三員環の環歪みを利用する炭素–炭素結合の切断を伴う触媒的環化異性化反応の開発

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略語表

Ac	acetyl
acac	acetylacetone
Ad	adamantyl
Ar	aryl
Bu	butyl
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bn	benzyl
Boc	*tert*-butoxycarbonyl
^{n}Bu	normal-butyl
^{t}Bu	*tert*-butyl
°C	degree Celsius
cat.	catalytic amount
cod	1,5-cyclooctadiene
Cp	cyclopentadienyl
Cp*	pentamethylcyclopentadienyl
Cy	cyclohexyl
Δ	heat
DABCO	1,4-diazabicyclo[2.2.2]octane
DART	direct analysis in real time
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	*N*,*N'*-dicyclohexylcarbodiimide
DCE	dichloroethane
DCM	dichloromethane
DIBAL	diisobutylaluminium hydride
DMAP	*N*,*N*-dimethyl-4-aminopyridine
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
dppe	1,2-bis(diphenylphosphino)ethane
dppp	1,3-bis(diphenylphosphino)propane
dppb	1,2-bis(diphenylphosphino)butane
DTBM-SEGPHOS	5,5'-bis[di(3,5-di-tert-butyl-4-methoxyphenyl)phosphino]-4,4'-bi-1,3-benzodioxole
Duanphos	2,2'-di-*tert*-butyl-2,3,2',3'-tetrahydro-1*H*,1'*H*-(1,1')biisophosphindolyl

E	entgegen
EI	electron ionization
ESI	electron spray ionization
Et	ethyl
eq.	equivalent
EWG	electron-withdrawing group
g	gram
h	hour
Hz	hertz
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
IPr	1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene
IR	infrared spectroscopy
J	coupling constant
L_n	ligands
LDA	lithium diisopropylamide
M	metals
*m*CPBA	*m*-chloroperoxybenzoic acid
Me	methyl
Me-Duphos	1,2-bis[2,5-dimethylphospholan-1-yl]benzene
min	minute
MOM	methoxymethyl
MS	molecular sieves
NMO	*N*-methylmorpholine *N*-oxide
NMR	nuclear magnetic resonance
Ph	phenyl
Ph-BPE	1,2-bis(2,5-diphenylphospholano)ethane
Pr	propyl
quant.	quantitative
rac	racemic
RT	room temperature
SEGPHOS	5,5'-bis(diphenylphosphino)-4,4'-bi-1,3-benzodioxole
TBAF	tetrabutylammonium fluoride
TBS	*tert*-butyldimethylsilyl
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid

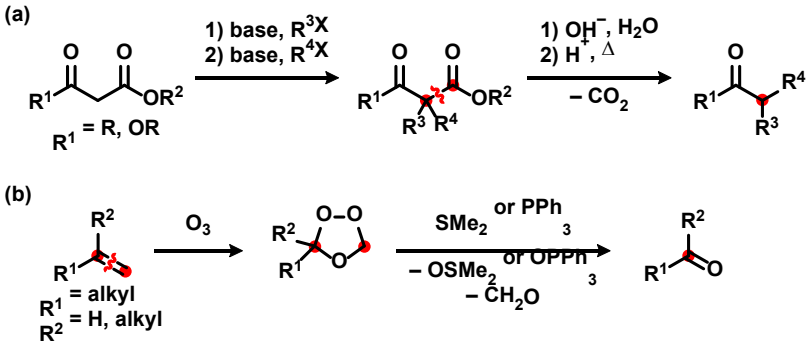
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TMS	trimethylsilyl
tol	tolyl
Ts	*p*-toluenesulfonyl
UV	ultraviolet light
Vis	visible light
Xantphos	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene
Z	zusammen

第 1 章

序論

第 1 節　炭素–炭素結合の切断を伴う反応

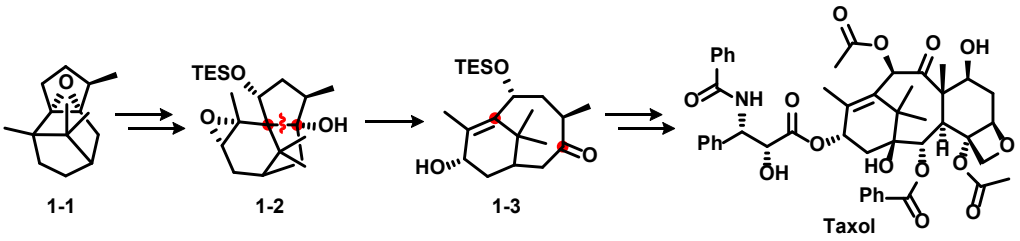
炭素–炭素結合は有機分子骨格における基本的かつ普遍的な結合であり、それゆえに炭素–炭素結合形成法の研究は有機合成化学の最も重要な位置を占める。炭素骨格構築において、炭素–炭素結合形成と表裏一体の関係にあるのが、炭素–炭素結合切断である。通常、小さな分子同士をつなぐことで目標分子を合成することが多いため、一見すると、炭素–炭素結合を切断することは一般的な合成戦略に相反するように思われる。しかし、炭素–炭素結合の切断は、有機合成における有用な分子変換手法になり得る。例えば、アセト酢酸エステル合成法やマロン酸エステル合成法には、炭素–炭素結合が切断される脱炭酸過程が含まれる。アセト酢酸エステルやマロン酸エステルは、活性メチレン部位を有するため弱い塩基で容易に脱プロトン化され、アルキル化される（**Scheme 1-1a**）。その後、脱炭酸することで、結果として温和な条件で種々のケトンやエステルを合成することができる。また、天然物全合成にて汎用される酸化手段にオゾン分解法がある（**Scheme 1-1b**）。この反応では、まず、酸化能の高いオゾンをオレフィンと反応させることで、炭素–炭素二重結合を切断する。続いて、生じたオゾニド中間体に対して、還元剤を作用させることで二種類のカルボニル化合物へと誘導する。とりわけ、一置換アルケンや 1,1-二置換アルケンを基質に用いると、ホルムアルデヒドが系外に放出され、アルデヒドやケトンが得られる。



Scheme 1-1　代表的な炭素–炭素結合切断反応

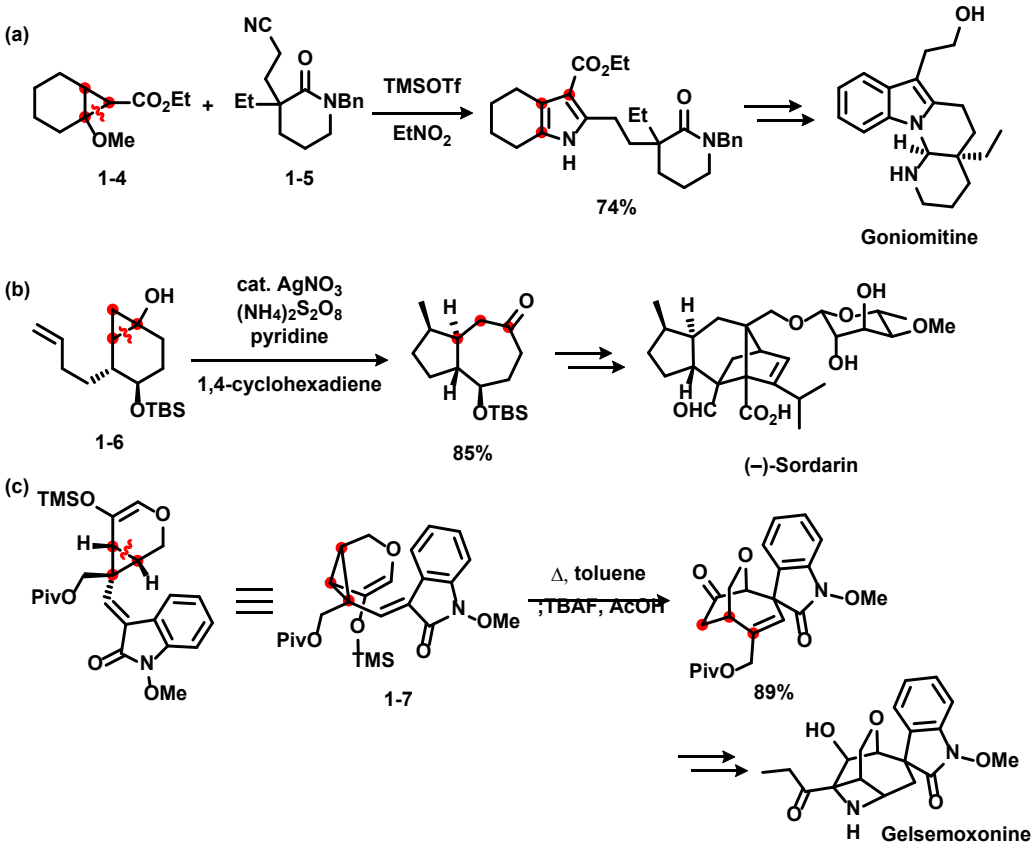
さらに、炭素–炭素結合を切断する戦略は、炭素–炭素結合の形成のみに焦点を当てた戦略では到達できない分子を合成できる場合がある。1994 年に、Holton らは、世界に先駆けて Taxol の全合成を報告した（**Scheme 1-2**）[1]。彼らは、市販される天然物 **1-1** を出発物質として、β-ヒドロキシエポキシド中間体 **1-2** へと誘導した。**1-2** は非常に不安定

であり、ヒドロキシ基の酸素電子の押し込みに伴い炭素–炭素結合の切断およびエポキシドの開環が進行し、**1-3** へと変換される。このように、彼らは、積極的に炭素–炭素結合を切断することで、当時到達不可能だと考えられていた 6 員環と 8 員環の二環式複雑骨格を有する **1-3** を合成することに成功した。その後、**1-3** を母核として Taxol の全合成が達成された。



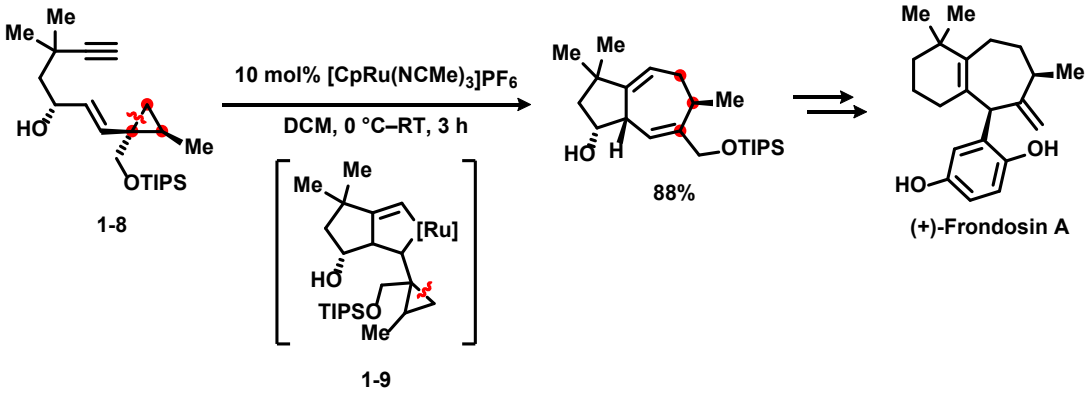
Scheme 1-2 先駆的な Taxol 全合成

高い反応性を有する試薬や複雑な基質設計を必要とする上記の反応例に対して、容易に調製可能 [2] なシクロプロパンの高い環歪みを利用すると、比較的温和な条件で炭素–炭素結合を切断できる。シクロプロパンは、炭素–炭素結合の切断と形成を伴う環拡大反応を可能にし、複雑な分子を合成する際の 3 炭素ビルディングブロックとして用いられる。例えば、Pagenkopf らは、TMSOTf の存在下で、ドナーアクセプター型シクロプロパン **1-4** とニトリル **1-5** の[3+2]付加環化反応によって、ピロール骨格を構築し、Goniomitine の全合成を達成している（**Scheme 1-3a**）[3a]。また、奈良坂らは、シクロプロパノール **1-6** に $AgNO_3$ を作用させることで、酸化的にアルコキシラジカルを調製し、その β-開裂に続く分子内ラジカル付加により、5,7-縮環炭素骨格を構築している。その後、カルボニル基を足掛かりとして、複雑な環骨格を有する (−)-Sordarin の合成に成功した（**Scheme 1-3b**）[3b]。福山らが 2011 年に報告した Gelsemoxonine の全合成では、中間体 **1-7** において、ジビニルシクロプロパンの熱的転位反応を利用することで、スピロ 7 員環骨格を構築している（**Scheme 1-3c**）[3c]。



Scheme 1-3 シクロプロパンの炭素–炭素結合の切断を利用する天然物の合成

単純な基質から複雑な分子を触媒的かつ効率的に合成する手法は、有機合成化学を基盤とする創薬に大きく貢献することができる。とりわけ、基質の環化に伴い構造異性体を与える触媒的環化異性化反応は、レドックスニュートラルで原子効率の高い反応であり、用いる基質の設計次第で、一挙に複雑環骨格を構築することを可能にする。例えば、Trost らは、ルテニウム触媒と **1-8** を反応させることで、ルテナサイクル **1-9** における β-炭素脱離を伴って 5,7-縮環炭素骨格を一挙に構築し、(+)-Frondosin A の全合成を達成している（**Scheme 1-4**）[4]。



Scheme 1-4 ルテニウム触媒による分子内環化反応を利用した
(+)-Frondosin A の全合成

以上の反応例が示すように、多様な活性化に基づく、選択的な炭素–炭素結合切断を可能にするシクロプロパンは、有用な 3 炭素ビルディングブロックである。第 2 節では、なぜシクロプロパンの炭素–炭素結合が特異な性質を有するのかについて説明する。

第 2 節　シクロプロパンの炭素–炭素結合

3 つの sp^3 炭素が環状に配置されたシクロプロパンは、(i) シクロアルカンの中で最も大きな環歪みを有し、炭素–炭素結合が比較的弱く、(ii) 炭素–炭素結合と炭素–水素結合が、アルケンの炭素–炭素 σ 結合と炭素–水素結合に類似するという特異な性質を有している。**Figure 1-1** に、Goddard らによって見積もられた種々のシクロアルカンの環歪みエネルギーを示す[5]。置換様式によって多少の差はあるが、シクロヘキサンやシクロペンタンに比べて、シクロブタンやシクロプロパンは環歪みエネルギーが高いことが分かる。

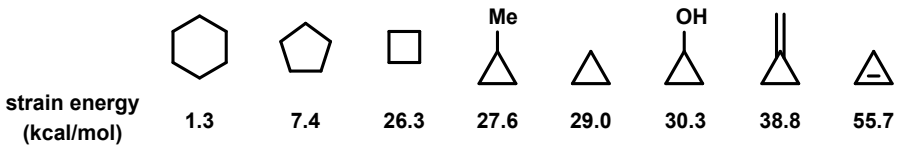


Figure 1-1 代表的なシクロアルカンの環歪みエネルギー

シクロプロパンの性質を理解する際には、Coulson モデルが用いられる（**Figure 1-2**）[6]。シクロプロパンは三角形構造であるために、理想的な結合角は 60 度となる。しかし、これは sp^3 混成軌道を有する原子同士の安定な結合角である 109.5 度から大きく離れている。Coulson モデルでは、その結合は原子間の直線上には存在せず、曲がった結合（バナナボンド）として表現され、その結合角が 104 度になるとされている。このように、sp^3 混成軌道を有する原子同士の結合と比較して、バナナボンドの軌道の重なりは小さいために、弱い炭素–炭素結合であることを説明できる。

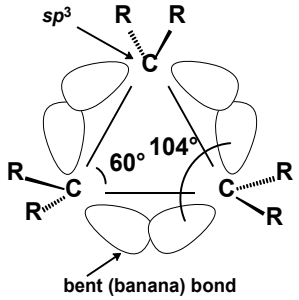


Figure 1-2 Coulson モデルによるシクロプロパン

シクロプロパンは 3 つの sp^3 炭素から構築されているとする Coulson モデルに対して、3 つの sp^2 炭素から構築されているとするのが Walsh モデルである（**Figure 1-3**）[7]。Walsh モデルでは、3 つの炭素中心で sp^2 混成軌道が重なり合い σ 結合を形成し、p 軌道の重なりにより π 結合を形成すると考える。実際、シクロプロパンの炭素–炭素結合間距離は 1.51 Å で、通常の炭素–炭素結合長の 1.53 Å よりも短いことが知られている[8]。Walsh モデルにより、シクロプロパンの炭素–炭素結合の π 結合性が増していることおよび炭素–水素結合の水素が高い酸性度を有していることを説明できる。

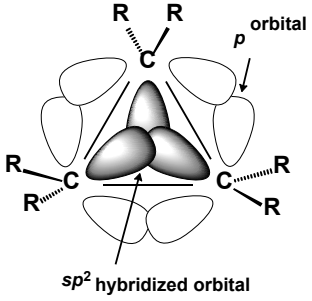
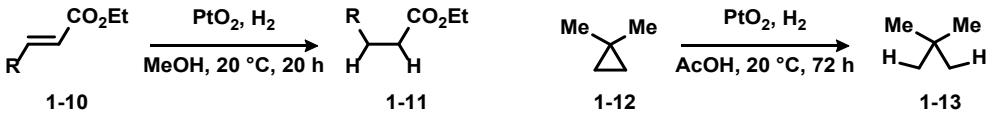


Figure 1-3 Walsh モデルによるシクロプロパン

以上のように、シクロプロパンは特異な炭素–炭素結合を有していると考えられており、典型的なシクロアルカンよりも反応性が高いことが知られている。そのため、適切な条件下で炭素–炭素結合の切断が可能である。

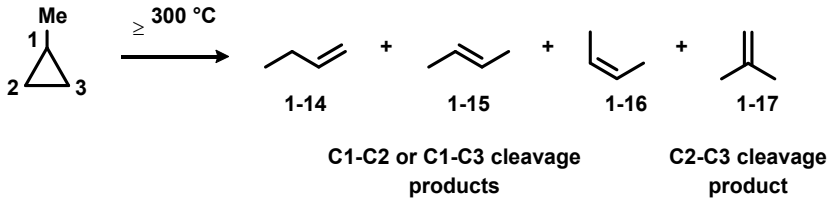
第 3 節　シクロプロパンの炭素–炭素結合切断の反応性と選択性

シクロプロパンの炭素–炭素結合切断を含む変換反応はこれまでに数多く報告されている。シクロプロパンの環歪みに起因する弱い結合と二重結合に類似した反応性を端的に表す例として、酸化白金を用いる接触水素化反応が挙げられる（**Scheme 1-5**）[9]。アルケン **1-10** に分子状水素が付加して **1-11** に還元されるのと同様に、シクロプロパン **1-12** は炭素–炭素結合の切断を伴って **1-13** に還元される。



Scheme 1-5 アルケンとシクロプロパンの接触水素化反応

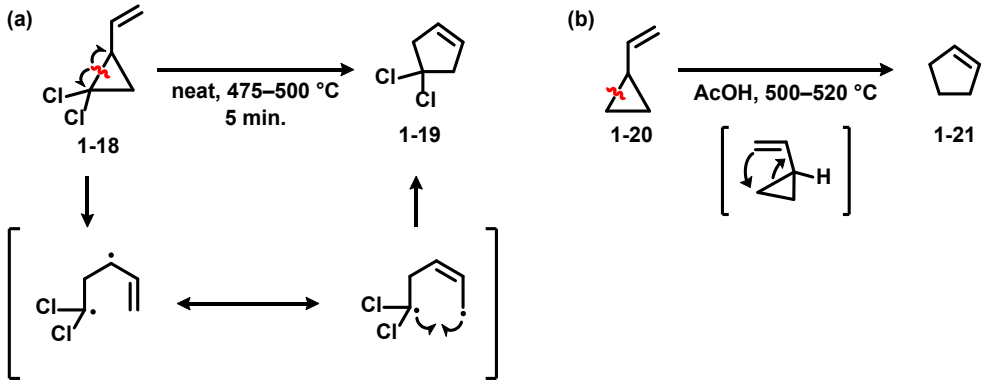
一方、単純なメチルシクロプロパンを 300 度以上に加熱すると、その炭素–炭素結合は無秩序に切断されて、4 種類の生成物を与える（**Scheme 1-6**）[10]。**1-14**、**1-15** および **1-16** は、C1–C2 もしくは C1–C3 の切断により生じ、**1-17** は C2–C3 の切断により生じる。このように、置換基を有するシクロプロパンの炭素－炭素結合を切断する際には、位置選択性が問題となる。



Scheme 1-6 高温条件下でのメチルシクロプロパンの炭素–炭素結合切断

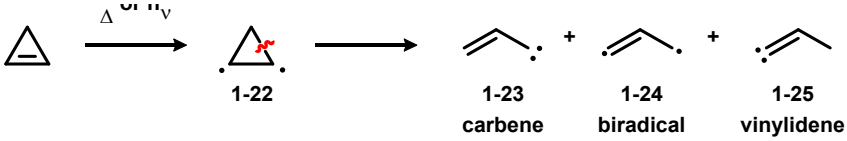
この問題は、シクロプロパン基質の設計を工夫することで解決される場合がある。例えば、ビニルシクロプロパンは、シクロプロパンの反応性に、ビニル基の π 電子に起因

する反応性が加わるため、特有の炭素–炭素結合切断様式が知られている。1959 年に、Neureiter は、ジクロロビニルシクロプロパン **1-18** を 475 ℃から 500 ℃程の高温にさらすことで、シクロペンテン **1-19** の生成を観測した（**Scheme 1-7a**）[11]。この反応では、安定なアリルラジカル中間体が生成するように、ホモリティックな炭素–炭素結合切断が進行していると考えられている。その翌年には、Overberger と Borchert が、**1-20** から **1-21** への環拡大反応が酢酸溶媒中で観測できることを報告した（**Scheme 1-7b**）[12]。彼らは、ビニル基の π 電子がシクロプロパンのバナナボンドの反結合性軌道に流れ込むことで、この反応が進行したと考察している。このように、ビニル基をシクロプロパンに導入することで、位置選択的にその炭素–炭素結合を切断することが可能になる。



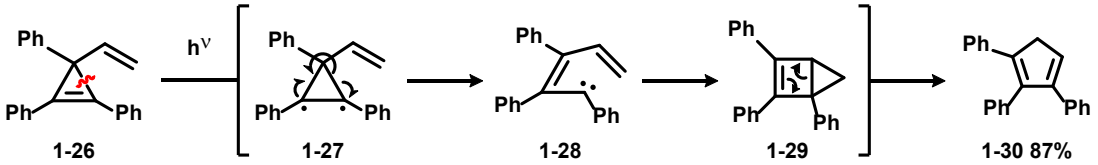
Scheme 1-7 熱分解によるビニルシクロプロパンの環拡大反応

また、環内に二重結合を有するシクロプロペンは、3 つの構成炭素のうち 2 つが sp^2 混成軌道を有している。sp^3 混成軌道を有する原子同士の安定な結合角は 109.5 度であるのに対して、sp^2 混成軌道を有する原子同士の結合角は 120 度であるために、その環歪みはシクロプロパンよりも大きく、55.7 kcal/mol 程度である（**Figure 1-1**）[5]。その大きな環歪みのために、紫外光照射条件や熱的条件にて、その炭素–炭素結合は切断され得る[13]。まず、シクロプロペン中の最も弱い π 結合がホモリティックに切断され **1-22** となった後に、カルベン **1-23**、ビラジカル **1-24** やビニリデン **1-25** などの高活性混合物が生成すると考えられている（**Scheme 1-8**）。



Scheme 1-8 紫外光照射条件や熱的条件によるシクロプロペンの炭素–炭素結合切断

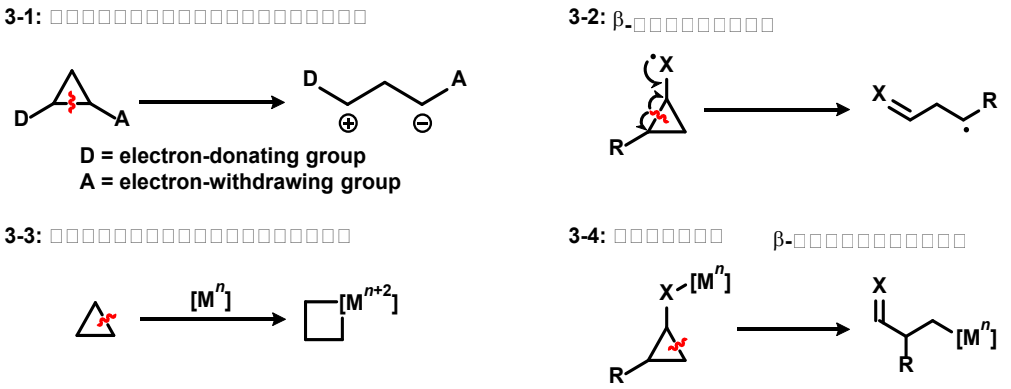
Padwa らは、三つのフェニル基を導入したビニルシクロプロペン **1-26** を設計することで、シクロプロペンの高い反応性を有効に利用した環拡大反応を報告した（**Scheme 1-9**）[14]。まず、**1-26** に紫外光を照射するとビラジカル中間体 **1-27** が生じる。次に、**1-27** は比較的安定なカルベン中間体 **1-28** を与えるようにして、炭素–炭素結合が選択的に切断される。**1-28** は、速やかに分子内のアルケンに捕捉され、**1-29** が形成される。最後に、**1-29** の電子環状反応によってシクロペンタジエン **1-30** が得られる。



Scheme 1-9 紫外光照射条件によるビニルシクロプロペン基質の反応

以上のように、シクロプロパンへビニル基を導入することで、ビニル基に隣接する炭素–炭素結合を選択的に切断することが可能となる。これらの先駆的な反応は、3 炭素ビルディングブロックとしてのシクロプロパンのポテンシャルを示したが、高温条件やエネルギーの強い紫外光を必要とするために実用的とは言い難い。

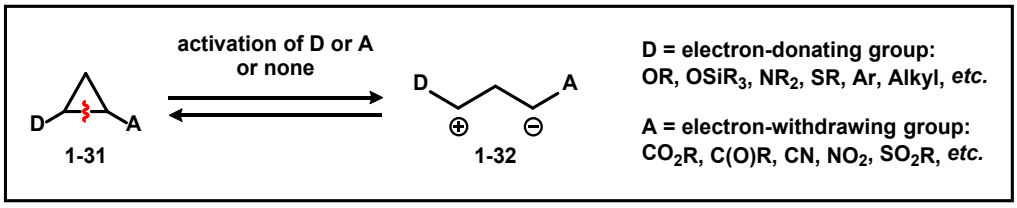
その後、多くの研究者が、シクロプロパンの合成化学的有用性を高めることを目指し、種々のシクロプロパン基質を設計し、様々な活性化手法を見出してきた。その結果、今日では、温和な条件下でその炭素–炭素結合を選択的に切断することが可能になってきている。以降では、どのようなシクロプロパンに対して、どのようにその炭素–炭素結合を選択的に切断するのかに焦点を当て、シクロプロパンの炭素–炭素結合切断様式を説明する。具体的には、ドナーアクセプター型シクロプロパンを用いる切断、ラジカル種の β-開裂を利用する切断、遷移金属錯体の酸化的付加を利用する切断および遷移金属錯体の β-炭素脱離を利用する切断の 4 つの項目に大別して説明する（**Scheme 1-10**）。



Scheme 1-10 近年の代表的なシクロプロパンの炭素–炭素結合切断様式

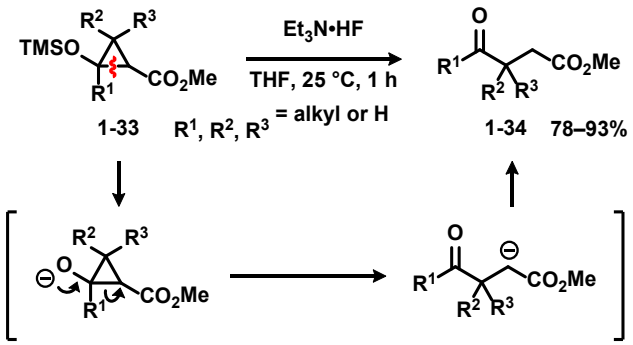
3-1 ドナーアクセプター型シクロプロパンの炭素–炭素結合切断

ビシナル位に電子供与基と電子求引基をそれぞれ導入したシクロプロパン **1-31** をドナーアクセプター型シクロプロパンと呼ぶ（**Scheme 1-11**）。ドナーアクセプター型シクロプロパンは、電子供与基の電子の押し込みと電子求引基の電子の引き込みによって、両置換基間の炭素–炭素結合が大きく分極し、ヘテロリティックに切断されやすくなっている。すなわち、両置換基間の炭素–炭素結合を選択的に切断することが可能である。その極限構造は双性イオンである 1,3-双極子 **1-32** として描かれ、負電荷は電子求引基によって安定化され、正電荷は電子供与基によって安定化されている。電子供与基にはアルコキシ基やアミノ基などが、電子求引基にはアルコキシカルボニル基やシアノ基などが該当する。



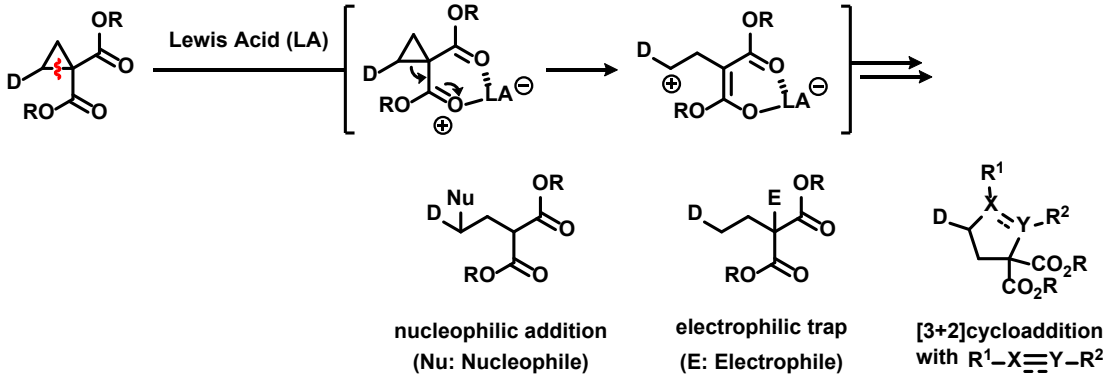
Scheme1-11 ドナーアクセプター型シクロプロパンとその炭素–炭素結合切断

1980 年に、Reissig らは、シロキシ基とメトキシカルボニル基を有するシクロプロパン **1-33** に $Et_3N\cdot HF$ を作用させ、シリル基を脱保護しようと試みたところ、選択的に炭素–炭素結合が切断されたケトン **1-34** が得られたことを報告した（**Scheme 1-12**）[15]。この選択的な炭素–炭素結合の切断は、シリル基脱保護後に生成するアルコキシドからの電子の押し込みとメトキシカルボニル基の電子の引き込みによって実現したものである。



Scheme 1-12 シロキシ基とメトキシカルボニル基を有するシクロプロパンの反応

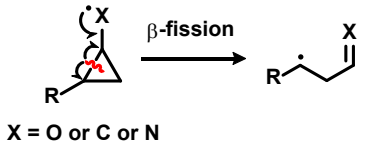
一方、電子供与基の活性化ではなく、ブレンステッド酸やルイス酸を用いる電子求引基の活性化によっても、炭素–炭素結合を切断できる。例えば、ルイス酸は電子求引基に配位し、LUMO を低下させることで、炭素–炭素結合の切断を引き起こす（**Scheme 1-13**）。多くの場合、ルイス酸に配位しやすいジエステル部位を有する基質が用いられ、求核剤や求電子剤との反応、あるいは付加環化反応に用いられる [16]。



Scheme 1-13 ルイス酸を用いたドナーアクセプター型シクロプロパンの炭素–炭素結合切断

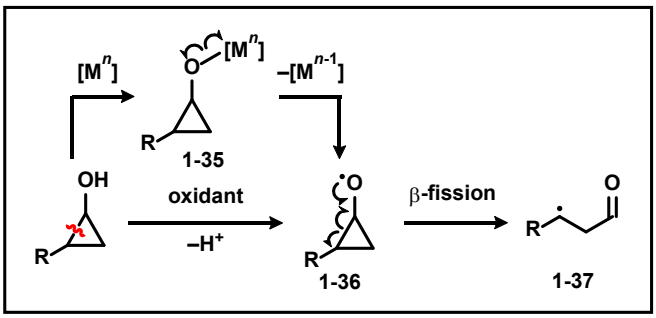
3-2 β-開裂を利用した炭素–炭素結合切断

シクロプロポキシラジカル、シクロプロピルメチルラジカルおよびシクロプロピルアミニルラジカルは、安定な二重結合の形成とシクロプロパンの環歪みの解消を駆動力として、速やかに β-開裂を起こす（**Scheme 1-14**）[17]。この場合、より安定なラジカル中間体が生じるように選択的に炭素–炭素結合が切断される。



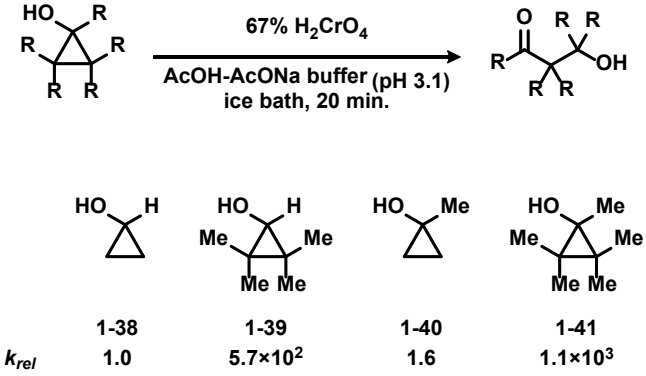
Scheme 1-14 シクロプロパンのホモリティックな炭素–炭素結合切断

シクロプロパノールとクロム(VI)[18a–b]、銅(II)[18c]、鉄(III)[18d–e]、マンガン(III)[18f] あるいはバナジウム(V)[18g] などの遷移金属錯体から調製されるメタルシクロプロポキシド **1-35** は、酸化的な金属–酸素結合の切断に伴い、シクロプロポキシラジカル **1-36** へと変換される（**Scheme 1-15**）。また、遷移金属錯体を用いない酸化 [19] や可視光照射を駆動力とする光触媒による酸化 [20] でも **1-36** を調製できることが知られている。**1-36** は、β-開裂によって、β-ケトラジカル **1-37** へと変換される。



Scheme 1-15 シクロプロパノールの β-開裂による炭素–炭素結合切断

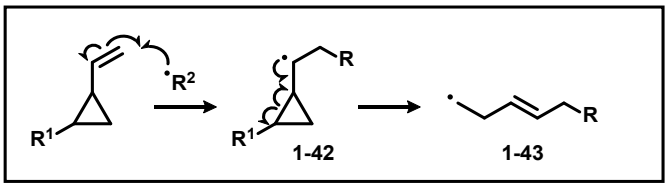
遷移金属錯体が促進するシクロプロポキシラジカルの β-開裂に関する先駆的な研究は、約 50 年前に報告された。Rocek らは、クロム(VI)を用いて、種々の置換基を有するシクロプロパノールの酸化反応の反応速度を詳細に調べた [18a–b]。**Scheme 1-16** に、酸化反応の詳細と単純なシクロプロパノール **1-38** を基準としたときの種々のシクロプロパノールの相対的な反応速度定数（k_{rel}）を示す。まず、**1-38** と比較して、テトラメチルシクロプロパノール **1-39** を用いた反応は、570 倍速くなることが分かった。これは、**1-38** では第一級ラジカルが生じるのに対して、**1-39** ではより安定な第三級ラジカルが生じることに起因する。次に、著者らは、**1-40** の反応が **1-38** の反応よりも 1.6 倍速いことに関して、生成物のアルデヒドの C=O 二重結合よりもケトンの C=O 二重結合の方が安定であるからと考察している。最後に、本反応条件にて、第三級ラジカルを中間体として、より安定な C=O 二重結合を有するケトンへと変換される **1-41** を用いた反応は、**1-38** を用いた反応よりも大幅に速くなることが確認された。



Scheme 1-16 クロム(VI)酸化剤を用いた種々のシクロプロパノールの酸化反応

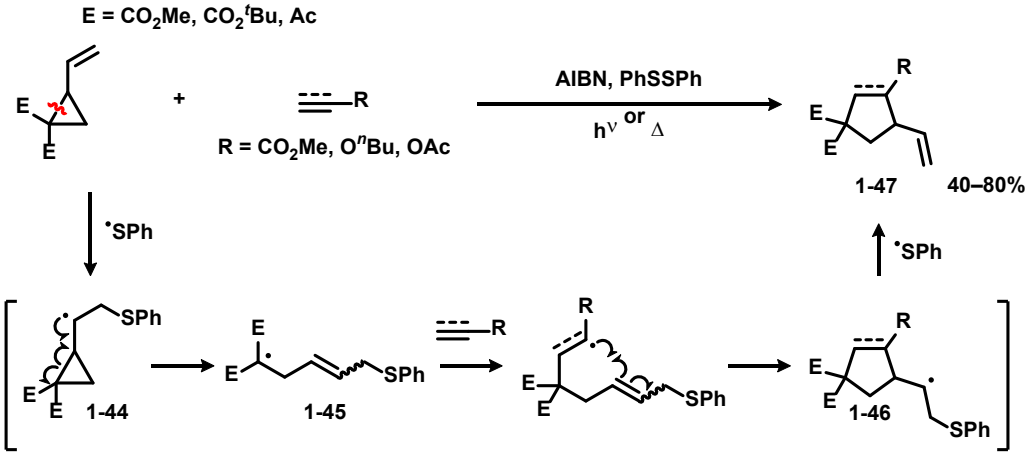
一方、ビニルシクロプロパンにラジカル種を作用させると、ビニル基へのラジカル付加が進行する（**Scheme 1-17**）。生成するラジカル種の安定性から、シクロプロピルメチ

ルラジカル誘導体 **1-42** が主なラジカル付加体となる。**1-42** は、β-開裂によって、3-ブテニルラジカル誘導体 **1-43** へと変換される。



Scheme 1-17 ビニルシクロプロパンの β-開裂による炭素–炭素結合切断

シクロプロパンの β-開裂を利用したメタルフリーな触媒的環化反応の先駆的な例として、チイルラジカルを触媒とする[3+2]付加環化反応が挙げられる（**Scheme 1-18**）[21]。これらの反応では、ラジカル開始剤である AIBN によって生じたチイルラジカルがビニルシクロプロパンにラジカル付加する。続いて、安定なラジカル中間体 **1-45** が生成するように、**1-44** は位置選択的に炭素–炭素結合が切断される。ここで、アルケンやアルキンとの連続的なラジカル付加反応が進行することで、**1-46** が生じる。最終的に、チイルラジカルが再生するとともに、ビニルシクロペンタンやビニルシクロペンテン **1-47** が得られる。

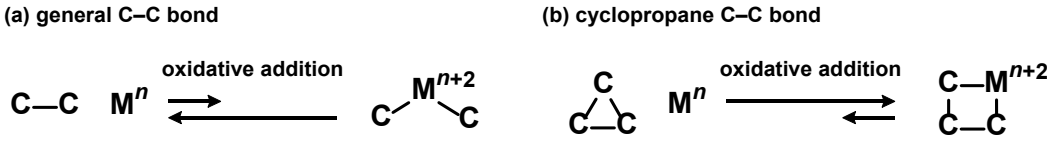


Scheme 1-18 ビニルシクロプロパンを用いたラジカルが媒介する[3+2]付加環化反応

3-3 遷移金属錯体の酸化的付加過程を利用した炭素–炭素結合切断

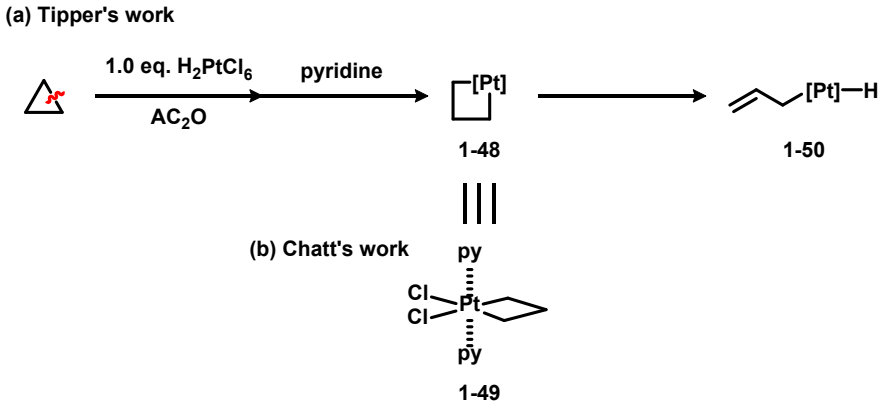
β-開裂を利用する手法は、非常に高活性なラジカル中間体を与えるために、基質適用範囲に制限があるケースがあった。一方、遷移金属錯体の酸化的付加を利用する手法は、二電子過程であるために、様々な分子変換反応への展開が期待できる。

一般的に、遷移金属錯体（M^n）の炭素–炭素結合（C–C）への酸化的付加は、熱力学的に不利である。なぜなら、炭素–炭素結合の結合エネルギーが約 90 kcal/mol であるのに対して、金属–炭素結合の結合エネルギーは 20–30 kcal/mol 程度だからである（**Scheme 1-19a**）[22]。一方、大きな環歪みを有するシクロプロパンの炭素–炭素結合への酸化的付加では、環歪みの解消を駆動力とし、より環歪みの小さいメタラシクロブタンを形成するので、熱力学的に不利な炭素–炭素結合活性化過程を克服することができる（**Scheme 1-19b**）。



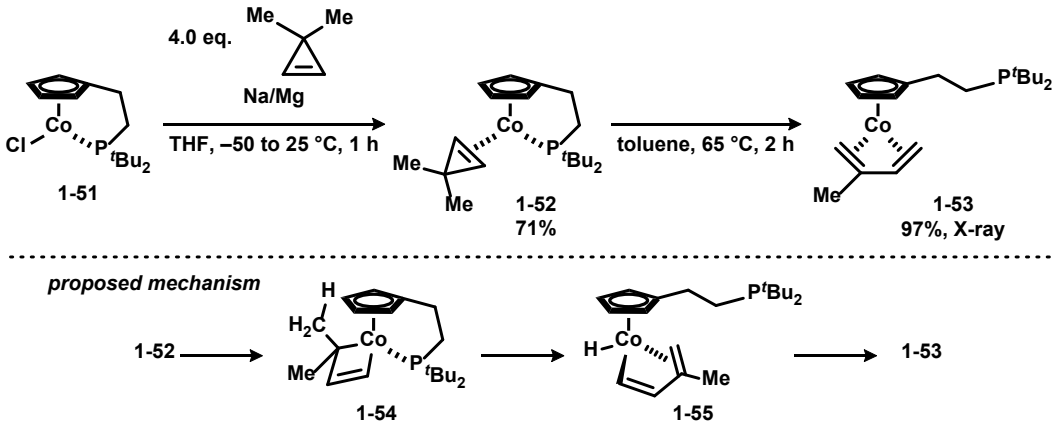
Scheme 1-19 遷移金属の炭素–炭素結合への酸化的付加

1955 年に、Tipper らは、H_2PtCl_6 を用いることで、初めて遷移金属錯体のシクロプロパンへの酸化的付加を観測し、メタラシクロブタン **1-48** を単離した（**Scheme 1-20a**）[23a]。その後、Chatt らが、そのプラチナシクロブタンの構造が **1-49** であると同定した（**Scheme 1-20b**）[23b]。しかし、このプラチナシクロブタンは不安定で、容易に β-水素脱離を起こし、**1-50** を与える。



Scheme 1-20 遷移金属の単純なシクロプロパンへの酸化的付加

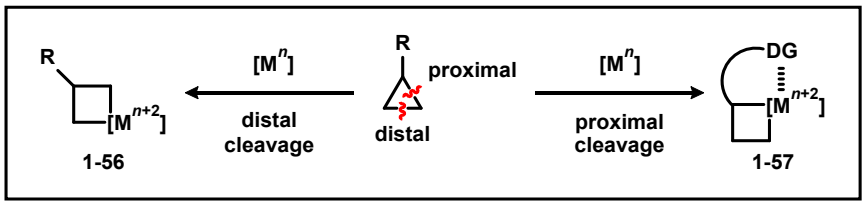
また、Butenschön らは、シクロプロパンよりも環歪みが大きいシクロプロペンを用いて、遷移金属錯体の酸化的付加過程を間接的に観測した。彼らは、ジメチルシクロプロペンの存在下、二価のコバルト錯体 **1-51** の還元により、一価のコバルト錯体 **1-52** を調製および単離した（**Scheme 1-21**）[24]。続いて、**1-52** のトルエン溶液を 65 ℃に加熱することで、**1-53** を得た。この **1-53** の構造は、X 線結晶構造解析により決定している。**1-53** の生成過程に関して、彼らは、以下のように述べている。まず、コバルトがシクロプロペンの炭素–炭素単結合に酸化的付加し、コバルタシクロブテン中間体 **1-54** が生成する。続いて、この **1-54** には β-水素が存在するので、速やかに β-水素脱離が起こり、**1-55** となる。最後に、**1-55** の還元的脱離によって、**1-53** が得られる。



Scheme 1-21 コバルト錯体のジメチルシクロプロペンへの酸化的付加

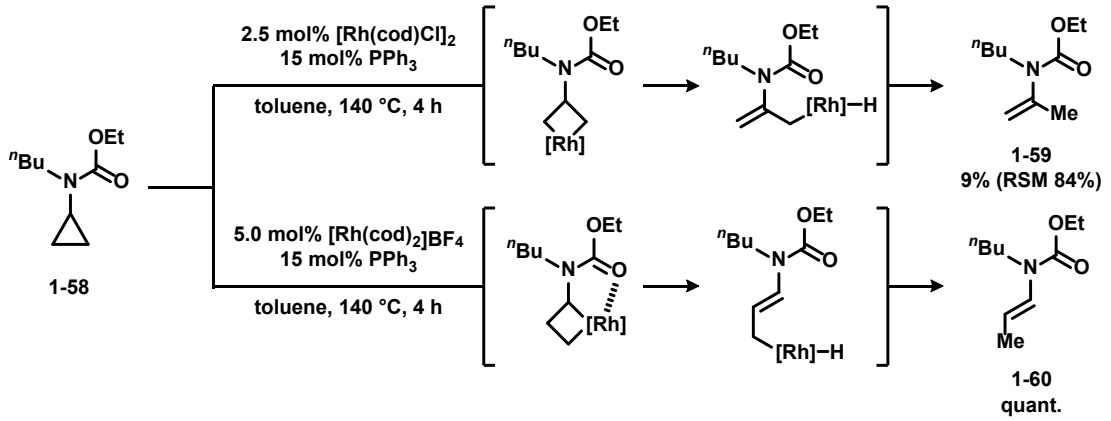
これらの先駆的な研究によって、安定な炭素–炭素結合を切断する手法として、遷移金属錯体の酸化的付加過程が有効であることが広く知られるようになった。その後、シクロプロパンに合成化学的価値を付与するために、その基質設計に焦点が置かれた。

単純なシクロプロパンに置換基を導入した場合、その炭素–炭素結合は非等価になるため、遷移金属錯体が酸化的付加する炭素–炭素結合の位置は 2 通りになる（**Scheme 1-22**）。一般に、導入された置換基との立体障害を避けるようにして、distal 位の炭素–炭素結合が切断され、**1-56** を与える。しかし、導入された置換基が配向基として機能する場合、選択的な proximal 位の炭素–炭素結合の切断が可能となり、**1-57** を与える。この場合、配向基によって、金属中心を当該結合の近傍に位置させることができるため、その酸化的付加の速度は向上する。



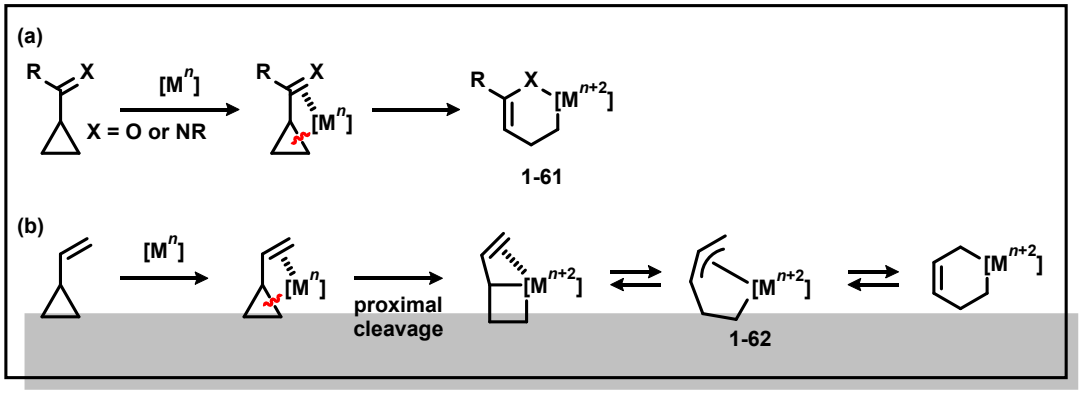
Scheme 1-22 遷移金属錯体による一置換シクロプロパンへの酸化的付加

Bower らは、ロジウム触媒とシクロプロピルアミド **1-58** を用いて、ロジウム触媒の種類による酸化的付加の位置選択性への影響とその効率を調査している（**Scheme 1-23**）[25]。まず、**1-58** に中性ロジウム錯体触媒を作用させると、ブランチ体 **1-59** が収率 9%で得られた。一方で、カチオン性ロジウム錯体触媒を用いた反応は、定量的にリニア体 **1-60** を与えた。ここで、Bower らは、得られる生成物の違いとその収率の差を以下のように考察している。中性ロジウム錯体触媒を用いた場合、ロジウム錯体は立体障害を避けるようにして、distal 位に酸化的付加する。続いて、β-水素脱離および還元的脱離により、**1-59** が得られる。しかし、この酸化的付加の効率は悪いため、**1-59** は低収率にとどまる。それに対して、ルイス酸性のより高いカチオン性ロジウム錯体を用いた場合、アミド部位のカルボニル基がより強く配位することで、効率的に proximal 位へ酸化的付加することが可能となり、高収率で **1-60** を得ることができる。すなわち、配向基を用いて、シクロプロパンの炭素–炭素結合に対して、金属中心を適切に配置させることができれば、効率的に当該結合を直接的に活性化することが可能となる。



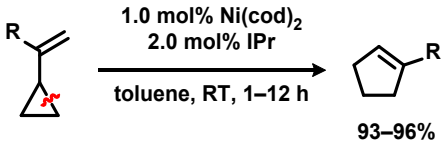
Scheme 1-23 中性あるいはカチオン性ロジウム錯体触媒による酸化的付加の位置選択性とその効率

配向基としてカルボニル基やイミノ基を利用することも可能である（**Scheme 1-24a**）[26]。シクロプロピルケトンやシクロプロピルイミンに対して、遷移金属錯体を作用させると、カルボニル基やイミノ基の不飽和結合の η^2-配位を足掛かりとして酸化的付加が起こり、環歪みの小さい 6 員環メタラサイクル **1-61** を与えるとされている。また、ビニルシクロプロパンを用いた場合、π-アリル錯体 **1-62** が生じる（**Scheme 1-24b**）[27]。



Scheme 1-24 遷移金属錯体の配向基置換型シクロプロパンへの酸化的付加

例えば、**Scheme 1-7** のようなビニルシクロプロパンの環拡大反応は、遷移金属錯体を触媒として用いれば、高温を必要とせずに進行することが分かっている [28]。とりわけ、Louie らは、ニッケルと NHC から構成される錯体を触媒に用いると、所望の環拡大反応が室温で進行することを報告した（**Scheme 1-25**）[28c]。この反応では、ビニル基の π 結合を足掛かりとして、シクロプロパンに対してニッケル中心を適切に配置させ、効率的に炭素–炭素結合を活性化している。

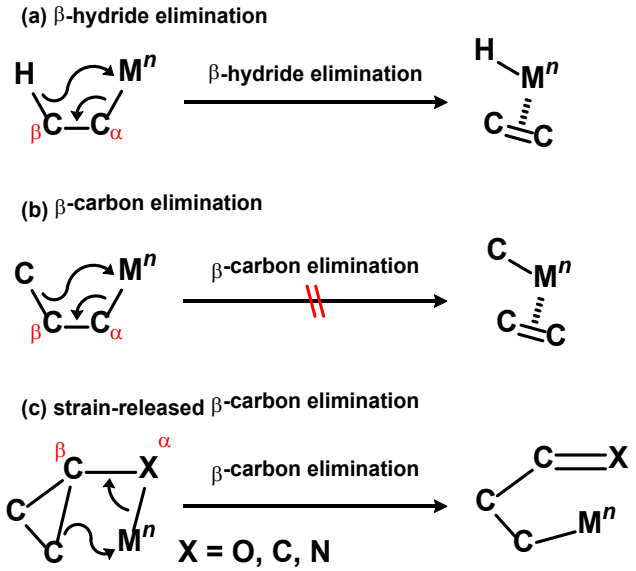


Scheme 1-25 ニッケル錯体触媒によるビニルシクロプロパンの環拡大反応

3-4 遷移金属錯体の β-炭素脱離過程を利用した炭素–炭素結合切断

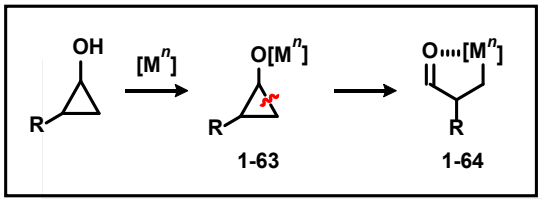
遷移金属錯体が炭素–炭素結合を切断する素過程として、酸化的付加の他に、β-炭素脱離が広く知られている。遷移金属錯体が関与する素過程の一つに β-水素脱離がある。β-水素脱離とは、遷移金属中心にアルキル基などが結合している基質において、遷移金

属のβ位に存在する水素がヒドリドとして脱離し、アルケンとメタルヒドリド種を形成する過程を指す（**Scheme 1-26a**）。一般的には、同様の機構にてβ-炭素脱離は進行しないが （**Scheme 1-26b**）、環歪みの解消を駆動力とする場合では、β-炭素脱離が進行する（**Scheme 1-26c**）[29]。遷移金属中心に結合しているXには酸素、炭素および窒素などが該当する。安定なC=X二重結合の形成とともに、シクロプロパンのバナナボンドの電子が遷移金属Mの空のd軌道に流れ込むことで、β-炭素脱離が可能となる。



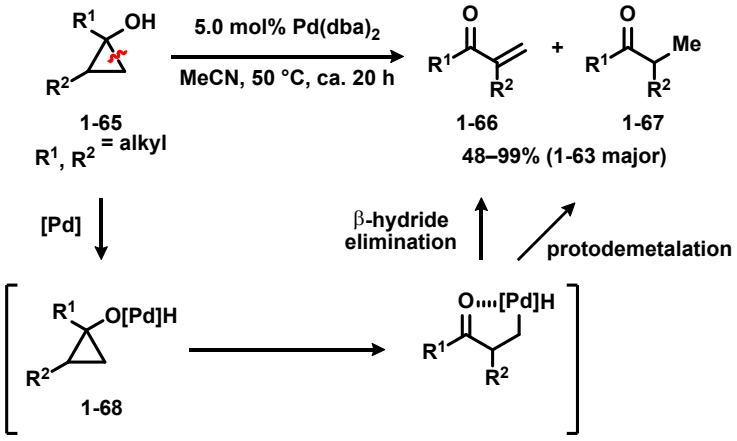
Scheme 1-26 β-水素脱離とβ-炭素脱離

シクロプロパノールに遷移金属錯体を作用させ、メタルシクロプロポキシド **1-63** が生成すると、安定なC=O二重結合の形成と環歪みの解消を駆動力として、β-炭素脱離が進行し、メタルホモエノラート **1-64** が生成する（**Scheme 1-27**）。一般的に、立体障害を避けるようにしてβ-炭素脱離が起こるので、置換基がより少ない方の炭素–炭素結合が切断される。1電子過程のβ-開裂に対して、炭素–炭素結合の切断位置選択性が異なることに注目すべきである。



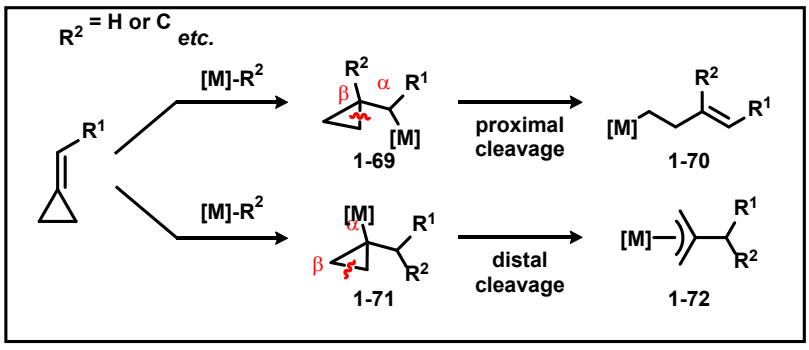
Scheme 1-27 シクロプロパノールのβ-炭素脱離による炭素–炭素結合切断

例えば、シクロプロパノール **1-65** に対して、反応温度 50 ℃で、$Pd(dba)_2$ を触媒として作用させると、開環体 **1-66** と **1-67** の混合物が得られることが報告されている（**Scheme 1-28**）[30a]。これらは、パラジウムシクロプロポキシド **1-68** の β-炭素脱離に基づく生成物である。その他にも、様々な遷移金属錯体がシクロプロパノールの β-炭素脱離を促進することが知られている [31]。



Scheme 1-28 遷移金属錯体触媒によるシクロプロパノールの開環反応

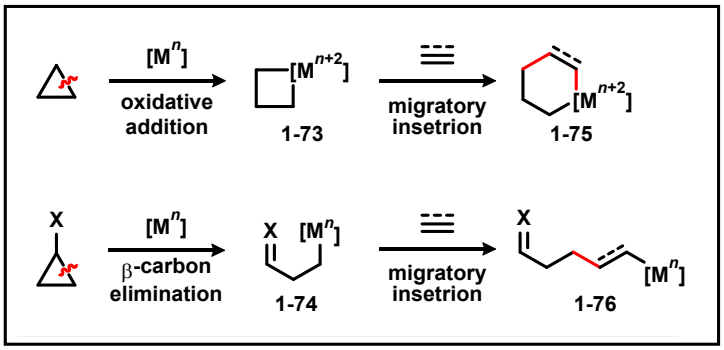
アルキリデンシクロプロパンにおいても、β-炭素脱離による炭素–炭素結合切断を観測できる（**Scheme 1-29**）[32]。アルキリデンシクロプロパンが、遷移金属錯体によってヒドロメタル化もしくはカルボメタル化されると、**1-69** へと変換される。**1-69** は、**Scheme 1-26c** にて説明した立体構造にて β-炭素脱離が進行するため、proximal 位が切断され、**1-70** を与える。一方で、マルコフニコフ則に従ってヒドロメタル化もしくはカルボメタル化が進行すると、**1-71** が生成する。しかし、**1-71** は、**Scheme 1-26c** に示すように、脱離する β 位の炭素と遷移金属の空配座がシスの位置の関係にないので、直接アルキルメタル種へと変換されずに、π-アリル錯体 **1-72** へと変換されると考えられている。



Scheme 1-29 アルキリデンシクロプロパンの β-炭素脱離による炭素–炭素結合切断

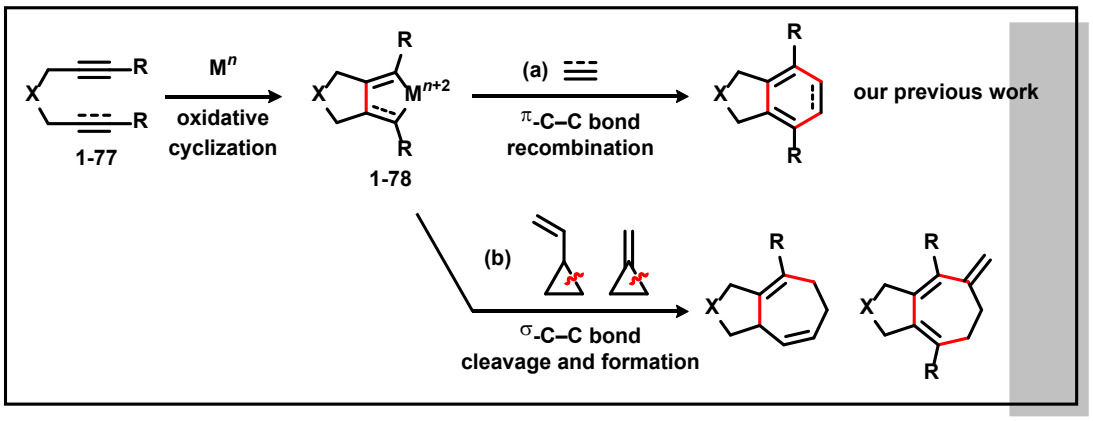
第 4 節　シクロプロパンを基質とする触媒的付加環化反応

これまでに、様々なシクロプロパンの炭素–炭素結合切断様式を説明した。とりわけ、温和な条件で選択的に炭素–炭素結合を切断するために、遷移金属錯体が有効であることを述べた。これらの素過程を通して、酸化的付加によるメタラサイクル **1-73** や β-炭素脱離によるアルキルメタル種 **1-74** などの金属–炭素結合を含む反応性の高い遷移金属錯体が生じる（**Scheme 1-30**）。さらに、これらの錯体に対して、アルキンやアルケンなどの不飽和分子を作用させると、転移挿入反応が起こり、新しい炭素–炭素結合が形成され、**1-75** や **1-76** となる。このような炭素–炭素結合の切断と形成を伴う反応は、切って縫い付ける反応（cut and sew transformation）と表現される [33]。



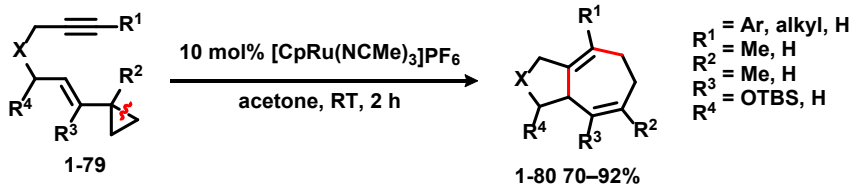
Scheme 1-30　遷移金属錯体触媒によるシクロプロパンと不飽和分子の反応

1,6-ジインや 1,6-エンイン **1-77** は、様々な遷移金属錯体の存在下で、メタラサイクル **1-78** へと変換される [34]。私の所属する研究室では、**1-78** に対して、アルキンやアルケンを反応させる [2+2+2]付加環化反応の開発研究に取り組んできた（**Scheme 1-31a**）[35]。これらの反応では、一度の操作で、炭素–炭素 π 結合の組み換えによって、ベンゼン誘導体やシクロヘキサジエン誘導体が得られる。一方、**1-78** に対して、ビニルシクロプロパンやアルキリデンシクロプロパンを反応させると、炭素–炭素 σ 結合の切断と形成を伴って、7 員環炭素骨格を構築できることが知られている（**Scheme 1-31b**）。



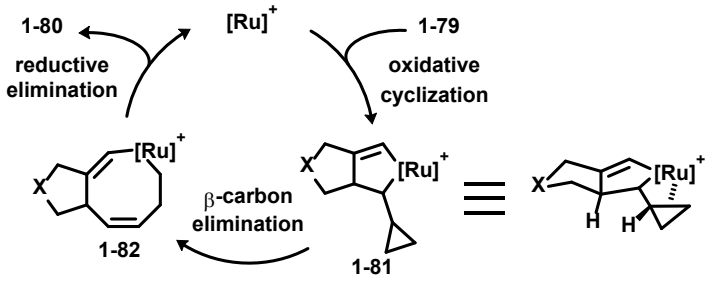
Scheme 1-31 遷移金属錯体触媒による 1,6-ジインや 1,6-エンインの環化反応

Trost らは、カチオン性ルテニウム触媒を用いたアルキン含有ビニルシクロプロパン **1-79** の分子内[5+2]付加環化反応を報告している（**Scheme 1-32**）[36]。この反応では、5 員環が縮環したシクロヘプタジエン **1-80** が良好な収率で得られる。



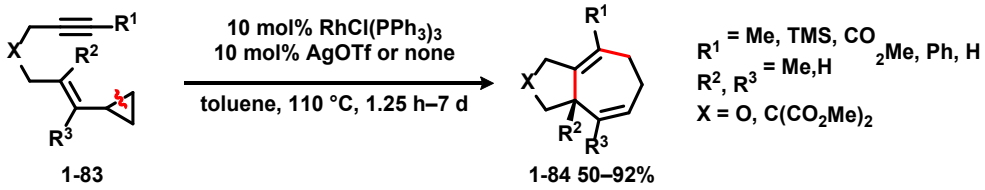
Scheme 1-32 ルテニウム触媒によるアルキン含有ビニルシクロプロパンの[5+2]付加環化反応

彼らは、種々のコントロール実験を踏まえて、以下のような反応機構を提唱している（**Scheme 1-33**）。まず、**1-79** において、アルキンとアルケン部位における酸化的環化によりルテナサイクル **1-81** が形成される。次に、β-炭素脱離によりシクロプロパンが開環し、8 員環ルテナサイクル **1-82** が生じる。ここでは、Trost らは、*E* 体のアルケンを含む基質から得られるルテナサイクルにおいて、その convex 面の擬エカトリアル位に位置するシクロプロパンとルテニウムが相互作用すると考察している。最後に、**1-82** のルテニウムの還元的脱離が進行することで、**1-80** が生成し、触媒サイクルが完結する。



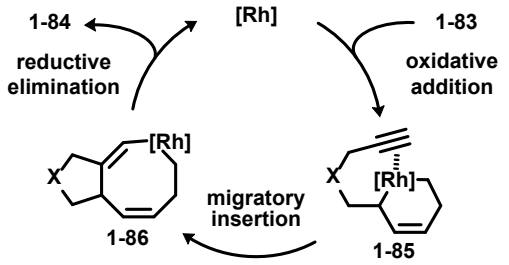
Scheme 1-33 ルテニウム触媒によるアルキン含有ビニルシクロプロパンの[5+2]付加環化反応の反応機構

一方で、Wender らは、同様の分子内[5+2]付加環化反応に対して、ロジウム触媒が有効であることを報告している（**Scheme 1-34**）[37]。彼らは、1,6-エンイン含有シクロプロパン **1-83** とロジウム触媒を反応させることで、同様の生成物 **1-84** を良好な収率で得ている。



Scheme 1-34 ロジウム触媒による 1,6-エンイン含有シクロプロパンの分子内[5+2]付加環化反応

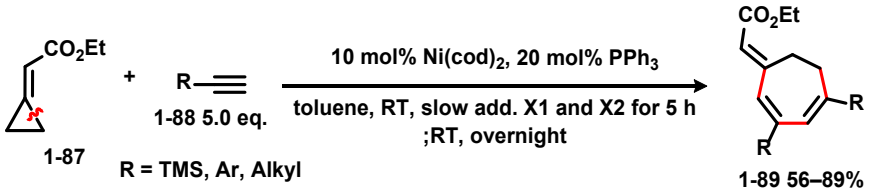
ロジウム触媒反応の機構の概略を **Scheme 1-35** に示す[38]。まず、**1-83** のビニルシクロプロパン部位にロジウムが酸化的付加することで、6 員環ロダサイクル **1-85** を形成する。続く分子内アルキンへの転移挿入を経て、**1-86** となった後に、ロジウム錯体が還元的脱離し、**1-84** が得られる。



Scheme 1-35 ロジウム触媒によるアルキン含有ビニルシクロプロパンの[5+2]付加環化反応の反応機構

Trost らと Wender らの報告から分かるように、同様の基質と生成物でも、用いる遷移金属錯体触媒によって、シクロプロパンの炭素–炭素結合の活性化様式が全く異なることがある。これまでに、Louie らがニッケル触媒を [39a]、Fürstner らが鉄触媒を [39b]、Strand らがイリジウム触媒を [39c]、吉戒らがコバルト触媒を [39d] それぞれ用いて、同様の反応を報告するに至っている。これらの触媒を用いる反応は、Trost らと Wender らが提唱している反応機構のどちらかに従い、それぞれ進行すると考えられている。

