *m/z* 594 [(M-C$(CH_3)_3$-3Me)$^+$], 281, 207, 79, 44; $[\alpha]_D^{22}$ +29.2 (*c* 1.00, $CHCl_3$).

<Scheme 52>

Dimethyl (*S*, 1*Z*, 5*Z*, 7*Z*)-3-(((*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl)oxy)
-2-methylbicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate (175)

To a solution of (*R*)-MTPACl (39.5 mg, 0.156 mmol) in pyridine (0.20 mL) was added a solution of (*S*)-**137a** (5.0 mg, 0.018 mmol) in pyridine (0.80 mL) at 0 °C, and the mixture was stirred at room temperature for 4 h. To the mixture was added 1 N 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **175** (8.9 mg, quant.) as a colorless oil. Spectral data of **175**: IR (neat) 3069, 3033, 2954, 2925, 2852, 1739 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53-7.47 (m, 2 H), 7.41-7.35 (m, 3 H), 6.19 (dd, *J* = 11.5, 1.5 Hz, 1 H), 6.01 (s, 1 H), 5.61-5.55 (m, 2 H), 3.75 (s, 3 H), 3.73 (s, 3 H), 3.49 (s, 3 H), 3.21 (s, 2 H), 2.71 (ddd, *J* = 16.5, 6.6, 6.6 Hz, 1 H), 2.67-2.61 (m, 1 H), 1.89 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8, 170.6, 166.3, 143.6, 140.2, 134.6, 132.2, 129.5 (2 C), 128.3 (2 C), 127.4, 127.2, 127.1, 126.0, 123.3 ($J^1_{C\text{-}F}$ = 287.0 Hz), 84.5 ($J^2_{C\text{-}F}$ = 27.4 Hz), 76.3, 62.6, 55.4, 53.1, 53.0, 39.0, 32.7, 21.0; LRMS (EI) *m/z* 260 [(M-OMTPA-H)$^+$], 201, 169, 142, 115; $[\alpha]_D^{23}$ -175.9 (*c* 0.12, $CHCl_3$).

Dimethyl (*S*, 1*Z*, 5*Z*, 7*Z*)-3-(((*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl)oxy)
-2-methylbicyclo[5.3.0]deca-1,5,7-triene-9,9-dicarboxylate (176)

To a solution of (*S*)-MTPACl (36.5 mg, 0.144 mmol) in pyridine (0.20 mL) was added a solution of (*S*)-**137a** (4.7 mg, 0.017 mmol) in pyridine (0.80 mL) at 0 °C, and the mixture was stirred at room temperature for 4 h. To the mixture was added 1 N 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **176** (5.7 mg, 68% yield) as a colorless oil. Spectral data of **176**: IR (neat) 3066, 3031,

2954, 2925, 2852, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.57-7.46 (m, 2 H), 7.44-7.35 (m, 3 H), 6.26 (dd, *J* = 11.3, 1.8 Hz, 1 H), 6.01 (s, 1 H), 5.70 (ddd, *J* = 11.3, 7.0, 4.6 Hz, 1 H), 5.59 (d, *J* = 7.0 Hz, 1 H), 3.75 (s, 3 H), 3.72 (s, 3 H), 3.52 (s, 3 H), 3.19 (d, *J* = 13.0 Hz, 1 H), 3.14 (d, *J* = 13.0 Hz, 1 H), 2.81 (ddd, *J* = 16.5, 7.0, 7.0 Hz, 1 H), 2.73-2.67 (m, 1 H), 1.75 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.7, 170.6, 166.2, 143.6, 139.6, 134.6, 132.2, 129.5 (2 C), 128.3 (2 C), 127.4, 126.9, 126.7, 126.0, 123.3 ($J^1_{C\text{-}F}$ = 286.5 Hz), 84.5 ($J^2_{C\text{-}F}$ = 27.0 Hz), 76.4, 62.6, 55.5, 53.1, 53.0, 38.9, 32.8, 20.4; LRMS (EI) *m/z* 260 [(M-OMTPA-H)$^+$], 201, 169, 142, 115; $[\alpha]_D^{23}$ -4.9 (*c* 0.57, $CHCl_3$).

<Scheme 54>

Dimethyl 2-(but-2-yn-1-yl)-2-(6-((*tert*-butyldiphenylsilyl)oxy)-4,4-dimethylhexa-1,2-dien-1-yl)malonate (181)

To a solution of **180** (2.93 g, 6.71 mmol) in THF (7.0 mL) was added LHMDS (1.3 M in THF, 12 mL, 16 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the solution was added methyl chloroformate (550 μL, 7.12 mmol), and the mixture was stirred at the same temperature for 10 min. Then, to the solution was added a solution of **142** (1.84 g, 10.2 mmol) in THF (1.0 mL) at -78 °C, and the mixture was stirred and warmed to room temperature for 19 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1) to give **181** (2.97 g, 81% yield) as a pale yellow oil. Spectral data of **181**: IR (neat) 3070, 2957, 2931, 2858, 1967, 1741 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70-7.65 (m, 4 H), 7.45-7.36 (m, 6 H), 5.77 (d, *J* = 7.0 Hz, 1 H), 5.23 (d, *J* = 7.0 Hz, 1 H), 3.73-3.69 (m, 8 H), 2.82 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.78 (dq, *J* = 16.5, 2.5 Hz, 1 H), 1.71 (t, *J* = 2.5 Hz, 3 H), 1.66-1.62 (m, 2 H), 1.04 (s, 9 H), 0.980 (s, 3 H), 0.976 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9, 169.7 (2 C), 135.5 (4 C), 133.9 (2 C), 129.5 (2 C), 127.6 (4 C), 106.2, 91.9, 78.5, 73.7, 61.1, 57.9, 52.8 (2 C), 45.1, 34.2, 28.2, 27.5, 26.8 (3 C), 25.2, 19.1, 3.5; LRMS (EI) *m/z* 279 [(M-(*t*-BuSiPh$_2$O)CH$_2$+2 H)$^+$], 167, 149.

Dimethyl 2-(but-2-yn-1-yl)-2-(6-hydroxy-4,4-dimethylhexa-1,2-dien-1-yl)malonate (182)

To a solution of **181** (2.04 g, 3.73 mmol) in THF (12 mL) was added TBAF (1.0 M in THF, 5.5 mL, 5.5 mmol) 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 EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 1/2) to give **182** (914 mg, 80% yield) as a pale yellow oil. Spectral data of **182**: IR (neat) 3417, 2957, 2925, 2237, 1967, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.81 (d, *J* = 6.0 Hz, 1 H), 5.37 (d, *J* = 6.0 Hz, 1 H), 3.741 (s, 3 H), 3.739 (s, 3 H), 3.71-3.65 (m, 2 H), 2.85-2.81 (m, 2 H), 1.72 (t, *J* = 2.5 Hz, 3 H), 1.66-1.55 (m, 3 H), 1.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9, 169.7, 169.6, 106.0, 92.1, 78.7, 73.6, 60.0, 57.9, 52.9 (2 C), 45.3, 34.2, 28.0, 27.9, 25.3, 3.5; LRMS (EI) *m/z* 308 [M$^+$], 248, 163, 103, 69, 41.

Dimethyl 2-(but-2-yn-1-yl)-2-(4,4-dimethyl-6-oxohexa-1,2-dien-1-yl)malonate (162a)

To a solution of **182** (764 mg, 2.48 mmol) in CH_2Cl_2 (25 mL) was added Dess-Martin Periodinane (1.50 g, 3.54 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **162a** (626 mg, 82% yield) as a colorless oil. Spectral data of **162a**: IR (neat) 2959, 2926, 2872, 2737, 1969, 1739, 1719 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.79 (t, *J* = 2.8 Hz, 1 H), 5.88 (d, *J* = 6.5 Hz, 1

H), 5.49 (d, *J* = 6.5 Hz, 1 H), 3.76 (s, 3 H), 3.75 (s, 3 H), 2.87 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.83 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.43 (dd, *J* = 15.5, 2.8 Hz, 1 H), 2.37 (dd, *J* = 15.5, 2.8 Hz, 1 H), 1.74 (t, *J* = 2.5 Hz, 3 H), 1.18 (s, 3 H), 1.17 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.6, 200.8, 169.4 (2 C), 105.0, 92.9, 78.8, 73.5, 57.9, 54.7, 52.9 (2 C), 34.2, 28.2, 28.0, 25.1, 3.5; LRMS (EI) *m/z* 253 [(M-MeC≡CCH_2)$^+$], 183, 125, 53; HRMS (EI) calcd for $C_{13}H_{17}O_5$ [(M-MeC≡CCH_2)$^+$] 253.1076, found 253.1069.

<Scheme 55>

Dimethyl (*E*)-4-ethylidene-3-((*E*)-4-oxopent-1-en-1-yl)cyclopent-2-ene-1,1-dicarboxylate (183)

According to the general procedure for cyclization, a crude product, which was prepared from **134l** (44.2 mg, 0.151 mmol) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) at 50 °C for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **183** (40.3 mg, 91% yield) as a colorless oil. Spectral data of **183**: IR (neat) 3003, 2955, 2917, 2855, 1736 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.16 (dt, *J* = 16.5, 7.0 Hz, 1 H), 6.04 (d, *J* = 16.5 Hz, 1 H), 5.99 (s, 1 H), 5.50 (qt, *J* = 7.0, 2.3 Hz, 1 H), 3.68 (s, 6 H), 3.21 (d, *J* = 7.0 Hz, 2 H), 3.12-3.06 (m, 2 H), 2.12 (s, 3 H), 1.66 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.2, 171.1 (2 C), 144.0, 141.4, 127.2, 126.5, 125.1, 116.0, 63.3, 52.9 (2 C), 47.8, 35.8, 29.7, 14.7; LRMS (EI) *m/z* 292 [M$^+$], 233, 129, 115, 43.

<Scheme 56>

<without MS4A>

Dimethyl (2*E*, 6*Z*)-7,8,10,10-tetramethyl-11-oxatricyclo[6.2.1.0^{2,6}]undeca-2,6-diene-4,4-dicarboxylate (163b)

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.1 mg, 0.150 mmol) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) under reflux for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 5/1, 1/1) to give **163b** (10.9 mg, 23% yield) as a colorless oil.

<with MS4A>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.1 mg, 0.150 mmol), MS4A (96.0 mg) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) under reflux for 1 h, was purified by column chromatography on silica gel (toluene/EtOAc = 7/1) to give **163b** (41.9 mg, 87% yield) as a colorless oil. Spectral data of **163b**: IR (neat) 3004, 2955, 2935, 2867, 1736 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.55 (s, 1 H), 4.35 (s, 1 H), 3.72 (s, 3 H), 3.71 (s, 3 H), 3.05 (s, 2 H), 1.74 (d, *J* = 12.0 Hz, 1 H), 1.68 (s, 3 H), 1.49 (d, *J* = 12.0 Hz, 1 H), 1.38 (s, 3 H), 1.23 (s, 3 H), 0.90 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 171.2, 145.6, 135.5, 133.2, 121.3, 84.4, 82.4, 65.2, 53.6, 52.82, 52.79, 43.7, 34.0, 31.9, 25.4, 22.6, 14.4; LRMS (EI) *m/z* 320 [M$^+$], 305, 273, 261, 245, 205, 173, 146; HRMS (EI) calcd for $C_{18}H_{24}O_5$ [M$^+$] 320.1624, found 320.1622.

<Table 6>

<run 1>

Dimethyl (2*E*, 6*Z*)-8-ethyl-7,10,10-trimethyl-11-oxatricyclo[6.2.1.0^{2,6}]undeca-2,6-diene-4,4-dicarboxylate (163c)

According to the general procedure for cyclization, a crude product, which was prepared from **162c** (50.2 mg, 0.150 mmol), MS4A (110 mg) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) under reflux for 24 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 15/1, 5/1) to give **163c** (45.2 mg, 90% yield) as a colorless oil. Spectral data of **163c**: IR (neat) 2955, 2929, 2868, 1738 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$)

δ 5.53 (s, 1 H), 4.34 (s, 1 H), 3.72 (s, 3 H), 3.71 (s, 3 H), 3.08 (dd, *J* = 17.5, 1.0 Hz, 1 H), 3.03 (dd, *J* = 17.5, 1.0 Hz, 1 H), 1.80 (dq, *J* = 15.0, 7.5 Hz, 1 H), 1.68 (d, *J* = 1.0 Hz, 3 H), 1.62 (dq, *J* = 15.0, 7.5 Hz, 1 H), 1.59 (d, *J* = 12.0 Hz, 1 H), 1.54 (d, *J* = 12.0 Hz, 1 H), 1.21 (s, 3 H), 0.94 (t, *J* = 7.5 Hz, 3 H), 0.90 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 171.1, 145.6, 135.4, 134.0, 121.1, 85.0, 84.1, 65.2, 52.80, 52.77, 50.8, 43.5, 34.1, 31.6, 27.8, 25.5, 14.2, 8.2; LRMS (EI) *m/z* 334 [M^+], 319, 287, 245, 219, 217, 203, 160; HRMS (EI) calcd for $C_{19}H_{26}O_5$ [M^+] 334.1780, found 334.1779.

<run 2>

Dimethyl (2*E*,6*Z*)-8-isopropyl-7,10,10-trimethyl-11-oxatricyclo[6.2.1.0^{2,6}]undeca-2,6-diene-4,4-dicarboxylate (163d)

According to the general procedure for cyclization, a crude product, which was prepared from **162d** (52.3 mg, 0.150 mmol), MS4A (105 mg) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0151 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) under reflux for 24 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 15/1, 5/1) to give **163d** (11.5 mg, 22% yield) and **162d** (5.3 mg, 10%). Spectral data of **163d**: IR (neat) 2958, 2872, 1737 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.52 (s, 1 H), 4.31 (s, 1 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 3.11 (d, *J* = 17.5 Hz, 1 H), 3.02 (d, *J* = 17.5 Hz, 1 H), 2.00-1.94 (m, 1 H), 1.76 (d, *J* = 12.0 Hz, 1 H), 1.71 (s, 3 H), 1.44 (d, *J* = 12.0 Hz, 1 H), 1.19 (s, 3 H), 1.02 (d, *J* = 6.5 Hz, 3 H), 0.95 (d, *J* = 6.5 Hz, 3 H), 0.91 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 171.2, 145.5, 136.2, 134.4, 120.8, 87.6, 83.6, 65.1, 52.81, 52.79, 48.2, 43.4, 34.2, 31.2, 25.4, 18.5, 16.5 (2 C), 14.5; LRMS (EI) *m/z* 348 [M^+], 333, 289, 277, 245, 233, 217, 71, 43; HRMS (EI) calcd for $C_{20}H_{28}O_5$ [M^+] 348.1937, found 348.1933.

<Table 7>

<run 1>

Dimethyl (2*E*, 6*Z*)-7,10,10-trimethyl-8-phenyl-11-oxatricyclo[6.2.1.0^{2,6}]undeca-2,6-diene-4,4-dicarboxylate (163e)

According to the general procedure for cyclization, a crude product, which was prepared from **162e** (57.7 mg, 0.151 mmol), MS4A (114 mg) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) under reflux for 24 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 15/1, 7/1) to give **163e** (24.0 mg, 42% yield) as a pale yellow oil. Spectral data of **163e**: IR (neat) 3019, 2956, 2936, 2869, 1732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.24 (m, 5 H), 5.64 (s, 1 H), 4.52 (s, 1 H), 3.76 (s, 3 H), 3.74 (s, 3 H), 3.11 (d, *J* = 19.0 Hz, 1 H), 3.07 (d, *J* = 19.0 Hz, 1 H), 2.17 (d, *J* = 11.5 Hz, 1 H), 2.11 (d, *J* = 11.5 Hz, 1 H), 1.29 (s, 3 H), 1.24 (s, 3 H), 1.01 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 171.1, 145.2, 142.4, 135.4, 133.4, 127.9 (2 C), 127.2, 126.6 (2 C), 121.4, 86.8, 84.0, 65.1, 52.9 (2 C), 51.8, 43.2, 34.2, 32.1, 25.7, 15.9; LRMS (EI) *m/z* 382 [M^+], 367, 335, 323, 267, 245, 217, 208, 105; HRMS (EI) calcd for $C_{23}H_{26}O_5$ [M^+] 382.1780, found 382.1786.

<run 2>

Dimethyl (2*E*, 6*Z*)-8-(4-carbomethoxyphenyl)-7,10,10-trimethyl-11-oxatricyclo[6.2.1.0^{2,6}]undeca-2,6-diene-4,4-dicarboxylate (163f)

According to the general procedure for cyclization, a crude product, which was prepared from **162f** (66.2 mg, 0.150 mmol), MS4A (129 mg) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) under reflux for 24 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 15/1, 5/1) to give **163f** (55.8 mg, 85% yield) as a pale yellow oil. Spectral data of **163f**: IR (neat) 3023, 2955, 2936, 2909, 2870, 2845, 1732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01-7.97 (m, 2 H), 7.43-7.38 (m, 2 H), 5.65 (s, 1 H), 4.52 (s, 1 H), 3.89 (s, 3 H), 3.75 (s, 3

H), 3.73 (s, 3 H), 3.10 (d, *J* = 22.0 Hz, 1 H), 3.05 (d, *J* = 22.0 Hz, 1 H), 2.19 (d, *J* = 12.0 Hz, 1 H), 2.07 (d, *J* = 12.0 Hz, 1 H), 1.26 (s, 3 H), 1.22 (s, 3 H), 1.00 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 171.0, 166.8, 147.5, 144.9, 134.5, 133.9, 129.2 (2 C), 129.0, 126.7 (2 C), 121.9, 86.6, 84.0, 65.1, 52.9 (2 C), 52.1, 52.0, 43.2, 34.1, 32.0, 25.5, 15.8; LRMS (EI) *m/z* 440 [M^+], 425, 409, 393, 381, 325, 266, 217, 163; HRMS (EI) calcd for $C_{25}H_{28}O_7$ [M^+] 440.1835, found 440.1842.

<run 3>

According to the general procedure for cyclization, a crude product, which was prepared from **162g** (62.0 mg, 0.150 mmol), MS4A (123 mg) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) under reflux for 24 h, was obtained as a complex mixture.

<Scheme 57>

Dimethyl (2*E*, 6*Z*)-7,10,10-trimethyl-8-dimethylphenylsilyl-11-oxatricyclo[6.2.1.0^{2,6}]undeca-2,6-diene-4,4-dicarboxylate (163h)

According to the general procedure for cyclization, a crude product, which was prepared from **162h** (66.2 mg, 0.150 mmol), MS4A (134 mg) and [Rh(dppbz)(nbd)]ClO_4 (11.2 mg, 0.0150 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) under reflux for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1) to give **163h** (53.6 mg, 81% yield) as a white solid. The structure of **163h** was determined by X-ray analysis. Spectral data of **163h**: IR ($CHCl_3$) 2999, 2954, 2929, 2867, 1737 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63-7.59 (m, 2 H), 7.40-7.30 (m, 3 H), 5.54 (s, 1 H), 4.35 (s, 1 H), 3.74 (s, 3 H), 3.70 (s, 3 H), 3.04 (dd, *J* = 17.0, 1.0 Hz, 1 H), 2.99 (dd, *J* = 17.0, 1.0 Hz, 1 H), 1.88 (d, *J* = 11.5 Hz, 1 H), 1.68 (d, *J* = 11.5 Hz, 1 H), 1.57 (d, *J* = 1.0 Hz, 3 H), 1.03 (s, 3 H), 0.95 (s, 3 H), 0.41 (s, 3 H), 0.39 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.6, 171.2, 145.5, 137.3, 136.3, 134.3 (2 C), 131.7, 129.0, 127.6 (2 C), 120.7, 84.9, 78.9, 64.7, 52.7 (2 C), 49.9, 44.0, 34.0, 31.1, 25.4, 17.0, -3.6, -4.0; LRMS (EI) *m/z* 440 [M^+], 425, 412, 397, 353, 325, 187, 135; HRMS (EI) calcd for $C_{25}H_{32}O_5Si$ [M^+] 440.2019, found 440.2026; mp 106.0 °C (recrystallized from *n*-hexane-EtOAc at 0 °C).

<Scheme 58>

Dimethyl 2-(but-2-yn-1-yl)-2-(6-hydroxyhepta-1,2-dien-1-yl)malonate (186)

To a solution of **134a** (313 mg, 1.12 mmol) in THF (11 mL) was added MeMgBr (1.12 M in THF, 1.50 mL, 1.68 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 2 h. To the mixture was added saturated NH_4Cl aqueous solution at -78 °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 (*n*-hexane/EtOAc = 5/1, 2/1) to give **186** (151 mg, 46% yield) and **134a** (108 mg, 35% yield) as a pale yellow oil. Spectral data of **186**: IR (neat) 3420, 2955, 2924, 2855, 1967, 1739 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.73-5.68 (m, 1 H), 5.43-5.35 (m, 1 H), 3.85-3.80 (m, 1 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 2.81 (s, 2 H), 2.20-2.05 (m, 2 H), 1.64-1.51 (m, 3 H), 1.71 (s, 3 H), 1.17 (d, *J* = 6.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.2*[1], 169.8, 169.7*, 95.5*, 90.5*, 78.4, 73.6*, 67.3*, 57.7*, 52.9 (2 C), 38.0*, 24.9*, 24.5, 23.4*, 3.4; LRMS (EI) *m/z* 294 [M^+], 203, 131, 115, 91, 43.

Dimethyl 2-(but-2-yn-1-yl)-2-(6-oxohepta-1,2-dien-1-yl)malonate (134l)

To a solution of **186** (151 mg, 0.513 mmol) in CH_2Cl_2 (5.0 mL) was added Dess-Martin Periodinane (323 mg, 0.762 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture were added saturated $NaHCO_3$

aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 4/1) to give **134l** (135 mg, 90% yield) as a colorless oil. Spectral data of **134l**: IR (neat) 3003, 2955, 2923, 2853, 1969, 1739, 1714 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.76-5.71 (m, 1 H), 5.44 (dt, *J* = 6.3, 6.3 Hz, 1 H), 3.74 (s, 3 H), 3.72 (s, 3 H), 2.87-2.80 (m, 2 H), 2.57 (qt, *J* = 18.2, 7.1 Hz, 2 H), 2.34-2.18 (m, 2 H), 2.16-2.11 (m, 3 H), 1.72 (t, *J* = 3.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 203.0, 169.6, 169.5, 94.8, 91.4, 78.5, 73.6, 57.8, 52.9 (2 C), 41.8, 29.9, 24.8, 21.9, 3.5; LRMS (EI) *m/z* 292 [M^+], 233, 131, 115, 43.

<Scheme 60>

Dimethyl 2-(but-2-yn-1-yl)-2-(6-hydroxy-4,4-dimethylhepta-1,2-dien-1-yl)malonate (193b)

To a solution of **162a** (770 mg, 2.51 mmol) in THF (25 mL) was added MeMgBr (1.12 M in THF, 3.00 mL, 3.36 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 2 h. To the mixture was added saturated NH_4Cl aqueous solution at -78 °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 (*n*-hexane/EtOAc = 7/1, 5/1, 2/1) to give **193b** (514 mg, 64% yield) and **162a** (177 mg, 23% yield) as a pale yellow oil. Spectral data of **193b**: IR (neat) 3550, 3439, 2960, 2925, 1967, 1731 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.84-5.78 (m, 1 H), 5.46-5.42 (m, 1 H), 3.99-3.91 (brs, 1 H), 3.74 (s, 3 H), 3.73 (s, 3 H), 2.85-2.81 (m, 2 H), 1.91-1.78 (brs, 1 H), 1.74-1.69 (m, 3 H), 1.60-1.38 (m, 2 H), 1.19-1.14 (m, 3 H), 1.08-1.01 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9*[1], 169.7*, 169.6, 106.5*, 92.1*, 78.7*, 73.6*, 65.6*, 57.9*, 52.9*, 52.1*, 34.7*, 29.3*, 29.1*, 27.4*, 25.5*, 25.0*, 3.5; LRMS (EI) *m/z* 322 [M^+], 307, 205, 145, 83, 43.

Dimethyl 2-(but-2-yn-1-yl)-2-(4,4-dimethyl-6-oxohepta-1,2-dien-1-yl)malonate (162b)

To a solution of **193b** (514 mg, 1.59 mmol) in CH_2Cl_2 (16 mL) was added Dess-Martin Periodinane (1.31 g, 3.09 mmol) at 0 °C, and the mixture was stirred at room temperature for 5 h. To the mixture was added Dess-Martin Periodinane (472 mg, 1.11 mmol) at 0 °C, and the mixture was stirred at room temperature for 14 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **162b** (483 mg, 94% yield) as a colorless oil. Spectral data of **162b**: IR (neat) 2957, 2925, 2874, 1968, 1739, 1716 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.80 (d, *J* = 6.0 Hz, 1 H), 5.52 (d, *J* = 6.0 Hz, 1 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 2.84 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.79 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.48 (d, *J* = 15.0 Hz, 1 H), 2.43 (d, *J* = 15.0 Hz, 1 H), 2.10 (s, 3 H), 1.71 (t, *J* = 2.5 Hz, 3 H), 1.12 (s, 3 H), 1.09 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 200.7, 169.6, 169.5, 105.6, 92.5, 78.6, 73.7, 57.9, 54.7, 52.9, 52.8, 34.4, 31.9, 27.8, 27.6, 25.1, 3.5; LRMS (EI) *m/z* 320 [M^+], 305, 267, 225, 205, 193, 43; HRMS (EI) calcd for $C_{18}H_{24}O_5$ [M^+] 320.1623, found 320.1625.

<Scheme 61>

Dimethyl 2-(but-2-yn-1-yl)-2-(6-hydroxy-4,4-dimethylocta-1,2-dien-1-yl)malonate (193c)

To a suspension of Mg (152 mg, 6.26 mmol) in THF (5.0 mL) was added EtBr (400 μL, 5.14 mmol) dropwise at room temperature. The reaction mixture was stirred at the same temperature for 1 h to give EtMgBr in THF solution. To a solution of **162a** (269 mg, 0.879 mmol) in THF (9.0 mL) was added EtMgBr in THF (5.0 mL) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the mixture was added saturated NH_4Cl aqueous

solution at -78 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 6/1, 5/1) to give **193c** (177 mg, 60% yield) as a pale yellow oil. Spectral data of **193c**: IR (neat) 3552, 3449, 2959, 2925, 2876, 1967, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.84-5.80 (m, 1 H), 5.46 (d, *J* = 6.0 Hz, 1 H), 3.74 (s, 6 H), 3.69-3.62 (brs, 1 H), 2.85-2.82 (m, 2 H), 1.84-1.79 (brs, 1 H), 1.73 (t, *J* = 2.5 Hz, 3 H), 1.52-1.40 (m, 4 H), 1.09-1.03 (m, 6 H), 0.92 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9*[1], 169.8*, 169.6, 106.6*, 92.1*, 78.7, 73.6, 70.7*, 57.9*, 52.93, 52.89, 50.0*, 34.7*, 31.6*, 29.2*, 27.5*, 25.5*, 9.9, 3.5; LRMS (EI) *m/z* 336 [M^+], 321, 277, 205, 145, 97, 57.

Dimethyl 2-(but-2-yn-1-yl)-2-(4,4-dimethyl-6-oxoocta-1,2-dien-1-yl)malonate (162c)

To a solution of **193c** (150 mg, 0.446 mmol) in CH_2Cl_2 (6.0 mL) was added Dess-Martin Periodinane (290 mg, 0.684 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 6/1) to give **162c** (122 mg, 82% yield) as a colorless oil. Spectral data of **162c**: IR (neat) 2957, 2920, 2877, 1968, 1739, 1715 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.80 (d, *J* = 6.5 Hz, 1 H), 5.53 (d, *J* = 6.5 Hz, 1 H), 3.72 (s, 3 H), 3.72 (s, 3 H), 2.83 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.79 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.47-2.35 (m, 4 H), 1.71 (t, *J* = 2.5 Hz, 3 H), 1.12 (s, 3 H), 1.09 (s, 3 H), 0.99 (t, *J* = 7.4 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.2, 200.6, 169.6, 169.5, 105.7, 92.4, 78.6, 73.7, 57.9, 53.5, 52.83, 52.81, 37.7, 34.5, 27.9, 27.6, 25.1, 7.6, 3.5; LRMS (EI) *m/z* 334 [M^+], 319, 281, 249, 225, 219, 57; HRMS (EI) calcd for $C_{19}H_{26}O_5$ [M^+] 334.1781, found 334.1782.