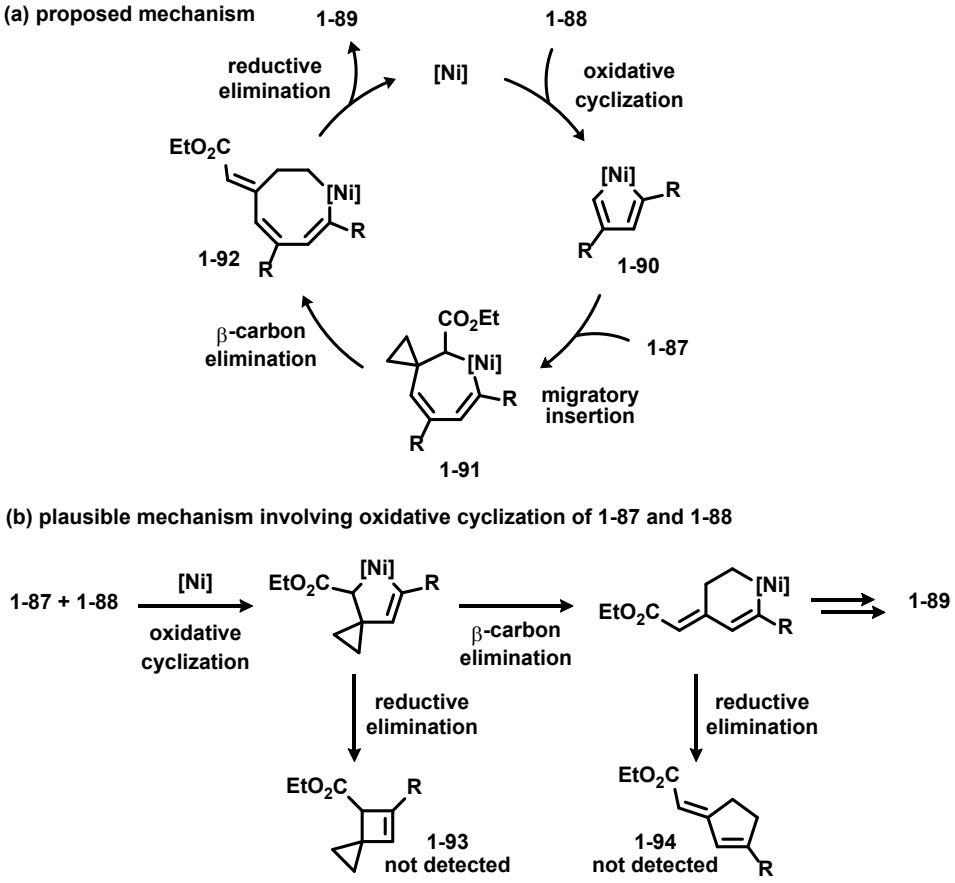
また、7 員環炭素骨格を構築する手法として、ニッケル触媒によるアルキンとアルキリデンシクロプロパンの[3+2+2]付加環化反応も知られている。ニッケル/ホスフィン触媒の存在下で、アルキリデンシクロプロパン **1-87** に対して、5 当量の末端アルキン **1-88** を反応させることで、7 員環炭素骨格を有する **1-89** を単一の生成物として得ることが可能である（**Scheme 1-36**）[40]。



Scheme 1-36 ニッケル触媒によるアルキンとアルキリデンシクロプロパンの[3+2+2]付加環化反応

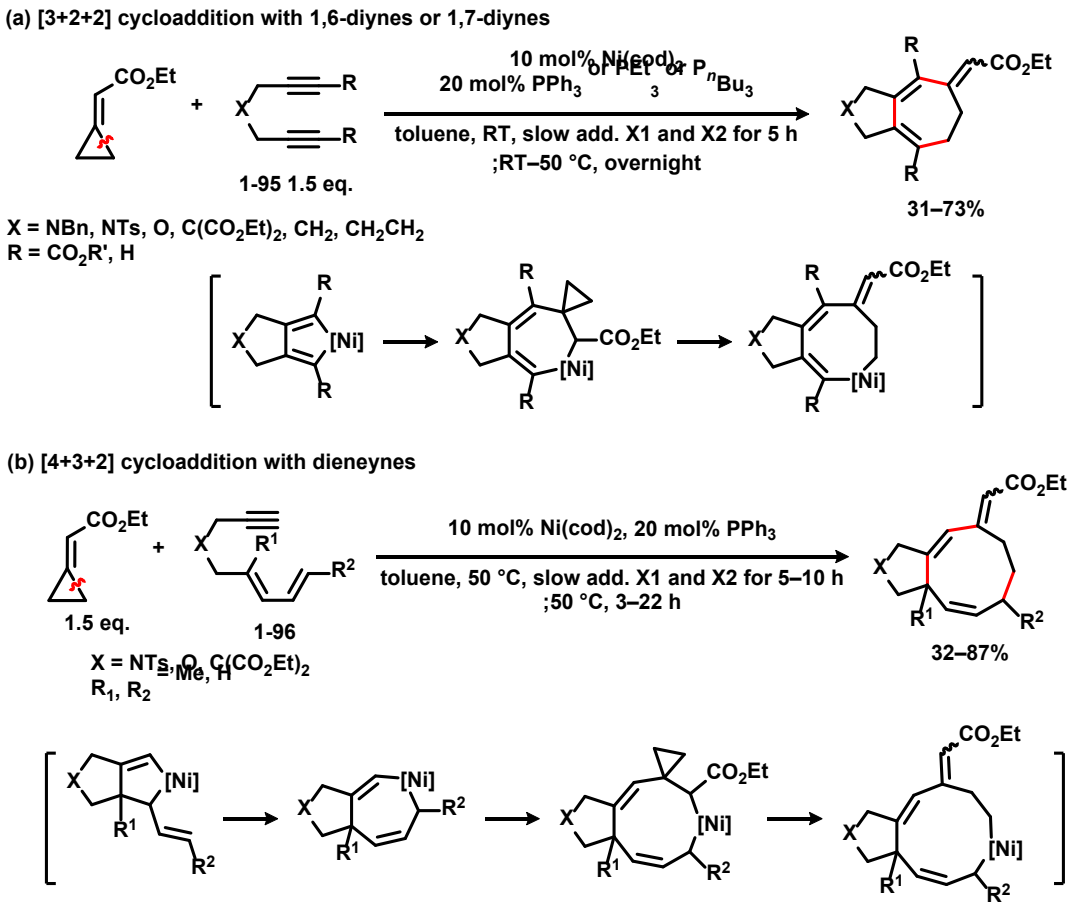
1-89 が単一の生成物として得られた実験事実から、**Scheme 1-37a** に示す反応機構が提唱されている。最初に、二分子の **1-88** とニッケル錯体の酸化的環化によって、ニケラシクロペンタジエン **1-90** が生じる。次に、**1-87** への転移挿入が進行し、ニケラシクロヘプタジエン **1-91** となる。ここで、β-炭素脱離が起こることで、8 員環ニケラサイクル **1-92** が形成される。最後に、**1-92** の還元的脱離によって、ニッケル触媒が再生し、

1-89 が得られる。その他に考えられる反応機構として、**1-87** と **1-88** の酸化的環化を経由する経路が考えられる（**Scheme 1-37b**）。しかし、生じ得る副生成物である **1-93** や **1-94** が全く観測されないことから、これらの可能性は除外されている。



Scheme 1-37 ニッケル触媒によるアルキンとアルキリデンシクロプロパンの[3+2+2]付加環化反応の反応機構

その後、上記の反応は、1,6-ジインや 1,7-ジイン基質 **1-95** に適用された（**Scheme 1-38a**）[41]。さらに、この反応をジエン-イン基質 **1-96** に応用することで、9 員環炭素骨格を一挙に構築できることが見出されている（**Scheme 1-38b**）[42]。これらの反応も酸化的環化を起点として、β-炭素脱離が進行していると考えられている。



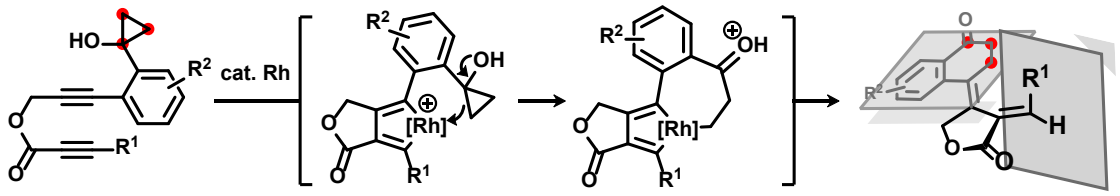
Scheme 1-38 ニッケル触媒によるアルキリデンシクロプロパンとアルキンやアルケンの付加環化反応

このように、シクロプロパンを基質とした既存の環化異性化反応では、ビニルシクロプロパンやアルキリデンシクロプロパンが用いられてきた。これらの反応では、隣接するπ結合が反応に関与し、メタラサイクルを形成し、シクロプロパンがβ-炭素脱離によって活性化される。すなわち、シクロプロパンを活性化するために、隣接するπ結合を必須としている。

第 5 節　研究目的

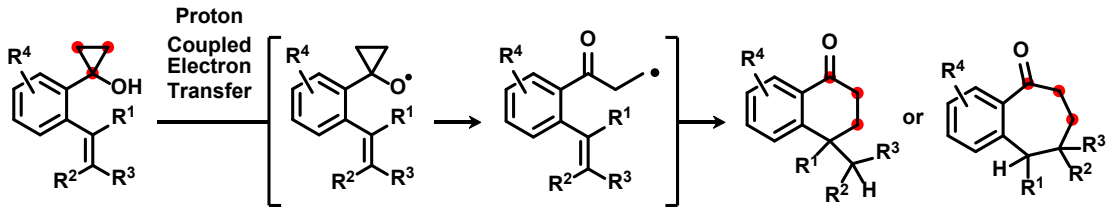
本章では、シクロプロパンは特異な性質を有していることやそれに起因して炭素–炭素結合が切断されやすいことを説明した。その切断様式はシクロプロパンの種類や活性化方法によって大きく変化する。また、既存のシクロプロパンを活用した触媒的付加環化反応では、最も反応性の高い π 結合が反応に関与した後に、シクロプロパンの炭素–炭素結合が活性化されていることを述べた。主として、ビニルシクロプロパンやアルキリデンシクロプロパンが用いられ、シクロプロパンに隣接する π 結合を必須とする。そこで、本研究では、触媒的環化異性化反応において、シクロプロパンを活用するため、シクロプロパノールとシクロプロペンに着目した。どのようにして炭素–炭素結合を活性化するのかに焦点を当て、新たな触媒的環化異性化反応を開発し、これまで到達困難であった炭素骨格を有する分子の創出を目指した。

まず、私は、酸素電子の押し込みに起因する反応性が知られているシクロプロパノールを利用することで、隣接する π 結合の助けがなくとも、触媒的環化異性化反応にてシクロプロパンを活用できるのではないかと考えた。そこで、市販の試薬からモジュラー合成可能な 1,6-ジイン含有シクロプロパノール基質を設計した（**Scheme 1-39**）。遷移金属錯体触媒と 1,6-ジインの環化によって形成されるメタラサイクルの金属中心を適切な位置に配置させ、シクロプロパノールの炭素–炭素結合を直接的に活性化できるのか、に焦点を当て研究に着手した。種々の遷移金属錯体触媒を探索したところ、カチオン性ロジウム錯体を用いると、らせん構造を有する環状エキソジエンを得ることができた。実験化学および計算化学の両側面から反応機構研究に取り組んだ。



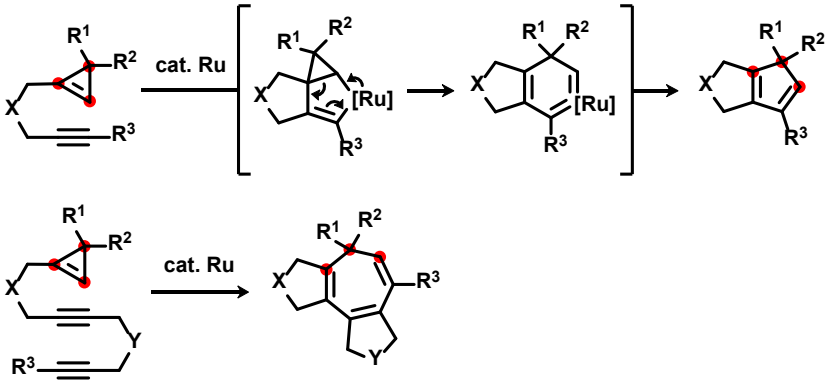
Scheme 1-39　ロジウム触媒を用いる 1,6-ジイン含有シクロプロパノールの環化異性化反応

次に、モジュラー合成可能なアルケン含有シクロプロパノール基質を設計した。レドックスニュートラルで高い原子効率の分子変換反応を可能にするプロトン共役電子移動によってシクロプロパノールを活性化することで、触媒的ラジカル環化反応を試みた（**Scheme 1-40**）。



Scheme 1-40 PCET を起点とするアルケン含有シクロプロパノールの触媒的環化異性化反応

最後に、アルキンに類似する性質を有するシクロプロペンに着目し、1,6-ジインのアルキンの 1 つをシクロプロペンに変更した、シクロプロペン-イン基質やシクロプロペン-ジイン基質を設計した（**Scheme 1-41**）。遷移金属錯体触媒の存在下で、シクロプロパンが縮環したメタラサイクルの形成を経て、環化反応が進行するのではないかと考えて検討したところ、シクロプロペンの新たな活性化法を見出すに至った。



Scheme 1-41 ルテニウム触媒を用いるシクロプロペン-イン類の環化異性化反応

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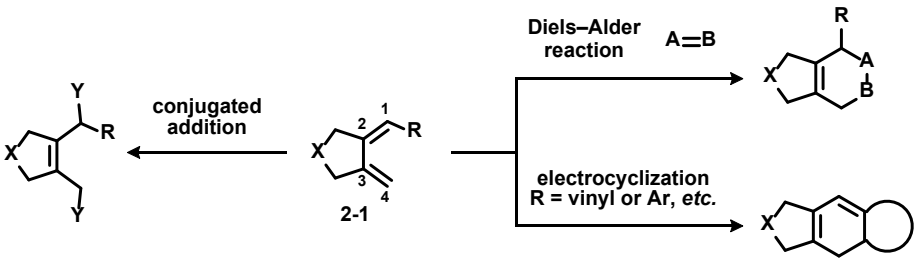
第 2 章

ロジウム触媒を用いる
1,6-ジイン含有シクロプロパノールの
環化異性化反応

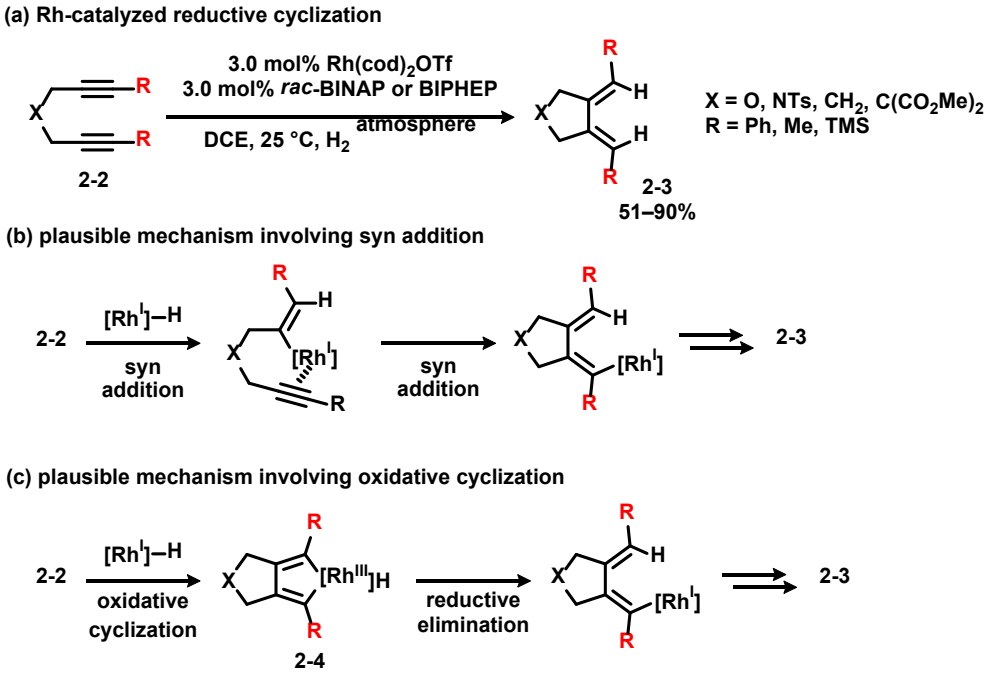
第 1 節　1,6-ジインの環化反応を利用した環外ジエンの合成

1,3-ブタジエンの 2,3 位が縮環した環外ジエン **2-1** は、1,4-付加反応をはじめとする様々な変換反応に応用できる（**Scheme 2-1**）。とりわけ、縮環構造によって、ジエン部位が s-cis 配座に固定されているので、Diels–Alder 反応の基質として汎用される [1]。その他に、末端にビニル基を有する環外ジエンでは、熱的条件や紫外光照射条件にて、電子環状反応が進行する [2]。すなわち、環外ジエンは、様々な多環式化合物へのアプローチを可能にする有用なビルディングブロックである。



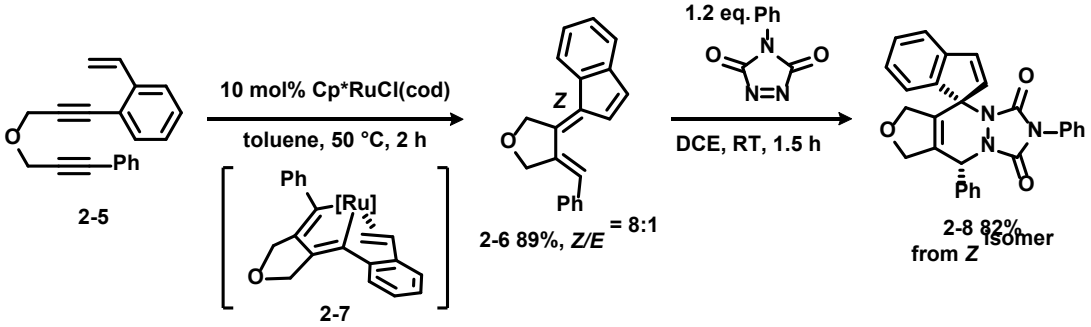
Scheme 2-1 環外ジエンを用いる変換反応

遷移金属錯体触媒を用いるジインの環化反応を利用することで、環外ジエン骨格を簡便に構築できる。例えば、Krische らは、カチオン性ロジウム錯体を水素雰囲気下で処理することで調製されるロジウムヒドリドが、1,6-ジイン **2-2** の触媒的還元環化反応に有効であることを報告した（**Scheme 2-2a**）[3]。彼らは、重水素化実験などを踏まえて、**2-3** の生成過程として二つの反応機構を提唱している。一つ目は、ロジウム錯体のジインに対する連続的な syn 付加を含む機構である（**Scheme 2-2b**）。二つ目は、ロジウムヒドリドの酸化的環化を含む機構である（**Scheme 2-2c**）。この反応機構では、ロダサイクル **2-4** において、還元的脱離が進行することで、水素が付加される。二つのどちらの機構で反応が進行しても、ジイン末端置換基を外側に向けた環外ジエン **2-3** が得られる。



Scheme 2-2 ロジウム触媒によるジインの還元的環化反応とその機構

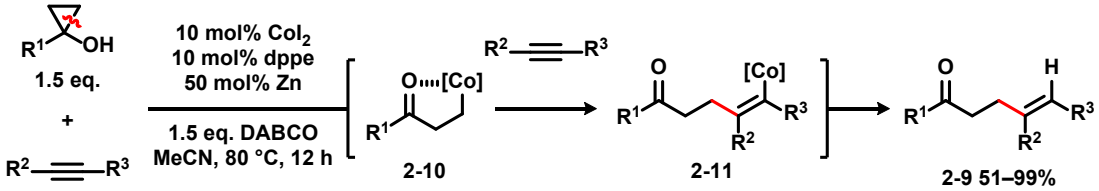
一方、当研究グループでは、ルテニウム触媒を用いる 1,6-ジインの環化反応を利用することで、様々な環骨格の構築に成功している。その研究過程で、スチレン部位を有する 1,6-ジイン基質 **2-5** を設計し、ルテニウム触媒を作用させることで、インデンを含む環外ジエン **2-6** が得られることを見出している（**Scheme 2-3**）[4]。重水素化実験や計算化学的手法により、この反応では、ルテナサイクル **2-7** において、通常の転移挿入ではなく、交差型の転移挿入が進行している可能性が高いことを明らかにした。アルケンをルテナサイクルのルテニウム中心に対して適切に配置させる基質設計が、ルテニウムの交差型転移挿入を進行させるために重要であると考えられる。また、Diels–Alder 反応によって、得られた環外ジエンを **2-8** へ誘導することに成功している。



Scheme 2-3 ルテニウム触媒によるスチレン含有 1,6-ジインの環化反応

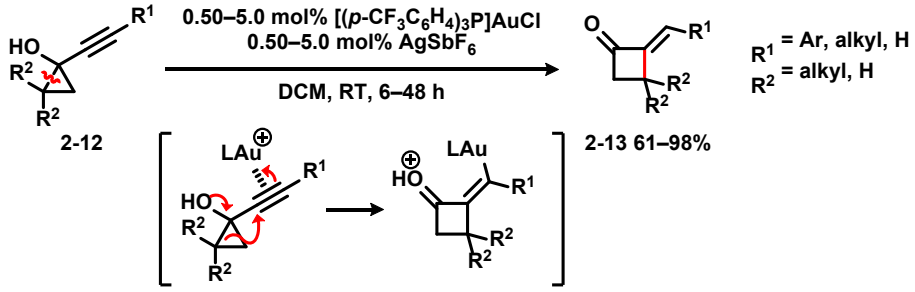
第 2 節　遷移金属錯体によるシクロプロパノールとアルキン基質の反応

第一章にて、シクロプロパノールは、酸素電子の押し込みに起因する反応性が広く知られていることを説明した。シクロプロパノールの開環反応の反応系中にアルキンを共存させることで、炭素–炭素結合の切断と形成を伴う反応が可能になる。例えば、吉戒らは、二価のコバルト錯体と亜鉛還元剤から調製される一価のコバルト錯体が、シクロプロパノールとアルキンのクロスカップリング反応に有効であることを報告した（**Scheme 2-4**）[5]。彼らは、アセトニトリル中で、コバルト触媒と両基質を反応させることで、γ,δ-不飽和ケトン **2-9** を得た。この反応では、β-炭素脱離によってコバルトホモエノラート **2-10** が形成された後に、アルキンへの転移挿入を経て、アルケニルコバルト **2-11** が生じる。**2-11** のプロト脱メタル化が進行することで **2-9** が得られると考えられている。



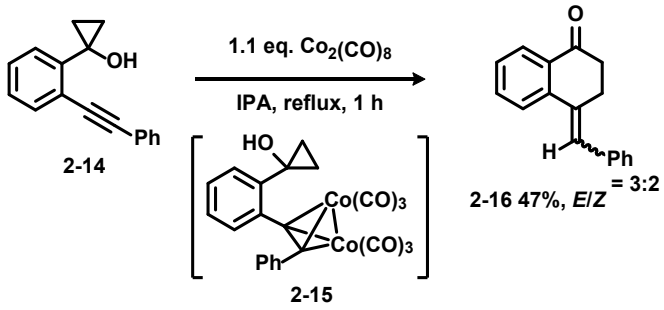
Scheme 2-4　コバルト触媒によるシクロプロパノールとアルキンのカップリング反応

一方で、分子内にアルキンを有する基質の場合、アルキンを足掛かりとしてシクロプロパノールを活性化できることが知られている。Toste らは、カチオン性金触媒を利用したアルキニルシクロプロパノール **2-12** のシクロブタノン **2-13** への環拡大反応を報告している（**Scheme 2-5**）[6]。この反応では、π 酸性の高いカチオン性金触媒がアルキンに配位し、アルキンの求電子性を高め、シクロプロパノールの酸素電子の押し込みに伴い、1,2-アルキル転位が進行する。



Scheme 2-5　金触媒によるアルキニルシクロプロパノールの環拡大反応

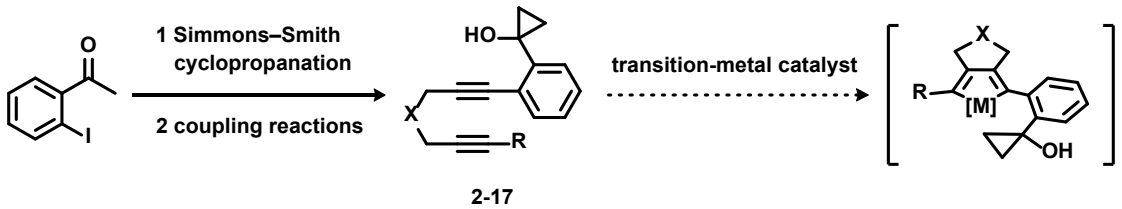
1997 年に、岩澤らは、フェニルシクロプロパノールのオルト位にアルキンを導入した基質 **2-14** に対して、1.1 当量のコバルト錯体を用いることで、**2-15** を中間体として、1-テトラロン誘導体 **2-16** が中程度の収率で得られることを報告した（**Scheme 2-6**）[7]。1-テトラロンは天然物や生理活性物質に広く見られる構造で、複雑分子のビルディングブロックとしても用いられる有用な分子である。



Scheme 2-6 コバルト錯体を用いるアルキン含有フェニルシクロプロパノールの環化反応

第 3 節　1,6-ジイン含有フェニルシクロプロパノール基質の設計

以上の背景から、1,6-ジイン含有シクロプロパノール基質 **2-17** を設計した。（**Scheme 2-7**）。**2-17** の 1,6-ジインは、遷移金属錯体触媒の酸化的環化によって、メタラサイクルを形成すると考えられる。酸素上の電子の押し込みに起因する反応性を特徴とするシクロプロパノールをメタラサイクルの金属中心に対して適切に配置させることで、π 結合性をもつ炭素–炭素結合を直接的に活性化できるのではないかと考えた。この観点から、1,6-ジインとシクロプロパノール部位は剛直なベンゼン環で架橋することとした。



Scheme 2-7 1,6-ジイン含有シクロプロパノール基質の設計

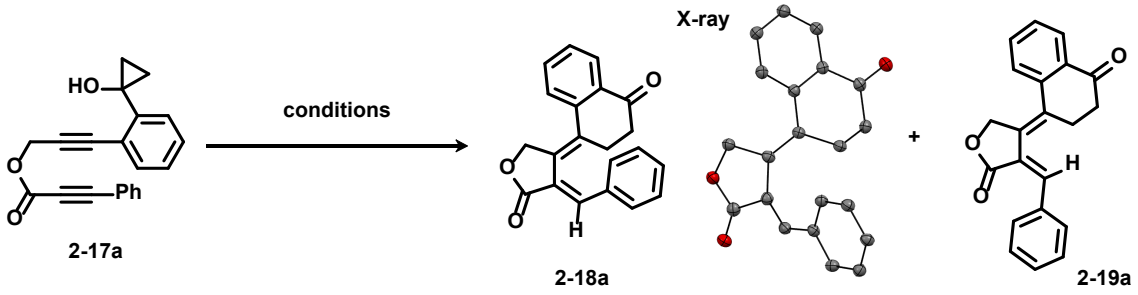
第 4 節　遷移金属錯体触媒の探索と反応条件の検討

アルキン末端にフェニル基を有し、1,6-ジインのテザー部位をエステルとした **2-17a** をモデル基質として、遷移金属錯体触媒を探索した（**Table 2-1**）。最初に、1,6-ジインとメタラサイクルを形成し環化異性化反応に汎用される$[Cp^*RuCl_2]_2$ を触媒として用いたが、反応は進行しなかった（entry 1）。次に、環状アルコールの開環を促進することで知られている遷移金属錯体触媒を検討した。酢酸パラジウム [8] を用いた反応は、複雑な混合物を与えた（entry 2）。次に、二価コバルトから亜鉛により系内で還元的に低原子価コバルト錯体 [5] を調製し、反応に用いたところ、シクロプロパノールの開環は確認できたものの、複雑な混合物を得た（entry 3）。また、環歪みを有する環状アルコールの開環反応に効果的な$[Rh(cod)OH]_2$ を触媒 [9] として用いたが、**2-17a** が多く残存する結果となった（entry 4）。

そこで、再び 1,6-ジインの環化に有効な遷移金属錯体を検討することとした。その結果、水素雰囲気下で$[Rh(cod)_2]BF_4$ と BINAP から調製されるカチオン性ロジウム錯体 [10] を用いると、**2-17a** は完全に消失し、47%の収率で、1-テトラロンを含む環外ジエン **2-18a** を単一の生成物として得ることができた（entry 5）。興味深いことに、X 線結晶構造解析により、**2-18a** は 1-テトラロンとフェニル基の立体反発により、熱力学的に不利なジエン構造を有しており、1-テトラロンとフェニル基の立体反発により、中心炭素骨格がらせん構造を成していることが明らかとなった [11]。また、**2-18a** の幾何異性体である **2-19a** の生成は確認できなかった。

さらに、ロジウム錯体の対アニオンや配位子などの反応条件を検討したところ、$[Rh(cod)_2]BF_4$ と BINAP から調製されるカチオン性ロジウム錯体が最も有効であることが分かり、**2-18a** の収率改善には至らなかった。また、entry 5 において、分子間反応などによる多量化が併発しているために **2-17a** の変換率が低くなっていると考え、反応溶液を希釈して反応を行ったところ、高い立体選択性を損なうことなく、**2-18a** の収率が 70%まで向上した（entry 6）。

Table 2-1　遷移金属錯体触媒の探索と反応条件の検討 [a]



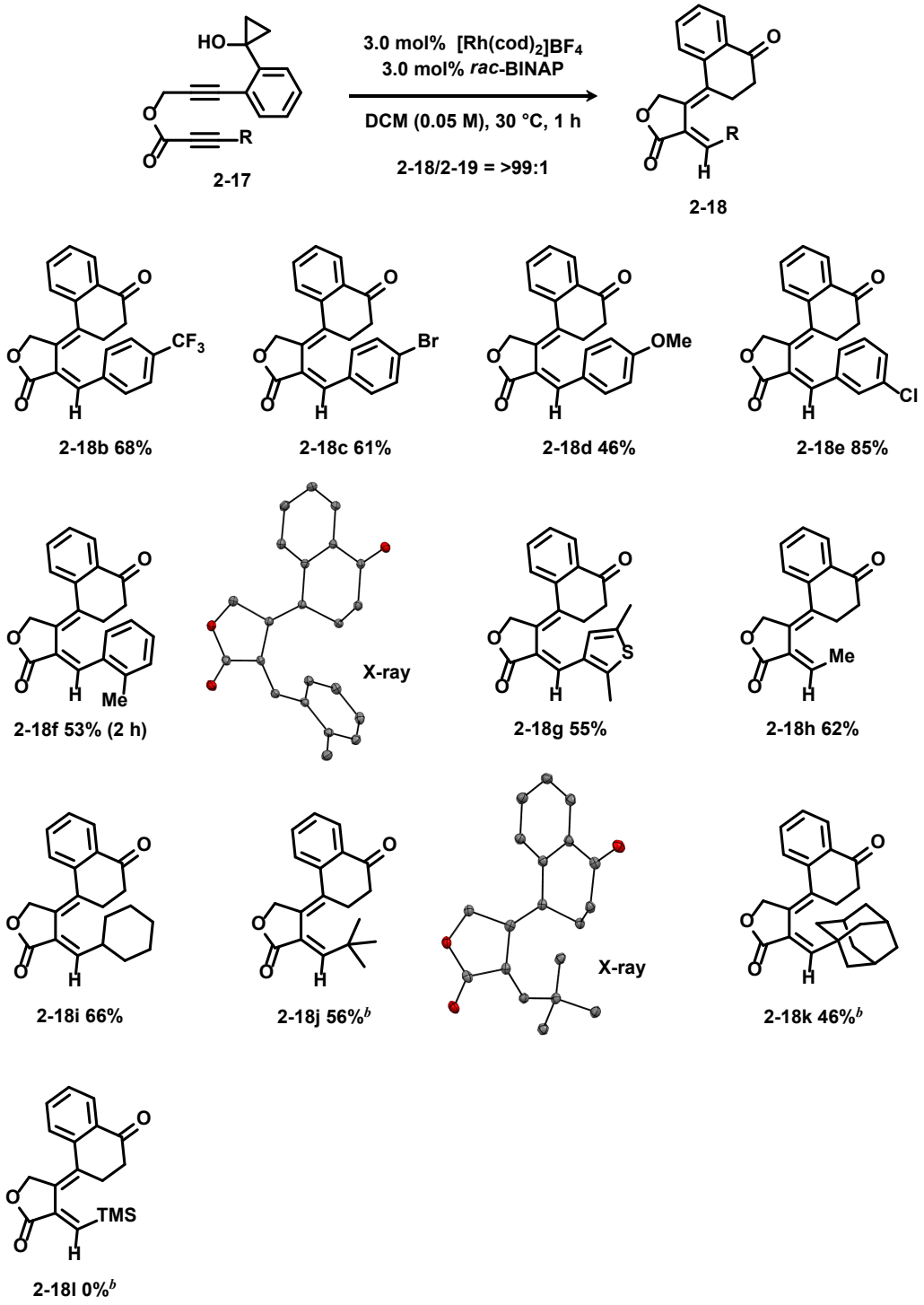
entry	catalysts	conditions	conv. (%)	results
1	5.0 mol% $[Cp^*RuCl_2]_2$	DCE (0.1 M) 80 ℃, 17 h	<5	no reaction
2	10 mol% $Pd(OAc)_2$	MeCN (0.1 M) 50 ℃, 24 h	>99	complex mixture
3	10 mol% $CoBr_2$ 10 mol% dppe 0.5 eq. Zn 1,5 eq. DABCO	DMSO (0.1 M) 80 ℃, 21 h	59	complex mixture
4	1.5 mol% $[RhOH(cod)]_2$ 3.0 mol% *rac*-BINAP	DCM (0.05 M) 30 ℃, 1 h	<5	no reaction
5[b]	3.0 mol% $[Rh(cod)_2]BF_4$ 3.0 mol% *rac*-BINAP	DCM (0.1 M) 30 ℃, 1 h	>99	47%[c] **2-18a**/**2-19a** = >99:1
6[b]	3.0 mol% $[Rh(cod)_2]BF_4$ 3.0 mol% *rac*-BINAP	DCM (0.05 M) 30 ℃, 1 h	>99	70%[c] **2-18a**/**2-19a** = >99:1

[a]0.1 mmol で反応を行った。[b]**2-17a** を反応溶液に加える前に、水素雰囲気下でロジウム錯体を事前に活性化した。[c] 単離収率。

第 5 節　基質適用範囲の調査

最適化した条件のもと、アルキン末端に様々な置換基を有する **2-17b–l** を用いて、基質適用範囲の調査を行った。その結果を **Scheme 2-8** に示す。まず、アルキン末端の置換基の電子密度が本反応に与える影響を調査するため、末端フェニル基のパラ位にそれぞれトリフルオロメチル基、ブロモ基およびメトキシ基を導入した **2-17b**、**2-17c** および **2-17d** を本反応条件に付した。その結果、対応する生成物 **2-18b**、**2-18c** および **2-18d** がそれぞれ 68%、61%および 46%で得られた。これらの結果から、電子求引性のジイン末端置換基を有する基質の方が、効率的にらせん性環外ジエンに変換されることが分かった。ジイン末端置換基上の電子密度は、生成物 **2-18b–d** の立体選択性には関与せず、いずれの場合においても、非常に高い立体選択性を発現した。また、3-クロロフェニル基を有する **2-17e** や 2-メチルフェニル基を有する **2-17f** を用いる反応も円滑に進行した。**2-18f** の構造は、X 線結晶構造解析により決定した。チオフェン基質 **2-17g** からは、中程度の収率で目的の **2-18g** を得ることができた。アルキン末端に立体的に小さなメチル基を有する **2-17h** を本反応に用いた場合も、高い立体選択性で反応が進行し、収率 62%で **2-18h** を与えた。続いて、メチル基よりも三次元的に嵩高いシクロヘキシル基を有する

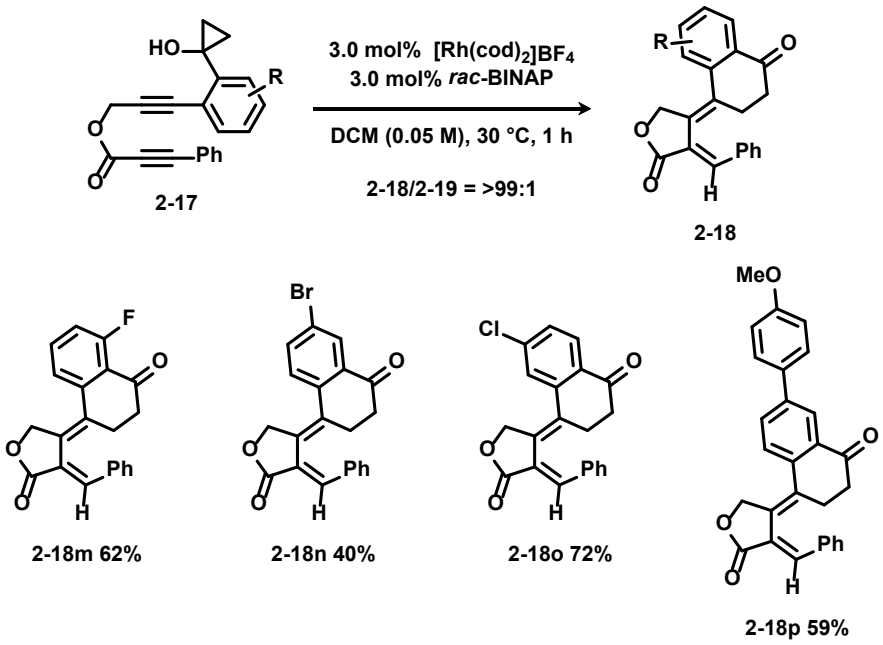
2-17i からは、収率 66%で立体選択的に **2-18i** が得られた。さらに三次元的に大きい *t*Bu 基を末端にもつ **2-17j** を用いた反応では、触媒量を 10 mol%に増やし、反応温度を 60 ℃に昇温することで、**2-17j** が完全に消失し、**2-18j** を 56%で得ることができた。**2-18j** の X 線結晶構造解析から、*t*Bu 基がジエン内側に向いていることを確認した。本手法は、アダマンチル基を有する **2-17k** にも適用可能で、高い立体選択性と良好な収率で、アダマンチル基を内側に向けた **2-18k** が得られた。しかし、TMS 基を有する **2-17l** に対して、本触媒系を作用させたところ、反応は進行せず、**2-18l** は得られなかった。TMS 基と同様に立体的に大きい *t*Bu 基やアダマンチル基を有する **2-17j** や **2-17k** を用いた反応が進行していることおよび一般的にジイン末端置換基の電子供与基は環化反応性の低下を招くことから、炭素よりも電子供与性の高いケイ素を末端に有する **2-17l** は、電子的な影響により反応が進行しなかったと考えられる。



[a]0.1 mmol の **2-17** を反応溶液に加える前に、水素雰囲気下でロジウム錯体を事前に活性化した。[b]10 mol%の$[Rh(cod)_2]BF_4$と *rac*-BINAP を用いて、DCE 中、反応温度 60 ℃で反応を行った。

Scheme 2-8 アルキン末端置換基の影響の調査 [a]

さらに、**2-17** のシクロプロパノールに隣接する芳香族環上の置換基が本反応に与える影響を調査した（**Scheme 2-9**）。まず、フルオロ基を導入した基質 **2-17m** を用いた反応は、収率 62%で目的の生成物 **2-18m** を与えた。しかし、ブロモ基を有する基質 **2-17n** を用いた反応では、**2-17n** が完全に消失したことを確認したが、反応系は複雑化し、**2-18n** の収率は中程度にとどまった。カチオン性ロジウム錯体の炭素–臭素結合への酸化的付加に起因する副反応が併発したことが、収率低下の原因の一つとして考えられる。その他、5 位のクロロ基（**2-17o**）や 4 位のメトキシフェニル基（**2-17p**）の導入は本反応に大きな影響を与えず、良好な収率で **2-18o** および **2-18p** を得ることができた。

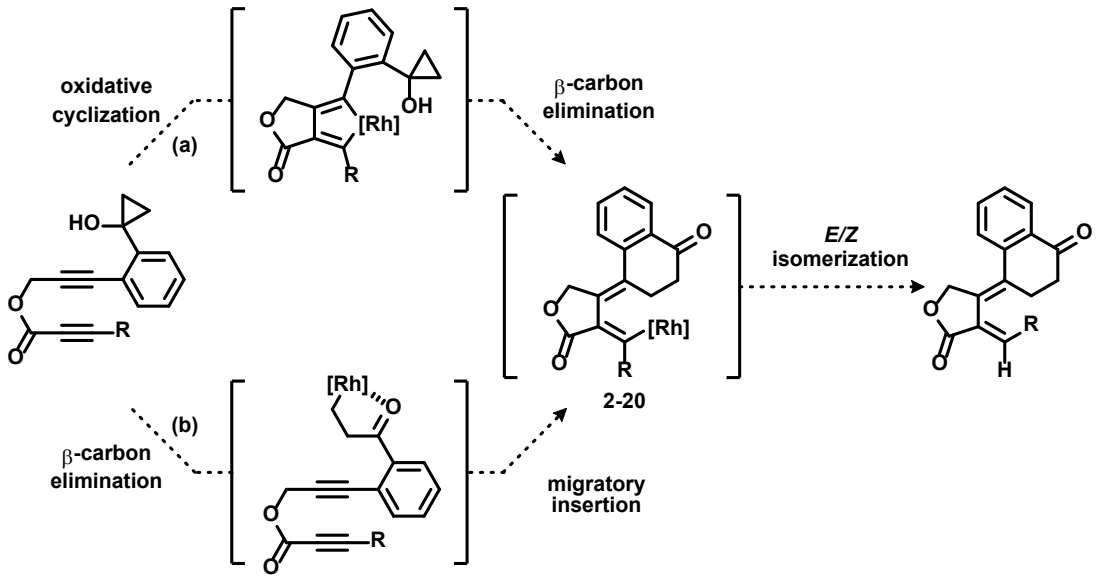


[a]0.1 mmol の **2-17** を反応溶液に加える前に、水素雰囲気下でロジウム錯体を事前に活性化した。

Scheme 2-9 芳香族環上置換基の影響の調査 [a]

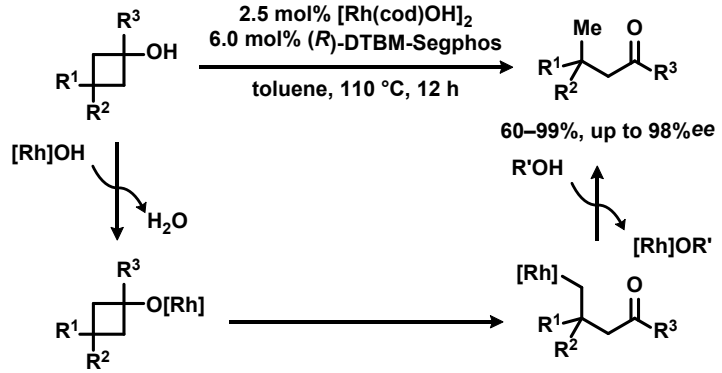
第 6 節　反応機構研究：1,6-ジインの環化とシクロプロパノールの開環のどちらが先行するか？

第 6 節と第 7 節では、本反応がどのようにして進行しているのかについて考察する。本反応では、1,6-ジインの環化から反応が進行し、ロダサイクル中のロジウムがシクロプロパノールを活性化していると想定している（**Scheme 2-10a**）。



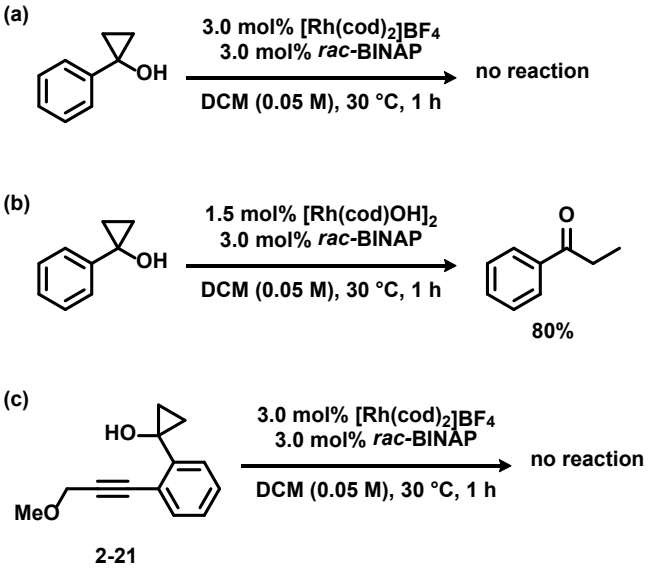
Scheme 2-10 本反応の想定反応機構

しかし、これまでのロジウム触媒反応の知見に基づけば、シクロプロパノールの開環から反応が進行する機構も否定できない（**Scheme 2-10b**）。実際、$[Rh(cod)OH]_2$ は、アルコールと反応して、水分子が脱離することで、容易にロジウムアルコキシドへと変換されるため、環歪みを有する環状アルコールの開環を促進する触媒として広く知られている。例えば、Cramer らは、$[Rh(cod)OH]_2$ とキラル配位子を触媒に用いることで、シクロブタノールの開環に伴う非対称化反応を報告している（**Scheme 2-11**）[9b]。このことを踏まえれば、$[Rh(cod)_2]BF_4$ を用いる本反応条件でも、シクロプロパノールの開環から反応が進行し、共通中間体 **2-20** になる可能性も十分に考えられる。さらに、**2-20** から、何らかの理由で *E/Z* 異性化しているものと考えられる（**Scheme 2-10**）。



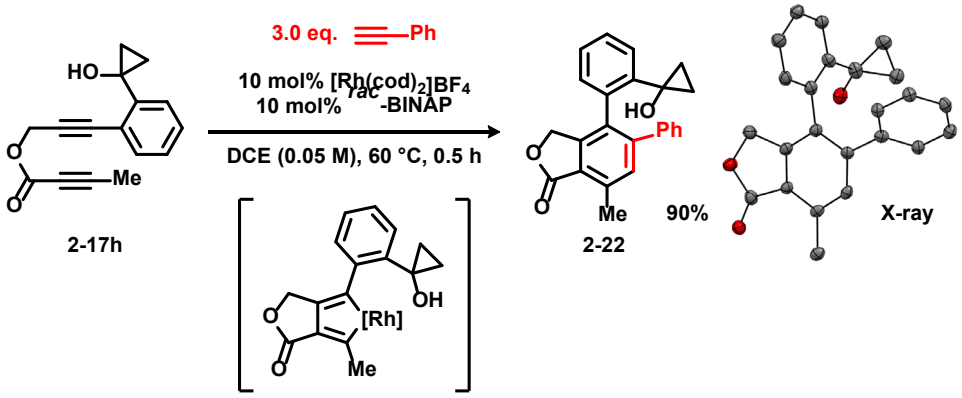
Scheme 2-11 $[Rh(cod)OH]_2$ を触媒として用いるシクロブタノールの開環反応

まず、1,6-ジインの環化とシクロプロパノールの開環のどちらが最初に進行し **2-20** になるのかを解明すべく、種々の検証実験を行った。単純なシクロプロパノールであるフェニルシクロプロパノールを本反応条件に付したところ、反応は全く進行しないことが明らかとなった（**Scheme 2-12a**）。一方で、1,6-ジイン含有シクロプロパノール **2-17a** に有効ではなかった$[Rh(cod)OH]_2$を作用させると、収率 80%でプロピオフェノンが得られた（**Scheme 2-12b**）。以上のことから、本反応に用いるカチオン性ロジウム錯体は、$[Rh(cod)OH]_2$と異なり、シクロプロパノールの開環によるホモエノラートの生成を促進しないと考えられる。続いて、アルキンが配向基としてはたらき、シクロプロパノールの開環を促進している可能性を考え、1,6-ジインの代わりにモノアルキンを導入した基質 **2-21** を用いたが、反応は進行しなかった（**Scheme 2-12c**）。単純なフェニルシクロプロパノールや **2-21** を用いた反応でシクロプロパノールの開環を観測できないことは、1,6-ジインから形成されるロダサイクルがシクロプロパノールの開環に関与していることを示唆している。



Scheme 2-12 検証実験

以上の検証実験から、本反応はロダサイクル中間体を経て進行することが示唆された（**Scheme 2-10a**）。そこで、ロダサイクル中間体を捕捉することを目的として、3 当量のフェニルアセチレンの存在下、10 mol%の触媒を用いて、反応温度 60 ℃で **2-17h** を反応させた。その結果、ロダサイクル中間体を捕捉したと考えられる **2-22** を収率 90%で得ることができた（**Scheme 2-13**）。X 線結晶構造解析により、**2-22** の構造を決定し、未反応のシクロプロパノール部位を有することを確認した。

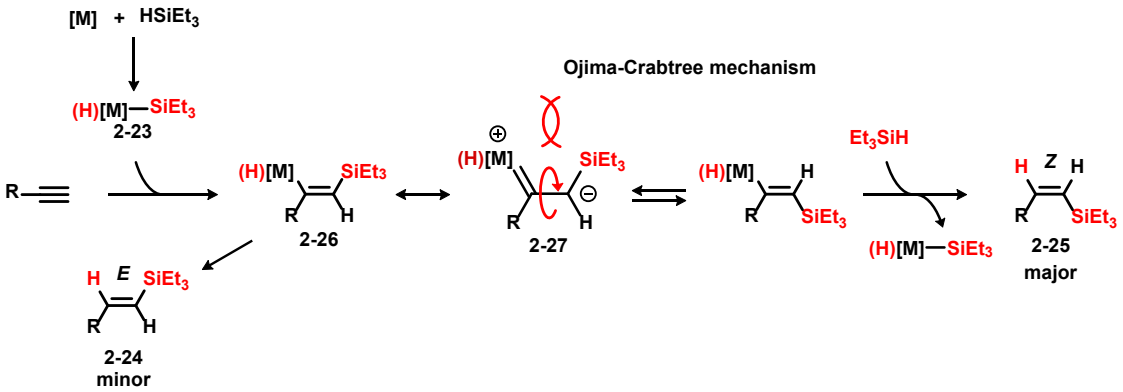


Scheme 2-13 中間体の捕捉実験

以上の検証実験から、当初の予想通り、本反応は、1,6-ジインの環化から反応が進行し、ロダサイクルがシクロプロパノールを活性化していると結論付けた。

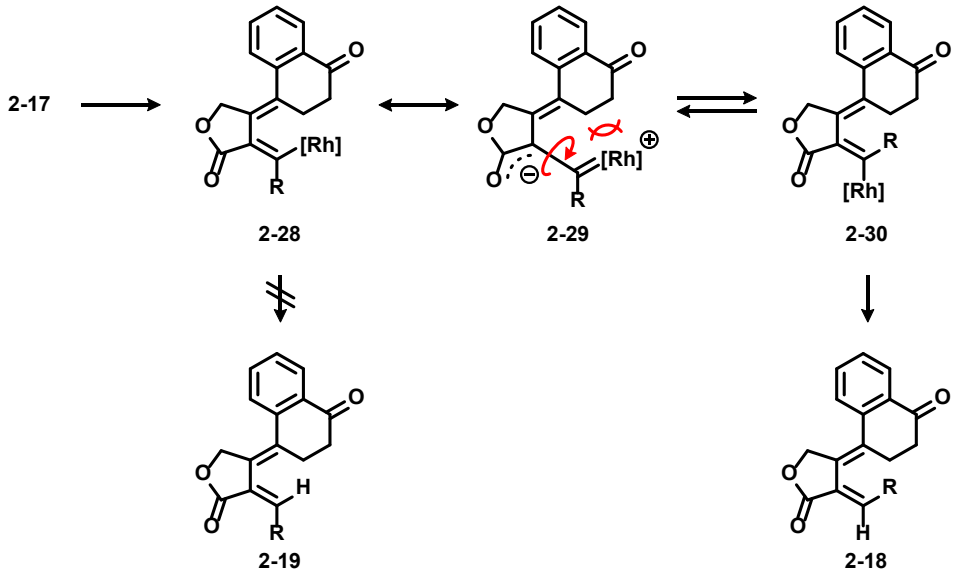
第 7 節　反応機構研究 : どのようにして熱力学的に不利なジエン骨格が構築されるか？

尾島らおよび Crabtree らは、ロジウム錯体触媒やイリジウム錯体触媒を用いる末端アルキンのヒドロシリル化反応を報告している（**Scheme 2-14**）[12]。遷移金属錯体とヒドロシランから調製される活性種 **2-23** が、末端アルキンに syn 付加することで、*E* 体の **2-24** が生成すると予想される。しかし、この反応では、*Z* 体の **2-25** が優先して得られる。これは、syn 付加が起こった後の **2-26** が、ケイ素の α 位のアニオン安定化効果を受けた双性イオンメタルカルベン **2-27** に変換され、シリル置換基と遷移金属錯体部位が立体障害を避けるようにして結合回転を起こすためであると考えられている。



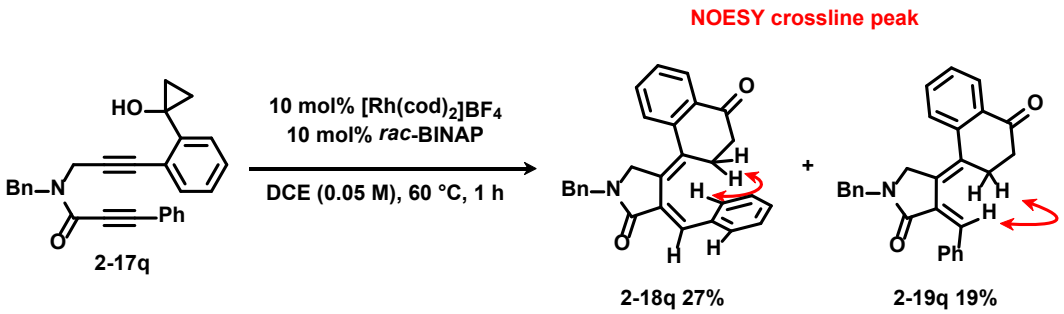
Scheme 2-14 遷移金属錯体触媒を用いる末端アルキンのヒドロシリル化反応

これを踏まえて、本反応でも尾島–Crabtree 様のメカニズムで異性化が起こることで、熱力学的に不利なジエン骨格が構築されていると考えた。予想される異性化機構を **Scheme 2-15** に示す。まず、本反応条件下で、**2-17** から導かれる共通中間体 **2-28** は、**2-19** へと変換されずに、エステルのカルボニル基の共鳴効果によるアニオン安定化を鍵として **2-29** に示す共鳴構造をとる。続いて、1-テトラロン部位とロジウム錯体部位が立体障害を避けるようにして結合回転を起こすことで、**2-30** へと異性化し、**2-18** が得られる。もし、予想される尾島–Crabtree 様のメカニズムで異性化しているのであれば、共鳴構造 **2-29** の寄与を小さくすることで、異性化が抑制されるはずである。すなわち、エステルテザーの代わりにアニオン安定化効果の小さいテザーを導入することで、得られる生成物の立体選択性（**2-18**:**2-19**）が低下すると考えた。そこで、テザーが本反応に与える影響を調査することとした。



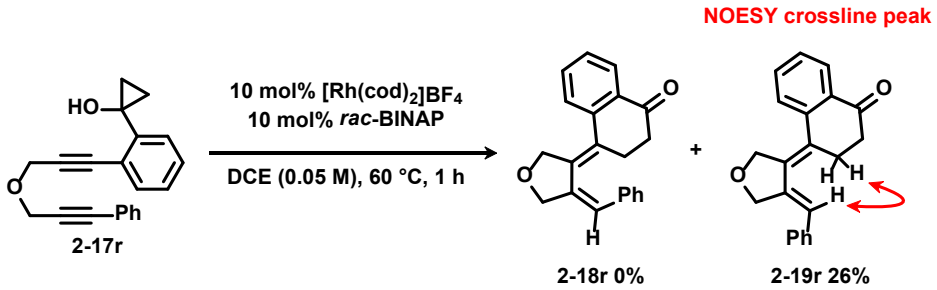
Scheme 2-15 予想される異性化機構

まず、カルボキサミドテザーを有する **2-17q** を調製し、反応を行った（**Scheme 2-16**）。10 mol%の触媒の存在下、反応温度 60 ℃で反応させることで、**2-17q** が完全に消失し、**2-18q** と **2-19q** をそれぞれ収率 27%および 19%で得た。**2-18q** と **2-19q** の立体化学は、NOESY 測定にて決定した。予想通り、エステルと比較してアニオン安定化効果の小さいカルボキサミドを導入したことで、**2-19q** が得られた。



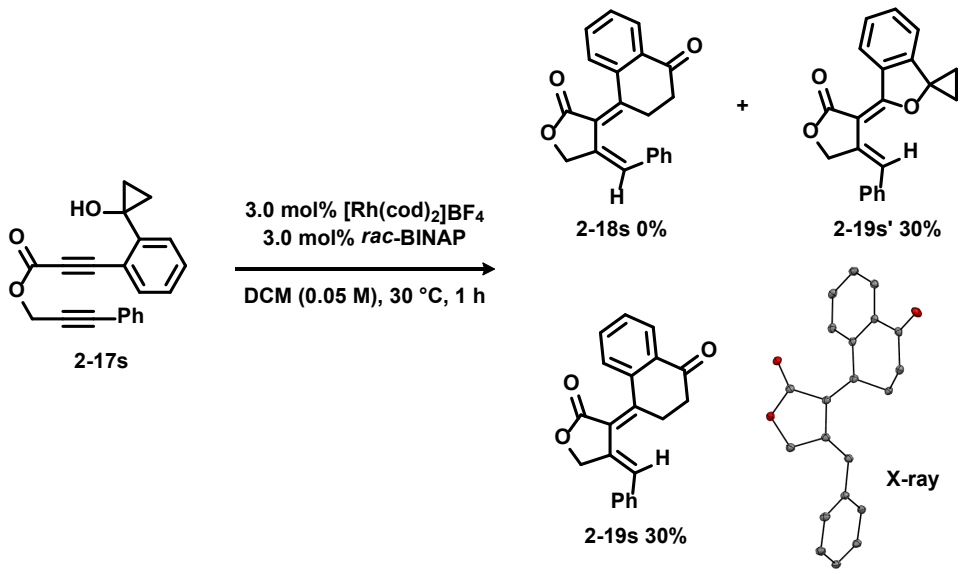
Scheme 2-16 カルボキサミドテザーを有する基質を用いた反応

続いて、エーテルテザーを有する **2-17r** を本反応条件に付したところ、**2-18r** の生成は確認できず、**2-19r** のみを収率 26%で得た（**Scheme 2-17**）。カルボニル基が存在しない **2-17r** では、対応する **2-29** の寄与が非常に小さいために、結合回転が起こらなかったと考えられる。



Scheme 2-17 エーテルテザーを有する基質を用いた反応

エステルテザーを有する **2-17a–p** を用いた反応に対して、**2-17q** および **2-17r** を用いた反応では、それぞれ反応の完結に 60 ℃への昇温を必要としたため、熱的に異性化して **2-19q** や **2-19r** が生成している可能性が内在している [13]。そこで、この可能性を否定するため新たな基質を設計した。すなわち、エステルよりも電子豊富なテザー部位が反応性の低下を招いていると考え、**2-17s** を設計した（**Scheme 2-18**）。**2-17s** を用いた反応は、加熱を必要とせず 30 ℃で完結し、外側に置換基を向けた環外ジエン **2-19s** および **2-19s'**を合計収率 60%で与えた。**2-19s** に関して、X 線結晶構造解析に成功した。また、らせん性環外ジエン **2-18s** の生成は確認できなかった。

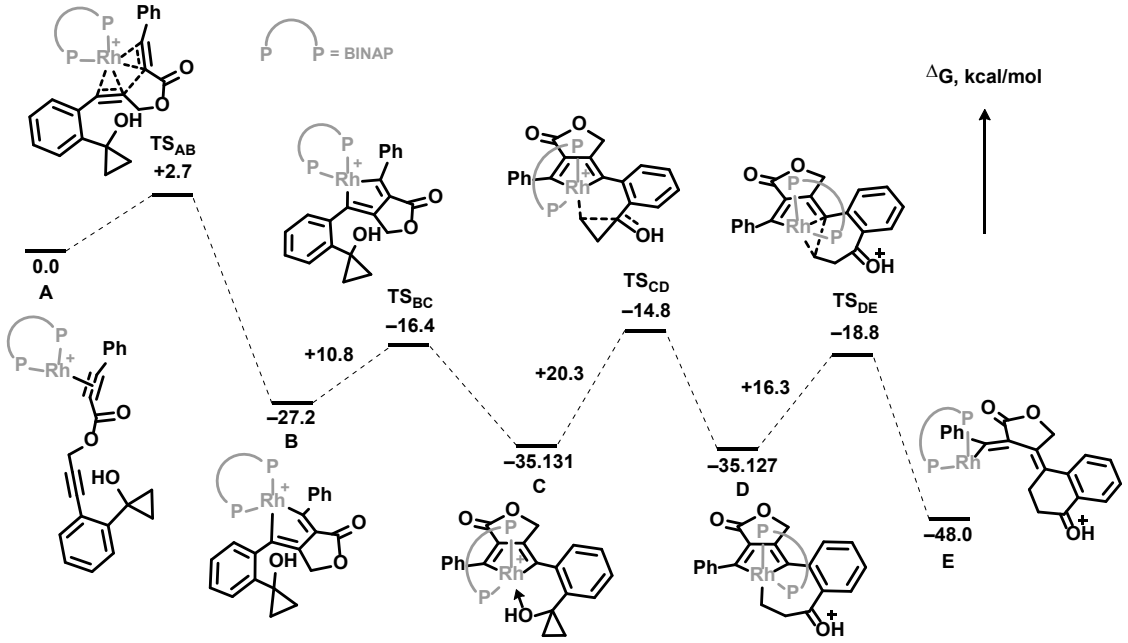


Scheme 2-18 エステルテザーを有する基質を用いた反応

以上のように、アニオンの安定化効果の小さいテザーを有する基質を用いた反応では、異性化が起こることなく **2-19** が得られることが分かった。また、**2-17** のアニオンの安定化の程度と **2-18** と **2-19** の生成比に相関が見られた。加えて、**2-17s** を基質とする反応では、反応温度 30 ℃で **2-19s** および **2-19s'**が得られていることから、**2-19q** や **2-19r** が熱的に異性化した生成物ではないことが示唆される。これらの実験事実は、本反応で得られるらせん性環外ジエンが、予想している尾島–Crabtree 様のメカニズムの *E/Z* 異性化を経て生成していることを強く支持している。

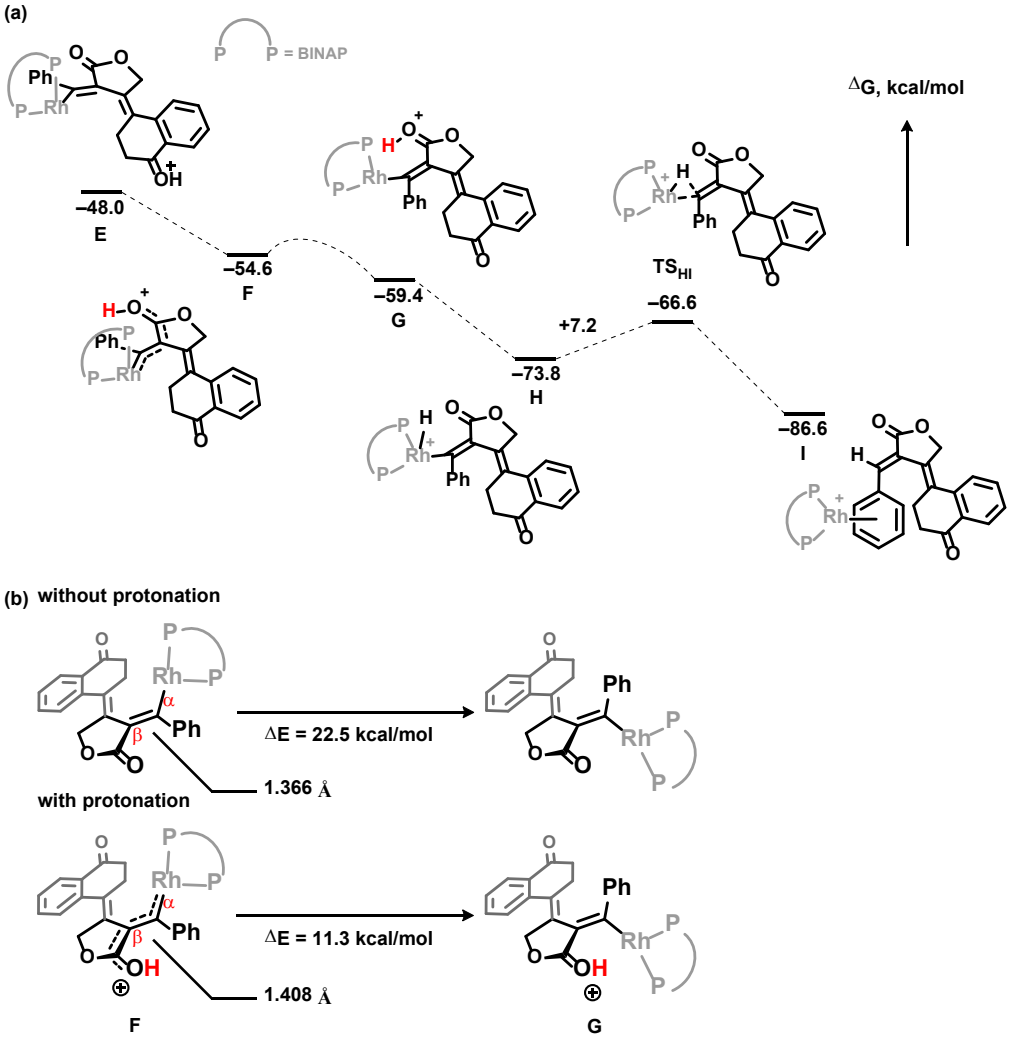
第 8 節　計算化学的手法による検討

これまでの実験結果を踏まえて、DFT 計算を行った（**Scheme 2-19**）。まず、錯体 **A** の酸化的環化によって、歪んだロダサイクル **B** を経由し、平面型ロダサイクル **C** となる。中間体 **C** におけるシクロプロパノールの開環の活性化障壁は 20.3 kcal/mol であり、本反応条件下で十分に進行し得る。DFT 計算によって、酸素の電子の押し込みによって、バナナボンドの電子がロジウムの空の d 軌道に流れ込むという新しいシクロプロパノールの活性化様式が支持された。次に、**D** の還元的脱離によって、ジエニルロジウム中間体 **E** を形成する。



Scheme 2-19 DFT 計算により支持される反応機構 1

続いて、**E** のプロトン移動により生じる **F** において、尾島–Crabtree 様の異性化が進行することで、**G** が生じる（**Scheme 2-20a**）。この *E/Z* 異性化の活性化障壁が 11.3 kcal/mol と見積もられたのに対し、カルボニル基上にプロトンがない場合の異性化の活性化障壁が 22.5 kcal/mol と見積もられたことから、カルボニル基のプロトン化が重要な役割を果たしていることが示された。（**Scheme 2-20b**）。実際に、カルボニル基上にプロトンがない場合の C_α–C_β が 1.366 Å であるのに対して、カルボニル基がプロトン化を受けている場合は 1.408 Å であり、カルボニル基のプロトン化によって、C_α–C_β の二重結合性が低下し、結合回転が容易になっていることが示唆された。最後に、ロジウム中心へのプロトン移動によって生じる **H** の還元的脱離が進行することで **I** となる。全体の反応は 86.6 kcal/mol の発エルゴン過程であり、実験結果から想定される反応機構と矛盾しない。



Scheme 2-20 DFT 計算により支持される反応機構 2

第 9 節　結論

カチオン性ロジウム触媒を用いる 1,6-ジイン含有シクロプロパノールの環化異性化反応では、らせん構造を有する環状エキソジエンが得られることが分かった。実験化学および計算化学的手法によって、本反応ではロダサイクルのロジウム中心がシクロプロパノールの炭素–炭素結合を直接的に活性化していることや尾島–Crabtree 様のメカニズムの *E/Z* 異性化によってらせん構造が構築されていることを明らかにした。

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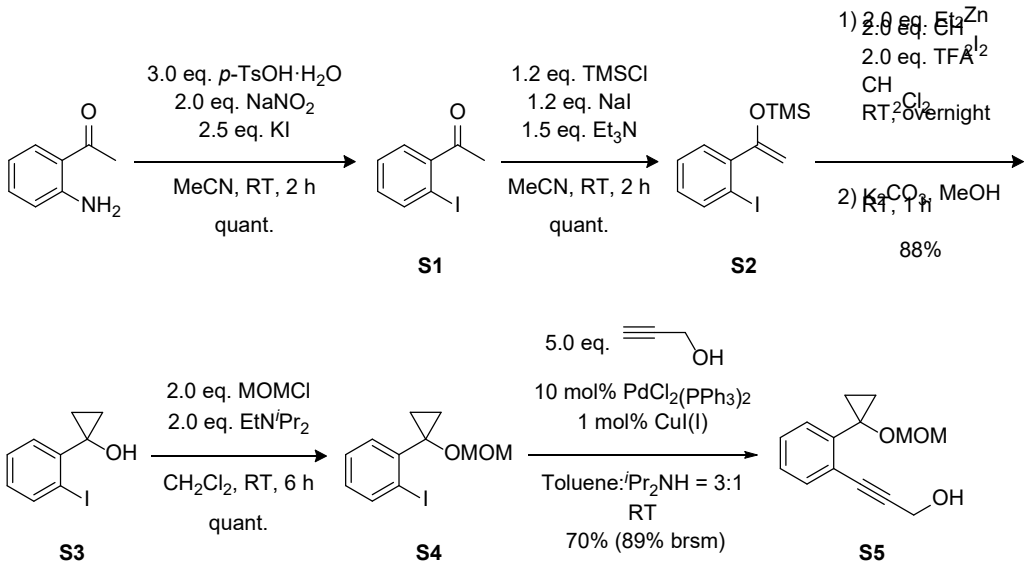
実験項

General considerations: All air- and moisture-sensitive reactions were performed under an argon (Ar) atmosphere. Analytical thin layer chromatography was performed using 0.25 mm silica gel plate (Merck TLC Silica gel 60 F_{254}). Column chromatography was performed on silica gel (Cica silica gel 60N) with solvents specified below. Melting points were recorded on SRS OptiMelt MPA100. NMR spectra were recorded on JEOL ESC-400 spectrometer (^{1}H/400 MHz and ^{13}C/101 MHz) for samples in $CDCl_3$ solutions at 25 ˚C. ^{1}H NMR chemical shifts are reported in terms of chemical shift (δ, ppm) relative to the signal at δ 0.00 ppm for internal tetramethylsilane. ^{13}C NMR spectra were fully decoupled and are reported in terms of chemical shift (δ, ppm) relative to the triplet at δ 77.0 ppm for $CDCl_3$. ^{19}F NMR spectra are reported in terms of chemical shift (δ, ppm) relative to the singlet at d −63.7 ppm for α,α,α-trifluorotoluene as an external standard. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; sept, septet; m, multiplet. Coupling constants are reported in Hz. Infrared spectra were recorded on JASCO FT/IR-230 spectrometer. High-resolution mass spectra were recorded on JEOL JMS-T100LP mass spectrometer.

Reagents and Solvents: $[RhOH(cod)]_2$,[1] $[Cp^*RuCl_2]_2$,[2] $[Ir(cod)Cl]_2$,[3] $[Rh(cod)_2]BF_4$,[4] $[Rh(cod)_2]PF_6$,[4] $[Rh(cod)_2]BAr^F$,[5] $[Rh(cod)_2]OTf$[4] and $[Rh(cod)_2]ClO_4$,[4] $PdCl_2(PPh_3)_2$,[5] were prepared according to the report. *rac*-BINAP was purchased from Aldrich and used after recrystallization from toluene and EtOH. dry DCM was distilled from calcium hydride under Ar atmosphere and stored over 4 Å molecular sieves. Other solvents and reagents were purchased from chemical suppliers (Aldrich, Kanto Chemical, TCI, and Wako) and used as received.

1. Synthesis and Characterization of 1,6-Diynes 2-17

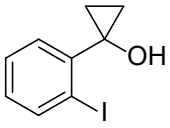
Synthesis of intermediate S5



Synthesis and characterization of S1 and S2

S1[6] and **S2**[7, 8] were prepared according to the previous reports.

Synthesis and characterization of S3

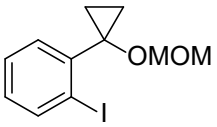


S3

To a dried 500 mL two-necked flask was added degassed dry DCM (120 mL) and Et_2Zn (40 mL, 1.07 M in hexane) under Ar. The solution was cooled to –10 °C and a solution of TFA (3.30 mL, 43.0 mmol) in degassed dry DCM (20 mL) was then dripped into the reaction mixture for 1 h (*very slowly*). On stirring for additional 1 h, a solution of CH_2I_2 (3.70 mL, 43.0 mmol) in degassed dry DCM (20 mL) was added to the reaction mixture for 1 h (*very slowly*). After stirring at rt for 3 h, **S2** (6.85 g, 21.5 mmol) was added to the mixture. The reaction mixture was stirred at rt overnight. The reaction was quenched with saturated aqueous NH_4Cl and extracted with hexane. The organic layer was washed with sat. aq. $NaHCO_3$, dried over $MgSO_4$, and concentrated in vacuo. To a MeOH solution (50 mL) of the crude material in a 200 mL flask was added K_2CO_3 (2.97 mg, 21.5 mmol) at rt. After being stirred for 1 h, the reaction mixture was diluted with water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 40:1) to furnish **S3** (4.95 g, 88%) as a pale-yellow solid. **Analytical data for S3:** pale-yellow solid (mp 52.4–52.8 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 7.8 Hz, 1H), 7.37 (dd, J = 7.5, 1.6 Hz, 1H), 7.31 (t, J = 7.5 Hz, 1H), 7.00 (dt, J = 7.8, 1.6 Hz, 1H), 2.99 (s, 1H), 1.29 (dd, J = 7.5, 5.3 Hz, 2H), 0.98 (dd, J = 7.5, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 143.9, 139.7, 131.0, 129.8, 128.4, 100.9,

61.0, 15.6; IR (neat) 3315 cm^{-1}; HRMS (DART) *m/z* $[M+ NH_4]^+$ calcd for $C_9H_9O_3I•NH_4$ 278.0042, found 278.0050.

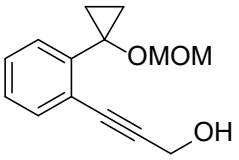
Synthesis and characterization of S4



S4

To a solution of **S3** (5.25 g, 20.2 mmol) and EtN^iPr_2 (7.0 mL, 40.4 mmol) in dry DCM (40 mL) was added MOMCl (3.0 mL, 40.4 mmol) at 0 °C, and the mixture was allowed to warm to rt. After being stirred at rt for 5 h, the reaction was quenched with water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S4** (5.96 g, quant.) as a yellow oil. **Analytical data for S4:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ7.91 (d, *J* = 7.4 Hz, 1H), 7.35–7.27 (m, 2H), 7.00 (dt, *J* = 7.4, 1.7 Hz, 1H), 4.61 (s, 2H), 3.17 (s, 3H), 1.34 (dd, *J* = 7.1, 5.7 Hz, 2H), 0.98 (dd, *J* = 7.1, 5.7 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 141.9, 140.1, 132.2, 129.7, 127.6, 101.5, 95.2, 65.0, 55.8, 14.0; IR (neat) 1034 cm^{-1}; HRMS (DART) *m/z* $[M+ NH_4]^+$ calcd for $C_{11}H_{13}IO_2•NH_4$ 322.0304, found 322.0295.

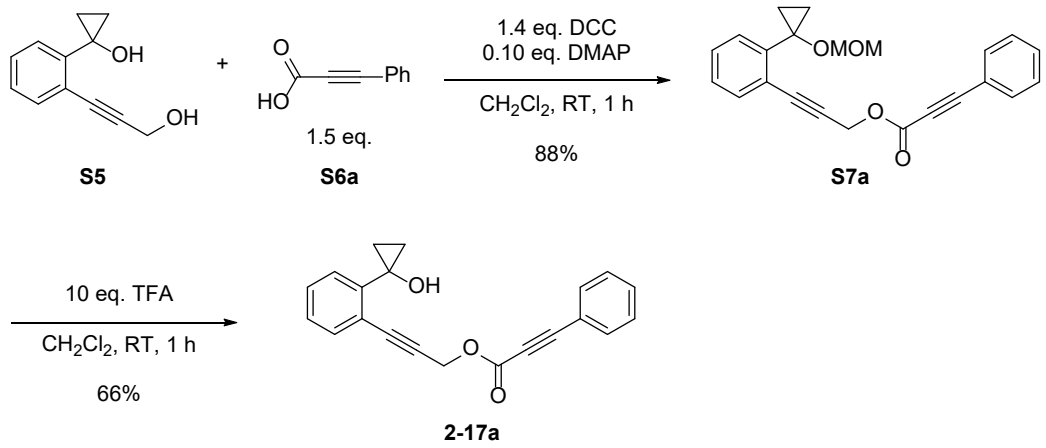
Synthesis and characterization of S5



S5

To a solution of **S4** (3.37 g, 11.1 mmol) in $^iPr_2NH$ (6.0 mL) and toluene (19 mL) was added $PdCl_2(PPh_3)_2$ (772 mg, 1.11 mmol) and CuI (20.9 mg, 0.110 mmol). After degassed at –78 °C, the reaction mixture was warmed to room temperature. To the stirred solution was added a solution of propargyl alcohol (930 mg, 16.6 mmol) in $^iPr_2NH$ (6.0 mL) and toluene (19 mL) over 1 h. Insoluble materials were filtered off through a pad of Celite®, and the filtrate was concentrated *in vacuo*. The obtained crude product was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to give **S5** (1.45 g, 70%) as a brown oil. **Analytical data for S5:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.3 Hz, 1H), 7.43 (d, *J* = 7.3 Hz, 1H), 7.33–7.24 (m, 2H), 4.70 (s, 2H), 4.51 (d, *J* = 5.5 Hz, 2H), 3.24 (s, 3H), 2.63 (t, *J* = 5.5 Hz, 1H), 1.29 (dd, *J* = 7.3, 5.5 Hz, 2H), 1.00 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 141.7, 132.3, 131.2, 128.4, 128.0, 124.4, 94.7, 92.5, 84.7, 61.2, 55.6, 51.7, 13.1; IR (neat) 3402, 1030 cm^{-1}; HRMS (DART) *m/z* $[M+ NH_4]^+$ calcd for $C_{14}H_{16}O_3•NH_4$ 250.1443, found 250.1418.

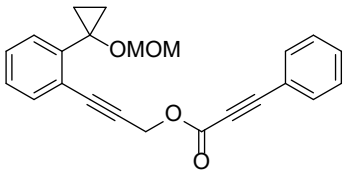
Representative procedure: synthesis of 2-17a–f and 2-17h–l.



Synthesis and characterization of S6b–d, S6f–h

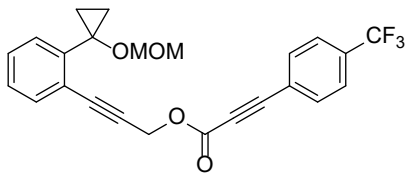
Compounds **S6b–d**[9], **S6e**[9], **S6f**[10], **S6i**[11], **S6j**[12] and **S6k**[13] were synthesized as reported.

Synthesis and characterization of S7a



S7a

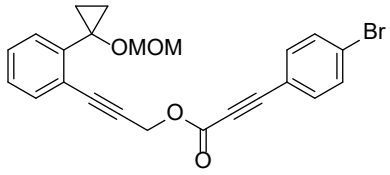
To a 50 mL flask was charged with **S5** (348 mg, 1.50 mmol), phenylpropiolic acid **S6a** (329 mg, 2.25 mmol) and DMAP (18.3 mg, 0.150 mmol). To the mixture was added a DCM (20 mL) solution of DCC (433 mg, 2.10 mmol) at 0 °C, and the resulting solution was stirred at room temperature for 1 h. After that, the reaction mixture was filtered through a pad of Celite® with EtOAc. The filtrate was washed with water, sat. aq. $NaHCO_3$ and brine. The solution was dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S7a** (476 mg, 88%) as an orange gum. **Analytical data for S7a:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.51–7.44 (m, 3H), 7.41–7.37 (m, 2H), 7.31–7.26 (m, 2H), 5.12 (s, 2H), 4.66 (s, 2H), 3.17 (s, 3H), 1.29 (dd, *J* = 7.2, 5.6 Hz, 2H), 1.00 (dd, *J* = 7.2, 5.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 153.4, 142.2, 133.2, 131.0, 130.7, 128.7, 128.7, 127.9, 123.5, 119.5, 95.2, 87.3, 86.7, 86.1, 80.2, 61.5, 55.6, 54.4, 13.0; IR (neat) 2356, 2220, 1714, 1164 cm^{-1}; HRMS (DART) *m/z* $[M+ NH_4]^+$ calcd for $C_{23}H_{20}O_4•NH_4$ 378.1705, found 378.1705



S7b

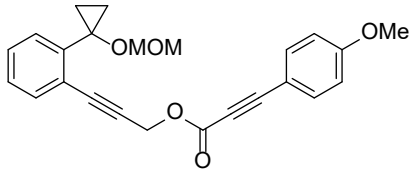
Analytical data for S7b: orange gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.50 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.45 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.32 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.26 (dt, *J* = 7.8, 1.3 Hz, 3H), 5.14 (s, 2H), 4.65 (s, 2H), 3.17 (s, 3H), 1.28 (dd, *J* = 7.3, 5.5 Hz, 2H), 1.00 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz,

$CHCl_3$) δ 153.0, 142.2, 133.3, 133.2, 130.7, 128.7, 127.9, 125.7, 125.7, 123.4, 123.3, 95.2, 86.3, 85.0, 81.7, 61.5, 55.6, 54.7, 13.0; ^{19}F-NMR (376 MHz, $CDCl_3$) δ –64.1; IR (neat) 2227, 1720, 1171 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{24}H_{19}F_3O_4$•NH_4 446.1579, found 446.1584



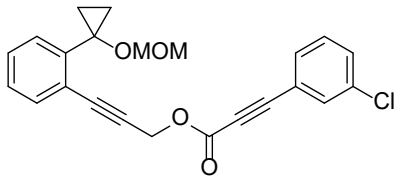
S7c

Analytical data for S7c: orange gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.50–7.44 (m, 4H), 7.33–7.29 (m, 1H), 7.28–7.24 (m, 1H), 5.12 (s, 2H), 4.65 (s, 2H), 3.16 (s, 3H), 1.28 (dd, *J* = 7.3, 5.5 Hz, 2H), 1.00 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.2, 142.2, 134.4, 133.2, 132.1, 130.7, 128.7, 127.9, 125.8, 123.5, 118.4, 95.2, 86.4, 86.2, 86.1, 81.1, 61.5, 55.6, 54.6, 13.0; IR (neat) 2343, 2222, 1716, 1162 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{23}H_{19}BrO_4$•NH_4 456.0811, found 456.0838



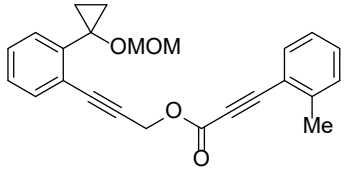
S7d

Analytical data for S7d: orange gum; ^{1}NMR (400 MHz, $CDCl_3$) δ 7.57-7.54 (m, 2H), 7.49 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.45 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.31 (dt, *J* = 7.5, 1.2 Hz, 1H), 7.25 (dt, *J* = 7.5, 1.2 Hz, 1H), 6.91–6.88 (m, 2H), 5.11 (s, 2H), 4.65 (s, 2H), 3.84 (s, 3H), 3.17 (s, 3H), 1.28 (dd, *J* = 7.1, 5.7 Hz, 2H), 1.00 (dd, *J* = 7.1, 5.7 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 161.8, 153.7, 142.2, 135.2, 133.2, 130.7, 128.6, 127.8, 123.6, 114.4, 111.3, 95.2, 88.3, 86.8, 86.0, 79.7, 61.5, 55.6, 55.5, 54.3, 13.0; IR (neat) 2211, 1710, 1155 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{24}H_{22}O_5$•NH_4 408.1811, found 408.1815



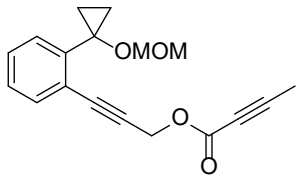
S7e

Analytical data for S7e: orange gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.59 (t, *J* = 1.8 Hz, 1H), 7.51–7.43 (m, 4H), 7.35–7.24 (m, 3H), 5.12 (s, 2H), 4.65 (s, 2H), 3.17 (s, 3H), 1.28 (dd, *J* = 7.3, 5.5 Hz, 2H), 1.00 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 152.9, 142.2, 134.6, 133.1, 132.7, 131.2, 130.7, 130.0, 128.7, 127.9, 123.4, 121.2, 95.1, 86.6, 86.2, 85.2, 81.0, 61.4, 55.5, 54.6, 13.0; IR (neat) 1718, 1172 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{23}H_{19}O_4Cl$•NH_4 412.1316, found 412.1335



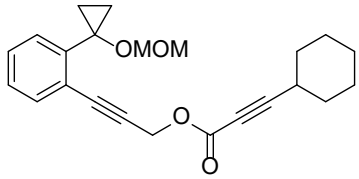
S7f

Analytical data for S7f: yellow gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.57–7.55 (m, 1H), 7.50 (dd, *J* = 7.3, 1.8 Hz, 1H), 7.45 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.37–7.24 (m, 4H), 7.19 (t, *J* = 7.6 Hz, 1H), 5.12 (s, 2H), 4.66 (s, 2H), 3.17 (s, 3H), 2.51 (s, 3H), 1.29 (dd, *J* = 7.1, 5.7 Hz, 2H), 1.00 (dd, *J* = 7.1, 5.7 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.4, 142.4, 142.3, 133.6, 133.1, 130.9, 130.7, 129.9, 128.6, 127.9, 126.0, 123.5, 119.3, 95.1, 86.9, 86.3, 86.0, 84.0, 61.4, 55.4, 54.3, 20.5, 13.0; IR (neat) 2216, 1714, 1173 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{24}H_{22}O_4$•NH_4 392.1862, found 392.1889



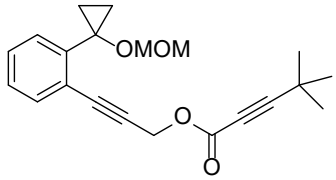
S7h

Analytical data for S7h: pale yellow gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.43 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.29 (dt, *J* = 7.2, 1.2 Hz, 1H), 7.23 (dt, *J* = 7.2, 1.2 Hz, 1H), 5.02 (s, 2H), 4.63 (s, 2H), 3.15 (s, 3H), 2.00 (s, 3H), 1.25 (dd, *J* = 7.6, 5.3 Hz, 2H), 0.97 (dd, *J* = 7.6, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.1, 142.1, 133.1, 130.7, 128.6, 127.8, 123.5, 95.2, 86.7, 86.6, 85.9, 72.0, 61.4, 55.6, 54.2, 13.0, 4.0; IR (neat) 2310, 2238, 1716, 1243 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{18}H_{18}O_4$•NH_4 316.1549, found 316.1539



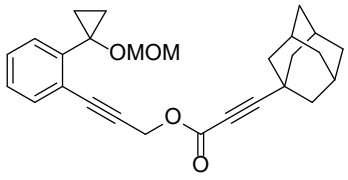
S7i

Analytical data for S7i: pale yellow gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 7.3 Hz, 1H), 7.32–7.28 (m, 1H), 7.26–7.23 (m, 1H), 5.04 (s, 2H), 4.64 (s, 2H), 3.16 (s, 3H), 2.57–2.51 (m, 1H), 1.86–1.83 (m, 2H), 1.73–1.71 (m, 2H), 1.61-1.49 (m, 3H), 1.38–1.31 (m, 3H), 1.27 (dd, *J* = 7.3, 5.5 Hz, 2H), 0.99 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.4, 142.1, 133.1, 130.7, 128.6, 127.8, 123.6, 95.2, 94.3, 86.8, 85.8, 72.6, 61.4, 55.6, 54.1, 31.5, 29.0, 25.7, 24.7, 13.0; IR (neat) 2933, 2856, 2364, 2233, 1716, 1234 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{23}H_{26}O_4$•NH_4 384.2174, found 384.2165



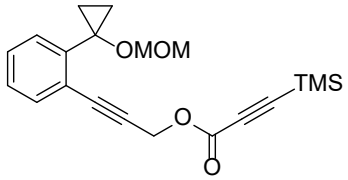
S7j

Analytical data for S7j: pale yellow gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.1 Hz, 1H), 7.44 (d, *J* = 7.1 Hz, 1H), 7.30 (t, *J* = 7.1 Hz, 1H), 7.24 (t, *J* = 7.1 Hz, 1H), 5.04 (s, 2H), 4.64 (s, 2H), 3.17 (s, 3H), 1.30 (s, 9H), 1.26 (dd, *J* = 7.4, 5.4 Hz, 2H), 0.99 (dd, *J* = 7.4, 5.4 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.4, 142.1, 133.2, 130.7, 128.6, 127.8, 123.6, 97.8, 95.2, 86.8, 85.8, 71.3, 61.4, 55.6, 54.1, 30.0, 27.7, 13.0; IR (neat) 2971, 2225, 1716, 1211 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{21}H_{24}O_4$•NH_4 358.2018, found 358.2031



S7k

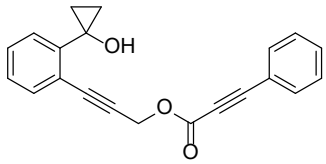
Analytical data for S7k: orange gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.44 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.30 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.24 (dt, *J* = 7.6, 1.2 Hz, 1H), 5.03 (s, 2H), 4.64 (s, 2H), 3.16 (s, 3H), 1.99 (br s, 3H), 1.93 (br s, 6H), 1.70 (br s, 6H), 1.27 (dd, J = 7.3, 5.5 Hz, 2H), 0.99 (dd, J = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.3, 142.1, 133.0, 130.7, 128.6, 127.8, 123.5, 96.9, 95.1, 86.9, 85.7, 71.7, 61.4, 55.4, 53.9, 41.5, 36.1, 29.7, 27.6, 12.9; IR (neat) 2908, 2852, 2227, 1716, 1240 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{27}H_{30}O_4$•NH_4 436.2488, found 436.2498



S7l

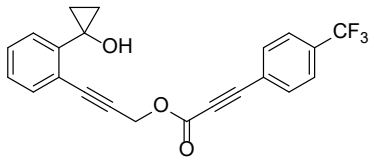
Analytical data for S7l: pale yellow gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.44 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.31 (dt, *J* = 7.4, 1.2 Hz, 1H), 7.25 (dt, *J* = 7.4, 1.2 Hz, 1H), 5.05 (s, 2H), 4.64 (s, 2H), 3.16 (s, 3H), 1.27 (dd, *J* = 7.3, 5.5 Hz, 2H), 0.98 (dd, *J* = 7.3, 5.5 Hz, 2H), 0.26 (s, 9H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 152.4, 142.2, 133.2, 130.7, 128.7, 127.9, 123.5, 95.4, 95.2, 94.0, 86.4, 86.1, 61.4, 55.6, 54.4, 13.0, -0.8; IR (neat) 1718, 1209 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{20}H_{24}O_4Si$•NH_4 374.1788, found 374.1774

Synthesis and characterization of 2-17a



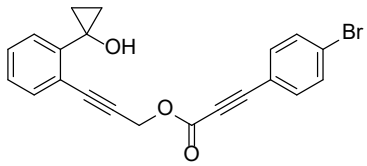
2-17a

To a 50 mL flask was added **S7a** (360 mg, 1.00 mmol) followed by degassed DCM (10 mL). TFA (0.770 mL, 10.0 mmol) was slowly added to the solution. After being stirred at rt for 1 h under Ar atmosphere, the reaction mixture was diluted with water and extracted with EtOAc. The organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **2-17a** (209 mg, 66%) as an orange gum. **Analytical data for 2-17a:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 8.8, 1.6 Hz, 2H), 7.50–7.45 (m, 2H), 7.40–7.36 (m, 3H), 7.31 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.25 (dt, *J* = 7.6, 1.2 Hz, 1H), 5.09 (s, 2H), 3.35 (s, 1H), 1.23 (dd, *J* = 7.2, 5.2 Hz, 2H), 1.00 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.7, 145.0, 133.3, 133.0, 131.0, 129.3, 128.7, 128.2, 127.7, 122.2, 119.4, 87.9, 87.4, 86.1, 80.0, 56.9, 54.4, 14.4; IR (neat) 3533, 3403, 2220, 1712, 1166 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{21}H_{16}O_3$•NH_4 334.1443, found 334.1438



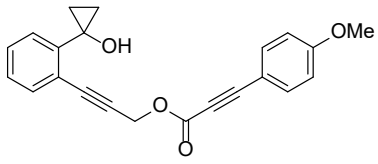
2-17b

Analytical data for 2-17b: red gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 7.3 Hz, 1H), 7.36 (d, *J* = 7.3 Hz, 1H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.26 (t, *J* = 7.3 Hz, 1H), 5.09 (s, 2H), 3.28 (br s, 1H), 1.23 (dd, *J* = 7.4, 5.4 Hz, 2H), 1.00 (dd, *J* = 7.4, 5.4 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.2, 145.0, 133.4, 133.0, 129.4, 128.2, 127.8, 125.7, 125.7, 125.6, 123.2, 122.1, 87.1, 86.3, 85.5, 81.5, 56.9, 54.6, 14.4; ^{19}F-NMR (376 MHz, $CDCl_3$) δ –64.1; IR (neat) 3536, 3411, 2225, 1716, 1170 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{22}H_{15}F_3O_3$•NH_4 402.1317, found 402.1299



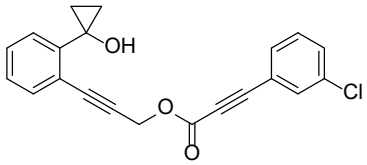
2-17c

Analytical data for 2-17c: orange gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 7.3 Hz, 1H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 1H), 5.09 (s, 2H), 3.30 (br s, 1H), 1.22 (dd, *J* = 7.1, 5.3 Hz, 2H), 1.00 (dd, *J* = 7.1, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.4, 145.0, 134.5, 133.0, 132.2, 129.3, 128.2, 127.7, 125.9, 122.2, 118.3, 87.3, 86.6, 86.2, 80.9, 56.9, 54.5, 14.4; IR (neat) 3535, 3396, 2322, 2220, 1713, 1167 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{21}H_{15}BrO_3$•NH_4 412.0548, found 412.0558



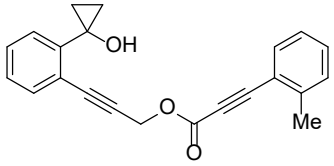
2-17d

Analytical data for 2-17d: orange gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.58–7.54 (m, 2H), 7.49 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.37 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.31 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.25 (dt, *J* = 7.8, 1.4 Hz, 1H), 6.91–6.88 (m, 2H), 5.08 (s, 2H), 3.84 (s, 3H), 3.37 (s, 1H), 1.22 (dd, *J* = 7.1, 5.3 Hz, 2H), 0.99 (dd, *J* = 7.1, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 161.9, 153.9, 145.1, 135.3, 132.9, 129.2, 128.2, 127.7, 122.3, 114.4, 111.1, 88.9, 87.6, 86.0, 79.5, 56.9, 55.5, 54.2, 14.4; IR (neat) 3515, 1743 cm^{-1}; HRMS (DART) *m/z* [M+H]$^+$ calcd for $C_{22}H_{18}O_4$•H 347.1283, found 347.1276



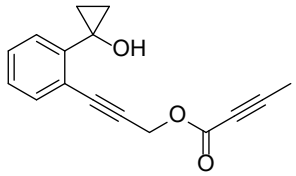
2-17e

Analytical data for 2-17e: orange gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.59 (t, *J* = 1.8 Hz, 1H), 7.50–7.44 (m, 3H), 7.39–7.30 (m, 2H), 7.26 (dt, *J* = 7.2, 1.2 Hz, 2H), 5.10 (s, 2H), 3.30 (s, 1H), 1.23 (dd, *J* = 7.1, 5.3 Hz, 2H), 1.00 (dd, *J* = 7.1, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.3, 145.0, 134.7, 133.0, 132.8, 131.3, 131.3, 130.0, 129.3, 128.3, 127.7, 122.2, 121.0, 87.2, 86.2, 85.8, 80.7, 56.9, 54.6, 14.4; IR (neat) 3535, 3408, 2224, 1714 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{21}H_{15}O_3Cl$•NH_4 368.1054, found 368.1058



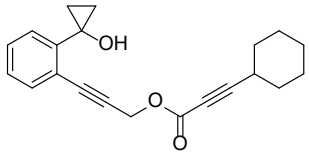
2-17f

Analytical data for 2-17f: yellow gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.49 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.38-7.29 (m, 3H), 7.27–7.23 (m, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 5.09 (s, 2H), 3.30 (br s, 1H), 2.50 (s, 3H), 1.23 (dd, *J* = 7.3, 5.0 Hz, 2H), 1.00 (dd, *J* = 7.3, 5.0 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.8, 145.1, 142.6, 133.7, 132.9, 131.0, 129.9, 129.3, 128.2, 127.7, 125.9, 122.3, 119.2, 87.6, 87.0, 86.0, 83.7, 56.9, 54.3, 20.6, 14.4; IR (neat) 3535, 3405, 2213, 1711 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{22}H_{18}O_3$•NH_4 348.1600, found 348.1600



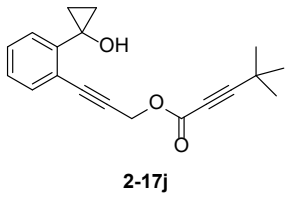
2-17h

Analytical data for 2-17h: pale yellow gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.36 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.31 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.24 (dt, *J* = 7.6, 1.2 Hz, 1H), 4.99 (s, 2H), 3.42 (br s, 1H), 2.01 (s, 3H), 1.19 (dd, *J* = 7.2, 4.8 Hz, 2H), 0.99 (dd, *J* = 7.2, 4.8 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.3, 145.0, 132.9, 129.2, 128.2, 127.7, 122.3, 87.5, 87.3, 85.9, 71.8, 56.9, 54.1, 14.4, 4.0; IR (neat) 3535, 3407, 2320, 2239, 1712, 1248 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{16}H_{14}O_3$•NH_4 272.1287, found 272.1259



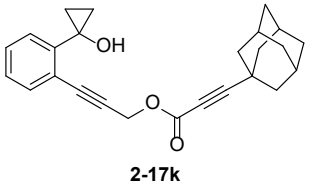
2-17i

Analytical data for 2-17i: pale yellow gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.36 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.31 (dt, *J* = 7.6, 1.4 Hz, 1H), 7.23 (dt, *J* = 7.6, 1.4 Hz, 1H), 5.00 (s, 2H), 3.34 (br s, 1H), 2.57–2.51 (m, 1H), 1.86-1.82 (m, 2H), 1.75–1.68 (m, 2H), 1.55–1.49 (m, 3H), 1.38–1.31 (m, 3H), 1.21 (dd, *J* = 7.3, 5.0 Hz, 2H), 0.98 (dd, *J* = 7.3, 5.0 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.6, 145.1, 132.9, 129.2, 128.2, 127.7, 122.3, 94.9, 87.6, 85.8, 72.5, 56.9, 54.1, 31.4, 29.0, 25.6, 24.7, 14.4; IR (neat) 3535, 3408, 2931, 2233, 1712, 1238 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{21}H_{22}O_3$•NH_4 340.1913, found 340.1911



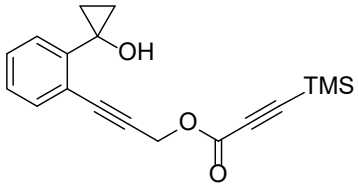
2-17j

Analytical data for 2-17j: light orange gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.3 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.33–7.29 (m, 1H), 7.25–7.22 (m, 1H), 5.00 (s, 2H), 3.35 (br s, 1H), 1.29 (s, 9H), 1.21 (dd, *J* = 7.1, 5.3 Hz, 2H), 0.98 (dd, *J* = 7.1, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.6, 145.1, 132.9, 129.2, 128.2, 127.7, 122.3, 98.4, 87.6, 85.8, 71.2, 56.9, 54.0, 29.9, 27.7, 14.4; IR (neat) 3539, 3415, 2972, 2225, 1712, 1213 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^+$ calcd for $C_{19}H_{20}O_3$•NH_4 314.1756, found 314.1727



2-17k

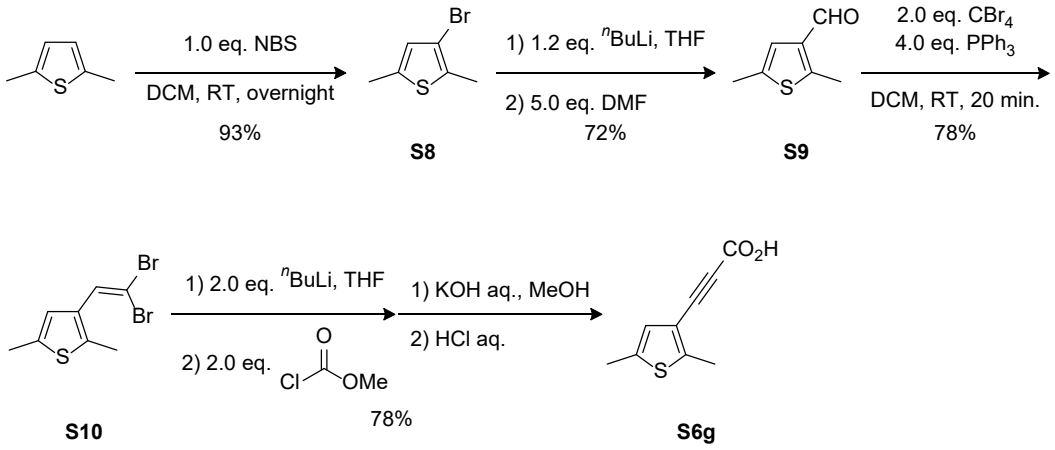
Analytical data for 2-17k: light orange gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.3 Hz, 1H), 7.37–7.35 (m, 1H), 7.33–7.29 (m, 1H), 7.25–7.22 (m, 1H), 5.00 (s, 2H), 3.35 (br s, 1H), 1.99 (br s, 3H), 1.93 (br s, 6H), 1.70 (br s, 6H), 1.21 (dd, J = 7.1, 5.3 Hz, 2H), 0.98 (dd, J = 7.1, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.8, 145.1, 132.9, 129.2, 128.1, 127.7, 122.3, 97.9, 87.7, 85.8, 71.5, 56.9, 54.0, 41.5, 36.1, 29.8, 27.6, 14.4; IR (neat) 3535, 3409, 2908, 2225, 1712, 1242 cm^{-1}; HRMS (DART) *m/z* [M– H_2O]$^{+}$ calcd for $C_{25}H_{25}O_2$ 357.1855, found 357.1855



2-17l

Analytical data for 2-17l: pale yellow gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.8 Hz, 1H), 7.37–7.35 (m, 1H), 7.33–7.29 (m, 1H), 7.25–7.23 (m, 1H), 5.02 (s, 2H), 3.27 (br s, 1H), 1.21 (dd, J = 7.1, 5.3 Hz, 2H), 0.98 (dd, J = 7.1, 5.3 Hz, 2H), 0.26 (s, 9H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 152.6, 145.0, 133.0, 129.3, 128.2, 127.7, 122.2, 96.0, 93.8, 87.3, 86.0, 56.9, 54.3, 14.4, -0.9; IR (neat) 3539, 3413, 2960, 1714, 1211 cm^{-1}; HRMS (DART) *m/z* [M+ NH_4]$^{+}$ calcd for $C_{18}H_{20}O_3Si•NH_4$ 330.1525, found 330.1530

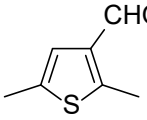
Synthesis of S6g



Synthesis and characterization of S8

A known compound **S8** was synthesized as reported[14].

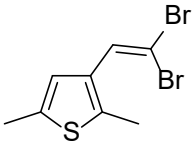
Synthesis and characterization of S9[15]



S9

A solution of **S8** (3.56 g, 18.6 mmol) in THF (40 mL) was cooled under Ar atmosphere to –78 °C. A solution of ^{n}BuLi (14.0 mL, 1.60 M in hexane) was added and the mixture was stirred for 1 h. After addition of dry DMF (7.20 mL, 93.0 mmol), the mixture was warmed to rt and stirred for another 1 h. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S9**[15] (1.87 g, 72%).

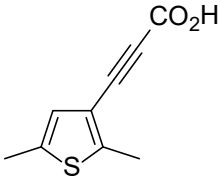
Synthesis and characterization of S10



S10

To a solution of PPh_3 (14.4 g, 54.9 mmol) in DCM (100 mL) was added CBr_4 (9.04 g, 27.3 mmol) and **S9** (1.87 g, 13.4 mmol) at 0 °C. The reaction mixture was stirred at rt for 20 min. The reaction was quenched with water. The aqueous phase was extracted with DCM. The combined organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane) to furnish **S10** (3.07 g, 78%). **Analytical data for S10:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 1H), 7.12 (s, 1H), 2.37 (s, 3H), 2.28 (s, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 137.3, 135.6, 132.1, 131.1, 124.4, 88.3, 15.5, 13.8; IR (neat) 2916 cm^{-1}; HRMS (DART) *m/z* [M+ H]$^{+}$ calcd for $C_8H_8Br_2S$•H 294.8792, found 294.8771

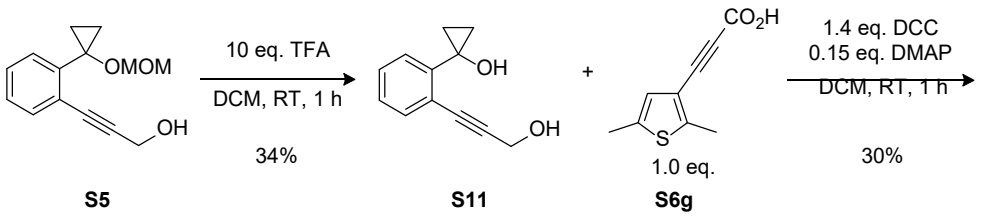
Synthesis and characterization of S6g



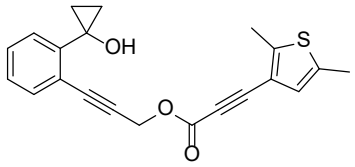
S6g

A solution of **S10** (3.07 g, 10.3 mmol) in THF (30 mL) was cooled under Ar atmosphere to 0 °C. A solution of ^{n}BuLi (12.8 mL, 1.60 M in hexane) was added and the mixture was stirred for 15 min. Methyl chloroformate (1.90 g, 20.6 mmol) was added to the mixture. After being stirred at 0 °C for 30 min, the reaction mixture was quenched with water and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. To a solution of the crude product in MeOH (40 mL) was added 20% aq. KOH (11.2 g, 200 mmol), and the solution was stirred at rt for 30 min. After that, 1 M aq. HCl was added slowly at 0 °C until the pH value was less than 1. This mixture was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. **S6g** was obtained as a brown solid (1.44g, 78%). **Analytical data for S6g:** brown solid (mp 120.1–121.1 °C);^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.71 (s, 1H), 2.54 (s, 3H), 2.39 (s, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 159.1, 149.4, 137.0, 127.3, 115.7, 85.2, 82.8, 15.2, 14.7; IR (neat) 2916, 1666 cm^{-1}; HRMS (DART) *m/z* [M+ H]$^{+}$ calcd for $C_9H_8O_2S$•H 181.0239, found 181.0244

Synthesis and characterization of 2-17g

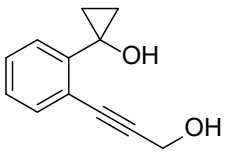


S5 **S11** **S6g**



2-17g

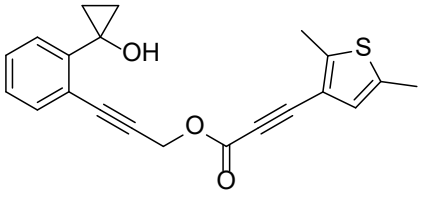
Synthesis and characterization of S11



S11

To a 50 mL flask was added **S5** (682 mg, 2.93 mmol) followed by degassed DCM (20 mL). TFA (2.20 mL, 29.3 mmol) was slowly added to the solution. After stirring at rt for 1 h under Ar atmosphere, the reaction mixture was diluted with water and extracted with EtOAc. The organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 5:1) to furnish **S11** (188 mg, 34%). **Analytical data for S11:** brown solid (mp 81.3–83.1 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.3 Hz, 1H), 7.35 (d, J = 7.8 Hz, 1H), 7.32–7.25 (m, 2H), 4.57 (d, J = 5.9 Hz, 2H), 3.19 (s, 1H), 1.83 (t, J = 5.9 Hz, 1H), 1.20 (t, J = 6.2 Hz, 2H), 1.01 (t, J = 6.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 144.0, 132.8, 128.6, 128.4, 127.8, 123.5, 92.8, 84.0, 57.1, 51.3, 14.1; IR (KBr) 3307 cm^{-1}; HRMS (DART) *m/z* [M+ H]$^+$ calcd for $C_{12}H_{12}O_2$•H 189.0916, found 189.0903

Synthesis and characterization of 2-17g

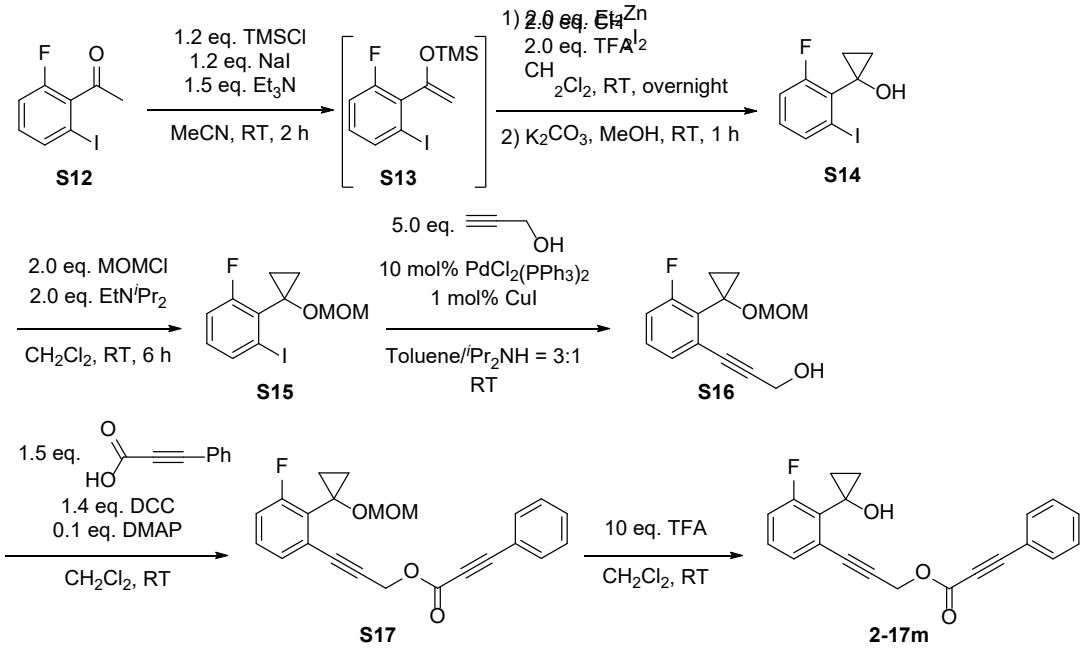


2-17g

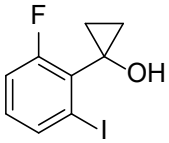
To a 30 mL flask was charged with **S11** (157 mg, 0.840 mmol), **S6g** (151 mg, 0.840 mmol) and DMAP (15.4 mg, 0.130 mmol). To the mixture was added a DCM (8 mL) solution of DCC (193 mg, 0.935 mmol) at 0 °C, and the resulting solution was stirred at rt for 1 h. The reaction mixture was filtered through a pad of Celite® with EtOAc. The filtrate was washed with water, sat. aq. $NaHCO_3$ and brine. The solution was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography

(Hexane/EtOAc = 10:1) to furnish **2-17g** (89.4 mg, 30%). **Analytical data for 2-17g:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.36 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.31 (dt, *J* = 7.3, 1.4 Hz, 1H), 7.25 (dt, *J* = 7.3, 1.4 Hz, 1H), 6.70 (s, 1H), 5.06 (s, 2H), 3.39 (br s, 1H), 2.53 (s, 3H), 2.38 (s, 3H), 1.22 (dd, J = 7.1, 5.3 Hz, 2H), 0.99 (dd, J = 7.1, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 154.0, 148.9, 145.1, 136.9, 132.9, 129.2, 128.2, 127.7, 127.3, 122.3, 87.7, 85.9, 83.8, 82.4, 56.9, 54.2, 15.2, 14.7, 14.4; IR (neat) 3535, 3406, 2210, 1709 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{21}H_{18}O_3S$•H 351.1055, found 351.1035

Synthesis of 2-17m



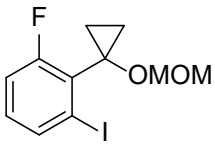
Synthesis and characterization of S14



S14

This compound was prepared in the same manner as described for **S3** using **S12**[16] instead of **S1** in 61% yield as a pale-yellow solid. **Analytical data for S14:** pale-yellow solid (mp 82.3–84.4 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 1H), 7.08–7.03 (m, 1H), 6.99–6.94 (m, 1H), 2.83 (br s, 1H), 1.44–1.32 (m, 2H), 1.09–0.97 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 161.1 (d, *J* = 256.1 Hz), 135.4 (d, *J* = 2.9 Hz), 131.3 (d, *J* = 13.5 Hz), 130.8 (d, *J* = 8.6 Hz), 116.4 (d, *J* = 23.1 Hz), 101.5, 55.3, 16.6 (d, *J* = 4.7 Hz, 2C); ^{19}F NMR (376 MHz, $CDCl_3$): δ –112.3; IR (KBr) 3402 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for C_9H_8FIO•NH_4 295.9948, found 295.9948.

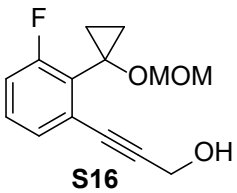
Synthesis and characterization of S15



S15

This compound was prepared in the same manner as described for **S4** using **S14** instead of **S3** in 91% yield as a yellow oil. **Analytical data for S15:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.70–7.68 (m, 1H), 7.06–7.01 (m, 1H), 6.98–6.93 (m, 1H), 4.74 (s, 2H), 3.12 (s, 3H), 1.44-1.42 (m, 2H), 1.05–1.02 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 161.4 (d, *J* = 254.2 Hz), 135.7 (d, *J* = 3.8 Hz), 130.7 (d, *J* = 8.7 Hz), 130.2 (d, *J* = 13.5 Hz), 115.8 (d, *J* = 24.0 Hz), 102.2, 96.0, 59.4, 55.6, 15.5 (2C); ^{19}F NMR (376 MHz, $CDCl_3$) δ –110.6: IR (neat) 1562, 1440 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{11}H_{12}FIO_2 \bullet NH_4$ 340.0210, found 340.0201.

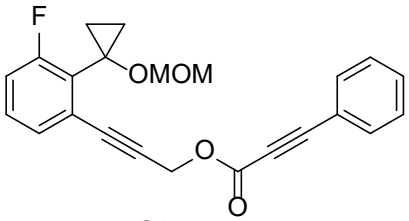
Synthesis and characterization of S16



S16

This compound was prepared in the same manner as described for **S5** using **S15** instead of **S4** in 59% yield as a brown oil. **Analytical data for S16:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.27–7.19 (m, 2H), 7.06–7.02 (m, 1H), 4.78 (s, 2H), 4.50 (d, *J* = 5.5 Hz, 2H), 3.29 (t, *J* = 5.5 Hz, 1H), 3.23 (s, 3H), 1.39–1.35 (m, 2H), 1.06–1.02 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 162.3 (d, *J* = 251.4 Hz), 129.5 (d, *J* = 10.6 Hz), 128.9 (d, *J* = 14.4 Hz), 127.8 (d, *J* = 2.9 Hz), 126.3 (d, *J* = 4.7 Hz), 116.1 (d, *J* = 23.1 Hz), 95.0, 93.4, 83.7 (d, *J* = 3.8 Hz), 55.3, 55.2, 51.4, 13.7 (d, *J* = 2.8 Hz, 2C); ^{19}F NMR (376 MHz, $CDCl_3$) δ –114.1; IR (neat) 3417 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{14}H_{15}FO_3 \bullet NH_4$ 268.1349, found 268.1327.

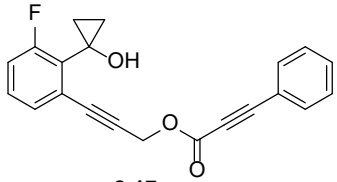
Synthesis and characterization of S17



S17

This compound was prepared in the same manner as described for **S7a** using **S16** instead of **S5** in 79% yield as an orange gum. **Analytical data for S17:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.62–7.59 (m, 2H), 7.49–7.45 (m, 1H), 7.41–7.37 (m, 2H), 7.29–7.21 (m, 2H), 7.08–7.03 (m, 1H), 5.11 (s, 2H), 4.76 (s, 2H), 3.13 (s, 3H), 1.38–1.34 (m, 2H), 1.06–1.03 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 162.1 (d, *J* = 251.3 Hz), 153.2, 133.1 (2C), 130.9, 129.6 (d, *J* = 14.4 Hz), 129.4 (d, *J* = 9.6 Hz), 128.7 (d, *J* = 3.9 Hz), 128.6 (2C), 125.3 (d, *J* = 4.8 Hz), 119.3, 116.5 (d, *J* = 23.1 Hz, 2C), 95.7, 87.4, 87.3, 85.0 (d, *J* = 3.8 Hz), 79.9, 55.6, 55.3, 54.1, 13.8 (d, *J* = 2.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ –114.6; IR (neat) 2222, 1715 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{23}H_{19}FO_4 \bullet NH_4$ 396.1611, found 396.1640.

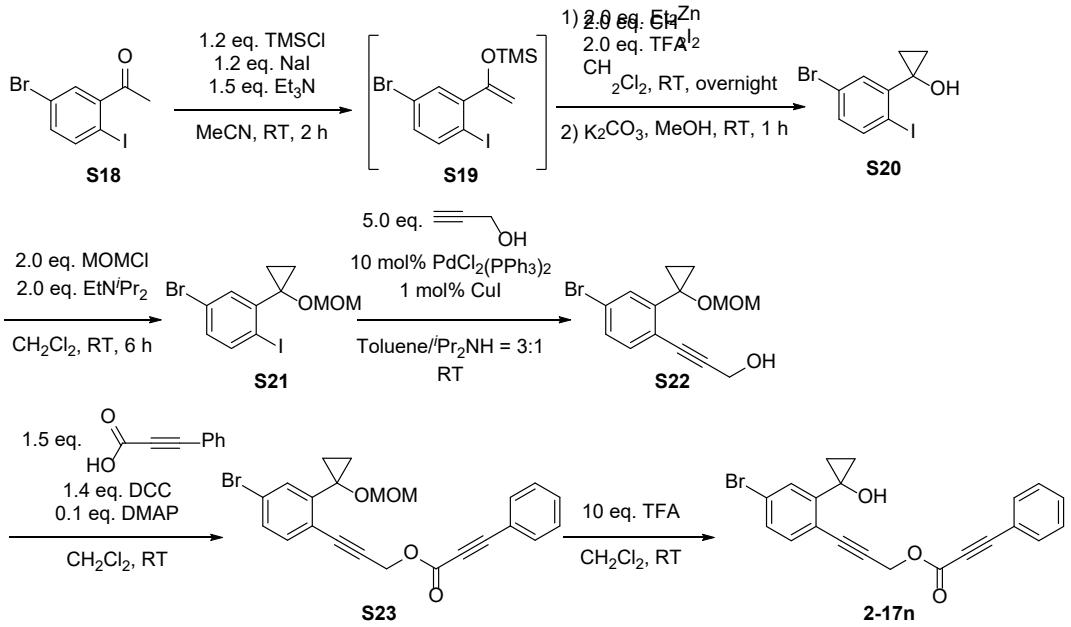
Synthesis and characterization of 2-17m



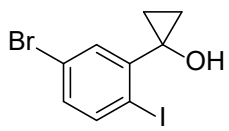
2-17m

This compound was prepared in the same manner as described for **2-17a** using **S17** instead of **S7a** in 69% yield as an orange gum. **Analytical data for 2-17m:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.61–7.59 (m, 2H), 7.49–7.45 (m, 1H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.28–7.19 (m, 2H), 7.08–7.03 (m, 1H), 5.09 (s, 2H), 2.99 (s, 1H), 1.30–1.27 (m, 2H), 1.07–1.03 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 161.2 (d, *J* = 250.4 Hz), 153.4, 133.1 (2C), 131.3 (d, *J* = 14.4 Hz), 130.9, 129.3 (d, *J* = 9.6 Hz), 128.7 (d, *J* = 3.9 Hz), 128.6 (2C), 124.5 (d, *J* = 5.8 Hz), 119.2, 117.0 (d, *J* = 23.1 Hz), 87.80, 87.77, 84.8 (d, *J* = 4.8 Hz), 79.8, 54.1, 51.0 (d, *J* = 2.8 Hz), 15.1 (d, *J* = 3.8 Hz, 2C); ^{19}F NMR (376 MHz, $CDCl_3$) δ –115.8; IR (neat) 3399, 2221, 1713 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for C21H15FO3•NH_4 352.1349, found 352.1361.

Synthesis of 2-17n



Synthesis and characterization of S20

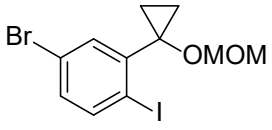


S20

This compound was prepared in the same manner as described for **S3** using **S18**[16] instead of **S1** in 57% yield as a yellow solid. **Analytical data for S20:** yellow solid (mp 85.4–87.2 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 2.3 Hz, 1H), 7.13 (dd, *J* = 8.2, 2.3 Hz, 1H), 3.04 (s, 1H), 1.29 (dd, *J* = 7.3, 5.5 Hz, 2H), 0.97 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 145.7, 140.8, 133.9, 132.6, 122.4, 98.6, 60.5, 15.5 (2C); IR (KBr)

3195 cm^{-1}; HRMS (DART) *m/z* $[M–OH]^+$ calcd for $C_9H_7{}^{81}BrI$ 322.8755, found 322.8752.

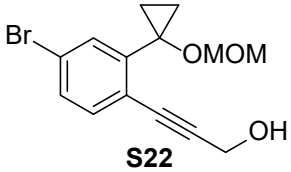
Synthesis and characterization of S21



S21

This compound was prepared in the same manner as described for **S4** using **S20** instead of **S3** in 88% yield as a yellow oil. **Analytical data for S21:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 2.7 Hz, 1H), 7.12 (dd, *J* = 8.2, 2.7 Hz, 1H), 4.60 (s, 2H), 3.16 (s, 3H), 1.34 (dd, *J* = 7.6, 5.7 Hz, 2H), 0.96 (dd, *J* = 7.6, 5.7 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 144.0, 141.1, 134.8, 132.4, 121.7, 99.1, 95.2, 64.5, 55.7, 13.9 (2C); IR (neat) 2945, 1442 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{11}H_{12}BrIO_2•NH_4$ 399.9409, found 399.9434.

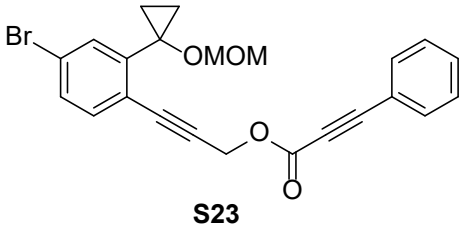
Synthesis and characterization of S22



S22

This compound was prepared in the same manner as described for **S5** using **S22** instead of **S4** in 45% yield as a brown oil. **Analytical data for S22:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 1.8 Hz, 1H), 7.39 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 4.68 (s, 2H), 4.49 (d, *J* = 4.6 Hz, 2H), 3.22 (s, 3H), 3.07 (t, *J* = 4.6 Hz, 1H), 1.29 (dd, *J* = 7.3, 6.0 Hz, 2H), 1.00 (dd, *J* = 7.3, 6.0 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 143.6, 133.9, 133.6, 131.1, 123.2, 122.1, 94.8, 93.5, 83.5, 60.9, 55.5, 51.5, 13.1 (2C); IR (neat) 3409 cm^{-1}; HRMS (FAB) *m/z* $[M+Na]^+$ calcd for $C_{14}H_{15}BrO_3•Na$ 333.0102, found 333.0099

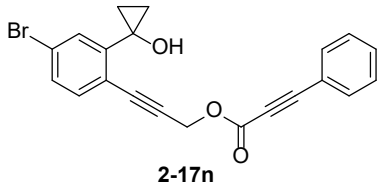
Synthesis and characterization of S23



S23

This compound was prepared in the same manner as described for **S7a** using **S22** instead of **S5** in 81% yield as an orange gum. **Analytical data for S23:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.60–7.58 (m, 3H), 7.48–7.44 (m, 1H), 7.40–7.33 (m, 4H), 5.10 (s, 2H), 4.65 (s, 2H), 3.17 (s, 3H), 1.29 (dd, *J* = 7.3, 5.5 Hz, 2H), 0.99 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.1, 144.2, 134.2, 133.5, 133.0 (2C), 130.84, 130.79, 128.5 (2C), 122.5, 122.2, 119.2, 95.2, 87.6, 87.3, 84.9, 79.9, 61.0, 55.5, 54.1, 12.9 (2C); IR (neat) 2220, 1714 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{23}H_{19}BrO_4•NH_4$ 456.0811, found 456.0819.

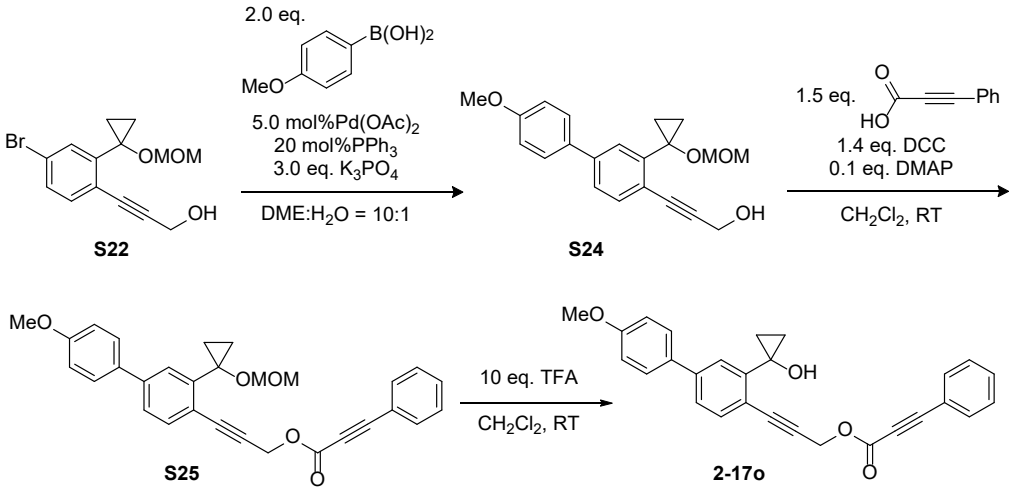
Synthesis and characterization of 2-17n



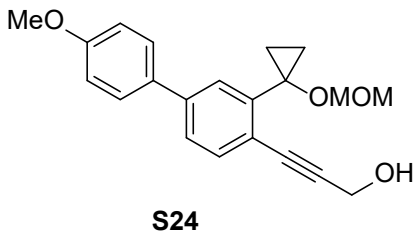
2-17n

This compound was prepared in the same manner as described for **2-17a** using **S23** instead of **S7a** in 69% yield as an orange gum. **Analytical data for 2-17n:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.59–7.57 (m, 2H), 7.50 (d, *J* = 2.3 Hz, 1H), 7.47–7.43 (m, 1H), 7.38–7.30 (m, 4H), 5.05 (s, 2H), 3.54 (br s, 1H), 1.27–1.16 (m, 2H), 1.04–0.96 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.4, 146.7, 134.1, 133.0 (2C), 131.4, 130.9, 130.6, 128.5 (2C), 123.1, 121.0, 119.0, 88.2, 87.8, 84.9, 79.7, 56.3, 54.1, 14.3 (2C); IR (neat) 3398, 2220, 1714 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{21}H_{15}BrO_3$•Na 417.0102, found 417.0090.

Synthesis of 2-17o



Synthesis and characterization of S24

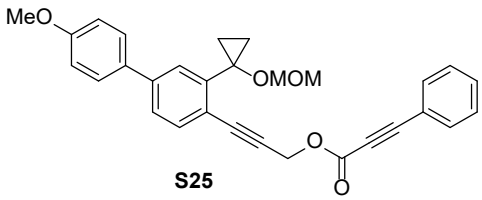


S24

To a solution of **S22** (156 mg, 0.500 mmol) and 4-Methoxyphenylbronic acid (152 mg, 1.00 mmol) in DME (3.0 mL) and H_2O (0.30 mL) was added $Pd(OAc)_2$ (5.61 mg, 0.0250 mmol), PPh_3 (26.2 mg, 0.100 mmol) and K_3PO_4 (318 mg, 1.50 mmol). Then the resulting solution was stirred at 60 °C for 4 h. After that, the reaction mixture was diluted with water and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 5:1) to furnish **S24** (120 mg, 72%) as a black gum. **Analytical data for S24:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 1.2 Hz, 1H), 7.52 (dd, *J* = 10.8, 2.0 Hz, 2H), 7.48-7.42 (m, 2H), 6.97 (dd, *J* = 10.8, 2.0 Hz, 2H), 4.73 (s, 2H), 4.53 (d, *J* = 3.6 Hz, 2H),

3.84 (s, 3H), 3.37 (br s, 1H), 3.25 (s, 3H), 1.33 (dd, J = 7.2, 5.6 Hz, 2H), 1.05 (dd, J = 7.2, 5.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 159.6, 141.9, 140.7, 132.9, 132.5, 129.3, 128.2, 126.1, 122.6, 114.4, 94.8, 92.9, 84.5, 61.4, 55.6, 55.4, 51.7, 13.1 (2C); IR (neat) 3403 cm^{-1}; HRMS (ESI) *m/z* [M+ NH_4]$^+$ calcd for $C_{21}H_{22}O_4$•Na 361.1416, found 361.1387.

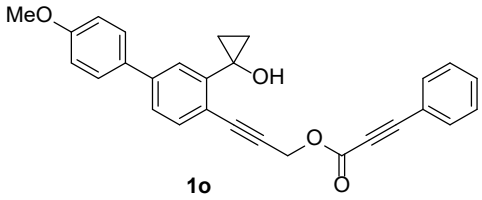
Synthesis and characterization of S25



S25

This compound was prepared in the same manner as described for **S7a** using **S24** instead of **S5** in 91% yield as an orange gum. **Analytical data for S25:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 1.6 Hz, 1H), 7.59 (dt, J = 6.8, 1.6 Hz, 2H), 7.55-7.51 (m, 3H), 7.47-7.42 (m, 2H), 7.38-7.34 (m, 2H), 6.97 (dt, J = 9.6, 2.4 Hz, 2H), 5.14 (s, 2H), 4.70 (s, 2H), 3.83 (s, 3H), 3.20 (s, 3H), 1.33 (dd, J = 7.2, 5.6 Hz, 2H), 1.05 (dd, J = 7.2, 5.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 159.7, 153.4, 142.5, 141.0, 133.7, 133.2 (2C), 132.5, 131.0, 129.0, 128.7 (2C), 128.2 (2C), 125.9, 121.6, 119.5, 114.4 (2C), 95.2, 87.4, 87.0, 86.2, 80.2, 61.6, 55.7, 55.4, 54.5, 13.1 (2C); IR (neat) 2220, 1712 cm^{-1}; HRMS (ESI) *m/z* [M+Na]$^+$ calcd for $C_{30}H_{26}O_5$•Na 489.1678, found 489.1692.

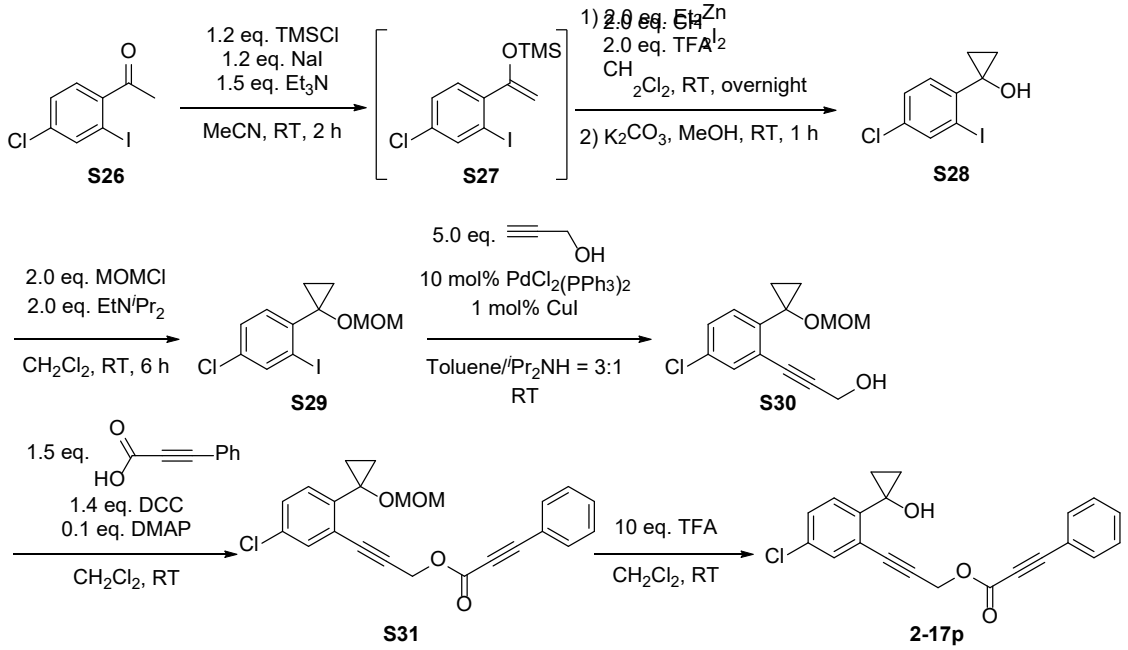
Synthesis and characterization of 2-17o



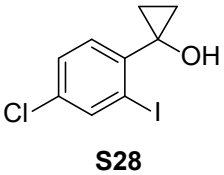
1o

This compound was prepared in the same manner as described for **2-17a** using **S25** instead of **S7a** in 66% yield as an orange gum. **Analytical data for 2-17o:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, J = 8.0, 1.6 Hz, 2H), 7.56 (d, J = 1.6 Hz, 1H), 7.53-7.50 (m, 3H), 7.46-7.42 (m, 2H), 7.40-7.36 (m, 2H), 6.97 (dd, J = 6.8, 2.4 Hz, 2H), 5.10 (s, 2H), 3.84 (s, 3H), 3.43 (br s, 1H), 1.26 (dd, J = 7.2, 5.2 Hz, 2H), 1.04 (dd, J = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 159.7, 153.7, 145.4, 141.7, 133.4, 133.3 (2C), 132.6, 131.1, 128.7 (2C), 128.3 (2C), 126.5, 125.8, 120.3, 119.4, 114.4 (2C), 87.9, 87.7, 86.2, 80.0, 57.1, 55.5, 54.5, 14.5 (2C); IR (neat) 3427, 2221, 1712 cm^{-1}; HRMS (ESI) *m/z* [M+Na]$^+$ calcd for $C_{28}H_{22}O_4$•Na 445.1416, found 445.1395.

Synthesis of 2-17p

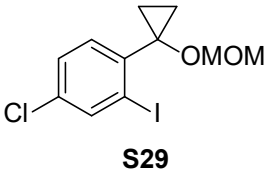


Synthesis and characterization of S28



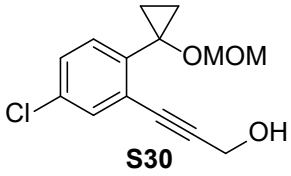
This compound was prepared in the same manner as described for **S3** using **S26**[17] instead of **S1** in 45% yield as a yellow solid. **Analytical data for S28:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 1.8 Hz, 1H), 7.27–7.22 (m, 2H), 3.15 (s, 1H), 1.25 (dd, *J* = 7.3, 5.5 Hz, 2H), 0.92 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 142.3, 138.7, 134.2, 131.4, 128.2, 100.7, 60.1, 15.5 (2C); IR (KBr) 3242 cm^{-1}; HRMS (DART) *m/z* $[M–OH]^+$ calcd for C_9H_7ClI 276.9281, found 276.9251.

Synthesis and characterization of S29



This compound was prepared in the same manner as described for **S4** using **S28** instead of **S3** in 98% yield as a yellow oil. **Analytical data for S29:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 1.8 Hz, 1H), 7.29–7.25 (m, 2H), 4.60 (s, 2H), 3.16 (s, 3H), 1.35–1.32 (m, 2H), 0.96–0.93 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 140.7, 139.2, 134.3, 132.6, 127.7, 101.3, 95.2, 64.4, 55.8, 14.0 (2C); IR (neat) 2947 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{11}H_{12}ClIO_2•NH_4$ 355.9914, found 355.9929.