Dimethyl 2-(but-2-yn-1-yl)-2-(6-hydroxy-4,4,7-trimethylocta-1,2-dien-1-yl)malonate (193d)

To a solution of **162a** (289 mg, 0.943 mmol) in THF (5 mL) was added *i*-PrMgBr (0.71 M in THF, 2.5 mL, 1.8 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the mixture was added saturated NH_4Cl aqueous solution at -78 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 5/1) to give **193d** (125 mg, 38% yield) as a colorless oil. Spectral data of **193d**: IR (neat) 3583, 3449, 2958, 2927, 2872, 1967, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.85-5.83 (m, 1 H), 5.45 (d, *J* = 6.0 Hz, 1 H), 3.74 (s, 6 H), 3.56-3.48 (brs, 1 H), 2.86-2.83 (m, 2 H), 1.73 (t, *J* = 2.3 Hz, 3 H), 1.70-1.54 (m, 2 H), 1.50-1.37 (m, 2 H), 1.09-1.02 (m, 6 H), 0.93-0.85 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0*[1], 169.8*, 169.7*, 106.6*, 92.1*, 78.7*, 73.7*, 73.5, 57.9*, 52.92, 52.88, 47.2*, 34.7*, 29.0*, 27.5*, 25.5*, 18.5*, 17.03, 17.00, 3.5; LRMS (EI) *m/z* 350 [M^+], 335, 291, 205, 145, 111, 69, 43.

Dimethyl 2-(but-2-yn-1-yl)-2-(4,4,7-trimethyl-6-oxoocta-1,2-dien-1-yl)malonate (162d)

To a solution of **193d** (125 mg, 0.357 mmol) in CH_2Cl_2 (6.0 mL) was added Dess-Martin Periodinane (220 mg, 0.519 mmol) at 0 °C, and the mixture was stirred at room temperature for 3.5 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1) to give **162d** (103 mg, 83% yield) as a colorless oil. Spectral data of **162d**: IR (neat) 2962, 2929, 2874, 1968, 1739, 1712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.82 (d, *J* = 6.0 Hz, 1 H), 5.59 (d, *J* = 6.0 Hz, 1 H), 3.75 (s, 3 H), 3.75 (s, 3 H), 2.87 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.82 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.60-2.53 (m, 1 H), 2.51 (d,

J = 16.0 Hz, 1 H), 2.48 (d, *J* = 16.0 Hz, 1 H), 1.73 (t, *J* = 2.5 Hz, 3 H), 1.14 (s, 3 H), 1.12 (s, 3 H), 1.07 (s, 3 H), 1.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.4, 200.6, 169.6, 169.5, 105.8, 92.3, 78.5, 73.7, 57.9, 52.79, 52.77, 51.5, 41.8, 34.4, 27.8, 27.5, 25.1, 18.0, 17.9, 3.4; LRMS (EI) *m/z* 348 [M^+], 333, 295, 289, 225, 71, 43; HRMS (EI) calcd for $C_{20}H_{28}O_5$ [M^+] 348.1936, found 348.1939.

<Scheme 62>

Dimethyl 2-(but-2-yn-1-yl)-2-(4,4-dimethyl-6-oxo-6-phenylhexa-1,2-dien-1-yl)malonate (162e)

To a solution of **162a** (234 mg, 0.764 mmol) in THF (11 mL) was added PhMgBr (1.08 M in THF, 1.00 mL, 1.08 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 1 h and at 0 °C for 1 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give a crude alcohol **193e**. To a solution of the crude alcohol **193e** in CH_2Cl_2 (8 mL) was added Dess-Martin Periodinane (537 mg, 1.27 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **162e** (143 mg, 49% yield in 2 steps) as a colorless oil. Spectral data of **162e**: IR (neat) 3061, 2957, 2924, 2873, 1967, 1739, 1691 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96-7.91 (m, 2 H), 7.57-7.51 (m, 1 H), 7.49-7.42 (m, 2 H), 5.82 (d, *J* = 6.5 Hz, 1 H), 5.62 (d, *J* = 6.5 Hz, 1 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 3.02 (s, 2 H), 2.86 (dq, *J* = 16.5, 2.8 Hz, 1 H), 2.81 (dq, *J* = 16.5, 2.8 Hz, 1 H), 1.70 (t, *J* = 2.8 Hz, 3 H), 1.21 (s, 3 H), 1.19 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.7, 199.1, 169.7, 169.6, 138.1, 132.8, 128.5 (2 C), 128.2 (2 C), 106.1, 92.5, 78.6, 73.7, 58.0, 52.9, 52.8, 49.0, 34.9, 28.0, 27.9, 25.2, 3.5; LRMS (EI) *m/z* 382 [M^+], 367, 329, 323, 267, 105, 77; HRMS (EI) calcd for $C_{23}H_{26}O_5$ [M^+] 382.1780, found 382.1780.

Dimethyl 2-(but-2-yn-1-yl)-2-(6-hydroxy-6-(4-methoxyphenyl)-4,4-dimethylhexa-1,2-dien-1-yl)malonate (193f)

To a suspension of methyl 4-iodobenzoate (524 mg, 2.00 mmol) and LiCl (87.2 mg, 2.06 mmol) in THF (2.0 mL) was added *i*-PrMgBr (0.70 M in THF, 3.0 mL, 2.1 mmol) dropwise at -25 °C. The reaction mixture was stirred at the same temperature for 30 min to give ArMgBr in THF solution (Ar = *p*-$MeO_2CC_6H_4$). To a solution of **162a** (369 mg, 1.20 mmol) in THF (12 mL) was added ArMgBr (2.0 mL) at -30 °C, and the reaction mixture was stirred at the same temperature for 1 h. To the mixture was added saturated NH_4Cl aqueous solution at -30 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1, 3/1) to give **193f** (477 mg, 90% yield) as a pale yellow oil. Spectral data of **193f**: IR (neat) 3520, 3010, 2955, 2924, 2870, 1967, 1719 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.0 Hz, 2 H), 7.40 (d, *J* = 8.0 Hz, 2 H), 5.89-5.82 (m, 1 H), 5.53-5.48 (m, 1 H), 4.92-4.85 (brs, 1 H), 3.88 (s, 3 H), 3.77-3.69 (m, 6 H), 2.91-2.79 (m, 2 H), 2.54-2.41 (m, 1 H), 1.88-1.60 (m, 5 H), 1.16-1.07 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.1*[1], 169.7*, 169.6, 166.9, 151.0*, 129.7 (2 C), 128.9*, 125.6* (2 C), 106.3*, 92.3*, 78.8*, 73.5, 71.7*, 57.9*, 53.0*, 52.9, 52.4, 52.1*, 35.1*, 29.1*, 28.0*, 25.5*, 3.5*; LRMS (EI) *m/z* 442 [M^+], 264, 205, 163, 43.

Dimethyl 2-(but-2-yn-1-yl)-2-(6-(4-methoxyphenyl)-4,4-dimethyl-6-oxohexa-1,2-dien-1-yl)malonate (162f)

To a solution of **193f** (408 mg, 0.922 mmol) in CH_2Cl_2 (10 mL) was added Dess-Martin Periodinane (906 mg, 2.14 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. To the mixture were added saturated $NaHCO_3$

aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1) to give **162f** (395 mg, 97% yield) as a colorless oil. Spectral data of **162f**: IR (neat) 3025, 2955, 2925, 2871, 2843, 1968, 1735, 1692 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.13-8.10 (m, 2 H), 8.00-7.97 (m, 2 H), 5.82 (d, *J* = 6.5 Hz, 1 H), 5.60 (d, *J* = 6.5 Hz, 1 H), 3.95 (s, 3 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 3.05 (s, 2 H), 2.86 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.80 (dq, *J* = 16.5, 2.5 Hz, 1 H), 1.70 (t, *J* = 2.5 Hz, 3 H), 1.22 (s, 3 H), 1.20 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6, 198.6, 169.6, 169.5, 166.2, 141.2, 133.6, 129.7 (2 C), 128.0 (2 C), 105.9, 92.6, 78.6, 73.7, 58.0, 52.9, 52.8, 52.4, 49.3, 34.9, 27.9, 27.8, 25.1, 3.5; LRMS (EI) *m/z* 440 [M^+], 425, 387, 355, 325, 163, 135; HRMS (EI) calcd for $C_{25}H_{28}O_7$ [M^+] 440.1835, found 440.1840.

Dimethyl 2-(but-2-yn-1-yl)-2-(6-hydroxy-6-(4-(methoxycarbonyl)phenyl)-4,4-dimethylhexa-1,2-dien-1-yl)malonate (193g)

To a suspension of Mg (134 mg, 5.51 mmol) and LiCl (212 mg, 5.00 mmol) in THF (5.0 mL) was added *p*-bromoanisole (630 μL, 5.03 mmol) dropwise at room temparature. The reaction mixture was stirred at the same temperature for 1 h to give ArMgBr in THF solution (Ar = *p*-$MeOC_6H_4$). To a solution of **162a** (460 mg, 1.50 mmol) in THF (15 mL) was added ArMgBr in THF (3.0 mL) at -78 °C, and the reaction mixture was stirred at the same temperature for 1 h. To the mixture was added saturated NH_4Cl aqueous solution at -78 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1, 5/1) to give **193g** (470 mg, 76% yield) as a pale yellow oil. Spectral data of **193g**: IR (neat) 3543, 3000, 2956, 2923, 2837, 1966, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29-7.24 (m, 2 H), 6.89-6.84 (m, 2 H), 5.88-5.83 (m, 1 H), 5.53-5.48 (m, 1 H), 4.84-4.76 (m, 1 H), 3.80 (s, 3 H), 3.77-3.72 (m, 6 H), 2.88 (dq, *J* = 17.0, 2.5 Hz, 1 H), 2.84 (dq, *J* = 17.0, 2.5 Hz, 1 H), 2.11-2.02 (brs, 1 H), 1.92-1.82 (m, 1 H), 1.76-1.72 (m, 3 H), 1.71-1.64 (m, 1 H), 1.14-1.05 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 169.7, 169.6, 158.8, 138.0*, 126.94, 126.90, 113.8 (2 C), 106.5*, 92.2*, 78.7*, 73.6*, 71.7*, 57.9*, 55.3, 52.9, 52.2, 52.1, 35.0*, 29.0*, 27.8*, 25.5*, 3.5; LRMS (EI) *m/z* 414 [M^+], 264, 205, 150, 135.

Dimethyl 2-(but-2-yn-1-yl)-2-(6-(4-(methoxycarbonyl)phenyl)-4,4-dimethyl-6-oxohexa-1,2-dien-1-yl)malonate (162g)

To a solution of **193g** (452 mg, 1.09 mmol) in CH_2Cl_2 (11.0 mL) was added Dess-Martin Periodinane (729 mg, 1.72 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1, 5/1) to give **162g** (394 mg, 88% yield) as a colorless oil. Spectral data of **162g**: IR (neat) 3009, 2957, 2925, 2871, 2842, 1968, 1739, 1681 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.5 Hz, 2 H), 6.91 (d, *J* = 8.5 Hz, 2 H), 5.81 (d, *J* = 6.5 Hz, 1 H), 5.60 (d, *J* = 6.5 Hz, 1 H), 3.85 (s, 3 H), 3.71 (s, 3 H), 3.71 (s, 3 H), 2.94 (s, 2 H), 2.84 (dq, *J* = 16.0, 3.0 Hz, 1 H), 2.79 (dq, *J* = 16.0, 3.0 Hz, 1 H), 1.69 (t, *J* = 3.0 Hz, 3 H), 1.18 (s, 3 H), 1.17 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6, 197.6, 169.7, 169.6, 163.2, 131.2, 130.5 (2 C), 113.5 (2 C), 106.2, 92.4, 78.6, 73.7, 58.0, 55.4, 52.83, 52.79, 48.7, 34.9, 28.1, 27.8, 25.1, 3.5; LRMS (EI) *m/z* 412 [M^+], 397, 359, 297, 135; HRMS (EI) calcd for $C_{24}H_{28}O_6$ [M^+] 412.1886, found 412.1886.

<Scheme 64>

Dimethyl 2-(but-2-yn-1-yl)-2-(6-(dimethyl(phenyl)silyl)-4,4-dimethyl-6-oxohexa-1,2-dien-1-yl)malonate (162h)

To a suspension of Li (162 mg, 23.3 mmol) in THF (2.3 mL) was added $PhMe_2SiCl$ (380 μL, 2.26 mmol) dropwise at room temparature. The reaction mixture was stirred at the same temperature for 3 h to give $PhMe_2SiLi$ in THF solution. To a solution of **162a** (458 mg, 1.50 mmol) in THF (10 mL) was added $PhMe_2SiLi$ in THF (2.3 mL) at -78 °C, and the reaction mixture was stirred at the same temperature for 1 h. To the mixture was added saturated NH_4Cl aqueous solution at -78 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 6/1) to give mixture of **193h** and **162a** (366 mg) as a pale yellow oil. To a solution of the mixture (366 mg) in CH_2Cl_2 (10 mL) were added pyridine (0.50 mL, 6.19 mmol) and then Dess-Martin Periodinane (500 mg, 1.18 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 6/1) to give **162h** (145 mg, 22% yield in 2 steps) and **162a** (119 mg, 26% yield in 2 steps) as a colorless oil. Spectral data of **162h**: IR (neat) 3070, 2956, 2924, 2871, 1967, 1739, 1645 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.55-7.51 (m, 2 H), 7.43-7.35 (m, 3 H), 5.75 (d, *J* = 6.5 Hz, 1 H), 5.53 (d, *J* = 6.5 Hz, 1 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 2.82 (dq, *J* = 17.0, 2.5 Hz, 1 H), 2.76 (dq, *J* = 17.0, 2.5 Hz, 1 H), 2.65 (s, 2 H), 1.70 (t, *J* = 2.5 Hz, 3 H), 1.04 (s, 3 H), 1.02 (s, 3 H), 0.47 (s, 3 H), 0.46 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 246.3, 200.5, 169.7, 169.6, 134.4, 134.0 (2 C), 129.8, 128.1 (2 C), 105.9, 92.2, 78.5, 73.7, 58.9, 58.0, 52.80, 52.77, 34.4, 27.9, 27.4, 25.2, 3.5, -4.8 (2 C); LRMS (EI) *m/z* 440 [M^+], 425, 387, 381, 221, 189, 135; HRMS (EI) calcd for $C_{25}H_{32}O_5Si$ [M^+] 440.2019, found 440.2021.

Experimental Section of Chapter 2, Section 2

General Procedure for Cyclization Using [Rh(phosphine)]X.

A solution of [Rh(ligand)(cod)]X (0.0150 mmol, 10 mol% to a substrate) or [Rh(cod)$_2$]X (0.0150 mmol, 10 mol% to a substrate) and ligand (0.0150 mmol, 10 mol% to a substrate) in degassed (Freeze-Pump up-Thaw cycle was conducted) $ClCH_2CH_2Cl$ (0.58 mL: 0.026 M to Rh) was stirred under H_2 atmosphere at room temperature for 1 h. Then the solvent was pump up, and the reaction vessel was flushed with Ar gas. To the mixture was added solvent (0.58 mL) and then added the solution of substrate (0.150 mmol) in degassed solvent (0.92 mL) and the reaction mixture was stirred at an ambitent temperature until the substrate disappeared on TLC. After filtration of Molecular Sieve with EtOAc, the residue was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel to give product.

<Scheme 65>

<eq. 1>

According to the general procedure for cyclization, a crude product, which was prepared from 1**62b** (48.1 mg, 0.150 mmol), MS4A (100 mg), [Rh(cod)$_2$]BF_4 (6.1 mg, 0.015 mmol), and DPPBz (6.7 mg, 0.015 mmol) in $ClCH_2CH_2Cl$ (1.50 mL) under reflux for 3 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 5/1) to give **163b** (41.6 mg, 87% yield) as a colorless oil.

<eq. 2>

Dimethyl (*Z*)-5,5,9-trimethyl-7-oxo-1,4,5,6,7,8-hexahydro-2*H*-cyclopenta[8]annulene-2,2-dicarboxylate (194b)

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (47.8 mg, 0.149 mmol), MS4A (90.2 mg), [Rh(cod)$_2$]BF_4 (5.9 mg, 0.015 mmol), and DPPBz (6.6 mg, 0.015 mmol) in DMF (1.50 mL) under 90 ℃ for 5 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 5/1) to give **194b** (24.6 mg, 52% yield) as a white solid. The structure of **194b** was determined by X-ray analysis. Spectral data of **194b**: IR ($CHCl_3$) 3020, 2957, 1732, 1691 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6, 150 °C) δ 5.90 (s, 1 H), 3.75 (s, 6 H), 3.33 (s, 2 H), 3.18 (s, 2 H), 2.52 (s, 2 H), 2.33 (s, 2 H), 1.83 (s, 3 H), 0.99 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.6, 171.4, 171.1, 145.1, 138.9, 133.5, 122.6, 62.4, 52.9 (2 C), 51.4, 50.6, 41.0, 38.5, 33.7, 29.4, 28.9, 24.3; LRMS (EI) *m/z* 320 [M$^+$], 261, 245, 229, 201, 117, 83, 59; HRMS (EI) calcd for $C_{18}H_{24}O_5$ [M$^+$] 320.1624, found 320.1626; mp 107.0 °C (recrystallized from *n*-hexane-THF at 0 °C).

<Table 8>

<run 2>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (49.6 mg, 0.155 mmol), MS4A (100 mg), [Rh(cod)$_2$]BF_4 (6.1 mg, 0.015 mmol) and DPPE (6.0 mg, 0.015 mmol) in DMF (1.50 mL) at 90 °C for 19 h, was obtained. Yields of **194b** and **163b** were determined to be 43% and 5% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 3>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (47.7 mg, 0.149 mmol), MS4A (94.0 mg), $[Rh(cod)_2]BF_4$ (6.1 mg, 0.015 mmol) and DPPP (6.2 mg, 0.015 mmol) in DMF (1.50 mL) at 90 °C for 1 h, was obtained. Yield of **194b** was determined to be 63% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 4>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.4 mg, 0.151 mmol), MS4A (101 mg), $[Rh(cod)_2]BF_4$ (6.1 mg, 0.015 mmol) and DPPB (6.5 mg, 0.015 mmol) in DMF (1.50 mL) at 90 °C for 19 h, was obtained. Yields of **194b**, **163b**, and **162b** were determined to be 8%, 6%, and 33% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 5>

According to the general procedure for cyclization, a crude product, which was prepared from **194b** (48.9 mg, 0.153 mmol), MS4A (95.8 mg), $[Rh(cod)_2]BF_4$ (6.1 mg, 0.015 mmol) and DPPF (8.3 mg, 0.015 mmol) in DMF (1.50 mL) at 90 °C for 19 h, was obtained. Yields of **194b**, **163b**, and **162b** were determined to be 4%, 4%, and 53% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 6>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.2 mg, 0.150 mmol), MS4A (100 mg), $[Rh(cod)_2]BF_4$ (6.3 mg, 0.016 mmol) and BIPHEP (7.9 mg, 0.015 mmol) in DMF (1.50 mL) at 90 °C for 22 h, was obtained. Yield of **162b** was determined to be 47% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 7>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.4 mg, 0.151 mmol), MS4A (101 mg), $[Rh(cod)_2]BF_4$ (6.1 mg, 0.015 mmol) and PPh_3 (7.9 mg, 0.030 mmol) in DMF (1.50 mL) at 90 °C for 19 h, was obtained. Yields of **194b**, **163b**, and **162b** were determined to be 5%, 12%, and 23% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 8>

A solution of MS4A (92.3 mg), [Rh(I*i*Pr)(cod)]Cl (6.0 mg, 0.015 mmol) and $AgBF_4$ (2.9 mg, 0.015 mmol) in DMF (1.50 mL) was stirred at room temperature for 10 min. Then to the solution was added a solution of **162b** (41.5 mg, 0.149 mmol) in DMF (0.92 mL) and the reaction mixture was stirred at 90 °C for 9 h and 120 °C for 12 h. After filtration of Molecular Sieve with EtOAc, the residue was washed with brine, dried over Na_2SO_4, and concentrated to obtain crude. Yield of **162b** was determined to be 41% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<Table 9>

<run 2>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.6 mg, 0.152 mmol), MS4A (94.5 mg), $[Rh(cod)_2]BF_4$ (6.1 mg, 0.015 mmol) and DPPP (6.3 mg, 0.015 mmol) in $ClCH_2CH_2Cl$ (1.50

mL) under reflux for 20 h, was obtained. Yield of **163b** was determined to be 87% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 3>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.2 mg, 0.150 mmol), MS4A (103 mg), $[Rh(cod)_2]BF_4$ (6.1 mg, 0.015 mmol) and DPPP (6.2 mg, 0.015 mmol) in CH_3CN (1.50 mL) under reflux for 17 h, was obtained. Yields of **194b** and **162b** were determined to be 4% and 72% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 4>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.8 mg, 0.152 mmol), MS4A (92.5 mg), $[Rh(cod)_2]BF_4$ (6.1 mg, 0.015 mmol) and DPPP (6.2 mg, 0.015 mmol) in THF (1.50 mL) under reflux for 19 h, was obtained. Yields of **194b** and **163b** were determined to be 60% and 5% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 5>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (47.0 mg, 0.147 mmol), MS4A (94.2 mg), $[Rh(cod)_2]BF_4$ (6.0 mg, 0.015 mmol) and DPPP (6.1 mg, 0.015 mmol) in DMSO (1.50 mL) at 90 ℃ for 2 h, was obtained. Yield of **194b** was determined to be 41% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 6>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (47.9 mg, 0.149 mmol), MS4A (100 mg), $[Rh(cod)_2]ClO_4$ (6.3 mg, 0.015 mmol) and DPPP (6.2 mg, 0.015 mmol) in DMF (1.50 mL) at 90 ℃ for 1 h, was obtained. Yield of **194b** was determined to be 66% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 7>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.4 mg, 0.151 mmol), MS4A (96.0 mg), $[Rh(cod)_2]SbF_6$ (8.3 mg, 0.015 mmol) and DPPP (6.2 mg, 0.015 mmol) in DMF (1.50 mL) at 90 ℃ for 1 h, was obtained. Yield of **194b** was determined to be 59% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 8>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.9 mg, 0.153 mmol), MS4A (100 mg), $[Rh(cod)_2]BAr^F$ (17.8 mg, 0.0151 mmol) and DPPP (6.2 mg, 0.015 mmol) in DMF (1.50 mL) at 90 ℃ for 1 h, was obtained. Yield of **194b** was determined to be 56% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<Table 10>

<run 2>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.1 mg, 0.150 mmol) and [Rh(dppp)(cod)]ClO_4 (10.9 mg, 0.0151 mmol) in DMF (1.50 mL) at 90 ℃ for 19 h, was obtained. Yield of **162b** was determined to be 46% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 3>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (47.8 mg, 0.149 mmol), MS3A (94.8 mg) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 90 ℃ for 1 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 4/1) to give **194b** (34.5 mg, 72% yield) as a white solid.

<run 4>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.5 mg, 0.151 mmol), MS5A (102 mg) and [Rh(dppp)(cod)]ClO_4 (10.9 mg, 0.0151 mmol) in DMF (1.50 mL) under 90 ℃ for 19 h, was obtained. Yield of **163b** was determined to be 55% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 5>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.1 mg, 0.150 mmol), $PhCO_2H$ (18.3 mg, 0.150 mmol) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 90 ℃ for 18 h, was obtained. Yield of **162b** was determined to be 21% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 6>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.1 mg, 0.150 mmol), $EtCO_2H$ (11.5 μL, 0.154 mmol) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 90 ℃ for 18 h, was obtained. Yield of **162b** was determined to be 22% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.

<run 7>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.1 mg, 0.150 mmol), Na_2CO_3 (15.9 mg, 0.150 mmol) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 90 ℃ for 18 h, was obtained. Yields of **194b**, **163b** and **162b** were determined to be 7%, 4%, and 42% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 8>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.1 mg, 0.150 mmol), K_2CO_3 (20.7 mg, 0.150 mmol) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 90 ℃ for 18 h, was obtained. Yields of **194b**, **163b** and **162b** were determined to be 17%, 5%, and 28% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 9>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.1 mg, 0.150 mmol), Cs_2CO_3 (48.9 mg, 0.150 mmol) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 90 ℃ for 18 h, was obtained. Yields of **194b** and **162b** were determined to be 9% and 35% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<run 10>

According to the general procedure for cyclization, a crude product, which was prepared from **162b** (48.1 mg, 0.150 mmol), $CaCO_3$ (15.0 mg, 0.150 mmol) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 90 ℃ for 18 h, was obtained. Yields of **163b** and **162b** were determined to be 6% and 64% by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

<Table 12>

<run 1>

Dimethyl (*E*)-9-((methoxymethoxy)methyl)-5,5-dimethyl-7-oxo-1,4,5,6,7,8-hexahydro-2*H*-cyclopenta[8]annulene-2,2-dicarboxylate (194c)

According to the general procedure for cyclization, a crude product, which was prepared from **162c** (57.1 mg, 0.150 mmol), MS3A (92.5 mg) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) at 90 ℃ for 19 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 3/1, 1/1) to give **194c** (24.5 mg, 43% yield) as a pale yellow oil.

<run 2>

According to the general procedure for cyclization, a crude product, which was prepared from **162c** (57.1 mg, 0.150 mmol), MS3A (105 mg) and [Rh(dppp)(cod)]ClO_4 (10.7 mg, 0.0148 mmol) in THF (1.50 mL) under reflux for 40 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 2/1) to give **194c** (44.0 mg, 77% yield) as a pale yellow oil. Spectral data of **194c**: IR (neat) 3444, 2956, 2846, 1732, 1698, 1645 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6, 75 ℃) δ 6.05 (s, 1 H), 4.38 (s, 2 H), 3.87 (s, 2 H), 3.48-3.26 (m, 12 H), 3.15 (s, 3 H), 2.42-2.00 (brs, 2 H), 0.84 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.0, 170.9, 170.5, 145.0, 143.1, 136.3, 123.1, 95.6, 69.9, 62.6, 55.4, 52.9 (2 C), 51.2, 46.5, 40.9, 37.5, 33.8, 29.3, 28.9; LRMS (EI) *m/z* 380 [M^+], 305, 243, 215, 157, 59; HRMS (EI) calcd for $C_{20}H_{28}O_7$ [M^+] 380.1835, found 380.1834.

<run 3>

Dimethyl (*Z*)-9-ethyl-5,5-dimethyl-7-oxo-1,4,5,6,7,8-hexahydro-2*H*-cyclopenta[8]annulene-2,2-dicarboxylate (194d)

According to the general procedure for cyclization, a crude product, which was prepared from **162d** (50.2 mg, 0.150 mmol), MS3A (100 mg) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) at 90 ℃ for 72 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 5/1) to give **194d** (14.6 mg, 29% yield) as a white solid.

<run 4>

According to the general procedure for cyclization, a crude product, which was prepared from **162d** (50.2 mg, 0.150 mmol), MS3A (101 mg) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in THF (1.50 mL) under reflux for 64 h,

was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 5/1) to give **194d** (16.0 mg, 32% yield) as a white solid. Spectral data of **194d**: IR ($CHCl_3$) 3020, 2958, 2872, 1732, 1692 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, 150 °C) δ 5.93 (s, 1 H), 3.75 (s, 6 H), 3.34 (s, 2 H), 3.21 (s, 2 H), 2.56-2.51 (m, 2 H), 2.34 (s, 2 H), 2.14 (q, *J* = 7.5 Hz, 2 H), 1.05-0.96 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.9, 171.4, 171.1, 145.3, 138.2, 133.7, 128.7, 62.4, 52.9 (2 C), 51.5, 48.7, 41.1, 37.7, 33.8, 31.2, 29.5, 28.9, 11.6; LRMS (EI) *m/z* 334 [M^+], 275, 259, 243, 215, 131, 83, 59; HRMS (EI) calcd for $C_{19}H_{26}O_5$ [M^+] 334.1780, found 334.1786; mp 60.0 °C (recrystallized from *n*-hexane-EtOAc at 0 °C).

<run 5>

According to the general procedure for cyclization, a crude product, which was prepared from **162e** (46.0 mg, 0.150 mmol), MS3A (92.5 mg) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 90 ℃ for 24 h, was obtained as a complex mixture.

<run 6>

Dimethyl (*Z*)-5,5-dimethyl-7-oxo-1,4,5,6,7,8-hexahydro-2*H*-cyclopenta[8]annulene-2,2-dicarboxylate (194e)

According to the general procedure for cyclization, a crude product, which was prepared from **162e** (46.1 mg, 0.150 mmol), MS4A (90.6 mg) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 90 ℃ for 24 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 5/1) to give **194e** (15.4 mg, 34% yield) as a pale yellow solid. Spectral data of **194e**: IR (neat) 2956, 2926, 2871, 1732, 1696 cm^{-1}; ^1H NMR (500 MHz, C_6D_6, 75 ℃) δ 5.98 (s, 1 H), 5.02 (t, *J* = 7.3 Hz, 1 H), 3.38 (s, 6 H), 3.25 (m, 2 H), 2.92 (s, 2 H), 2.45-2.18 (brs, 2 H), 2.08 (s, 2 H), 0.84 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.0, 171.0 (2 C), 145.9, 144.9, 135.6, 113.6, 63.0, 52.9 (2 C), 51.0, 43.5, 40.4, 39.6, 34.2, 29.3, 29.2; LRMS (EI) *m/z* 306 [M^+], 246, 215, 187, 83, 59; HRMS (EI) calcd for $C_{17}H_{22}O_5$ [M^+] 306.1467, found 306.1463; mp 93.5 °C (recrystallized from *n*-hexane-THF at 0 °C).