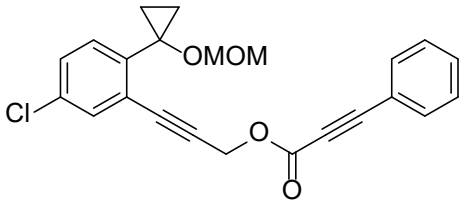
Synthesis and characterization of S30



S30

This compound was prepared in the same manner as described for **S5** using **S29** instead of **S4** in 45% yield as a brown oil. **Analytical data for S30:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.41–7.38 (m, 2H), 7.28–7.25 (m, 1H), 4.67 (s, 2H), 4.51 (d, *J* = 5.5 Hz, 2H), 3.21 (s, 3H), 2.97 (t, *J* = 5.5 Hz, 1H), 1.28 (dd, J = 7.3, 5.5 Hz, 2H), 0.97 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 140.2, 133.6, 132.3, 131.9, 128.4, 125.9, 94.7, 93.6, 83.2, 60.6, 55.5, 51.4, 13.1 (2C); IR (neat) 3411 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{14}H_{15}ClO_3 \bullet NH_4$ 284.1054, found 284.1025.

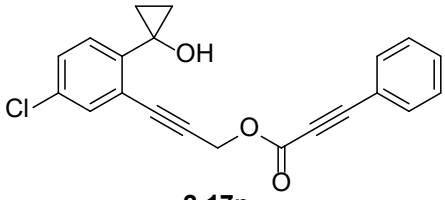
Synthesis and characterization of S31



S31

This compound was prepared in the same manner as described for **S7a** using **S30** instead of **S5** in 82% yield as an orange gum. **Analytical data for S31:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.62–7.59 (m, 2H), 7.49–7.45 (m, 2H), 7.41–7.36 (m, 3H), 7.28–7.26 (m, 1H), 5.11 (s, 2H), 4.64 (s, 2H), 3.15 (s, 3H), 1.28 (dd, *J* = 7.6, 5.7 Hz, 2H), 0.97 (dd, *J* = 7.6, 5.7 Hz, 2H; ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.2, 140.8, 133.4, 133.1 (2C), 132.6, 131.8, 130.9, 128.7, 128.6 (2C), 125.0, 119.3, 95.2, 87.7, 87.4, 84.6, 80.0, 60.8, 55.5, 54.0, 13.0 (2C); IR (neat) 2220, 1716 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{23}H_{19}ClO_4 \bullet Na$ 417.0870, found 417.0861.

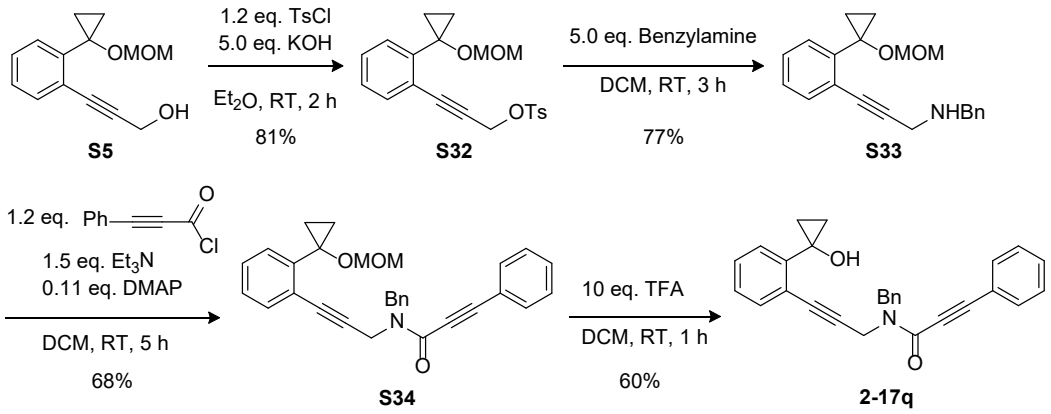
Synthesis and characterization of 2-17p



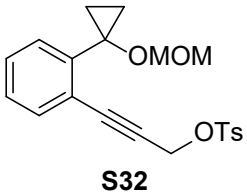
2-17p

This compound was prepared in the same manner as described for **2-17a** using **S31** instead of **S7a** in 65% yield as an orange gum. **Analytical data for 2-17p:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.61–7.59 (m, 2H), 7.49–7.45 (m, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.31–7.25 (m, 2H), 5.07 (s, 2H), 3.34 (br s, 1H), 1.22 (dd, *J* = 7.6, 5.3 Hz, 2H), 0.96 (dd, *J* = 7.6, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.5, 143.4, 133.2, 133.1 (2C), 132.5, 131.0, 129.5, 129.2, 128.6 (2C), 123.8, 119.1, 88.4, 88.0, 84.6, 79.8, 56.2, 54.0, 14.4 (2C); IR (neat) 3403, 2220, 1712 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{21}H_{15}ClO_3 \bullet NH_4$ 368.1054, found 368.1077.

Synthesis of 2-17q



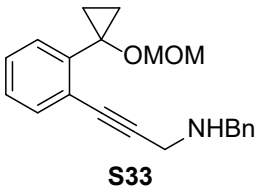
Synthesis and characterization of S32



S32

To a dry Et_2O solution (10 mL) of **S5** (1.16 g, 5.00 mmol) and *p*-toluenesulfonyl chloride (1.20 g, 6.00 mmol) was added KOH (1.43 g, 25 mmol) at 0 °C, and the resulting mixture was stirred at rt for 2 h. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **S32** (1.57 g, 81%) as a yellow oil. **Analytical data for S32:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.7 Hz, 2H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 8.7 Hz, 2H), 7.30-7.20 (m, 3H), 5.01 (s, 2H), 4.58 (s, 2H), 3.12 (s, 3H), 2.41 (s, 3H), 1.20 (dd, *J* = 7.3, 5.5 Hz, 2H), 0.91 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 145.1, 142.1, 133.4, 133.2, 130.6, 129.9, 128.9, 128.2, 127.8, 123.0, 95.1, 87.7, 85.0, 61.4, 58.9, 55.6, 21.7, 12.9; IR (neat) 1367, 1176, 1032 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{21}H_{22}O_5S•NH_4$ 404.1532, found 404.1521.

Synthesis and characterization of S33

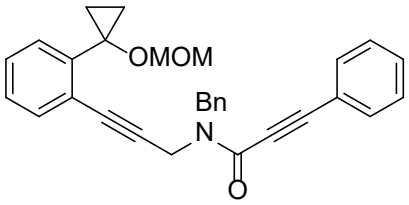


S33

To a stirred solution of **S32** (1.14 g, 2.94 mmol) in DCM (15 mL) was added benzylamine (1.6 mL, 15.0 mmol) at 0 °C. The mixture was stirred at rt for 3 h, and the solvent was removed *in vacuo*. The reaction mixture was filtered through a pad of Celite® with EtOAc. The filtrate was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **S33** (746 mg, 77%) as a yellow oil. **Analytical data for S33:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48–7.39 (m, 4H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.28–7.25 (m, 3H), 4.66 (s, 2H), 4.01 (s, 2H), 3.73 (s, 2H), 3.17 (s, 3H), 1.27 (dd, *J* = 7.3, 5.5 Hz, 2H), 1.01 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 141.5, 139.9, 133.1, 130.7, 128.6, 128.5, 127.9, 127.8, 127.2, 124.9, 95.1, 92.5, 82.4, 61.6, 55.6, 52.5, 38.6,

13.0; IR (neat) 3319, 1153, 1032 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{21}H_{23}NO_2$•H 322.1807, found 322.1791

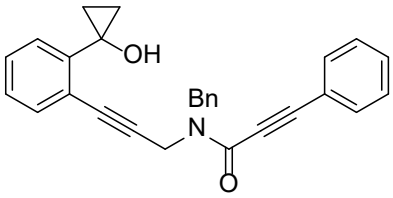
Synthesis and characterization of S34



S34

To a 30 mL flask was added **S33** (953 mg, 2.96 mmol) followed by dry DCM (5.0 mL), Et_3N (610 µL, 4.43 mmol), and DMAP (38.6 mg, 0.340 mmol). 3-Phenyl-2-propynoyl chloride[18] (583 mg, 3.54 mmol) was added slowly at 0 °C. After stirring for 5 h at rt, the reaction was quenched with water and extracted with DCM. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **S34** (930 mg, 68%) as an orange gum. **S34** was analyzed as a mixture of rotamers (major/minor = 3:2). **Analytical data for S34:** ^{1}H-NMR (400 MHz, $CDCl_3$) **major** δ 7.55–7.52 (m, 2H), 7.46–7.23 (m, 12H), 5.14 (s, 2H), 4.66 (s, 2H), 4.49 (s, 2H), 3.18 (s, 3H), 1.29-1.25 (m, 2H), 1.02-0.97 (m, 2H); **minor** δ 7.61–7.58 (m, 2H), 7.46–7.23 (m, 12H), 4.93 (s, 2H), 4.63 (s, 2H), 4.62 (s, 2H), 3.14 (s, 3H), 1.29-1.25 (m, 2H), 1.02-0.97 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) **major** δ 154.3, 142.0, 136.1, 133.1, 132.6, 130.48, 130.34, 128.8, 128.7, 128.2, 128.1, 127.9, 124.2, 120.38, 95.2, 91.0, 87.9, 83.1, 81.6, 61.6, 55.63, 51.4, 33.5, 12.9; **minor** δ 154.5, 142.2, 136.2, 133.0, 132.6, 130.50, 130.32, 129.0, 128.8, 128.4, 128.2, 127.9, 123.9, 120.43, 95.2, 91.3, 87.8, 83.8, 81.3, 61.6, 55.57, 46.7, 38.8, 12.9; IR (neat) 1631 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{30}H_{27}NO_3$•H 450.2069, found 450.2076

Synthesis and characterization of 2-17q

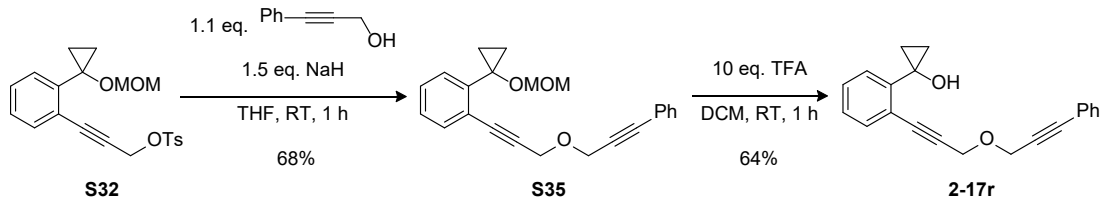


2-17q

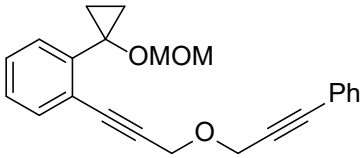
To a 50 mL flask was added **S34** (439 mg, 0.97 mmol) followed by degassed DCM (12 mL). TFA (0.700 mL, 9.70 mmol) was added slowly, and the flask was flushed with Ar. After stirring at rt for 1 h, the reaction mixture was diluted with water and extracted with EtOAc. The organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **2-17q** (238 mg, 60%) as an orange gum. **2-17q** was analyzed as a mixture of rotamers (major/minor = 2:1). **Analytical data for 2-17q:** ^{1}H-NMR (400 MHz, $CDCl_3$) **major** δ 7.52–7.50 (m, 2H), 7.45–7.20 (m, 12H), 5.05 (s, 2H), 4.40 (s, 2H), 3.49 (br s, 1H), 1.21 (dd, *J* = 7.3, 5.0 Hz, 2H), 0.98 (dd, *J* = 7.3, 5.0 Hz, 2H); **minor** δ 7.59–7.56 (m, 2H), 7.45–7.20 (m, 12H), 4.87 (s, 2H), 4.62 (s, 2H), 2.92 (br s, 1H), 1.15 (dd, *J* = 7.3, 5.5 Hz, 2H), 0.97 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) **major** δ 154.6, 144.8, 135.6, 132.7,

132.5, 130.3, 128.9, 128.8, 128.5, 128.2, 128.0, 127.7, 127.5, 122.7, 120.0, 91.1, 88.6, 82.6, 81.1, 56.7, 52.5, 34.4, 14.2; **minor** δ 154.3, 144.3, 135.8, 133.0, 132.5, 130.3, 128.9, 128.6, 128.5, 128.2, 127.9, 127.7, 127.6, 122.4, 120.0, 91.5, 88.4, 83.4, 81.0, 57.0, 47.1, 38.6, 14.2; IR (neat) 3548, 2214, 1621 cm^{-1}; HRMS (DART) *m/z* $[M+ H]^+$ calcd for $C_{28}H_{23}NO_2$•H 406.1807, found 406.1805

Synthesis of 2-17r



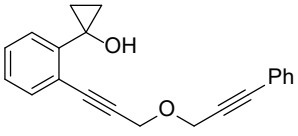
Synthesis and characterization of S35



S35

To a solution of 3-phenyl-2-propyn-1-ol (264 mg, 2.00 mmol) in dry THF (10 mL) was added NaH (60% dispersion in mineral oil, 121 mg, 3.00 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was stirred at 0 °C for 1 h. To this reaction mixture was added a THF (5.0 mL) solution of **S32** (822 mg, 2.13 mmol), and the mixture was stirred for 1 h at rt. The reaction was quenched with water. The aqueous phase was extracted with EtOAc. The combined organic layer was washed with brine and dried over $MgSO_4$. After concentration *in vacuo*, the obtained crude product was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **S35** (470 mg, 68%) as a yellow oil. **Analytical data for S35:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50–7.42 (m, 4H), 7.33–7.23 (m, 5H), 4.65 (s, 2H), 4.63 (s, 2H), 4.62 (s, 2H), 3.17 (s, 3H), 1.29 (dd, *J* = 7.1, 5.7 Hz, 2H), 1.01 (dd, *J* = 7.1, 5.7 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 142.0, 133.1, 131.9, 130.5, 128.6, 128.4, 128.3, 127.9, 124.2, 122.7, 95.2, 89.2, 86.8, 85.7, 84.8, 61.6, 57.5, 57.2, 55.6, 12.9; IR (neat) 1230,1153 cm^{-1}; HRMS (DART) *m/z* $[M– MOMOH]^+$ calcd for $C_{21}H_{17}O$ 285.1279, found 285.1292

Synthesis and characterization of 2-17r

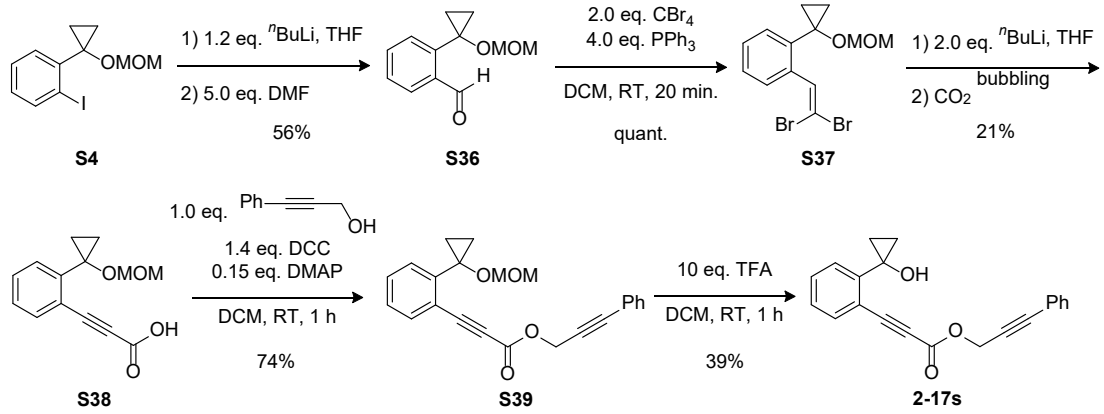


2-17r

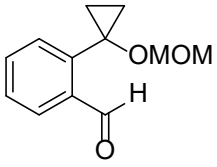
To a 50 mL flask was added **S35** (468 mg, 1.35 mmol) followed by degassed DCM (13 mL). TFA (1.00 mL, 13.5 mmol) was slowly added to the solution. After stirring at rt for 1 h under Ar atmosphere, the reaction mixture was diluted with water and extracted with EtOAc. The organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and

concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **2-17r** (261 mg, 64%) as a yellow gum. **Analytical data for 2-17r:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 7.1, 1.1 Hz, 1H), 7.48–7.44 (m, 2H), 7.37–7.29 (m, 5H), 7.25 (dt, *J* = 7.4, 1.7 Hz, 1H), 4.63 (s, 2H), 4.59 (s, 2H), 3.18 (s, 1H), 1.22 (dd, *J* = 7.3, 5.0 Hz, 2H), 1.02 (dd, *J* = 7.3, 5.0 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 144.5, 133.1, 131.9, 128.9, 128.7, 128.4, 128.1, 127.8, 122.7, 122.5, 89.9, 87.2, 85.5, 84.2, 57.5, 57.4, 57.2, 14.4; IR (neat) 3413,1225 cm^{-1}; HRMS (DART) *m/z* $[M-H_2O]^+$ calcd for $C_{21}H_{17}O$ 285.1279, found 285.1289

Synthesis of 2-17s



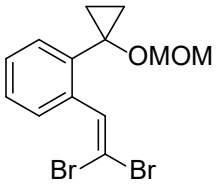
Synthesis and characterization of S36



S36

A solution of **S4** (2.97 g, 9.76 mmol) in THF (20 mL) was cooled under Ar atmosphere to –78 °C. A solution of ^{n}BuLi (7.46 mL, 1.60 M in hexane) was added and the mixture was stirred for 1 h. To the resulting mixture was added DMF (3.58 mL, 4.90 mmol) at –78 °C, and the mixture was stirred for 1 h. The reaction mixture was quenched by water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S36** (1.21 g, 56%) as an orange liquid. **Analytical data for S36:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 10.88 (s, 1H), 7.97 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.55–7.51 (m, 1H), 7.46–7.42 (m, 2H), 4.60 (s, 2H), 3.11 (s, 3H), 1.36 (dd, *J* = 7.1, 5.3 Hz, 2H), 1.08 (dd, *J* = 7.1, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 193.0, 142.8, 135.3, 133.5, 129.3, 128.6, 127.8, 95.4, 59.7, 55.9, 12.8; IR (neat) 1693, 1032 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{12}H_{14}O_3 \bullet NH_4$ 224.1287, found 224.1276

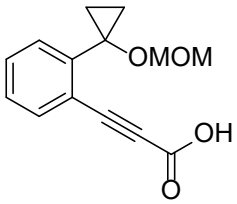
Synthesis and characterization of S37



S37

To a solution of PPh_3 (2.67 g, 10.2 mmol) in DCM (12 mL) was added CBr_4 (1.76 g, 5.08 mmol) and **S36** (559 mg, 2.54 mmol) at 0 °C. The reaction mixture was stirred at rt for 20 min. The reaction was quenched with water. The aqueous phase was extracted with DCM. The combined organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated to ca. 5 mL. The solution was poured slowly into hexane (40 mL). The resulting suspension was filtrated and the filtrate was concentrated. The resulting suspension was filtrated, concentrated, and purified by silica gel column chromatography (hexane was used as an eluent) to afford **S37** (827 mg, quant.) as a yellow liquid. **Analytical data for S37:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.64 (dd, *J* = 7.1, 2.1 Hz, 1H), 7.37–7.27 (m, 3H), 4.55 (s, 2H), 3.18 (s, 3H), 1.22 (dd, *J* = 7.1, 5.3 Hz, 2H), 0.91 (dd, *J* = 7.1, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 137.8, 136.9, 136.7, 129.7, 129.3, 128.1, 128.0, 95.0, 90.3, 60.8, 55.9, 12.4; IR (neat) 1032 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{13}H_{14}Br_2O_2 \bullet NH_4$ 377.9704, found 377.9717

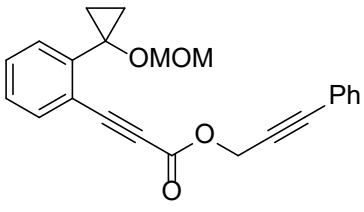
Synthesis and characterization of S38



S38

A solution of **S37** (635 mg, 2.00 mmol) in THF (19 mL) was cooled under Ar atmosphere to –78 °C. A solution of ^{n}BuLi (2.84 mL, 1.60 M in hexane) was added and the mixture was stirred for 1 h. The mixture was warmed to –40 °C and CO_2 gas bubbled into the solution for 1 h. The reaction mixture was quenched by the slow addition of 2.0 M aqueous HCl and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was recrystallized from toluene and hexane at rt, affording pure **S38** (105 mg, 21%) as a white powder (mp 81.9–83.0 °C). **Analytical data for S38:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.58 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.48 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.36 (dt, *J* = 7.6, 1.2 Hz, 1H), 4.77 (s, 2H), 3.34 (s, 3H), 1.36 (dd, *J* = 7.2, 6.0 Hz, 2H), 1.01 (dd, *J* = 7.2, 6.0 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 155.3, 143.5, 133.9, 131.3, 130.9, 128.5, 121.2, 94.8, 86.4, 84.9, 61.2, 55.7, 13.0; IR (KBr) 2943, 2210, 1678 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{14}H_{14}O_4 \bullet NH_4$ 264.1236, found 264.1214

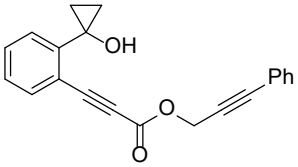
Synthesis and characterization of S39



S39

To a 20 mL flask was charged with **S38** (105 mg, 0.420 mmol), 3-phenyl-2-propyn-1-ol (55.5 mg, 0.420 mmol) and DMAP (5.13 mg, 0.042 mmol). To the mixture was added a DCM (4 mL) solution of DCC (122 mg, 0.590 mmol) at 0 ℃, and the resulting solution was stirred at rt for 1 h. The reaction mixture was filtered through a pad of Celite® with EtOAc. The filtrate was washed with water, sat. aq. $NaHCO_3$ and brine. The solution was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S39** (115 mg, 74%) as a light-yellow gum. **Analytical data for S39:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.3 Hz, 1H), 7.49–7.47 (m, 3H), 7.43–7.39 (m, 1H), 7.35–7.29 (m, 4H), 5.07 (s, 2H), 4.66 (s, 2H), 3.14 (s, 3H), 1.34 (dd, *J* = 7.1, 5.7 Hz, 2H), 1.03 (dd, *J* = 7.1, 5.7 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.5, 144.2, 134.3, 132.0, 130.6, 130.5, 129.0, 128.4, 128.0, 122.1, 121.0, 95.4, 87.2, 86.3, 84.3, 82.4, 61.4, 55.6, 54.2, 13.1; IR (neat) 2220, 1712, 1171 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{23}H_{20}O_4$•NH_4 378.1705, found 378.1717

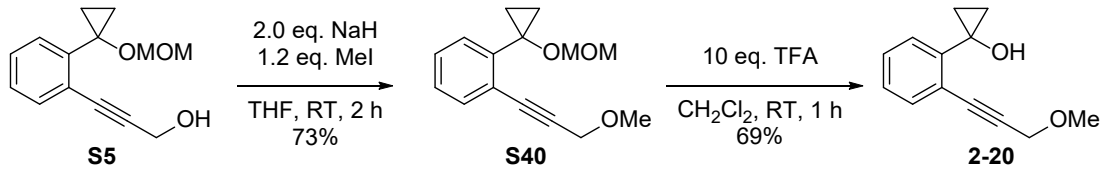
Synthesis and characterization of 2-17s



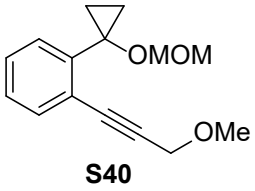
2-17s

To a 20 mL flask was added **S39** (115 mg, 0.31 mmol) followed by degassed DCM (4 mL). TFA (0.240 mL, 3.10 mmol) was slowly added to the solution. After stirring at rt for 1 h under Ar atmosphere, the reaction mixture was dilutedwith water and extracted with EtOAc. The organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **2-17s** (238 mg, 60%) as a light-yellow gum. **Analytical data for 2-17s:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.49–7.43 (m, 4H), 7.34–7.31 (m, 4H), 5.08 (s, 2H), 2.94 (s, 1H), 1.29 (dd, *J* = 7.3, 5.5 Hz, 2H), 1.05 (dd, *J* = 7.3, 5.5 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 153.3, 146.5, 134.4, 132.1, 131.2, 129.0, 128.8, 128.4, 128.0, 122.0, 119.8, 87.4, 86.1, 84.9, 82.1, 56.9, 54.4, 14.7; IR (neat) 3398, 2216, 1712, 1173 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{21}H_{16}O_3$•H 317.1178, found 317.1175

Synthesis of 2-20

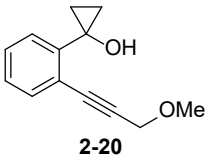


Synthesis and characterization of S40



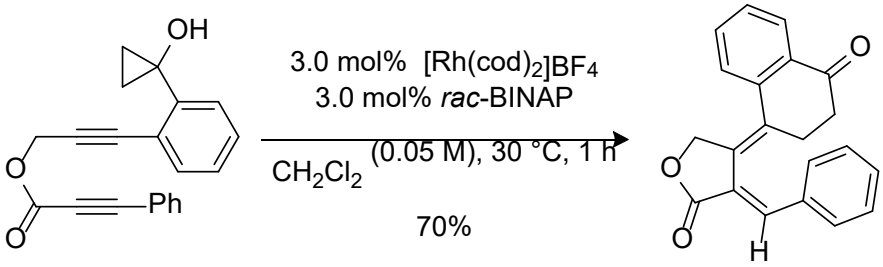
To a solution of **S5** (348 mg, 1.50 mmol) in dry THF (5 mL) was added NaH (60% dispersion in mineral oil, 122 mg, 3.00 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was stirred at rt for 1 h. To this reaction mixture was added iodomethane (112 µL, 1.80 mmol) and the mixture was stirred at rt for 2 h. The reaction was quenched with water. The aqueous phase was extracted with EtOAc. The combined organic layer was washed with brine and dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to afford **S40** (268 mg, 73%) as a yellow oil. **Analytical data for S40:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.1, 2.1 Hz, 1H), 7.43 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.31–7.23 (m, 2H), 4.64 (s, 2H), 4.40 (s, 2H), 3.49 (s, 3H), 3.17 (s, 3H), 1.26 (dd, *J* = 7.2, 5.6 Hz, 2H), 1.00 (dd, *J* = 7.2, 5.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 141.8, 133.1, 130.6, 128.1, 127.8, 124.3, 95.1, 89.7, 85.1, 61.5, 60.6, 57.6, 55.5, 12.9; IR (neat) 1034 cm^{-1}; HRMS (DART) *m/z* $[M+ NH_4]^+$ calcd for $C_{15}H_{18}O_3•NH_4$ 264.1600, found 264.1600

Synthesis and characterization of 2-20



To a 50 mL flask was added **S40** (268 mg, 1.10 mmol) followed by degassed DCM (10 mL). TFA (770 µL, 11.0 mmol) was slowly added to the solution. After being stirred at rt for 1 h under Ar atmosphere, the reaction was diluted with water and extracted with EtOAc. The organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **2-20** (154 mg, 69%) as a yellow liquid. **Analytical data for 2-20:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.35 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.29 (dt, *J* = 7.5, 1.6 Hz, 1H), 7.24 (dt, *J* = 7.5, 1.6 Hz, 1H), 4.39 (s, 2H), 3.47 (s, 3H), 1.19 (dd, *J* = 7.1, 5.3 Hz, 2H), 1.00 (dd, *J* = 7.1, 5.3 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 144.4, 133.0, 128.8, 128.0, 127.7, 122.8, 90.5, 85.0, 60.6, 57.9, 57.1, 14.3; IR (neat) 3411, 1095 cm^{-1}; HRMS (DART) *m/z* $[M+ NH_4]^+$ calcd for $C_{13}H_{14}O_2•NH_4$ 2201338, found 220.1318

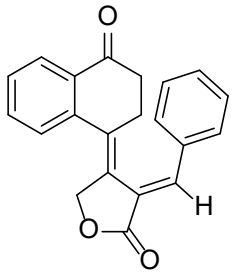
2. Representative Procedure for the Rhodium-Catalyzed Cycloisomerization of 2-17



2-17a **2-18a**

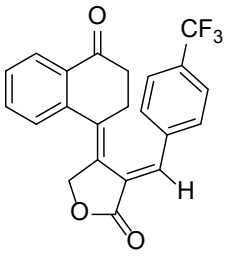
$[Rh(cod)_2]BF_4$ (1.21 mg, 0.00300 mmol) and *rac*-BINAP (1.88 mg, 0.00300 mmol) were dissolved in degassed DCM (1.0 mL) and the mixture was stirred at 30 ℃ for 10 min under Ar atmosphere. The reaction tube was evacuated and refilled with H_2 using a balloon, which was repeated 3 times. After stirring at 30 ℃ for 1 h under H_2 atmosphere, the reaction tube was evacuated and refilled with Ar using a balloon, which was repeated 3 times. To the resulting mixture was added a DCM (1.0 mL) solution of **2-17a** (31.6 mg, 0.100 mmol). After stirring at 30 ℃ for 1 h, the resulting solution was concentrated *in vacuo*. The crude was then purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to give **2-18a** (22.1 mg, 70%) as a yellow solid (mp 246.5–248.3 ℃).

3. Characterization of Exocyclic Dienes 2-18 and 2-19



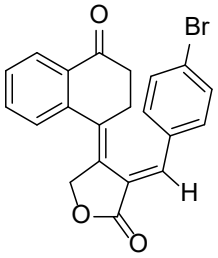
2-18a

Recrystallization from isopropanol at rt afforded pure **2-18a** as a yellow crystal. **Analytical data for 2-18a:**; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.8 Hz, 1H), 7.68 (s, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.55–7.50 (m, 3H), 7.41–7.36 (m, 3H), 7.22 (d, *J* = 7.8 Hz, 1H), 5.23 (s, 2H), 2.60 (t, *J* = 6.9 Hz, 2H), 2.42 (t, *J* = 6.9 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.4, 171.0, 139.5, 137.5, 136.1, 134.9, 133.7, 132.2, 130.5, 130.0, 129.8, 128.9, 128.04, 127.96, 123.6, 70.5, 38.9, 32.7; IR (KBr) 1763, 1687 cm^{-1}; HRMS (DART) *m/z* $[M+ NH_4]^+$ calcd for $C_{21}H_{16}O_3 \bullet NH_4$ 334.1443, found 334.1414



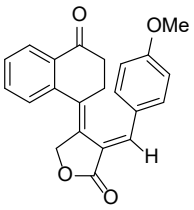
2-18b

According to the representative procedure, yellow solid (mp 168.6–169.8 °C) was obtained (68% yield). **Analytical data for 2-18b:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.8 Hz, 1H), 7.68–7.65 (m, 6H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 5.22 (s, 2H), 2.62 (t, *J* = 6.9 Hz, 2H), 2.37 (t, *J* = 6.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 195.9, 170.4, 139.0, 138.2, 137.4, 135.1, 133.8, 132.3, 130.2, 129.9, 128.2, 128.1, 128.0, 125.9, 125.9, 125.9, 125.8, 70.5, 38.7, 32.7; ^{19}F-NMR (376 MHz, $CDCl_3$) δ –63.9; IR (KBr) 1766, 1689 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{22}H_{15}F_3O_3$•H 385.1052, found 385.1031



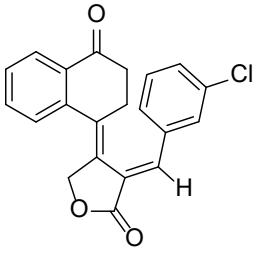
2-18c

According to the representative procedure, yellow solid (mp 163.0–164.5 °C) was obtained (61% yield). **Analytical data for 2-18c:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.65 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.60 (s, 1H), 7.55–7.51 (m, 3H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.20 (d, *J* = 7.3 Hz, 1H), 5.19 (s, 2H), 2.62 (t, *J* = 6.6 Hz, 2H), 2.41 (t, *J* = 6.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.1, 170.7, 139.2, 136.5, 135.9, 133.8, 133.8, 132.2, 131.3, 130.0, 128.6, 128.1, 128.0, 124.8, 124.2, 70.4, 38.8, 32.8; IR (KBr) 1761, 1689 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{21}H_{15}BrO_3$•H 395.0283, found 395.0275



2-18d

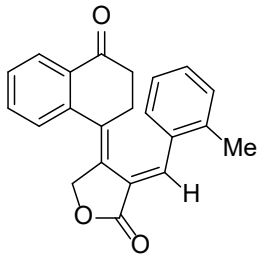
According to the representative procedure, yellow solid (mp 179.3–180.9 °C) was obtained (46% yield). **Analytical data for 2-18d:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.65 (dt, *J* = 7.8, 0.9 Hz, 1H), 7.63 (s, 1H), 7.53–7.49 (m, 3H), 7.21 (d, *J* = 7.8 Hz, 1H), 6.90 (d, *J* = 8.7 Hz, 2H), 5.17 (s, 2H), 3.84 (s, 3H), 2.62 (t, *J* = 6.6 Hz, 2H), 2.50 (t, *J* = 6.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.6, 171.4, 161.4, 139.7, 137.4, 135.1, 133.7, 132.2, 132.1, 129.6, 128.00, 127.96, 127.4, 121.0, 114.3, 70.4, 55.5, 39.0, 32.8; IR (KBr) 1745, 1675 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{22}H_{18}O_4$•H 347.1283, found 347.1269



2-18e

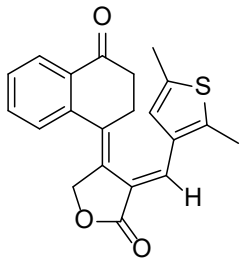
According to the representative procedure, yellow solid (mp 175.2–176.5 °C) was obtained (85% yield). **Analytical data for 2-18e:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.66 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.60 (s, 1H), 7.54 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.50 (s, 1H), 7.44–7.41 (m, 1H), 7.34–7.33 (m, 2H), 7.22 (d, *J* = 6.9 Hz, 1H), 5.19 (s, 2H), 2.62 (t, *J* = 6.9 Hz, 2H), 2.41 (t, *J* = 6.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.1, 170.6, 139.2, 136.9, 136.7, 135.5, 134.9, 133.8, 132.3, 130.4, 130.1, 130.1, 129.6, 128.4, 128.1, 128.0, 127.9, 124.9, 70.5, 38.8, 32.7; IR (KBr)

1753, 1684 cm^{-1}; HRMS (DART) *m/z* $[M+ NH_4]^+$ calcd for $C_{21}H_{15}O_3Cl•NH_4$ 368.1054, found 368.1074



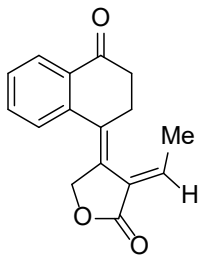
2-18f

The reaction was performed at 30 °C for 2 h. Yellow solid (mp 186.5–188.0 °C) was obtained (53% yield). Recrystallization from isopropanol at rt afforded pure **2-18f** as a yellow crystal. **Analytical data for 2-18f:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.85 (s, 1H), 7.63 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.52–7.47 (m, 2H), 7.29–7.25 (m, 2H), 7.20 (d, *J* = 7.3 Hz, 1H), 7.11 (t, *J* = 7.3 Hz, 1H), 5.21 (s, 2H), 2.57 (t, *J* = 6.9 Hz, 2H), 2.46 (s, 3H), 2.24 (t, *J* = 6.9 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.4, 171.0, 139.5, 138.6, 136.2, 135.5, 134.3, 133.7, 132.2, 131.1, 130.3, 129.7, 128.5, 128.0, 127.9, 127.6, 126.1, 124.4, 70.4, 38.8, 31.9, 20.2; IR (KBr) 1749, 1678 cm^{-1}; HRMS (DART) *m/z* $[M+ NH_4]^+$ calcd for $C_{22}H_{18}O_3•NH_4$ 348.1600, found 368.1598



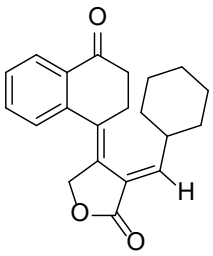
2-18g

According to the representative procedure, brown solid (mp 175.4–175.9 °C) was obtained (55% yield). **Analytical data for 2-18g:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.64 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.57 (s, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 7.8 Hz, 1H), 6.77 (s, 1H), 5.12 (s, 2H), 2.64 (t, *J* = 6.2 Hz, 2H), 2.56 (t, *J* = 6.2 Hz, 2H), 2.53 (s, 3H), 2.33 (s, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.7, 171.6, 144.8, 139.9, 136.4, 135.6, 133.7, 132.8, 132.2, 130.1, 129.8, 129.5, 127.9, 124.1, 120.8, 70.4, 39.2, 32.2, 15.3, 14.0; IR (KBr) 1757, 1681 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{21}H_{18}O_3S•H$ 351.1055, found 351.1051



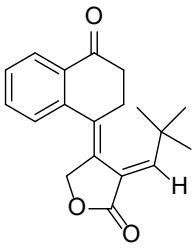
2-18h

According to the representative procedure, white solid (mp 173.8–174.9 °C) was obtained (62% yield). **Analytical data for 2-18h:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.61 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 6.93 (q, *J* = 7.5 Hz, 1H), 5.05 (s, 2H), 2.86 (t, *J* = 6.2 Hz, 2H), 2.77 (t, *J* = 6.2 Hz, 2H), 2.02 (d, *J* = 7.5 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.4, 170.2, 139.6, 137.3, 134.1, 133.7, 132.1, 129.6, 128.7, 128.0, 128.0, 127.9, 70.6, 39.4, 31.9, 18.3; IR (KBr) 1762, 1693 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{14}O_3•NH_4$ 272.1287, found 272.1268



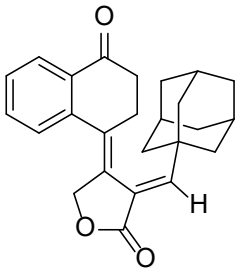
2-18i

According to the representative procedure, white solid (mp 151.6–153.0 °C) was obtained (66% yield). **Analytical data for 2-18i:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.59 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 6.63 (d, *J* = 11.4 Hz, 1H), 5.01 (s, 2H), 2.92 (t, *J* = 6.6 Hz, 2H), 2.77 (t, *J* = 6.6 Hz, 2H), 2.31-2.25 (m, 1H), 1.81-1.69 (m, 5H), 1.33-1.19 (m, 5H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.4, 170.8, 147.6, 139.6, 134.0, 133.7, 132.1, 129.5, 129.0, 128.1, 127.9, 124.0, 70.6, 40.7, 39.3, 31.8, 31.6, 25.7, 25.6; IR (KBr) 1766, 1687 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{21}H_{22}O_3 \bullet NH_4$ 340.1913, found 340.1892



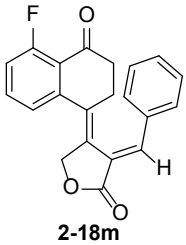
2-18j

The reaction was performed using $[Rh(cod)_2]BF_4$ (10 mol%) and *rac*-BINAP (10 mol%) at 60 °C in DCE and white solid (mp 166.7–167.3 °C) was obtained (56% yield). Recrystallization from isopropanol at rt afforded pure **2-18j** as a colorless crystal. **Analytical data for 2-18j:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J* = 7.6 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.82 (s, 1H), 4.94 (s, 2H), 3.02 (t, *J* = 6.6 Hz, 2H), 2.77 (t, *J* = 6.6 Hz, 2H), 1.24 (s, 9H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.2, 170.7, 152.2, 139.7, 136.9, 133.7, 132.0, 129.7, 129.2, 128.1, 127.9, 122.7, 70.4, 39.5, 35.5, 33.1, 28.6; IR (KBr) 1765, 1684 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{19}H_{20}O_3 \bullet H$ 297.1491, found 297.1483



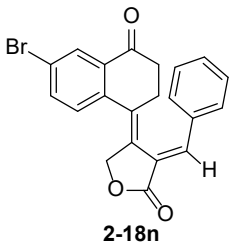
2-18k

The reaction was performed using $[Rh(cod)_2]BF_4$ (10 mol%) and *rac*-BINAP (10 mol%) at 60 °C in DCE and orange solid (mp 275.3–278.1 °C) was obtained (46% yield). **Analytical data for 2-18k:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.60 (dt, *J* = 7.6, 1.4 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.62 (s, 1H), 4.94 (s, 2H), 3.04 (t, *J* = 6.2 Hz, 2H), 2.78 (d, *J* = 6.2 Hz, 2H), 2.02 (br s, 3H), 1.82 (br s, 6H), 1.74 (br d, *J* = 12.4 Hz, 3H), 1.67 (br d, *J* = 12.4 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.3, 170.8, 151.8, 139.8, 136.8, 133.7, 132.0, 130.0, 129.6, 128.2, 127.8, 122.5, 70.4, 40.2, 39.5, 37.9, 36.4, 33.4, 27.9; IR (KBr) 3427, 2906, 1765, 1712 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{25}H_{26}O_3 \bullet NH_4$ 392.2226, found 392.2206



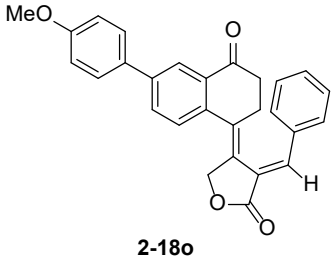
2-18m

According to the representative procedure, pale-yellow solid (mp 194.4–195.8 °C) was obtained (62% yield). **Analytical data for 2-18m:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.63–7.58 (m, 1H), 7.55–7.52 (m, 2H), 7.41–7.38 (m, 3H), 7.20 (ddd, *J* = 11.0, 8.2, 0.9 Hz, 1H), 7.02 (d, *J* = 7.8 Hz, 1H), 5.15 (s, 2H), 2.58 (t, *J* = 6.9 Hz, 2H), 2.39 (t, *J* = 6.9 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 194.1, 170.6, 162.2 (d, *J* = 269.7 Hz), 141.6, 138.1, 135.4 (d, *J* = 2.9 Hz), 134.7, 134.6, 130.6, 129.9 (2C), 129.7, 128.8 (2C), 123.8 (d, *J* = 3.8 Hz), 123.3, 120.5 (d, *J* = 4.7 Hz), 118.3 (d, *J* = 23.1 Hz), 70.2, 39.7, 32.2; ^{19}F-NMR (376 MHz, $CDCl_3$) δ –110.8; IR (KBr) 1752, 1678 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{21}H_{15}FO_3{\bullet}NH_4$ 352.1349, found 352.1367



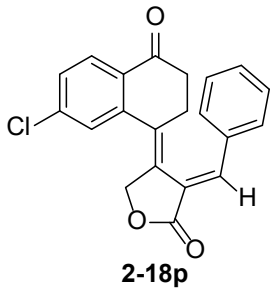
2-18n

According to the representative procedure, yellow solid (mp 199.8–201.2 °C) was obtained (40% yield). **Analytical data for 2-18n:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 2.3 Hz, 1H), 7.76 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.71 (s, 1H), 7.53–7.51 (m, 2H), 7.41–7.38 (m, 3H), 7.08 (d, *J* = 8.2 Hz, 1H), 5.16 (s, 2H), 2.59 (t, *J* = 6.9 Hz, 2H), 2.40 (t, *J* = 6.9 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 195.0, 170.6, 138.0, 136.4, 134.74, 134.69, 133.3, 130.9, 130.6, 129.9, 129.4, 128.8, 124.1, 123.3, 70.1, 38.6, 32.3; IR (KBr) 1759, 1680 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{21}H_{15}BrO_3{\bullet}Na$ 417.0102, found 417.0099.



2-18o

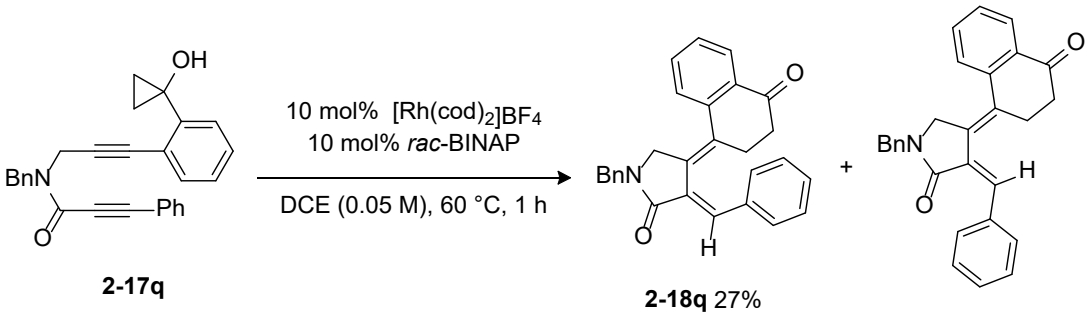
According to the representative procedure, orange solid (mp 212.3–214.0 °C) was obtained (59% yield). **Analytical data for 2-18o:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 2.2 Hz, 1H), 7.84 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.69 (s, 1H), 7.63–7.61 (m, 2H), 7.56–7.54 (m, 2H), 7.39–7.38 (m, 3H), 7.28–7.26 (m, 1H), 7.02 (d, *J* = 8.5 Hz, 2H), 5.24 (s, 2H), 3.88 (s, 3H), 2.63 (t, *J* = 6.9 Hz, 2H), 2.43 (t, *J* = 6.9 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.5, 171.0, 160.0, 142.1, 137.4, 137.2, 135.7, 134.9, 132.4, 131.4, 131.3, 130.4, 129.9, 128.8, 128.6, 128.5, 128.1, 125.4, 123.6, 114.5, 70.4, 55.4, 38.9, 32.6; IR (KBr) 1765, 1681 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{28}H_{22}O_4{\bullet}Na$ 445.1416, found 445.1398



2-18p

According to the representative procedure, yellow solid (mp 188.0–189.5 °C) was obtained (72% yield). **Analytical data for 2-18p:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.2 Hz, 1H), 7.72 (s, 1H), 7.54–7.52 (m, 2H), 7.47 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.41–7.39 (m, 3H), 7.19 (d, *J* = 1.8 Hz, 1H), 5.21 (s, 2H), 2.59 (t, *J* = 6.6 Hz, 2H), 2.40 (t, *J* = 6.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 195.2, 170.5, 140.7, 140.1, 138.3, 134.7, 134.6, 130.7, 130.4, 130.0, 129.9, 129.8, 129.5, 128.9, 127.6, 123.2, 77.3, 77.0, 76.7, 70.0, 38.6, 32.5; IR (KBr) 1763, 1689 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{21}H_{15}ClO_3$•H 351.0788, found 351.0789

Rhodium-Catalyzed Cycloisomerization of 2-17q

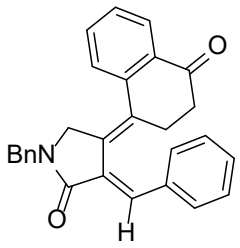


2-17q

2-18q 27%

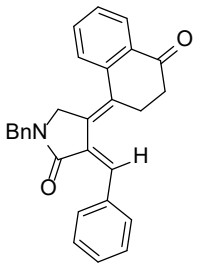
2-19q 19%

$[Rh(cod)_2]BF_4$ (4.07 mg, 0.0100 mmol) and *rac*-BINAP (6.23 mg, 0.0100 mmol) were dissolved in degassed DCE (1.0 mL) and the mixture was stirred at 30 °C for 10 min under Ar atmosphere. The reaction tube was evacuated and refilled with H_2 using a balloon, which was repeated 3 times. After stirring at 30 °C for 1 h under H_2 atmosphere, the reaction tube was evacuated and refilled with Ar using a balloon, which was repeated 3 times. To the resulting mixture was added a DCE (1.0 mL) solution of **2-17q** (40.6 mg, 0.100 mmol). After stirring at 60 °C for 1 h, the resulting solution was concentrated *in vacuo*. The crude product was then purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to give **2-18q** (11.0 mg, 27%) and **2-19q** (7.70 mg, 19%).



2-18q

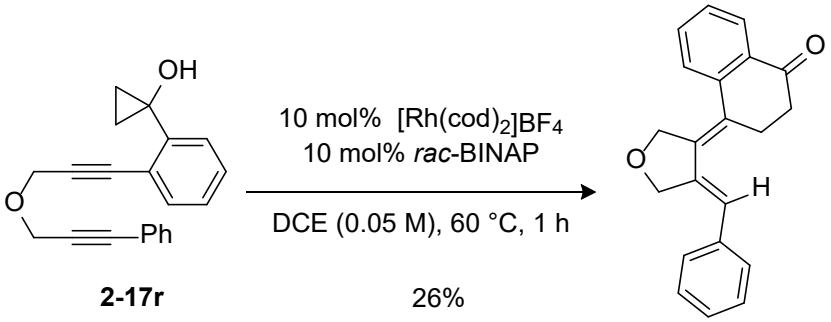
Analytical data for 2-18q: yellow solid (mp 169.9–170.9 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.58 (s, 1H), 7.56 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.51 (d, *J* = 7.6 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.37–7.28 (m, 9H), 4.67 (s, 2H), 4.22 (s, 2H), 2.55 (t, *J* = 6.6 Hz, 2H), 2.41 (t, *J* = 6.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 197.0, 168.6, 140.4, 136.2, 136.0, 134.6, 133.5, 132.6, 132.2, 130.0, 129.6, 129.3, 129.1, 129.0, 128.7, 128.3, 128.1, 127.9, 127.7, 51.5, 47.1, 39.0, 32.4; IR (KBr) 1691, 1619 cm^{-1}; HRMS (DART) *m/z* $[M+ H]^+$ calcd for $C_{28}H_{23}NO_2$•H 406.1807, found 406.1808



2-19q

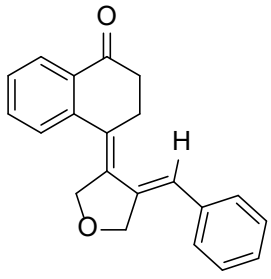
Analytical data for 2-19q: yellow solid (mp 175.6–179.4 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.02 (d, *J* = 6.8 Hz, 2H), 7.51 (dt, *J* = 7.6, 1.4 Hz, 1H), 7.43–7.21 (m, 10H), 7.10 (s, 1H), 4.58 (s, 2H), 4.18 (s, 2H), 3.32 (t, *J* = 6.6 Hz, 2H), 2.74 (t, *J* = 6.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 197.0, 168.6, 140.4, 136.2, 136.0, 134.6, 133.5, 132.6, 132.2, 130.0, 129.6, 129.3, 129.1, 129.0, 128.7, 128.3, 128.1, 127.9, 127.7, 51.5, 47.1, 39.0, 32.4; IR (KBr) 1691, 1619 cm^{-1}; HRMS (DART) *m/z* [M+ H]$^{+}$ calcd for $C_{28}H_{23}NO_2$•H 406.1807, found 406.1793

Rhodium-Catalyzed Cycloisomerization of 2-17r



2-17r 26% **2-19r**

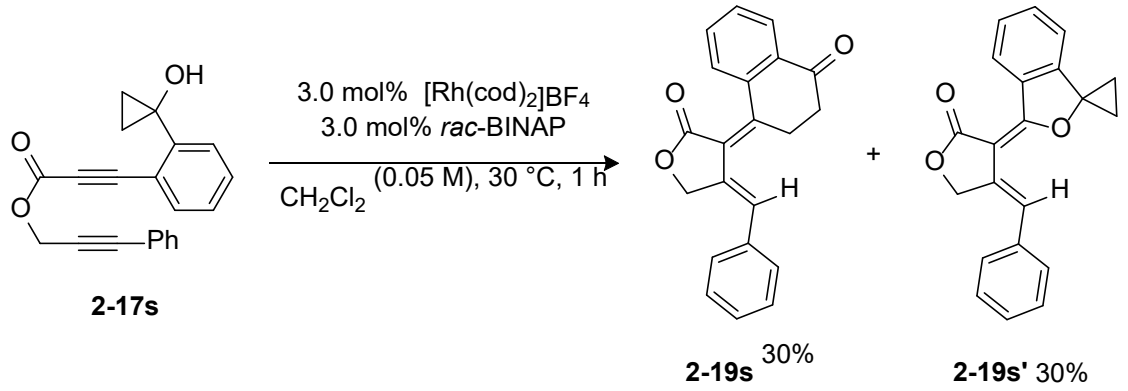
$[Rh(cod)_2]BF_4$ (4.07 mg, 0.0100 mmol) and *rac*-BINAP (6.23 mg, 0.0100 mmol) were dissolved in degassed DCE (1.0 mL) and the mixture was stirred at 30 ℃ for 10 min under Ar atmosphere. The reaction tube was evacuated and refilled with H_2 using a ballon, which was repeated 3 times. After stirring at 30 ℃ for 1 h under H_2 atmosphere, the reaction tube was evacuated and refilled with Ar using a balloon, which was repeated 3 times. To the resulting mixture was added a DCE (1.0 mL) solution of **2-17r** (30.2 mg, 0.100 mmol). After stirring at 60 ℃ for 1 h, the resulting solution was concentrated *in vacuo*. The crude product was then purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to give **2-19r** (7.86 mg, 26%).



2-19r

Analytical data for 2-19r: white solid (mp 119.0–122.4 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.56 (dt, *J* = 7.8, 1.6 Hz, 1H), 7.44–7.39 (m, 3H), 7.32–7.24 (m, 3H), 7.08 (d, *J* = 7.8 Hz, 1H), 6.87 (t, *J* = 2.7 Hz, 1H), 4.82 (d, *J* = 2.7 Hz, 2H), 4.66 (s, 2H), 3.38 (t, *J* = 6.9 Hz, 2H), 2.80 (t, *J* = 6.9 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) 197.3, 142.2, 138.8, 137.7, 136.6, 133.4, 131.7, 130.3, 128.8, 128.4, 128.3, 127.8, 127.4, 127.0, 70.9, 70.0, 39.5, 30.3; IR (KBr) 1680 cm^{-1}; HRMS (DART) *m/z* [M+ H]$^{+}$ calcd for $C_{21}H_{18}O_2$ 303.1385, found 303.1397

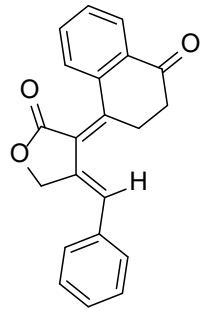
Rhodium-Catalyzed Cycloisomerization of 2-17s



2-17s

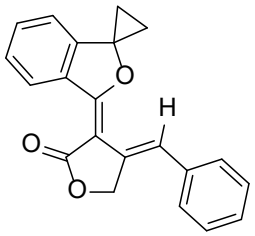
2-19s 30% **2-19s'** 30%

$[Rh(cod)_2]BF_4$ (1.21 mg, 0.00300 mmol) and *rac*-BINAP (1.88 mg, 0.00300 mmol) were dissolved in degassed DCM (1.0 mL) and the mixture was stirred at 30 ℃ for 10 min under Ar atmosphere. The reaction tube was evacuated and refilled with H_2 using a balloon, which was repeated 3 times. After stirring at 30 ℃ for 1 h under H_2 atmosphere, the reaction tube was evacuated and refilled with Ar using a balloon, which was repeated 3 times. To the resulting mixture was added a DCM (1.0 mL) solution of **2-17s** (31.6 mg, 0.100 mmol). After stirring at 30 ℃ for 1 h, the resulting solution was concentrated *in vacuo*. The crude product was then purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to give **2-19s** (9.16 mg, 30%) and **2-19s'** (9.23 mg, 30%).



2-19s

Recrystallization from hexane and EtOAc at rt afforded pure **3s** as a yellow crystal. **Analytical data for 2-19s:** yellow solid (mp 170.8–172.3 ℃); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.08-8.06 (m, 1H), 7.88-7.86 (m, 1H), 7.60-7.53 (m, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.38-7.34 (m, 1H), 7.23 (d, J = 7.6 Hz, 2H), 6.98 (t, J = 2.3 Hz, 1H), 5.20 (d, J = 2.3 Hz, 2H), 3.46 (t, J = 6.9 Hz, 2H), 2.84 (t, J = 6.9 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.0, 167.5, 150.2, 137.9, 135.3, 134.7, 132.3, 132.1, 131.9, 131.1, 129.2, 129.0, 128.8, 128.6, 126.5, 123.1, 68.9, 38.7, 33.7; IR (KBr) 1751, 1681 cm^{-1}; HRMS (DART) *m/z* $[M+ H]^+$ calcd for $C_{21}H_{16}O_3$•H 317.1178, found 317.1170

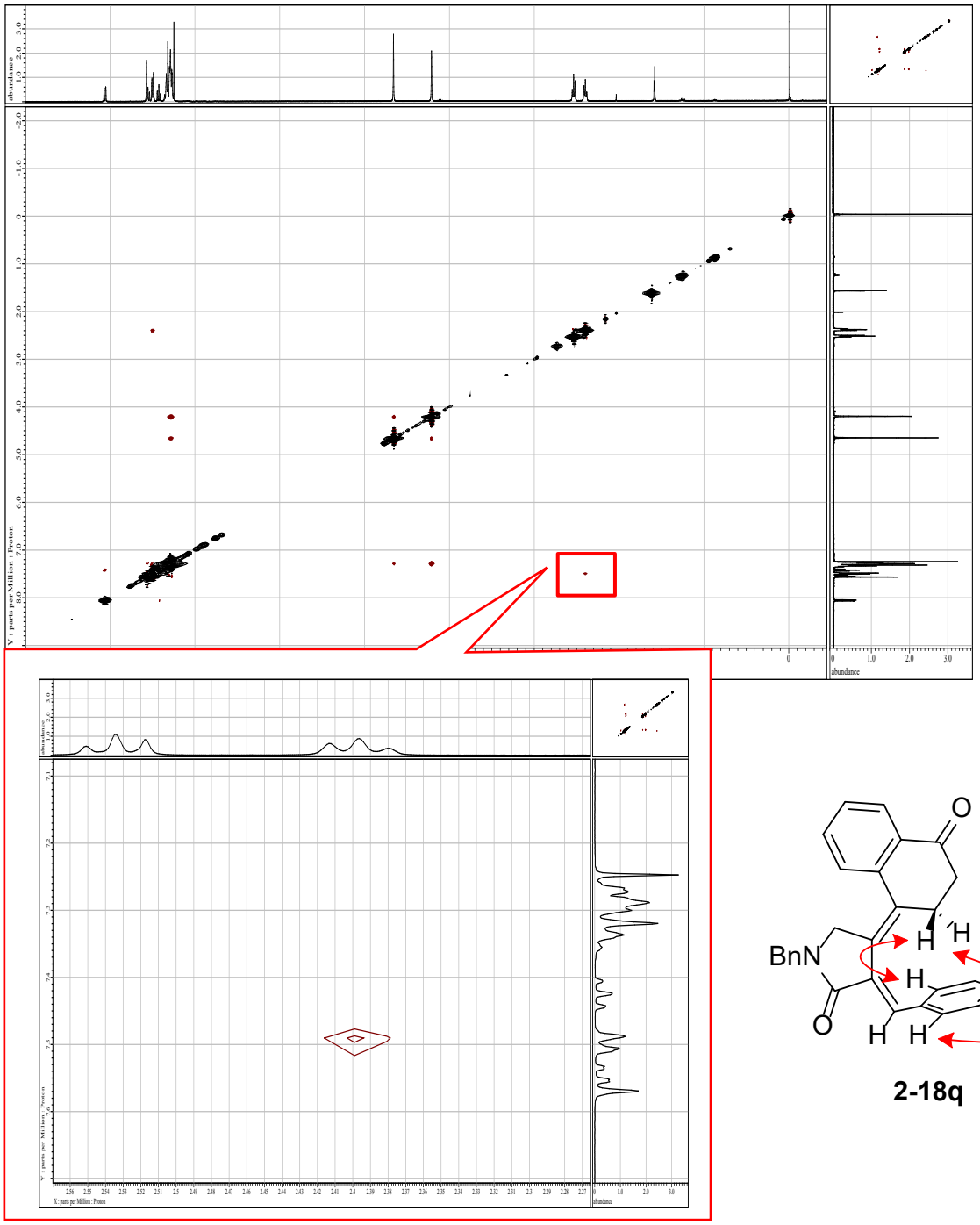


2-19s'

Analytical data for 2-19s': orange solid (mp 199.2–200.0 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.48 (dd, *J* = 7.1, 1.6 Hz, 1H), 7.54–7.47 (m, 2H), 7.40–7.36 (m, 2H), 7.30 (t, *J* = 2.3 Hz, 1H), 7.25–7.18 (m, 3H), 7.02–7.00 (m, 1H), 5.23 (d, *J* = 2.3 Hz, 2H), 1.89 (dd, *J* = 8.2, 6.0 Hz, 2H), 1.47 (dd, *J* = 8.2, 6.0 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 171.6, 166.8, 146.4, 137.7, 134.9, 131.9, 131.9, 129.0, 128.8, 128.4, 126.8, 121.7, 116.7, 100.5, 72.1, 69.9, 15.9; IR (KBr) 1732, 1570 cm^{-1}; HRMS (DART) *m/z* $[M+ H]^+$ calcd for $C_{21}H_{16}O_3$•H 317.1178, found 317.1167

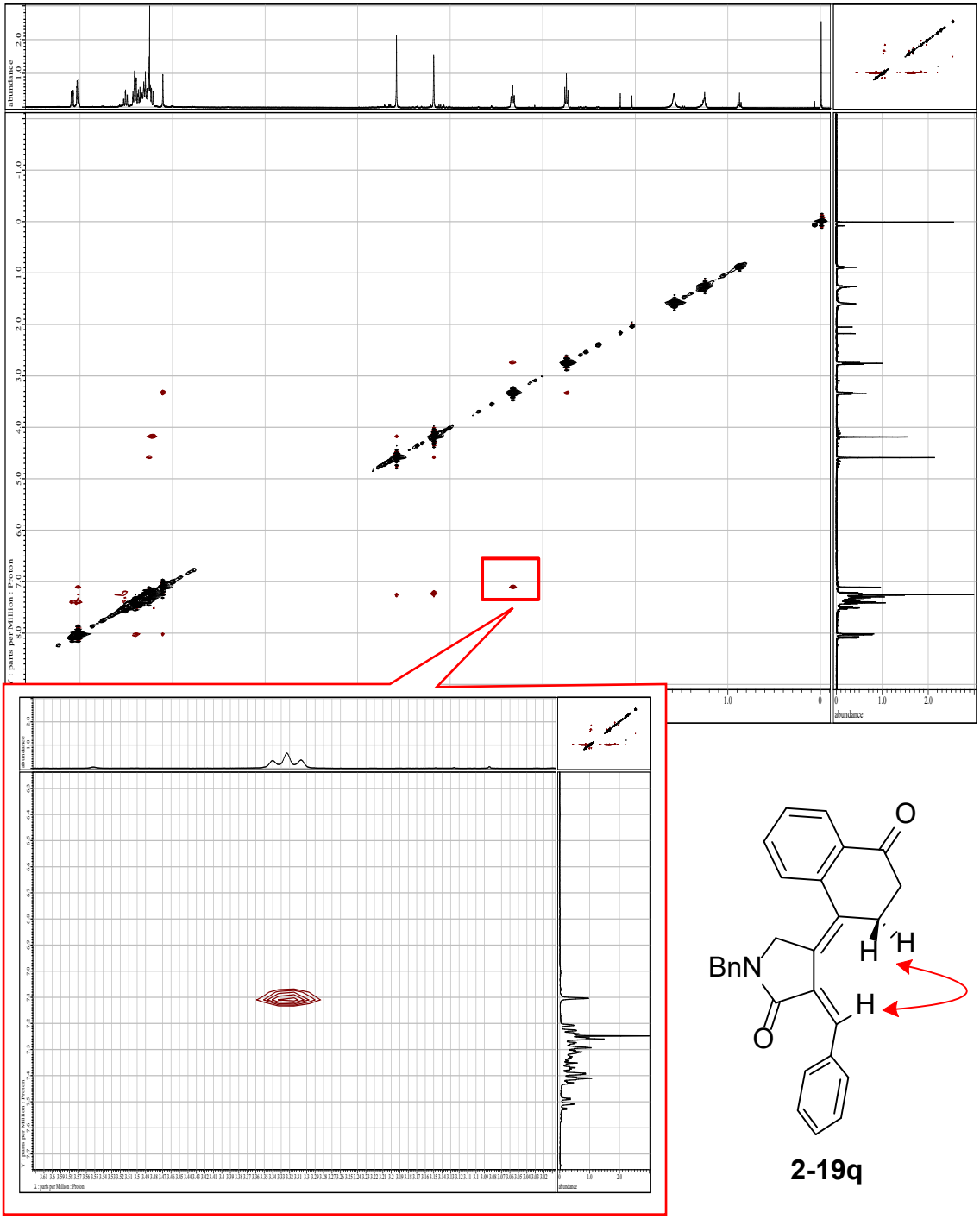
4. Determination of Structures of 2-18q, 2-19q, 2-19r, and 2-19s'

The structure of **2-18q** was assigned by NOESY experiments. The arrows shown below indicate the observed cross peaks.



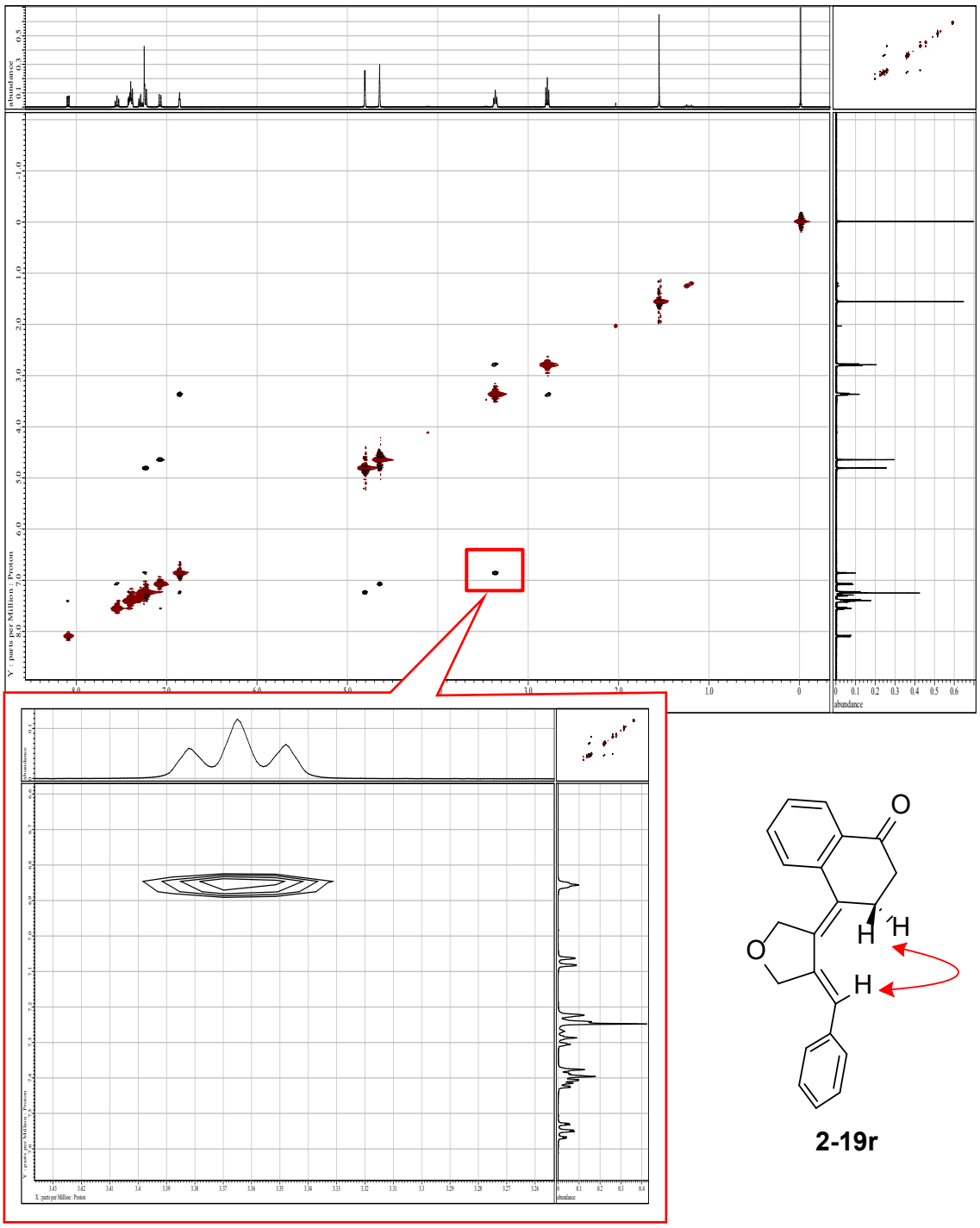
2-18q

The structure of **2-19q** was assigned by NOESY experiments. The arrow shown below indicate the observed cross peaks.



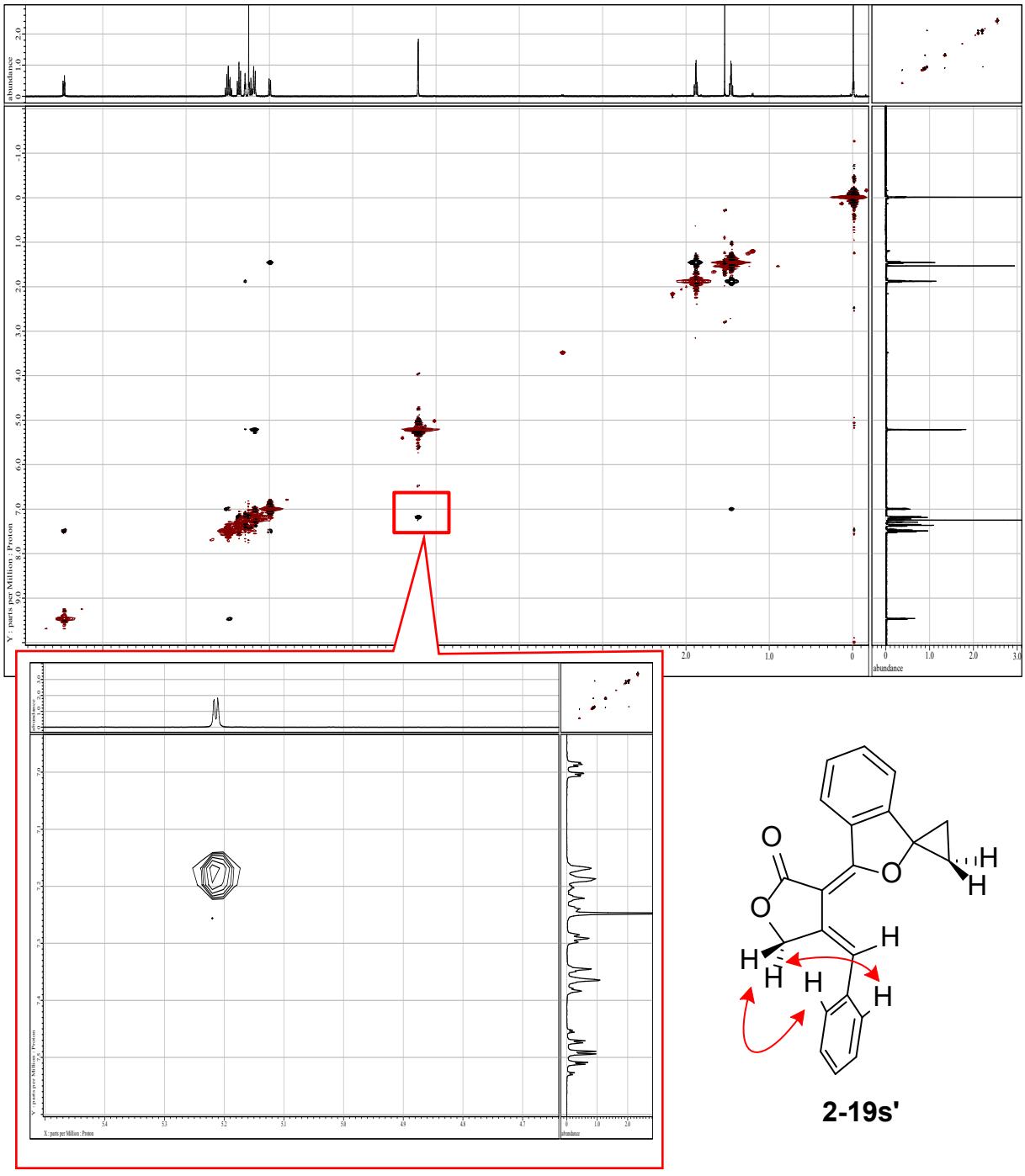
2-19q

The structure of **2-19r** was assigned by NOESY experiments. The arrow shown below indicate the observed cross peaks.



2-19r

The structure of **2-19s'** was assigned by NOESY experiments. The arrows shown below indicate the observed cross peaks.

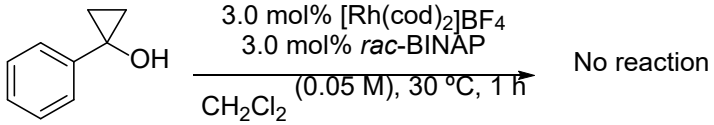


2-19s'

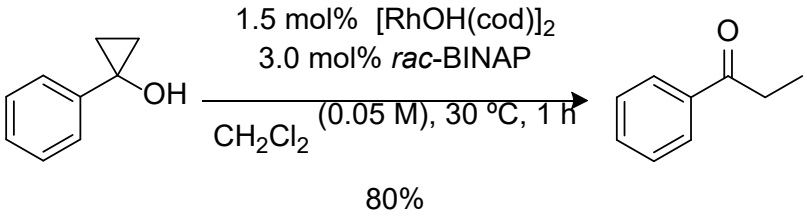
5. Control Experiments

Ring-Opening Reaction of Phenylcyclopropanol

Phenylcyclopropanol was prepared according to the previous report[19]. Characterization of the ring-opened product was identical to the previous reports[20].

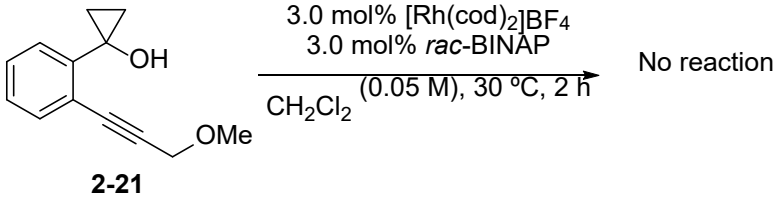


$[Rh(cod)_2]BF_4$ (1.21 mg, 0.00300 mmol) and *rac*-BINAP (1.88 mg, 0.00300 mmol) were dissolved in degassed DCM (1.0 mL) and the mixture was stirred at 30 ℃ for 10 min under Ar atmosphere. The reaction tube was evacuated and refilled with H_2 using a balloon, which was repeated 3 times. After stirring at 30 ℃ for 1 h under H_2 atmosphere, the reaction tube was evacuated and refilled with Ar using a balloon, which was repeated 3 times. To the resulting mixture was added a DCM (1.0 mL) solution of phenylcyclopropanol (13.4 mg, 0.100 mmol). After stirring at 30 ℃ for 1 h, the resulting solution was concentrated *in vacuo*. The crude material was then purified by silica gel column chromatography (Hexane/EtOAc = 4:1) to recover starting material (12.4 mg, RSM 92%).



$[RhOH(cod)]_2$ (1.21 mg, 0.00300 mmol), *rac*-BINAP (1.88 mg, 0.00300 mmol) and phenylcyclopropanol (13.4 mg, 0.100 mmol) were dissolved in degassed DCM (2.0 mL). After stirring at 30 ℃ for 1 h, the resulting solution was concentrated *in vacuo*. The crude material was then purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to give the ring-opened product (10.6 mg, 80%).

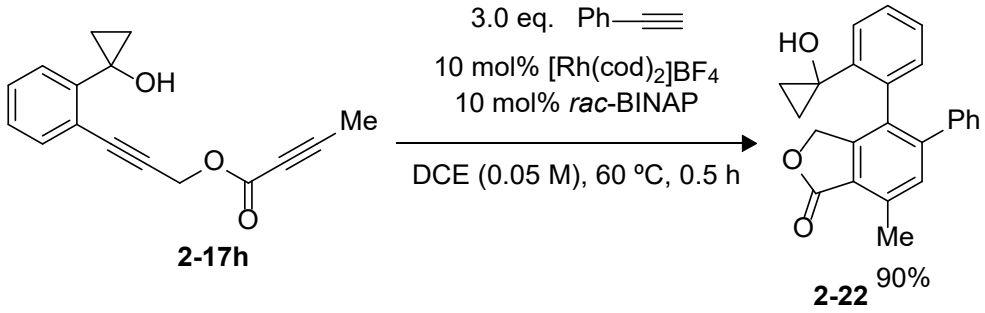
Reaction of Alkyne substrate 2-21



$[Rh(cod)_2]BF_4$ (1.21 mg, 0.00300 mmol) and *rac*-BINAP (1.88 mg, 0.00300 mmol) were dissolved in degassed DCM (1.0 mL) and the mixture was stirred at 30 ℃ for 10 min under Ar atmosphere. The reaction tube was evacuated and refilled with H_2 using a balloon, which was

repeated 3 times. After stirring at 30 ℃ for 1 h under H_2 atmosphere, the reaction tube was evacuated and refilled with Ar using a balloon, which was repeated 3 times. To the resulting mixture was added a DCM (1.0 mL) solution of **2-21** (20.2 mg, 0.100 mmol). After stirring at 30 ℃ for 2 h, the resulting solution was concentrated. The crude was then purified by a silica gel column chromatography (Hexane/EtOAc = 10:1) to recover starting material **2-21**.

Rhodium-Catalyzed Cycloisomerization of 2-17h in the presence of Phenylacetylene



2-17h **2-22** 90%

$[Rh(cod)_2]BF_4$ (4.07 mg, 0.0100 mmol) and *rac*-BINAP (6.23 mg, 0.0100 mmol) were dissolved in degassed DCE (1.0 mL) and the mixture was stirred at 30 ℃ for 10 min under Ar atmosphere. The reaction tube was evacuated and refilled with H_2 using a balloon, which was repeated 3 times. After stirring at 30 ℃ for 1 h under H_2 atmosphere, the reaction tube was evacuated and refilled with Ar using a balloon, which was repeated 3 times. To the resulting mixture was added a DCE (1.0 mL) solution of **2-17h** (31.6 mg, 0.100 mmol) and phenylacetylene (32.0 μL, 0.300 mmol). After stirring at 60 ℃ for 0.5 h, the resulting solution was concentrated *in vacuo*. The crude material was then purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to give **2-22** (32.2 mg, 90%). Recrystallization from hexane and EtOAc at rt afforded pure **2-22** as a colorless crystal.

Analytical data for 2-22: colorless crystal (mp 170.6–172.0 ℃); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.47-7.44 (m, 2H), 7.39-7.36 (m, 2H), 7.31-7.29 (m, 1H), 7.27-7.22 (m, 5H), 5.11 (d, J = 15.6 Hz, 1H), 4.74 (d, J = 15.6 Hz, 1H), 2.80 (s, 3H), 1.09 (s, 1H), 0.80-0.75 (m, 1H), 0.61-0.56 (m, 1H), 0.28-0.24 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 171.3, 147.4, 145.3, 139.5, 139.4, 135.2, 132.9, 132.3, 131.5, 130.8, 129.8, 128.7, 128.5, 128.1, 127.9, 122.5, 69.0, 56.3, 17.3, 15.1, 14.5; IR (KBr) 3464, 1720 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{24}H_{20}O_3$•H 357.1491, found 357.1486

6. Variable-Temperature ^{1}H NMR Spectroscopy of 2-18j

Exocyclic dienes **2-18** have fluxional nature. Helical isomerization process (Figure S1) can be monitored by variable-temperature NMR study in CD_2Cl_2. The methylene protons (H_A and H_B) of **2-18j** are enantiotopic, appearing as a sharp singlet peak at 22 ºC (Figure S2). As the temperature decreases, the protons gradually appear as two doublets, and become diastereotopic below –60 ºC. This implies the two isomers are in rapid equilibrium at 22 ºC, but are distinguished each other below –60 ºC in the NMR time scale.

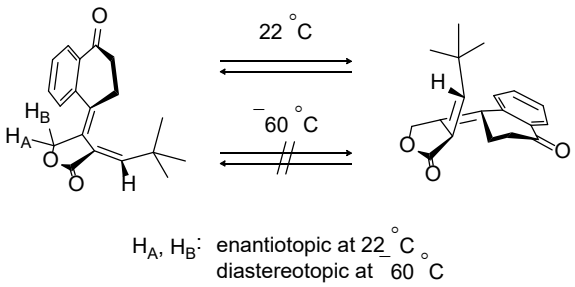


Figure S1 Helical isomerization of **2-18j**

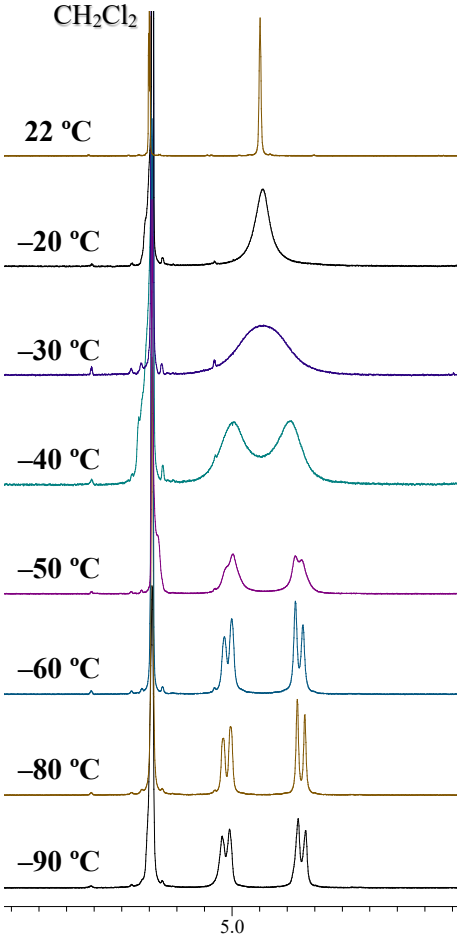


Figure S2 Variable-temperature ^{1}H NMR behavior of **2-18j** (only H_A and H_B shown)

7. X-Ray Diffraction Analysis of 2-18a

A single crystal of **2-18a** was mounted on a glass fiber, and diffraction data were collected in θ ranges specified in Table S1 at 123 K on a Rigaku R-AXIS Rapid diffractometer with graphite monochromatized Cu-Ka radiation (λ = 1.54187 Å). The Lorenz polarization absorption correction was applied. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined using the riding model. Final refinement details are compiled in Table S1. The supplementary crystallographic data for this paper (CCDC2007772) can also be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk)

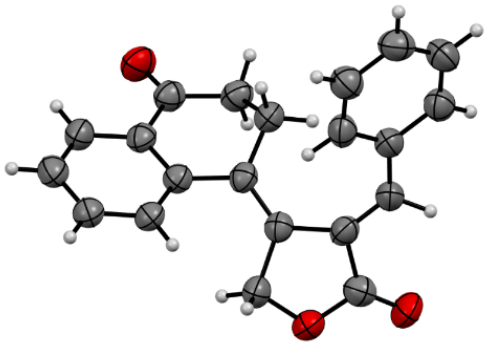


Figure S3 ORTEP plot of **2-18a**.

Table S1 Selected crystallographic data and collection parameters for **2-18a**.

formula	$C_{21}H_{16}O_3$	crystal size, mm	0.60 x 0.30 x 0.10
FW	316.36	maximum 2θ, deg	136.4
crystal system	orthorhombic	reflections collected	62519
space group	Pbca (#61)	independent reflections [R(int)]	5578 [R(int) = 0.1638]
a, Å	8.8744(6)	max. and min. transmission	0.929/0.601
b, Å	11.4021(7)	goodness-of-fit on F^2	1.069
c, Å	60.208(4)	R_1 [I >2σ(I)]	0.1092
volume, Å^3	6092.2(7)	R, wR_2 (all data)	0.1600, 0.3326
Z	16	Weighting scheme	$R_1 = \Sigma \lvert\lvert Fo\rvert - \lvert Fc\rvert\rvert / \Sigma \lvert Fo\rvert$ $wR_2 = [\ \Sigma\ (w(Fo^2 - Fc^2)^2) / \Sigma\ w(Fo^2)^2\ ]^{1/2}$
D (calcd), Mg m^{-3}	1.380		
μ, cm^{-1}	7.395	largest diff. peak and hole, e Å^{-3}	0.61 and -0.61
F(000)	2656.00		

X-Ray Diffraction Analysis of 2-18f

A single crystal of **2-18f** was mounted on a glass fiber, and diffraction data were collected in θ ranges specified in Table S2 at 123 K on a Rigaku R-AXIS Rapid diffractometer with graphite monochromatized Cu-Ka radiation (λ = 1.54187 Å). The Lorenz polarization absorption correction was applied. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined using the riding model. Final refinement details are compiled in Table S2. The supplementary crystallographic data for this paper (CCDC2007776) can also be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk)

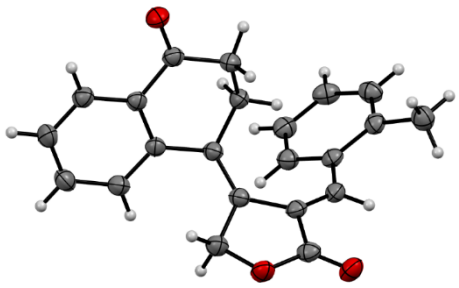


Figure S4 ORTEP plot of **2-18f**.

Table S2 Selected crystallographic data and collection parameters for **2-18f**.

formula	$C_{22}H_{18}O_3$	crystal size, mm	0.20 x 0.20 x 0.20
FW	330.38	maximum 2θ, deg	136.4
crystal system	monoclinic	reflections collected	17148
space group	$P2_1/c$ (#14)	independent reflections [*R*(int)]	3013 [*R*(int) = 0.1009]
a, Å	15.8736(5)	max. and min. transmission	0.406/0.868
b, Å	9.6592(3)	goodness-of-fit on F^2	1.268
c, Å	10.7426(3)	R_1 [I >2σ(I)]	0.0773
volume, Å^3	1644.14(9)	*R*, wR_2 (all data)	0.1118, 0.3302
Z	4	Weighting scheme	$R_1 = \Sigma \lvert\lvert Fo\rvert - \lvert Fc\rvert\rvert / \Sigma \lvert Fo\rvert$ $wR_2 = [\ \Sigma\ (w(Fo^2 - Fc^2)^2) / \Sigma\ w(Fo^2)^2\ ]^{1/2}$
D (calcd), Mg m^{-3}	1.335		
μ, cm^{-1}	7.073	largest diff. peak and hole, e Å^{-3}	0.48 and -0.49
F(000)	696.00		

X-Ray Diffraction Analysis of 2-18j

A single crystal of **2-18j** was mounted on a glass fiber, and diffraction data were collected in θ ranges specified in Table S3 at 123 K on a Rigaku R-AXIS Rapid diffractometer with graphite monochromatized Cu-Ka radiation (λ = 1.54187 Å). The Lorenz polarization absorption correction was applied. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined using the riding model. Final refinement details are compiled in Table S3. The supplementary crystallographic data for this paper (CCDC2007773) can also be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk)

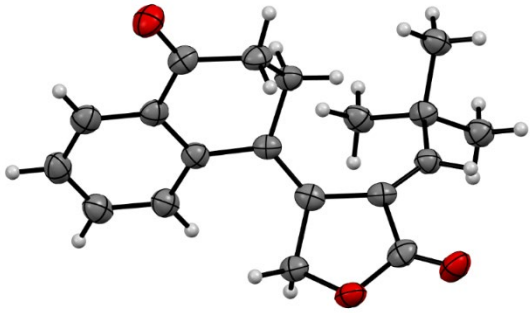


Figure S5 ORTEP plot of **2-18j**.

Table S3 Selected crystallographic data and collection parameters for **2-18j**.

formula	$C_{19}H_{20}O_3$	crystal size, mm	0.40 x 0.20 x 0.10
FW	296.37	maximum 2θ, deg	136.4
crystal system	monoclinic	reflections collected	8864
space group	$P2_1$ (#4)	independent reflections [R(int)]	2669 [R(int) = 0.0605]
a, Å	8.6683(12)	max. and min. transmission	0.934/0.694
b, Å	8.3860(10)	goodness-of-fit on F^2	1.174
c, Å	11.3586(14)	R_1 [I >2σ(I)]	0.0386
β, deg	110.379(8)	R, wR_2 (all data)	0.0586, 0.1248
volume, Å^3	774.01(18)	Weighting scheme	$R_1 = \Sigma \lvert\lvert Fo\rvert - \lvert Fc\rvert\rvert / \Sigma \lvert Fo\rvert$ $wR_2 = [\ \Sigma\ (w(Fo^2 - Fc^2)^2) / \Sigma\ w(Fo^2)^2\ ]^{1/2}$
Z	2		
D (calcd), Mg m^{-3}	1.272	largest diff. peak and hole, e Å^{-3}	0.23 and -0.24
μ, cm^{-1}	6.818	flack parameter	-0.06(13)
F(000)	316.00		

X-Ray Diffraction Analysis of 2-19s

A single crystal of **2-19s** was mounted on a glass fiber, and diffraction data were collected in θ ranges specified in Table S4 at 123 K on a Rigaku R-AXIS Rapid diffractometer with graphite monochromatized Cu-Ka radiation (λ = 1.54187 Å). The Lorenz polarization absorption correction was applied. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined using the riding model. Final refinement details are compiled in Table S4. The supplementary crystallographic data for this paper (CCDC2007774) can also be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk)

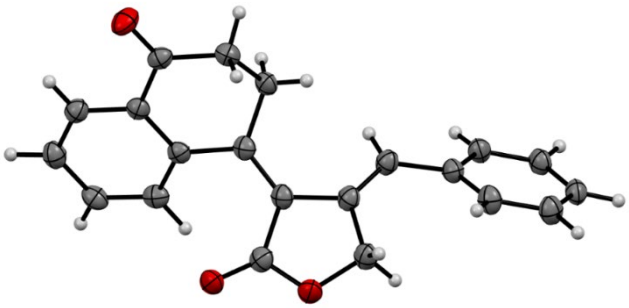


Figure S6 ORTEP plot of **2-19s**.

Table S4 Selected crystallographic data and collection parameters for **2-19s**.

formula	$C_{21}H_{16}O_3$	crystal size, mm	0.20 x 0.20 x 0.10
FW	316.36	maximum 2θ, deg	136.4
crystal system	monoclinic	reflections collected	8943
space group	$P2_1$ (#4)	independent reflections [*R*(int)]	2701 [*R*(int) = 0.0352]
a, Å	9.6092(3)	max. and min. transmission	0.929/0.734
b, Å	8.1201(3)	goodness-of-fit on F^2	1.076
c, Å	10.9799(4)	R_1 [$I > 2\sigma(I)$]	0.0317
β, deg	116.4260(18)	*R*, wR_2 (all data)	0.0333, 0.0822
volume, Å^3	767.22(4)	Weighting scheme	$R_1 = \Sigma \, \|\|Fo\| - \|Fc\|\| / \Sigma \, \|Fo\|$ $wR_2 = [\, \Sigma \, (w(Fo^2 - Fc^2)^2) / \Sigma \, w(Fo^2)^2 \,]^{1/2}$
Z	2		
D (calcd), Mg m^{-3}	1.369	largest diff. peak and hole, e Å^{-3}	0.19 and -0.21
μ, cm^{-1}	7.340	flack parameter	0.05(8)
F(000)	332.00		

X-Ray Diffraction Analysis of 2-22

A single crystal of **2-22** was mounted on a glass fiber, and diffraction data were collected in θ ranges specified in Table S5 at 123 K on a Rigaku R-AXIS Rapid diffractometer with graphite monochromatized Cu-Ka radiation (λ = 1.54187 Å). The Lorenz polarization absorption correction was applied. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined using the riding model. Final refinement details are compiled in Table S5. The supplementary crystallographic data for this paper (CCDC2007775) can also be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk)

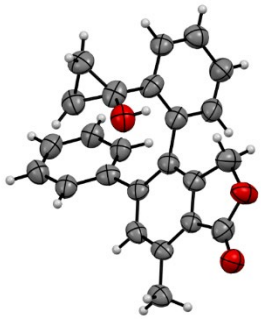


Figure S7 ORTEP plot of **2-22**.

Table S5 Selected crystallographic data and collection parameters for **2-22**.

formula	$C_{24}H_{20}O_3$	crystal size, mm	0.70 x 0.10 x 0.10
FW	356.42	maximum 2θ, deg	136.5
crystal system	monoclinic	reflections collected	19341
space group	$P2_1/n$ (#14)	independent reflections [R(int)]	3332 [R(int) = 0.1118]
a, Å	13.0170(6)	max. and min. transmission	0.934/0.433
b, Å	10.8103(5)	goodness-of-fit on F^2	0.881
c, Å	13.8173(6)	R_1 [I >2σ(I)]	0.1038
β, deg	110.376(2)	R, wR_2 (all data)	0.1887, 0.3372
volume, Å^3	1822.68(15)	Weighting scheme	$R_1 = \Sigma \lvert\lvert Fo\rvert - \lvert Fc\rvert\rvert / \Sigma \lvert Fo\rvert$ $wR_2 = [\ \Sigma\ (w(Fo^2 - Fc^2)^2) / \Sigma\ w(Fo^2)^2\ ]^{1/2}$
Z	4		
D (calcd), Mg m^{-3}	1.299	largest diff. peak and hole, e Å^{-3}	0.33 and -0.44
μ, cm^{-1}	6.777		
F(000)	752.00		

8. DFT Calculations

The Gaussian 16 program package was used for all calculations.[21] The geometries of the stationary points and transition states were fully optimized using the Becke's three-parameter hybrid density functional method (B3LYP),[22] with a [3*s*3*p*2*d*] contracted-valence basis set with the relativistic effective core potential of Hay and Wadt (LanL2DZ)[23] for Rh, and the 6-31G(d)[24] basis sets for other elements. The vibrational frequencies and the thermal correction to Gibbs free energy (TCGFE) including the zero-point energy were calculated at the same level of theory. The obtained structures were characterized by the number of imaginary frequencies (one or zero for the transition and ground states, respectively). The connectivity of each step was also confirmed using intrinsic reaction coordinate (IRC)[25] calculation from the transition states, followed by optimization of the resultant geometries. Single-point energies for geometries obtained using the above method were calculated at the same level of theory using a [6*s*5*p*3*d*] contracted-valence basis set with the Stuttgart-Dresden-Bonn energy-consistent pseudopotential (SDD)[26] for Rh, and the 6-311++G(d,p) basis sets[27] for other elements. The D3 version of Grimme's dispersion with Becke-Johnson damping[28] was used for empirical dispersion correction. To examine the solvent effect, the above single-point energy calculations were performed using the SMD model[29] with CH_2Cl_2 as the solvent. CYLview (Ver. 1.0b)[30] was used for the visualization of the optimized structures.

Table S6. Summary of theoretical calculations.

Model	TCGFE/au	SMD Energy/au	IF/cm^{-1}
A	0.834094	–3525.768839	
TS_{AB}	0.839935	–3525.770357	196.3824i
B	0.842284	–3525.820307	
TS_{BC}	0.843373	–3525.804259	139.3597i
C	0.846548	–3525.837278	
TS_{CD}	0.845812	–3525.804187	196.3342i
D	0.848022	–3525.838747	
TS_{DE}	0.847489	–3525.812232	414.6393i
E	0.841963	–3525.853145	
F	0.842689	–3525.864414	
G	0.845008	–3525.874465	
H	0.841103	–3525.893471	
TS_{HI}	0.839893	–3525.880753	713.8393i
I	0.846142	–3525.918818	

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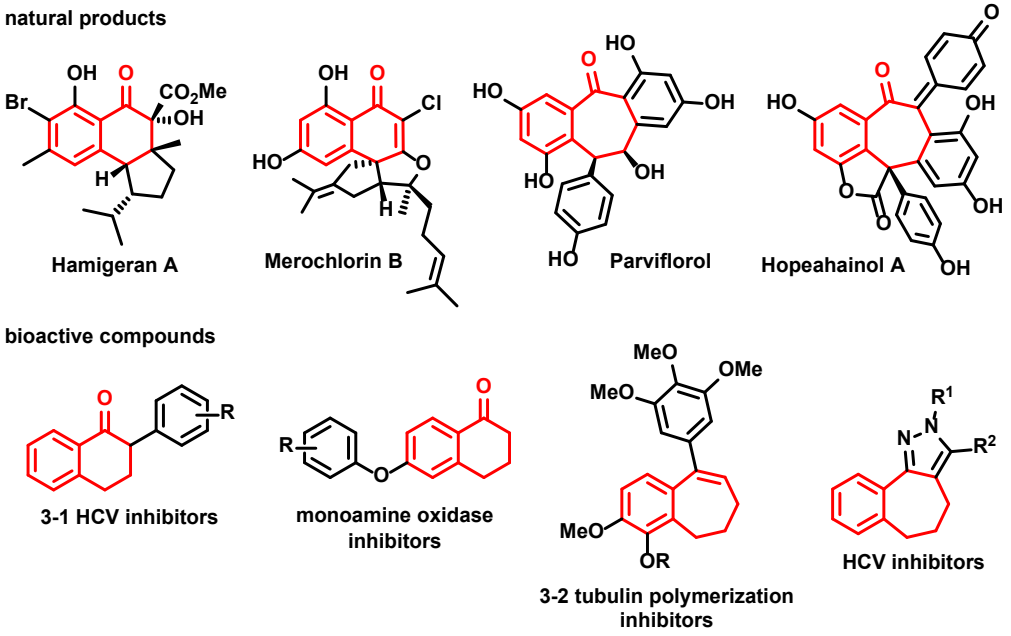
第 3 章

PCET を起点とする
アルケン含有シクロプロパノールの
触媒的環化異性化反応

第 1 節　ベンゼン縮環環状ケトン

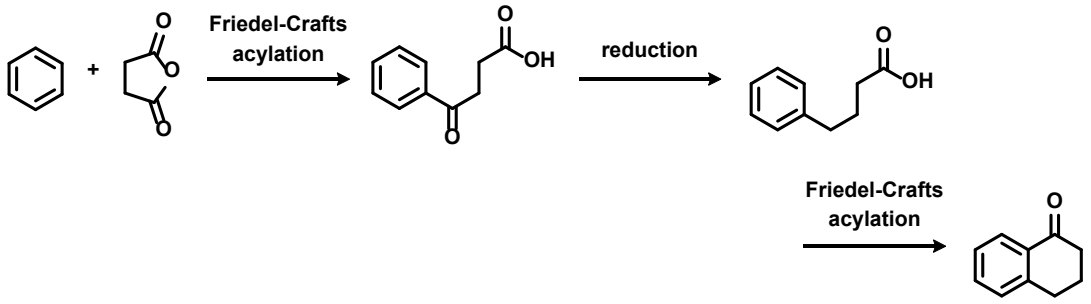
ベンゼン環が縮環した環状ケトンである、1-テトラロンや 1-ベンゾスベロンは、天然物によく見られる構造である（**Scheme 3-1**）[1]。例えば、ニュージーランド近海に生息する海綿動物から単離された Hamigeran A[1a] や日本固有種である五葉松から単離された Parviflorol[1c] などが挙げられる。また、1-テトラロンや 1-ベンゾスベロンの誘導体の多くが、生物活性を有することが知られている[2]。例えば、**3-1** は C 型肝炎ウイルスの阻害活性を示し[2a]、**3-2** は抗がん剤として機能することが知られている[2d]。



Scheme 3-1 1-テトラロンや 1-ベンゾスベロンを含む天然物および生物活性物質

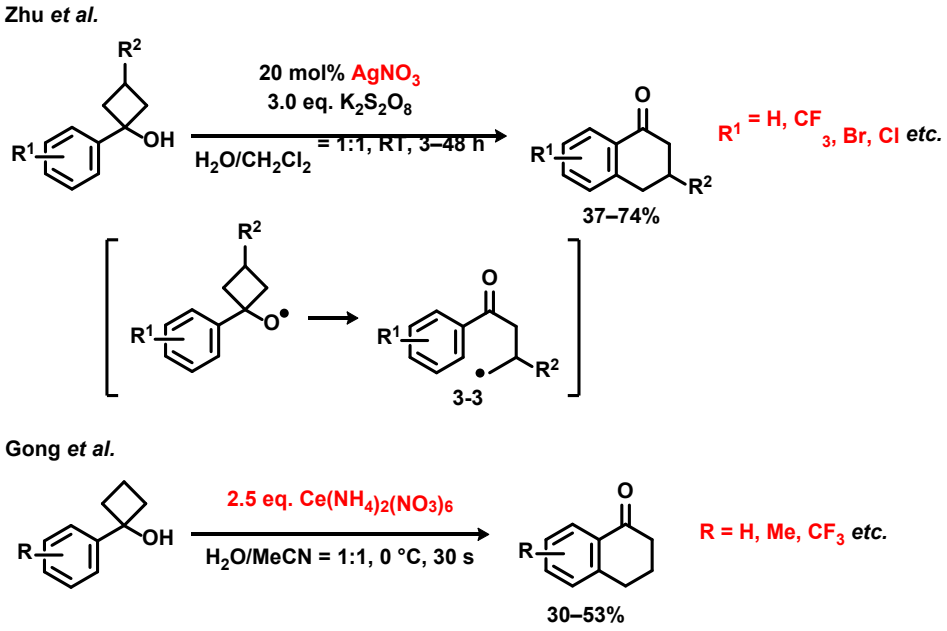
第 2 節　ベンゼン縮環環状ケトンの合成

Haworth 反応は、ベンゼン縮環環状ケトンの古典的な合成法として知られている（**Scheme 3-2**）[3]。この合成法では、まず、Friedel–Crafts アシル化反応によって、ベンゼンと無水コハク酸を反応させた後に、還元と二回目の Friedel–Crafts アシル化反応を行うことで、1-テトラロンが得られる。しかし、Friedel–Crafts アシル化反応は強いルイス酸やブレンステッド酸を必要とするために、基質適用範囲が著しく制限される。



Scheme 3-2 Haworth 反応

それに対して、最近では、より温和な条件で進行するラジカル反応を利用した合成法が報告されている。Zhu ら [4] と Gong ら [5] は、それぞれ独立に、金属酸化剤を用いるフェニルシクロブタノールのラジカル的環拡大反応を報告している（**Scheme 3-3**）。これらの反応では、環歪みの解消を駆動力として、高活性な第一級ラジカルを生じさせていることが特徴である。しかし、反応後に化学量論量以上の金属酸化剤由来の廃棄物が生じ、中間体 **3-3** において、求核的なアルキルラジカルが芳香族環に直接付加するために電子供与基をベンゼン環上に導入した基質には適用できないなどの課題が残されている。

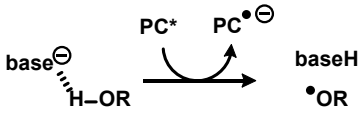


Scheme 3-3 金属酸化剤によるフェニルシクロブタノール基質のラジカル環化反応

第 3 節　プロトン共役電子移動によるアルコキシラジカルの調製

プロトン共役電子移動（Proton-Coupled Electron Transfer, PCET）は、プロトンと電子の移動が協奏的に起こる過程を指し、水素化や脱水素化など生体内の酸化還元反応で頻繁に見られる過程である[6]。

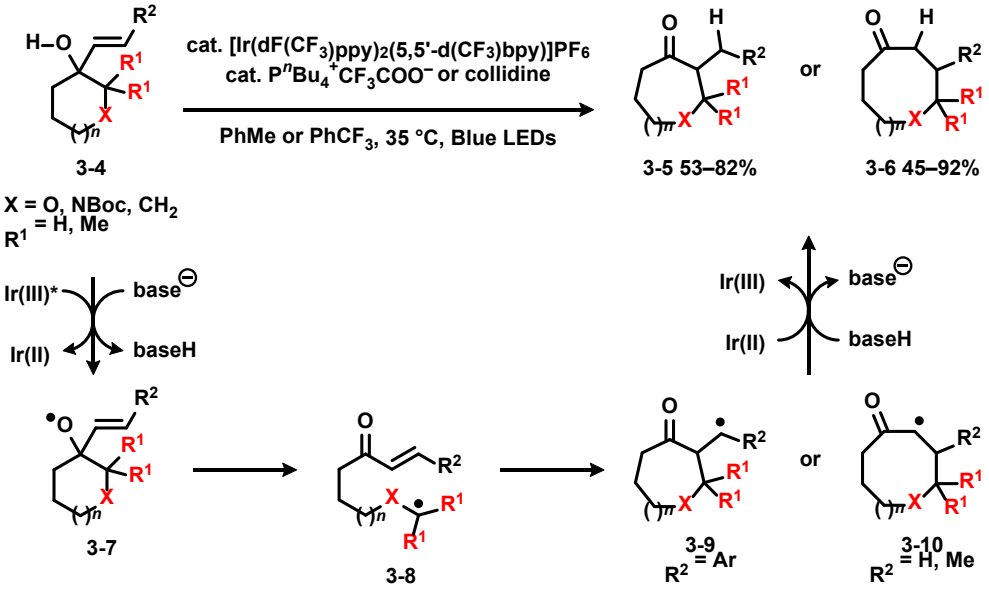
最近、PCET を分子変換反応に応用する研究が盛んである。とりわけ、アルコールの PCET では、塩基触媒によるアルコールのプロトン引き抜きと励起した光レドックス触媒(PC*)による一電子酸化が協奏的に起こり、アルコキシラジカルを直接的かつ温和に調製できる（**Scheme 3-4**）。PCET はレドックスニュートラルで原子効率の高い分子変換反応を可能にする[7]。



Scheme 3-4 アルコールの PCET

PCET を利用した分子変換反応の先駆的な例として、Knowles らが、イリジウム光触媒を用いる環状アリルアルコール **3-4** の環拡大反応を報告している（**Scheme 3-5**）[7d]。基質の設計次第で、一炭素あるいは二炭素環拡大した生成物 **3-5** および **3-6** がそれぞれ選択的に得られる。この反応では、最初にリン酸イオンと励起したイリジウム光触媒によって、アルコールの PCET が起こり、アルコキシラジカル **3-7** が生成する。次に、β-開裂によって、α-オキシラジカル、α-アミノラジカルおよび第三級ラジカルなどの安定なラジカル中間体 **3-8** を与える。続いて、生じたラジカルが分子内のアルケンへ付加する。この時のラジカル付加の位置選択性は、アルケン上の置換基（R^2）に依存する。R^2 がアリール基の場合、**3-9** が生じる。これは、アルキルラジカルとアリール基の立体障害を避けた環化様式および安定なベンジルラジカル中間体の生成に起因していると考えられる。一方で、R^2 が水素やメチル基の場合、**3-10** が生成する。最後に、イリジウム光触媒による一電子還元と続くプロトン化が起こることで、**3-9** および **3-10** からそれぞれ **3-5** および **3-6** が得られ、触媒サイクルが完結する。

この反応では、β-開裂を効率的に進行させるために、生じるアルキルラジカル **3-8** を安定化させる必要があると考えられる。そのため、**3-4** にヘテロ原子を導入しなければならないなど基質設計の制限を余儀なくされている。PCET を利用するラジカル環化反応で、炭素のみの骨格を有するベンゼン縮環環状ケトンを合成するには、新しい基質設計が必要となる。

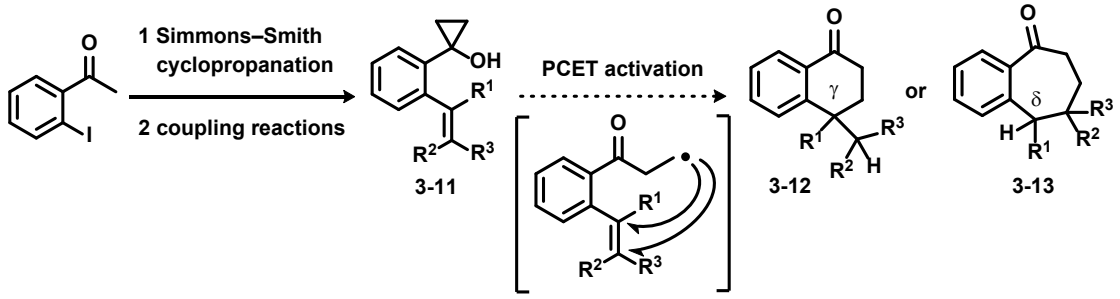


Scheme 3-5 PCET を利用する環状アリルアルコールの触媒的環拡大反応

第 4 節　アルケン含有シクロプロパノール基質の設計

そこで、第 2 章で設計した 1,6-ジイン含有シクロプロパノール基質と同じくモジュラー合成が可能なアルケン含有シクロプロパノール基質 **3-11** を設計した（**Scheme 3-6**）。シクロプロパノールは環歪みを駆動力として開環し、高活性な第一級アルキルラジカルとなるので、炭素のみの骨格を有する環状ケトンの合成に適している。また、確立されたクロスカップリング反応により、様々な不飽和部位を導入できるので、多様な置換基をベンジル位に有するベンゼン縮環環状ケトンの合成が可能になると考えられる。

3-11 のアルコールの PCET によって、環歪みを駆動力として高活性な第一級アルキルラジカルが生じると考えられる。この時、6-*exo-trig* 環化が進行すれば、γ 位に置換基を有する様々な 1-テトラロン誘導体 **3-12** となる。また、7-*endo-trig* 環化が進行すれば、δ 位に置換基を有する様々な 1-ベンゾスベロン誘導体 **3-13** が得られるはずである。

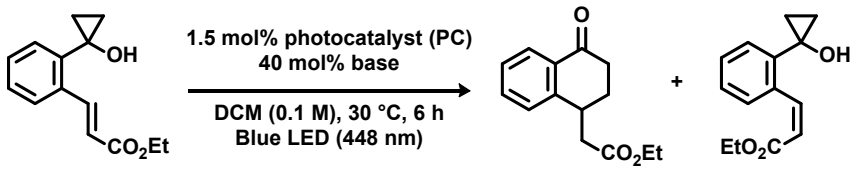


Scheme 3-6 アルケン含有フェニルシクロプロパノールの基質設計

第 5 節　反応条件の検討

エチルアクリレート部位を有する **3-11a** をモデル基質として、反応条件を検討した（**Scheme 3-7**）。PCET により生じる求核的な第一級アルキルラジカルは、求電子性の高まっているエチルエステルの β 位に付加することで、6-*exo-trig* 環化が進行し、優先的に 1-テトラロンが得られると予想した。まず、Knowles らの報告 [7d] を参考に、イリジウム光触媒[Ir(dF(CF$_3$)ppy)$_2$(dtbpy)]PF$_6$ と市販のリン酸塩を用いて反応を行うこととした。また、PCET では塩基と基質間でのプロトンの移動が重要となるので、非プロトン性溶媒であるジクロロメタンを溶媒とした。その結果、期待した 1-テトラロン **3-12a** と幾何異性体の副生成物 **3-14a** が、それぞれ 33%収率および 8%収率で得られた（entry 1）。また、この時、7-*endo-trig* 環化による **3-13a** の生成は確認されなかった。

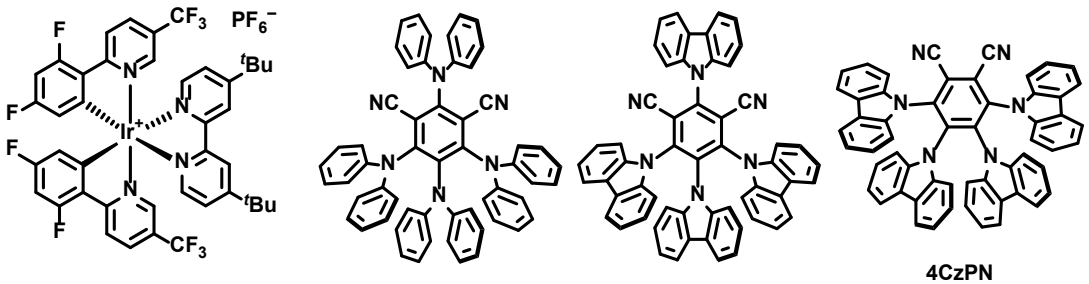
続いて、光触媒の影響を調査することとした。その際、カルバゾイルジシアノベンゼン型の有機光触媒 [8] に着目した。[Ir(dF(CF$_3$)ppy)$_2$(dtbpy)]PF$_6$　[$E_{1/2}$(*P/P$^-$) = 1.21 V vs SCE in MeCN][9] に対して、酸化能が低い 4DPAIPN [$E_{1/2}$(*P/P$^-$) = 1.10 V vs SCE in MeCN][10] を用いた反応では、**3-12a** の収率は低下し、**3-14a** の収率が増加した（entry 2）。このことから、より効率的に PCET による活性化を起こすためには、より酸化力の高い光触媒が必要であることが示唆された。そこで、4CzIPN [$E_{1/2}$(*P/P$^-$) = 1.35 V vs SCE in MeCN][8] を用いたところ、**3-12a** の収率が 54%にまで向上した（entry 3）。一方、4CzIPN よりも酸化電位が高い 4CzPN [$E_{1/2}$(*P/P$^-$) = 1.40 V vs SCE in MeCN][8] は、効果的ではなかった（entry 4）。続いて、4CzIPN を用いて PCET によるアルコールの活性化に有効だと報告されている種々の塩基を検討した（entries 5–7）。その結果、P^{n}Bu$_4^+$(PhO)$_2$POO$^-$が最適であることが分かった（entry 7）。**3-12a** の変換率が中程度で反応系が複雑化していたため、より温和な条件で反応させることを目的として、反応温度 0 ℃で反応を行ったところ、**3-14a** の生成は確認されず、**3-12a** の収率が 72%に向上した（entry 8）。最終的に、4CzIPN を 5.0 mol%に増やすことで、単離収率 85%で **3-12a** を得ることができた（entry 9）。これを最適な反応条件として、基質適用範囲を調査することとした。



3-11a　　3-12a　　3-14a

entry	PC	base	**3-12a** (%)[c,d]	**3-14a** (%)[c]
1[b]	$[Ir(dF(CF_3)ppy)_2(dtbpy)]PF_6$	$P^nBu_3Et^+(EtO)_2POO^-$	33	8
2	4DPAIPN	$P^nBu_3Et^+(EtO)_2POO^-$	12	31
3	4CzIPN	$P^nBu_3Et^+(EtO)_2POO^-$	54	10
4	4CzPN	$P^nBu_3Et^+(EtO)_2POO^-$	33	37
5	4CzIPN	collidine	15	16
6	4CzIPN	$P^nBu_4^+CF_3COO^-$	39	0
7	4CzIPN	$P^nBu_4^+(PhO)_2POO^-$	57	1
8[e]	4CzIPN	$P^nBu_4^+(PhO)_2POO^-$	72	0
9[e,f]	4CzIPN	$P^nBu_4^+(PhO)_2POO^-$	86 (85)	0

[a]0.1 mmol で反応を行った。[b]385 nm の青色光を照射した。[c]NMR 収率。[d]括弧内は単離収率。[e]反応温度 0 ℃で反応を行った。[f]5.0 mol%の 4CzIPN を用いて反応を行った。



$[Ir(dF(CF_3)ppy)_2(dtbpy)]PF_6$　　4DPAIPN　　4CzIPN　　4CzPN

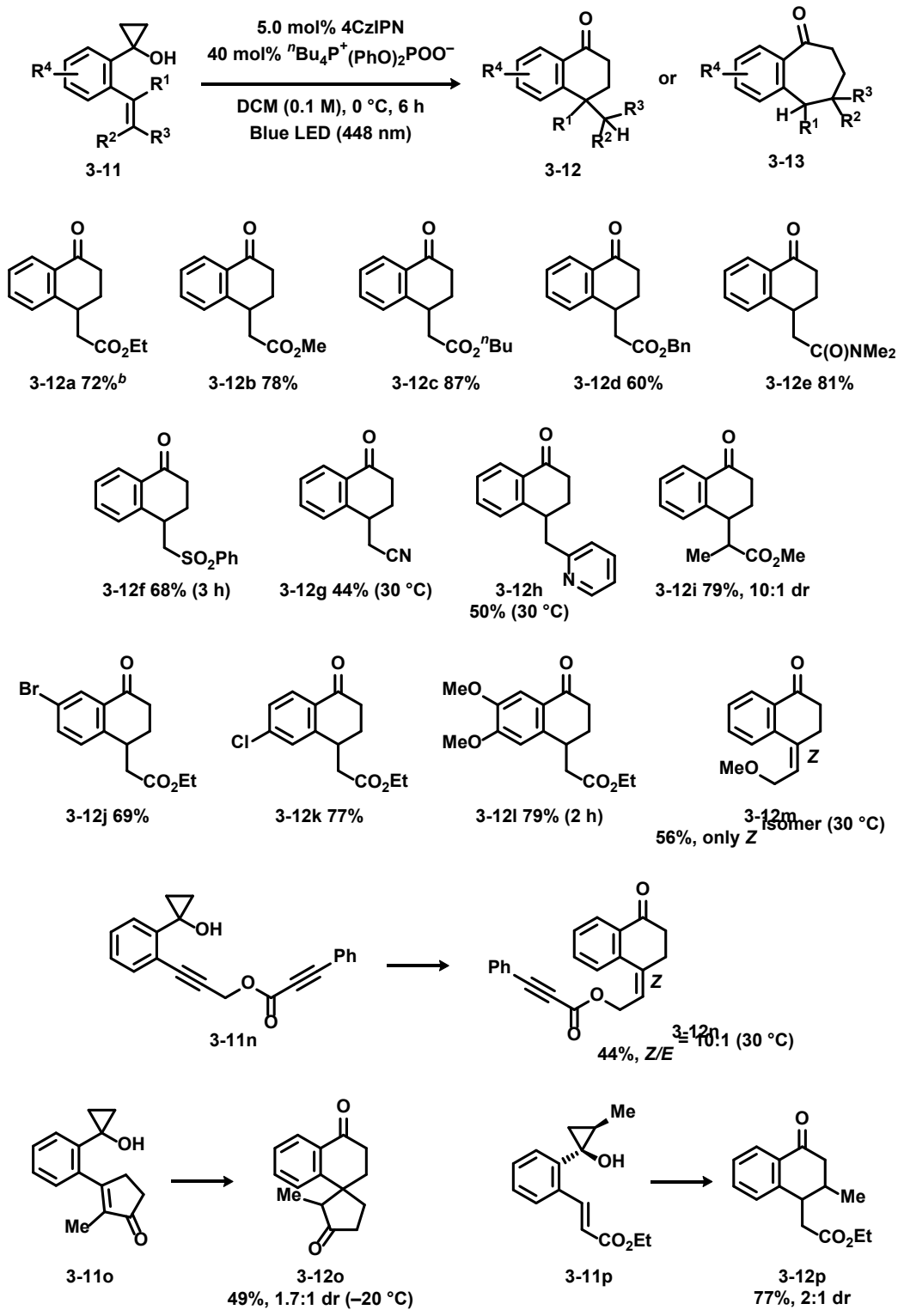
1.21 V　　1.10 V　　1.35 V　　1.40 V

$[E_{1/2}(*P/P^-)$ vs SCE in MeCN]

Scheme 3-7 反応条件の検討[a]

第 6 節　基質適用範囲の調査

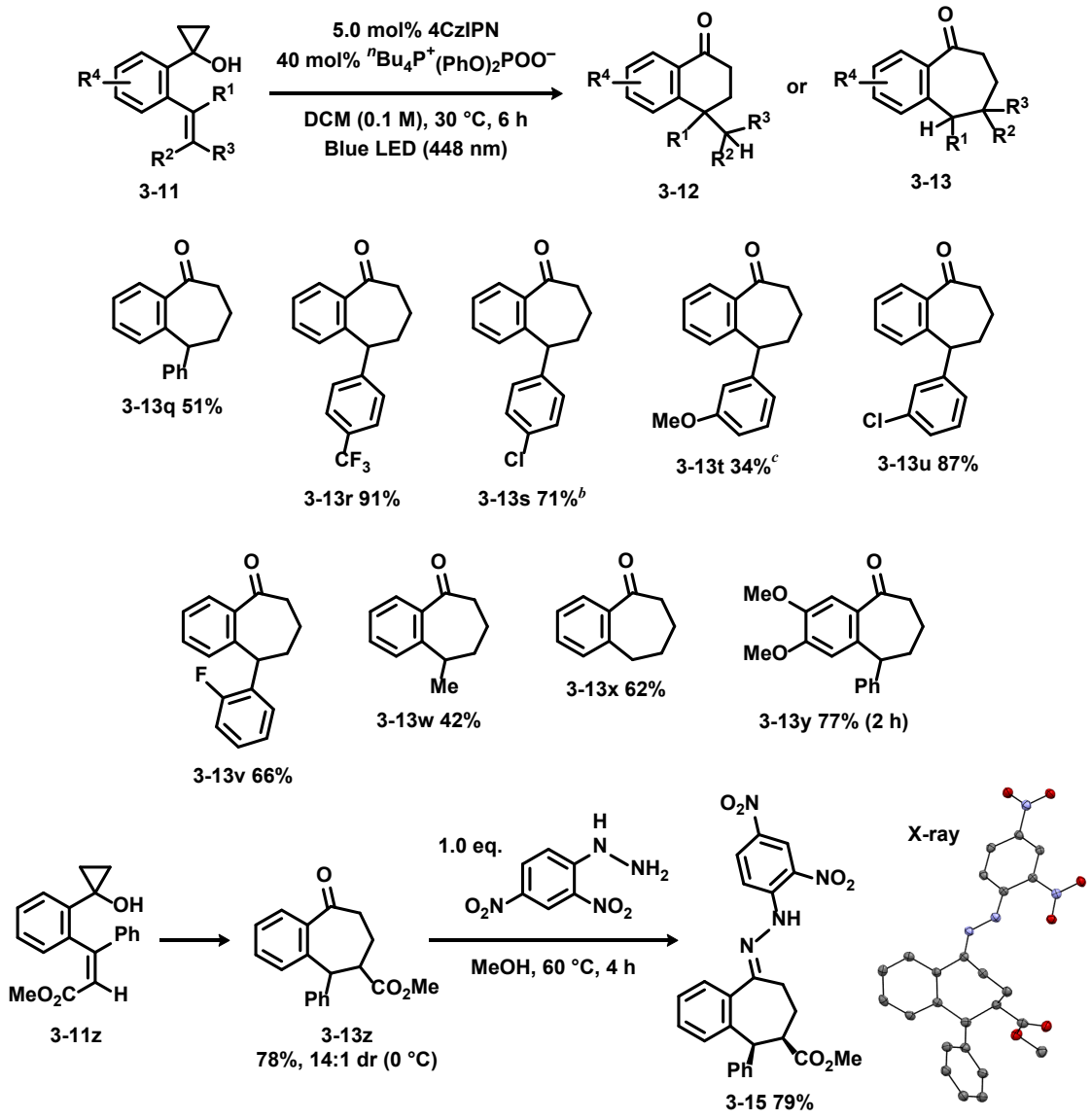
最初に、1.5 mol%の 4CzIPN を用いて、1 mmol スケールで **3-11a** の反応を行った（**Scheme 3-8**）。反応は問題なく進行し、収率 72%で **3-12a** を得ることができ、本反応の有用性を示すことができた。メチルエステル **3-11b**、^{n}Bu エステル **3-11c** およびベンジルエステル **3-11d** からも、それぞれ良好な収率で目的の生成物が得られた。本反応は、ジメチルアミノカルボニル基（**3-11e**）やベンゼンスルホニル基（**3-11f**）を有する基質にも適用可能であり、**3-12e** と **3-12f** をそれぞれ 81%収率および 68%収率で与えた。ニトリル（**3-11g**）やピリジン（**3-11h**）を含む基質を用いたところ、反応温度 0 ℃では反応が完結せず、それぞれ基質が残存した。そこで、反応温度を 30 ℃に昇温したところ、それぞれ基質が完全に消失し、**3-12g** と **3-12h** をそれぞれ中程度の収率で得ることができた。また、エステルの α 位にメチル基を導入しても、本反応の触媒効率には影響はなく、**3-12i** が良好な収率で得られた。続いて、ベンゼン環上の置換基が本反応に与える影響を調査した。4 位にブロモ基（**3-11j**）と 5 位にクロロ基（**3-11k**）を導入した基質を用いた反応では、それぞれ収率 69%と 77%で対応する生成物を得ることができた。加えて、電子供与基を有する基質 **3-11l** を用いた反応も円滑に進行し、所望の 1-テトラロンを良好な収率で与えた。また、本反応はオレフィンをアルキンに代えた基質 **3-11m** にも適用可能で、6-*exo-dig* 環化による生成物 **3-12m** を得ることができた。一方で、第 2 章で設計した 1,6-ジインを有する基質 **3-11n** を用いたところ、連続的なラジカル環化反応は進行せず、プロピオレート部位を残した 1-テトラロン誘導体 **3-12n** が収率 44%で得られた。さらに、環状アルケンを含む基質に本反応を適用することで、γ 位に 4 級炭素を有する 1-テトラロンを合成できると考えた。そこで、環状アルケンとして 2-メチルシクロペンテン-1-オンを導入した基質 **3-11o** を設計した。反応温度–20 ℃で反応を行うことで、所望の 1-テトラロン **3-12o** を得ることに成功した。シクロプロパン環にメチル基を有する基質 **3-11p** を用いた反応では、より安定な第二級アルキルラジカルが発生するように、選択的に炭素–炭素結合が切断され、収率 77%、ジアステレオマー比 2:1 で **3-12p** を得ることができた。以上のように、**3-11a–p** を用いた反応では、7-*endo-trig* 環化による 1-ベンゾスベロン誘導体 **3-13** の生成は確認されず、選択的に 1-テトラロン誘導体 **3-12** をそれぞれ得ることに成功した。



[a]0.1 mmol で反応を行った。[b]1 mmol スケールで反応を行った。

Scheme 3-8 1-テトラロン基質適用範囲の調査 [a]

対照的に、1,1-ジアリールエテン型基質 **3-11q** を用いると、**3-12q** の生成は確認できず、**3-13q** を収率 51%で得た（**Scheme 3-9**）。4-トリフルオロメチルフェニル基（**3-16r**）や 4-クロロフェニル基（**3-11s**）を有する基質からも、良好な収率で、対応する生成物 **3-13r** および **3-13s** を得ることができた。一方で、3-メトキシフェニル基を導入すると、反応は完結せず、**3-13t** は低収率にとどまった。その他、3-クロロフェニル基（**3-13u**）や 2-フルオロフェニル基（**3-13v**）が δ 位に置換した 1-ベンゾスベロンが良好な収率で得られることが分かった。アリール基の代わりにメチル基を導入した基質 **3-11w** を用いると、反応が複雑化したが、中程度の収率で **3-13w** を得ることができた。さらに、単純なビニル基を有する基質 **3-11x** は、本反応条件下で無置換の 1-ベンゾスベロン **3-13x** へと変換された。4,5-ジメトキシ基を有する基質 **3-11y** を用いた反応は、2 時間で完結し、良好な収率で対応する生成物 **3-13y** を与えた。最後に、β-フェニルアクリレート基質 **3-11z** を本反応条件に付すと、収率 78%、ジアステレオマー比 14:1 で、γ,δ-二置換 1-ベンゾスベロン **3-13z** を得ることに成功した。**3-13z** の主な異性体の立体化学を決定するため、**3-13z** と 2,4-ジニトロフェニルヒドラジンから結晶性の高いヒドラゾン **3-15** へと誘導し、単結晶 X 線結晶構造解析により、シス体が主生成物であることを確認できた。

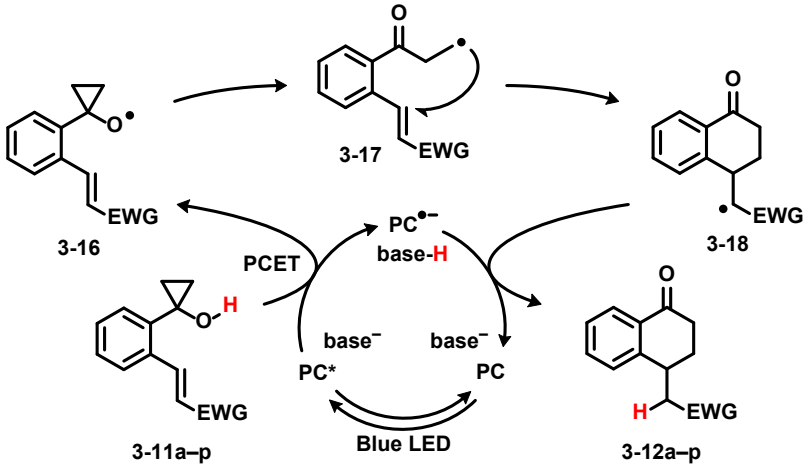


[a]0.1 mmol で反応を行った。[b]9%の **3-12s** を含む混合物として得られた。[c]5%の **3-12t** を含む混合物として得られた。

Scheme 3-9 1-ベンゾスベロン基質適用範囲の調査 [a]

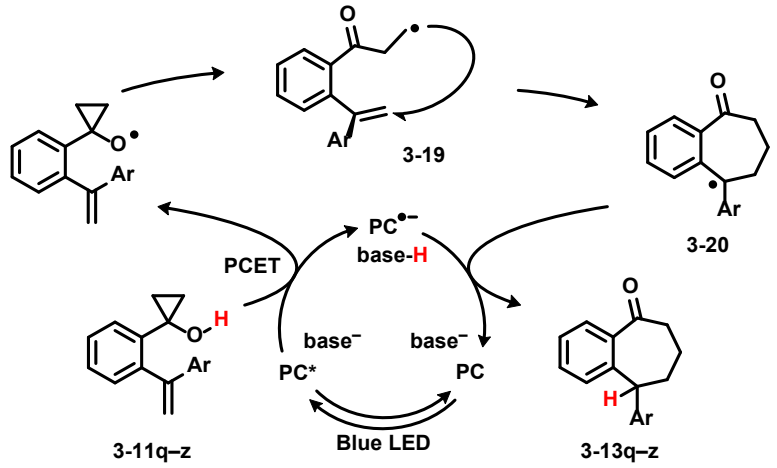
第 7 節　反応機構の考察

基質適用範囲の調査を踏まえた上で予想される、**3-11a–p** を用いた場合の反応機構を **Scheme 3-10** に示す。まず、アルコール部位の PCET によって、シクロプロポキシラジカル **3-16** が生じる。続いて、環歪みを駆動力として β-開裂が起こり、第一級アルキルラジカル **3-17** となる。**3-11a–p** はオレフィンの末端に電子求引基を有していて、その β 位の求電子性が高まっている。そのため、6-*exo-trig* 環化が進行し、**3-18** を与える。最後に、**3-18** は光触媒からの一電子還元とリン酸によるプロトン化を受けて、1-テトラロン **3-12a–p** が得られる。



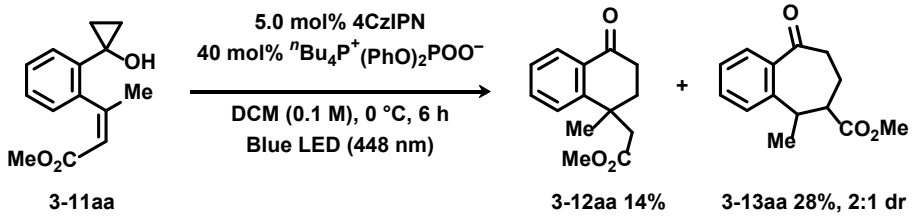
Scheme 3-10 1-テトラロンが得られる反応機構

それに対して、1,1-ジアリールエテン型基質などの **3-11q–z** を用いた場合の想定される反応機構を **Scheme 3-11** に示す。アルコール部位の PCET と続く β-開裂によって生じる **3-19** は、優先的に 7-*endo-trig* 環化が進行する。これは、第一級アルキルラジカルとアリール基の立体障害を避けた環化様式および比較的安定なジベンジルラジカル中間体 **3-20** の生成に起因すると考えられる [11]。



Scheme 3-11 1-ベンゾスベロンが得られる反応機構

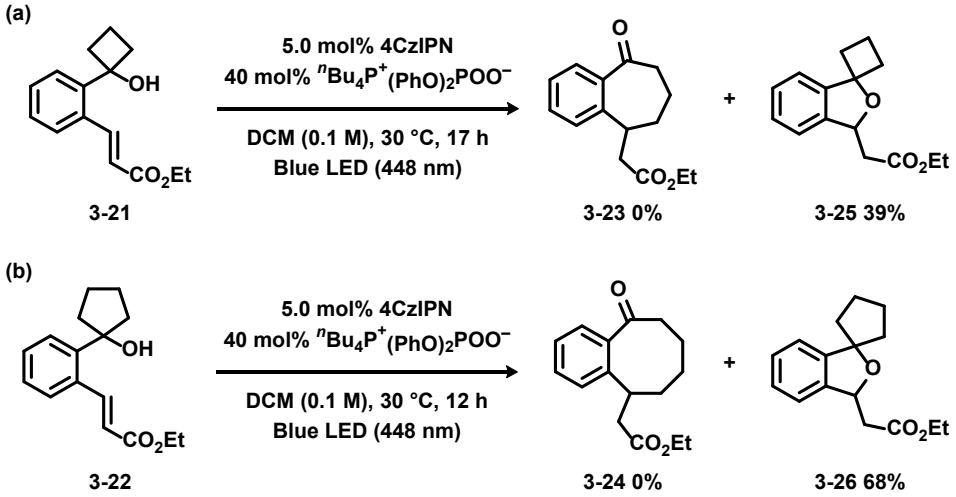
実際、β-フェニルアクリレート基質 **3-11z** を用いた反応では 7-*endo-trig* 環化のみが進行するのに対して、β-メチルアクリレート基質 **3-11aa** を用いた反応では、**3-12aa** と **3-13aa** の混合物が得られた（**Scheme 3-12**）。これは、アクリレートのβ位の置換基をフェニル基からより立体的に小さいメチル基に変更することで、6-*exo-dig* 環化が許容されたものと考えられる。



Scheme 3-12 3-11aa を用いた反応

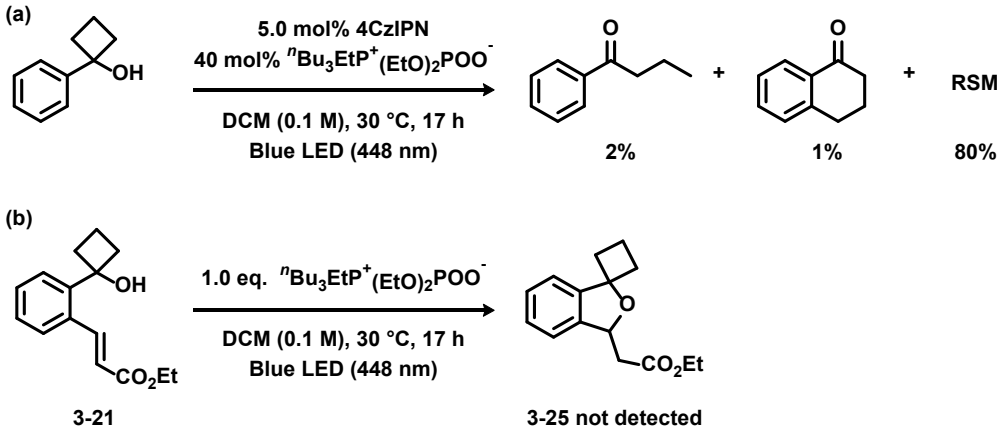
第 8 節　シクロブタノールおよびシクロペンタノール誘導体の反応

本反応の基質適用範囲の拡大を目指し、基質の環状アルコール部位に着目し、シクロブタノール基質 **3-21** とシクロペンタノール基質 **3-22** を設計した（**Scheme 3-13**）。これらの基質は、本反応条件下において 7-*exo-trig* 環化および 8-*exo-trig* 環化が進行すれば、1-ベンゾスベロン **3-23** および 1-ベンゾオクタノン **3-24** へと変換されると予想される。しかし、反応を実施したところ、**3-23** と **3-24** の生成は確認できず、β-開裂を起こす前の環状アルコキシラジカルがオレフィンに付加することで生成したと考えられるフタラン生成物 **3-25** および **3-26** をそれぞれ収率 39%および 68%で得た [12]。



Scheme 3-13 シクロブタノール基質とシクロペンタノール基質を用いた反応

これらの反応の知見を得るべく、コントロール実験を実施した。まず、単純なフェニルシクロブタノール基質を本反応条件に付したところ、ブチロフェノンと 1-テトラロンを観測でき、80%のフェニルシクロブタノールを回収した（**Scheme 3-14a**）。このことから、PCET によるシクロブタノールの開環は効率的に進行しないことが示唆された。次に、**3-21** と 1 当量のリン酸塩を用いた反応は進行しなかったことから、**3-25** はシクロブトキシド中間体を経て形成されるものではないと考えられる（**Scheme 3-14b**）。これらのことから、**3-21** を用いた反応では、シクロブタノールの PCET による活性化は起こっているものの、シクロブトキシラジカルの開環が効率的に進行せず、**3-23** が得られなかったものと考えられる。



Scheme 3-14 シクロブタノール基質を用いた検証実験

第 9 節　結論

本章では、市販の試薬からモジュラー合成可能なアルケン含有シクロプロパノール基質を設計した。シクロプロパノールの環歪みを駆動力として不安定な第一級アルキルラジカルを調製することで、PCET を起点とした触媒的環拡大反応の開発を試みた。反応条件の検討で、有機光触媒が有効であることを見出した。基質中のアルケンの置換様式によって、第一級アルキルラジカルの分子内アルケンへのラジカル付加の位置選択性をコントロールし、ベンジル位に多様な置換基を有する 1-テトラロンと 1-ベンゾスベロンのメタルフリーな触媒的合成法を確立することができた。

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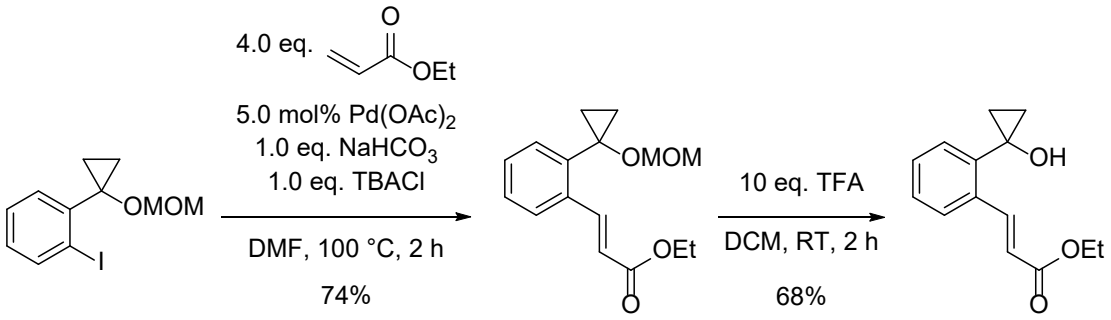
実験項

General considerations: All air- and moisture-sensitive reactions were performed under an argon (Ar) atmosphere. Analytical thin layer chromatography was performed using 0.25 mm silica gel plate (Merck TLC Silica gel 60 F_{254}). Column chromatography was performed on silica gel (Cica silica gel 60N) with solvents specified below. Melting points were recorded on SRS OptiMelt MPA100. NMR spectra were recorded on JEOL ESC-400 spectrometer (^{1}H/400 MHz and ^{13}C/101 MHz) for samples in $CDCl_3$ solutions at 25 ˚C. ^{1}H NMR chemical shifts are reported in terms of chemical shift (δ, ppm) relative to the signal at δ 0.00 ppm for internal tetramethylsilane. ^{13}C NMR spectra were fully decoupled and are reported in terms of chemical shift (δ, ppm) relative to the triplet at δ 77.0 ppm for $CDCl_3$. ^{19}F NMR spectra are reported in terms of chemical shift (δ, ppm) relative to the singlet at δ −63.7 ppm for *a*,*a*,*a*-trifluorotoluene as an external standard. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; sept, septet; m, multiplet. Coupling constants are reported in Hz. Infrared spectra were recorded on JASCO FT/IR-230 spectrometer. High-resolution mass spectra were recorded on JEOL JMS-T100LP mass spectrometer. Techno Sigma PER-AMP was used as a light source.