<Table 13>

<run 1>

Dimethyl (*Z*)-3,5,5,9-tetramethyl-7-oxo-1,4,5,6,7,8-hexahydro-2*H*-cyclopenta[8]annulene-2,2-dicarboxylate (194f)

According to the general procedure for cyclization, a crude product, which was prepared from **162f** (50.2 mg, 0.150 mmol), MS3A (99.9 mg) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 90 ℃ for 2 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 5/1) to give **194f** (32.4 mg, 65% yield) as a pale yellow solid. Spectral data of **194f**: IR ($CHCl_3$) 3020, 2956, 2929, 1729, 1692 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, 150 °C) δ 3.76 (s, 6 H), 3.34 (s, 2 H), 3.12 (q, *J* = 1.3 Hz, 2 H), 2.53 (s, 2 H), 2.35 (s, 2 H), 1.94 (s, 3 H), 1.80 (t, *J* = 1.3 Hz, 3 H), 1.00 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.0, 171.4, 171.3, 140.5, 140.2, 139.5, 119.5, 65.8, 52.64, 52.62, 51.6, 50.7, 38.8, 37.7, 35.2, 29.4, 29.0, 24.3, 13.6; LRMS (EI) *m/z* 334 [M^+], 275, 243, 215, 131, 83, 59; HRMS (EI) calcd for $C_{19}H_{26}O_5$ [M^+] 334.1780, found 334.1784; mp 75.5 °C (recrystallized from *n*-hexane-EtOAc at 0 °C).

<run 2>

(*Z*)-2',2',5,5,9-Pentamethyl-1,5,6,8-tetrahydrospiro[cyclopenta[8]annulene-2,5'-[1,3]dioxan]-7(4*H*)-one (194g)

According to the general procedure for cyclization, a crude product, which was prepared from **162g** (45.7 mg, 0.150 mmol), MS3A (104 mg) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 50 ℃ for 24 h,

was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 25/1, 10/1 and 25/1) to give **194g** (22.8 mg, 50% yield) as a white solid. Spectral data of **194g**: IR ($CHCl_3$) 3017, 2960, 2866, 1691 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, 150 °C) δ 5.86 (s, 1 H), 3.75 (d, *J* = 11.4 Hz, 2 H), 3.56 (d, *J* = 11.4 Hz, 2 H), 3.29 (s, 2 H), 2.53 (s, 2 H), 2.47 (s, 2 H), 2.34 (s, 2 H), 1.79 (s, 3 H), 1.44 (s, 3 H), 1.41 (s, 3 H), 0.98 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.4, 143.4, 140.5, 139.2, 121.0, 97.6, 68.9, 68.6, 51.6, 50.7, 45.2, 41.5, 40.0, 33.5, 29.6, 29.1, 25.4, 24.1, 22.2; LRMS (EI) *m/z* 304 [M^+], 229, 216, 201, 83; HRMS (EI) calcd for $C_{19}H_{28}O_3$ [M^+] 304.2038, found 304.2032; mp 83.0 °C (recrystallized from *n*-hexane-EtOAc at 0 °C).

<run 3>

(*Z*)-2,2-Bis((benzyloxy)methyl)-4,8,8-trimethyl-2,3,5,7,8,9-hexahydro-6*H*-cyclopenta[8]annulen-6-one (194h)

According to the general procedure for cyclization, a crude product, which was prepared from **162h** (66.7 mg, 0.150 mmol), MS3A (105 mg) and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) under 50 °C for 18 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 25/1, 10/1 and 25/1) to give **194h** (20.3 mg, 31% yield) as a colorless oil.

<run 4>

According to the general procedure for cyclization, a crude product, which was prepared from **162h** (64.2 mg, 0.144 mmol), MS4A (106 mg) and [Rh(dppp)(cod)]ClO_4 (10.6 mg, 0.0147 mmol) in DMF (1.50 mL) under 50 °C for 18 h, was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 25/1) to give **194h** (37.1 mg, 58% yield) as a colorless oil. Spectral data of **194h**: IR (neat) 2957, 2919, 2849, 1642 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, 150 °C) δ 7.42-7.24 (m, 10 H), 5.78 (s, 1 H), 4.54 (s, 4 H), 3.50 (s, 4 H), 3.27 (s, 2 H), 2.50 (s, 2 H), 2.45 (s, 2 H), 2.30 (s, 2 H), 1.76 (s, 3 H), 0.96 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.9, 142.7, 141.5, 140.9, 138.6, 128.29, 128.26 (4 C), 127.52, 127.49, 127.4 (4 C), 119.6, 74.3, 74.0, 73.3 (2 C), 51.6, 50.9, 50.7, 41.4, 38.3, 33.6, 29.5, 29.0, 24.1; LRMS (EI) *m/z* 444 [M^+], 353, 323, 216, 91; HRMS (EI) calcd for $C_{30}H_{36}O_3$ [M^+] 444.2664, found 444.2662.

<Scheme 70>

1-Iodo-4-(methoxymethoxy)but-2-yne (207)

To a solution of **206** (3.48 g, 26.7 mmol) in THF (5.0 mL) was added PPh_3 (8.39 g, 32.0 mmol), imidazole (2.65 g, 38.9 mmol), and I_2 (8.10 g, 31.9 mmol) at 0 °C, and the reaction mixture was stirred at the same temperature for 30 min. After the solution was concentrated, the residue was filtered with hexane. After the concentrated, the crude was obtained as a pale yellow oil. The crude was used in the next reaction without purification.

Dimethyl 2-(6-((*tert*-butyldiphenylsilyl)oxy)-4,4-dimethylhexa-1,2-dien-1-yl)-2-(4-(methoxymethoxy)but-2-yn-1-yl)malonate (209c)

To a solution of **180** (2,17 g, 4.97 mmol) in THF (5.0 mL) was added LHMDS (1.3 M in THF, 8.5 mL, 11 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the solution was added methyl chloroformate (400 μL, 5.18 mmol), and the mixture was stirred at the same temperature for 10 min. Then, to the solution was added a solution of **207** (2.00 g, 8.34 mmol) in THF (5.0 mL) at -78 °C, and the mixture was stirred and warmed to room temperature for 18 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 15/1, 10/1) to give

209c (2.10 g, 70% yield) as a pale yellow oil. Spectral data of **209c**: IR (neat) 3071, 2956, 2858, 1967, 1740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70-7.63 (m, 4 H), 7.45-7.35 (m, 6 H), 5.76 (d, *J* = 6.0 Hz, 1 H), 5.32 (d, *J* = 6.0 Hz, 1 H), 4.64 (s, 2 H), 4.15-4.12 (m, 2 H), 3.79-3.65 (m, 8 H), 3.34 (s, 3 H), 2.89 (s, 2 H), 1.63 (t, *J* = 7.0 Hz, 2 H), 1.04 (s, 9 H), 0.971 (s, 3 H), 0.966 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9, 169.43, 169.35, 135.5 (4 C), 133.90, 133.88, 129.5 (2 C), 127.6 (4 C), 106.5, 94.3, 91.7, 81.4, 78.3, 61.1, 57.6, 55.5, 54.2, 52.89, 52.87, 45.1, 34.2, 28.2, 27.5, 26.8 (3 C), 25.2, 19.1; LRMS (EI) *m/z* 549 [(M-^{t}Bu)$^+$], 485, 281, 229, 213, 199, 183, 135, 91, 45.

Dimethyl 2-(6-hydroxy-4,4-dimethylhexa-1,2-dien-1-yl)-2-(4-(methoxymethoxy)but-2-yn-1-yl)malonate (210c)

To a solution of **209c** (2.10 g, 3.46 mmol) in THF (24 mL) was added TBAF (1.0 M in THF, 4.5 mL, 4.5 mmol) 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 EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 1/1) to give **210c** (1.04 g, 82% yield) as a pale yellow oil. Spectral data of **210c**: IR (neat) 3435, 2956, 2826, 1966, 1738 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.81 (d, *J* = 6.0 Hz, 1 H), 5.39 (d, *J* = 6.0 Hz, 1 H), 4.66 (s, 2 H), 4.15 (t, *J* = 2.0 Hz, 2 H), 3.75 (s, 6 H), 3.71-3.63 (m, 2 H), 3.34 (s, 3 H), 2.93 (t, *J* = 2.0 Hz, 2 H), 1.81-1.68 (brs, 1 H), 1.64 (t, *J* = 7.5 Hz, 2 H), 1.03 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 169.5, 169.4, 106.5, 94.3, 91.9, 81.5, 78.4, 59.9, 57.5, 55.5, 54.2, 53.00, 52.98, 45.1, 34.3, 28.2, 27.8, 25.2; LRMS (EI) *m/z* 368 [M^+], 306, 255, 240, 214, 199, 45.

Dimethyl 2-(4,4-dimethyl-6-oxohexa-1,2-dien-1-yl)-2-(4-(methoxymethoxy)but-2-yn-1-yl)malonate (211c)

To a solution of the **210c** (1.04 g, 2.82 mmol) in CH_2Cl_2 (24 mL) was added Dess-Martin Periodinane (1.55 g, 3.65 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 4/1, 3/1) to give **211c** (932 mg, 90% yield) as a pale yellow oil. Spectral data of **211c**: IR (neat) 2957, 2889, 2736, 1968, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.76 (t, *J* = 2.8 Hz, 1 H), 5.86 (d, *J* = 6.5 Hz, 1 H), 5.50 (d, *J* = 6.5 Hz, 1 H), 4.65 (s, 2 H), 4.14 (t, *J* = 2.3 Hz, 2 H), 3.75 (s, 6 H), 3.34 (s, 3 H), 2.95 (dq, *J* = 16.8, 2.3 Hz, 1 H), 2.81 (dq, *J* = 16.8, 2.3 Hz, 1 H), 2.41 (dd, *J* = 15.5, 2.8 Hz, 1 H), 2.35 (dd, *J* = 15.5, 2.8 Hz, 1 H), 1.17 (s, 3 H), 1.15 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.5, 200.9, 169.2, 169.1, 105.3, 94.4, 92.8, 81.2, 78.6, 57.6, 55.5, 54.8, 54.2, 53.02, 53.00, 34.3, 28.2, 28.0, 25.2; LRMS (EI) *m/z* 366 [M^+], 304, 245, 115, 45.

Dimethyl 2-(6-hydroxy-4,4-dimethylhepta-1,2-dien-1-yl)-2-(4-(methoxymethoxy)but-2-yn-1-yl)malonate (212c)

To a solution of **211c** (932 mg, 2.54 mmol) in THF (24 mL) was added MeMgBr (1.0 M in Et_2O, 3.0 mL, 3.0 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 1 h. To the mixture was added saturated NH_4Cl aqueous solution at -78 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 2/1) to give **212c** (584 mg, 60% yield) and **211c** (165 mg, 18% yield) as a pale yellow oil. Spectral data of **212c**: IR (neat) 3452, 3439, 2959, 2928, 1966, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.84-5.78 (m, 1 H), 5.47 (m, *J* = 6.5 Hz, 1 H), 4.65 (s, 2 H), 4.14 (s, 2 H), 3.99-3.89 (m, 1 H), 3.74 (s, 6 H), 3.34 (s, 3 H), 2.94 (s, 2 H), 1.92-1.78 (brs, 1 H), 1.60-1.38 (m, 2 H), 1.16 (d, *J* = 6.5 Hz, 3 H), 1.07 (s, 3 H), 1.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0*[1], 169.5*, 169.3, 106.8*, 94.3, 91.9*, 81.4*, 78.4*, 65.6*, 57.6*, 55.5, 54.2, 53.02, 52.99*, 52.1*, 34.8*, 29.2*, 27.6*, 25.5*, 25.1*; LRMS (EI) *m/z* 382 [M^+], 337, 255, 179, 83, 45.

Dimethyl 2-(4,4-dimethyl-6-oxohepta-1,2-dien-1-yl)-2-(4-(methoxymethoxy)but-2-yn-1-yl)malonate (162c)

To a solution of **212c** (584 mg, 1.53 mmol) in CH_2Cl_2 (15.0 mL) was added Dess-Martin Periodinane (881 mg, 2.08 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1) to give **162c** (472 mg, 81% yield) as a colorless oil. Spectral data of **162c**: IR (neat) 2956, 2930, 2891, 2845, 1967, 1739, 1712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.83 (d, *J* = 6.5 Hz, 1 H), 5.57 (d, *J* = 6.5 Hz, 1 H), 4.66 (s, 2 H), 4.16 (t, *J* = 2.3 Hz, 2 H), 3.75 (s, 6 H), 3.35 (s, 3 H), 2.97 (dt, *J* = 17.5, 2.3 Hz, 1 H), 2.92 (dt, *J* = 17.5, 2.3 Hz, 1 H), 2.49 (d, *J* = 14.5 Hz, 1 H), 2.45 (d, *J* = 14.5 Hz, 1 H), 2.13 (s, 3 H), 1.14 (s, 3 H), 1.12 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.6, 200.8, 169.3, 169.2, 105.9, 94.3, 92.3, 81.4, 78.4, 57.6, 55.5, 54.7, 54.2, 52.94, 52.92, 34.5, 31.9, 27.8, 27.7, 25.1; LRMS (EI) *m/z* 365 [(M-Me)$^+$], 321, 267, 235, 203, 161, 59.; HRMS (EI) calcd for $C_{19}H_{25}O_7$ [(M-Me)$^+$] 365.1600, found 365.1592.

Dimethyl 2-(6-((*tert*-butyldiphenylsilyl)oxy)-4,4-dimethylhexa-1,2-dien-1-yl)-2-(pent-2-yn-1-yl)malonate (209d)

To a solution of **180** (1.74 g, 3.98 mmol) in THF (8.0 mL) was added LHMDS (1.3 M in THF, 6.8 mL, 8.8 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the solution was added methyl chloroformate (330 μL, 4.26 mmol), and the mixture was stirred at the same temperature for 10 min. Then, to the solution were added 1-chloroprop-2-yne **208** (630 μL, 6.02 mmol) and NaI (903 mg, 6.02 mmol) at -78 °C, and the mixture was stirred and warmed to room temperature for 20 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 30/1, 20/1, 15/1) to give **209d** (1.31 g, 59% yield) as a pale yellow oil. Spectral data of **209d**: IR (neat) 3068, 2957, 2933, 2854, 1966, 1741 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70-7.65 (m, 4 H), 7.45-7.36 (m, 6 H), 5.77 (d, *J* = 6.5 Hz, 1 H), 5.29 (d, *J* = 6.5 Hz, 1 H), 3.76-3.68 (m, 8 H), 2.83 (dt, *J* = 16.0, 2.3 Hz, 1 H), 2.79 (dt, *J* = 16.0, 2.3 Hz, 1 H), 2.08 (qt, *J* = 7.5, 2.3 Hz, 2 H), 1.66 (dt, *J* = 13.5, 7.3 Hz, 1 H), 1.63 (dt, *J* = 13.5, 7.3, 1 H), 1.05 (t, *J* = 7.5 Hz, 3 H), 1.04 (s, 9 H), 0.981 (s, 3 H), 0.976 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8, 169.7, 169.6, 135.6 (4 C), 133.9 (2 C), 129.5 (2 C), 127.6 (4 C), 106.3, 92.0, 84.6, 74.0, 61.2, 58.1, 52.8, 52.7, 45.1, 34.2, 28.3, 27.5, 26.8 (3 C), 25.3, 19.1, 14.1, 12.3; LRMS (EI) *m/z* 560 [M$^+$], 545, 503, 213, 135, 44.

Dimethyl 2-(6-hydroxy-4,4-dimethylhexa-1,2-dien-1-yl)-2-(pent-2-yn-1-yl)malonate (210d)

To a solution of **209d** (1.31 g, 2.34 mmol) in THF (23 mL) was added TBAF (1.0 M in THF, 3.0 mL, 3.0 mmol) at 0 °C, and the mixture was stirred at room temperature for 45 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 2/1) to give **210d** (598 mg, 79% yield) as a pale yellow oil. Spectral data of **210d**: IR (neat) 3398, 2957, 2924, 2877, 1966, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.83 (d, *J* = 6.0 Hz, 1 H), 5.38 (d, *J* = 6.0 Hz, 1 H), 3.76 (s, 6 H), 3.73-3.66 (m, 2 H), 2.88 (dt, *J* = 16.5, 2.3 Hz, 1 H), 2.84 (dt, *J* = 16.5, 2.3 Hz, 1 H), 2.11 (qt, *J* = 7.5, 2.3, 2 H), 1.67 (dt, *J* = 14.0, 7.3 Hz, 1 H), 1.62 (dt, *J* = 14.0, 7.3 Hz, 1 H), 1.42 (t, *J* = 5.5 Hz, 1 H), 1.08 (t, *J* = 7.5 Hz, 3 H), 1.050 (s, 3 H), 1.047 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9, 169.7, 169.6, 106.1, 92.1, 84.8, 73.9, 60.0, 58.1, 52.9, 52.8, 45.3, 34.3, 28.1, 27.9, 25.4, 14.1, 12.3; LRMS (EI) *m/z* 322 [M$^+$], 262, 244, 177, 117, 69, 41.

Dimethyl 2-(4,4-dimethyl-6-oxohexa-1,2-dien-1-yl)-2-(pent-2-yn-1-yl)malonate (211d)

To a solution of the **210d** (564 mg, 1.75 mmol) in CH_2Cl_2 (19 mL) was added Dess-Martin Periodinane (1.07 g, 2.52 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 6/1) to give **211d** (504 mg, 90% yield) as a pale yellow oil. Spectral data of **211d**: IR (neat) 2959, 2928, 2877, 2840, 2737, 1966, 1739, 1720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.77 (t, *J* = 3.0 Hz, 1 H), 5.87 (d, *J* = 6.0 Hz, 1 H), 5.47 (d, *J* = 6.0 Hz, 1 H), 3.74 (s, 3 H), 3.73 (s, 3 H), 2.86 (dt, *J* = 17.0, 2.3 Hz, 1 H), 2.82 (dt, *J* = 17.0, 2.3 Hz, 1 H), 2.41 (dd, *J* = 15.5, 3.0 Hz, 1 H), 2.35 (dd, *J* = 15.5, 3.0 Hz, 1 H), 2.09 (qt, *J* = 7.8, 2.3 Hz, 2 H), 1.17 (s, 3 H), 1.16 (s, 3 H), 1.05 (t, *J* = 7.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.6, 200.8, 169.5, 169.4, 105.1, 93.1, 84.9, 73.8, 58.0, 54.8, 52.9, 52.8, 34.3, 28.2, 28.0, 25.2, 14.0, 12.3; LRMS (EI) *m/z* 320 [M^+], 260, 229, 117, 41.

Dimethyl 2-(6-hydroxy-4,4-dimethylhepta-1,2-dien-1-yl)-2-(pent-2-yn-1-yl)malonate (212d)

To a solution of **211d** (504 mg, 1.57 mmol) in THF (16 mL) was added MeMgBr (1.0 M in Et_2O, 1.9 mL, 1.9 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 1 h. To the mixture was added saturated NH_4Cl aqueous solution at -78 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 6/1) to give **212d** (275 mg, 52% yield) and **211d** (141 mg, 28% yield) as a pale yellow oil. Spectral data of **212d**: IR (neat) 3432, 2961, 2924, 1966, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.84-5.81 (m, 1 H), 5.45 (d, *J* = 6.0 Hz, 1 H), 4.01-3.92 (m, 1 H), 3.74 (s, 6 H), 2.87 (dt, *J* = 16.5, 2.4 Hz, 1 H), 2.82 (dt, *J* = 16.5, 2.4 Hz, 1 H), 2.10 (qt, *J* = 7.7, 2.4 Hz, 2 H), 1.91-1.63 (brs, 1 H), 1.60-1.39 (m, 2 H), 1.18-1.16 (m, 3 H), 1.10-1.03 (m, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9*[1], 169.7*, 169.6, 106.5*, 92.2*, 84.9*, 73.9, 65.6*, 58.1*, 52.9*, 52.8, 52.2*, 34.8*, 29.4*, 27.5*, 25.6*, 25.0*, 14.1, 12.3; LRMS (EI) *m/z* 336 [M^+], 278, 219, 117, 45.

Dimethyl 2-(4,4-dimethyl-6-oxohepta-1,2-dien-1-yl)-2-(pent-2-yn-1-yl)malonate (162d)

To a solution of **212d** (275 mg, 0.817 mmol) in CH_2Cl_2 (8.0 mL) was added Dess-Martin Periodinane (458 mg, 1.08 mmol) at 0 °C, and the mixture was stirred at room temperature for 4 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 8/1, 6/1) to give **162d** (250 mg, 92% yield) as a colorless oil. Spectral data of **162d**: IR (neat) 2957, 2877, 1967, 1738 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.84 (d, *J* = 6.5 Hz, 1 H), 5.55 (d, *J* = 6.5 Hz, 1 H), 3.750 (s, 3 H), 3.745 (s, 3 H), 2.88 (dt, *J* = 16.5, 2.3 Hz, 1 H), 2.83 (dt, *J* = 16.5, 2.3 Hz, 1 H), 2.50 (d, *J* = 14.5 Hz, 1 H), 2.45 (d, *J* = 14.5 Hz, 1 H), 2.13 (s, 3 H), 2.10 (qt, *J* = 7.3, 2.3 Hz, 2 H), 1.15 (s, 3 H), 1.12 (s, 3 H), 1.07 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 200.7, 169.6, 169.5, 105.6, 92.5, 84.7, 74.0, 58.1, 54.7, 52.81, 52.79, 34.5, 32.0, 27.9, 27.7, 25.2, 14.1, 12.3; LRMS (EI) *m/z* 319 [$(M\text{-}Me)^+$], 275, 267, 219, 193, 161, 59; HRMS (EI) calcd for $C_{18}H_{23}O_5$ [$(M\text{-}Me)^+$] 319.1546, found 319.1549.

<Scheme 71>

Dimethyl 2-(6-hydroxy-4,4-dimethylhepta-1,2-dien-1-yl)-2-(prop-2-yn-1-yl)malonate (212e)

To a solution of **211e** (170 mg, 0.582 mmol) in THF (6 mL) was added MeMgBr (1.0 M in Et_2O, 1.2 mL, 1.2 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the mixture was added saturated NH_4Cl aqueous solution at -78 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 4/1, 3/1) to give **212e** (122 mg, 68% yield) as a pale yellow oil. Spectral data of **212e**: IR (neat) 3425, 3294, 2960, 2927, 1966, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.85-5.82 (m, 1 H), 5.49 (d, *J* = 6.5 Hz, 1 H), 4.00-3.91 (m, 1 H), 3.763 (s, 3 H), 3.756 (s, 3 H), 2.90 (d, *J* = 3.0 Hz, 2 H), 2.00 (t, *J* = 3.0 Hz, 1 H), 1.85-1.65 (brs, 1 H), 1.61-1.38 (m, 2 H), 1.19-1.16 (m, 3 H), 1.08 (s, 3 H), 1.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0*[1], 169.43, 169.38, 106.9*, 91.8*, 79.0, 71.2*, 65.6*, 57.5*, 53.1, 53.0*, 52.1*, 34.8*, 29.3*, 27.6*, 25.1*, 24.9; LRMS (EI) *m/z* 308 [M^+], 269, 199, 139.

Dimethyl 2-(4,4-dimethyl-6-oxohepta-1,2-dien-1-yl)-2-(prop-2-yn-1-yl)malonate (162e)

To a solution of **212e** (160 mg, 0.519 mmol) in CH_2Cl_2 (5.0 mL) was added Dess-Martin Periodinane (345 mg, 0.813 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1, 4/1) to give **162e** (147 mg, 92% yield) as a colorless oil. Spectral data of **162e**: IR (neat) 3284, 2958, 2930, 2873, 2848, 1967, 1739, 1717 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.83 (d, *J* = 6.5 Hz, 1 H), 5.57 (d, *J* = 6.5 Hz, 1 H), 3.75 (s, 6 H), 2.91 (dd, *J* = 17.0, 2.5 Hz, 1 H), 2.87 (dd, *J* = 17.0, 2.5 Hz, 1 H), 2.48 (d, *J* = 15.0 Hz, 1 H), 2.45 (d, *J* = 15.0 Hz, 1 H), 2.11 (s, 3 H), 1.98 (t, *J* = 2.5 Hz, 1 H), 1.13 (s, 3 H), 1.11 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.6, 200.8, 169.3, 169.2, 106.0, 92.2, 79.1, 71.2, 57.5, 54.7, 52.99, 52.96, 34.5, 32.0, 27.8, 27.7, 24.7; LRMS (EI) *m/z* 291 [$(M\text{-}Me)^+$], 267, 247, 235, 59; HRMS (EI) calcd for $C_{16}H_{19}O_5$ [$(M\text{-}Me)^+$] 291.1233, found 291.1224.

<Scheme 72>

7-((*tert*-Butyldiphenylsilyl)oxy)-5,5-dimethylhept-2-yn-4-ol (214)

To a solution of 1-bromoprop-1-ene (1.00 mL, 11.7 mmol) in THF (40 mL) was added *n*-BuLi (1.63 M in hexane, 15.0 mL, 24.5 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 1 h. To the solution was added a solution of **213** (3.55 g, 10.0 mmol) in THF (100 mL), and the mixture was stirred and warmed to room temperature for 16 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 15/1, 10/1) to give **214** (3.65 g, 93% yield) as a yellow oil. Spectral data of **214**: IR (neat) 3390, 3071, 2959, 2931, 2858 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.78-7.64 (m, 4 H), 7.57-7.34 (m, 6 H), 4.13-4.04 (m, 1 H), 3.88 (d, *J* = 7.0 Hz, 1 H), 3.80-3.63 (m, 2 H), 1.97-1.89 (m, 1 H), 1.87 (d, *J* = 2.0 Hz, 3 H), 1.44 (dt, *J* = 15.0, 5.0 Hz, 1 H), 1.07 (s, 9 H), 1.00 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6 (2 C), 135.5 (2 C), 133.0, 132.9, 129.78, 129.76, 127.73 (2 C), 127.71 (2 C), 81.4, 79.1, 70.5, 61.0, 40.8, 38.3, 26.6 (3 C), 24.8, 23.8, 19.0, 3.6; LRMS (EI) *m/z* 355 [$(M\text{-}CH_3C{\equiv}C)^+$], 335, 199, 132.

Methyl 8-((*tert*-butyldiphenylsilyl)oxy)-3,6,6-trimethylocta-3,4-dienoate (215)

A solution of **214** (3.65 g, 9.25 mmol) and propionic acid (150 μL, 1.99 mmol) in trimethyl orthoacetate (7.00 mL. 55.9

mmol) was stirred at 120 °C for 14 h with azeotropic removal of methanol. The mixture was concentrated, and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 30/1, 20/1) to give **215** (2.70 g, 65% yield) as a pale yellow oil. Spectral data of **215**: IR (neat) 3071, 3050, 2958, 2931, 2858, 1969, 1741 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70-7.64 (m, 4 H), 7.45-7.35 (m, 6 H), 4.98-4.95 (m, 1 H), 3.71 (t, *J* = 7.5 Hz, 2 H), 3.64 (s, 3 H), 2.91 (dd, *J* = 15.0, 2.5 Hz, 1 H), 2.87 (dd, *J* = 15.0, 2.5 Hz, 1 H), 1.67 (d, *J* = 3.0 Hz, 3 H), 1.64 (td, *J* = 7.5, 1.2 Hz, 2 H), 1.05 (s, 9 H), 0.95 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6, 171.6, 135.5 (4 C), 134.0, 133.8, 129.6, 129.5, 127.60 (2 C), 127.57 (2 C), 101.2, 94.8, 61.4, 51.6, 45.1, 40.3, 34.2, 28.3, 28.1, 26.83, 26.79, 25.5, 19.13, 19.10; LRMS (EI) *m/z* 450 [M^+], 393, 213, 168, 135, 109.