Reagents and Solvents: Photocatalysts $[Ir(dF(CF_3)ppy)_2(dtbbpy)](PF_6)$,[1] 4DPAIPN,[2] 4CzIPN[2] were prepared according to the report. All other phosphates excepted $P^nBu_3Et^+(EtO)_2POO^-$ were prepared using a method reported by Knowles and co-worker.[3] Dry DCM was distilled from calcium hydride under Ar atmosphere and stored over 4 Å molecular sieves. Other solvents and reagents were purchased from chemical suppliers (Aldrich, Kanto Chemical, TCI, and Wako) and used as received.

1. Synthesis and Characterization of 1-(2-alkenylaryl)cyclopropanols 3-11

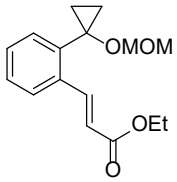
Representative procedure (S2a–i)



S1 **S2a** **3-11a**

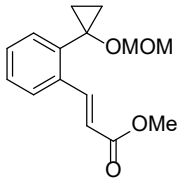
S1 was prepared according to the previous report.[4]

Synthesis and characterization of S2a–i



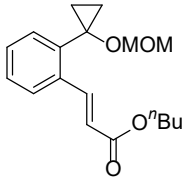
S2a

To a solution of **S1** (304 g, 1.00 mmol) in DMF (2.00 mL) was added $Pd(OAc)_2$ (11.3 mg, 0.0500 mmol), $NaHCO_3$ (84.1 mg, 1.00 mmol) and TBACl (278 mg, 1.00 mmol). After degassed at –78 °C, the mixture was added Ethyl acrylate (440 μL, 4.05 mmol). The reaction mixture was stirred at 100 °C for 2 h. After that, the reaction mixture was filtered through a pad of silica gel with a mixed solution of hexane (40 mL) and EtOAc (10 mL). The filtrate concentrated *in vacuo*. The obtained crude product was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to give **S2a** (205 mg, 74%). **Analytical data for S2a:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 16.0 Hz, 1H), 7.65–7.63 (m, 1H), 7.41–7.38 (m, 1H), 7.32–7.29 (m, 2H), 6.43 (d, *J* = 16.0 Hz, 1H), 4.55 (s, 2H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.12 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H), 1.30 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.93 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 167.0, 142.8, 139.4, 135.4, 130.3, 129.5, 128.4, 126.6, 119.3, 94.9, 60.5, 60.4, 55.6, 14.4, 12.5; IR (neat) 1714, 1177 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{20}O_4$•NH_4 294.1705, found 294.1693.



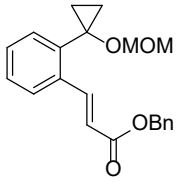
S2b

Analytical data for S2b: pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 16.0 Hz, 1H), 7.64 (dd, *J* = 5.6, 3.6 Hz, 1H), 7.40 (dd, *J* = 5.6, 3.6 Hz, 1H), 7.32–7.30 (m, 2H), 6.44 (d, *J* = 16.0 Hz, 1H), 4.55 (s, 2H), 3.81 (s, 3H), 3.12 (s, 3H), 1.30 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.93 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 167.4, 143.0, 139.4, 135.4, 130.2, 129.6, 128.4, 126.6, 118.9, 94.9, 60.5, 55.6, 51.7, 12.5; IR (neat) 1719, 1173 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{15}H_{18}O_4$•H 263.1283, found 263.1265.



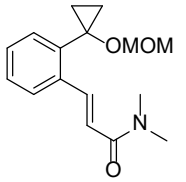
S2c

S2c was obtained as a mixture with a trace amount of (*Z*)-isomer. **Analytical data for S2c:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 16.0 Hz, 1H), 7.66–7.63 (m, 1H), 7.41–7.38 (m, 1H), 7.32–7.29 (m, 2H), 6.43 (d, *J* = 16.0 Hz, 1H), 4.55 (s, 2H), 4.23 (t, *J* = 6.8 Hz, 2H), 3.12 (s, 3H), 1.74–1.67 (m, 2H), 1.48–1.44 (m, 2H), 1.30 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.97 (t, *J* = 7.6 Hz, 3H), 0.93 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 167.1, 142.7, 139.4, 135.4, 130.2, 129.5, 128.4, 126.5, 119.2, 94.9, 64.3, 60.5, 55.6, 30.8, 19.3, 13.8, 12.5; IR (neat) 1715, 1173 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{18}H_{24}O_4$•NH_4 322.2018, found 322.2034.



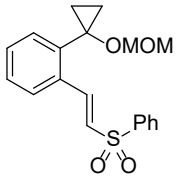
S2d

Benzyl acrylate was prepared according to the previous report.[5] **Analytical data for S2d:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 16.0 Hz, 1H), 7.63–7.61 (m, 1H), 7.42–7.27 (m, 8H), 6.48 (d, *J* = 16.0 Hz, 1H), 5.26 (s, 2H), 4.53 (s, 2H), 3.09 (s, 3H), 1.29 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.91 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 166.8, 143.5, 139.6, 136.4, 135.3, 130.3, 129.7, 128.7, 128.5, 128.3, 128.2, 126.7, 118.9, 95.0, 66.3, 60.6, 55.7, 12.6; IR (neat) 1714, 1173 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{21}H_{22}O_4$•NH_4 356.1862, found 356.1889.



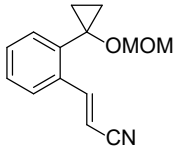
S2e

Analytical data for S2e: brown oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 15.6 Hz, 1H), 7.64–7.61 (m, 1H), 7.42–7.39 (m, 1H), 7.32–7.28 (m, 2H), 6.89 (d, *J* = 15.6 Hz, 1H), 4.56 (s, 2H), 3.19 (s, 3H), 3.13 (s, 3H), 3.08 (s, 3H), 1.31 (dd, *J* = 7.2, 5.6 Hz, 2H), 0.94 (dd, *J* = 7.2, 5.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 167.1, 140.2, 138.9, 136.4, 130.4, 128.8, 128.3, 126.7, 119.0, 94.8, 60.7, 55.6, 37.6, 35.9, 12.6; IR (neat) 1650, 1152 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{16}H_{21}NO_3$•H 276.1600, found 276.1609.



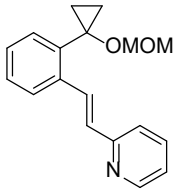
S2f

(Vinylsulfonyl)benzene was prepared according to the previous report.[6] 22 mol% $(o\text{-Tol})_3$P was used as a ligand in addition to representative conditions. **Analytical data for S2f:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 15.6 Hz, 1H), 7.99 (dt, *J* = 6.8, 1.6 Hz, 2H), 7.64–7.59 (m, 1H), 7.54 (dt, *J* = 9.2, 1.6 Hz, 2H), 7.51 (dd, *J* = 9.2, 1.6 Hz, 1H), 7.40 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.36–7.28 (m, 2H), 6.87 (d, *J* = 15.6 Hz, 1H), 4.52 (s, 2H), 3.07 (s, 3H), 1.29 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.92 (dd, *J* = 7.3, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 141.5, 141.0, 140.0, 133.6, 133.3, 130.4, 130.2, 129.3, 128.7, 128.6, 127.9, 127.4, 95.0, 60.5, 55.7, 12.6; IR (neat) 1307, 1147 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{19}H_{20}O_4S$•H 345.1161, found 345.1165.



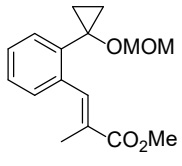
S2g

S2g was obtained as a mixture of *E*/*Z* isomer (*E*/*Z* = 2.5:1). **Analytical data for S2g:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) **major (*E*)** δ 8.26 (d, *J* = 16.4 Hz, 1H), 7.56–7.54 (m, 1H), 7.44–7.32 (m, 3H), 5.90 (d, *J* = 16.4 Hz, 1H), 4.55 (s, 2H), 3.13 (s, 3H), 1.29 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.93 (dd, *J* = 7.2, 5.2 Hz, 2H); **minor (*Z*)** δ 8.11–8.08 (m, 1H), 8.01 (d, *J* = 12.0 Hz, 1H), 7.44–7.32 (m, 3H), 5.56 (d, *J* = 12.0 Hz, 1H), 4.55 (s, 2H), 3.14 (s, 3H), 1.25 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.96 (dd, *J* = 7.2, 5.2 Hz, 2H), ^{13}C-NMR (101 MHz, $CHCl_3$) **major (*E*)** δ 149.1, 139.3, 134.4, 130.6, 130.3, 128.6, 125.9, 97.1, 95.1, 60.46, 55.8, 12.54 **minor (*Z*)** δ 148.0, 139.2, 134.4, 130.3, 129.8, 128.6, 128.2, 96.2, 95.2, 60.55, 55.9, 12.51; IR (neat) 2218, 1154 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{14}H_{15}O_2N{\bullet}NH_4$ 247.1447, found 247.1425.



S2h

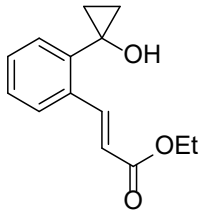
2-Vinylpyridine was prepared according to the previous report.[7] 22 mol% $(o\text{-Tol})_3P$ was used as a ligand in addition to representative conditions. **Analytical data for S2h:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.60 (dd, *J* = 4.8, 1.2 Hz, 1H), 8.32 (d, *J* = 16.4 Hz, 1H), 7.77 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.65 (td, *J* = 8.0, 1.2 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.39 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.33 (td, *J* = 7.6, 1.2 Hz, 1H), 7.25 (td, *J* = 7.6, 1.2 Hz, 1H), 7.20 (d, *J* = 16.4 Hz, 1H), 7.12 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 4.59 (s, 2H), 3.16 (s, 3H), 1.31 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.98 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 156.4, 149.8, 137.8, 137.6, 136.5, 130.9, 130.3, 129.6, 128.5, 127.8, 125.9, 122.0, 121.3, 94.9, 60.8, 55.8, 12.7; IR (neat) 1153 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{18}H_{19}NO_2{\bullet}H$ 282.1494, found 282.1500.



S2i

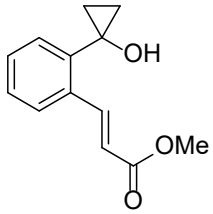
Analytical data for S2i: yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.41 (dd, *J* = 6.8, 0.8 Hz, 1H), 7.32–7.27 (m, 3H), 4.55 (s, 2H), 3.84 (s, 3H), 3.14 (s, 3H), 2.02 (s, 3H), 1.21 (dd, *J* = 7.2, 5.6 Hz, 2H), 0.90 (dd, *J* = 7.2, 5.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 169.3, 138.8, 138.6, 137.1, 129.9, 129.7, 128.2, 127.9, 127.8, 94.9, 60.9, 55.7, 52.2, 14.2, 12.5; IR (neat) 1713, 1154 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{20}O_4{\bullet}NH_4$ 294.1705, found 294.1685.

Synthesis and characterization of 3-11a–i



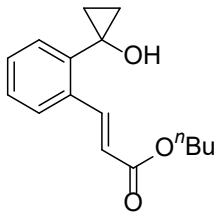
3-11a

To a 50 mL flask was added **S2a** (205 mg, 0.740 mmol) followed by degassed DCM (10 mL). TFA (560 μL, 7.32 mmol) was slowly added to the solution. After being stirred at rt for 2 h under Ar atmosphere, the reaction mixture was diluted with water and extracted with EtOAc. The organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **3-11a** (117 mg, 68%). **Analytical data for 3-11a:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 16.0 Hz, 1H), 7.58–7.56 (m, 1H), 7.40–7.37 (m, 1H), 7.30–7.24 (m, 2H), 6.35 (d, *J* = 16.0 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.91 (s, 1H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.19 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.87 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 167.5, 142.8, 141.7, 134.7, 130.0, 129.6, 128.3, 126.6, 119.1, 60.7, 56.0, 14.3, 14.0; IR (neat) 3421, 1697 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{14}H_{16}O_3 \bullet NH_4$ 250.1443, found 250.1420.



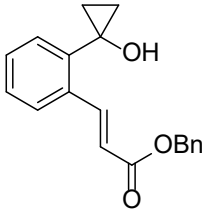
3-11b

Analytical data for 3-11b: pale-yellow gum; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 16.0 Hz, 1H), 7.62–7.59 (m, 1H), 7.43–7.41 (m, 1H), 7.34–7.28 (m, 2H), 6.39 (d, *J* = 16.0 Hz, 1H), 3.77 (s, 3H), 3.33 (s, 1H), 1.23 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.92 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 167.8, 142.9, 141.5, 134.8, 130.1, 129.4, 128.4, 126.7, 118.9, 56.2, 51.9, 14.1; IR (neat) 3421, 1698 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{13}H_{14}O_3 \bullet NH_4$ 236.1287, found 236.1269.



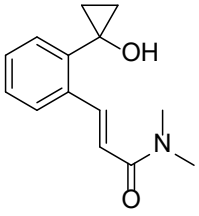
3-11c

Analytical data for 3-11c: pale- yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 16.0 Hz, 1H), 7.63–7.61 (m, 1H), 7.44–7.41 (m, 1H), 7.34–7.29 (m, 2H), 6.41 (d, *J* = 16.0 Hz, 1H), 4.19 (t, *J* = 6.8 Hz, 2H), 3.06 (s, 1H), 1.72–1.64 (m, 2H), 1.46–1.42 (m, 2H), 1.23 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.93 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 167.4, 142.5, 141.4, 134.9, 130.0, 129.4, 128.5, 126.7, 119.5, 64.6, 56.3, 30.8, 19.3, 14.1, 13.9; IR (neat) 3422, 1697 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{16}H_{20}O_3 \bullet H$ 261.1491, found 261.1481.



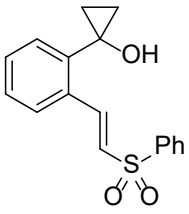
3-11d

Analytical data for 3-11d: pale- yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 16.0 Hz, 1H), 7.58 (dd, *J* = 6.8, 1.6 Hz, 1H), 7.40–7.26 (m, 8H), 6.43 (d, *J* = 16.0 Hz, 1H), 5.20 (s, 2H), 3.42 (s, 1H), 1.20 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.89 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 167.0, 143.1, 141.5, 136.2, 134.8, 130.2, 129.4, 128.7, 128.5, 128.30, 128.27, 126.8, 119.1, 66.5, 56.4, 14.1; IR (neat) 3421, 1698 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{19}H_{18}O_3$•H 295.1334, found 295.1317.



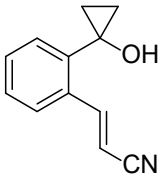
3-11e

Analytical data for 3-11e: white solid (mp 111.5–112.9 ℃); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 15.6 Hz, 1H), 7.56–7.61 (m, 1H), 7.48–7.43 (m, 1H), 7.33–7.28 (m, 2H), 6.85 (d, *J* = 15.6 Hz, 1H), 4.23 (s, 1H), 3.17 (s, 3H), 3.05 (s, 3H), 1.25 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.92 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 167.3, 141.6, 140.3, 135.6, 129.8, 129.4, 128.1, 126.6, 118.9, 55.9, 37.6, 36.0, 14.3; IR (KBr) 3347, 1644 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{14}H_{17}NO_2$•H 232.1338, found 232.1312.



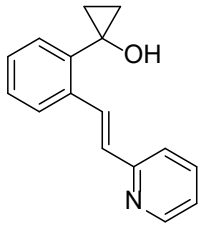
3-11f

Analytical data for 3-11f: pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 15.6 Hz, 1H), 7.96 (dt, *J* = 7.6, 1.6 Hz, 2H), 7.63–7.58 (m, 1H), 7.55–7.51 (m, 2H), 7.49 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.42 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.35 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.29 (td, *J* = 7.6, 1.6 Hz, 1H), 6.87 (d, *J* = 15.6 Hz, 1H), 2.69 (s, 1H), 1.22 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.90 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 141.8, 141.1, 140.7, 133.4, 133.2, 130.9, 129.4, 128.8, 128.6, 127.8, 127.5, 56.3, 14.1, One Csp^2 signal is missing due to overlapping.; IR (neat) 3464, 1304 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{16}O_3S$•NH_4 318.1164, found 318.1174.



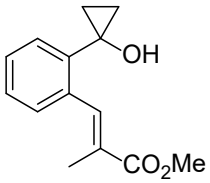
3-11g

Analytical data for 3-11g: pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 17.2 Hz, 1H), 7.56 (dd, *J* = 7.2, 2.0 Hz, 1H), 7.44–7.33 (m, 3H), 5.92 (d, *J* = 17.2 Hz, 1H), 2.24 (s, 1H), 1.25 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.96 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 148.8, 140.9, 134.3, 130.9, 129.1, 128.8, 126.2, 118.5, 97.5, 56.5, 14.1; IR (neat) 3412, 2220 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{12}H_{11}NO$•NH_4 203.1184, found 203.1169.



3-11h

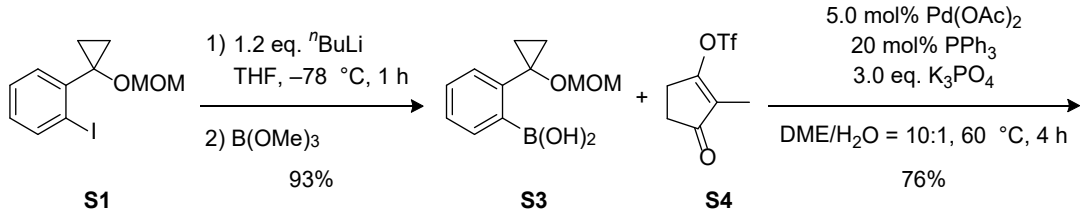
Analytical data for 3-11h: pale-brown solid (mp 141.9–143.2 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 4.8, 0.8 Hz, 1H), 8.26 (d, *J* = 16.4 Hz, 1H), 7.67 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.61 (td, *J* = 7.6, 1.6 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.38 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.27 (td, *J* = 7.2, 1.2 Hz, 1H), 7.21 (td, *J* = 7.2, 1.2 Hz, 1H), 7.08 (ddd, *J* = 7.2, 4.8, 0.8 Hz, 1H), 7.08 (d, *J* = 16.4 Hz, 1H), 5.04 (s, 1H), 1.22 (dd, *J* = 7.2, 4.8 Hz, 2H), 0.92 (dd, *J* = 7.2, 4.8 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 156.1, 149.4, 140.7, 136.8, 136.7, 130.9, 129.4, 128.9, 128.22, 128.18, 125.8, 122.1, 122.0, 56.2, 14.1; IR (KBr) 3158 cm^{-1}; HRMS (ESI) *m/z* $[2M+Na]^+$ calcd for $C_{32}H_{30}N_2O_2$•Na 497.2205, found 497.2213.



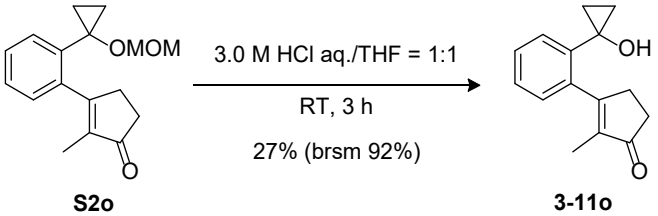
3-11i

Analytical data for 3-11i: brown oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.20 (q, *J* = 1.2 Hz, 1H), 7.42 (td, *J* = 6.0, 1.6 Hz, 1H), 7.34–7.26 (m, 3H), 3.82 (s, 3H), 2.62 (s, 1H), 2.01 (d, *J* = 1.2 Hz, 3H), 1.16 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.91 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 169.1, 140.9, 138.1, 136.4, 129.7, 129.0, 128.7, 128.3, 127.8, 56.8, 52.2, 14.2, 14.1; IR (neat) 3431, 1708 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{14}H_{16}O_3$•H 233.1178, found 233.1148.

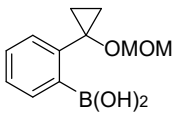
Synthesis and characterization of 3-11o



S1 **S3** **S4**



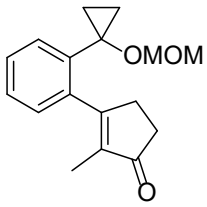
S2o **3-11o**



S3

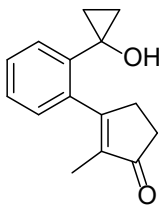
A solution of **S1** (608 mg, 2.00 mmol) in THF (10 mL) was cooled to –78 °C under Ar atmosphere. A solution of ^{n}BuLi (1.50 mL, 1.60 M in hexane) was added and the mixture was stirred for 1 h. $B(OMe)_3$ (340 μL, 3.05 mmol) was then added to the mixture. After being stirred at room temperature for 1 h, the reaction mixture was quenched with water and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel

column chromatography (Hexane/EtOAc = 10:1) to furnish **S3** (412 mg, 93%). **Analytical data for S3:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.42–7.32 (m, 3H), 6.75 (s, 2H), 4.65 (s, 2H), 3.21 (s, 3H), 1.30 (dd, *J* = 7.2, 5.2 Hz, 2H), 1.02 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 143.4, 136.1, 130.2, 129.4, 128.1, 94.8, 63.3, 56.2, 12.8 (One peak derived from an aromatic carbon is obscure due to influence of the boron atom adjacent to that aromatic carbon.); IR (neat) 3398 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{11}H_{15}BO_4$•NH_4 240.1407, found 240.1392.



S2o

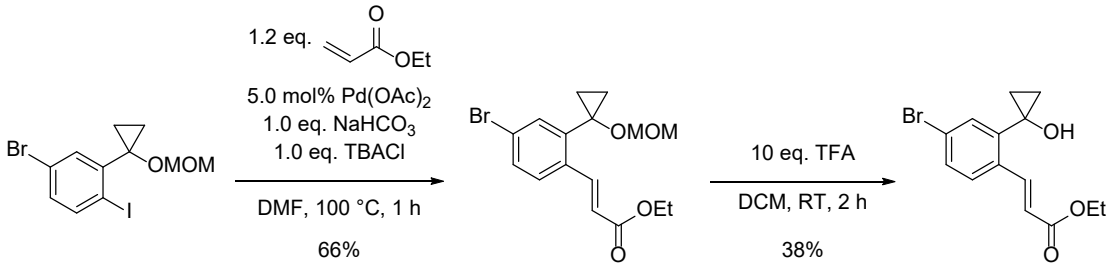
To a solution of **S3** (412 mg, 2.00 mmol) and **S4**[8] (488 mg, 2.00 mmol) in DME (12 mL) and H_2O (1.2 mL) was added $Pd(OAc)_2$ (25.2 mg, 0.112 mmol), PPh_3 (106 mg, 0.404 mmol) and K_3PO_4 (1.27 g, 6.08 mmol). Then the resulting solution was stirred at 60 ℃ for 4 h. After that, the reaction mixture was diluted with water and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 5:1) to furnish **S2o** (416 mg, 76%). **Analytical data for S2o:** pale-yellow solid (mp 82.9–84.1 ℃); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.47–7.45 (m, 1H), 7.38–7.31 (m, 2H), 7.08–7.06 (m, 1H), 4.56 (s, 2H), 3.21 (s, 3H), 3.06–3.03 (m, 2H), 2.57–2.55 (m, 2H), 1.61 (t, *J* = 2.0 Hz, 3H), 1.14 (dd, *J* = 7.2, 5.6 Hz, 2H), 0.87 (dd, *J* = 7.2, 5.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 210.3, 172.4, 139.1, 137.4, 136.5, 130.5, 128.34, 128.26, 128.1, 94.8, 60.8, 55.9, 34.7, 32.1, 12.9, 9.3; IR (KBr) 1688, 1156 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{17}H_{20}O_3$•H 273.1491, found 273.1465.



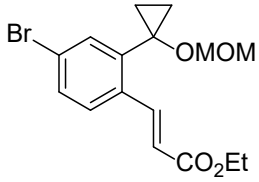
3-11o

To a THF solution (5.0 mL) of **S2o** (416 mg, 1.52 mmol) was added aq. HCl (5.0 mL, 3.0 M). The resulting mixture was stirred at room temperature overnight. The reaction was quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 3:1) to furnish **3-11o** (93.6 mg, 27%). **Analytical data for 3-11o:** colorless solid (mp 103.1–103.9 ℃); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.49–7.49 (m, 1H), 7.37–7.35 (m, 2H), 7.08–7.06 (m, 1H), 3.05–3.02 (m, 2H), 2.57–2.55 (m, 2H), 2.42 (s, 1H), 1.63 (t, *J* = 2.0 Hz, 3H), 1.07 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.88 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 210.5, 172.6, 139.1, 138.4, 137.7, 129.4, 128.6, 128.2, 128.1, 57.0, 34.7, 32.6, 14.7, 9.3; IR (KBr) 3468, 1693 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{15}H_{16}O_2$•H 229.1229, found 229.1202.

Synthesis and characterization of 3-11j

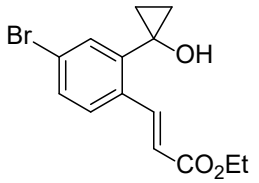


S5 **S2j** **3-11j**



S2j

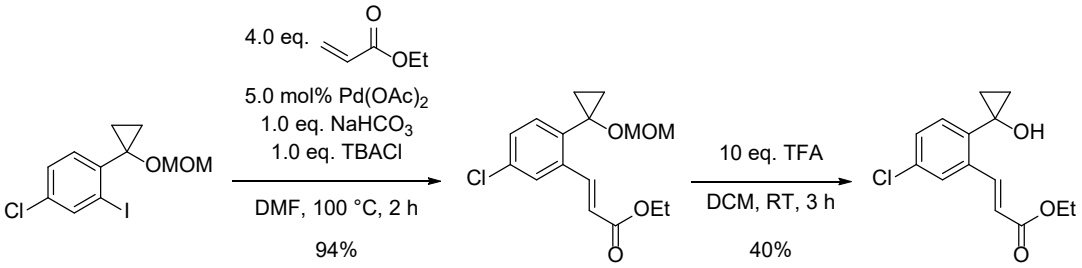
This compound was prepared in the same manner as described for **S2a** using **S5**[4] instead of **S1** in 66% yield. **S2j** was obtained as a mixture with a trace amount of (*Z*)-isomer. **Analytical data for S2j:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 16.0 Hz, 1H), 7.54–7.43 (m, 3H), 6.41 (d, *J* = 16.0 Hz, 1H), 4.56 (s, 2H), 4.28 (q, *J* = 7.2 Hz, 2H), 3.13 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H), 1.31 (dd, *J* = 7.2, 5.6 Hz, 2H), 0.94 (dd, *J* = 7.2, 5.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 166.8, 141.6, 141.5, 134.4, 133.1, 131.5, 128.1, 123.5, 119.8, 95.1, 60.6, 60.3, 55.7, 14.4, 12.7; IR (neat) 1714, 1177 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{16}H_{19}BrO_4$•H 355.0545, found 355.0570.

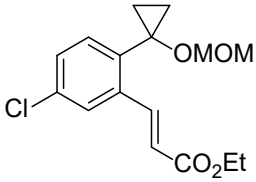


3-11j

This compound was prepared in the same manner as described for **3-11a** using **S2j** instead of **S2a** in 38% yield. **Analytical data for 3-11j:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 16.0 Hz, 1H), 7.56 (d, *J* = 1.2 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 6.39 (d, *J* = 16.0 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 3.17 (s, 1H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.25 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.94 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 167.1, 143.3, 141.4, 133.9, 132.5, 131.5, 128.3, 123.9, 120.0, 60.8, 56.0, 14.4, 14.2; IR (neat) 3414, 1711 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{14}H_{15}BrO_3$•NH_4 328.0548, found 328.0538.

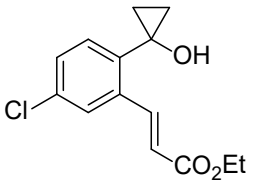
Synthesis and characterization of 3-11k





S2k

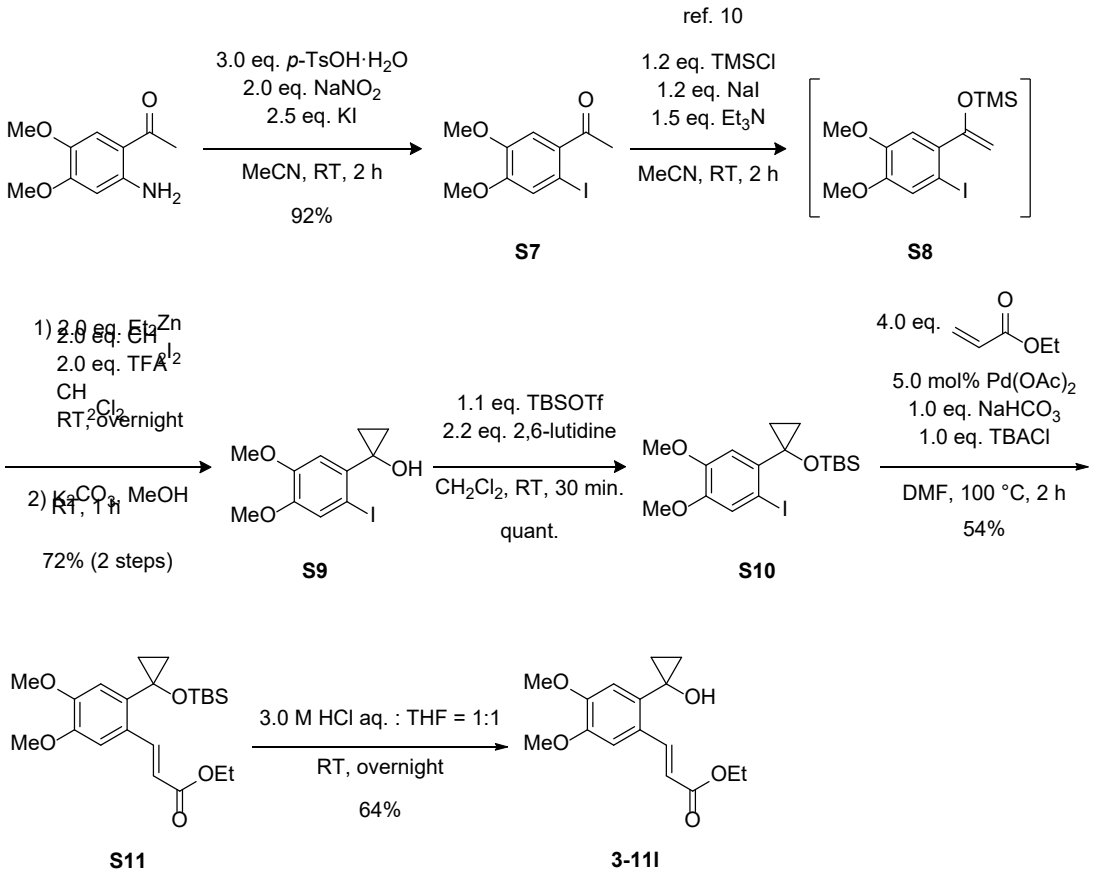
This compound was prepared in the same manner as described for **S2a** using **S6**[4] instead of **S1** in 94% yield. **Analytical data for S2k:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 16.0 Hz, 1H), 7.60 (d, J = 1.6 Hz, 1H), 7.33 (d, J = 8.4 Hz, 1H), 7.28–7.26 (m, 1H), 6.42 (d, J = 16.0 Hz, 1H), 4.55 (s, 2H), 4.28 (q, J = 7.2 Hz, 2H), 3.12 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H), 1.30 (dd, J = 7.2, 5.6 Hz, 2H), 0.91 (dd, J = 7.2, 5.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 166.6, 141.3, 138.1, 137.2, 134.3, 131.6, 129.2, 126.5, 120.5, 95.0, 60.6, 60.0, 55.6, 14.3, 12.6; IR (neat) 1715, 1179 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{16}H_{19}ClO_4$•H 313.1021, found 313.1008.

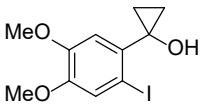


3-11k

This compound was prepared in the same manner as described for **3-11a** using **S2k** instead of **S2a** in 40% yield. **Analytical data for 3-11k:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 16.0 Hz, 1H), 7.57 (d, J = 2.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.28–7.26 (m, 1H), 6.39 (d, J = 16.0 Hz, 1H), 4.25 (q, J = 7.2 Hz, 2H), 3.24 (s, 1H), 1.33 (t, J = 7.2 Hz, 3H), 1.23 (dd, J = 7.2, 5.2 Hz, 2H), 0.90 (dd, J = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 166.9, 141.2, 139.9, 136.6, 134.3, 130.8, 129.7, 126.6, 120.6, 60.9, 55.7, 14.3, 14.1; IR (neat) 3414, 1712 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{14}H_{15}ClO_3$•NH_4 284.1054, found 284.1076.

Synthesis and characterization of 3-11l

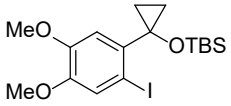




S9

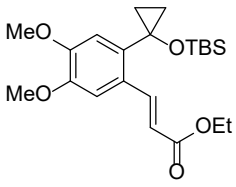
To a 200 mL two-necked flask was charged with **S7**[9] (4.21 g, 13.8 mmol) and NaI (2.48 g, 16.6 mmol), followed by dry MeCN (40 mL). To the mixture was added Et_3N (2.90 mL, 20.7 mmol) and TMSCl (2.10 mL, 16.6 mmol), successively. The resulting solution was stirred at room temperature for 2 h. After that, the reaction mixture was quenched with water and washed with brine. The solution was dried over $MgSO_4$, and concentrated *in vacuo*. The residue **S8** was used for the next reaction without further purification. To a dried 300 mL two-necked flask was added degassed dry DCM (100 mL) and Et_2Zn (28 mL, 1.07 M in hexane) under Ar. The solution was cooled to –10 °C and a solution of TFA (2.10 mL, 27.6 mmol) in degassed dry DCM (15 mL) was then dripped into the reaction mixture for 1 h (*very slowly*). On stirring for additional 1 h, a solution of CH_2I_2 (2.40 mL, 27.6 mmol) in degassed dry DCM (20 mL) was added to the reaction mixture for 1 h (*very slowly*). After stirring at rt for 3 h, **S8** was added to the mixture. The reaction mixture was stirred at rt overnight. The reaction was quenched with sat. aq. NH_4Cl and extracted with EtOAc. The organic layer was washed with sat. aq. $NaHCO_3$, dried over $MgSO_4$, and concentrated *in vacuo*. To a MeOH solution (40 mL) of the crude material in a 200 mL flask was added K_2CO_3 (2.01 mg, 14.5 mmol) at rt. After being stirred for 1 h, the reaction mixture was diluted with water and

extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S9** (3.17 g, 72%, 2 steps from **S7**). **Analytical data for S9:** pale-yellow solid (mp 121.5–122.8 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.26 (s, 1H), 6.92 (s, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 2.91 (s, 1H), 1.29 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.97 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 149.3, 149.0, 136.6, 121.8, 114.2, 88.8, 61.1, 56.3, 56.1, 16.2; IR (KBr) 3476 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{11}H_{13}I\ O_3 \bullet NH_4$ 338.0253, found 338.0269.



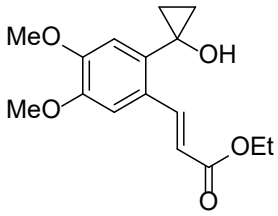
S10

A solution of **S9** (957 mg, 2.99 mmol) in dry DCM (30 mL) was added 2,6-lutidine (770 μL, 6.60 mmol) under Ar atmosphere. TBSOTf (760 μL, 3.30 mmol) was added to the mixture at 0 °C. After being stirred at room temperature for 30 min, the reaction mixture was quenched with water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S10** (1.51 g, quant.). **Analytical data for S10:** white solid (mp 65.4–67.0 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28 (s, 1H), 6.81 (s, 1H), 3.85 (s, 3H), 3.85 (s, 3H), 1.12 (dd, *J* = 7.1, 5.2 Hz, 2H), 0.88 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.78 (s, 9H), –0.14 (s, 6H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 148.8, 148.3, 136.8, 122.5, 114.1, 90.4, 61.5, 56.2, 56.1, 25.7, 17.8, 15.7, –3.9; IR (neat) 1252 cm^{-1}; HRMS (DART) *m/z* $[M–TBSO]^+$ calcd for $C_{11}H_{12}IO_2 \bullet H$ 302.9882, found 302.9900.



S11

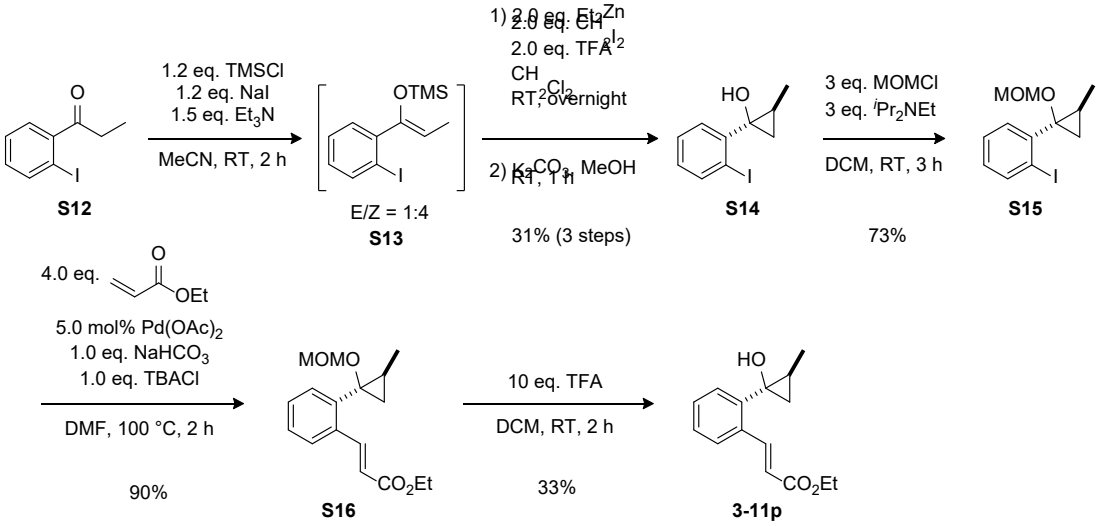
This compound was prepared in the same manner as described for **S2a** using **S10** instead of **S1** in 54% yield. **Analytical data for S11:** white solid (mp 100.5–102.2 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 16.0 Hz, 1H), 7.12 (s, 1H), 6.84 (s, 1H), 6.31 (d, *J* = 16.0 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.91 (s, 6H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.13 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.90 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.75 (s, 9H), –0.17 (s, 6H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 167.3, 149.8, 148.5, 143.1, 135.8, 128.1, 116.8, 111.6, 108.9, 60.3, 57.0, 56.1, 56.0, 25.5, 17.7, 14.4, 14.3, –4.1; IR (neat) 1702, 1252 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{22}H_{34}O_5Si \bullet NH_4$ 424.2519, found 424.2539.

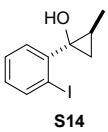


3-11l

To a THF solution (1.0 mL) of **S11** (81.3 mg, 0.200 mmol) was added aq. HCl (1.0 mL, 3 M). The resulting mixture was stirred at room temperature overnight. The reaction was quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 5:1) to furnish **3-11l** (37.5 mg, 64%). **Analytical data for 3-11l:** white solid (mp 142.3–144.4 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 16.0 Hz, 1H), 7.12 (s, 1H), 6.96 (s, 1H), 6.35 (d, *J* = 16.0 Hz, 1H), 4.28 (q, *J* = 7.2 Hz, 2H), 3.93 (s, 3H), 3.92 (s, 3H), 2.24 (s, 1H), 1.35 (t, *J* = 7.2 Hz, 3H), 1.28 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.96 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 167.5, 150.5, 148.9, 141.9, 135.5, 127.0, 117.2, 112.5, 108.7, 60.6, 56.2, 56.1, 14.6, 14.4, A signal of O*C*H$_3$ is missing due to overlapping.; IR (neat) 3485, 1686 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{20}O_5$•NH_4 310.1655, found 310.1682.

Synthesis and characterization of 3-11p

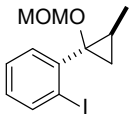




S14

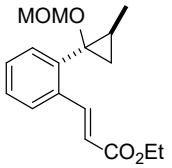
This compound was prepared in the same manner as described for **S9** using **S12**[11] instead of **S7** in 31% yield over 3 steps as a single diastereomer. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 4:1). **Analytical data for S14:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.37 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.31 (td, *J* = 7.8, 1.1 Hz, 1H), 6.99 (td, *J* = 7.8, 1.8 Hz, 1H), 2.68 (s, 1H), 1.43 (d, *J* = 6.0 Hz, 3H), 1.23–1.19 (m, 1H), 1.12–1.03 (m, 1H), 0.83–0.80 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 145.6, 139.5, 130.9, 129.5, 128.2, 100.3, 63.3, 20.3, 20.1, 12.9; IR

(neat) 3443 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{10}H_{15}{}^{127}INO$ 292.0198; Found 292.0173.



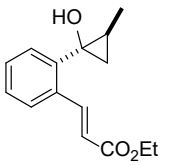
S15

To a solution of **S14** (432 mg, 1.6 mmol) and $^iPr_2NEt$ (0.82 mL, 4.8 mmol) in DCM (7 mL) was added MOMCl (0.36 mL, 4.5 mmol) at 0 ºC. After being stirred at rt for 3h, the reaction was quenched with sat. aq. $NaHCO_3$. The mixture was extracted with Et_2O, washed with brine, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to afford **S15** (371.6 mg, 73% yield). **Analytical data for S15:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.34–7.26 (m, 2H), 6.97 (td, *J* = 7.8, 2.3 Hz, 1H), 4.65 (d, *J* = 6.9 Hz, 1H), 4.63 (d, *J* = 6.9 Hz, 1H), 3.16 (s, 3H), 1.45 (d, *J* = 5.9 Hz, 3H), 1.25–1.22 (m, 1H), 1.10–1.01 (m, 1H), 0.88–0.85 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 143.8, 139.9, 131.9, 129.3, 127.5, 101.0, 95.4, 67.6, 55.8, 20.5, 18.4, 13.5; IR (neat) 1153 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{12}H_{19}{}^{127}INO_2$ 336.0461; Found 336.0474.



S16

This compound was prepared in the same manner as described for **S2a** using **S15** instead of **S1** in 90% yield (ca. 6% of a stereoisomer was contained). This compound was purified by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for S16:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 16.0 Hz, 1H), 7.65–7.63 (m, 1H), 7.37–7.29 (m, 3H), 6.40 (d, *J* = 16.0 Hz, 1H), 4.63 (d, *J* = 6.4 Hz, 1H), 4.57 (d, *J* = 6.4 Hz, 1H), 4.33–4.24 (m, 2H), 3.13 (s, 3H), 1.41 (d, *J* = 6.4 Hz, 3H), 1.35 (t, *J* = 7.2 Hz, 3H), 1.23 (dd, *J* = 9.6, 5.5 Hz, 1H), 1.03–0.96 (m, 1H), 0.82–0.78 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 167.0, 143.0, 141.2, 135.1, 129.9, 129.4, 128.1, 126.3, 118.9, 95.2, 63.2, 60.4, 55.7, 19.9, 16.9, 14.3, 12.6; IR (neat) 1714 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{17}H_{26}NO_4$ 308.1862; Found 308.1870.

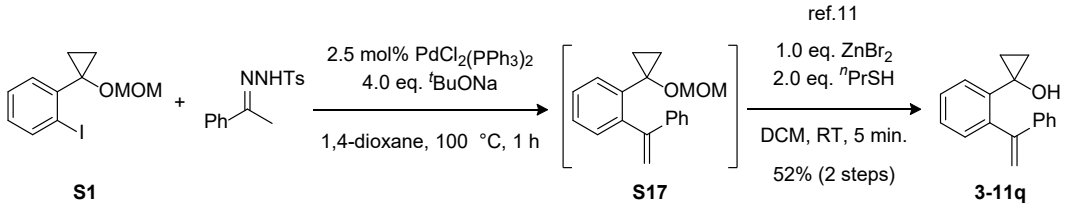


3-11p

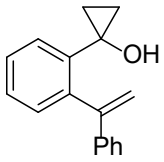
This compound was prepared in the same manner as described for **3-11a** using **S16** instead of **S2a** in 90% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 5:1). **Analytical data for 3-11p:** colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 16.0 Hz, 1H), 7.65–7.63 (m, 1H), 7.41–7.30 (m, 3H), 6.42 (d, *J* = 16.0 Hz, 1H), 4.31–4.25 (m, 2H), 1.43 (d, *J* = 5.9 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.19–1.08 (m, 2H), 0.75–0.72 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 166.9, 142.7, 142.4, 134.7, 129.9, 129.1, 128.3, 126.6, 119.5, 60.5, 58.9, 19.3, 19.3, 14.3, 12.1; IR (neat) 3446, 1698 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{15}H_{22}NO_3$ 264.1600; Found 264.1592.

Synthesis and characterization of 3-11q–v

Representative procedure (3-11q–v)

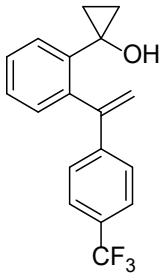


Synthesis and characterization of 3-11q–v



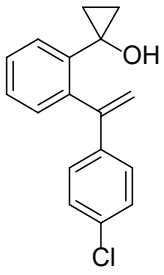
3-11q

To a solution of **S1** (457 mg, 1.50 mmol) and acetophenone tosylhydrazone[11] (655 mg, 2.27 mmol) in dioxane (18 mL) was added $PdCl_2(PPh_3)_2$ (28.6 mg, 0.0407 mmol). After degassed at –78 °C, the mixture was added ^{t}BuONa (637 mg, 6.63 mmol). The reaction mixture was stirred at 100 °C for 3 h. After that, the reaction mixture was filtered through a pad of celite with EtOAc. The filtrate concentrated *in vacuo*. The obtained crude product was purified by silica gel column chromatography (Hexane/EtOAc = 50:1) to give **S17**, which still contained a small amount of inseparable impurities. The crude **S17** was used for the next reaction without further purification at this stage. To a 10 mL two-necked flask was charged with dried $ZnBr_2$ (338 mg, 1.50 mmol), followed by the crude **S17** in dry DCM (2.0 mL). After the addition of ^{n}PrSH (272 µL, 3.00 mmol), the reaction mixture was stirred at room temperature for 5 min. The resulting mixture was diluted with DCM and added sat. aq. $NaHCO_3$, then the mixture was filtered through a pad of Celite. The aqueous layer was separated and further extracted with DCM. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **3-11q** (184 mg, 52%, 2 steps from **S1**). **Analytical data for 3-11q:** orange oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.52–7.49 (m, 1H), 7.38–7.27 (m, 8H), 5.76 (d, J = 1.2 Hz, 1H), 5.33 (d, J = 1.2 Hz, 1H), 1.91 (s, 1H), 0.81 (dd, J = 7.2, 5.2 Hz, 2H), 0.79 (dd, J = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 150.3, 142.3, 142.2, 139.6, 130.8, 130.6, 128.7, 128.3, 128.0, 127.2, 115.9, 56.9, 15.3, One Csp^2 signal is missing due to overlapping.; IR (neat) 3444 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{16}O{\bullet}NH_4$ 254.1545, found 254.1539.



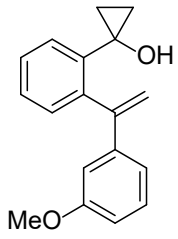
3-11r

This compound was prepared in the same manner as described for **3-11q** using tosylhydrazone synthesized from 4'-trifluoromethylacetophenone[12] in 61% yield for 2 steps. **Analytical data for 3-11r:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.4 Hz, 2H), 7.48 (dd, J = 6.4, 2.4 Hz, 1H), 7.41 (d, J = 8.4 Hz, 2H), 7.35–7.33 (m, 2H), 7.24 (dd, J = 6.4, 2.4 Hz, 1H), 5.87 (s, 1H), 5.47 (s, 1H), 2.06 (s, 1H), 0.83 (dd, J = 7.2, 5.2 Hz, 2H), 0.76 (dd, J = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 148.8, 145.3, 141.5, 139.8, 130.9, 130.2,130.0 (q, J = 33 Hz), 128.5, 128.1, 127.4, 125.5 (q, J = 3.8 Hz), 118.0, 56.9, 15.2, A signal of CF_3 is obscure due to overlapping with aromatic peaks; ^{19}F-NMR (376 MHz, $CDCl_3$) δ –63.5; IR (neat) 3420 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{18}H_{15}F_3O•NH_4$ 322.1419, found 322.1406.



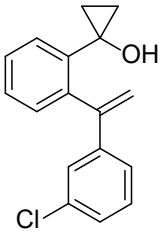
3-11s

This compound was prepared in the same manner as described for **3-11q** using tosylhydrazone synthesized from 4'-chloroacetophenone[11] in 54% yield for 2 steps. **Analytical data for 3-11s:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, J = 7.2, 2.0 Hz, 1H), 7.38–7.33 (m, 2H), 7.32–7.23 (m, 5H), 5.78 (d, J = 0.8 Hz, 1H), 5.36 (d, J = 0.8 Hz, 1H), 1.81 (s, 1H), 0.84 (td, J = 6.4, 1.2 Hz, 2H), 0.77 (td, J = 6.4, 1.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 149.0, 141.8, 140.4, 139.7, 134.1, 130.8, 130.3, 128.8, 128.4, 128.1, 116.4, 56.9, 15.3, One Csp^2 signal is missing due to overlapping.; IR (neat) 3445 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{15}ClO•NH_4$ 288.1155, found 288.1168.



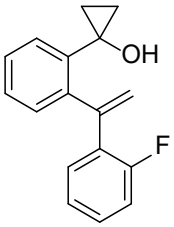
3-11t

This compound was prepared in the same manner as described for **3-11q** using tosylhydrazone synthesized from 3'-methoxyacetophenone[11] in 69% yield for 2 steps. **Analytical data for 3-11t:** colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.51–7.49 (m, 1H), 7.36–7.27 (m, 3H), 7.25–7.21 (m, 1H), 6.91 (t, J = 2.0 Hz, 1H), 6.86–6.82 (m, 2H), 5.76 (d, J = 1.2 Hz, 1H), 5.32 (d, J = 1.2 Hz, 1H), 3.77 (s, 3H), 2.03 (s, 1H), 0.86–0.83 (m, 2H), 0.81–0.77 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 159.9, 150.1, 143.7, 142.3, 139.6, 130.8, 130.6, 129.7, 128.3, 128.0, 119.7, 116.1, 113.4, 113.1, 56.9, 55.4, 15.3; IR (neat) 3431 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{18}H_{18}O_2•NH_4$ 284.1651, found 284.1627.



3-11u

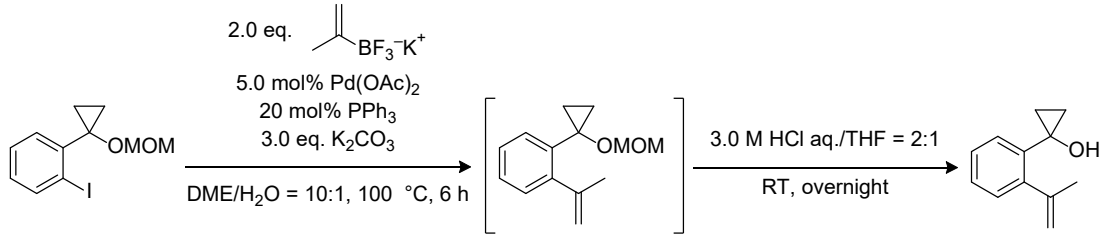
This compound was prepared in the same manner as described for **3-11q** using tosylhydrazone synthesized from 3'-chlorocetophenone[13] in 45% yield for 2 steps. **Analytical data for 3-11u:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.51–7.48 (m, 1H), 7.39–7.32 (m, 3H), 7.29–7.22 (m, 3H), 7.15 (td, *J* = 6.8, 2.0 Hz, 1H), 5.80 (d, *J* = 1.2 Hz, 1H), 5.39 (d, *J* = 1.2 Hz, 1H), 2.01 (s, 1H), 0.87–0.83 (m, 2H), 0.80–0.76 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 148.9, 143.8, 141.6, 139.7, 134.7, 130.9, 130.3, 129.8, 128.4, 128.2, 128.1, 127.1, 125.3, 117.1, 56.9, 15.3; IR (neat) 3426 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{17}H_{15}ClO$•H 271.0876, found 271.0890.



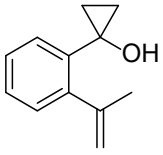
3-11v

This compound was prepared in the same manner as described for **3-11q** using tosylhydrazone synthesized from 2'-fluoroacetophenone[13] in 49% yield for 2 steps. **Analytical data for 3-11v:** colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48–7.46 (m, 1H), 7.35–7.32 (m, 3H), 7.29–7.23 (m, 1H), 7.13–7.04 (m, 3H), 5.84 (s, 1H), 5.63 (s, 1H), 1.97 (s, 1H), 0.86–0.83 (m, 2H), 0.79–0.76 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 160.1 (d, *J* = 251 Hz), 144.0, 142.5, 139.2, 130.7, 130.6 (d, *J* = 2.9 Hz), 130.3, 129.9 (d, *J* = 11.5 Hz), 129.5 (d, *J* = 8.7 Hz), 128.2 (d, *J* = 5.8 Hz), 124.0 (d, *J* = 3.8 Hz), 120.8, 120. 8, 116.5 (d, *J* = 22.2 Hz), 56.9, 15.1; ^{19}F-NMR (376 MHz, $CDCl_3$) δ –115.1; IR (neat) 3423 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{17}H_{15}FO$•H 255.1185, found 255.1194.

Synthesis and characterization of 3-11w



S1 **S18** 27% (2 steps) **3-11w**

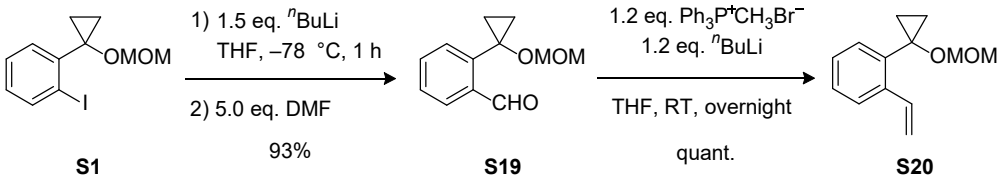


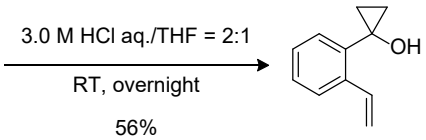
3-11w

To a solution of **S1** (915 mg, 3.01 mmol) and potassium isopropenyltrifluoroborate (895 mg, 6.05 mmol) in DME (30 mL) and H_2O (3.0 mL) was added $Pd(OAc)_2$ (33.7 mg, 0.150 mmol), PPh_3 (157 mg, 0.600 mmol) and K_2CO_3 (1.16 g, 8.40 mmol). The resulting solution was then stirred at 100 °C for 6 h. After that, the reaction mixture was diluted with water and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 50:1) to furnish **S18**, which still contained a small amount of inseparable impurities. The crude **S18** was used for

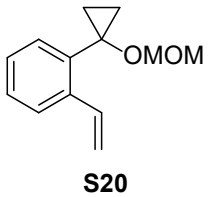
the next reaction without further purification at this stage. To a THF solution (3.0 mL) of **S18** was added aq. HCl (6.0 mL, 3 M). The resulting mixture was stirred at room temperature overnight. The reaction was quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **3-11w** (142 mg, 27%, 2 steps from **S1**). **Analytical data for 3-11w:** colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38–7.36 (m, 1H), 7.27–7.21 (m, 2H), 7.17–7.14 (m, 1H), 5.29 (dq, *J* = 2.8, 1.6 Hz, 1H), 5.06 (dq, *J* = 2.8, 1.6 Hz, 1H), 2.74 (s, 1H), 2.20 (s, 3H), 1.11 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.96 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 147.2, 144.6, 138.9, 128.8, 127.8, 127.2, 115.6, 57.2, 25.3, 15.1, One Csp^2 signal is missing due to overlapping.; IR (neat) 3420 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{12}H_{14}O{\bullet}NH_4$ 192.1388, found 192.1377.

Synthesis and characterization of 3-11x



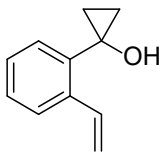


S19[4] was prepared according to the previous report.



In a 30 mL two-necked flask, to a suspension of CH_3PPh_3Br (429 mg, 1.20 mmol) in dry THF (5.0 mL) was added a solution of *n*BuLi (0.770 mL, 1.60 M in hexane) at 0 °C and the reaction mixture was stirred at room temperature for 0.5 h. To the resultant yellow solution was added a THF solution (2.0 mL) of **S19** (206 mg, 1.00 mmol) at 0 °C and the mixture was stirred at room temperature overnight. The reaction was quenched with water. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S20** (205 mg, quant.). **Analytical data for S20:** pale-yellow liquid; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.50 (dd, *J* = 17.6, 11.2 Hz, 1H), 7.34 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.29 (td, *J* = 7.6, 1.2 Hz, 1H), 7.21 (td, *J* = 7.6, 1.2 Hz, 1H),

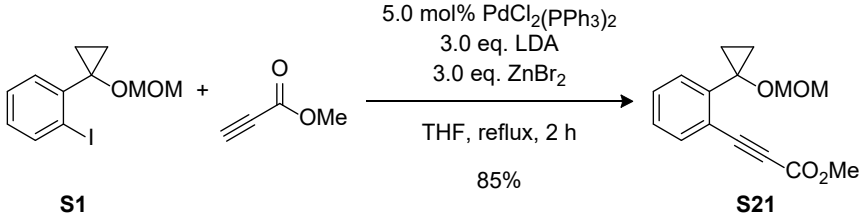
5.73 (dd, J = 17.6, 1.2 Hz, 1H), 5.33 (dd, J = 11.2, 1.2 Hz, 1H), 4.56 (s, 2H), 3.16 (s, 3H), 1.23 (dd, J = 7.2, 5.2 Hz, 2H), 0.93 (dd, J = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 138.6, 137.0, 135.0, 130.1, 128.4, 127.3, 125.3, 114.7, 94.9, 60.7, 55.7, 12.6; IR (neat) 1034 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{13}H_{16}O_2 \bullet NH_4$ 222.1494, found 222.1466.



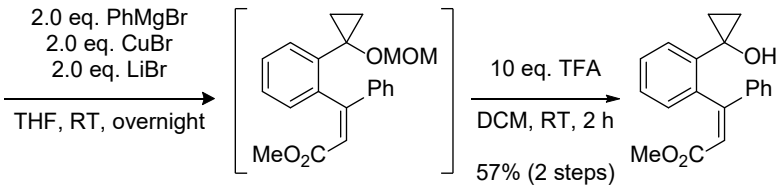
3-11x

To a THF solution (2.0 mL) of **S20** (205 mg, 1.00 mmol) was added aq. HCl (4.0 mL, 3 M). The resulting mixture was stirred at room temperature overnight. The reaction was quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **3-11x** (89.7 mg, 56%). **Analytical data for 3-11x:** colorless liquid; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, J = 7.6, 1.2 Hz, 1H), 7.48 (dd, J = 17.6, 11.2 Hz, 1H), 7.37 (dd, J = 7.6, 1.2 Hz, 1H), 7.30 (td, J = 7.6, 1.2 Hz, 1H), 7.23 (dd, J = 7.6, 1.2 Hz, 1H), 5.76 (dd, J = 17.6, 1.2 Hz, 1H), 5.38 (dd, J = 11.2, 1.2 Hz, 1H), 2.22 (s, 1H), 1.19 (dd, J = 7.2, 5.2 Hz, 2H), 0.95 (dd, J = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 139.1, 138.2, 134.6, 128.8, 128.4, 127.8, 125.8, 115.7, 56.8, 14.0; IR (KBr) 3431 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{11}H_{12}O \bullet H$ 161.0966, found 161.0953.

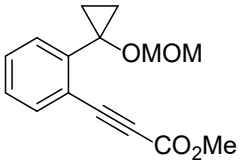
Synthesis and characterization of 3-11z



S1 **S21**

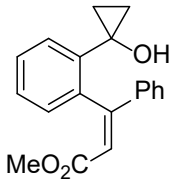


S22 **3-11z**



S21

To a solution of $^{i}Pr_2NH$ (1.30 mL, 7.80 mmol) in THF (15 mL) was added ^{n}BuLi (5.00 mL, 1.6 M in hexane) at 0 °C in a flame-dried flask under Ar atmosphere. After 10 min, the reaction mixture was treated with methyl propiolate (650 µL, 7.80 mmol) at –78 °C. After additional 10 min, dried $ZnBr_2$ (1.76 g, 7.82 mmol) in THF (6.0 mL) was added and the mixture was stirred for 10 min. **S1** (794 mg, 2.60 mmol) and $PdCl_2(PPh_3)_2$ (91.2 mg, 0.130 mmol) was added to the resultant solution. The temperature was raised to room temperature and the mixture was refluxed for 2 h. The reaction mixture was diluted with Et_2O, washed with sat. aq. NH_4Cl and then with sat. aq. $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **S21** (572 mg, 85%). **Analytical data for S21:** dark-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.48 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.41 (td, *J* = 7.6, 1.2 Hz, 1H), 7.30 (td, *J* = 7.6, 1.2 Hz, 1H), 4.66 (s, 2H), 3.85 (s, 3H), 3.14 (s, 3H), 1.33 (dd, *J* = 7.2, 5.6 Hz, 2H), 1.02 (dd, *J* = 7.2, 5.6 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 154.7, 144.0, 134.2, 130.6, 130.4, 128.0, 121.2, 95.4, 85.2, 84.6, 61.4, 55.6, 52.9, 13.0; IR (neat) 1712 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{15}H_{16}O_4$•NH_4 278.1392, found 278.1409.

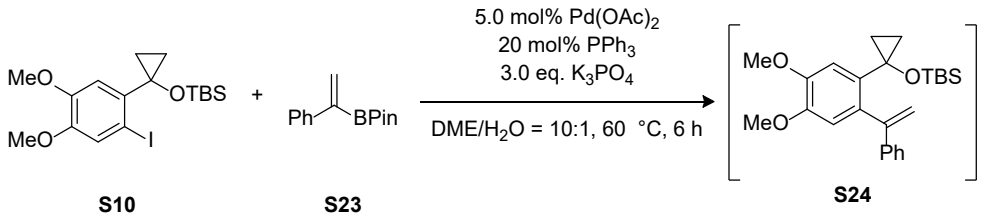


3-11z

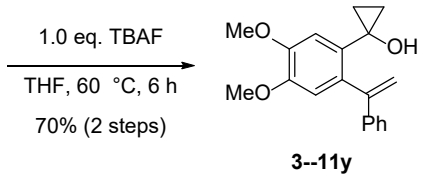
To a solution of dried CuBr (430 mg, 3.0 mmol) and dried LiBr (259 mg, 2.98 mmol) in THF (5.0 mL) was added PhMgBr (2.90 mL, 1.00 M in THF) at 0 °C and the reaction mixture was stirred at 0 °C for 0.5 h. To the resultant solution was added a THF solution (1.0 mL) of **S21** (258 mg, 0.990 mmol) at 0 °C and the mixture was stirred at room temperature for 1.0 h. The reaction was quenched with sat. aq. NH_4Cl. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S22**, which still contained a small amount of inseparable impurities. The crude **S22** was used for the next reaction without further purification at this stage. To a 50 mL flask was added **S22** followed by degassed DCM (10 mL). TFA (765 µL, 10.0 mmol) was slowly added to the solution. After being stirred at rt for 2 h under Ar atmosphere, the reaction mixture was diluted with water and extracted with EtOAc. The organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **3-11z** (94.2 mg, 32%, 2 steps from **S21**). **Analytical data for 3-11z:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.41–7.30 (m, 8H), 6.14 (s, 1H), 3.68 (s, 3H), 1.21 (s, 1H), 0.91–0.88 (m, 2H), 0.86–0.82 (m, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 166.6, 157.3, 142.8, 140.0, 139.3, 131.7, 130.5, 129.9, 129.44, 129.36, 128.1,

128.0, 119.6, 56.8, 51.5, 15.7; IR (neat) 3448, 1723 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{19}H_{18}O_3$•H 295.1334, found 295.1323.

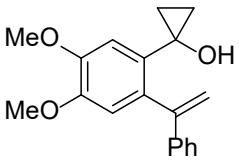
Synthesis and characterization of 3-11y



S10 **S23** **S24**



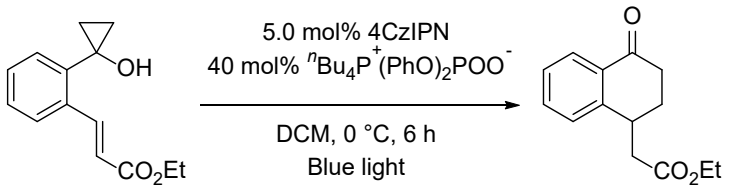
3--11y



3-11y

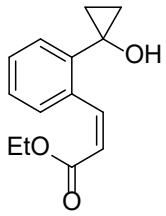
To a solution of **S10** (335 mg, 1.10 mmol) and **S23**[14] (460 mg, 2.00 mmol) in DME (6.0 mL) and H_2O (0.6 mL) was added $Pd(OAc)_2$ (12.3 mg, 0.0550 mmol), PPh_3 (57.7 mg, 0.220 mmol) and K_3PO_4 (636 mg, 3.00 mmol). Then the resulting solution was stirred at 60 ℃ for 6 h. After that, the reaction mixture was diluted with water and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S24**, which still contained inseparable impurities. The crude **S24** was used for the next reaction without further purification. To a dry THF solution (6.0 mL) of the crude **S24** was added a solution of TBAF (1.0 mL, 1.0 M in THF). The resulting mixture was stirred at 60 ℃ for 4 h. The reaction was quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 5:1) to furnish **3-11y** (207 mg, 70%, 2 steps from **S10**). **Analytical data for 3-11y:** colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35–7.28 (m, 5H), 7.05 (s, 1H), 6.81 (s, 1H), 5.72 (d, *J* = 1.2 Hz, 1H), 5.31 (d, *J* = 1.2 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 1.76 (s, 1H), 0.80 (br, s, 4H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 150.1, 148.5, 148.3, 142.6, 134.9, 132.1, 128.7, 128.3, 127.2, 115.5, 113.9, 113.7, 56.8, 56.1, 56.0, 15.7; IR (neat) 3544 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{19}H_{20}O_3$•H 297.1491, found 297.1486.