Dimethyl 2-(but-2-yn-1-yl)-2-(7-((*tert*-butyldiphenylsilyl)oxy)-5,5-dimethylhepta-2,3-dien-2-yl)malonate (209f)

To a solution of **215** (2.24 g, 4.97 mmol) in THF (10.0 mL) was added LHMDS (1.3 M in THF, 8.5 mL, 11 mmol) at -78 °C, and the reaction mixture was stirred at the same temperature for 30 min. To the solution was added methyl chloroformate (400 μL, 5.18 mmol), and the mixture was stirred at the same temperature for 15 min. Then, to the solution was added 1-bromobut-2-yne **216** (900 μL, 10.0 mmol) and NaI (1.50 g, 10.0 mmol) at -78 °C, and the mixture was stirred and warmed to room temperature for 16 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 30/1, 20/1) to give **209f** (1.85 g, 66% yield) as a pale yellow oil. Spectral data of **209f**: IR (neat) 3071, 2956, 2930, 2858, 1964, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.69-7.62 (m, 4 H), 7.44-7.33 (m, 6 H), 5.16 (q, *J* = 3.0 Hz, 1 H), 3.73 (s, 3 H), 3.72 (s, 3 H), 3.71 (t, *J* = 6.5 Hz, 2 H), 2.79 (dq, *J* = 16.5, 2.8 Hz, 1 H), 2.75 (dq, *J* = 16.5, 2.8 Hz, 1 H), 1.77 (d, *J* = 3.0 Hz, 3 H), 1.71 (t, *J* = 2.8 Hz, 3 H), 1.67-1.60 (m, 2 H), 1.04 (s, 9 H), 0.97 (s, 3 H), 0.95 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6, 169.7 (2 C), 135.5 (4 C), 133.99, 133.97, 129.5 (2 C), 127.6 (4 C), 104.4, 99.9, 78.1, 74.5, 61.3, 61.0, 52.5 (2 C), 45.1, 34.6, 28.3, 27.4, 26.8 (3 C), 25.6, 19.1, 17.2, 3.6; LRMS (EI) *m/z* 560 [M^+], 545, 501, 213, 199, 135, 44.

Dimethyl 2-(but-2-yn-1-yl)-2-(7-hydroxy-5,5-dimethylhepta-2,3-dien-2-yl)malonate (210f)

To a solution of **209f** (1.80 g, 3.21 mmol) in THF (32 mL) was added TBAF (1.0 M in THF, 4.2 mL, 4.2 mmol) at 0 °C, and the mixture was stirred at room temperature for 5 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 1/1) to give **210f** (926 mg, 89% yield) as a pale yellow oil. Spectral data of **210f**: IR (neat) 3389, 2956, 2924, 2868, 1964, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.24 (q, *J* = 3.0 Hz, 1 H), 3.75 (s, 6 H), 3.69 (t, *J* = 6.8 Hz, 2 H), 2.83 (dq, *J* = 16.6, 2.8 Hz, 1 H), 2.79 (dq, *J* = 16.6, 2.8 Hz, 1 H), 1.85 (d, *J* = 3.0 Hz, 3 H), 1.73 (t, *J* = 2.8 Hz, 3 H), 1.66-1.55 (m, 3 H), 1.03 (s, 3 H), 1.02 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.7, 169.7, 169.6, 104.2, 99.9, 78.3, 74.5, 61.1, 60.1, 52.63, 52.61, 45.2, 34.7, 28.02, 27.99, 25.5, 17.3, 3.6; LRMS (EI) *m/z* 322 [M^+], 263, 231, 177, 117, 69, 41.

Dimethyl 2-(but-2-yn-1-yl)-2-(5,5-dimethyl-7-oxohepta-2,3-dien-2-yl)malonate (211f)

To a solution of the **210f** (897 mg, 2.78 mmol) in CH_2Cl_2 (24 mL) was added Dess-Martin Periodinane (1.66 g, 3.91 mmol) at 0 °C, and the mixture was stirred at room temperature for 4 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column

chromatography on silica gel (*n*-hexane/EtOAc = 5/1, 4/1) to give **211f** (830 mg, 93% yield) as a pale yellow oil. Spectral data of **211f**: IR (neat) 2958, 2926, 2871, 2736, 1966, 1738 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.77 (t, *J* = 3.0 Hz, 1 H), 5.33 (q, *J* = 3.0 Hz, 1 H), 3.744 (s, 3 H), 3.739 (s, 3 H), 2.83 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.79 (dq, *J* = 16.5, 2.5 Hz, 1 H), 2.42 (dd, *J* = 15.5, 3.0 Hz, 1 H), 2.34 (dd, *J* = 15.5, 3.0 Hz, 1 H), 1.84 (d, *J* = 3.0 Hz, 3 H), 1.72 (t, *J* = 2.5 Hz, 3 H), 1.17 (s, 3 H), 1.15 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.9, 200.7, 169.4 (2 C), 103.1, 101.0, 78.4, 74.4, 61.1, 54.6, 52.63, 52.61, 34.8, 28.3, 28.1, 25.4, 17.1, 3.6; LRMS (EI) *m/z* 320 [M^+], 261, 229, 201, 177, 117, 83, 41.

Dimethyl 2-(but-2-yn-1-yl)-2-(7-hydroxy-5,5-dimethylocta-2,3-dien-2-yl)malonate (212f)

To a solution of **211f** (830 mg, 2.59 mmol) in THF (24 mL) was added MeMgBr (1.0 M in Et_2O, 3.1 mL, 3.1 mmol) at -30 °C, and the reaction mixture was stirred at the same temperature for 1 h. To the mixture was added saturated NH_4Cl aqueous solution at -30 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 5/1, 3/1) to give **212f** (269 mg, 31% yield) and **211f** (86.9 mg, 10% yield) as a pale yellow oil. Spectral data of **212f**: IR (neat) 3437, 2958, 2925, 1963, 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.34-5.29 (m, 1 H) 3.99-3.94 (m, 1 H), 3.76 (s, 6 H), 2.88-2.79 (m, 2 H), 1.89-1.82 (m, 3 H), 1.74 (t, *J* = 2.3 Hz, 3 H), 1.62-1.40 (m, 3 H), 1.19-1.16 (m, 3 H), 1.07 (s, 3 H), 1.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8*[1], 169.7, 169.6, 104.5*, 99.5, 78.5, 74.4*, 65.7*, 61.1, 52.7*, 52.2, 52.0, 35.2*, 29.5*, 27.3*, 25.5*, 25.0*, 17.3*, 3.6; LRMS (EI) *m/z* 336 [M^+], 277, 245, 233, 177, 117, 57.

Dimethyl 2-(but-2-yn-1-yl)-2-(5,5-dimethyl-7-oxoocta-2,3-dien-2-yl)malonate (162f)

To a solution of **212f** (269 mg, 0.800 mmol) in CH_2Cl_2 (8.0 mL) was added Dess-Martin Periodinane (510 mg, 1.20 mmol) at 0 °C, and the mixture was stirred at room temperature for 16 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 6/1, 5/1) to give **162f** (201 mg, 75% yield) as a colorless oil. Spectral data of **162f**: IR (neat) 2956, 2925, 2872, 1964, 1738, 1714 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.38 (q, *J* = 3.0 Hz, 1 H), 3.76 (s, 3 H), 3.75 (s, 3 H), 2.84 (dq, *J* = 16.0, 2.3 Hz, 1 H), 2.80 (dq, *J* = 16.0, 2.3 Hz, 1 H), 2.50 (d, *J* = 15.5 Hz, 1 H), 2.46 (d, *J* = 15.5 Hz, 1 H), 2.13 (s, 3 H), 1.84 (d, *J* = 3.0 Hz, 3 H), 1.74 (t, *J* = 2.3 Hz, 3 H), 1.14 (s, 3 H), 1.11 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.8, 200.4, 169.6, 169.5, 103.8, 100.5, 78.2, 74.5, 61.1, 54.6, 52.6 (2 C), 35.0, 31.9, 27.9, 27.6, 25.4, 17.0, 3.6; LRMS (EI) *m/z* 303 [(M-MeO)$^+$], 281, 275, 219, 59; HRMS (EI) calcd for $C_{18}H_{23}O_4$ [(M-MeO)$^+$] 303.1596, found 303.1585.

<Scheme 73>

((6-(5-(But-2-yn-1-yl)-2,2-dimethyl-1,3-dioxan-5-yl)-3,3-dimethylhexa-4,5-dien-1-yl)oxy)(*tert*-butyl)diphenylsilane (209g)

To a suspension of $LiAlH_4$ (342 mg, 9.01 mmol) in Et_2O (5 mL) was added a solution of **181** (1.56 g, 2.85 mmol) in Et_2O (5 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 2 h. Then to the mixture was added with H_2O (340 μL), 15% NaOH aq. (340 μL), and H_2O (1.02 mL) and stirred at room temperature for 3 h. The mixture was filtered through Celite®, washed with Et_2O, and concentrated. The residue was roughly purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 5/1) to give the crude diol (626 mg). To a solution of diol (626 mg) in CH_2Cl_2 (13 mL) were added 2,2-dimethoxypropane (800 μL, 6.53 mmol) and PPTS (35.1 mg, 0.140 mmol) at

0 ℃ and the reaction mixture was stirred at room temperature for 18 h. Then the reaction mixture was concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1) to give **209g** (584 mg, 39% yield in 2 steps) as a pale yellow oil. Spectral data of **209g**: IR (neat) 3071, 2992, 2958, 2858, 1959 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71-7.64 (m, 4 H), 7.45-7.36 (m, 6 H), 5.17 (d, *J* = 6.0 Hz, 1 H), 5.14 (d, *J* = 6.0 Hz, 1 H), 3.76-3.61 (m, 6 H), 2.52 (dq, *J* = 16.5, 2.8 Hz, 1 H), 2.43 (dq, *J* = 16.5, 2.8 Hz, 1 H), 1.76 (t, *J* = 2.8 Hz, 3 H), 1.65 (t, *J* = 7.3 Hz, 2 H), 1.41 (s, 3 H), 1.38 (s, 3 H), 1.05 (s, 9 H), 0.99 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.7, 135.5 (4 C), 133.9 (2 C), 129.5 (2 C), 127.6 (4 C), 104.3, 97.9, 94.4, 78.1, 75.7, 66.81, 66.76, 61.2, 45.3, 36.5, 33.6, 28.3, 28.0, 27.8, 26.8 (3 C), 24.4, 19.6, 19.1, 3.6; LRMS (EI) *m/z* 530 [M^+], 515, 442, 199, 135, 44.

6-(5-(But-2-yn-1-yl)-2,2-dimethyl-1,3-dioxan-5-yl)-3,3-dimethylhexa-4,5-dien-1-ol (210g)

To a solution of **209g** (584 mg, 1.10 mmol) in THF (11 mL) was added TBAF (1.0 M in THF, 1.3 mL, 1.3 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. The reaction mixture was concentrated and the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 3/1, 1/1) to give **210g** (305 mg, 95% yield) as a pale yellow oil. Spectral data of **210g**: IR (neat) 3434, 2994, 2959, 2920, 2864, 1956 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.26 (d, *J* = 6.5 Hz, 1 H), 5.20 (d, *J* = 6.5 Hz, 1 H), 3.78-3.66 (m, 6 H), 2.51 (dq, *J* = 16.5, 2.8 Hz, 1 H), 2.43 (dq, *J* = 16.5, 2.8 Hz, 1 H), 1.78 (t, *J* = 2.8 Hz, 3 H), 1.64 (td, *J* = 7.3, 1.3 Hz, 2 H), 1.52-1.45 (brs, 1 H), 1.42 (s, 3 H), 1.41 (s, 3 H), 1.06 (s, 3 H), 1.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9, 104.1, 98.0, 94.9, 78.3, 75.5, 66.8, 66.7, 60.1, 45.5, 36.7, 33.7, 28.23, 28.15, 27.1, 24.5, 20.3, 3.6; LRMS (EI) *m/z* 292 [M^+], 207, 73, 69, 43.

6-(5-(But-2-yn-1-yl)-2,2-dimethyl-1,3-dioxan-5-yl)-3,3-dimethylhexa-4,5-dienal (211g)

To a solution of the **210g** (305 mg, 1.04 mmol) in CH_2Cl_2 (10 mL) were added $NaHCO_3$ (119 mg, 1.42 mmol) and Dess-Martin Periodinane (561 mg, 1.32 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, 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 purified by column chromatography on silica gel (*n*-hexane/EtOAc = 6/1) to give **211g** (271 mg, 90% yield) as a pale yellow oil. Spectral data of **211g**: IR (neat) 2991, 2961, 2871, 2736, 1960, 1721 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.79 (t, *J* = 3.0 Hz, 1 H), 5.36 (d, *J* = 6.0 Hz, 1 H), 5.25 (d, *J* = 6.0 Hz, 1 H), 3.78-3.65 (m, 4 H), 2.56-2.33 (m, 4 H), 1.77 (t, *J* = 2.5 Hz, 3 H), 1.41 (s, 3 H), 1.40 (s, 3 H), 1.19 (s, 3 H), 1.18 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.7, 200.8, 103.2, 98.0, 95.8, 78.3, 75.5, 66.7, 66.6, 55.0, 36.8, 33.8, 28.5, 28.3, 27.1, 24.4, 20.2, 3.5; LRMS (EI) *m/z* 290 [M^+], 202, 173, 159, 146, 117, 43.

7-(5-(But-2-yn-1-yl)-2,2-dimethyl-1,3-dioxan-5-yl)-4,4-dimethylhepta-5,6-dien-2-ol (212g)

To a solution of **211g** (271 mg, 0.933 mmol) in THF (9 mL) was added MeMgBr (1.0 M in Et_2O, 1.4 mL, 1.4 mmol) at 0 °C, and the reaction mixture was stirred at the same temperature for 1.5 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 6/1, 1/1) to give **212g** (209 mg, 73% yield) and **211g** (41.3 mg, 15% yield) as a pale yellow oil. Spectral data of **212g**: IR (neat) 3450, 2991, 2960, 2921, 2871, 1958 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.34 (d, *J* = 6.4 Hz, 1 H), 5.23-5.19 (m, 1 H), 4.02-3.91 (m, 1 H), 3.77-3.67 (m, 4 H), 2.55-2.35 (m, 2 H), 1.90-1.82 (brs, 1 H), 1.77 (t, *J* = 2.4 Hz, 3 H), 1.60-1.39 (m, 8 H), 1.18-1.07 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0*[1], 104.5*, 98.0, 94.9, 78.4*, 75.4*, 66.7, 65.7*, 52.3*, 36.8*, 34.2*, 29.5*, 27.6*, 27.1, 26.4, 25.1*, 24.5*, 20.9*, 3.6; LRMS (EI) *m/z*

306 [M^+], 291, 203, 160, 83, 43.

7-(5-(But-2-yn-1-yl)-2,2-dimethyl-1,3-dioxan-5-yl)-4,4-dimethylhepta-5,6-dien-2-one (162g)

To a solution of **212g** (209 mg, 0.682 mmol) in CH_2Cl_2 (7.0 mL) were added $NaHCO_3$ (80.5 mg, 0.959 mmol) and Dess-Martin Periodinane (379 mg, 0.894 mmol) at 0 °C, and the mixture was stirred at room temperature for 1.5 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 8/1) to give **162g** (150 mg, 72% yield) as a colorless oil. Spectral data of **162g**: IR (neat) 2991, 2959, 2871, 1959, 1715 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.41 (d, *J* = 7.0 Hz, 1 H), 5.21 (d, *J* = 7.0 Hz, 1 H), 3.77-3.65 (m, 4 H), 2.55-2.41 (m, 4 H), 2.13 (s, 3 H), 1.78 (t, *J* = 2.3 Hz, 3 H), 1.42 (s, 3 H), 1.40 (s, 3 H), 1.15 (s, 3 H), 1.13 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 200.7, 103.7, 98.0, 95.2, 78.2, 75.6, 66.8, 66.7, 54.9, 36.7, 34.0, 32.1, 28.0 (2 C), 27.4, 24.4, 20.0, 3.6; LRMS (EI) *m/z* 289 [(M-Me)$^+$], 247, 201, 189, 173, 160, 143.; HRMS (EI) calcd for $C_{18}H_{25}O_3$ [(M-Me)$^+$] 289.1804, found 289.1799.

<Scheme 74>

2-(But-2-yn-1-yl)-2-(6,6-dimethoxy-4,4-dimethylhexa-1,2-dien-1-yl)propane-1,3-diol (217)

7,7-Bis((benzyloxy)methyl)-3,3-dimethylundeca-4,5-dien-9-ynal (211h)

To a solution of **162a** (507 mg, 1.65 mmol) in MeOH (16 mL) were added $HC(OMe)_3$ (600 μL, 5.48 mmol) and $TsOH·H_2O$ (31.6 mg, 0.166 mmol) at 0 °C, and the mixture was stirred at room temperature for 15 h. To the mixture were added $NaHCO_3$ and then H_2O at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was dried over Na_2SO_4, and concentrated to give crude acetal (546 mg) as a pale yellow oil. To a suspension of $LiAlH_4$ (177 mg, 4.66 mmol) in Et_2O (3 mL) was added a solution of crude acetal (546 mg) in Et_2O (2 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 3 h. Then to the mixture was added with H_2O (180 μL), 15% NaOH aqueous solution (180 μL), and H_2O (540 μL) and stirred at room temperature for 1 h. The mixture was filtered through Celite®, washed with Et_2O, and concentrated to give the crude diol **217** (386 mg). To a suspension of NaH (60% dispersion in mineral oil, 156 mg, 3.90 mmol) in DMF (4.5 mL) was added a solution of crude diol **217** (386 mg) in DMF (2.0 mL) at 0 °C, and the mixture was stirred at the same temperature for 30 min. To the mixture was added BnBr (460 μL, 3.87 mmol) at 0 °C, and the resulting mixture was stirred and warmed to 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 to give a crude dibenzyl ether (1.06 g). To a solution of crude dibenzyl ether (1.06 g) in THF (13 mL) was added 3 N HCl aqueous solution (6.0 mL, 18 mmol) at 0 °C, and the mixture was stirred at room temperature for 3 h. To the mixture was added saturated $NaHCO_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 15/1, 10/1) to give **211h** (330 mg, 46% yield in 4 steps) as a pale yellow oil. Spectral data of **211h**: IR (neat) 3030, 2960, 2919, 2858, 1962, 1720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.73 (t, *J* = 3.0 Hz, 1 H), 7.37-7.22 (m, 10 H), 5.40 (d, *J* = 6.5 Hz, 1 H), 5.28 (d, *J* = 6.5 Hz, 1 H), 4.509 (s, 2 H), 4.505 (s, 2 H), 3.52-3.44 (m, 4 H), 2.42-2.26 (m, 4 H), 1.73 (t, *J* = 2.3 Hz, 3 H), 1.13 (s, 3 H), 1.12 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.4, 200.9, 138.6, 138.5, 128.2 (4 C), 127.43 (2 C), 127.40 (2 C), 127.3 (2 C), 102.6, 96.7, 77.6, 75.8, 73.3 (2 C), 72.8, 72.7, 54.8, 43.6, 33.9, 28.6, 28.1, 23.9, 3.6; LRMS (EI) *m/z* 430 [M^+], 309, 91.

8,8-Bis((benzyloxy)methyl)-4,4-dimethyldodeca-5,6-dien-10-yn-2-ol (212h)

To a solution of **211h** (437 mg, 1.01 mmol) in THF (10 mL) was added MeMgBr (1.0 M in Et_2O, 1.5 mL, 1.5 mmol) at 0 °C, and the reaction mixture was stirred at the same temperature for 1 h. To the mixture was added saturated NH_4Cl aqueous solution at 0 °C, and the aqueous layer was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 10/1, 6/1) to give **212h** (356 mg, 79% yield) and **211h** (64.6 mg, 15% yield) as a pale yellow oil. Spectral data of **212h**: IR (neat) 3434, 3030, 2960, 2919, 2860, 1960 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.21 (m, 10 H), 5.38-5.36 (m, 1 H), 5.29-5.23 (m, 1 H), 4.52 (s, 4 H), 3.99-3.85 (m, 1 H), 3.55-3.42 (m, 4 H), 2.38 (s, 2 H), 1.93-1.79 (brs, 1 H), 1.74 (s, 3 H), 1.59-1.42 (m, 2 H), 1.15-1.13 (m, 3 H), 1.05-1.03 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9*[1], 138.64*, 138.57, 128.2 (4 C), 127.5, 127.45, 127.40, 127.37, 127.3 (2 C), 103.9*, 95.9*, 77.7*, 75.8*, 73.3*, 73.0*, 72.8*, 65.7*, 52.2, 52.1, 43.6*, 34.2*, 29.9*, 27.2, 24.8*, 24.0*, 3.6; LRMS (EI) *m/z* 446 [M^+], 325, 217, 91.

8,8-Bis((benzyloxy)methyl)-4,4-dimethyldodeca-5,6-dien-10-yn-2-one (162h)

To a solution of **212h** (356 mg, 0.797 mmol) in CH_2Cl_2 (8.0 mL) was added Dess-Martin Periodinane (431 mg, 1.02 mmol) at 0 °C, and the mixture was stirred at room temperature for 2 h. To the mixture were added saturated $NaHCO_3$ aqueous solution and 10% $Na_2S_2O_3$ aqueous solution at 0 °C, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc = 7/1, 6/1) to give **162h** (304 mg, 86% yield) as a colorless oil. Spectral data of **162h**: IR (neat) 3063, 3030, 2958, 2918, 2859, 1961, 1715 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38-7.22 (m, 10 H), 5.37 (d, *J* = 6.0 Hz, 1 H), 5.32 (d, *J* = 6.0 Hz, 1 H), 4.522 (s, 2 H), 4.516 (s, 2 H), 3.50 (s, 2 H), 3.49 (s, 2 H), 2.46-2.32 (m, 4 H), 2.06 (s, 3 H), 1.75 (t, *J* = 2.3 Hz, 3 H), 1.11 (s, 3 H), 1.10 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.2, 200.6, 138.7, 138.6, 128.2 (4 C), 127.39 (2 C), 127.36 (2 C), 127.3 (2 C), 103.3, 96.3, 77.5, 75.9, 73.3 (2 C), 73.0, 72.8, 54.9, 43.6, 34.2, 32.0, 28.0, 27.9, 23.9, 3.6; LRMS (EI) *m/z* 444 [M^+], 429, 402, 323, 215, 91; HRMS (EI) calcd for $C_{30}H_{36}O_3$ [(M-Me)$^+$] 444.2664, found 444.2666.

<Scheme 75>

According to the general procedure for cyclization, a crude product, which was prepared from **162c** (49.9 mg, 0.149 mmol), MS4A (102 mg), and [Rh(dppp)(cod)]ClO_4 (10.8 mg, 0.0149 mmol) in DMF (1.50 mL) at 90 °C for 24 h, was was obtained. Yields of **163c** and **162c** were determined to be 9% and 10% by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard, respectively.

X-ray Structure Report

for

164

October 1, 2013

Data Collection

A colorless prismatic crystal of $C_{18}H_{22}O_6$ having approximate dimensions of 0.200 x 0.200 x 0.200 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC7R diffractometer using graphite monochromated Mo-Kα radiation and a rotating anode generator.

Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using the setting angles of 25 carefully centered reflections in the range $22.00 < 2\theta < 25.00^o$ corresponded to a primitive monoclinic cell with dimensions:

a = 13.3227(13) Å
b = 9.557(2) Å β = 102.477(7)^o
c = 13.5981(12) Å
V = 1690.5(4) Å^3

For Z = 4 and F.W. = 334.37, the calculated density is 1.314 g/cm^3. The reflection conditions of:

h0l: l = 2n
0k0: k = 2n

uniquely determine the space group to be:

$P2_1/c$ (#14)

The data were collected at a temperature of 23 $\pm$ 1^{o}C using the ω-2θ scan technique to a maximum 2θ value of 55.0^o. Omega scans of several intense reflections, made prior to data collection, had an average width at half-height of 0.28^o with a take-off angle of 6.0^o. Scans of (1.68 + 0.30 tan θ)^o were made at speeds ranging from 4.0 to 32.0^o/min (in ω). The weak reflections ($I < 10.0\sigma(I)$) were rescanned (maximum of 7 scans) and the counts were accumulated to ensure good counting statistics. Stationary background counts were recorded on each side of the reflection. The ratio of peak counting time to background counting time was 2:1. The diameter of the incident beam collimator was 0.5 mm and the crystal to detector distance was 235 mm. The computer-controlled slits were set to 6.0 mm (horizontal) and 6.0 mm (vertical).

Data Reduction

Of the 4052 reflections were collected, where 3887 were unique (R_{int} = 0.0168). The intensities of three representative reflections were measured after every 150 reflections. No decay correction was applied.

The linear absorption coefficient, μ, for Mo-Kα radiation is 0.982 cm^{-1}. The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods[1] and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement[2] on F^2 was based on 3887 observed reflections and 217 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R1 = \Sigma \; ||Fo| - |Fc|| \; / \; \Sigma \; |Fo| = 0.0471$$

$$wR2 = [\; \Sigma \; (\; w \; (Fo^2 - Fc^2)^2 \;) / \; \Sigma \; w(Fo^2)^2]^{1/2} = 0.1492$$

The standard deviation of an observation of unit weight[3] was 1.05. A Sheldrick weighting scheme was used. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.22 and -0.20 $e^-/Å^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber[4]. Anomalous dispersion effects were included in Fcalc[5]; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley[6]. The values for the mass attenuation coefficients are those of Creagh and Hubbell[7]. All calculations were performed using the CrystalStructure[8] crystallographic software package except for refinement, which was performed using SHELXL-97[9].

References

(1) SIR2008: M.C. Burla, R. Caliandro, M. Camalli, B. Carrozzini, G.L. Cascarano, L. De Caro, C. Giacovazzo, G. Polidori, D. Siliqi, R. Spagna (2007)

(2) Least Squares function minimized: (SHELXL97)

$\Sigma w(F_o^2-F_c^2)^2$ where w = Least Squares weights.

(3) Standard deviation of an observation of unit weight:

$[\Sigma w(F_o^2-F_c^2)^2/(N_o-N_v)]^{1/2}$

where: N_o = number of observations
N_v = number of variables

(4) Cromer, D. T. & Waber, J. T.; "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

(5) Ibers, J. A. & Hamilton, W. C.; Acta Crystallogr., 17, 781 (1964).

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(7) Creagh, D. C. & Hubbell, J.H..; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200-206 (1992).

(8) CrystalStructure 4.1: Crystal Structure Analysis Package, Rigaku Corporation (2000-2013). Tokyo 196-8666, Japan.

(9) SHELX97: Sheldrick, G.M. (2008). Acta Cryst. A64, 112-122.