2. Representative Procedure for the Ring Expansion of 3-11



4CzIPN (3.94 mg, 0.00500 mmol), $^{n}Bu_4P^{+}(PhO)_2POO^{-}$ (20.3 mg, 0.0400 mmol), and **3-11a** (23.2 mg, 0.100 mmol) were dissolved in degassed dry DCM (1.0 mL) under Ar atmosphere. A LED lamp was put into the reaction mixture in the Schlenk tube, and the reaction mixture was stirred at 0 ºC under irradiation. After stirring at 0 °C for 6 h, the resulting solution was concentrated. The residue was then purified by a silica gel column chromatography (Hexane/EtOAc = 10:1) to give **3-12a** (19.7 mg, 85%) as a pale-yellow oil.

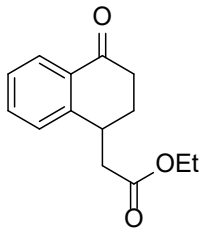
3. Characterization of 3-14a



3-14a

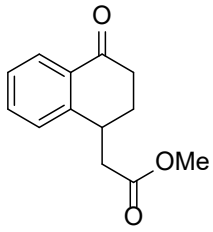
Analytical data for 3-14a: yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 11.6 Hz, 1H), 7.44 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.32–7.24 (m, 3H), 6.11 (d, *J* = 11.6 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 2.93 (s, 1H), 1.15 (t, *J* = 7.2 Hz, 3H), 1.11 (dd, *J* = 7.2, 5.2 Hz, 2H), 0.90 (dd, *J* = 7.2, 5.2 Hz, 2H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 166.7, 143.5, 139.6, 136.8, 129.0, 128.8, 128.5, 127.7, 121.5, 60.5, 57.2, 14.1, 14.0; IR (neat) 3402, 1707 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^{+}$ calcd for $C_{14}H_{16}O_3 \bullet NH_4$ 250.1443, found 250.1445.

4. Characterization of 1-Tetralones 3-12 and 1-Benzosuberones 3-13



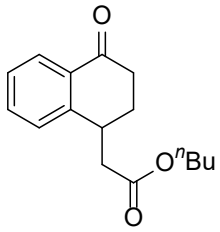
3-12a

According to the representative procedure, **3-12a** was obtained in 85% yield as a pale-yellow oil. **Analytical data for 3-12a:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.57–3.51 (m, 1H), 2.82–2.73 (m, 2H), 2.69–2.61 (m, 2H), 2.35–2.27 (m, 1H), 2.11–2.04 (m, 1H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 197.7, 172.1, 146.3, 133.9, 132.1, 127.8, 127.6, 127.3, 60.8, 39.8, 35.2, 34.9, 27.5, 14.3; IR (neat) 1732, 1685 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^{+}$ calcd for $C_{14}H_{16}O_3 \bullet NH_4$ 250.1443, found 250.1434.



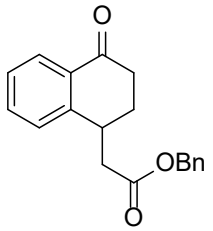
3-12b

According to the representative procedure, **3-12b** was obtained in 78% yield as a pale-yellow oil. **Analytical data for 3-12b:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.51 (td, *J* = 7.6, 1.2 Hz, 1H), 7.35 (td, *J* = 7.6, 1.2 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 3.73 (s, 3H), 3.57–3.51 (m, 1H), 2.82–2.73 (m, 2H), 2.71–2.61 (m, 2H), 2.35–2.27 (m, 1H), 2.11–2.03 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 197.7, 172.5, 146.2, 133.9, 132.1, 127.8, 127.7, 127.3, 52.0, 39.5, 35.2, 34.8, 27.5; IR (neat) 1736, 1685 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{13}H_{14}O_3{\bullet}NH_4$ 236.1287, found 236.1261.



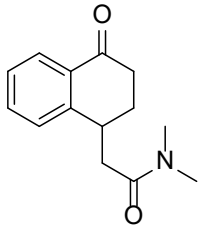
3-12c

According to the representative procedure, **3-12c** was obtained in 87% yield as a pale-yellow oil. **Analytical data for 3-12c:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.51 (td, *J* = 7.6, 1.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 4.13 (t, *J* = 6.4 Hz, 2H), 3.57–3.51 (m, 1H), 2.82–2.74 (m, 2H), 2.70–2.61 (m, 2H), 2.35–2.27 (m, 1H), 2.11–2.04 (m, 1H), 1.66–1.58 (m, 2H), 1.41–1.32 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 197.7, 172.2, 146.3, 133.9, 132.1, 127.8, 127.6, 127.3, 64.8, 39.8, 35.2, 34.9, 30.7, 27.5, 19.2, 13.8; IR (neat) 1732, 1686 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{20}O_3{\bullet}NH_4$ 278.1756, found 278.1760.



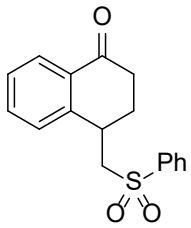
3-12d

According to the representative procedure, **3-12d** was obtained in 60% yield as a pale-yellow oil. **Analytical data for 3-12d:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 7.6 Hz, 1H), 7.46 (td, *J* = 7.6, 1.6 Hz, 1H), 7.40–7.31 (m, 6H), 7.26 (d, *J* = 7.6 Hz, 1H), 5.17 (s, 2H), 3.58–3.52 (m, 1H), 2.84–2.58 (m, 4H), 2.33–2.24 (m, 1H), 2.08–2.02 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 197.6, 171.9, 146.1, 135.7, 133.9, 132.1, 128.7, 128.51, 128.45, 127.8, 127.7, 127.3, 66.7, 39.7, 35.2, 34.9, 27.5; IR (neat) 1733, 1685 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{19}H_{18}O_3{\bullet}NH_4$ 312.1600, found 312.1590.



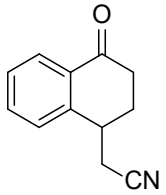
3-12e

According to the representative procedure, **3-12e** was obtained in 81% yield as a yellow amorphas solid. **Analytical data for 3-12e:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.50 (td, *J* = 7.6, 1.2 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 3.70–3.66 (m, 1H), 2.99 (s, 3H), 2.91 (s, 3H), 2.80–2.62 (m, 4H), 2.38–2.29 (m, 1H), 2.15–2.07 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 198.1, 171.1, 147.3, 133.9, 132.1, 128.1, 127.5, 127.1, 38.2, 37.4, 35.7, 35.3, 34.7, 27.6; IR (KBr) 1682, 1623 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{14}H_{17}NO_2{\bullet}NH_4$ 249.1603, found 249.1578.



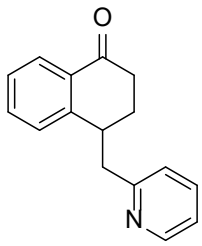
3-12f

The reaction was performed for 3 h. **3-12f** was obtained in 68% yield as a yellow oil. **Analytical data for 3-12f:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.99–7.97 (m, 2H), 7.72–7.67 (m, 1H), 7.63–7.59 (m, 2H), 7.49 (td, *J* = 7.6, 1.6 Hz, 1H), 7.35 (td, *J* = 7.6, 0.8 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 3.78–3.73 (m, 1H), 3.48 (dd, *J* = 14.0, 9.6 Hz, 1H), 3.31 (dd, *J* = 14.8, 3.6 Hz, 1H), 2.80–2.64 (m, 2H), 2.48–2.45 (m, 1H), 2.43–2.35 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 197.0, 144.5, 139.8, 134.2, 134.1, 132.2, 129.6, 128.2, 128.0, 127.8, 59.7, 34.2, 33.1, 26.3, One Csp^2 signal is missing due to overlapping.; IR (neat) 1685, 1303 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{16}O_3S•NH_4$ 318.1164, found 318.1159.



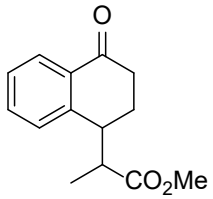
3-12g

The reaction was performed at 30 °C. **3-12g** was obtained in 44% yield as a pale-yellow oil. **Analytical data for 3-12g:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.59 (td, *J* = 7.6, 1.2 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 1H), 3.43–3.37 (m, 1H), 2.87–2.66 (m, 4H), 2.50–2.41 (m, 1H), 2.29–2.22 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.4, 143.1, 134.3, 132.1, 128.3, 128.1, 127.5, 118.0, 35.1, 31.2, 27.5, 23.1; IR (neat) 2248, 1685 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{12}H_{11}NO•NH_4$ 203.1184, found 203.1188.



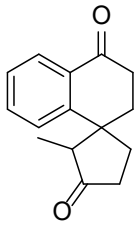
3-12h

The reaction was performed at 30 °C. **3-12h** was obtained in 50% yield as a pale-yellow oil. **Analytical data for 3-12h:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.62 (dd, *J* = 4.8, 1.2 Hz, 1H), 8.06 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.61 (td, *J* = 7.6, 2.0 Hz, 1H), 7.44 (td, *J* = 7.6, 2.0 Hz, 1H), 7.33 (td, *J* = 7.6, 1.2 Hz, 1H), 7.25–7.10 (m, 2H), 7.05 (d, *J* = 7.6 Hz, 1H), 3.63–3.56 (m, 1H), 3.26 (dd, *J* = 13.6, 6.4 Hz, 1H), 3.07 (dd, *J* = 13.6, 9.2 Hz, 1H), 2.85 (ddd, *J* = 17.2, 12.0, 5.2 Hz, 1H), 2.61 (dt, *J* = 17.6, 5.2 Hz, 1H), 2.23–2.14 (m, 1H), 1.99–1.92 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 198.3, 159.7, 149.7, 147.4, 136.5, 133.6, 132.1, 128.4, 127.5, 127.0, 123.9, 121.7, 43.5, 38.4, 34.9, 26.6; IR (neat) 1683 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{15}NO•H$ 238.1232, found 238.1205.



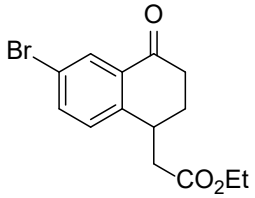
3-12i

According to the representative procedure, **3-12i** was obtained in 79% yield as a yellow oil. **3-12i** was analyzed as a mixture of diastereomers (major/minor = 10:1). **Analytical data for 3-12i:** ^{1}H-NMR (400 MHz, $CDCl_3$) **major** δ 8.04 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.50 (td, *J* = 7.2, 1.2 Hz, 1H), 7.36 (td, *J* = 7.2, 1.2 Hz, 1H), 7.25 (d, *J* = 7.2 Hz, 1H), 3.74 (s, 3H), 3.15–3.10 (m, 1H), 2.98–2.71 (m, 2H), 2.62 (ddd, *J* = 18.8, 5.2, 3.6 Hz, 1H), 2.31–2.17 (m, 1H), 2.08–2.01 (m, 1H), 1.14 (d, *J* = 7.2 Hz, 3H), **minor** δ 8.04 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.47 (td, *J* = 7.2, 1.2 Hz, 1H), 7.34 (td, *J* = 7.2, 1.2 Hz, 1H), 7.22 (d, *J* = 7.2 Hz, 1H), 3.57 (s, 3H), 3.34–3.29 (m, 1H), 2.98–2.71 (m, 2H), 2.62 (ddd, *J* = 18.8, 5.2, 3.6 Hz, 1H), 2.31–2.17 (m, 2H), 1.23 (d, *J* = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) **major** δ 197.9, 176.2, 144.6, 133.0, 132.3, 129.9, 127.8, 127.6, 52.0, 42.8, 41.5, 34.4, 26.5, 16.4, **minor** δ 197.7, 176.0, 144.6, 133.5, 132.4, 129.9, 127.8, 127.4, 51.7, 42.9, 40.7, 35.1, 24.3, 14.4; IR (neat) 1734, 1685 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{14}H_{16}O_3 \bullet NH_4$ 250.1443, found 250.1428.



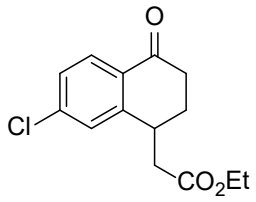
3-12o

The reaction was performed at –20 °C. **3-12o** was obtained in 49% yield as a colorless oil and analyzed as a mixture of diastereomers (major/minor = 1.7:1). **Analytical data for 3-12o:** ^{1}H-NMR (400 MHz, $CDCl_3$) **major** δ 8.14 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.46 (td, *J* = 7.6, 1.6 Hz, 1H), 7.42–7.34 (m, 1H), 6.83 (dd, *J* = 7.6, 1.2 Hz, 1H), 2.97–2.85 (m, 1H), 2.85–2.81 (m, 1H), 2.58–2.28 (m, 5H), 2.18–2.03 (m, 2H), 1.04 (d, J = 7.2 Hz, 3H); **minor** δ 8.10 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.61 (td, *J* = 7.6, 1.6 Hz, 1H), 7.42–7.34 (m, 2H), 1.95–1.87 (m, 1H), 1.68 (ddd, *J* = 14.4, 5.2, 4.0 Hz, 1H), 3.01 (q, *J* = 6.8 Hz, 1H), 2.80–2.76 (m, 1H), 2.76–2.68 (m, 1H), 2.58–2.28 (m, 3H), 2.18–2.03 (m, 1H), 1.00 (d, *J* = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) **major** δ 219.6, 197.30, 145.6, 133.4, 132.4, 128.8, 127.27, 126.7, 55.3, 46.4, 36.8, 35.1, 34.9, 34.4, 9.3; **minor** 217.7, 197.33, 147.4, 134.4, 132.9, 128.2, 127.33, 124.5, 53.7, 45.7, 34.7, 34.4, 32.8, 25.5, 7.7; IR (neat) 1738, 1683 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{15}H_{16}O_2 \bullet H$ 229.1229, found 229.1229.



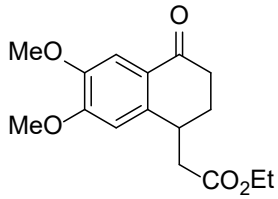
3-12j

According to the representative procedure, **3-12j** was obtained in 69% yield as a yellow oil. **Analytical data for 3-12j:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 2.4 Hz, 1H), 7.61 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.53–3.47 (m, 1H), 2.81–2.61 (m, 4H), 2.33–2.25 (m, 1H), 2.11–2.03 (m, 1H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.3, 171.8, 144.9, 136.6, 133.6, 130.5, 129.8, 121.5, 61.0, 39.6, 35.0, 34.4, 27.4, 14.3; IR (neat) 1732, 1687 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{14}H_{15}BrO_3 \bullet NH_4$ 328.0548, found 328.0554.



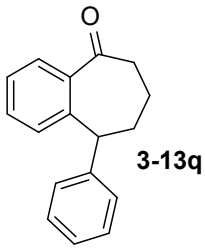
3-12k

According to the representative procedure, **3-12k** was obtained in 77% yield as a yellow oil. **Analytical data for 3-12k:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 9.2 Hz, 1H), 7.33–7.30 (m, 2H), 4.20 (q, J = 7.2 Hz, 2H), 3.54–3.48 (m, 1H), 2.80–2.72 (m, 2H), 2.69–2.60 (m, 2H), 2.34–2.26 (m, 1H), 2.11–2.04 (m, 1H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.5, 171.7, 147.8, 140.2, 130.5, 129.4, 127.9, 127.8, 61.0, 39.5, 35.1, 34.8, 27.4, 14.3; IR (neat) 1732, 1687 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{14}H_{15}ClO_3$•NH_4 284.1054, found 284.1062.



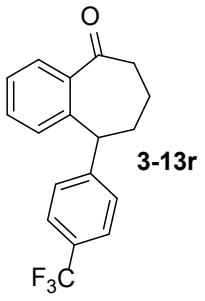
3-12l

The reaction was performed for 2 h. **3-12l** was obtained in 79% yield as a yellow solid. **Analytical data for 3-12l:** (mp 84.6–85.5 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 6.75 (s, 1H), 4.18 (q, J = 7.2 Hz, 2H), 3.93 (s, 3H), 3.92 (s, 3H), 3.51–3.45 (m, 1H), 2.77–2.66 (m, 3H), 2.64–2.56 (m, 1H), 2.35–2.26 (m, 1H), 2.09–2.02 (m, 1H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 196.5, 172.2, 153.8, 148.3, 141.2, 125.4, 109.6, 108.8, 60.8, 56.2, 56.1, 39.9, 34.7, 34.4, 27.8, 14.3; IR (KBr) 1731, 1660 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{21}O_5$•H 293.1389, found 293.1361.



3-13q

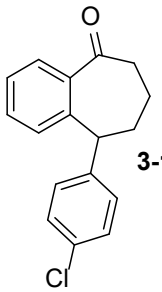
The reaction was performed at 30 °C. **3-13q** was obtained in 51% yield as a white amorphas solid. **Analytical data for 3-13q:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, J = 7.2, 1.6 Hz, 1H), 7.35 (d, J = 7.6 Hz, 2H), 7.37–7.27 (m, 3H), 7.22 (d, J = 7.6 Hz, 2H), 6.83 (dd, J = 7.2, 1.6 Hz, 1H), 4.41 (dd, J = 10.4, 4.0 Hz, 1H), 2.82–2.66 (m, 2H), 2.38–2.30 (m, 1H), 2.23–2.15 (m, 1H), 2.03–1.96 (m, 1H), 1.77–1.71 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 207.4, 142.9, 142.3, 139.7, 131.9, 129.0, 128.8, 128.7, 128.3, 126.8, 47.1, 41.1, 31.5, 20.6, One Csp^2 signal is missing due to overlapping.; IR (KBr) 1672 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{16}O$•NH_4 254.1545, found 254.1518.



3-13r

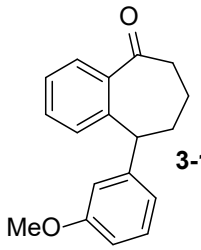
The reaction was performed at 30 °C. **3-13r** was obtained in 91% yield as a yellow amorphas solid. **Analytical data for 3-13r:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, J = 7.2, 1.6 Hz, 1H), 7.61 (d, J = 8.4 Hz, 2H), 7.37–7.30 (m, 4H), 6.77 (d, J = 7.2 Hz, 1H), 4.46 (dd, J = 10.0, 4.0 Hz, 1H), 2.82–2.66 (m, 2H), 2.40–2.31 (m, 1H), 2.25–2.16 (m, 1H), 2.06–1.97 (m, 1H), 1.81–1.67 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 206.9, 146.6, 141.7, 139.9, 132.0, 129.2 (q, J = 32 Hz), 129.1, 128.8, 128.5, 127.2, 125.6 (q, J = 3.8 Hz), 47.2, 41.1, 31.4, 20.5, A signal of CF_3 is obscure due to overlapping with aromatic peaks.; ^{19}F-NMR

(376 MHz, $CDCl_3$) δ –63.4; IR (KBr) 1673 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{18}H_{15}F_3O•H$ 305.1153, found 305.1179.



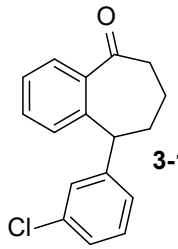
3-13s

The reaction was performed at 30 °C. **3-13s** was obtained in 71% yield as a pale-yellow amorphas solid. **3-13s** was analyzed as a mixture containing 9% of 1-tetralone product **3-12s** which was inseparable from **3-13s**. **Analytical data for 3-13s:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.36–7.28 (m, 4H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.79 (dd, *J* = 7.2, 1.6 Hz, 1H), 4.38 (dd, *J* = 10.4, 4.4 Hz, 1H), 2.81–2.74 (m, 1H), 2.73–2.65 (m, 1H), 2.34–2.25 (m, 1H), 2.22–2.13 (m, 1H), 2.04–1.96 (m, 1H), 1.79–1.68 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 207.1, 142.2, 140.9, 139.7, 132.6, 131.9, 130.1, 128.82, 128.79, 128.4, 127.1, 46.6, 41.1, 31.4, 20.5; IR (neat) 1683 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{15}ClO•NH_4$ 288.1155, found 288.1142.



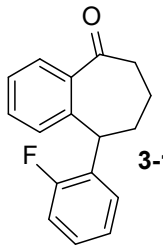
3-13t

The reaction was performed at 30 °C. **3-13t** was obtained in 34% yield as a white amorphas solid. **3-13t** was analyzed as a mixture containing 5% of 1-tetralone product **3-12t** which was inseparable from **3-13t**. **Analytical data for 3-13t:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.33 (td, *J* = 7.2, 1.6 Hz, 1H), 7.31–7.29 (m, 1H), 7.26 (d, *J* = 7.2 Hz, 1H), 6.86 (dd, *J* = 7.2, 1.2 Hz, 1H), 6.83 (t, *J* = 2.0 Hz, 1H), 6.81 (t, *J* = 2.0 Hz, 1H), 6.76 (t, *J* = 2.0 Hz, 1H), 4.37 (dd, *J* = 10.8, 4.0 Hz, 1H), 3.78 (s, 3H), 2.83–2.76 (m, 1H), 2.73–2.65 (m, 1H), 2.36–2.27 (m, 1H), 2.23–2.14 (m, 1H), 2.04–1.95 (m, 1H), 1.79–1.69 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 207.3, 159.9, 144.0, 142.7, 139.7, 131.9, 129.6, 129.0, 128.3, 126.9, 121.1, 114.8, 111.9, 55.3, 47.1, 41.1, 31.4, 20.6; IR (neat) 1678 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{18}H_{18}O_2•H$ 267.1385, found 267.1375.



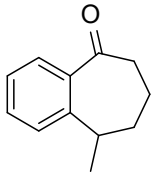
3-13u

The reaction was performed at 30 °C. **3-13u** was obtained in 87% yield as a pale-yellow amorphas solid. **Analytical data for 3-13u:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.37–7.23 (m, 5H), 7.08 (td, *J* = 6.8, 2.0 Hz, 1H), 6.80 (dd, *J* = 7.6, 1.2 Hz, 1H), 4.38 (dd, *J* = 10.8, 4.4 Hz, 1H), 2.75–2.81 (m, 1H), 2.66–2.73 (m, 1H), 2.26–2.34 (m, 1H), 2.13–2.22 (m, 1H), 1.96–2.04 (m, 1H), 1.68–1.81 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 206.9, 144.5, 142.0, 139.7, 134.6, 132.0, 129.9, 128.8, 128.5, 127.11, 127.07, 127.04, 46.9, 41.1, 31.3, 20.5; IR (neat) 1679 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{15}ClO•NH_4$ 288.1155, found 288.1146.



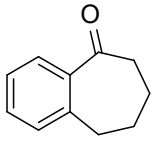
3-13v

The reaction was performed at 30 °C. **3-13v** was obtained in 66% yield as a colorless oil. **3-13v** was analyzed as a mixture containing a trace amount of 1-tetralone product **3-12v** which was inseparable from **3-13v**. **Analytical data for 3-13v:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.35–7.27 (m, 3H), 7.23 (td, *J* = 7.6, 1.2 Hz, 1H), 7.15 (td, *J* = 7.6, 1.2 Hz, 1H), 7.09–7.04 (m, 1H), 6.82–6.80 (m, 1H), 4.65 (dd, *J* = 10.8, 4.0 Hz, 1H), 2.86–2.72 (m, 2H), 2.38–2.33 (m, 1H), 2.17–2.09 (m, 1H), 2.06–1.99 (m, 1H), 1.77–1.71 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 206.9, 160.9 (d, *J* = 247 Hz), 141.8, 139.7, 132.0, 130.0 (d, *J* = 4.8 Hz), 129.6 (d, *J* = 14.4 Hz), 128.6 (d, *J* = 7.7 Hz), 128.5, 128.1, 127.0, 124.3 (d, *J* = 3.9 Hz), 115.8 (d, *J* = 22.1 Hz), 41.2, 40.9, 30.8, 20.7; ^{19}F-NMR (376 MHz, $CDCl_3$) δ –116.3; IR (neat) 1680 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{17}H_{15}FO$•H 255.1185, found 255.1184.



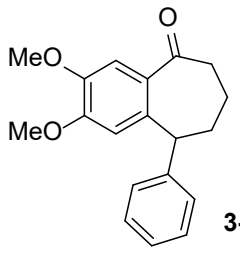
3-13w

The reaction was performed at 30 °C. **3-13w** was obtained in 42% yield as a colorless oil. Spectra are consistent with reported literature values.[15] **Analytical data for 3-13w:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.49–7.27 (m, 3H), 3.17–3.06 (m, 1H), 2.79–2.52 (m, 2H), 2.01–1.86 (m, 2H), 1.66–1.47 (m, 2H), 1.39 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 208.7, 143.3, 139.6, 132.1, 128.0, 126.6, 125.4, 41.3, 34.5, 34.3, 20.5, 19.4.



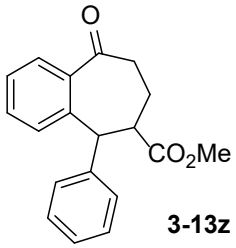
3-13x

The reaction was performed at 30 °C. **3-13x** was obtained in 62% yield as a colorless oil. Spectra are consistent with reported literature values.[16] **Analytical data for 3-13x:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.42 (td, *J* = 7.6, 1.6 Hz, 1H), 7.30 (td, *J* = 7.6, 1.6 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 2.93 (t, *J* = 6.0 Hz, 2H), 2.75–2.72 (m, 2H), 1.92–1.78 (m, 4H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 206.3, 141.4, 138.9, 132.3, 129.8, 128.7, 126.7, 40.9, 32.6, 25.3, 21.0.



3-13y

The reaction was performed at 30 °C for 2 h. **3-13y** was obtained in 77% yield as a yellow oil. **Analytical data for 3-13y:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38–7.34 (m, 2H), 7.32 (s, 1H), 7.29–7.25 (m, 1H), 7.23–7.21 (m, 2H), 6.33 (s, 1H), 4.42 (dd, *J* = 10.0, 4.0 Hz, 1H), 3.92 (s, 3H), 3.67 (s, 3H), 2.81–2.74 (m, 1H), 2.71–2.63 (m, 1H), 2.41–2.32 (m, 1H), 2.23–2.14 (m, 1H), 2.02–1.93 (m, 1H), 1.79–1.68 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 204.9, 151.7, 147.4, 142.7, 138.1, 131.9, 128.7, 128.6, 126.8, 112.3, 111.3, 56.1, 55.8, 47.2, 41.3, 31.5, 20.4; IR (neat) 1667 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{19}H_{20}O_3$•H 297.1491, found 297.1480.



3-13z

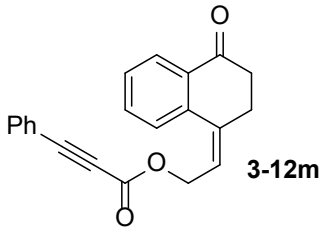
According to the representative procedure, **3-13z** was obtained in 78% yield as a colorless oil. **3-13z** was analyzed as a mixture of diastereomers (major/minor = 14:1). **Analytical data for 3-13z (major diastereomer):** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.46 (td, *J* = 8.0, 2.0 Hz, 1H), 7.38 (td, *J* = 8.0, 2.0 Hz, 1H), 7.32–7.22 (m, 4H), 7.00 (d, *J* = 8.0 Hz, 2H), 5.18 (s, 1H), 3.81 (s, 3H), 3.27 (ddd, *J* = 12.8, 5.2, 2.0 Hz, 1H), 2.90–2.82 (m, 1H), 2.59–2.53 (m, 1H), 2.27–2.19 (m, 1H), 1.99–1.90 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 204.3, 174.5, 141.9, 139.9, 139.5, 131.94, 131.86, 129.3, 128.6, 128.5, 127.4, 127.0, 52.4, 51.0, 47.4, 40.4, 22.3; IR (neat) 1733, 1682 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{19}H_{18}O{\bullet}NH_4$ 312.1600, found 312.1596.

5. Ring Expansion of the Alkyne Substrates 3-11m and 3-11n

Preparation of the alkyne substrates

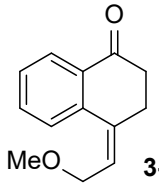
3-11m and **3-11n** was prepared according to the previous report.[4]

characterization of 3-12m and 3-12n



3-12m

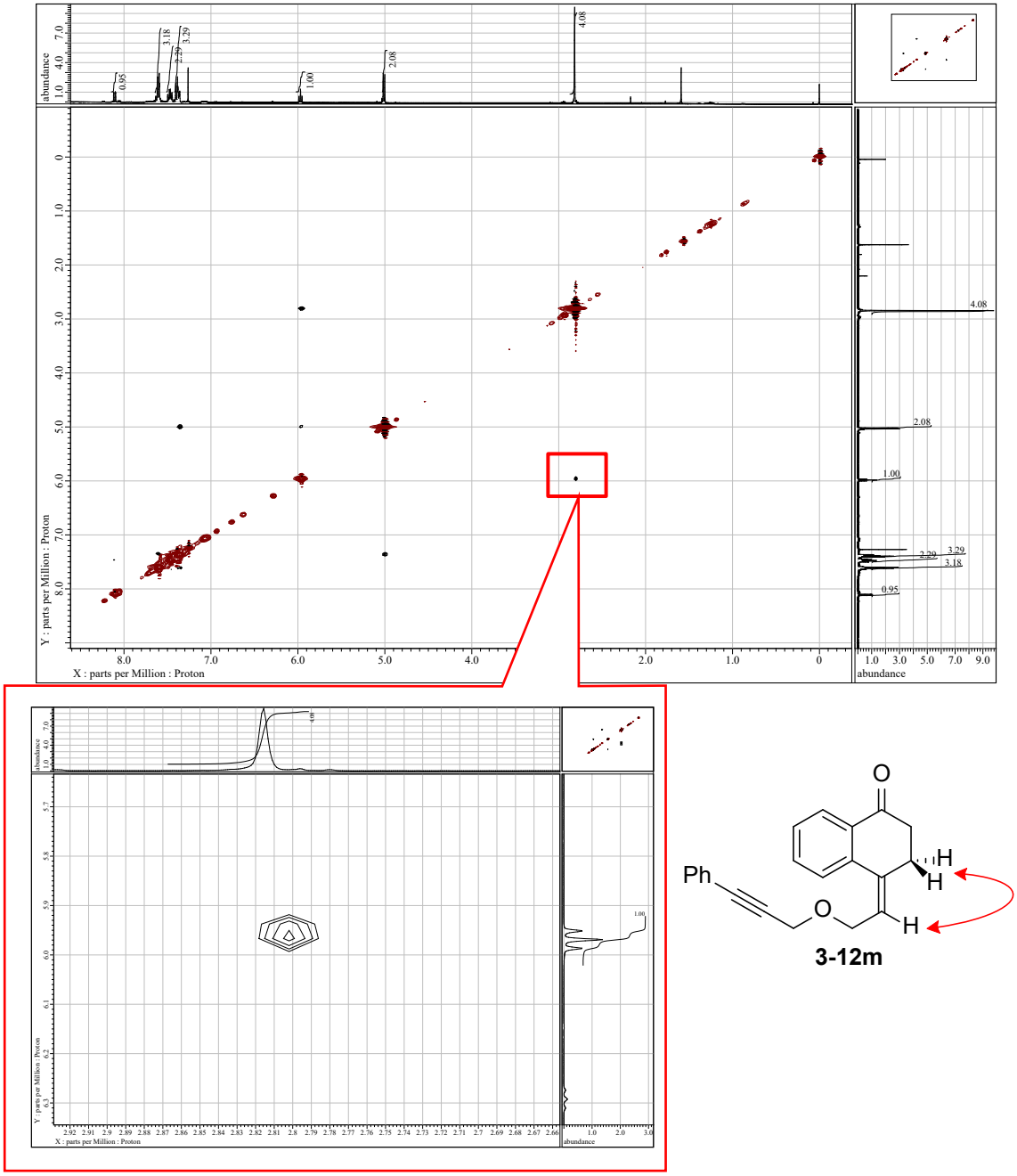
The reaction was performed at 30 ℃. **3-12m** was obtained in 44% yield as a pale-yellow oil. **Analytical data for 3-12m:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.64–7.59 (m, 3H), 7.50–7.44 (m, 2H), 7.41–7.36 (m, 3H), 5.97 (t, *J* = 6.8 Hz, 1H), 5.01 (d, *J* = 6.8 Hz, 2H), 2.82 (br s, 4H) ^{13}C-NMR (101 MHz, $CDCl_3$) δ 197.3, 153.9, 140.3, 139.2, 133.5, 133.1, 132.5, 130.9, 129.1, 128.7, 128.0, 127.8, 120.8, 119.5, 87.0, 80.4, 63.3, 40.1, 35.1; IR (neat) 1685, 1708 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{21}H_{16}O_3{\bullet}NH_4$ 334.1443, found 334.1459.



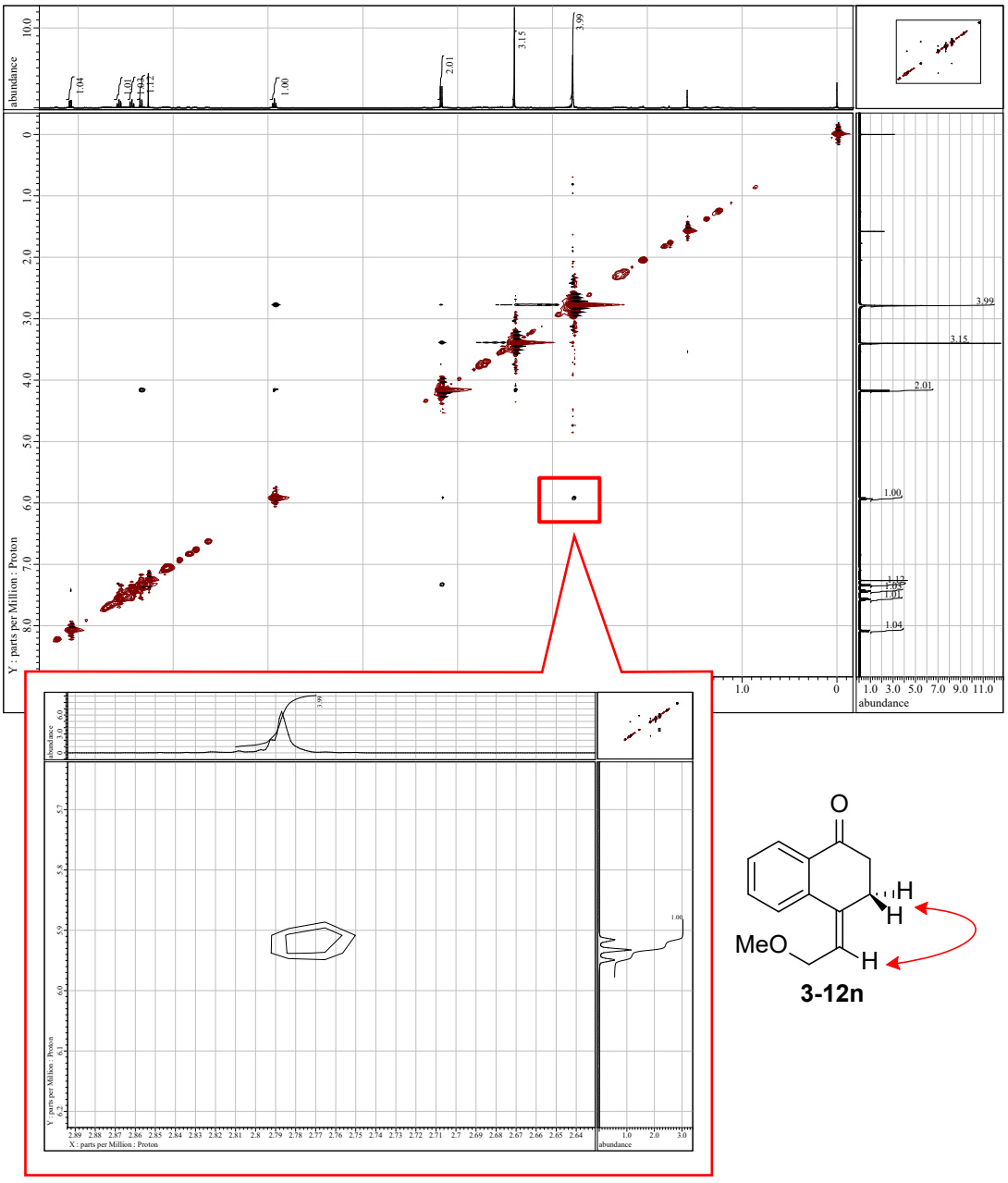
3-12n

The reaction was performed at 30 ℃. **3-12n** was obtained in 56% yield as a pale-yellow oil. **Analytical data for 3-12n:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.57 (td, *J* = 7.6, 1.2 Hz, 1H), 7.43 (td, *J* = 7.6, 1.2 Hz, 1H), 7.34 (dd, *J* = 7.6, 1.2 Hz, 1H), 5.93 (t, *J* = 7.2 Hz, 1H), 4.17 (d, *J* = 7.2 Hz, 2H), 3.40 (s, 3H), 2.79 (br s, 4H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 197.8, 139.9, 137.8, 133.2, 132.3, 128.5, 128.2, 127.5, 124.8, 69.6, 58.4, 40.4, 35.1; IR (neat) 1685 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{13}H_{14}O_2{\bullet}NH_4$ 220.1338, found 220.1313.

The structure of **3-12m** was assigned by NOESY experiments. The arrows shown below indicate the observed cross peaks.



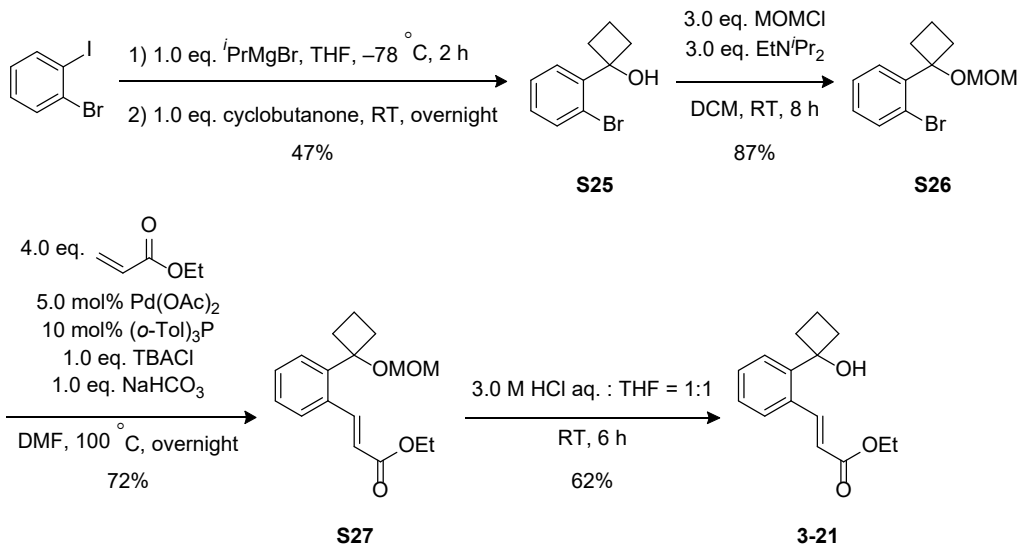
The structure of **3-12n** was assigned by NOESY experiments. The arrows shown below indicate the observed cross peaks.



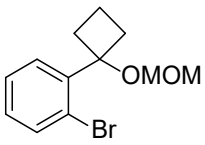
3-12n

6. Radical Cyclization of the Cyclobutanol Substrate 3-21 and the Cyclopentanol Substrate 3-22

Preparation of the cyclobutanol substrate 3-21

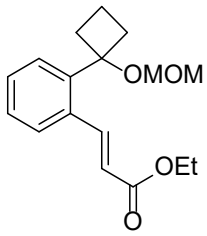


S25 was prepared according to the previous report.[17]



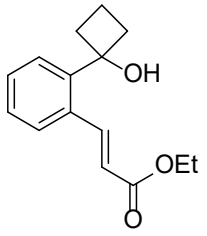
S26

To a solution of **S25** (500 mg, 2.20 mmol) and EtN^iPr_2 (1.10 mL, 6.35 mmol) in dry DCM (10 mL) was added MOMCl (500 µL, 6.65 mmol) at 0 °C, and the mixture was allowed to warm to rt. After being stirred at rt for 8 h, the reaction was quenched with water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S26** (516 mg, 87%). **Analytical data for S26:** dark-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.41 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.29 (td, *J* = 8.0, 1.2 Hz, 1H), 7.12 (td, *J* = 8.0, 1.2 Hz, 1H), 4.47 (s, 2H), 3.32 (s, 3H), 2.65 (t, *J* = 7.6 Hz, 4H), 2.16–2.03 (m, 1H), 1.70–1.60 (m, 1H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 140.7, 134.6, 129.2, 126.8, 123.1, 92.7, 83.5, 55.9, 34.2, 15.1, One Csp^2 signal is missing due to overlapping.; IR (neat) 1013 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{12}H_{15}BrO_2 \bullet NH_4$ 288.0599, found 288.0602.



S27

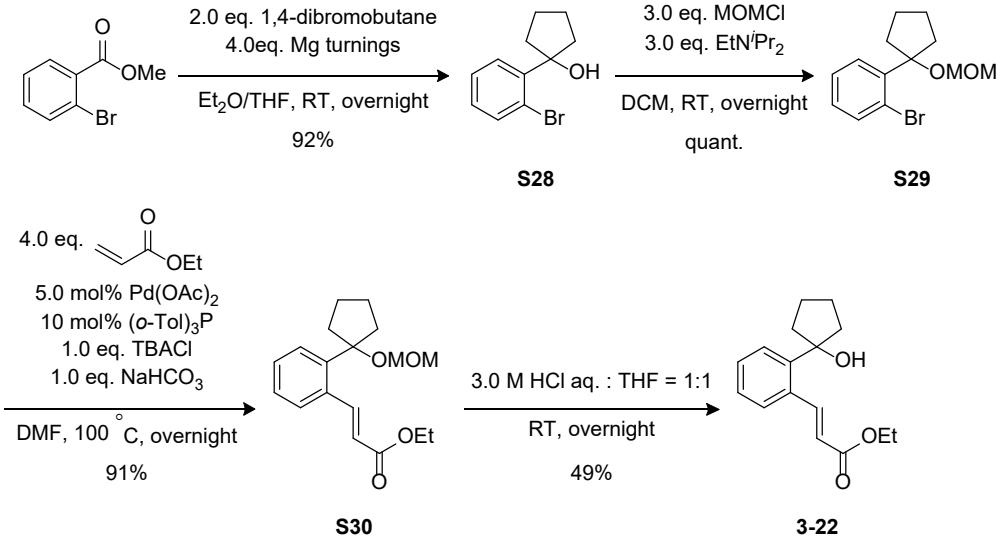
To a solution of **S26** (516 mg, 1.91 mmol) in DMF (2.00 mL) was added $Pd(OAc)_2$ (22.4 mg, 0.100 mmol), (*o*-Tol)$_3$P (60.9 mg, 0.200 mmol), $NaHCO_3$ (168 mg, 2.00 mmol) and TBACl (556 mg, 2.00 mmol). After degassed at –78 °C, the mixture was added ethyl acrylate (870 μL, 8.00 mmol). The reaction mixture was stirred at 100 ℃ overnight. After that, the reaction mixture was filtered through a pad of silica gel with a mixed solution of hexane (40 mL) and EtOAc (10 mL). The filtrate concentrated *in vacuo*. The obtained crude product was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to give **S27** (418 mg, 72%). **Analytical data for S27:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 16.0 Hz, 1H), 7.61 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.42 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.35 (td, *J* = 7.6, 1.6 Hz, 1H), 7.31 (td, *J* = 7.6, 1.6 Hz, 1H), 6.28 (d, *J* = 16.0 Hz, 1H), 4.42 (s, 2H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.29 (s, 3H), 2.65–2.53 (m, 4H), 2.15–2.05 (m, 1H), 1.73–1.62 (m, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 166.9, 143.9, 141.6, 134.3, 129.2, 128.2, 127.7, 127.5, 119.0, 92.6, 82.2, 60.5, 55.9, 34.9, 15.1, 14.4; IR (neat) 1714, 1176 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{17}H_{22}O_4$•NH_4 308.1862, found 308.1890.

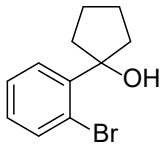


3-21

To a THF solution (5.0 mL) of **S27** (311 mg, 1.07 mmol) was added aq. HCl (5.0 mL, 3.00 M). The resulting mixture was stirred at room temperature for 6 h. The reaction was quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **3-21** (163 mg, 62%). **Analytical data for 3-21:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J* = 16.0 Hz, 1H), 7.59 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.38 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.34 (td, *J* = 7.6, 1.6 Hz, 1H), 7.29 (td, *J* = 7.6, 1.6 Hz, 1H), 6.28 (d, *J* = 16.0 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 2.70–2.63 (m, 2H), 2.48 (s, 1H), 2.47–2.41 (m, 2H), 2.20–2.10 (m, 1H), 1.74–1.64 (m, 1H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 167.0, 144.2, 143.8, 133.9, 129.6, 128.1, 127.8, 125.7, 119.3, 78.1, 60.6, 36.9, 14.6, 14.4; IR (neat) 3446, 1698 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{15}H_{18}O_3$•NH_4 264.1600, found 264.1586.

Preparation of the cyclopentanol substrate 3-22

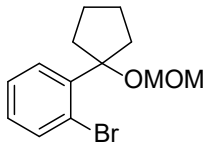




S28

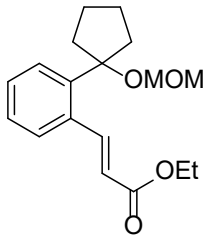
In a 100 mL two-necked flask containing Mg metal turnings (972 mg, 40.0 mmol) in dry Et_2O (10 mL), solution of 1,4-dibromobutane (4.32 g, 20.0 mmol) in anhydrous THF (20 mL) was added cautiously in a dropwise manner at 0 °C. After addition, the reaction mixture was allowed to warm up to room temperature and stirred for 2 h. The reaction mixture becomes turbid indicating generation of a Grignard reagent. To a solution of methyl 2-bromobenzoate (1.40 mL, 10.0 mmol) in THF (40 mL) was added the above generated solution of Grignard reagent slowly in a dropwise manner at –78 °C. After addition, the reaction mixture was warmed up to room temperature and then stirred overnight. The suspension was quenched slowly with the addition of sat. NH_4Cl solution, followed by extraction with EtOAc. The combined organic extracts were washed with water and brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S28** as a white solid (2.15 g, 89%). Spectra are consistent with reported literature values.[18]

Analytical data for S28: white solid; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 7.6, 1.2 Hz, 1H), 7.45 (dd, J = 7.6, 1.6 Hz, 1H), 7.25 (td, J = 7.6, 1.2 Hz, 1H), 7.11 (td, J = 7.6, 1.6 Hz, 1H), 4.43 (s, 2H), 3.36 (s, 3H), 2.64–2.59 (m, 2H), 2.08–2.00 (m, 2H), 1.96–1.91 (m, 2H), 1.76–1.67 (m, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 141.4, 135.5, 129.7, 129.0, 126.9, 123.3, 93.0, 89.6, 56.4, 37.5, 23.1.



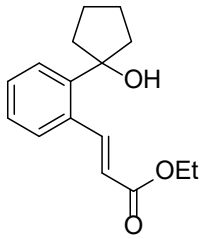
S29

To a solution of **S28** (493 mg, 2.04 mmol) and EtN^iPr_2 (1.20 mL, 6.93 mmol) in dry DCM (10 mL) was added MOMCl (530 μL, 7.04 mmol) at 0 °C, and the mixture was allowed to warm to rt. After being stirred at rt overnight, the reaction was quenched with water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **S29** (576 mg, quant.). **Analytical data for S29:** dark-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.45 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.25 (td, *J* = 7.6, 1.2 Hz, 1H), 7.11 (td, *J* = 7.6, 1.6 Hz, 1H), 4.43 (s, 2H), 3.36 (s, 3H), 2.64–2.59 (m, 2H), 2.08–2.00 (m, 2H), 1.96–1.91 (m, 2H), 1.76–1.67 (m, 2H); ^{13}C-NMR (101 MHz, $CHCl_3$) δ 141.4, 135.5, 129.7, 129.0, 126.9, 123.3, 93.0, 89.6, 56.4, 37.5, 23.1; IR (neat) 1031 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{13}H_{17}BrO_2$•NH_4 302.0756, found 302.0762.



S30

To a solution of **S29** (285 g, 1.00 mmol) in DMF (2.00 mL) was added $Pd(OAc)_2$ (11.2 mg, 0.0500 mmol), (*o*-Tol)$_3$P (60.9 mg, 0.100 mmol), $NaHCO_3$ (84.0 mg, 1.00 mmol) and TBACl (278 mg, 1.00 mmol). After degassed at –78 °C, the mixture was added ethyl acrylate (870 μL, 8.00 mmol). The reaction mixture was stirred at 100 °C overnight. After that, the reaction mixture was filtered through a pad of silica gel with a mixed solution of hexane (40 mL) and EtOAc (10 mL). The filtrate concentrated *in vacuo*. The obtained crude product was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) to give **S30** (279 mg, 91%). **Analytical data for S30:** pale-yellow solid (mp 50.5–51.7 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 16.0 Hz, 1H), 7.57–7.55 (m, 1H), 7.44–7.41 (m, 1H), 7.33–7.29 (m, 2H), 6.23 (d, *J* = 16.0 Hz, 1H), 4.40 (s, 2H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.32 (s, 3H), 2.44–2.36 (m, 2H), 1.98–1.89 (m, 4H), 1.71–1.68 (m, 2H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 167.1, 145.9, 141.9, 135.4, 129.2, 128.3, 128.0, 127.6, 119.2, 92.9, 89.2, 60.4, 56.2, 38.7, 23.2, 14.4; IR (KBr) 1711, 1156 cm^{-1}; HRMS (DART) *m/z* $[M+ NH_4]^+$ calcd for $C_{18}H_{24}O_4$• NH_4 322.2018, found 322.2022.

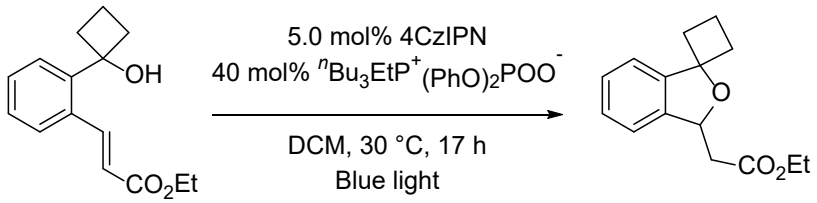


3-22

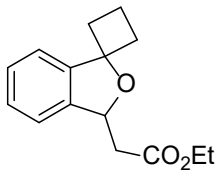
To a THF solution (2.0 mL) of **S30** (202 mg, 0.660 mmol) was added aq. HCl (2.0 mL, 3.00 M). The resulting mixture was stirred at room temperature overnight. The reaction was quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish **3-22** (84.2 mg, 49%). **Analytical data for 3-22:** pale-yellow solid (mp 73.2–

73.8 °C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 16.0 Hz, 1H), 7.54 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.50 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.32 (td, *J* = 7.6, 1.6 Hz, 1H), 7.27 (td, *J* = 7.6, 1.6 Hz, 1H), 6.22 (d, *J* = 16.0 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 2.12–2.09 (m, 4H), 1.99–1.93 (m, 2H), 1.84–1.75 (m, 2H), 1.78 (s, 1H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 167.1, 145.8, 145.0, 134.8, 129.3, 128.5, 127.7, 125.6, 119.3, 83.7, 60.5, 41.3, 23.9, 14.4; IR (KBr) 3454, 1695 cm^{-1}; HRMS (DART) *m/z* $[M+NH_4]^+$ calcd for $C_{16}H_{20}O_3 \bullet NH_4$ 278.1756, found 278.1763.

The ring expansion of cyclobutanol substrate 3-21 and cyclopentanol substrate 3-22

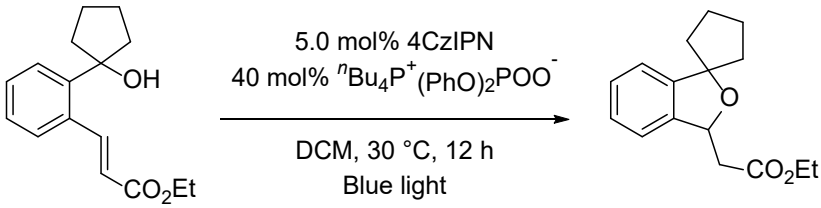


3-21 **3-25**

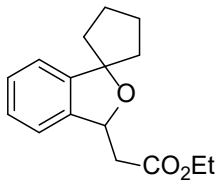


3-25

According to the representative procedure for the radical cyclization of **3-11**, pale-yellow oil was obtained in 39% yield. **Analytical data for 3-25:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 5.60 (t, *J* = 6.4 Hz, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 2.74–2.59 (m, 4H), 2.43–2.35 (m, 2H), 2.00–1.83 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 170.9, 145.9, 140.5, 128.5, 127.6, 121.0, 120.0, 87.5, 79.0, 60.7, 42.8, 38.8, 37.8, 14.3, 13.0; IR (neat) 1735 cm^{-1}; HRMS (DART) *m/z* $[M+H]^+$ calcd for $C_{15}H_{18}O_3 \bullet H$ 247.1334, found 247.1348.



3-22 **3-26**

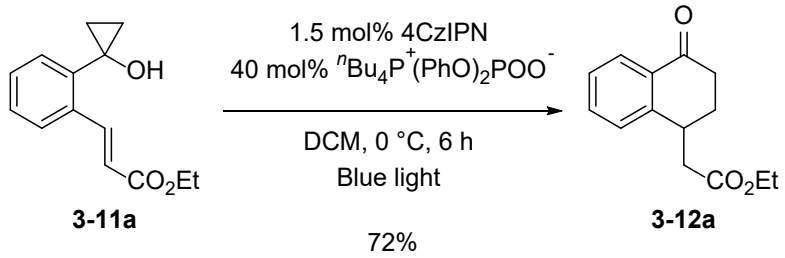


3-26

According to the representative procedure for the radical cyclization of **3-11**, pale-yellow oil was obtained in 68% yield. **Analytical data for 3-26:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.29 (td, *J* = 7.2, 1.2 Hz, 1H), 7.25 (td, *J* = 7.2, 1.2 Hz, 1H), 7.16 (d, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 7.2 Hz, 1H), 5.58 (t, *J* = 6.8 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 2.74 (d, *J* = 6.8 Hz, 2H), 2.10–1.88 (m, 5H), 1.82–1.77 (m, 3H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 171.0, 145.7, 141.3, 128.1, 127.4, 121.1, 120.8, 95.5, 78.1, 60.6, 42.8, 42.2, 41.1, 25.1,

25.0, 14.3; IR (neat) 1735 cm^{-1}; HRMS (ESI) *m/z* $[M+ Na]^+$ calcd for $C_{16}H_{20}O_3$•Na 283.1310, found 283.1296.

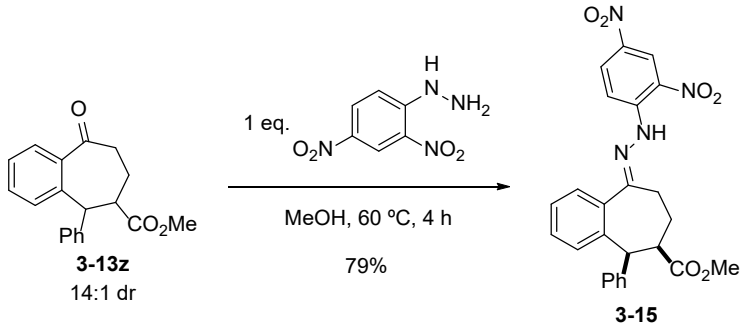
7. Scale-Up Experiment



3-11a 72% **3-12a**

4CzIPN (12.7 mg, 0.0161 mmol), $^nBu_4P^+(PhO)_2POO^-$ (218 mg, 0.428 mmol), and **3-11a** (249 mg, 1.07 mmol) were dissolved in degassed dry DCM (10 mL) under Ar atmosphere. A LED lamp was put into the reaction mixture in the Schlenk tube, and the reaction mixture was stirred at 0 ºC under irradiation. After vigorous stirring at 0 ºC for 6 h, the resulting solution was concentrated *in vacuo*. The residue was then purified by a silica gel column chromatography (Hexane/EtOAc = 10:1) to give **3-12a** (179 mg, 72%) as a pale-yellow oil.

8. Synthesis of 3-15 from 3-13z for X-ray crystallographic analysis



3-13z 14:1 dr 79% **3-15**

A solution of **3-13z** (12.8 mg, 0.043 mmol) and 2,4-dinitrophenylhydrazine (8.4 mg, 0.043 mmol) in MeOH (0.5 mL) was stirred at 60 ºC for 4 h oil bath. The precipitate was collected by filtration and washed with water. The obtained solid was dried under reduced pressure to afford **3-15** (16.1 mg, 79% yield) as an orange solid. The solid was recrystallized from CH_2Cl_2 and hexane. **Analytical data for 3-15:** mp 187.1–187.9 ºC; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 11.46 (s, 1H), 9.17 (d, *J* = 2.7 Hz, 1H), 8.36 (dd, *J* = 9.6, 2.7 Hz, 1H), 8.12 (d, *J* = 9.6 Hz, 1H), 7.72–7.69 (m, 1H), 7.42–7.37 (m, 2H), 7.31–7.22 (m, 4H), 7.09 (d, *J* = 6.9 Hz, 2H), 4.95 (d, *J* = 3.2 Hz, 1H), 3.77 (s, 3H), 3.33–3.27 (m, 1H), 2.85–2.76 (m, 2H), 2.40–2.32 (m, 1H), 1.97–1.87 (m, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ 174.4, 157.7, 145.1, 139.7, 138.3, 137.8, 131.5, 130.1, 129.7, 129.6, 128.5, 128.4, 128.3, 127.2, 126.9, 123.5, 116.7, 76.7, 52.1, 49.0, 46.2, 26.3, 23.3; IR (neat) 1727 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{25}H_{22}N_4O_6Na$ 497.1437; Found 497.1430.

X-Ray Diffraction Analysis of 3-15

Diffraction data were collected in θ ranges specified in Table S1 at 123 K on a Rigaku R-AXIS Rapid diffractometer with graphite monochromatized Cu-Ka radiation (λ = 1.54187 Å). The Lorenz polarization absorption correction was applied. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined using the riding model. Final refinement details are compiled in Table S1. The supplementary crystallographic data for this paper (CCDC2084574) can also be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

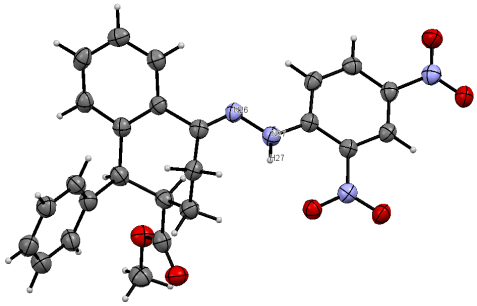


Figure S1. ORTEP plot of **3-15**.