A. Crystal Data

Empirical Formula	$C_{18}H_{22}O_6$
Formula Weight	334.37
Crystal Color, Habit	colorless, prismatic
Crystal Dimensions	0.200 X 0.200 X 0.200 mm
Crystal System	monoclinic
Lattice Type	Primitive
No. of Reflections Used for Unit Cell Determination (2θ range)	25 (22.0 - 25.0°)
Omega Scan Peak Width at Half-height	0.28°
Lattice Parameters	a = 13.3227(13) Å b = 9.557(2) Å c = 13.5981(12) Å β = 102.477(7) ° V = 1690.5(4) Å^3
Space Group	$P2_1/c$ (#14)
Z value	4
D_{calc}	1.314 g/cm^3
F_{000}	712.00
μ(MoKα)	0.982 cm^{-1}

B. Intensity Measurements

Diffractometer	AFC7R
Radiation	MoKα (λ = 0.71069 Å) graphite monochromated
Attenuator	Zr foil (factor = 7.21)
Take-off Angle	6.0°
Detector Aperture	6.0 mm horizontal 6.0 mm vertical
Crystal to Detector Distance	235 mm
Voltage, Current	60kV, 300mA
Temperature	23.0°C
Scan Type	ω-2θ
Scan Rate	4.0 - 32.0°/min (in ω) (up to 7 scans)
Scan Width	(1.68 + 0.30 tan θ)°
$2\theta_{max}$	55.0°
No. of Reflections Measured	Total: 4052 Unique: 3887 (R_{int} = 0.0168)
Corrections	Lorentz-polarization

C. Structure Solution and Refinement

Structure Solution	Direct Methods
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	w = 1/ [$\sigma^2(Fo^2)$ + $(0.0689 \cdot P)^2$ + 0.4230 · P] where P = $(Max(Fo^2,0) + 2Fc^2)/3$
$2\theta_{max}$ cutoff	55.0^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	3887
No. Variables	217
Reflection/Parameter Ratio	17.91
Residuals: R1 (I>2.00σ(I))	0.0471
Residuals: R (All reflections)	0.0811
Residuals: wR2 (All reflections)	0.1492
Goodness of Fit Indicator	1.046
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.22 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.20 $e^-/Å^3$

Table 1. Atomic coordinates and B_{iso}/B_{eq}

atom	x	y	z	B_{eq}
O1	0.40736(14)	0.92711(19)	0.17862(13)	5.21(4)
O2	0.10553(12)	0.46904(17)	0.25481(11)	4.50(3)
O3	0.05902(10)	0.31429(13)	0.13029(10)	3.42(3)
O4	0.12414(14)	0.43356(19)	-0.06769(10)	4.97(3)
O5	0.24054(11)	0.29878(16)	0.03212(12)	4.63(3)
O6	0.53615(13)	0.7859(2)	0.17602(14)	6.36(5)
C1	0.17858(12)	0.49214(16)	0.10880(12)	2.49(3)
C2	0.14061(13)	0.64500(18)	0.08391(14)	3.00(3)
C3	0.22366(12)	0.73602(17)	0.14452(12)	2.60(3)
C4	0.22171(16)	0.87460(19)	0.15396(15)	3.66(4)
C5	0.3138(2)	0.9507(2)	0.21642(19)	4.67(5)
C6	0.3349(2)	0.9186(3)	0.32813(18)	5.14(5)
C7	0.38707(15)	0.7756(2)	0.35554(14)	3.60(4)
C8	0.40522(13)	0.7020(2)	0.25883(13)	3.05(3)
C9	0.30847(11)	0.64573(18)	0.19216(12)	2.49(3)
C10	0.28593(12)	0.51138(18)	0.17274(13)	2.75(3)
C11	0.45620(16)	0.8045(3)	0.20118(15)	4.15(4)
C12	0.11112(12)	0.42433(17)	0.17391(13)	2.67(3)
C13	-0.00989(17)	0.2511(3)	0.18633(18)	4.54(4)
C14	0.17619(13)	0.4067(2)	0.01376(13)	3.07(3)
C15	0.2455(2)	0.2107(3)	-0.0537(2)	6.53(7)
C16	0.3220(2)	0.6812(3)	0.40765(18)	5.55(6)
C17	0.49209(19)	0.7972(3)	0.42653(18)	5.71(6)
C18	0.1300(2)	0.9608(3)	0.1069(3)	6.59(7)

$B_{eq} = 8/3\ \pi^2(U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}(aa^*bb^*)\cos\gamma + 2U_{13}(aa^*cc^*)\cos\beta + 2U_{23}(bb^*cc^*)\cos\alpha)$

Table 2. Atomic coordinates and B_{iso} involving hydrogen atoms

atom	x	y	z	B_{iso}
H2A	0.13200	0.66390	0.01248	3.598
H2B	0.07561	0.66089	0.10326	3.598
H5	0.29864	1.05094	0.20918	5.605
H6A	0.27044	0.92045	0.35033	6.166
H6B	0.37859	0.99144	0.36425	6.166
H8	0.45248	0.62362	0.27940	3.655
H10	0.33076	0.43804	0.19570	3.300
H13A	0.02928	0.21245	0.24794	5.442
H13B	-0.04851	0.17804	0.14681	5.442
H13C	-0.05618	0.32082	0.20146	5.442
H15A	0.17910	0.17058	-0.08013	7.834
H15B	0.29467	0.13722	-0.03288	7.834
H15C	0.26612	0.26598	-0.10492	7.834
H16A	0.26055	0.65450	0.36034	6.655
H16B	0.30400	0.73074	0.46277	6.655
H16C	0.36059	0.59893	0.43258	6.655
H17A	0.48256	0.83279	0.48990	6.853
H17B	0.53157	0.86284	0.39709	6.853
H17C	0.52793	0.70949	0.43708	6.853
H18A	0.15228	1.05149	0.08990	7.914
H18B	0.08577	0.97098	0.15354	7.914
H18C	0.09320	0.91526	0.04692	7.914

Table 3. Anisotropic displacement parameters

atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O1	0.0739(11)	0.0619(10)	0.0656(10)	-0.0365(9)	0.0227(8)	-0.0027(8)
O2	0.0689(10)	0.0608(9)	0.0466(8)	-0.0100(8)	0.0243(7)	-0.0118(7)
O3	0.0447(7)	0.0397(7)	0.0486(7)	-0.0111(5)	0.0165(6)	-0.0019(5)
O4	0.0784(11)	0.0712(10)	0.0356(7)	-0.0046(9)	0.0040(7)	-0.0069(7)
O5	0.0488(8)	0.0590(9)	0.0654(9)	0.0062(7)	0.0061(7)	-0.0314(8)
O6	0.0536(9)	0.1294(17)	0.0686(11)	-0.0388(10)	0.0351(8)	-0.0355(11)
C1	0.0280(7)	0.0303(7)	0.0350(8)	-0.0021(6)	0.0037(6)	-0.0027(6)
C2	0.0320(8)	0.0337(8)	0.0441(9)	0.0003(7)	-0.0008(7)	0.0045(7)
C3	0.0341(8)	0.0306(8)	0.0353(8)	-0.0017(6)	0.0102(6)	0.0019(6)
C4	0.0554(11)	0.0318(9)	0.0522(11)	-0.0001(8)	0.0125(9)	0.0043(8)
C5	0.0767(15)	0.0307(9)	0.0709(14)	-0.0128(10)	0.0178(12)	-0.0101(9)
C6	0.0773(16)	0.0590(14)	0.0608(14)	-0.0044(12)	0.0191(12)	-0.0268(11)
C7	0.0415(9)	0.0608(12)	0.0360(9)	-0.0147(8)	0.0118(7)	-0.0134(8)
C8	0.0289(8)	0.0483(10)	0.0386(9)	-0.0065(7)	0.0073(7)	-0.0109(7)
C9	0.0273(7)	0.0357(8)	0.0320(7)	-0.0021(6)	0.0069(6)	-0.0040(6)
C10	0.0273(7)	0.0343(8)	0.0403(8)	0.0030(6)	0.0015(6)	-0.0045(7)
C11	0.0469(11)	0.0725(14)	0.0409(10)	-0.0282(10)	0.0155(8)	-0.0200(10)
C12	0.0322(7)	0.0314(8)	0.0377(8)	0.0035(6)	0.0073(6)	0.0015(6)
C13	0.0544(12)	0.0583(12)	0.0649(13)	-0.0158(10)	0.0246(10)	0.0083(11)
C14	0.0336(8)	0.0454(9)	0.0393(9)	-0.0117(7)	0.0109(7)	-0.0086(7)
C15	0.0774(17)	0.0832(19)	0.091(2)	-0.0060(14)	0.0262(15)	-0.0556(16)
C16	0.0706(15)	0.099(2)	0.0466(12)	-0.0274(14)	0.0245(11)	-0.0053(12)
C17	0.0577(14)	0.106(2)	0.0477(12)	-0.0238(14)	-0.0001(10)	-0.0259(13)
C18	0.089(2)	0.0395(12)	0.117(2)	0.0177(13)	0.0099(18)	0.0181(14)

The general temperature factor expression: $\exp(-2\pi^2(a^{*2}U_{11}h^2 + b^{*2}U_{22}k^2 + c^{*2}U_{33}l^2 + 2a^*b^*U_{12}hk + 2a^*c^*U_{13}hl + 2b^*c^*U_{23}kl))$

Table 4. Bond lengths (Å)

atom	atom	distance	atom	atom	distance
O1	C5	1.465(3)	O1	C11	1.343(3)
O2	C12	1.197(2)	O3	C12	1.327(2)
O3	C13	1.446(3)	O4	C14	1.201(2)
O5	C14	1.330(2)	O5	C15	1.453(4)
O6	C11	1.200(3)	C1	C2	1.559(2)
C1	C10	1.516(2)	C1	C12	1.535(3)
C1	C14	1.523(2)	C2	C3	1.505(2)
C3	C4	1.331(2)	C3	C9	1.458(2)
C4	C5	1.518(3)	C4	C18	1.498(3)
C5	C6	1.515(3)	C6	C7	1.543(3)
C7	C8	1.555(3)	C7	C16	1.527(4)
C7	C17	1.532(3)	C8	C9	1.506(2)
C8	C11	1.505(3)	C9	C10	1.332(2)

Table 5. Bond lengths involving hydrogens (Å)

atom	atom	distance	atom	atom	distance
C2	H2A	0.970	C2	H2B	0.970
C5	H5	0.980	C6	H6A	0.970
C6	H6B	0.970	C8	H8	0.980
C10	H10	0.930	C13	H13A	0.960
C13	H13B	0.960	C13	H13C	0.960
C15	H15A	0.960	C15	H15B	0.960
C15	H15C	0.960	C16	H16A	0.960
C16	H16B	0.960	C16	H16C	0.960
C17	H17A	0.960	C17	H17B	0.960
C17	H17C	0.960	C18	H18A	0.960
C18	H18B	0.960	C18	H18C	0.960

Table 6. Bond angles (º)

atom	atom	atom	angle	atom	atom	atom	angle
C5	O1	C11	117.45(19)	C12	O3	C13	115.20(16)
C14	O5	C15	115.99(17)	C2	C1	C10	103.44(12)
C2	C1	C12	108.54(14)	C2	C1	C14	111.84(14)
C10	C1	C12	108.53(13)	C10	C1	C14	113.32(14)
C12	C1	C14	110.82(13)	C1	C2	C3	104.89(12)
C2	C3	C4	126.89(15)	C2	C3	C9	107.98(14)
C4	C3	C9	125.13(15)	C3	C4	C5	120.00(17)
C3	C4	C18	122.49(18)	C5	C4	C18	117.49(18)
O1	C5	C4	112.10(19)	O1	C5	C6	109.47(19)
C4	C5	C6	114.6(2)	C5	C6	C7	113.4(2)
C6	C7	C8	109.91(16)	C6	C7	C16	111.4(2)
C6	C7	C17	109.6(2)	C8	C7	C16	109.44(18)
C8	C7	C17	107.81(18)	C16	C7	C17	108.65(18)
C7	C8	C9	113.66(15)	C7	C8	C11	108.44(16)
C9	C8	C11	110.05(14)	C3	C9	C8	122.44(15)
C3	C9	C10	111.26(13)	C8	C9	C10	126.21(15)
C1	C10	C9	112.02(14)	O1	C11	O6	118.7(2)
O1	C11	C8	115.84(19)	O6	C11	C8	125.5(2)
O2	C12	O3	124.26(18)	O2	C12	C1	122.66(15)
O3	C12	C1	113.06(15)	O4	C14	O5	124.03(19)
O4	C14	C1	124.73(17)	O5	C14	C1	111.23(14)

Table 7. Bond angles involving hydrogens (º)

atom	atom	atom	angle	atom	atom	atom	angle
C1	C2	H2A	110.8	C1	C2	H2B	110.8
C3	C2	H2A	110.8	C3	C2	H2B	110.8
H2A	C2	H2B	108.9	O1	C5	H5	106.7
C4	C5	H5	106.7	C6	C5	H5	106.7
C5	C6	H6A	108.9	C5	C6	H6B	108.9
C7	C6	H6A	108.9	C7	C6	H6B	108.9
H6A	C6	H6B	107.7	C7	C8	H8	108.2
C9	C8	H8	108.2	C11	C8	H8	108.2
C1	C10	H10	124.0	C9	C10	H10	124.0
O3	C13	H13A	109.5	O3	C13	H13B	109.5
O3	C13	H13C	109.5	H13A	C13	H13B	109.5
H13A	C13	H13C	109.5	H13B	C13	H13C	109.5
O5	C15	H15A	109.5	O5	C15	H15B	109.5
O5	C15	H15C	109.5	H15A	C15	H15B	109.5
H15A	C15	H15C	109.5	H15B	C15	H15C	109.5
C7	C16	H16A	109.5	C7	C16	H16B	109.5
C7	C16	H16C	109.5	H16A	C16	H16B	109.5
H16A	C16	H16C	109.5	H16B	C16	H16C	109.5
C7	C17	H17A	109.5	C7	C17	H17B	109.5
C7	C17	H17C	109.5	H17A	C17	H17B	109.5
H17A	C17	H17C	109.5	H17B	C17	H17C	109.5
C4	C18	H18A	109.5	C4	C18	H18B	109.5
C4	C18	H18C	109.5	H18A	C18	H18B	109.5
H18A	C18	H18C	109.5	H18B	C18	H18C	109.5

Table 8. Torsion Angles(º)
(Those having bond angles > 160 or < 20 degrees are excluded.)

atom1	atom2	atom3	atom4	angle	atom1	atom2	atom3	atom4	angle
C5	O1	C11	O6	-175.80(17)	C5	O1	C11	C8	3.0(2)
C11	O1	C5	C4	-78.1(2)	C11	O1	C5	C6	50.3(2)
C13	O3	C12	O2	1.8(2)	C13	O3	C12	C1	-176.87(13)
C15	O5	C14	O4	-0.2(3)	C15	O5	C14	C1	-179.28(17)
C2	C1	C10	C9	4.60(19)	C10	C1	C2	C3	-6.08(17)
C2	C1	C12	O2	-60.90(18)	C2	C1	C12	O3	117.82(13)
C12	C1	C2	C3	109.06(13)	C2	C1	C14	O4	-21.8(2)
C2	C1	C14	O5	157.34(13)	C14	C1	C2	C3	-128.38(14)
C10	C1	C12	O2	50.88(19)	C10	C1	C12	O3	-130.40(13)
C12	C1	C10	C9	-110.55(15)	C10	C1	C14	O4	-138.23(17)
C10	C1	C14	O5	40.89(19)	C14	C1	C10	C9	125.90(15)
C12	C1	C14	O4	99.48(19)	C12	C1	C14	O5	-81.40(16)
C14	C1	C12	O2	175.92(13)	C14	C1	C12	O3	-5.36(17)
C1	C2	C3	C4	-174.28(15)	C1	C2	C3	C9	5.78(18)
C2	C3	C4	C5	-178.48(16)	C2	C3	C4	C18	3.0(3)
C2	C3	C9	C8	179.96(14)	C2	C3	C9	C10	-3.16(19)
C4	C3	C9	C8	0.0(3)	C4	C3	C9	C10	176.89(18)
C9	C3	C4	C5	1.5(3)	C9	C3	C4	C18	-177.05(15)
C3	C4	C5	O1	59.2(3)	C3	C4	C5	C6	-66.4(3)
C18	C4	C5	O1	-122.2(2)	C18	C4	C5	C6	112.2(2)
O1	C5	C6	C7	-49.9(2)	C4	C5	C6	C7	77.0(3)
C5	C6	C7	C8	0.6(3)	C5	C6	C7	C16	-120.9(2)
C5	C6	C7	C17	118.9(2)	C6	C7	C8	C9	-73.3(2)
C6	C7	C8	C11	49.45(19)	C16	C7	C8	C9	49.3(2)
C16	C7	C8	C11	172.05(14)	C17	C7	C8	C9	167.33(17)
C17	C7	C8	C11	-69.9(2)	C7	C8	C9	C3	62.7(2)
C7	C8	C9	C10	-113.66(18)	C7	C8	C11	O1	-54.56(19)
C7	C8	C11	O6	124.18(19)	C9	C8	C11	O1	70.3(2)
C9	C8	C11	O6	-110.93(19)	C11	C8	C9	C3	-59.1(2)
C11	C8	C9	C10	124.50(18)	C3	C9	C10	C1	-1.1(2)
C8	C9	C10	C1	175.68(15)					

Table 9. Intramolecular contacts less than 3.60 Å

atom	atom	distance	atom	atom	distance
O1	C3	3.008(2)	O1	C7	2.870(3)
O1	C9	3.018(3)	O1	C17	3.541(3)
O2	C2	2.986(3)	O2	C3	3.501(2)
O2	C9	3.447(2)	O2	C10	2.889(2)
O2	C13	2.637(3)	O3	O4	3.211(2)
O3	O5	3.008(2)	O3	C2	3.445(2)
O3	C10	3.502(2)	O3	C14	2.607(2)
O4	C2	2.861(2)	O4	C10	3.584(2)
O4	C12	3.328(2)	O4	C15	2.656(4)
O5	C10	2.766(2)	O5	C12	3.093(3)
O6	C5	3.501(3)	O6	C7	3.465(3)
O6	C9	3.366(2)	O6	C17	3.581(3)
C2	C18	3.041(3)	C3	C6	3.143(3)
C3	C7	3.228(2)	C3	C11	3.097(3)
C3	C12	3.397(2)	C3	C16	3.573(3)
C4	C7	3.264(3)	C4	C8	3.037(3)
C4	C10	3.571(3)	C4	C11	3.123(3)
C5	C8	2.676(3)	C5	C9	2.932(3)
C6	C9	3.172(3)	C6	C11	2.826(4)
C7	C10	3.595(3)	C9	C12	3.342(2)
C9	C14	3.516(2)	C9	C16	2.916(3)
C10	C11	3.573(3)	C10	C16	3.522(3)
C11	C17	2.998(3)			

Table 10. Intramolecular contacts less than 3.60 Å involving hydrogens

atom	atom	distance	atom	atom	distance
O1	H6A	3.259	O1	H6B	2.705
O1	H8	3.209	O1	H17B	3.133
O1	H18A	3.556	O2	H2B	2.723
O2	H10	3.283	O2	H13A	2.648
O2	H13B	3.578	O2	H13C	2.549
O2	H16A	2.861	O3	H2B	3.345
O4	H2A	2.449	O4	H2B	3.345
O4	H15A	2.634	O4	H15B	3.598
O4	H15C	2.610	O5	H10	2.647
O6	H8	2.510	O6	H17B	3.108
C2	H10	3.313	C2	H18B	3.382
C2	H18C	2.681	C3	H5	3.233
C3	H6A	3.252	C3	H8	3.376
C3	H10	3.194	C3	H16A	2.973
C3	H18A	3.200	C3	H18B	2.921
C3	H18C	2.592	C4	H2A	2.862
C4	H2B	2.803	C4	H6A	2.645
C4	H6B	3.348	C4	H16A	3.456
C5	H16A	3.598	C5	H17B	3.475
C5	H18A	2.631	C5	H18B	2.979
C5	H18C	3.337	C6	H8	3.360
C6	H16A	2.781	C6	H16B	2.659
C6	H16C	3.356	C6	H17A	2.741
C6	H17B	2.640	C6	H17C	3.340
C7	H5	3.356	C8	H6A	3.177
C8	H6B	3.170	C8	H10	2.778
C8	H16A	2.641	C8	H16B	3.347
C8	H16C	2.741	C8	H17A	3.331
C8	H17B	2.713	C8	H17C	2.615
C9	H2A	3.008	C9	H2B	3.080
C9	H6A	3.500	C9	H16A	2.505
C9	H16C	3.223	C10	H2A	3.025
C10	H2B	3.105	C10	H8	2.605
C10	H16A	2.978	C10	H16C	3.557
C11	H5	3.172	C11	H6B	3.189
C11	H17B	2.694	C11	H17C	3.272
C12	H2A	3.225	C12	H2B	2.462

Table 10. Intramolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
C12	H10	2.880	C12	H13A	2.603
C12	H13B	3.140	C12	H13C	2.539
C14	H2A	2.527	C14	H2B	3.144
C14	H10	2.872	C14	H15A	2.597
C14	H15B	3.156	C14	H15C	2.585
C16	H6A	2.465	C16	H6B	3.147
C16	H8	2.770	C16	H17A	2.625
C16	H17B	3.317	C16	H17C	2.699
C17	H6A	3.140	C17	H6B	2.428
C17	H8	2.565	C17	H16A	3.314
C17	H16B	2.731	C17	H16C	2.594
C18	H2A	3.117	C18	H2B	2.955
C18	H5	2.525	C18	H6A	3.455
H2A	H18C	2.522	H2B	H18B	3.038
H2B	H18C	2.575	H5	H6A	2.386
H5	H6B	2.221	H5	H18A	2.251
H5	H18B	2.876	H5	H18C	3.381
H6A	H16A	2.550	H6A	H16B	2.352
H6A	H16C	3.399	H6A	H17A	3.158
H6A	H17B	3.443	H6A	H18B	3.256
H6B	H16A	3.579	H6B	H16B	3.093
H6B	H17A	2.473	H6B	H17B	2.339
H6B	H17C	3.369	H8	H10	2.505
H8	H16A	3.009	H8	H16C	2.645
H8	H17A	3.443	H8	H17B	2.858
H8	H17C	2.313	H10	H16A	3.327
H10	H16C	3.514	H16A	H17A	3.536
H16A	H17C	3.528	H16B	H17A	2.523
H16B	H17B	3.571	H16B	H17C	3.084
H16C	H17A	2.774	H16C	H17B	3.501
H16C	H17C	2.456			

Table 11. Intermolecular contacts less than 3.60 Å

atom	atom	distance	atom	atom	distance
O1	C8[1]	3.598(3)	O2	C13[2]	3.158(3)
O2	C15[3]	3.333(3)	O3	O4[4]	3.404(2)
O3	C2[4]	3.516(2)	O3	C18[5]	3.541(3)
O4	O3[4]	3.404(2)	O4	C2[4]	3.566(3)
O4	C12[4]	3.435(2)	O4	C13[4]	3.598(3)
O5	C17[6]	3.484(3)	O6	C10[1]	3.519(2)
O6	C17[7]	3.409(3)	C2	O3[4]	3.516(2)
C2	O4[4]	3.566(3)	C8	O1[6]	3.598(3)
C10	O6[6]	3.519(2)	C12	O4[4]	3.435(2)
C13	O2[8]	3.158(3)	C13	O4[4]	3.598(3)
C15	O2[9]	3.333(3)	C17	O5[1]	3.484(3)
C17	O6[10]	3.409(3)	C18	O3[11]	3.541(3)

Symmetry Operators:

(1) -X+1,Y+1/2,-Z+1/2
(2) -X,Y+1/2,-Z+1/2
(3) X,-Y+1/2,Z+1/2
(4) -X,-Y+1,-Z
(5) X,Y-1,Z
(6) -X+1,Y+1/2-1,-Z+1/2
(7) X,-Y+1/2+1,Z+1/2-1
(8) -X,Y+1/2-1,-Z+1/2
(9) X,-Y+1/2,Z+1/2-1
(10) X,-Y+1/2+1,Z+1/2
(11) X,Y+1,Z

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens

atom	atom	distance	atom	atom	distance
O1	H8[1]	2.623	O1	H10[1]	3.539
O1	H15B[2]	3.563	O1	H16B[3]	3.323
O1	H16C[3]	3.278	O1	H17C[1]	3.330
O2	H13A[4]	2.934	O2	H13B[4]	2.607
O2	H13C[4]	3.501	O2	H15A[5]	2.613
O2	H15B[5]	3.546	O2	H15C[5]	3.391
O2	H18B[6]	3.069	O3	H2A[7]	2.856
O3	H2B[7]	3.301	O3	H18A[8]	2.907
O3	H18B[8]	3.308	O3	H18C[7]	3.553
O4	H2B[7]	2.752	O4	H6A[3]	2.816
O4	H13A[9]	2.909	O4	H13C[7]	2.988
O5	H5[8]	3.347	O5	H17B[10]	3.042
O5	H17C[10]	3.140	O5	H18A[8]	2.826
O6	H5[10]	3.292	O6	H6B[10]	3.127
O6	H8[1]	3.282	O6	H10[1]	2.639
O6	H15B[11]	3.362	O6	H15C[11]	3.037
O6	H17A[3]	2.724	O6	H17C[3]	3.228
C2	H13B[7]	3.542	C2	H16B[3]	3.227
C3	H13C[4]	3.470	C3	H16B[3]	2.915
C4	H13C[4]	3.296	C4	H16B[3]	3.195
C5	H8[1]	3.515	C6	H15C[12]	3.334
C9	H16B[3]	3.324	C10	H17B[10]	3.135
C11	H8[1]	3.273	C11	H10[1]	3.151
C11	H16B[3]	3.449	C11	H17A[3]	3.246
C12	H15A[5]	3.394	C13	H2A[7]	2.952
C13	H2B[6]	3.283	C13	H16A[6]	3.390
C13	H18A[8]	3.354	C13	H18B[8]	3.039
C13	H18B[6]	3.336	C13	H18C[7]	3.507
C14	H2B[7]	3.449	C14	H6A[3]	3.233
C14	H18A[8]	3.583	C15	H13A[9]	3.572
C15	H16C[9]	3.356	C15	H17B[10]	3.569
C15	H17C[10]	3.091	C15	H18A[8]	2.953
C16	H2A[12]	3.492	C16	H13B[4]	3.558
C16	H15B[5]	3.190	C17	H10[1]	3.441
C17	H15B[1]	3.275	C18	H13A[2]	3.518
C18	H13B[2]	3.289	C18	H13C[4]	3.265
C18	H15A[2]	3.410	C18	H18C[13]	3.454

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H2A	O3[7]	2.856	H2A	C13[7]	2.952
H2A	C16[3]	3.492	H2A	H6A[3]	3.267
H2A	H13B[7]	2.678	H2A	H13C[7]	2.870
H2A	H16A[3]	3.429	H2A	H16B[3]	2.719
H2B	O3[7]	3.301	H2B	O4[7]	2.752
H2B	C13[4]	3.283	H2B	C14[7]	3.449
H2B	H13A[4]	2.741	H2B	H13B[4]	3.498
H2B	H13C[4]	3.123	H5	O5[2]	3.347
H5	O6[1]	3.292	H5	H8[1]	3.358
H5	H15B[2]	3.383	H5	H15C[12]	3.180
H6A	O4[12]	2.816	H6A	C14[12]	3.233
H6A	H2A[12]	3.267	H6A	H13C[4]	2.947
H6A	H15C[12]	3.061	H6B	O6[1]	3.127
H6B	H8[1]	3.518	H6B	H15C[12]	2.840
H6B	H17A[14]	2.931	H6B	H17B[14]	3.497
H8	O1[10]	2.623	H8	O6[10]	3.282
H8	C5[10]	3.515	H8	C11[10]	3.273
H8	H5[10]	3.358	H8	H6B[10]	3.518
H8	H17B[10]	3.498	H10	O1[10]	3.539
H10	O6[10]	2.639	H10	C11[10]	3.151
H10	C17[10]	3.441	H10	H15C[5]	3.592
H10	H17B[10]	2.544	H13A	O2[6]	2.934
H13A	O4[5]	2.909	H13A	C15[5]	3.572
H13A	C18[8]	3.518	H13A	H2B[6]	2.741
H13A	H15A[5]	2.947	H13A	H15C[5]	3.358
H13A	H18A[8]	3.345	H13A	H18B[8]	2.821
H13A	H18B[6]	3.337	H13B	O2[6]	2.607
H13B	C2[7]	3.542	H13B	C16[6]	3.558
H13B	C18[8]	3.289	H13B	H2A[7]	2.678
H13B	H2B[6]	3.498	H13B	H16A[6]	2.815
H13B	H16B[6]	3.445	H13B	H18A[8]	3.180
H13B	H18B[8]	2.656	H13B	H18C[8]	3.581
H13B	H18C[7]	2.722	H13C	O2[6]	3.501
H13C	O4[7]	2.988	H13C	C3[6]	3.470
H13C	C4[6]	3.296	H13C	C18[6]	3.265
H13C	H2A[7]	2.870	H13C	H2B[6]	3.123
H13C	H6A[6]	2.947	H13C	H16A[6]	3.108

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H13C	H18B[6]	2.537	H15A	O2[9]	2.613
H15A	C12[9]	3.394	H15A	C18[8]	3.410
H15A	H13A[9]	2.947	H15A	H16A[9]	3.445
H15A	H16C[9]	3.511	H15A	H18A[8]	2.669
H15A	H18C[8]	3.332	H15B	O1[8]	3.563
H15B	O2[9]	3.546	H15B	O6[11]	3.362
H15B	C16[9]	3.190	H15B	C17[10]	3.275
H15B	H5[8]	3.383	H15B	H16A[9]	3.131
H15B	H16B[9]	3.520	H15B	H16C[9]	2.503
H15B	H17A[10]	3.449	H15B	H17B[10]	3.402
H15B	H17C[10]	2.536	H15B	H18A[8]	2.903
H15C	O2[9]	3.391	H15C	O6[11]	3.037
H15C	C6[3]	3.334	H15C	H5[3]	3.180
H15C	H6A[3]	3.061	H15C	H6B[3]	2.840
H15C	H10[9]	3.592	H15C	H13A[9]	3.358
H15C	H17A[10]	3.435	H15C	H17B[10]	3.580
H15C	H17C[10]	3.213	H16A	C13[4]	3.390
H16A	H2A[12]	3.429	H16A	H13B[4]	2.815
H16A	H13C[4]	3.108	H16A	H15A[5]	3.445
H16A	H15B[5]	3.131	H16B	O1[12]	3.323
H16B	C2[12]	3.227	H16B	C3[12]	2.915
H16B	C4[12]	3.195	H16B	C9[12]	3.324
H16B	C11[12]	3.449	H16B	H2A[12]	2.719
H16B	H13B[4]	3.445	H16B	H15B[5]	3.520
H16B	H18C[12]	3.540	H16C	O1[12]	3.278
H16C	C15[5]	3.356	H16C	H15A[5]	3.511
H16C	H15B[5]	2.503	H16C	H17C[15]	3.591
H17A	O6[12]	2.724	H17A	C11[12]	3.246
H17A	H6B[14]	2.931	H17A	H15B[1]	3.449
H17A	H15C[1]	3.435	H17A	H17A[14]	3.233
H17A	H17B[14]	3.314	H17B	O5[1]	3.042
H17B	C10[1]	3.135	H17B	C15[1]	3.569
H17B	H6B[14]	3.497	H17B	H8[1]	3.498
H17B	H10[1]	2.544	H17B	H15B[1]	3.402
H17B	H15C[1]	3.580	H17B	H17A[14]	3.314
H17C	O1[10]	3.330	H17C	O5[1]	3.140
H17C	O6[12]	3.228	H17C	C15[1]	3.091

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H17C	H15B[1]	2.536	H17C	H15C[1]	3.213
H17C	H16C[15]	3.591	H18A	O3[2]	2.907
H18A	O5[2]	2.826	H18A	C13[2]	3.354
H18A	C14[2]	3.583	H18A	C15[2]	2.953
H18A	H13A[2]	3.345	H18A	H13B[2]	3.180
H18A	H15A[2]	2.669	H18A	H15B[2]	2.903
H18A	H18C[13]	3.410	H18B	O2[4]	3.069
H18B	O3[2]	3.308	H18B	C13[2]	3.039
H18B	C13[4]	3.336	H18B	H13A[2]	2.821
H18B	H13A[4]	3.337	H18B	H13B[2]	2.656
H18B	H13C[4]	2.537	H18B	H18C[13]	3.390
H18C	O3[7]	3.553	H18C	C13[7]	3.507
H18C	C18[13]	3.454	H18C	H13B[2]	3.581
H18C	H13B[7]	2.722	H18C	H15A[2]	3.332
H18C	H16B[3]	3.540	H18C	H18A[13]	3.410
H18C	H18B[13]	3.390	H18C	H18C[13]	3.008

Symmetry Operators:

(1) -X+1,Y+1/2,-Z+1/2
(2) X,Y+1,Z
(3) X,-Y+1/2+1,Z+1/2-1
(4) -X,Y+1/2,-Z+1/2
(5) X,-Y+1/2,Z+1/2
(6) -X,Y+1/2-1,-Z+1/2
(7) -X,-Y+1,-Z
(8) X,Y-1,Z
(9) X,-Y+1/2,Z+1/2-1
(10) -X+1,Y+1/2-1,-Z+1/2
(11) -X+1,-Y+1,-Z
(12) X,-Y+1/2+1,Z+1/2
(13) -X,-Y+2,-Z
(14) -X+1,-Y+2,-Z+1
(15) -X+1,-Y+1,-Z+1

X-ray Structure Report

for

163h

August 29, 2013

Experimental

Data Collection

A colorless prismatic crystal of $C_{25}H_{32}O_5Si$ having approximate dimensions of 0.200 x 0.200 x 0.200 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC7R diffractometer using graphite monochromated Mo-Kα radiation and a rotating anode generator.

Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using the setting angles of 25 carefully centered reflections in the range $29.79 < 2\theta < 29.97^o$ corresponded to a primitive triclinic cell with dimensions:

a	= 11.065(4) Å	α	= 110.43(3)^o
b	= 12.052(4) Å	β	= 108.94(4)^o
c	= 10.146(6) Å	γ	= 77.35(3)^o
V	= 1190.8(9) Å^3		

For Z = 2 and F.W. = 440.61, the calculated density is 1.229 g/cm^3. Based on a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be:

P-1 (#2)

The data were collected at a temperature of 23 $\pm$ 1^{o}C using the ω-2θ scan technique to a maximum 2θ value of 55.0^o. Omega scans of several intense reflections, made prior to data collection, had an average width at half-height of 0.28^o with a take-off angle of 6.0^o. Scans of (1.73 + 0.30 tan θ)^o were made at a speed of 4.0^o/min (in ω). The weak reflections ($I < 10.0\sigma(I)$) were rescanned (maximum of 7 scans) and the counts were accumulated to ensure good counting statistics. Stationary background counts were recorded on each side of the reflection. The ratio of peak counting time to background counting time was 2:1. The diameter of the incident beam collimator was 0.5 mm and the crystal to detector distance was 235 mm. The computer-controlled slits were set to 3.0 mm (horizontal) and 5.0 mm (vertical).

Data Reduction

Of the 5784 reflections that were collected, 5476 were unique (R_{int} = 0.0058); equivalent reflections were merged. The intensities of three representative reflections were measured after every 150 reflections. No decay correction was applied.

The linear absorption coefficient, μ, for Mo-Kα radiation is 1.308 cm^{-1}. The data were corrected for Lorentz and polarization effects. A correction for secondary extinction[1] was applied (coefficient = 41.256000).

Structure Solution and Refinement

The structure was solved by direct methods[2] and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement[3] on F^2 was based on 5476 observed reflections and 313 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R1 = \Sigma \; ||Fo| - |Fc|| \; / \; \Sigma \; |Fo| = 0.0402$$

$$wR2 = [\; \Sigma \; (\; w \; (Fo^2 - Fc^2)^2 \;) / \; \Sigma \; w(Fo^2)^2]^{1/2} = 0.1655$$

The standard deviation of an observation of unit weight[4] was 1.02. A Sheldrick weighting scheme was used. Plots of Σ w $(|Fo| - |Fc|)^2$ versus |Fo|, reflection order in data collection, sin θ/λ and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.57 and -0.61 $e^-/Å^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber[5]. Anomalous dispersion effects were included in Fcalc[6]; the values for Δf' and Δf" were those of Creagh and McAuley[7]. The values for the mass attenuation coefficients are those of Creagh and Hubbell[8]. All calculations were performed using the CrystalStructure[9,10] crystallographic software package.

References

(1) Larson, A.C. (1970), Crystallographic Computing, 291-294. F.R. Ahmed, ed. Munksgaard, Copenhagen (equation 22, with V replaced by the cell volume).

(2) SIR92: Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M., Polidori, G., and Camalli, M. (1994) J. Appl. Cryst., 27, 435.

(3) Least Squares function minimized:

$\Sigma w(F_o^2-F_c^2)^2$ where w = Least Squares weights.

(4) Standard deviation of an observation of unit weight:

$[\Sigma w(F_o^2-F_c^2)^2/(N_o-N_v)]^{1/2}$

where: N_o = number of observations
N_v = number of variables

(5) Cromer, D. T. & Waber, J. T.; "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

(6) Ibers, J. A. & Hamilton, W. C.; Acta Crystallogr., 17, 781 (1964).

(7) Creagh, D. C. & McAuley, W.J .; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219-222 (1992).

(8) Creagh, D. C. & Hubbell, J.H..; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200-206 (1992).

(9) CrystalStructure 4.0: Crystal Structure Analysis Package, Rigaku Corporation (2000-2010). Tokyo 196-8666, Japan.

(10) CRYSTALS Issue 11: Carruthers, J.R., Rollett,J.S., Betteridge, P.W., Kinna, D., Pearce, L., Larsen, A., and Gabe, E. Chemical Crystallography Laboratory, Oxford, UK. (1999)

EXPERIMENTAL DETAILS

A. Crystal Data

Empirical Formula	$C_{25}H_{32}O_5Si$
Formula Weight	440.61
Crystal Color, Habit	colorless, prismatic
Crystal Dimensions	0.200 X 0.200 X 0.200 mm
Crystal System	triclinic
Lattice Type	Primitive
No. of Reflections Used for Unit Cell Determination (2θ range)	25 (29.8 - 30.0°)
Omega Scan Peak Width at Half-height	0.28°
Lattice Parameters	a = 11.065(4) Å b = 12.052(4) Å c = 10.146(6) Å α = 110.43(3) ° β = 108.94(4) ° γ = 77.35(3) ° V = 1190.8(9) Å^3
Space Group	P-1 (#2)
Z value	2
D_{calc}	1.229 g/cm^3
F_{000}	472.00
μ(MoKα)	1.308 cm^{-1}

B. Intensity Measurements

Diffractometer	AFC7R
Radiation	MoKα (λ = 0.71069 Å) graphite monochromated
Attenuator	Zr foil (factor = 7.21)
Take-off Angle	6.0°
Detector Aperture	5.0 mm horizontal 3.0 mm vertical
Crystal to Detector Distance	235 mm
Voltage, Current	50kV, 100mA
Temperature	23.0°C
Scan Type	ω-2θ
Scan Rate	4.0°/min (in ω) (up to 7 scans)
Scan Width	(1.73 + 0.30 tan θ)°
$2\theta_{max}$	55.0°
No. of Reflections Measured	Total: 5784 Unique: 5476 (R_{int} = 0.0058)
Corrections	Lorentz-polarization Secondary Extinction (coefficient: 4.12560e+001)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	$1/[0.0059Fo^2+1.0000\sigma(Fo^2)]/(4Fo^2)$
$2\theta_{max}$ cutoff	55.0^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	5476
No. Variables	313
Reflection/Parameter Ratio	17.50
Residuals: R1 (I>2.00σ(I))	0.0402
Residuals: R (All reflections)	0.0432
Residuals: wR2 (All reflections)	0.1655
Goodness of Fit Indicator	1.018
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.57 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.61 $e^-/Å^3$

Table 1. Atomic coordinates and B_{iso}/B_{eq}

atom	x	y	z	B_{eq}
Si1	0.27355(3)	0.35710(2)	0.17253(3)	0.909(9)
O1	0.37147(7)	0.12987(6)	0.07211(8)	0.89(2)
O2	0.06551(9)	-0.28639(9)	-0.3285(1)	2.02(2)
O3	-0.00356(8)	-0.23313(8)	-0.53445(9)	1.50(2)
O4	0.22526(9)	-0.07086(8)	-0.5201(1)	1.64(2)
O5	0.28176(8)	-0.26035(7)	-0.51405(9)	1.24(2)
C1	0.1634(1)	-0.13412(9)	-0.3498(1)	0.92(2)
C2	0.0877(1)	-0.00765(9)	-0.3062(1)	1.08(2)
C3	0.1655(1)	0.05204(9)	-0.1537(1)	0.89(2)
C4	0.14612(9)	0.16154(9)	-0.0620(1)	0.86(2)
C5	0.24504(9)	0.19311(9)	0.0872(1)	0.85(2)
C6	0.2168(1)	0.13836(9)	0.1903(1)	1.08(2)
C7	0.2969(1)	0.01249(9)	0.1652(1)	0.95(2)
C8	0.3573(1)	0.00661(9)	0.0442(1)	0.83(2)
C9	0.27220(9)	-0.03431(9)	-0.1080(1)	0.87(2)
C10	0.2708(1)	-0.13957(9)	-0.2123(1)	0.99(2)
C11	0.0731(1)	-0.22881(9)	-0.3999(2)	1.08(2)
C12	0.2239(1)	-0.14837(9)	-0.4715(1)	1.00(2)
C13	0.0298(1)	0.24920(9)	-0.0951(2)	1.15(2)
C14	0.2145(1)	-0.0879(1)	0.1213(2)	1.35(2)
C15	0.4070(1)	0.0078(1)	0.3033(2)	1.44(2)
C16	0.4177(1)	0.3626(1)	0.3335(2)	1.59(2)
C17	0.1344(1)	0.4523(1)	0.2398(2)	1.39(2)
C18	0.3054(1)	0.40783(9)	0.0331(2)	1.04(2)
C19	0.3966(1)	0.3413(1)	-0.0427(2)	1.51(3)
C20	0.4198(2)	0.3772(2)	-0.1480(2)	1.96(3)
C21	0.3513(2)	0.4796(2)	-0.1813(2)	1.97(3)
C22	0.2597(2)	0.5468(1)	-0.1090(2)	1.75(3)
C23	0.2381(1)	0.5110(1)	-0.0028(2)	1.34(2)
C24	-0.1033(2)	-0.3111(2)	-0.5917(2)	1.94(3)
C25	0.3463(2)	-0.2818(1)	-0.6249(2)	1.46(2)

$B_{eq} = 8/3\ \pi^2(U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}(aa^*bb^*)\cos\gamma + 2U_{13}(aa^*cc^*)\cos\beta + 2U_{23}(bb^*cc^*)\cos\alpha)$

Table 2. Atomic coordinates and B_{iso} involving hydrogen atoms

atom	x	y	z	B_{iso}
H1	0.0017	-0.0113	-0.3039	1.31
H2	0.0824	0.0382	-0.3701	1.20
H3	0.1256	0.1317	0.1642	1.38
H4	0.2442	0.1870	0.2912	1.38
H5	0.4412	-0.0423	0.0538	1.11
H6	0.3279	-0.2071	-0.2019	1.24
H7	-0.0152	0.2705	-0.0215	1.35
H8	-0.0261	0.2133	-0.1888	1.39
H9	0.0559	0.3195	-0.0968	1.33
H10	0.1404	-0.0784	0.0424	1.82
H11	0.1870	-0.0847	0.2032	1.70
H12	0.2638	-0.1635	0.0903	1.76
H13	0.4572	-0.0690	0.2862	1.80
H14	0.3720	0.0216	0.3835	1.73
H15	0.4608	0.0684	0.3265	1.73
H16	0.4891	0.3114	0.3018	1.89
H17	0.3992	0.3364	0.4033	1.91
H18	0.4390	0.4429	0.3781	1.91
H19	0.1082	0.4145	0.2934	1.69
H20	0.0639	0.4625	0.1580	1.77
H21	0.1597	0.5289	0.3024	1.72
H22	0.4427	0.2723	-0.0218	2.02
H23	0.4812	0.3322	-0.1962	2.57
H24	0.3666	0.5030	-0.2521	2.61
H25	0.2136	0.6155	-0.1308	2.17
H26	0.1769	0.5565	0.0455	1.61
H27	-0.1589	-0.2861	-0.5284	2.32
H28	-0.0649	-0.3916	-0.5971	2.36
H29	-0.1525	-0.3073	-0.6876	2.39
H30	0.2853	-0.2678	-0.7113	1.85
H31	0.4111	-0.2290	-0.5890	1.86
H32	0.3859	-0.3629	-0.6480	1.86

Table 3. Anisotropic displacement parameters

atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Si1	0.0112(2)	0.0085(2)	0.0143(2)	0.0022(2)	0.0047(2)	0.0037(2)
O1	0.0097(4)	0.0085(4)	0.0172(4)	0.0036(3)	0.0066(3)	0.0061(3)
O2	0.0271(5)	0.0288(5)	0.0287(5)	-0.0068(4)	0.0047(4)	0.0187(4)
O3	0.0199(5)	0.0216(5)	0.0164(4)	-0.0066(4)	0.0030(4)	0.0061(4)
O4	0.0278(5)	0.0164(4)	0.0245(5)	0.0038(4)	0.0131(4)	0.0121(4)
O5	0.0206(4)	0.0126(4)	0.0176(4)	0.0049(3)	0.0125(4)	0.0062(3)
C1	0.0133(5)	0.0095(5)	0.0129(5)	0.0033(4)	0.0057(4)	0.0053(4)
C2	0.0142(5)	0.0105(5)	0.0135(5)	0.0048(4)	0.0036(4)	0.0043(4)
C3	0.0112(5)	0.0111(5)	0.0135(5)	0.0024(4)	0.0048(4)	0.0069(4)
C4	0.0096(5)	0.0102(5)	0.0141(5)	0.0030(4)	0.0053(4)	0.0056(4)
C5	0.0094(5)	0.0095(5)	0.0145(5)	0.0035(4)	0.0062(4)	0.0049(4)
C6	0.0171(5)	0.0124(5)	0.0152(5)	0.0026(4)	0.0097(4)	0.0062(4)
C7	0.0137(5)	0.0118(5)	0.0132(5)	0.0018(4)	0.0058(4)	0.0071(4)
C8	0.0113(5)	0.0081(5)	0.0138(5)	0.0037(4)	0.0057(4)	0.0064(4)
C9	0.0109(5)	0.0108(5)	0.0133(5)	0.0030(4)	0.0053(4)	0.0068(4)
C10	0.0134(5)	0.0123(5)	0.0133(5)	0.0044(4)	0.0053(4)	0.0072(4)
C11	0.0143(5)	0.0120(5)	0.0153(5)	0.0025(4)	0.0073(4)	0.0045(4)
C12	0.0128(5)	0.0121(5)	0.0130(5)	0.0013(4)	0.0035(4)	0.0053(4)
C13	0.0107(5)	0.0105(5)	0.0209(5)	0.0040(4)	0.0042(4)	0.0058(4)
C14	0.0210(6)	0.0153(5)	0.0190(5)	-0.0032(4)	0.0080(5)	0.0070(4)
C15	0.0199(6)	0.0204(6)	0.0146(5)	0.0007(4)	0.0028(5)	0.0089(4)
C16	0.0187(6)	0.0173(6)	0.0210(6)	-0.0009(4)	-0.0002(5)	0.0075(5)
C17	0.0185(6)	0.0123(5)	0.0222(6)	0.0033(4)	0.0114(5)	0.0032(4)
C18	0.0117(5)	0.0108(5)	0.0177(5)	-0.0005(4)	0.0045(4)	0.0050(4)
C19	0.0180(6)	0.0157(5)	0.0279(6)	0.0027(4)	0.0121(5)	0.0092(5)
C20	0.0257(7)	0.0272(6)	0.0284(7)	-0.0029(5)	0.0168(5)	0.0080(5)
C21	0.0306(7)	0.0272(7)	0.0236(6)	-0.0118(5)	0.0070(5)	0.0109(5)
C22	0.0244(6)	0.0176(6)	0.0258(6)	-0.0038(5)	0.0015(5)	0.0123(5)
C23	0.0162(5)	0.0134(5)	0.0205(5)	0.0014(4)	0.0042(4)	0.0068(4)
C24	0.0208(6)	0.0301(7)	0.0233(6)	-0.0102(5)	0.0073(5)	0.0029(5)
C25	0.0221(6)	0.0198(6)	0.0167(5)	0.0040(4)	0.0120(5)	0.0072(5)

The general temperature factor expression: $\exp(-2\pi^2(a^{*2}U_{11}h^2 + b^{*2}U_{22}k^2 + c^{*2}U_{33}l^2 + 2a^*b^*U_{12}hk + 2a^*c^*U_{13}hl + 2b^*c^*U_{23}kl))$

Table 4. Bond lengths (Å)

atom	atom	distance	atom	atom	distance
Si1	C5	1.9122(13)	Si1	C16	1.8698(15)
Si1	C17	1.8748(14)	Si1	C18	1.8759(17)
O1	C5	1.4669(13)	O1	C8	1.4462(15)
O2	C11	1.195(2)	O3	C11	1.3432(15)
O3	C24	1.4482(18)	O4	C12	1.2036(18)
O5	C12	1.3460(14)	O5	C25	1.4418(19)
C1	C2	1.5594(15)	C1	C10	1.5226(16)
C1	C11	1.5242(18)	C1	C12	1.529(2)
C2	C3	1.5108(15)	C3	C4	1.3421(15)
C3	C9	1.4614(15)	C4	C5	1.5293(15)
C4	C13	1.5023(15)	C5	C6	1.553(2)
C6	C7	1.5623(15)	C7	C8	1.552(2)
C7	C14	1.5294(19)	C7	C15	1.5388(16)
C8	C9	1.4968(15)	C9	C10	1.3380(14)
C18	C19	1.4046(18)	C18	C23	1.4030(17)
C19	C20	1.394(3)	C20	C21	1.388(2)
C21	C22	1.388(2)	C22	C23	1.394(3)

Table 5. Bond lengths involving hydrogens (Å)

atom	atom	distance	atom	atom	distance
C2	H1	0.970	C2	H2	0.970
C6	H3	0.970	C6	H4	0.970
C8	H5	0.980	C10	H6	0.930
C13	H7	0.960	C13	H8	0.960
C13	H9	0.960	C14	H10	0.960
C14	H11	0.960	C14	H12	0.960
C15	H13	0.960	C15	H14	0.960
C15	H15	0.960	C16	H16	0.960
C16	H17	0.960	C16	H18	0.960
C17	H19	0.960	C17	H20	0.960
C17	H21	0.960	C19	H22	0.930
C20	H23	0.930	C21	H24	0.930
C22	H25	0.930	C23	H26	0.930
C24	H27	0.960	C24	H28	0.960
C24	H29	0.960	C25	H30	0.960
C25	H31	0.960	C25	H32	0.960

Table 6. Bond angles (º)

atom	atom	atom	angle	atom	atom	atom	angle
C5	Si1	C16	105.95(6)	C5	Si1	C17	111.81(6)
C5	Si1	C18	108.30(6)	C16	Si1	C17	108.18(7)
C16	Si1	C18	111.01(7)	C17	Si1	C18	111.46(7)
C5	O1	C8	103.43(9)	C11	O3	C24	116.17(12)
C12	O5	C25	114.66(11)	C2	C1	C10	104.46(8)
C2	C1	C11	109.65(10)	C2	C1	C12	111.22(11)
C10	C1	C11	113.11(11)	C10	C1	C12	108.56(10)
C11	C1	C12	109.75(9)	C1	C2	C3	104.20(9)
C2	C3	C4	130.62(10)	C2	C3	C9	108.46(9)
C4	C3	C9	120.82(9)	C3	C4	C5	116.87(9)
C3	C4	C13	123.52(9)	C5	C4	C13	119.48(9)
Si1	C5	O1	104.16(8)	Si1	C5	C4	116.10(9)
Si1	C5	C6	114.24(8)	O1	C5	C4	109.10(9)
O1	C5	C6	102.47(9)	C4	C5	C6	109.61(10)
C5	C6	C7	104.35(10)	C6	C7	C8	102.59(10)
C6	C7	C14	112.55(10)	C6	C7	C15	110.14(9)
C8	C7	C14	113.24(9)	C8	C7	C15	108.02(10)
C14	C7	C15	110.01(11)	O1	C8	C7	103.18(9)
O1	C8	C9	106.83(10)	C7	C8	C9	114.26(10)
C3	C9	C8	116.47(9)	C3	C9	C10	111.45(9)
C8	C9	C10	132.01(10)	C1	C10	C9	111.10(10)
O2	C11	O3	124.36(12)	O2	C11	C1	125.87(10)
O3	C11	C1	109.64(12)	O4	C12	O5	123.69(12)
O4	C12	C1	125.95(10)	O5	C12	C1	110.31(11)
Si1	C18	C19	120.75(10)	Si1	C18	C23	122.18(10)
C19	C18	C23	117.06(14)	C18	C19	C20	121.27(12)
C19	C20	C21	120.24(14)	C20	C21	C22	119.89(16)
C21	C22	C23	119.52(13)	C18	C23	C22	122.02(12)

Table 7. Bond angles involving hydrogens (º)

atom	atom	atom	angle	atom	atom	atom	angle
C1	C2	H1	112.1	C1	C2	H2	112.3
C3	C2	H1	109.3	C3	C2	H2	109.4
H1	C2	H2	109.4	C5	C6	H3	110.5
C5	C6	H4	110.5	C7	C6	H3	110.9
C7	C6	H4	111.0	H3	C6	H4	109.5
O1	C8	H5	110.7	C7	C8	H5	110.8
C9	C8	H5	110.7	C1	C10	H6	124.5
C9	C10	H6	124.4	C4	C13	H7	109.7
C4	C13	H8	109.1	C4	C13	H9	109.7
H7	C13	H8	109.4	H7	C13	H9	109.4
H8	C13	H9	109.4	C7	C14	H10	109.3
C7	C14	H11	109.6	C7	C14	H12	109.6
H10	C14	H11	109.4	H10	C14	H12	109.4
H11	C14	H12	109.4	C7	C15	H13	109.6
C7	C15	H14	109.7	C7	C15	H15	109.2
H13	C15	H14	109.4	H13	C15	H15	109.4
H14	C15	H15	109.4	Si1	C16	H16	109.5
Si1	C16	H17	109.5	Si1	C16	H18	109.5
H16	C16	H17	109.4	H16	C16	H18	109.4
H17	C16	H18	109.4	Si1	C17	H19	109.5
Si1	C17	H20	109.4	Si1	C17	H21	109.5
H19	C17	H20	109.4	H19	C17	H21	109.4
H20	C17	H21	109.4	C18	C19	H22	119.3
C20	C19	H22	119.5	C19	C20	H23	119.8
C21	C20	H23	120.0	C20	C21	H24	120.0
C22	C21	H24	120.1	C21	C22	H25	120.3
C23	C22	H25	120.2	C18	C23	H26	118.8
C22	C23	H26	119.1	O3	C24	H27	109.4
O3	C24	H28	109.7	O3	C24	H29	109.4
H27	C24	H28	109.4	H27	C24	H29	109.4
H28	C24	H29	109.4	O5	C25	H30	109.8
O5	C25	H31	109.2	O5	C25	H32	109.5
H30	C25	H31	109.4	H30	C25	H32	109.4
H31	C25	H32	109.4				

Table 8. Torsion Angles(°)
(Those having bond angles > 160 or < 20 degrees are excluded.)

atom1	atom2	atom3	atom4	angle	atom1	atom2	atom3	atom4	angle
C16	Si1	C5	O1	-49.93(9)	C16	Si1	C5	C4	-169.89(8)
C16	Si1	C5	C6	61.03(8)	C17	Si1	C5	O1	-167.58(7)
C17	Si1	C5	C4	72.46(10)	C17	Si1	C5	C6	-56.62(8)
C5	Si1	C18	C19	-49.87(8)	C5	Si1	C18	C23	128.56(7)
C18	Si1	C5	O1	69.23(8)	C18	Si1	C5	C4	-50.73(9)
C18	Si1	C5	C6	-179.81(6)	C16	Si1	C18	C19	66.05(9)
C16	Si1	C18	C23	-115.52(8)	C17	Si1	C18	C19	-173.27(7)
C17	Si1	C18	C23	5.15(9)	C5	O1	C8	C7	-48.71(9)
C5	O1	C8	C9	72.06(10)	C8	O1	C5	Si1	165.66(7)
C8	O1	C5	C4	-69.76(11)	C8	O1	C5	C6	46.36(8)
C24	O3	C11	O2	1.81(15)	C24	O3	C11	C1	-174.32(8)
C25	O5	C12	O4	-0.34(13)	C25	O5	C12	C1	-177.75(7)
C2	C1	C10	C9	-5.74(14)	C10	C1	C2	C3	5.40(13)
C2	C1	C11	O2	-100.88(12)	C2	C1	C11	O3	75.18(12)
C11	C1	C2	C3	126.90(10)	C2	C1	C12	O4	6.60(13)
C2	C1	C12	O5	-176.07(7)	C12	C1	C2	C3	-111.52(10)
C10	C1	C11	O2	15.26(15)	C10	C1	C11	O3	-168.68(8)
C11	C1	C10	C9	-124.93(10)	C10	C1	C12	O4	-107.79(11)
C10	C1	C12	O5	69.55(10)	C12	C1	C10	C9	113.00(11)
C11	C1	C12	O4	128.12(10)	C11	C1	C12	O5	-54.54(10)
C12	C1	C11	O2	136.66(11)	C12	C1	C11	O3	-47.28(11)
C1	C2	C3	C4	-179.90(13)	C1	C2	C3	C9	-3.62(14)
C2	C3	C4	C5	179.51(12)	C2	C3	C4	C13	3.6(3)
C2	C3	C9	C8	-177.09(10)	C2	C3	C9	C10	0.14(15)
C4	C3	C9	C8	-0.38(19)	C4	C3	C9	C10	176.85(12)
C9	C3	C4	C5	3.62(19)	C9	C3	C4	C13	-172.30(11)
C3	C4	C5	Si1	148.81(11)	C3	C4	C5	O1	31.56(16)
C3	C4	C5	C6	-79.90(13)	C13	C4	C5	Si1	-35.10(16)
C13	C4	C5	O1	-152.35(11)	C13	C4	C5	C6	96.19(13)
Si1	C5	C6	C7	-137.46(6)	O1	C5	C6	C7	-25.48(8)
C4	C5	C6	C7	90.27(9)	C5	C6	C7	C8	-2.71(8)
C5	C6	C7	C14	-124.74(9)	C5	C6	C7	C15	112.10(10)
C6	C7	C8	O1	30.57(9)	C6	C7	C8	C9	-85.00(10)
C14	C7	C8	O1	152.14(8)	C14	C7	C8	C9	36.57(12)
C15	C7	C8	O1	-85.77(10)	C15	C7	C8	C9	158.66(8)
O1	C8	C9	C3	-38.20(14)	O1	C8	C9	C10	145.26(12)
C7	C8	C9	C3	75.22(13)	C7	C8	C9	C10	-101.31(14)

Table 8. Torsion angles (°) (continued)

atom1	atom2	atom3	atom4	angle	atom1	atom2	atom3	atom4	angle
C3	C9	C10	C1	3.63(16)	C8	C9	C10	C1	-179.70(13)
Si1	C18	C19	C20	179.07(7)	Si1	C18	C23	C22	-178.37(7)
C19	C18	C23	C22	0.11(15)	C23	C18	C19	C20	0.57(14)
C18	C19	C20	C21	-0.79(17)	C19	C20	C21	C22	0.32(18)
C20	C21	C22	C23	0.34(17)	C21	C22	C23	C18	-0.56(16)

Table 9. Intramolecular contacts less than 3.60 Å

atom	atom	distance	atom	atom	distance
Si1	C13	3.2644(19)	O1	C3	2.7148(18)
O1	C15	3.062(3)	O1	C16	3.118(2)
O1	C18	3.4026(18)	O1	C19	3.244(2)
O2	C2	3.345(2)	O2	C10	2.8717(19)
O2	C12	3.543(3)	O2	C24	2.675(2)
O3	O4	3.4623(19)	O3	O5	3.0476(16)
O3	C2	3.0096(19)	O3	C12	2.7230(18)
O4	C2	2.844(2)	O4	C10	3.361(3)
O4	C11	3.507(3)	O4	C25	2.6334(18)
O5	C10	2.926(2)	O5	C11	2.8034(19)
C2	C13	3.1580(19)	C3	C6	3.165(3)
C3	C7	3.245(3)	C3	C11	3.563(2)
C3	C12	3.447(3)	C3	C14	3.581(3)
C4	C7	3.226(3)	C4	C8	2.8223(18)
C4	C10	3.565(2)	C4	C18	3.469(2)
C5	C9	2.7855(18)	C5	C15	3.482(3)
C5	C19	3.483(3)	C6	C9	3.180(3)
C6	C13	3.471(3)	C6	C16	3.487(3)
C6	C17	3.586(2)	C7	C10	3.567(3)
C9	C11	3.507(3)	C9	C12	3.359(3)
C9	C14	2.903(3)	C10	C14	3.458(3)
C13	C17	3.429(3)	C13	C18	3.590(2)
C17	C23	3.358(3)	C18	C21	2.822(3)
C19	C22	2.782(2)	C20	C23	2.767(3)

Table 10. Intramolecular contacts less than 3.60 Å involving hydrogens

atom	atom	distance	atom	atom	distance
Si1	H3	3.430	Si1	H4	2.833
Si1	H7	3.334	Si1	H9	2.969
Si1	H22	2.930	Si1	H26	2.954
O1	H3	3.144	O1	H4	2.817
O1	H13	3.559	O1	H15	2.748
O1	H16	2.763	O1	H17	3.377
O1	H22	2.587	O2	H1	3.173
O2	H6	2.988	O2	H27	2.648
O2	H28	2.636	O3	H1	2.870
O3	H2	3.302	O4	H2	2.407
O4	H30	2.602	O4	H31	2.576
O4	H32	3.578	O5	H6	2.894
C2	H6	3.334	C2	H8	2.717
C3	H3	3.178	C3	H5	3.318
C3	H6	3.205	C3	H7	3.114
C3	H8	2.566	C3	H9	3.104
C3	H10	3.040	C4	H1	2.874
C4	H2	2.874	C4	H3	2.530
C4	H4	3.312	C4	H10	3.429
C5	H5	3.159	C5	H7	2.803
C5	H8	3.406	C5	H9	2.870
C5	H10	3.541	C5	H15	3.328
C5	H16	3.126	C5	H17	3.170
C5	H19	3.190	C5	H20	3.395
C5	H22	3.183	C6	H5	3.253
C6	H7	3.280	C6	H10	2.683
C6	H11	2.831	C6	H12	3.387
C6	H13	3.373	C6	H14	2.730
C6	H15	2.704	C6	H17	3.182
C6	H19	3.201	C8	H3	3.062
C8	H4	3.100	C8	H6	2.885
C8	H10	2.801	C8	H11	3.389
C8	H12	2.721	C8	H13	2.728
C8	H14	3.335	C8	H15	2.613
C9	H1	3.025	C9	H2	3.073
C9	H3	3.448	C9	H10	2.662
C9	H12	2.975	C10	H1	3.052

Table 10. Intramolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
C10	H2	3.126	C10	H5	2.770
C10	H10	3.151	C10	H12	3.209
C11	H1	2.502	C11	H2	3.147
C11	H6	2.886	C11	H27	2.597
C11	H28	2.603	C11	H29	3.166
C12	H1	3.262	C12	H2	2.540
C12	H6	2.874	C12	H30	2.579
C12	H31	2.563	C12	H32	3.151
C13	H1	3.130	C13	H2	3.169
C13	H3	3.191	C13	H20	2.921
C14	H3	2.548	C14	H4	3.190
C14	H5	3.008	C14	H13	2.674
C14	H14	2.721	C14	H15	3.338
C15	H3	3.240	C15	H4	2.502
C15	H5	2.524	C15	H10	3.338
C15	H11	2.645	C15	H12	2.746
C16	H4	2.995	C16	H15	3.452
C16	H19	3.259	C16	H21	3.101
C16	H22	3.468	C17	H4	3.321
C17	H7	3.042	C17	H9	3.138
C17	H17	3.155	C17	H18	3.196
C17	H26	2.876	C18	H9	2.905
C18	H16	3.240	C18	H18	3.240
C18	H20	3.166	C18	H21	3.352
C18	H23	3.273	C18	H25	3.280
C19	H16	3.434	C19	H24	3.250
C19	H26	3.236	C20	H25	3.244
C21	H22	3.246	C21	H26	3.238
C22	H23	3.242	C23	H9	3.091
C23	H20	3.149	C23	H21	3.404
C23	H22	3.238	C23	H24	3.245
H1	H8	2.539	H2	H8	2.625
H2	H9	3.578	H3	H7	2.816
H3	H10	2.394	H3	H11	2.682
H3	H12	3.473	H3	H14	3.268
H3	H15	3.567	H3	H19	3.182
H4	H10	3.465	H4	H11	3.228

Table 10. Intramolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H4	H13	3.444	H4	H14	2.461
H4	H15	2.494	H4	H16	3.330
H4	H17	2.478	H4	H19	2.820
H5	H6	2.763	H5	H10	3.410
H5	H12	2.869	H5	H13	2.436
H5	H14	3.461	H5	H15	2.578
H6	H10	3.479	H6	H12	3.112
H7	H19	3.069	H7	H20	2.519
H9	H19	3.599	H9	H20	2.543
H9	H26	3.095	H10	H13	3.573
H10	H14	3.561	H11	H13	2.861
H11	H14	2.502	H11	H15	3.540
H12	H13	2.559	H12	H14	3.080
H12	H15	3.593	H15	H16	3.115
H15	H17	3.022	H16	H22	3.033
H17	H19	3.093	H17	H21	3.264
H18	H19	3.543	H18	H21	2.971
H20	H26	2.569	H21	H26	2.811
H22	H23	2.313	H23	H24	2.318
H24	H25	2.324	H25	H26	2.314

Table 11. Intermolecular contacts less than 3.60 Å

atom	atom	distance	atom	atom	distance
O1	C8[1]	3.4481(19)	O2	C22[2]	3.427(3)
O4	C2[3]	3.4292(19)	O4	C14[4]	3.536(3)
O4	C15[4]	3.538(3)	O5	C16[1]	3.4294(19)
C2	O4[3]	3.4292(19)	C8	O1[1]	3.4481(19)
C8	C8[1]	3.511(2)	C13	C14[5]	3.554(3)
C14	O4[6]	3.536(3)	C14	C13[5]	3.554(3)
C15	O4[6]	3.538(3)	C16	O5[1]	3.4294(19)
C16	C25[1]	3.521(3)	C19	C21[7]	3.564(3)
C20	C21[7]	3.599(3)	C21	C19[7]	3.564(3)
C21	C20[7]	3.599(3)	C21	C24[3]	3.468(3)
C22	O2[8]	3.427(3)	C24	C21[3]	3.468(3)
C25	C16[1]	3.521(3)			

Symmetry Operators:

(1)	-X+1,-Y,-Z	(2)	X,Y-1,Z
(3)	-X,-Y,-Z-1	(4)	X,Y,Z-1
(5)	-X,-Y,-Z	(6)	X,Y,Z+1
(7)	-X+1,-Y+1,-Z	(8)	X,Y+1,Z

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens

atom	atom	distance	atom	atom	distance
Si1	H32[1]	3.511	O1	H5[2]	2.620
O1	H6[2]	3.365	O2	H3[3]	3.020
O2	H4[3]	3.471	O2	H19[3]	2.887
O2	H25[4]	2.604	O3	H2[5]	2.713
O3	H8[5]	3.025	O3	H9[5]	3.400
O3	H21[6]	3.253	O4	H1[5]	2.776
O4	H2[5]	3.201	O4	H8[5]	3.228
O4	H11[7]	2.649	O4	H14[7]	2.724
O4	H15[2]	3.391	O5	H8[5]	3.517
O5	H16[2]	2.853	O5	H17[2]	3.361
O5	H18[6]	3.576	O5	H18[2]	3.559
O5	H21[6]	2.883	C1	H2[5]	3.565
C2	H2[5]	3.148	C2	H11[3]	3.366
C4	H29[5]	3.583	C6	H27[3]	3.466
C8	H5[2]	2.882	C8	H22[2]	3.575
C9	H5[2]	3.318	C10	H16[2]	3.164
C10	H25[4]	3.558	C11	H3[3]	3.501
C11	H25[4]	3.597	C12	H1[5]	3.520
C12	H2[5]	3.438	C12	H8[5]	3.355
C12	H11[7]	3.522	C12	H15[2]	3.523
C13	H10[3]	3.345	C13	H11[3]	3.122
C13	H26[8]	2.923	C13	H29[5]	3.261
C13	H30[5]	3.403	C14	H1[3]	3.264
C14	H7[3]	3.139	C14	H8[3]	3.182
C14	H25[4]	3.596	C14	H30[9]	3.028
C15	H14[10]	3.401	C15	H31[9]	3.381
C15	H31[2]	3.567	C16	H6[2]	3.405
C16	H18[11]	3.224	C16	H24[12]	3.593
C16	H31[2]	3.361	C16	H32[1]	3.193
C16	H32[2]	3.225	C17	H9[8]	3.517
C17	H28[1]	3.085	C17	H32[1]	3.590
C18	H29[5]	3.272	C18	H32[1]	3.444
C19	H24[12]	3.532	C19	H29[5]	3.140
C20	H29[5]	3.025	C20	H31[13]	3.502
C20	H32[13]	3.379	C21	H27[5]	3.457
C21	H28[5]	3.377	C21	H29[5]	3.015
C22	H7[8]	3.407	C22	H12[14]	3.371

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
C22	H20[8]	3.474	C22	H23[12]	3.585
C22	H28[5]	3.277	C22	H29[5]	3.122
C23	H7[8]	3.190	C23	H20[8]	3.196
C23	H29[5]	3.239	C23	H30[1]	3.198
C23	H32[1]	3.375	C24	H2[5]	3.509
C24	H4[3]	3.583	C24	H9[5]	3.333
C24	H21[6]	3.386	C25	H8[5]	3.503
C25	H11[7]	3.295	C25	H12[7]	3.436
C25	H13[7]	3.551	C25	H16[2]	3.293
C25	H17[2]	3.088	C25	H18[6]	3.258
C25	H21[6]	3.148	C25	H23[13]	2.877
C25	H26[6]	3.387	H1	O4[5]	2.776
H1	C12[5]	3.520	H1	C14[3]	3.264
H1	H2[5]	3.049	H1	H3[3]	3.119
H1	H10[3]	3.262	H1	H11[3]	2.498
H2	O3[5]	2.713	H2	O4[5]	3.201
H2	C1[5]	3.565	H2	C2[5]	3.148
H2	C12[5]	3.438	H2	C24[5]	3.509
H2	H1[5]	3.049	H2	H2[5]	2.653
H2	H29[5]	3.309	H3	O2[3]	3.020
H3	C11[3]	3.501	H3	H1[3]	3.119
H3	H10[3]	3.059	H3	H27[3]	3.445
H4	O2[3]	3.471	H4	C24[3]	3.583
H4	H27[3]	2.661	H5	O1[2]	2.620
H5	C8[2]	2.882	H5	C9[2]	3.318
H5	H5[2]	2.490	H5	H22[2]	2.743
H6	O1[2]	3.365	H6	C16[2]	3.405
H6	H16[2]	2.456	H6	H22[2]	2.974
H6	H24[4]	3.300	H6	H25[4]	3.089
H7	C14[3]	3.139	H7	C22[8]	3.407
H7	C23[8]	3.190	H7	H10[3]	2.863
H7	H11[3]	2.956	H7	H12[3]	3.066
H7	H25[8]	2.914	H7	H26[8]	2.458
H7	H30[5]	3.317	H8	O3[5]	3.025
H8	O4[5]	3.228	H8	O5[5]	3.517
H8	C12[5]	3.355	H8	C14[3]	3.182
H8	C25[5]	3.503	H8	H10[3]	3.202

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H8	H11[3]	2.545	H8	H12[3]	3.331
H8	H21[8]	3.543	H8	H26[8]	3.054
H8	H29[5]	3.216	H8	H30[5]	2.727
H9	O3[5]	3.400	H9	C17[8]	3.517
H9	C24[5]	3.333	H9	H20[8]	2.851
H9	H21[8]	3.303	H9	H26[8]	2.789
H9	H28[5]	3.541	H9	H29[5]	2.679
H10	C13[3]	3.345	H10	H1[3]	3.262
H10	H3[3]	3.059	H10	H7[3]	2.863
H10	H8[3]	3.202	H10	H10[3]	3.286
H10	H25[4]	3.527	H11	O4[9]	2.649
H11	C2[3]	3.366	H11	C12[9]	3.522
H11	C13[3]	3.122	H11	C25[9]	3.295
H11	H1[3]	2.498	H11	H7[3]	2.956
H11	H8[3]	2.545	H11	H30[9]	2.545
H11	H31[9]	3.301	H12	C22[4]	3.371
H12	C25[9]	3.436	H12	H7[3]	3.066
H12	H8[3]	3.331	H12	H22[2]	3.422
H12	H23[2]	3.208	H12	H25[4]	2.846
H12	H26[4]	3.548	H12	H30[9]	2.649
H12	H31[9]	3.414	H13	C25[9]	3.551
H13	H14[10]	3.187	H13	H22[2]	3.252
H13	H23[2]	2.965	H13	H30[9]	3.381
H13	H31[9]	2.852	H14	O4[9]	2.724
H14	C15[10]	3.401	H14	H13[10]	3.187
H14	H14[10]	3.123	H14	H15[10]	3.327
H14	H30[9]	3.542	H14	H31[9]	3.054
H14	H31[2]	3.478	H15	O4[2]	3.391
H15	C12[2]	3.523	H15	H14[10]	3.327
H15	H31[2]	2.828	H16	O5[2]	2.853
H16	C10[2]	3.164	H16	C25[2]	3.293
H16	H6[2]	2.456	H16	H18[11]	3.548
H16	H24[12]	3.269	H16	H31[2]	3.185
H16	H32[2]	3.215	H17	O5[2]	3.361
H17	C25[2]	3.088	H17	H18[11]	3.254
H17	H24[9]	3.463	H17	H27[3]	3.533
H17	H31[2]	2.753	H17	H32[2]	2.805

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H18	O5[1]	3.576	H18	O5[2]	3.559
H18	C16[11]	3.224	H18	C25[1]	3.258
H18	H16[11]	3.548	H18	H17[11]	3.254
H18	H18[11]	2.471	H18	H24[12]	3.110
H18	H32[1]	2.370	H18	H32[2]	3.125
H19	O2[3]	2.887	H19	H25[8]	3.445
H19	H27[3]	3.117	H19	H28[1]	2.824
H19	H28[3]	3.377	H20	C22[8]	3.474
H20	C23[8]	3.196	H20	H9[8]	2.851
H20	H20[8]	3.408	H20	H25[8]	3.305
H20	H26[8]	2.789	H20	H28[1]	3.074
H20	H29[1]	3.518	H21	O3[1]	3.253
H21	O5[1]	2.883	H21	C24[1]	3.386
H21	C25[1]	3.148	H21	H8[8]	3.543
H21	H9[8]	3.303	H21	H28[1]	2.838
H21	H29[1]	3.597	H21	H30[1]	3.131
H21	H32[1]	2.893	H22	C8[2]	3.575
H22	H5[2]	2.743	H22	H6[2]	2.974
H22	H12[2]	3.422	H22	H13[2]	3.252
H22	H24[12]	3.600	H23	C22[12]	3.585
H23	C25[13]	2.877	H23	H12[2]	3.208
H23	H13[2]	2.965	H23	H29[5]	3.487
H23	H30[13]	2.889	H23	H31[13]	2.619
H23	H32[13]	2.637	H24	C16[12]	3.593
H24	C19[12]	3.532	H24	H6[14]	3.300
H24	H16[12]	3.269	H24	H17[7]	3.463
H24	H18[12]	3.110	H24	H22[12]	3.600
H24	H27[5]	3.509	H24	H28[5]	3.535
H24	H29[5]	3.471	H24	H32[13]	3.156
H25	O2[14]	2.604	H25	C10[14]	3.558
H25	C11[14]	3.597	H25	C14[14]	3.596
H25	H6[14]	3.089	H25	H7[8]	2.914
H25	H10[14]	3.527	H25	H12[14]	2.846
H25	H19[8]	3.445	H25	H20[8]	3.305
H25	H28[5]	3.378	H26	C13[8]	2.923
H26	C25[1]	3.387	H26	H7[8]	2.458
H26	H8[8]	3.054	H26	H9[8]	2.789

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H26	H12[14]	3.548	H26	H20[8]	2.789
H26	H30[1]	2.748	H26	H32[1]	3.189
H27	C6[3]	3.466	H27	C21[5]	3.457
H27	H3[3]	3.445	H27	H4[3]	2.661
H27	H17[3]	3.533	H27	H19[3]	3.117
H27	H24[5]	3.509	H28	C17[6]	3.085
H28	C21[5]	3.377	H28	C22[5]	3.277
H28	H9[5]	3.541	H28	H19[6]	2.824
H28	H19[3]	3.377	H28	H20[6]	3.074
H28	H21[6]	2.838	H28	H24[5]	3.535
H28	H25[5]	3.378	H28	H28[15]	3.589
H29	C4[5]	3.583	H29	C13[5]	3.261
H29	C18[5]	3.272	H29	C19[5]	3.140
H29	C20[5]	3.025	H29	C21[5]	3.015
H29	C22[5]	3.122	H29	C23[5]	3.239
H29	H2[5]	3.309	H29	H8[5]	3.216
H29	H9[5]	2.679	H29	H20[6]	3.518
H29	H21[6]	3.597	H29	H23[5]	3.487
H29	H24[5]	3.471	H30	C13[5]	3.403
H30	C14[7]	3.028	H30	C23[6]	3.198
H30	H7[5]	3.317	H30	H8[5]	2.727
H30	H11[7]	2.545	H30	H12[7]	2.649
H30	H13[7]	3.381	H30	H14[7]	3.542
H30	H21[6]	3.131	H30	H23[13]	2.889
H30	H26[6]	2.748	H31	C15[7]	3.381
H31	C15[2]	3.567	H31	C16[2]	3.361
H31	C20[13]	3.502	H31	H11[7]	3.301
H31	H12[7]	3.414	H31	H13[7]	2.852
H31	H14[7]	3.054	H31	H14[2]	3.478
H31	H15[2]	2.828	H31	H16[2]	3.185
H31	H17[2]	2.753	H31	H23[13]	2.619
H32	Si1[6]	3.511	H32	C16[6]	3.193
H32	C16[2]	3.225	H32	C17[6]	3.590
H32	C18[6]	3.444	H32	C20[13]	3.379
H32	C23[6]	3.375	H32	H16[2]	3.215
H32	H17[2]	2.805	H32	H18[6]	2.370
H32	H18[2]	3.125	H32	H21[6]	2.893

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H32	H23[13]	2.637	H32	H24[13]	3.156
H32	H26[6]	3.189			

Symmetry Operators:

(1) X,Y+1,Z+1
(2) -X+1,-Y,-Z
(3) -X,-Y,-Z
(4) X,Y-1,Z
(5) -X,-Y,-Z-1
(6) X,Y-1,Z-1
(7) X,Y,Z-1
(8) -X,-Y+1,-Z
(9) X,Y,Z+1
(10) -X+1,-Y,-Z+1
(11) -X+1,-Y+1,-Z+1
(12) -X+1,-Y+1,-Z
(13) -X+1,-Y,-Z-1
(14) X,Y+1,Z
(15) -X,-Y-1,-Z-1

X-ray Structure Report

for

194b

April 17, 2015

Experimental

Data Collection

A colorless prismatic crystal of $C_{18}H_{24}O_5$ having approximate dimensions of 0.200 x 0.200 x 0.200 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC7R diffractometer using graphite monochromated Mo-Kα radiation and a rotating anode generator.

Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using the setting angles of 25 carefully centered reflections in the range $29.41 < 2\theta < 29.91^o$ corresponded to a primitive triclinic cell with dimensions:

a =	9.446(2) Å	α =	107.24(2)^o
b =	10.625(4) Å	β =	93.10(2)^o
c =	8.741(2) Å	γ =	92.46(3)^o
V =	835.0(4) Å^3		

For Z = 2 and F.W. = 320.38, the calculated density is 1.274 g/cm^3. Based on a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be:

P-1 (#2)

The data were collected at a temperature of 23 $\pm$ 1^{o}C using the ω-2θ scan technique to a maximum 2θ value of 55.0^o. Omega scans of several intense reflections, made prior to data collection, had an average width at half-height of 0.28^o with a take-off angle of 6.0^o. Scans of (1.57 + 0.30 tan θ)^o were made at a speed of 2.0^o/min (in ω). The weak reflections ($I < 10.0\sigma(I)$) were rescanned (maximum of 5 scans) and the counts were accumulated to ensure good counting statistics. Stationary background counts were recorded on each side of the reflection. The ratio of peak counting time to background counting time was 2:1. The diameter of the incident beam collimator was 0.5 mm and the crystal to detector distance was 235 mm. The computer-controlled slits were set to 3.0 mm (horizontal) and 3.0 mm (vertical).

Data Reduction

Of the 4057 reflections that were collected, 3826 were unique (R_{int} = 0.0252); equivalent reflections were merged. The intensities of three representative reflections were measured after every 150 reflections. No decay correction was applied.

The linear absorption coefficient, μ, for Mo-Kα radiation is 0.919 cm^{-1}. The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods[1] and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement[2] on F^2 was based on 3826 observed reflections and 232 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R1 = \Sigma \; ||Fo| - |Fc|| \; / \; \Sigma \; |Fo| = 0.0429$$

$$wR2 = [\Sigma \; (w \; (Fo^2 - Fc^2)^2 \;)/ \; \Sigma \; w(Fo^2)^2]^{1/2} = 0.1753$$

The standard deviation of an observation of unit weight[3] was 1.02. A Sheldrick weighting scheme was used. Plots of Σ w $(|Fo| - |Fc|)^2$ versus |Fo|, reflection order in data collection, sin θ/λ and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.42 and -0.27 $e^-/Å^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber[4]. Anomalous dispersion effects were included in Fcalc[5]; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley[6]. The values for the mass attenuation coefficients are those of Creagh and Hubbell[7]. All calculations were performed using the CrystalStructure[8,9] crystallographic software package.

References

(1) SIR92: Altomare, A., Cascarano, G., Giacovazzo, C., Guagliardi, A., Burla, M., Polidori, G., and Camalli, M. (1994) J. Appl. Cryst., 27, 435.

(2) Least Squares function minimized:

$\Sigma w(F_o^2-F_c^2)^2$ where w = Least Squares weights.

(3) Standard deviation of an observation of unit weight:

$[\Sigma w(F_o^2-F_c^2)^2/(N_o-N_v)]^{1/2}$

where: N_o = number of observations
N_v = number of variables

(4) Cromer, D. T. & Waber, J. T.; "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

(5) Ibers, J. A. & Hamilton, W. C.; Acta Crystallogr., 17, 781 (1964).

(6) Creagh, D. C. & McAuley, W.J .; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219-222 (1992).

(7) Creagh, D. C. & Hubbell, J.H..; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200-206 (1992).

(8) CrystalStructure 4.0: Crystal Structure Analysis Package, Rigaku Corporation (2000-2010). Tokyo 196-8666, Japan.

(9) CRYSTALS Issue 11: Carruthers, J.R., Rollett,J.S., Betteridge, P.W., Kinna, D., Pearce, L., Larsen, A., and Gabe, E. Chemical Crystallography Laboratory, Oxford, UK. (1999)

EXPERIMENTAL DETAILS

A. Crystal Data

Empirical Formula	$C_{18}H_{24}O_5$
Formula Weight	320.38
Crystal Color, Habit	colorless, prismatic
Crystal Dimensions	0.200 X 0.200 X 0.200 mm
Crystal System	triclinic
Lattice Type	Primitive
No. of Reflections Used for Unit Cell Determination (2θ range)	25 (29.4 - 29.9°)
Omega Scan Peak Width at Half-height	0.28°
Lattice Parameters	a = 9.446(2) Å b = 10.625(4) Å c = 8.741(2) Å α = 107.24(2) ° β = 93.10(2) ° γ = 92.46(3) ° V = 835.0(4) Å^3
Space Group	P-1 (#2)
Z value	2
D_{calc}	1.274 g/cm^3
F_{000}	344.00
μ(MoKα)	0.919 cm^{-1}

B. Intensity Measurements

Diffractometer	AFC7R
Radiation	MoKα (λ = 0.71069 Å) graphite monochromated
Attenuator	Zr foil (factor = 7.21)
Take-off Angle	6.0°
Detector Aperture	3.0 mm horizontal 3.0 mm vertical
Crystal to Detector Distance	235 mm
Voltage, Current	50kV, 100mA
Temperature	23.0°C
Scan Type	ω-2θ
Scan Rate	2.0°/min (in ω) (up to 5 scans)
Scan Width	(1.57 + 0.30 tan θ)°
$2\theta_{max}$	55.0°
No. of Reflections Measured	Total: 4057 Unique: 3826 (R_{int} = 0.0252)
Corrections	Lorentz-polarization

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	$1/[0.0064Fo^2+1.0000\sigma(Fo^2)]/(4Fo^2)$
$2\theta_{max}$ cutoff	55.0^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	3826
No. Variables	232
Reflection/Parameter Ratio	16.49
Residuals: R1 (I>2.00σ(I))	0.0429
Residuals: R (All reflections)	0.0470
Residuals: wR2 (All reflections)	0.1753
Goodness of Fit Indicator	1.016
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.42 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.27 $e^-/Å^3$

Table 1. Atomic coordinates and B_{iso}/B_{eq}

atom	x	y	z	B_{eq}
O1	0.47636(9)	0.2974(1)	1.0382(1)	2.27(2)
O2	0.91054(9)	0.44117(8)	0.3257(1)	1.77(2)
O3	0.8711(1)	-0.00213(8)	0.2698(1)	2.38(2)
O4	1.06319(8)	0.27955(7)	0.28380(9)	1.25(2)
O5	0.7918(1)	0.10750(8)	0.10270(9)	1.92(2)
C1	0.8409(1)	0.2338(1)	0.3723(1)	1.08(2)
C2	0.8930(1)	0.2311(1)	0.5424(2)	1.27(2)
C3	0.7734(1)	0.28392(9)	0.6491(1)	0.98(2)
C4	0.7884(1)	0.3105(1)	0.8099(2)	1.13(2)
C5	0.6758(1)	0.3671(1)	0.9242(2)	1.30(2)
C6	0.5403(1)	0.2817(1)	0.9173(2)	1.30(2)
C7	0.4860(1)	0.18307(9)	0.7597(2)	1.17(2)
C8	0.4132(1)	0.2463(1)	0.6395(2)	1.09(2)
C9	0.5116(1)	0.35030(9)	0.5982(2)	1.08(2)
C10	0.6546(1)	0.3045(1)	0.5447(2)	1.02(2)
C11	0.6912(1)	0.2790(1)	0.3926(2)	1.17(2)
C12	0.9382(1)	0.3315(1)	0.3231(1)	1.07(2)
C13	0.8390(1)	0.0982(1)	0.2462(2)	1.41(2)
C14	0.9281(1)	0.2908(2)	0.8882(2)	1.65(3)
C15	0.2811(1)	0.3124(1)	0.7103(2)	1.54(2)
C16	0.3676(1)	0.1348(1)	0.4847(2)	1.53(2)
C17	1.1716(1)	0.3690(1)	0.2547(2)	1.54(2)
C18	0.7835(2)	-0.0134(2)	-0.0303(2)	2.71(3)

$B_{eq} = 8/3\ \pi^2(U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(cc^*)^2 + 2U_{12}(aa^*bb^*)\cos\gamma + 2U_{13}(aa^*cc^*)\cos\beta + 2U_{23}(bb^*cc^*)\cos\alpha)$

Table 2. Atomic coordinates and B_{iso} involving hydrogen atoms

atom	x	y	z	B_{iso}
H1	0.9098	0.1421	0.5441	1.59
H2	0.9789	0.2875	0.5817	1.67
H3	0.7205	0.3887	1.0321	1.54
H4	0.6483	0.4474	0.9025	1.62
H5	0.5669	0.1367	0.7130	1.47
H6	0.4188	0.1214	0.7844	1.46
H7	0.4660	0.3771	0.5118	1.38
H8	0.5297	0.4267	0.6923	1.35
H9	0.6315	0.2886	0.3091	1.42
H10	0.9718	0.2176	0.8183	2.10
H11	0.9896	0.3692	0.9088	2.10
H12	0.9122	0.2731	0.9876	2.15
H13	0.2154	0.2474	0.7279	1.88
H14	0.3081	0.3784	0.8106	1.92
H15	0.2369	0.3530	0.6371	1.89
H16	0.3159	0.1704	0.4111	1.78
H17	0.4504	0.0956	0.4366	1.72
H18	0.3082	0.0689	0.5095	1.72
H19	1.1996	0.4368	0.3532	1.94
H20	1.2527	0.3212	0.2151	2.02
H21	1.1343	0.4084	0.1767	1.97
H22	0.8736	-0.0525	-0.0359	2.99
H23	0.7117	-0.0739	-0.0140	2.98
H24	0.7601	0.0059	-0.1289	2.99

Table 3. Anisotropic displacement parameters

atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O1	0.0207(5)	0.0468(6)	0.0184(4)	0.0005(4)	0.0080(4)	0.0084(4)
O2	0.0221(5)	0.0170(4)	0.0308(5)	0.0047(4)	0.0036(4)	0.0107(4)
O3	0.0396(6)	0.0159(4)	0.0350(5)	0.0022(4)	0.0055(4)	0.0070(4)
O4	0.0132(4)	0.0153(4)	0.0208(4)	0.0006(3)	0.0051(3)	0.0074(3)
O5	0.0316(5)	0.0227(5)	0.0150(4)	-0.0011(4)	0.0026(3)	-0.0000(4)
C1	0.0126(5)	0.0162(5)	0.0135(5)	0.0016(4)	0.0018(4)	0.0059(4)
C2	0.0126(5)	0.0249(6)	0.0144(5)	0.0059(4)	0.0024(4)	0.0105(4)
C3	0.0098(5)	0.0142(5)	0.0146(5)	0.0009(4)	0.0010(4)	0.0063(4)
C4	0.0120(5)	0.0162(5)	0.0158(5)	-0.0001(4)	0.0013(4)	0.0066(4)
C5	0.0165(5)	0.0177(5)	0.0141(5)	0.0009(4)	0.0027(4)	0.0027(4)
C6	0.0138(5)	0.0215(5)	0.0160(5)	0.0047(4)	0.0037(4)	0.0075(4)
C7	0.0134(5)	0.0138(5)	0.0183(5)	0.0013(4)	0.0031(4)	0.0062(4)
C8	0.0105(5)	0.0136(5)	0.0163(5)	0.0020(4)	0.0015(4)	0.0028(4)
C9	0.0112(5)	0.0133(5)	0.0175(5)	0.0034(4)	0.0021(4)	0.0058(4)
C10	0.0106(5)	0.0138(5)	0.0155(5)	0.0015(4)	0.0002(4)	0.0059(4)
C11	0.0123(5)	0.0176(5)	0.0153(5)	0.0028(4)	0.0002(4)	0.0060(4)
C12	0.0144(5)	0.0151(5)	0.0105(4)	0.0002(4)	0.0002(4)	0.0029(4)
C13	0.0152(5)	0.0177(5)	0.0200(5)	-0.0015(4)	0.0060(4)	0.0043(4)
C14	0.0152(5)	0.0333(6)	0.0169(5)	0.0016(4)	-0.0010(4)	0.0120(5)
C15	0.0130(5)	0.0198(5)	0.0260(6)	0.0050(4)	0.0050(4)	0.0063(4)
C16	0.0192(5)	0.0166(5)	0.0194(5)	0.0004(4)	-0.0010(4)	0.0015(4)
C17	0.0165(5)	0.0194(5)	0.0253(6)	-0.0031(4)	0.0043(4)	0.0110(4)
C18	0.0435(8)	0.0285(7)	0.0209(6)	-0.0088(6)	0.0072(5)	-0.0076(5)

The general temperature factor expression: $\exp(-2\pi^2(a^{*2}U_{11}h^2 + b^{*2}U_{22}k^2 + c^{*2}U_{33}l^2 + 2a^*b^*U_{12}hk + 2a^*c^*U_{13}hl + 2b^*c^*U_{23}kl))$

Table 4. Bond lengths (Å)

atom	atom	distance	atom	atom	distance
O1	C6	1.2179(15)	O2	C12	1.1996(15)
O3	C13	1.1928(16)	O4	C12	1.3435(14)
O4	C17	1.4508(15)	O5	C13	1.3412(15)
O5	C18	1.4506(15)	C1	C2	1.5495(16)
C1	C11	1.5159(14)	C1	C12	1.5261(16)
C1	C13	1.5316(14)	C2	C3	1.5228(14)
C3	C4	1.3471(15)	C3	C10	1.4726(15)
C4	C5	1.5176(15)	C4	C14	1.5055(15)
C5	C6	1.5252(16)	C6	C7	1.5099(14)
C7	C8	1.5514(17)	C8	C9	1.5490(16)
C8	C15	1.5279(15)	C8	C16	1.5368(14)
C9	C10	1.5070(14)	C10	C11	1.3436(15)

Table 5. Bond lengths involving hydrogens (Å)

atom	atom	distance	atom	atom	distance
C2	H1	0.970	C2	H2	0.970
C5	H3	0.970	C5	H4	0.970
C7	H5	0.970	C7	H6	0.970
C9	H7	0.970	C9	H8	0.970
C11	H9	0.930	C14	H10	0.960
C14	H11	0.960	C14	H12	0.960
C15	H13	0.960	C15	H14	0.960
C15	H15	0.960	C16	H16	0.960
C16	H17	0.960	C16	H18	0.960
C17	H19	0.960	C17	H20	0.960
C17	H21	0.960	C18	H22	0.960
C18	H23	0.960	C18	H24	0.960

Table 6. Bond angles (º)

atom	atom	atom	angle	atom	atom	atom	angle
C12	O4	C17	115.54(9)	C13	O5	C18	116.40(10)
C2	C1	C11	103.76(8)	C2	C1	C12	108.78(8)
C2	C1	C13	112.79(10)	C11	C1	C12	112.04(10)
C11	C1	C13	110.18(8)	C12	C1	C13	109.23(9)
C1	C2	C3	105.48(9)	C2	C3	C4	122.03(9)
C2	C3	C10	107.32(9)	C4	C3	C10	130.55(9)
C3	C4	C5	124.97(10)	C3	C4	C14	119.48(9)
C5	C4	C14	115.47(9)	C4	C5	C6	118.14(8)
O1	C6	C5	119.04(9)	O1	C6	C7	121.63(10)
C5	C6	C7	119.29(9)	C6	C7	C8	113.85(9)
C7	C8	C9	113.13(8)	C7	C8	C15	109.29(10)
C7	C8	C16	107.71(9)	C9	C8	C15	108.70(9)
C9	C8	C16	109.05(9)	C15	C8	C16	108.89(8)
C8	C9	C10	115.16(9)	C3	C10	C9	125.68(9)
C3	C10	C11	110.74(9)	C9	C10	C11	123.57(10)
C1	C11	C10	112.48(10)	O2	C12	O4	124.27(11)
O2	C12	C1	125.40(10)	O4	C12	C1	110.25(10)
O3	C13	O5	124.17(10)	O3	C13	C1	126.21(11)
O5	C13	C1	109.61(10)				

Table 7. Bond angles involving hydrogens (º)

atom	atom	atom	angle	atom	atom	atom	angle
C1	C2	H1	111.5	C1	C2	H2	111.3
C3	C2	H1	109.5	C3	C2	H2	109.5
H1	C2	H2	109.5	C4	C5	H3	106.8
C4	C5	H4	107.0	C6	C5	H3	107.7
C6	C5	H4	107.5	H3	C5	H4	109.5
C6	C7	H5	107.0	C6	C7	H6	107.0
C8	C7	H5	109.7	C8	C7	H6	109.7
H5	C7	H6	109.4	C8	C9	H7	109.6
C8	C9	H8	109.4	C10	C9	H7	106.6
C10	C9	H8	106.6	H7	C9	H8	109.4
C1	C11	H9	123.7	C10	C11	H9	123.8
C4	C14	H10	109.6	C4	C14	H11	109.5
C4	C14	H12	109.4	H10	C14	H11	109.4
H10	C14	H12	109.4	H11	C14	H12	109.4
C8	C15	H13	109.6	C8	C15	H14	109.4
C8	C15	H15	109.5	H13	C15	H14	109.4
H13	C15	H15	109.4	H14	C15	H15	109.4
C8	C16	H16	109.4	C8	C16	H17	109.4
C8	C16	H18	109.7	H16	C16	H17	109.4
H16	C16	H18	109.4	H17	C16	H18	109.4
O4	C17	H19	109.3	O4	C17	H20	109.7
O4	C17	H21	109.4	H19	C17	H20	109.4
H19	C17	H21	109.4	H20	C17	H21	109.4
O5	C18	H22	109.3	O5	C18	H23	109.5
O5	C18	H24	109.7	H22	C18	H23	109.4
H22	C18	H24	109.4	H23	C18	H24	109.4

Table 8. Torsion Angles(°)
(Those having bond angles > 160 or < 20 degrees are excluded.)

atom1	atom2	atom3	atom4	angle	atom1	atom2	atom3	atom4	angle
C17	O4	C12	O2	4.55(13)	C17	O4	C12	C1	-172.41(7)
C18	O5	C13	O3	-1.44(17)	C18	O5	C13	C1	-179.93(10)
C2	C1	C11	C10	1.63(11)	C11	C1	C2	C3	-3.83(10)
C2	C1	C12	O2	-102.10(11)	C2	C1	C12	O4	74.82(9)
C12	C1	C2	C3	115.60(9)	C2	C1	C13	O3	0.95(15)
C2	C1	C13	O5	179.40(8)	C13	C1	C2	C3	-123.05(9)
C11	C1	C12	O2	12.02(12)	C11	C1	C12	O4	-171.06(7)
C12	C1	C11	C10	-115.54(9)	C11	C1	C13	O3	-114.47(12)
C11	C1	C13	O5	63.98(12)	C13	C1	C11	C10	122.62(9)
C12	C1	C13	O3	122.05(11)	C12	C1	C13	O5	-59.50(11)
C13	C1	C12	O2	134.39(10)	C13	C1	C12	O4	-48.69(10)
C1	C2	C3	C4	-171.91(8)	C1	C2	C3	C10	4.74(10)
C2	C3	C4	C5	178.03(9)	C2	C3	C4	C14	1.43(15)
C2	C3	C10	C9	177.20(9)	C2	C3	C10	C11	-3.94(11)
C4	C3	C10	C9	-6.54(17)	C4	C3	C10	C11	172.31(10)
C10	C3	C4	C5	2.25(18)	C10	C3	C4	C14	-174.36(9)
C3	C4	C5	C6	67.20(15)	C14	C4	C5	C6	-116.08(10)
C4	C5	C6	O1	151.62(10)	C4	C5	C6	C7	-30.41(15)
O1	C6	C7	C8	102.34(13)	C5	C6	C7	C8	-75.57(12)
C6	C7	C8	C9	57.93(11)	C6	C7	C8	C15	-63.33(10)
C6	C7	C8	C16	178.53(8)	C7	C8	C9	C10	51.69(10)
C15	C8	C9	C10	173.27(8)	C16	C8	C9	C10	-68.15(11)
C8	C9	C10	C3	-73.20(11)	C8	C9	C10	C11	108.08(11)
C3	C10	C11	C1	1.41(12)	C9	C10	C11	C1	-179.70(8)

Table 9. Intramolecular contacts less than 3.60 Å

atom	atom	distance	atom	atom	distance
O1	C8	3.3799(16)	O1	C15	3.3714(17)
O2	O5	3.5986(17)	O2	C2	3.3328(18)
O2	C11	2.8331(16)	O2	C13	3.5291(18)
O2	C17	2.6650(15)	O3	O4	3.3993(16)
O3	C2	2.8744(15)	O3	C11	3.4202(17)
O3	C12	3.4606(18)	O3	C18	2.6745(18)
O4	O5	3.1403(15)	O4	C2	2.9953(16)
O4	C13	2.7389(15)	O5	C11	2.8839(15)
O5	C12	2.8278(15)	C2	C14	2.8957(17)
C3	C6	3.3062(17)	C3	C7	3.1783(16)
C3	C8	3.4021(16)	C3	C12	3.4731(17)
C3	C13	3.5925(17)	C4	C7	3.0601(16)
C4	C9	3.2359(16)	C5	C8	3.3401(17)
C5	C9	3.1226(17)	C5	C10	3.1770(17)
C6	C9	3.0859(18)	C6	C10	3.5577(18)
C6	C15	3.0512(17)	C7	C10	3.0526(18)
C8	C11	3.5570(17)	C10	C12	3.4395(17)
C10	C13	3.4751(17)	C10	C16	3.1207(17)
C11	C16	3.5960(18)			

Table 10. Intramolecular contacts less than 3.60 Å involving hydrogens

atom	atom	distance	atom	atom	distance
O1	H3	2.472	O1	H4	2.774
O1	H5	3.040	O1	H6	2.457
O1	H13	3.468	O1	H14	2.832
O2	H2	3.193	O2	H9	3.008
O2	H19	2.731	O2	H21	2.525
O3	H1	2.430	O3	H2	3.520
O3	H22	2.567	O3	H23	2.717
O4	H1	3.399	O4	H2	2.743
O5	H9	2.781	C2	H9	3.310
C2	H10	2.532	C2	H11	3.167
C3	H3	3.273	C3	H4	2.738
C3	H5	2.634	C3	H7	3.381
C3	H8	2.792	C3	H9	3.209
C3	H10	2.574	C3	H11	2.875
C3	H12	3.206	C4	H1	2.814
C4	H2	2.723	C4	H5	2.656
C4	H8	3.048	C5	H5	2.713
C5	H6	3.383	C5	H8	2.635
C5	H10	3.315	C5	H11	2.974
C5	H12	2.584	C5	H14	3.577
C6	H8	2.835	C6	H12	3.544
C6	H13	3.360	C6	H14	2.697
C7	H3	3.358	C7	H4	3.024
C7	H7	3.409	C7	H8	2.838
C7	H13	2.695	C7	H14	2.676
C7	H15	3.344	C7	H16	3.330
C7	H17	2.696	C7	H18	2.632
C8	H4	3.303	C9	H4	2.773
C9	H5	2.798	C9	H6	3.413
C9	H9	2.737	C9	H13	3.335
C9	H14	2.709	C9	H15	2.635
C9	H16	2.695	C9	H17	2.677
C9	H18	3.347	C10	H1	3.023
C10	H2	3.081	C10	H4	3.050
C10	H5	2.755	C10	H16	3.442
C10	H17	2.780	C11	H1	3.040
C11	H2	3.087	C11	H7	2.546

Table 10. Intramolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
C11	H8	3.139	C11	H17	3.046
C12	H1	3.188	C12	H2	2.454
C12	H9	2.903	C12	H19	2.634
C12	H20	3.163	C12	H21	2.547
C13	H1	2.551	C13	H2	3.201
C13	H9	2.835	C13	H22	2.558
C13	H23	2.648	C13	H24	3.168
C14	H1	2.946	C14	H2	2.737
C14	H3	2.486	C14	H4	3.172
C15	H5	3.350	C15	H6	2.672
C15	H7	2.732	C15	H8	2.631
C15	H16	2.650	C15	H17	3.324
C15	H18	2.693	C16	H5	2.663
C16	H6	2.685	C16	H7	2.637
C16	H8	3.348	C16	H9	3.576
C16	H13	2.644	C16	H14	3.325
C16	H15	2.696	H1	H10	2.324
H1	H11	3.403	H2	H10	2.398
H2	H11	2.726	H2	H19	3.592
H3	H5	3.443	H3	H8	3.525
H3	H10	3.357	H3	H11	2.807
H3	H12	2.219	H4	H5	3.262
H4	H7	3.596	H4	H8	2.048
H4	H11	3.365	H4	H12	3.348
H4	H14	3.268	H5	H8	3.173
H5	H13	3.566	H5	H14	3.573
H5	H16	3.559	H5	H17	2.507
H5	H18	2.876	H6	H13	2.498
H6	H14	2.916	H6	H15	3.560
H6	H16	3.546	H6	H17	3.003
H6	H18	2.462	H7	H9	2.431
H7	H13	3.580	H7	H14	3.074
H7	H15	2.514	H7	H16	2.462
H7	H17	2.861	H7	H18	3.533
H8	H9	3.443	H8	H13	3.536
H8	H14	2.484	H8	H15	2.818
H8	H16	3.544	H8	H17	3.586

Table 10. Intramolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H9	H16	3.448	H9	H17	3.104
H13	H16	2.872	H13	H17	3.535
H13	H18	2.488	H14	H16	3.543
H14	H18	3.552	H15	H16	2.497
H15	H17	3.555	H15	H18	3.012

Table 11. Intermolecular contacts less than 3.60 Å

atom	atom	distance	atom	atom	distance
O1	C17[1]	3.5167(16)	O2	O2[2]	3.2729(15)
O2	C12[2]	3.4836(16)	O2	C15[3]	3.3268(18)
O3	C15[4]	3.5948(19)	O4	C18[5]	3.4622(19)
O5	C14[6]	3.3434(18)	C3	C17[2]	3.5394(19)
C12	O2[2]	3.4836(16)	C14	O5[7]	3.3434(18)
C15	O2[3]	3.3268(18)	C15	O3[4]	3.5948(19)
C17	O1[8]	3.5167(16)	C17	C3[2]	3.5394(19)
C18	O4[5]	3.4622(19)			

Symmetry Operators:

(1)	X-1,Y,Z+1	(2)	-X+2,-Y+1,-Z+1
(3)	-X+1,-Y+1,-Z+1	(4)	-X+1,-Y,-Z+1
(5)	-X+2,-Y,-Z	(6)	X,Y,Z-1
(7)	X,Y,Z+1	(8)	X+1,Y,Z-1

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens

atom	atom	distance	atom	atom	distance
O1	H4[1]	2.918	O1	H8[1]	3.175
O1	H9[2]	2.744	O1	H20[3]	2.662
O1	H23[4]	2.853	O2	H2[5]	2.885
O2	H3[6]	2.947	O2	H11[5]	3.413
O2	H12[6]	2.967	O2	H14[7]	3.284
O2	H15[7]	2.591	O2	H19[5]	2.986
O3	H1[8]	3.236	O3	H6[4]	2.922
O3	H10[8]	2.721	O3	H13[4]	2.704
O3	H18[4]	2.856	O3	H22[9]	3.383
O4	H12[6]	2.869	O4	H15[10]	3.279
O4	H16[10]	3.000	O4	H22[9]	2.835
O4	H23[9]	3.570	O4	H24[9]	3.473
O5	H3[6]	3.314	O5	H6[4]	3.474
O5	H10[6]	3.528	O5	H12[6]	2.531
O5	H22[9]	3.290	C2	H13[10]	3.345
C2	H15[10]	3.410	C2	H18[4]	3.536
C2	H19[5]	3.534	C3	H19[5]	2.973
C3	H21[5]	3.228	C4	H19[5]	3.393
C4	H21[5]	3.010	C4	H24[2]	3.435
C5	H14[1]	2.986	C5	H21[5]	3.276
C6	H4[1]	3.463	C6	H9[2]	3.465
C6	H23[4]	3.482	C7	H17[4]	3.054
C7	H23[4]	3.401	C7	H24[2]	3.525
C9	H7[7]	3.314	C9	H19[5]	3.393
C10	H19[5]	2.887	C11	H19[5]	3.260
C12	H3[6]	3.396	C12	H12[6]	2.807
C12	H19[5]	3.508	C13	H6[4]	3.244
C13	H12[6]	3.405	C13	H18[4]	3.465
C13	H22[9]	3.332	C14	H11[11]	3.552
C14	H13[10]	3.110	C14	H21[2]	3.017
C14	H21[5]	3.476	C14	H24[2]	3.317
C15	H2[12]	2.983	C15	H3[1]	3.306
C15	H4[1]	3.592	C15	H10[12]	3.324
C15	H11[12]	3.316	C16	H5[4]	3.001
C16	H17[4]	3.263	C16	H24[13]	3.170
C17	H4[5]	3.184	C17	H7[10]	3.460
C17	H8[5]	3.409	C17	H11[6]	3.397

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
C17	H12[6]	3.201	C17	H15[10]	3.421
C17	H16[10]	3.152	C17	H22[9]	3.335
C17	H23[9]	3.480	C18	H6[4]	3.363
C18	H10[6]	3.570	C18	H12[6]	3.186
C18	H16[13]	3.314	C18	H20[9]	3.183
C18	H22[9]	3.267	H1	O3[8]	3.236
H1	H1[8]	3.438	H1	H13[10]	3.213
H1	H18[4]	2.892	H2	O2[5]	2.885
H2	C15[10]	2.983	H2	H13[10]	2.627
H2	H14[10]	3.540	H2	H15[10]	2.487
H2	H19[5]	3.360	H2	H21[5]	3.541
H3	O2[2]	2.947	H3	O5[2]	3.314
H3	C12[2]	3.396	H3	C15[1]	3.306
H3	H9[2]	3.061	H3	H11[11]	3.583
H3	H14[1]	2.483	H3	H15[1]	3.336
H3	H21[5]	3.494	H4	O1[1]	2.918
H4	C6[1]	3.463	H4	C15[1]	3.592
H4	C17[5]	3.184	H4	H4[1]	3.415
H4	H14[1]	2.637	H4	H19[5]	3.224
H4	H20[5]	3.062	H4	H21[5]	2.748
H5	C16[4]	3.001	H5	H16[4]	3.374
H5	H17[4]	2.420	H5	H18[4]	2.810
H5	H24[2]	2.873	H6	O3[4]	2.922
H6	O5[4]	3.474	H6	C13[4]	3.244
H6	C18[4]	3.363	H6	H17[4]	2.905
H6	H23[4]	2.572	H7	C9[7]	3.314
H7	C17[12]	3.460	H7	H7[7]	2.732
H7	H8[7]	3.120	H7	H19[12]	2.990
H7	H20[12]	3.091	H8	O1[1]	3.175
H8	C17[5]	3.409	H8	H7[7]	3.120
H8	H9[7]	3.448	H8	H19[5]	2.989
H8	H20[5]	3.180	H8	H21[5]	3.520
H9	O1[6]	2.744	H9	C6[6]	3.465
H9	H3[6]	3.061	H9	H8[7]	3.448
H10	O3[8]	2.721	H10	O5[2]	3.528
H10	C15[10]	3.324	H10	C18[2]	3.570
H10	H13[10]	2.510	H10	H14[10]	3.556

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H10	H15^{10}	3.510	H10	H21^{2}	3.425
H10	H22^{2}	3.575	H10	H22^{8}	3.275
H10	H24^{2}	3.099	H11	O2^{5}	3.413
H11	C14^{11}	3.552	H11	C15^{10}	3.316
H11	C17^{2}	3.397	H11	H3^{11}	3.583
H11	H11^{11}	2.756	H11	H13^{10}	2.848
H11	H14^{10}	3.178	H11	H15^{10}	3.394
H11	H21^{2}	2.559	H11	H21^{5}	2.950
H12	O2^{2}	2.967	H12	O4^{2}	2.869
H12	O5^{2}	2.531	H12	C12^{2}	2.807
H12	C13^{2}	3.405	H12	C17^{2}	3.201
H12	C18^{2}	3.186	H12	H21^{2}	2.675
H12	H22^{2}	3.407	H12	H22^{8}	3.266
H12	H24^{2}	2.990	H13	O3^{4}	2.704
H13	C2^{12}	3.345	H13	C14^{12}	3.110
H13	H1^{12}	3.213	H13	H2^{12}	2.627
H13	H10^{12}	2.510	H13	H11^{12}	2.848
H13	H23^{4}	3.576	H14	O2^{7}	3.284
H14	C5^{1}	2.986	H14	H2^{12}	3.540
H14	H3^{1}	2.483	H14	H4^{1}	2.637
H14	H10^{12}	3.556	H14	H11^{12}	3.178
H15	O2^{7}	2.591	H15	O4^{12}	3.279
H15	C2^{12}	3.410	H15	C17^{12}	3.421
H15	H2^{12}	2.487	H15	H3^{1}	3.336
H15	H10^{12}	3.510	H15	H11^{12}	3.394
H15	H19^{12}	2.884	H16	O4^{12}	3.000
H16	C17^{12}	3.152	H16	C18^{13}	3.314
H16	H5^{4}	3.374	H16	H19^{12}	3.246
H16	H20^{12}	2.731	H16	H22^{13}	3.502
H16	H23^{13}	3.307	H16	H24^{13}	2.657
H17	C7^{4}	3.054	H17	C16^{4}	3.263
H17	H5^{4}	2.420	H17	H6^{4}	2.905
H17	H17^{4}	2.760	H17	H18^{4}	3.031
H17	H24^{13}	3.141	H18	O3^{4}	2.856
H18	C2^{4}	3.536	H18	C13^{4}	3.465
H18	H1^{4}	2.892	H18	H5^{4}	2.810
H18	H17^{4}	3.031	H18	H24^{13}	3.205

Table 12. Intermolecular contacts less than 3.60 Å involving hydrogens (continued)

atom	atom	distance	atom	atom	distance
H19	O2^{5}	2.986	H19	C2^{5}	3.534
H19	C3^{5}	2.973	H19	C4^{5}	3.393
H19	C9^{5}	3.393	H19	C10^{5}	2.887
H19	C11^{5}	3.260	H19	C12^{5}	3.508
H19	H2^{5}	3.360	H19	H4^{5}	3.224
H19	H7^{10}	2.990	H19	H8^{5}	2.989
H19	H15^{10}	2.884	H19	H16^{10}	3.246
H20	O1^{14}	2.662	H20	C18^{9}	3.183
H20	H4^{5}	3.062	H20	H7^{10}	3.091
H20	H8^{5}	3.180	H20	H16^{10}	2.731
H20	H22^{9}	2.980	H20	H23^{9}	2.740
H20	H24^{9}	3.326	H21	C3^{5}	3.228
H21	C4^{5}	3.010	H21	C5^{5}	3.276
H21	C14^{6}	3.017	H21	C14^{5}	3.476
H21	H2^{5}	3.541	H21	H3^{5}	3.494
H21	H4^{5}	2.748	H21	H8^{5}	3.520
H21	H10^{6}	3.425	H21	H11^{6}	2.559
H21	H11^{5}	2.950	H21	H12^{6}	2.675
H22	O3^{9}	3.383	H22	O4^{9}	2.835
H22	O5^{9}	3.290	H22	C13^{9}	3.332
H22	C17^{9}	3.335	H22	C18^{9}	3.267
H22	H10^{6}	3.575	H22	H10^{8}	3.275
H22	H12^{6}	3.407	H22	H12^{8}	3.266
H22	H16^{13}	3.502	H22	H20^{9}	2.980
H22	H22^{9}	2.556	H23	O1^{4}	2.853
H23	O4^{9}	3.570	H23	C6^{4}	3.482
H23	C7^{4}	3.401	H23	C17^{9}	3.480
H23	H6^{4}	2.572	H23	H13^{4}	3.576
H23	H16^{13}	3.307	H23	H20^{9}	2.740
H24	O4^{9}	3.473	H24	C4^{6}	3.435
H24	C7^{6}	3.525	H24	C14^{6}	3.317
H24	C16^{13}	3.170	H24	H5^{6}	2.873
H24	H10^{6}	3.099	H24	H12^{6}	2.990
H24	H16^{13}	2.657	H24	H17^{13}	3.141
H24	H18^{13}	3.205	H24	H20^{9}	3.326

Symmetry Operators:

(1) -X+1,-Y+1,-Z+2	(2) X,Y,Z+1
(3) X-1,Y,Z+1	(4) -X+1,-Y,-Z+1
(5) -X+2,-Y+1,-Z+1	(6) X,Y,Z-1
(7) -X+1,-Y+1,-Z+1	(8) -X+2,-Y,-Z+1
(9) -X+2,-Y,-Z	(10) X+1,Y,Z
(11) -X+2,-Y+1,-Z+2	(12) X-1,Y,Z
(13) -X+1,-Y,-Z	(14) X+1,Y,Z-1

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