Table S1. Selected crystallographic data and collection parameters for **3-15**.

formula	$C_{25}H_{22}N_4O_6$	crystal size, mm	0.2 x 0.2 x 0.1
FW	474.47	maximum 2θ, deg	136.3
crystal system	monoclinic	reflections collected	24007
space group	P21/c (#14)	independent reflections [*R*(int)]	3954 [R(int) = 0.0656]
a, Å	23.5028(16)	max. and min. transmission	0.915/0.613
b, Å	7.0069(5)	goodness-of-fit on F^2	1.020
c, Å	13.6822(9)	R_1 [I >2σ(I)]	0.0626
volume, Å^3	2166.4(3)	R, wR_2 (all data)	0.1200, 0.1683
β, °	105.954(8)	Weighting scheme	$R_1 = \Sigma \lvert\lvert Fo\rvert - \lvert Fc\rvert\rvert / \Sigma \lvert Fo\rvert$ $wR_2 = [\Sigma(w(Fo^2 - Fc^2)^2)/\Sigma w(Fo^2)^2]^{1/2}$
Z	4		
D (calcd), Mg m^{-3}	1.455	largest diff. peak and hole, e Å^{-3}	0.28 and –0.25
μ, cm^{-1}	8.841		
F(000)	992.00		

9. References

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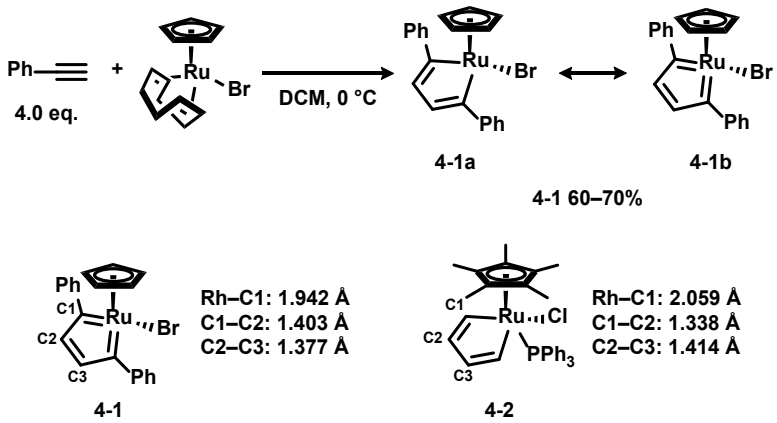
第 4 章

ルテニウム触媒を用いる
シクロプロペンとアルキンの
環化異性化反応

第 1 節　ルテナシクロペンタトリエン

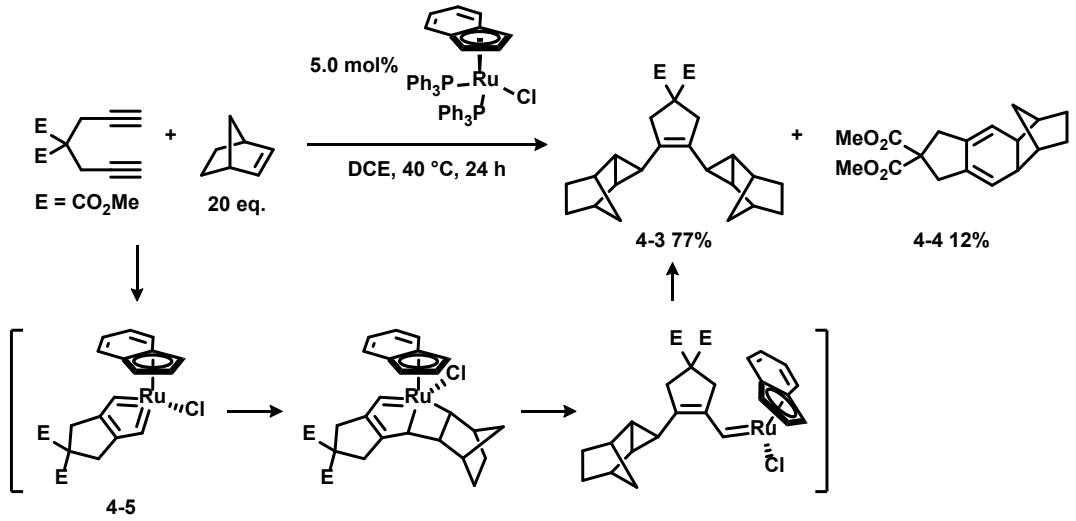
一般的に、コバルト、ロジウムおよびイリジウムなどの低原子価遷移金属錯体と二分子のアルキンの酸化的環化が進行すると、メタラシクロペンタジエンが形成される（**Scheme 1-31a**）。しかし、ルテニウムと二分子のアルキンからなるルテナサイクルは、通常のメタラサイクルとは異なることが知られている。

1986 年に、Singleton らは、二分子のフェニルアセチレンと CpRuBr(cod)の酸化的環化によって、ルテナサイクル **4-1** が得られることを報告した（**Scheme 4-1**）[1]。彼らは、**4-1** の X 線結晶構造解析により、Ru–C1 の結合長が 1.942 Å であることを確認している。これは、既知のルテナシクロペンタジエン錯体 **4-2** [2] における Ru–C1 結合長の 2.059 Å と比べて短い。加えて、**4-1** の C1–C2 および C2–C3 の結合長がそれぞれ 1.403 Å および 1.377 Å であるのに対して、**4-2** の C1–C2 および C2–C3 の結合長は 1.338 Å および 1.414 Å である。また、**4-1** の ^{13}C-NMR 測定で、ルテニウムに隣接する炭素のシグナルが、カルベノイドに特徴的な低磁場に観測されることが分かっている。これらの結果は、**4-1** の寄与はルテナシクロペンタジエン構造 **4-1a** よりもルテナシクロペンタトリエン構造 **4-1b** の方が大きいことを示唆している。



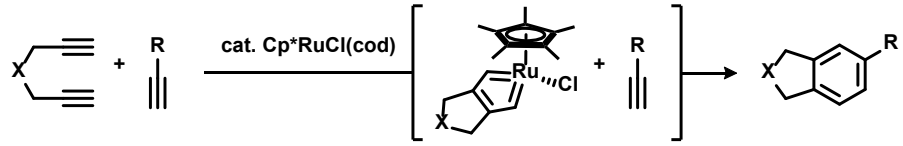
Scheme 4-1 ルテナシクロペンタトリエンと類似の錯体

Singleton らによって、ルテナシクロペンタトリエンはビスカルベン性を有することが明らかにされた。その反応性を顕著に表す例として、1,6-ジインの環化/二重シクロプロパン化反応が挙げられる（**Scheme 4-2**）[3]。山本らは、インデニル配位子をもつルテニウム錯体触媒の存在下、1,6-ジインと過剰量のノルボルネンを反応させることで、二重シクロプロパン化体 **4-3** と[2+2+2]付加環化体 **4-4** をそれぞれ 77%収率および 12%収率で得た。この **4-3** は、ルテニウム錯体と 1,6-ジインの酸化的環化によって形成されるルテナシクロペンタトリエン **4-5** において、順次シクロプロパン化が進行することで得られる生成物である。



Scheme 4-2 ルテニウム触媒による 1,6-ジイン基質の二重シクロプロパン化反応

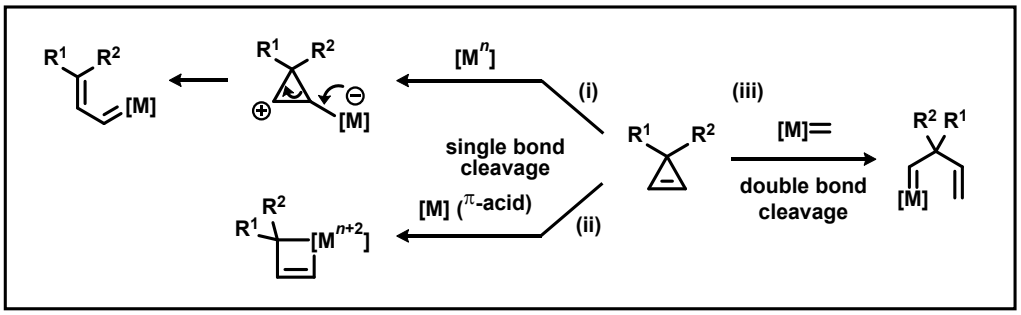
その後も、山本らを中心に、ルテナシクロペンタトリエンを活用した分子変換反応の開発研究がなされた[4]。Cp*RuCl(cod)を触媒として用いる[2+2+2]付加環化反応は、ルテナシクロペンタトリエンと不飽和分子などが反応することで、様々な芳香族化合物を与える[5]。とりわけ、不飽和分子としてアルキンを用いる、アルキンの環化三量化反応は、有用なベンゼン誘導体合成法である（**Scheme4-3**）[5a–e]。



Scheme 4-3 ルテニウム触媒によるアルキンの環化三量化反応

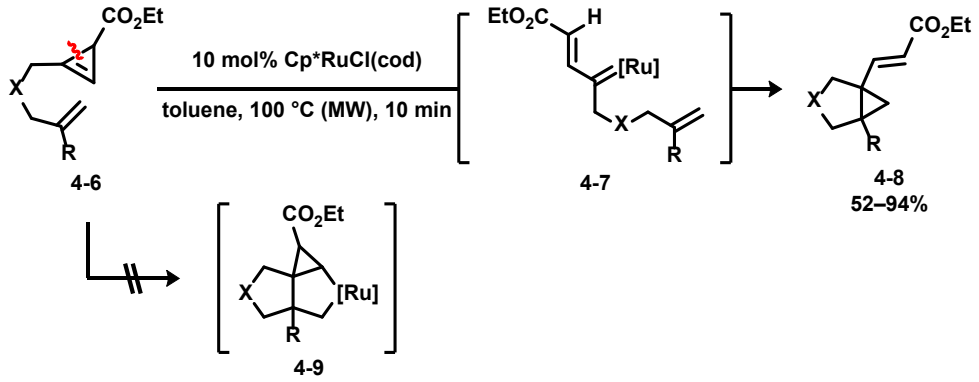
第 2 節　遷移金属錯体を用いるシクロプロペンの反応

環内に二重結合を有するシクロプロペンは、シクロプロパンよりも環歪みが大きく反応性が高い。遷移金属錯体を用いる炭素–炭素 σ 結合の切断様式は、**Scheme 4-4** に示す 3 つに大別できる。(i) π-酸性の高い遷移金属錯体による σ 結合の切断、(ii) 遷移金属錯体の酸化的付加による σ 結合の切断、(iii) 開環メタセシスによる二重結合の切断である。



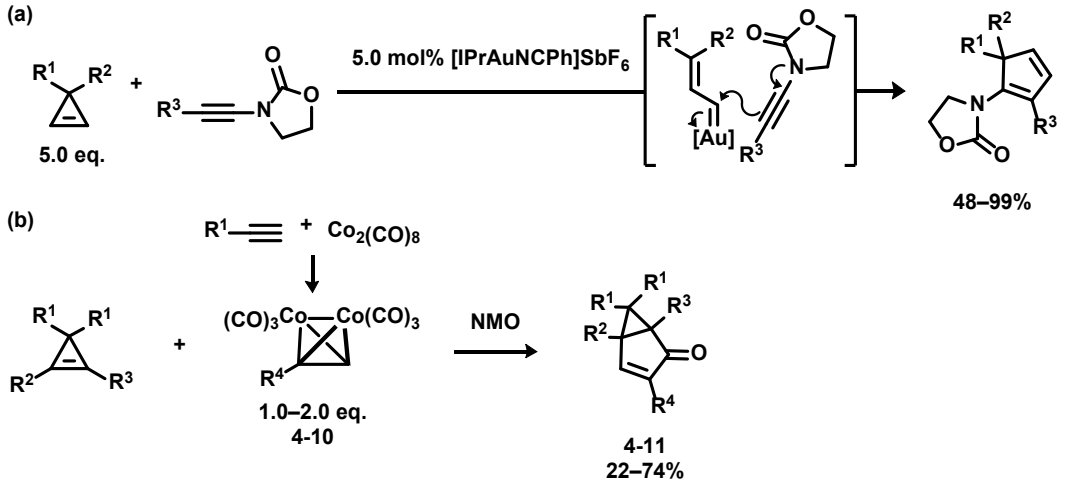
Scheme 4-4 遷移金属錯体によるシクロプロペンの炭素–炭素 σ 結合切断

（**Scheme 4-4i**）の反応性を利用した分子変換反応は多岐に渡る[6]。例えば、シクロプロペンを含む 1,6-ジエン基質 **4-6** に、ルテニウム錯体を触媒として作用させると、ルテニウムビニルカルベノイド **4-7** を中間体とし、シクロプロパン生成物 **4-8** へと誘導される（**Scheme 4-5**）[6g]。この反応では、シクロプロペン単独の反応性が高いために、一般に 1,6-エンインの環化反応で形成されるロダシクロペンテン中間体（**4-9**）を形成しないと考えられている。



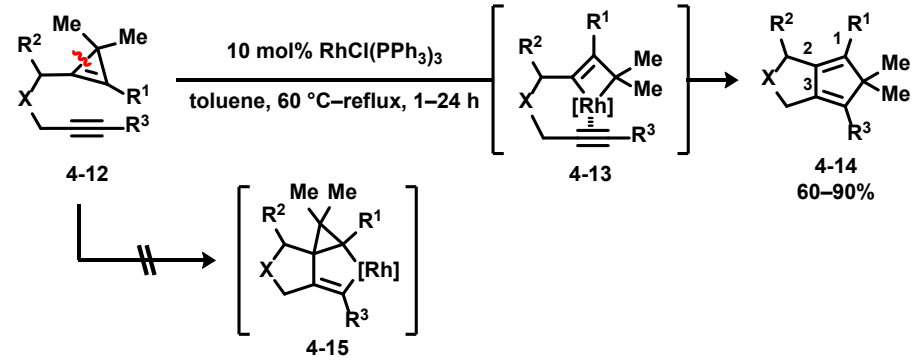
Scheme 4-5 ルテニウム触媒によるシクロプロペンとアルケンの環化異性化反応

シクロプロペンとアルキンを基質に用いた反応は、様々な炭素環骨格を構築できる。例えば、金触媒を用いるシクロプロペンとイナミドの[3+2]付加環化反応では、シクロペンタジエン誘導体が得られる（**Scheme 4-6a**）[7]。この反応も、メタルビニルカルベノイドを中間体とすると考えられている。一方、シクロプロペンの σ 結合が切断されるこの反応に対して、オクタカルボニルコバルト錯体とアルキンから調製される **4-10** とシクロプロペンの Pauson–Khand 反応では、シクロプロペンの π 結合のみが切断され、シクロプロパン環をそのままに残した **4-11** が得られることが知られている（**Scheme 4-6b**）[8]。



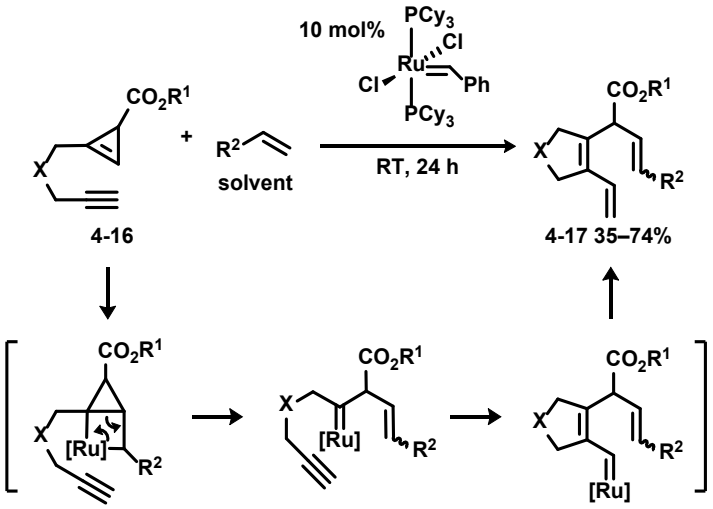
Scheme 4-6 シクロプロペンとアルキンの反応

柴田らは、（**Scheme 4-4ii**）の反応性を利用することで、シクロペンタジエンの合成に成功している（**Scheme 4-7**）[9]。ロジウム触媒を用いるシクロプロペン-イン **4-12** の環化異性化反応では、ロジウム錯体の酸化的付加によって生成するロダシクロブテン **4-13** において、分子内アルキンへの転移挿入と続く還元的脱離が進行し、2,3-縮環シクロペンタジエン **4-14** が得られる。この反応でも、シクロプロペン単独の反応性の高さゆえに、**4-15** に示すルテナサイクルは形成されないと考えられている。



Scheme 4-7 ロジウム触媒によるシクロプロペン-インの環化異性化反応

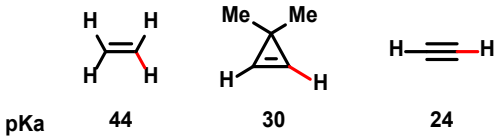
一方で、シクロプロペンの二重結合を切断する方法は、確立された開環メタセシスを利用するものに限られる（**Scheme 4-4iii**）。Shi らは、スチレンなどの溶媒中で、グラブス第一世代触媒とシクロプロペン-イン基質 **4-16** を反応させることで、環化生成物 **4-17** を得た（**Scheme 4-8**）[10]。彼らは、想定反応機構の一つとして、シクロプロペンの開環メタセシスに続くアルキンとの環化を提唱している。



Scheme 4-8 グラブス第一世代触媒によるシクロプロペン-インの環化反応

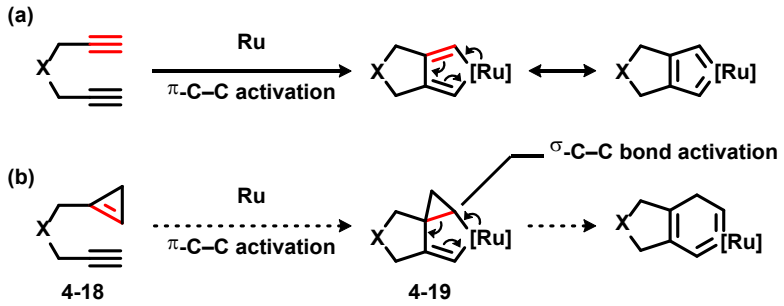
第 3 節　シクロプロペン-イン基質を用いる新たな反応設計

シクロプロパンの炭素–炭素結合の π 結合性が増していることを踏まえれば、シクロプロペン中のアルケンはアルキンに似た性質を示すはずである。実際、Allen らは、計算化学的手法を用いることで、シクロプロペンのビニル炭素原子が環外の置換基との結合に $sp^{1.19}$ 混成軌道を使っていることを明らかにしている [11]。これは、対応するアルキンの混成軌道（sp 混成軌道）に近い。実際、ジメチルシクロプロペンのビニル位炭素–水素結合は、エチレンよりもアセチレンに近い酸性度を示す（**Scheme 4-9**）[12]。



Scheme 4-9 エチレン、ジメチルシクロプロペンおよびアセチレンの酸性度

このようなシクロプロペンの性質とルテニウム錯体存在下における 1,6-ジインの反応性（**Scheme 4-10a**）を踏まえれば、シクロプロペン-イン **4-18** とルテニウム錯体はシクロプロパンが縮環したルテナサイクル **4-19** になると考えられる（**Scheme 4-10b**）。さらに、**4-19** において、π 結合性が増しているシクロプロパンの炭素–炭素結合が活性化されるのではないかと期待した。

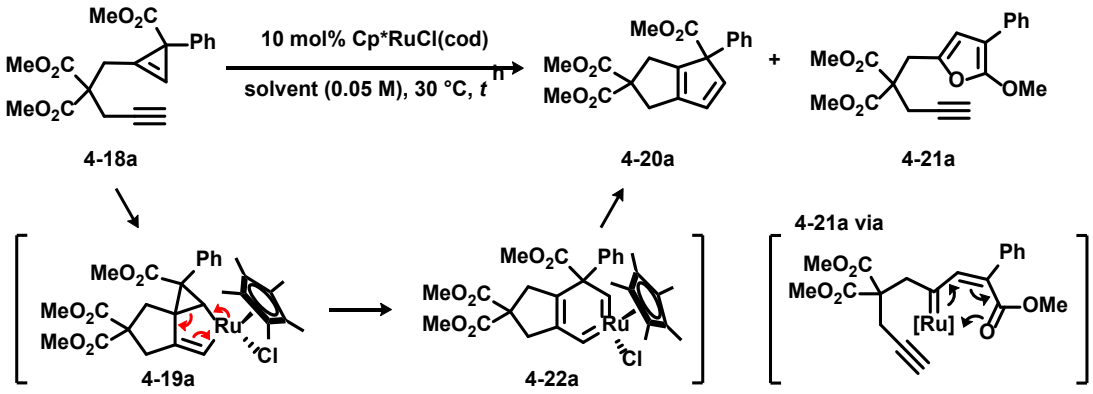


Scheme 4-10 ルテニウム錯体存在下での 1,6-ジインの反応と期待されるシクロプロペン-インの反応

第 4 節　反応条件の検討

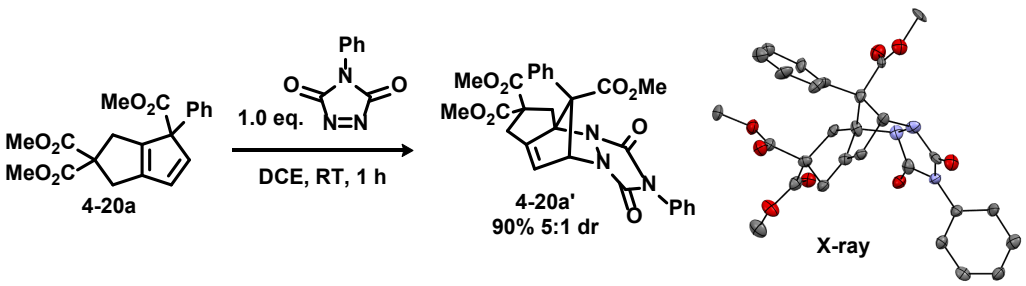
マロン酸ジメチルをテザーとするシクロプロペン-イン **4-18a** をモデル基質として、ジクロロメタン中、反応温度 30 ℃にて、10 mol%の Cp*RuCl(cod)を用いると、3 時間で **4-18a** は完全に消失し、1,2-縮環シクロペンタジエン **4-20a** とフラン誘導体 **4-21a** が得られた（**Table 4-1**, entry 1）。Diels–Alder 反応により **4-20a** を **4-20a'** へと誘導し、X 線結晶構造解析にてその構造を確認した（**Scheme 4-11**）。**4-20a** は、ルテナサイクル **4-19a** を形成した後に、6 員環ルテニウムビスカルベノイド **4-22a** を与えるようにして、シクロプロパン環が開環することで得られる生成物だと考えられる。また、**4-21a** は、既知のルテニウムビニルカルベノイドを中間体とする環化異性化反応によって得られたものであり [6b]、シクロプロペンの反応性の高さが伺える。続いて、溶媒を検討したところ、$PhCF_3$ を用いると、反応時間 1 時間で **4-18a** が完全に消失し、**4-20a** が 67%収率で得られた（entries 2–5）。続いて、反応溶液の濃度を検討したところ、0.03 M に希釈することで、単離収率 79%で所望の生成物を得ることができた（entries 6 and 7）。また、Cp*RuCl(cod)の前駆体のオリゴマーである $[Cp^*RuCl_2]_2$ は、Cp*RuCl(cod)よりも触媒効率が劣ることが分かり（entry 8）、1,6-ジインの環化に有効なカチオン性ルテニウム錯体 $[Cp^*Ru(NCMe)_3]PF_6$ を用いた反応では **4-20a** の生成を確認することができなかった（entry 9）。以上の検討から、entry 6 を最適条件として、以降の調査を続けることとした。

Table 4-1 ルテニウム触媒によるシクロプロペン-インの環化異性化反応と反応条件の検討 [a]



entry	solvent	*t* (h)	conv. (%)	**4-20a** (%)[b,c]	**4-21a** (%)[b]
1	DCM	3	>99	46	3
2	DCE	3	>99	66	6
3	DMF	1	>99	58	8
4	$PhCF_3$	1	>99	67	<1
5	toluene	5	>99	56	2
6[d]	$PhCF_3$	1.5	>99	82 (79)	3
7[e]	$PhCF_3$	1	98	52	4
8[f]	DCE	6	75	32	<1
9[g]	DCE	6	6	0	4

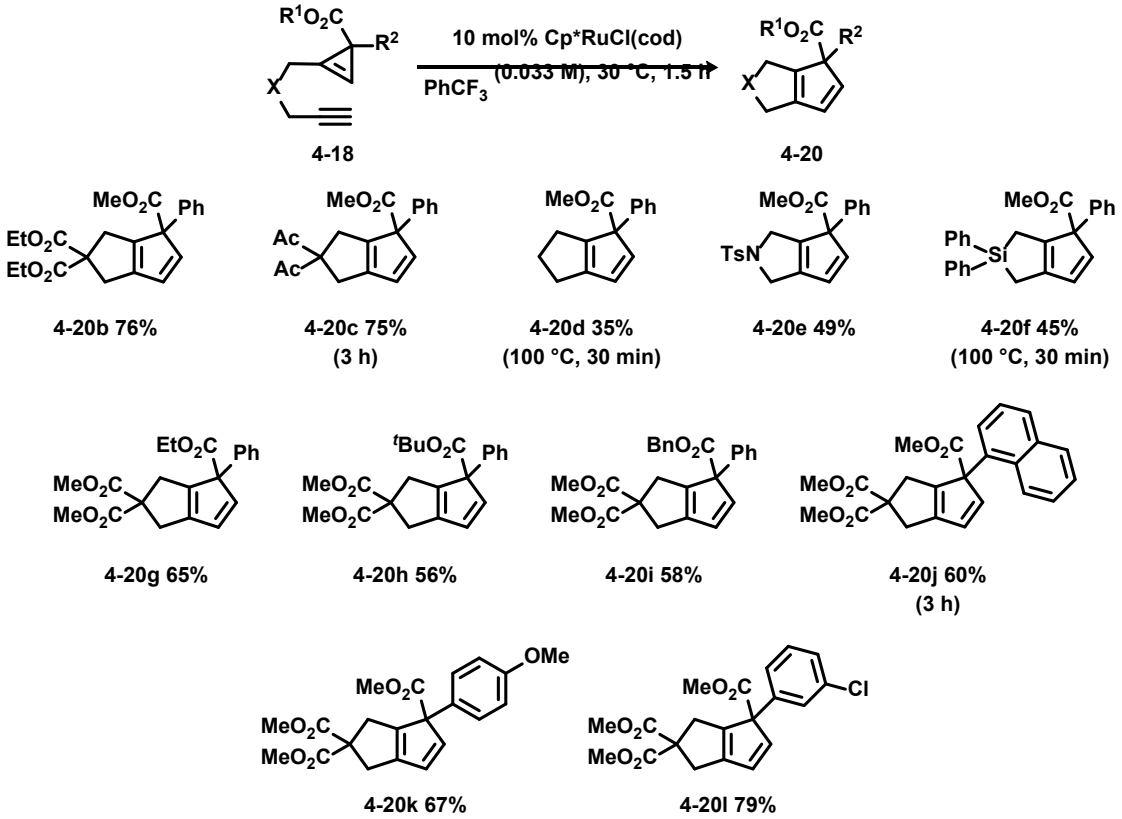
[a]0.1 mmol で反応を行った。[b]NMR 収率。[c]括弧内は単離収率。[d]反応濃度 0.03 M で反応を行った。[e]反応濃度 0.1 M で反応を行った。[f]10 mol%の$[Cp^*RuCl_2]_n$を用いた。[g]10 mol%の$[Cp^*Ru(NCMe)_3]PF_6$を用いた。



Scheme 4-11 4-20a の誘導化と X 線結晶構造解析

第 5 節　基質適用範囲の調査

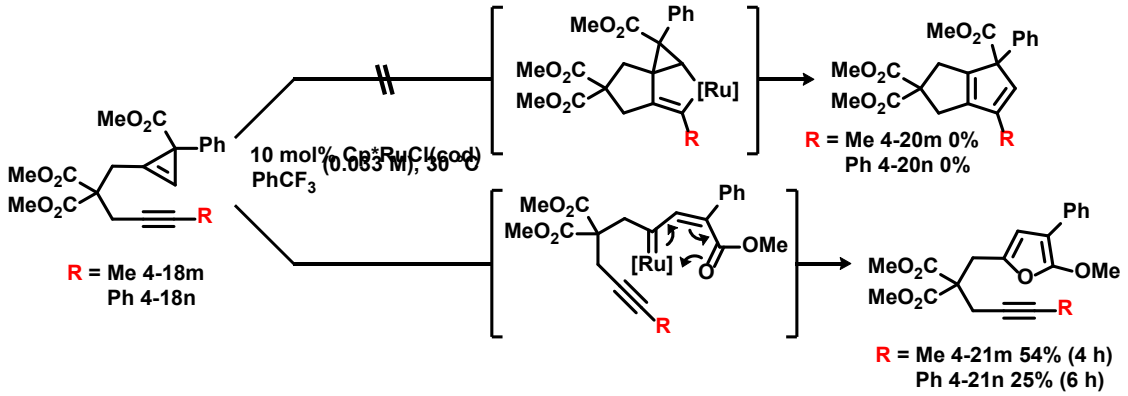
最初に、シクロプロペン-インのテザー部位 X が本反応に与える影響を調査した（**Scheme 4-12**）。マロン酸ジエチル（**4-18b**）とアセチルアセトン（**4-18c**）をテザーとする基質を用いた反応は、良好な収率で **4-20b** と **4-20c** を与えた。続いて、X にトシルアミド（**4-18d**）とメチレン部位（**4-18e**）を有する基質からは、低収率で **4-20d** と **4-20e** が得られた。**4-20d** と同様に、シリコンテザー（**4-20f**）を有する縮環シクロペンタジエンを得るためには、反応温度を 100 ℃に昇温する必要があった。これらのことから、本反応は、テザー部位 X の Thorpe–Ingold 効果の影響を大きく受けるものと考えられる。次に、シクロプロペン上に様々な置換基を有する基質を検討した。エチルエステル（**4-18g**）、^{t}Bu エステル（**4-18h**）およびベンジルエステル（**4-18i**）を有する基質からも、それぞれ良好な収率で **4-20g**、**4-20h**、**4-20i** が得られた。1-ナフチル基を導入した基質（**4-18j**）の反応は、反応時間 3 時間を要し、収率 60%で **4-20j** を与えた。そのほか、4-メトキシフェニル基（**4-20k**）や 3-クロロフェニル基（**4-20l**）が 4 級炭素上に導入された縮環シクロペンタジエンの合成に成功した。



[a]0.1 mmol で反応を行った。

Scheme 4-12 エステルを有する基質の基質適用範囲の調査 [a]

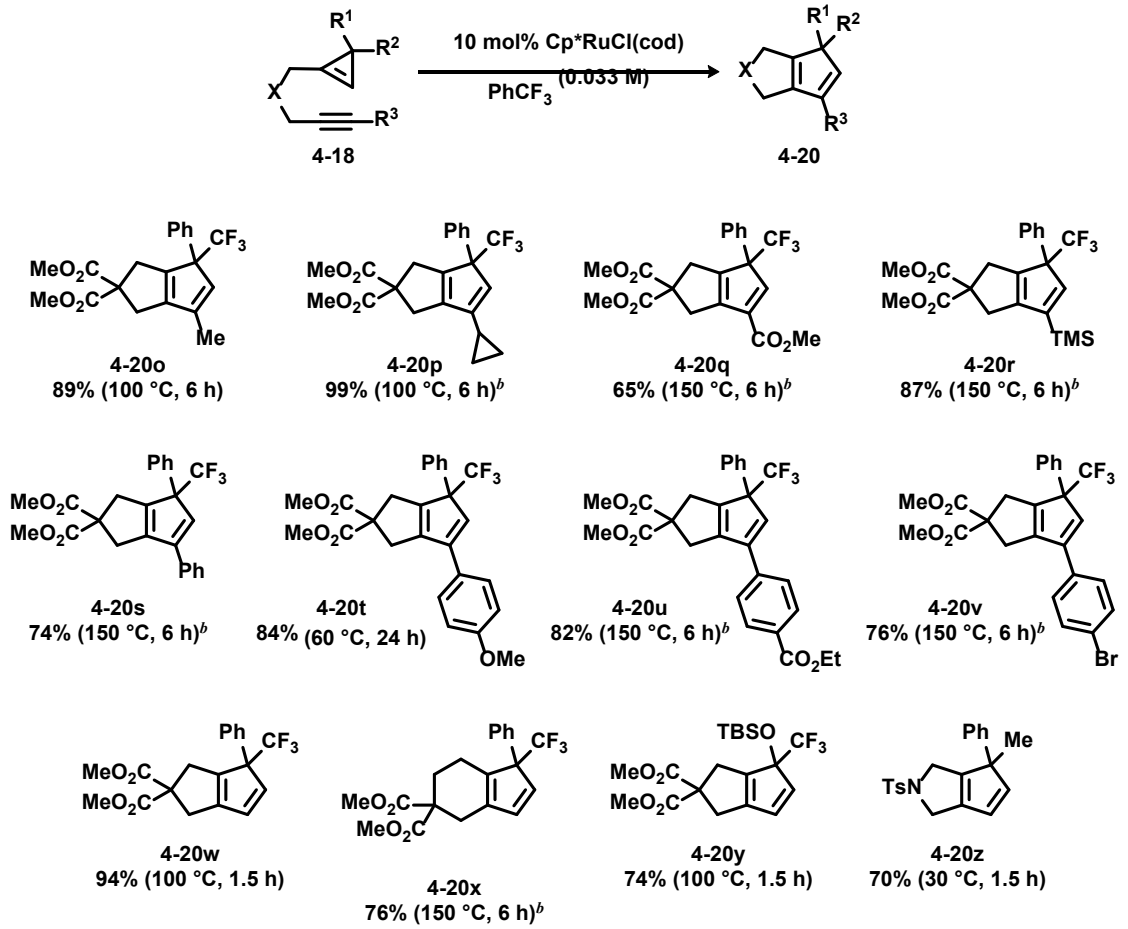
しかし、アルキン末端にメチル基（**4-18m**）とフェニル基（**4-18n**）を有する基質に本反応を適用したところ、目的の生成物である **4-20m** および **4-20n** の生成は確認できず、フラン誘導体 **4-21m** および **4-21n** を唯一の生成物として得る結果となった（**Scheme 4-13**）。これは、アルキン末端置換基の立体効果によりルテナサイクルの形成が抑制され、シクロプロペンとルテニウム触媒の反応によるビニルカルベノイドの形成が優先して進行したためだと考えられる。



Scheme 4-13 内部アルキン基質を用いる本反応の問題

これを踏まえて、本反応を内部アルキン基質にも適用できるようにするべく、フラン誘導体の生成を防ぐ目的で、エステルを同様の電子求引基であるトリフルオロメチル基に変更した基質を設計した。その基質適用範囲の調査の結果を **Scheme 4-14** に示す。アルキン末端にメチル基を有する基質 **4-18o** を用いた反応は、反応温度を 100 ℃に昇温することで、良好な収率で所望の **4-20o** を与えた。また、アルキン末端にシクロプロピル基を導入した基質 **4-18p** は、シクロプロパンをそのままに残した **4-20p** へ変換されたことから、本反応では選択的にシクロプロペンの二重結合が活性化されていることが伺える。プロピオレート基質 **4-18q** は、反応温度 100 ℃では反応が進行しなかったため、封管を用いて 150 ℃で反応させたところ、収率 65%で **4-20q** を得ることができた。そのほか、トリメチルシリル基を有する縮環シクロペンタジエン **4-20r** も合成することができた。また、アルキン末端にフェニル基を導入した基質 **4-18s** からも、良好な収率で **4-20s** が得られることが分かった。4-メトキシフェニル基を有する基質 **4-18t** を用いる反応は、60 ℃で進行したものの、電子求引性の 4-エトキシカルボニルフェニル基（**4-18u**）や 4-ブロモフェニル基（**4-18v**）を導入した場合、反応を進行させるために、150 ℃の高温が必要であった。1,6-シクロプロペン-イン **4-18w** を用いた反応は、問題なく進行し、高い収率で **4-20w** を得た。**4-18w** と比較して、ルテナサイクルの形成が著しく遅くなると予想された 1,7-シクロプロペン-イン **4-18x** からは、収率 76%で **4-20x** を得ることに成功した。そのほか、シクロプロペン上のシロキシ基（**4-18y**）は本反応に許容されることが分

かった。また、**4-18z** を用いた反応が円滑に進行していることから電子求引基は必須ではないことが示唆された。



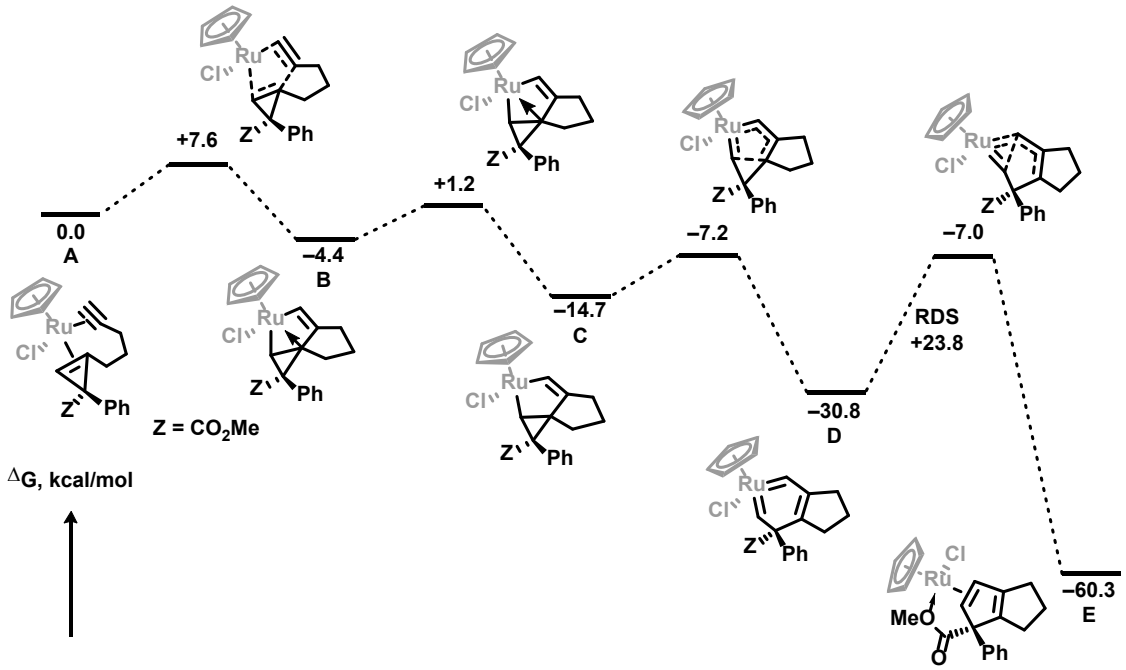
[a]0.1 mmol で反応を行った。[b]20 mol%の Cp*RuCl(cod)を用いて、反応を行った。

Scheme 4-14 トリフルオロメチル基などを有する基質の基質適用範囲の調査

第 6 節　計算化学的手法によるシクロプロペン-インの環化異性化反応の検証

想定しているシクロプロペンの活性化機構を検証するために DFT 計算を行った（**Scheme 4-15**）。計算効率を考慮し、シクロペンタジエニル錯体を用いた反応をモデルとした。まず、錯体 **A** の酸化的環化により、歪んだルテナサイクル **B** を経由し、平面型のルテナサイクル **C** が形成される。次に、6 員環ルテニウムビスカルベノイド **D** を与えるようにして、シクロプロパン環が開環する。最後に、**D** の還元的脱離により、錯体 **E** が生成する。この反応の律速段階は還元的脱離であり、その活性化障壁は 23.8

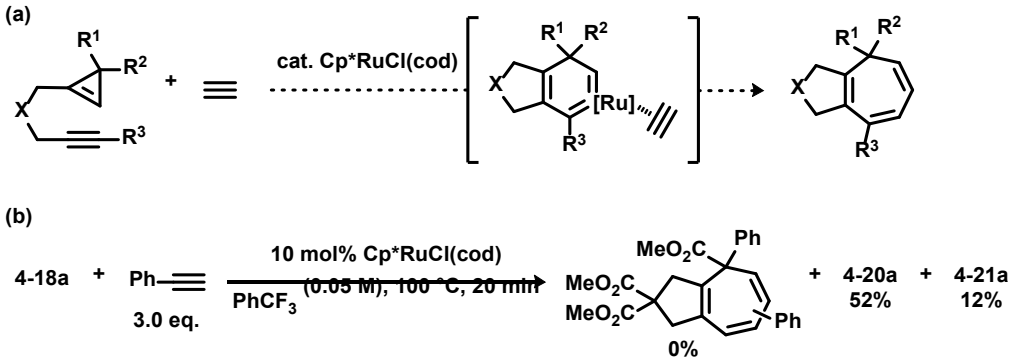
kcal/mol と見積もられた。全体の反応は、60.3 kcal/mol の発エルゴン過程であり、想定している活性化機構が妥当であることが分かった。



Scheme 4-15 DFT 計算によって支持される反応機構

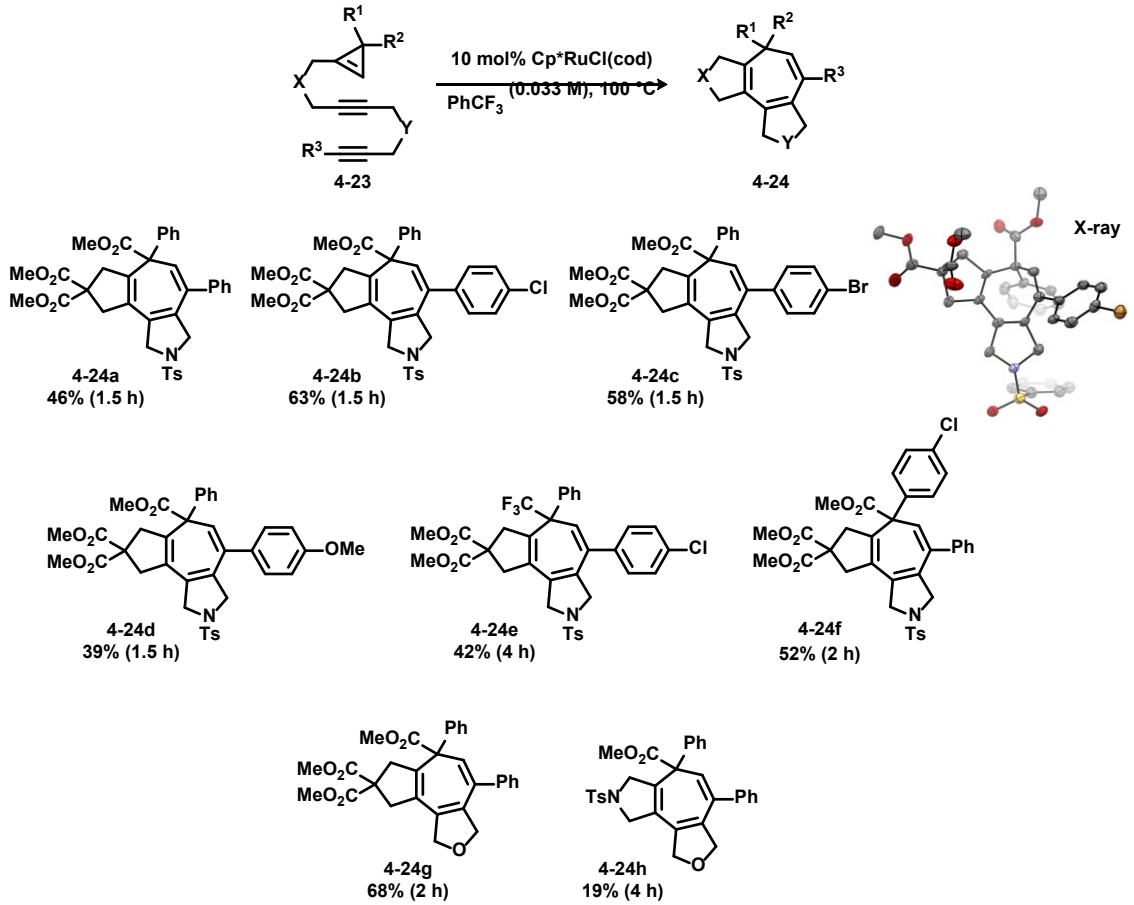
第 7 節　分子間反応の検討とシクロプロペン-ジイン基質の設計

第 1 節にて説明したように、ルテニウム触媒を用いる 1,6-ジインとアルキンの[2+2+2]付加環化反応では、ルテニウム錯体と 1,6-ジインから生じる 5 員環ルテニウムビスカルベノイドにアルキンが反応することで、様々なベンゼン誘導体などの芳香族化合物が得られる。一方、DFT 計算により、本反応は 6 員環ルテニウムビスカルベノイド中間体を経て進行することが示唆された。そこで、sp^3 炭素が組み込まれた中間体にアルキンを反応させることで、非芳香族化合物であるシクロヘプタトリエンが得られるのではないかと考えた（**Scheme 4-16a**）。そこで、3 当量のフェニルアセチレンの存在下、**4-18a** を用いて反応を行ったが、所望の生成物は得られず、**4-20a** および **4-21a** がそれぞれ 52%収率および 12%収率で得られた（**Scheme 4-16b**）。



Scheme 4-16 分子間反応の作業仮説と検討

所望のシクロヘプタトリエンが得られなかったのは、6 員環ルテニウムビスカルベノイドにアルキンが挿入できなかったためだと考えた。そこで、アルキンの挿入反応がより容易になるように、シクロプロペン-インの分子内にアルキンを導入したシクロプロペン-ジイン基質 **4-23** を設計した。ルテニウム触媒を **4-23a** に作用させたところ、期待通り **4-24a** を得ることに成功した（**Scheme 4-17**）。その他、末端フェニル基のパラ位にそれぞれクロロ基、ブロモ基およびメトキシ基を導入した **4-23b**、**4-23c** および **4-23d** を本反応条件に付したところ、対応する生成物 **4-24b**、**4-24c** および **4-24d** をそれぞれ 68%、61%および 46%で得ることができた。また、X 線結晶構造解析により **4-24c** の構造を明らかにした。続いて、シクロプロペン上にトリフルオロメチル基（**4-23e**）や 4-クロロフェニル基（**4-23f**）を有する基質を用いた反応で、それぞれ対応する **4-24e** および **4-24f** が得られることが分かった。1,6-ジインのテザー部位 Y をトシルアミドからエーテルに変更しても、**4-24g** は良好な収率で得られたが、シクロプロペン-インのテザー部位 X をマロン酸ジメチルからトシルアミドに変更すると、**4-24h** の収率が大きく低下することが分かった。このことから、**4-24** を得るためには、Y よりも X の方に、より Thorpe–Ingold 効果の影響が大きい置換基を導入する必要があることが示唆された。

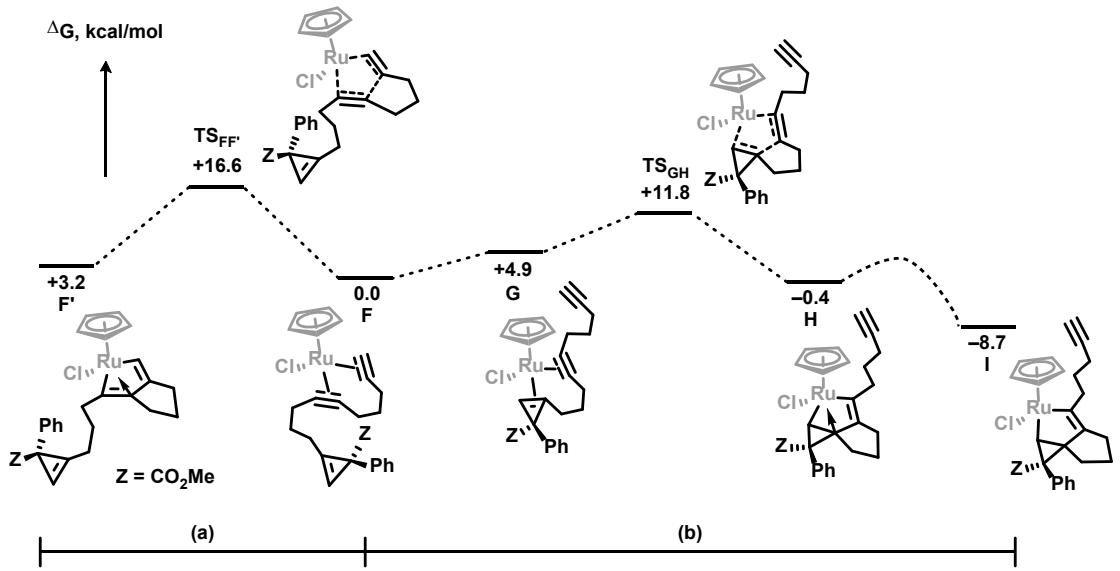


[a]0.1 mmol で反応を行った。

Scheme 4-17 シクロプロペン-ジインの基質適用範囲の調査 [a]

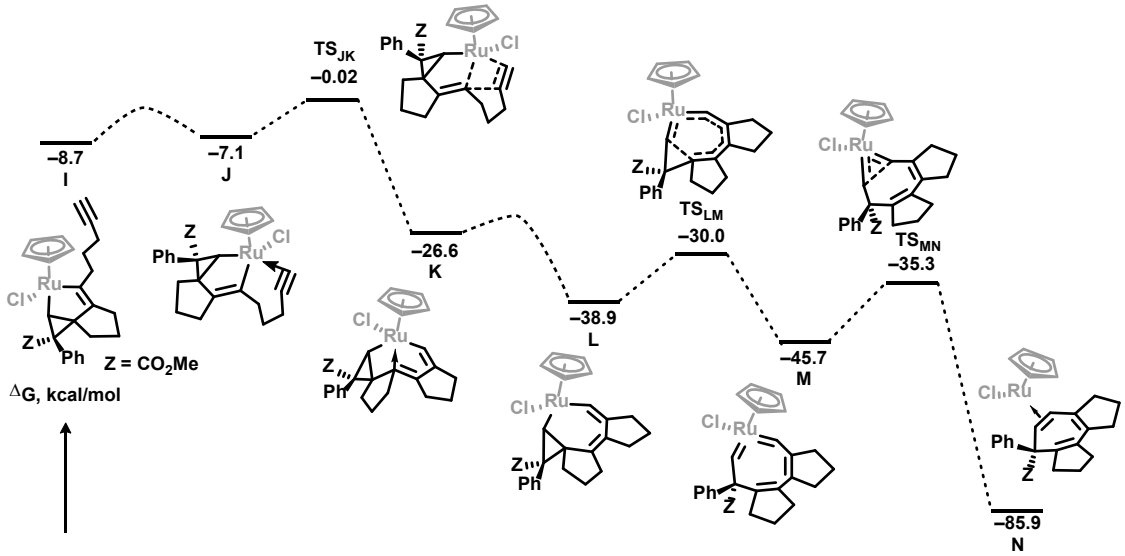
第 8 節　計算化学的手法によるシクロプロペン-ジインの環化異性化反応の検証

シクロプロペン-ジインを用いた反応がどのようにして進行しているのかについて考察する。これまでのルテニウム触媒反応の知見に基づけば、シクロプロペン-ジインの環化異性化反応は、1,6-ジインの環化（**Scheme 4-18a**）もしくはシクロプロペン-インの環化（**Scheme 4-18b**）のどちらかから反応が進行していると考えられる。どちらの経路で反応が進行するのかを解明すべく、DFT 計算を行ったところ、錯体 **F** を基準とした 1,6-ジインの環化の活性化障壁が 16.6 kcal/mol であるのに対して、シクロプロペン-インの環化の活性化障壁は 11.8 kcal/mol であり、本反応ではシクロプロペン-インの環化の方が速度論的に有利であることが分かった。続くシクロプロパンが縮環したルテナサイクル **I** の形成は、8.7 kcal/mol の発エルゴン反応であることが示された。



Scheme 4-18 DFT 計算により支持される反応機構 1

その後の DFT 計算によって支持される反応機構を **Scheme 4-19** に示す。**I** における分子内のアルキン挿入によって、錯体 **J** および錯体 **K** を経由し、シクロプロパンが縮環したルテナサイクル **L** となる。当初、6 員環ルテニウムビスカルベノイドとアルキンが反応することを期待していたが（**Scheme 4-16a**）、6 員環ルテニウムビスカルベノイドへ環拡大する前の **I** において、アルキン挿入が起こることが示唆された。続いて、8.9 kcal/mol の活性化障壁で、シクロプロパンが開環し、ルテナシクロオクタテトラエン **M** が生じる。最後に、還元的脱離によって、錯体 **N** となる。



Scheme 4-19 DFT 計算により支持される反応機構 2

第 9 節　結論

ルテニウム触媒を用いるシクロプロペン-インの環化異性化反応では、1,2-縮環シクロペンタジエンが得られることを見出した。計算化学的手法により、シクロプロパンが縮環したルテナサイクルにおいて、6 員環ルテニウムビスカルベノイドを与えるようにして、シクロプロパンが開環することで、シクロプロペンの二重結合が切断されている可能性が高いことを明らかにした。また、シクロプロペン-ジインを用いた反応は、縮環シクロヘプタトリエンを与えた。DFT 計算によって、この反応では、6 員環ルテニウムビスカルベノイドが形成される前に分子内アルキンの挿入が起こることが示唆された。

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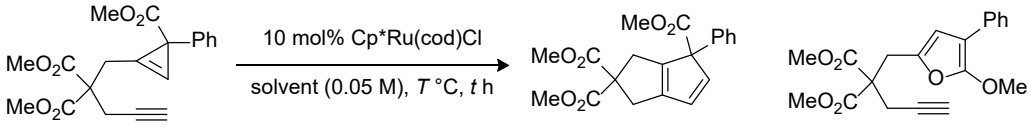
実験項

General considerations: All air- and moisture-sensitive reactions were performed under an argon (Ar) atmosphere. Analytical thin layer chromatography was performed using 0.25 mm silica gel plate (Merck TLC Silica gel 60 F_{254}). Column chromatography was performed on silica gel (Cica silica gel 60N) with solvents specified below. Melting points were recorded on SRS OptiMelt MPA100. NMR spectra were recorded on JEOL ESC-400 spectrometer (^{1}H/400 MHz and ^{13}C/100 MHz) for samples in $CDCl_3$ solutions at 25 ˚C. ^{1}H NMR chemical shifts are reported in terms of chemical shift (δ, ppm) relative to the signal at δ 0.00 ppm for internal tetramethylsilane. ^{13}C NMR spectra were fully decoupled and are reported in terms of chemical shift (δ, ppm) relative to the triplet at δ 77.0 ppm for $CDCl_3$. ^{19}F NMR spectra are reported in terms of chemical shift (δ, ppm) relative to the singlet at δ −63.7 ppm for *a*,*a*,*a*-trifluorotoluene as an external standard. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; sept, septet; m, multiplet. Coupling constants are reported in Hz. Infrared spectra were recorded on JASCO FT/IR-230 spectrometer. High-resolution mass spectra were recorded on JEOL JMS-T100LP (TOF) mass spectrometer.

Reagents and Solvents: Ruthenium catalysts Cp*RuCl(cod)[1] and $[Cp^*RuCl_2]_n$[2] were prepared according to the report. Dry DCM was distilled from calcium hydride under Ar atmosphere and stored over 4 Å molecular sieves. Other solvents and reagents were purchased from chemical suppliers (Aldrich, Kanto Chemical, TCI, and Wako) and used as received.

1. Optimization of Reaction Conditions

Table S1 Optimization of reaction conditions[a,b]



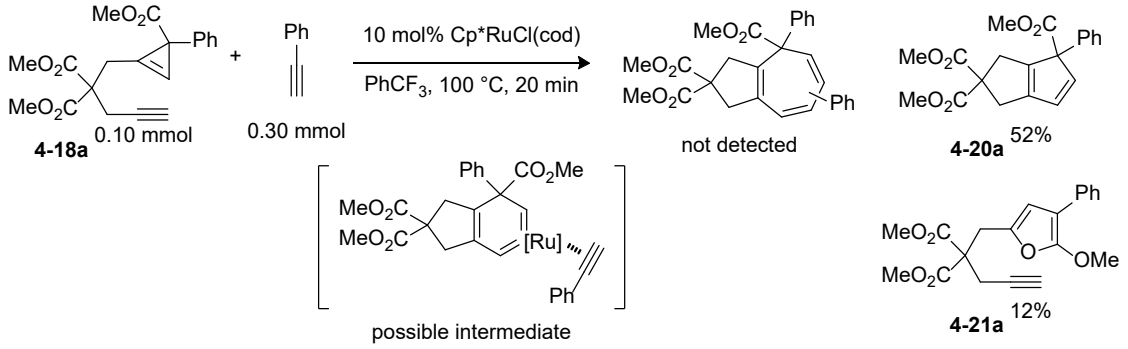
4-18a **4-20a** **4-21a**

entry	solvent	*T* (°C)	*t* (h)	conv. (%)	**4-20a** (%)	**4-21a** (%)	memo
1	$PhCF_3$	100	0.25	>99	62	10	
2	$PhCF_3$	30	1	>99	67	trace	
3	DMF	30	1	>99	58	8	
4	DCE	30	3	>99	66	6	
5	DCM	30	3	>99	46	3	
6	toluene	30	5	>99	56	2	
7	$PhCF_3$	30	1.5	>99	82 (79)[c]	3	$PhCF_3$ 0.033 M
8	$PhCF_3$	30	1	98	52	4	$PhCF_3$ 0.10 M
9	DCE	30	6	75	32	ND[d]	$[Cp^*RuCl_2]_n$ was used.
10	DCE	80	14	92	ND[d]	2	$[Cp^*Ru(NCMe)_3]PF_6$ was used.

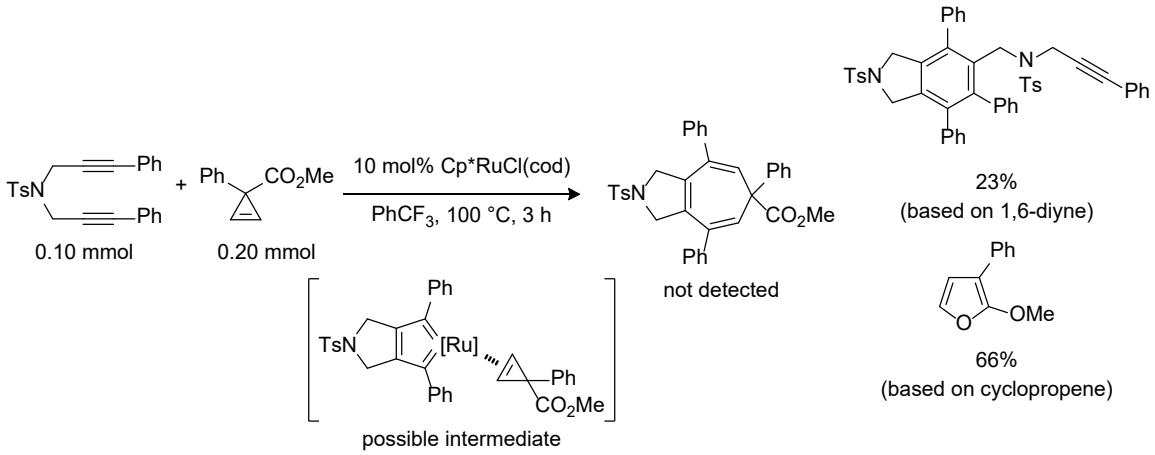
[a]Reactions were performed on a 0.1 mmol scale. [b]NMR yield. [c]Isolated yield shown in parentheses. [d]ND = not detected.

2. Intermolecular Reactions

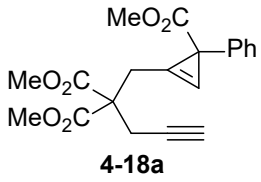
The computational study of the Ru-catalyzed cycloaddition of cyclopropenynes indicates that the reaction proceeds via the six-membered ruthenium biscarbenoid **D** (Scheme 4-15). We assumed that the insertion of an alkyne into this intermediate could lead to the formation of a cycloheptatriene. However, the reaction of **4-18a** in the presence of phenylacetylene resulted in the formation of **4-20a** as a major product and the desired cycloheptatriene product was not observed. This indicates that the expected intermolecular insertion of phenylacetylene into the six-membered ruthenacycle does not proceed. The fact that cycloheptatriene products were obtained via not the intermolecular reaction of cyclopropenynes and monoalkynes but intramolecular reactions of cyclopropenediynes **4-23** implies that the insertion of a pendant alkyne in the ruthenacycle **I** should proceed prior to the formation of the six-membered ruthenium biscarbenoid, which is consistent with the result of the DFT study (Scheme 4-19).



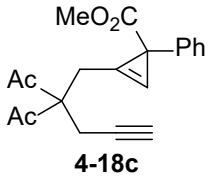
We also demonstrated the intermolecular reaction of 1,6-diyne and cyclopropene. However, the corresponding cycloheptatriene was not obtained and only 1,6-diyne dimer and furan were obtained, which implies that cyclopropenes readily reacts with the Ru catalyst to afford the corresponding furans and the insertion of cyclopropene into the five-membered ruthenacycle intermediate unlikely to proceed in this reaction conditions. This result is consistent with the result of the computational study: the cycloaddition of cyclopropenediynes **4-23** is initiated by the ene-yne coupling rather than by the yne-yne coupling (Scheme 4-18).



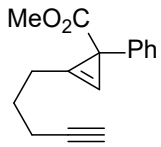
3. Synthesis and Characterization of Cyclopropenynes 4-18



4-18a was synthesized under modified conditions, referring to the previous report[3]. To a 20 mL two-necked flask was added dry DCM (2.0 mL), $Rh_2(OAc)_4$ (8.8 mg, 0.020 mmol) and **S1a** (376 mg, 1.8 mmol) under Ar atmosphere. The homogeneous green solution was stirred at room temperature for 5 min. A solution of **S2** (395 mg, 2.2 mmol) in dry DCM (2.0 mL) was added to the reaction mixture over 1 h using a syringe pump. After completion of the addition, the reaction mixture was additionally stirred at room temperature for 30 min. The solvent was removed under reduced pressure. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 7:1) to furnish **4-18a** (382 mg, 54%). **Analytical data for 4-18a:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31–7.19 (m, 5H), 6.83 (t, *J* = 1.6 Hz, 1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.66 (s, 3H), 3.42 (dd, *J* = 17.6, 1.6 Hz, 1H), 3.36 (dd, *J* = 17.6, 1.6 Hz, 1H), 2.99 (dd, *J* = 17.6, 2.4 Hz, 1H), 2.93 (dd, *J* = 17.6, 2.4 Hz, 1H), 2.01 (t, *J* = 2.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.4, 169.62, 169.60, 141.4, 128.6 (2C), 128.5 (2C), 126.9, 116.5, 101.9, 78.8, 72.5, 56.2, 53.6, 53.5, 52.4, 32.9, 28.2, 23.4; IR (neat) 1738, 1721 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{20}H_{24}NO_6$ 374.1604; Found 374.1595.

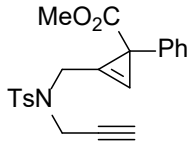


This compound was prepared in the same manner as described for **4-18a** using **S1c**[4] instead of **S1a** in 45% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-18c:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32–7.20 (m, 5H), 6.76 (t, *J* = 1.2 Hz, 1H), 3.67 (s, 3H), 3.46 (dd, *J* = 18.0 Hz, 1.2 Hz, 1H), 3.32 (dd, *J* = 18.0, 1.2 Hz, 1H), 2.99 (dd, *J* = 18.0, 2.4 Hz, 1H), 2.89 (dd, *J* = 18.0, 2.4 Hz, 1H), 2.18 (s, 3H), 2.07 (s, 3H), 1.99 (t, *J* = 2.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 202.8, 202.7, 174.7, 140.3, 127.9 (3C), 126.4 (2C), 116.4, 100.8, 78.6, 72.2, 69.3, 51.9, 32.2, 26.1, 26.0, 25.9, 20.9; IR (neat) 1719, 1702 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{20}H_{24}NO_4$ 342.1705; Found 342.1701.



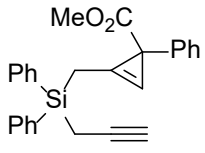
4-18d

This compound was prepared in the same manner as described for **4-18a** using 1,6-heptadiyne instead of **S1a** in 55% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-18d:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32–7.25 (m, 4H), 7.23–7.19 (m, 1H), 6.73 (t, *J* = 1.6 Hz, 1H), 3.69 (s, 3H), 2.70 (td, *J* = 7.2, 1.6 Hz, 2H), 2.24 (td, *J* = 7.2, 1.6 Hz, 2H), 1.96 (t, *J* = 2.4 Hz, 1H), 1.86–1.79 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 176.2, 142.0, 128.7 (2C), 128.5 (2C), 126.8, 120.5, 98.3, 83.7, 69.7, 52.4, 33.4, 26.1, 23.9, 18.3; IR (neat) 1718 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{16}H_{20}NO_2$ 258.1494; Found 258.1485.



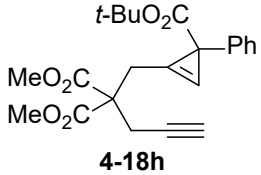
4-18e

This compound was prepared in the same manner as described for **4-18a** using **S1e**[5] instead of **S1a** in 54% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-18e:** pale-yellow amorphous solid; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.31–7.27 (m, 4H), 7.24–7.21 (m, 3H), 6.80 (t, *J* = 1.6 Hz, 1H), 4.52 (dd, *J* = 17.2 Hz, 1.6 Hz, 1H), 4.46 (dd, *J* = 17.2 Hz, 1.6 Hz, 1H), 4.16 (dd, *J* = 18.4, 2.4 Hz, 1H), 4.06 (dd, *J* = 18.4, 2.4 Hz, 1H), 3.68 (s, 3H), 2.43 (s, 3H), 2.05 (t, *J* = 2.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.9, 144.3, 140.6, 136.0, 130.0 (2C), 128.6 (2C), 128.5 (2C), 128.1 (2C), 127.0, 116.0, 103.1, 76.5, 74.9, 52.5, 41.8, 37.0, 34.1, 21.9; IR (KBr) 1718 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{22}H_{22}NO_4S$ 396.1270; Found 396.1251.



4-18f

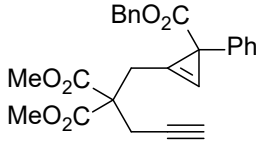
This compound was prepared in the same manner as described for **4-18a** using **S1f**[6] instead of **S1a** in 77% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-18f:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.54 (td, *J* = 8.0, 1.2 Hz, 4H), 7.45–7.33 (m, 7H), 7.24–7.22 (m, 1H), 7.19–7.16 (m, 3H), 6.51 (s, 1H), 3.46 (s, 3H), 2.72–2.64 (m, 2H), 2.06 (dd, *J* = 16.4, 3.0 Hz, 1H), 2.00 (dd, *J* = 16.4, 3.0 Hz, 1H), 1.90 (t, *J* = 3.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.7, 141.3, 134.7 (2C), 132.9, 132.6, 130.2 (2C), 130.1 (2C), 128.3 (2C), 128.00 (2C), 127.98 (2C), 127.9 (2C), 126.2, 117.6, 96.9, 80.8, 68.9, 51.7, 33.5, 10.0, 3.4; IR (neat) 1715 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{27}H_{28}NO_2Si$ 426.1889; Found 422.1868.



4-18h

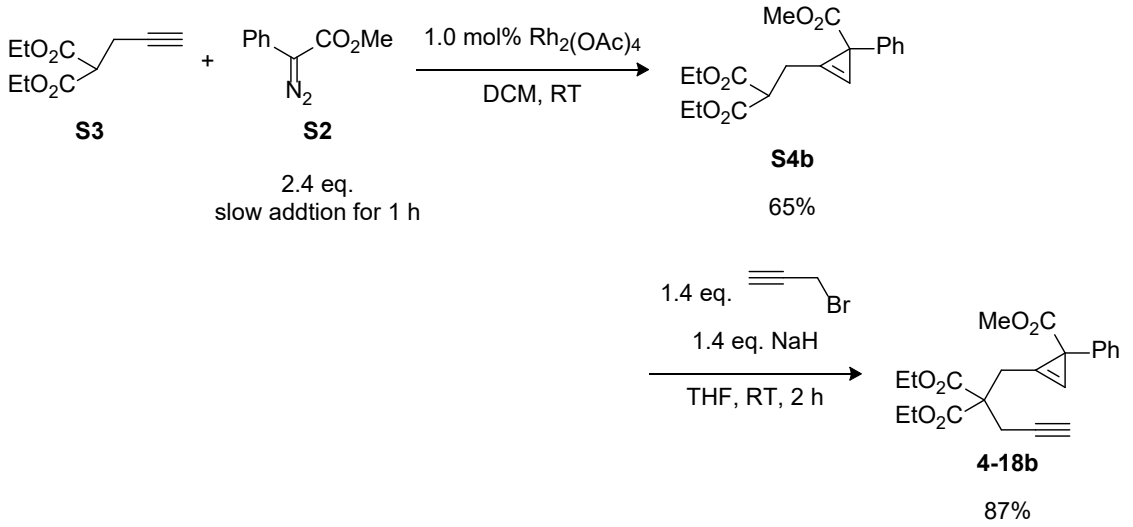
This compound was prepared in the same manner as described for **4-18a** using a corresponding diazo ester[7] instead of **S2** in 14% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-18h:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.29–7.22 (m, 4H), 7.20–7.15 (m, 1H), 6.77

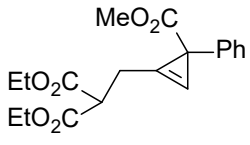
(t, J = 1.6 Hz, 1H), 3.74 (s, 3H), 3.65 (s, 3H), 3.39 (dd, J = 17.6, 1.6 Hz, 1H), 3.34 (dd, J = 17.6, 1.6 Hz, 1H), 2.96 (d, J = 2.4 Hz, 2H), 2.01 (t, J = 2.4 Hz, 1H), 1.43 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.7, 169.32, 169.29, 141.4, 128.1 (2C), 127.8 (2C), 126.1, 116.3, 101.1, 80.6, 78.4, 71.9, 55.8, 53.1, 53.0, 33.3, 28.1 (3C), 27.7, 23.0; IR (neat) 1741, 1712 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{27}O_6$ 399.1808; Found 399.1817.



4-18i

This compound was prepared in the same manner as described for **4-18a** using a corresponding diazo ester[8] instead of **S2** in 51% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-18i:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35–7.25 (m, 9H), 7.22–7.19 (m, 1H), 6.83 (s, 1H), 5.17 (d, J = 12.8 Hz, 1H), 5.09 (d, J = 12.8 Hz, 1H), 3.66 (s, 3H), 3.63 (s, 3H), 3.41 (d, J = 17.6 Hz, 1H), 3.36 (d, J = 17.6 Hz, 1H), 2.95 (dd, J = 17.6, 2.4 Hz, 1H), 2.90 (dd, J = 17.6, 2.4 Hz, 1H), 1.96 (t, J = 2.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.9, 169.8 (2C), 141.4, 136.9, 129.1 (2C), 128.8 (2C), 128.7 (2C), 128.6, 128.5 (2C), 127.1, 116.6, 101.8, 78.9, 72.6, 67.1, 56.4, 53.66, 53.75, 33.2, 28.4, 23.6; IR (neat) 1738, 1718 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{25}O_6$ 433.1651; Found 433.1625.

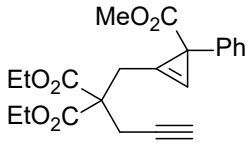




S4b

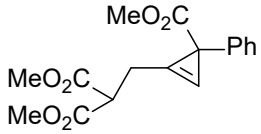
To a 50 mL two-necked flask was added dry DCM (10 mL), $Rh_2(OAc)_4$ (12.6 mg, 0.030 mmol) and **S3**[9] (900 mg, 3.1 mmol) under Ar atmosphere. The homogeneous green solution was stirred at room temperature for 5 min. A solution of **S2** (395 mg, 2.2 mmol) in dry DCM (2.0 mL) was added to the reaction mixture over 1 h using a syringe pump. After completion of the addition, the reaction mixture was additionally stirred at room temperature for 30 min. The

solvent was removed under reduced pressure. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 7:1) to furnish **S4b** (688 mg, 65%). **Analytical data for S4b:** orange oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31–7.18 (m, 5H), 6.80 (t, *J* = 1.2 Hz, 1H), 4.21–4.09 (m, 4H), 3.68 (s, 3H), 3.67 (t, *J* = 7.2 Hz, 1H), 3.17 (dd, *J* = 7.2, 1.2 Hz, 2H), 1.28–1.17 (m, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.6, 167.5 (2C), 140.6, 127.7 (2C), 127.6 (2C), 126.0, 117.2, 99.4, 61.3 (2C), 51.5, 49.3, 32.7, 23.6, 13.5 (2C); IR (neat) 1728 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{19}H_{26}NO_6$ 364.1760; Found 364.1744.



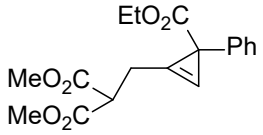
4-18b

To a solution of **S4b** (296 mg, 0.85 mmol) in dry THF (1.0 mL) was added NaH (60% dispersion in mineral oil, 46.7 mg, 1.15 mmol) at 0 °C under Ar atmosphere. The reaction mixture was stirred at room temperature for 10 min. To this reaction mixture was added propargyl bromide (100 μL, 1.33 mmol) and stirring was continued for 2 h at room temperature. The reaction was quenched with water. The aqueous phase was extracted with Et_2O. The combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in vacuo, the obtained crude product was purified by silica gel column chromatography (Hexane/AcOEt 10:1) to afford **4-18b** (269 mg, 87%). **Analytical data for 4-18b:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31–7.24 (m, 4H), 7.23–7.18 (m, 1H), 6.81 (t, *J* = 1.6 Hz, 1H), 4.26–4.07 (m, 4H), 3.67 (s, 3H), 3.41 (dd, *J* = 17.6, 1.6 Hz, 1H), 3.35 (dd, *J* = 17.6, 1.6 Hz, 1H), 2.98 (dd, *J* = 17.6, 2.4 Hz, 1H), 2.92 (dd, *J* = 17.6, 2.4 Hz, 1H), 2.00 (t, *J* = 2.4 Hz, 1H), 1.24 (t, *J* = 7.2 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.4, 169.24, 169.22, 141.4, 128.6 (2C), 128.5 (2C), 126.9, 116.6, 101.6, 78.9, 72.4, 62.6, 62.5, 56.1, 52.4, 32.9, 28.0, 23.2, 14.4, 14.3; IR (neat) 1735, 1723 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{22}H_{28}NO_6$ 402.1917; Found 402.1930.



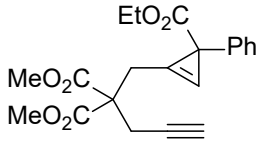
S4a

This compound was prepared in the same manner as described for **S4b** using a corresponding alkyne **S5**[9] instead of **S3** in 67% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for S4a:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31–7.19 (m, 5H), 6.81 (t, *J* = 1.2 Hz, 1H), 3.71 (t, *J* = 7.2 Hz, 1H), 3.71 (s, 3H), 3.68 (s, 6H), 3.24–3.13 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.9, 168.22, 168.20, 140.7, 127.93 (2C), 127.89 (2C), 126.3, 117.5, 99.8, 52.6 (2C), 51.9, 49.2, 33.1, 23.9; IR (neat) 1736 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{17}H_{19}O_6$ 319.1182; Found 319.1199.



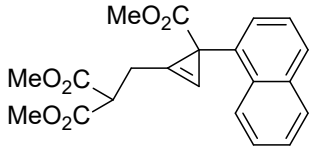
S4g

This compound was prepared in the same manner as described for **S4b** using a corresponding alkyne **S5**[9] and a corresponding diazo ester[8] instead of **S3** and **S2** in 78% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for S4g:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31–7.18 (m, 5H), 6.80 (t, *J* = 2.4 Hz, 1H), 4.15 (qd, *J* = 7.2, 2.4 Hz, 2H), 3.71 (t, *J* = 7.2 Hz, 1H), 3.71 (s, 3H), 3.67 (s, 3H), 3.18 (d, *J* = 7.2 Hz, 2H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.2, 168.01, 167.99, 140.7, 127.7 (2C), 127.6 (2C), 125.9, 117.2, 99.5, 60.4, 52.4 (2C), 49.0, 32.9, 23.7, 13.9; IR (neat) 1738 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{18}H_{21}O_6$ 333.1338; Found 333.1309.



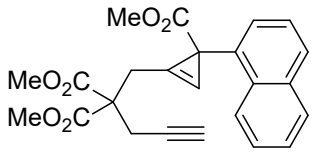
4-18g

This compound was prepared in the same manner as described for **4-18b** using **S4g** instead of **S4b** in 89% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-18g:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.30–7.24 (m, 4H), 7.22–7.17 (m, 1H), 6.82–6.81 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.73 (s, 3H), 3.65 (s, 3H), 3.41 (dd, *J* = 17.2, 1.2 Hz, 1H), 3.36 (dd, *J* = 17.2, 1.2 Hz, 1H), 2.99 (dd, *J* = 17.2, 2.4 Hz, 1H), 2.94 (dd, *J* = 17.2, 2.4 Hz, 1H), 2.02 (t, *J* = 2.4 Hz, 1H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.1, 169.9, 169.8, 141.6, 128.7 (2C), 128.6 (2C), 127.0, 116.7, 101.9, 79.0, 72.5, 61.5, 56.4, 53.8, 53.7, 33.1, 28.3, 23.6, 14.9; IR (neat) 1739, 1716 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{21}H_{23}O_6$ 371.1495; Found 371.1500.



S4j

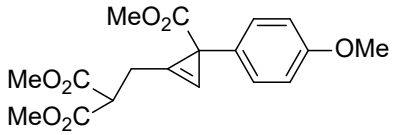
This compound was prepared in the same manner as described for **S4b** using a corresponding alkyne **S5**[9] and a corresponding diazo ester[10] instead of **S3** and **S2** in 46% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **S4j** was used for the next reaction without further purification because impurities could not be separated in this step.



4-18j

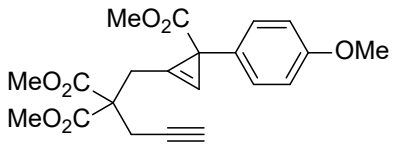
This compound was prepared in the same manner as described for **4-18b** using **S4j** instead of **S4b** in 66% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-18j:** orange oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.0 Hz, 1H), 7.85 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.54–7.46 (m, 2H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.33 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.06 (t, *J* = 1.2 Hz, 1H), 3.77 (s, 3H), 3.63 (dd, *J* = 17.2, 1.2 Hz, 1H), 3.60 (s, 3H), 3.56 (s,

3H), 3.44 (dd, *J* = 17.2, 1.2 Hz, 1H), 3.06 (dd, *J* = 17.2, 2.4 Hz, 1H), 2.94 (dd, *J* = 17.2, 2.4 Hz, 1H), 1.98 (t, *J* = 2.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.7, 169.22, 169.19, 138.7, 133.7, 132.3, 128.6, 127.6, 126.1, 125.8, 125.6 (2C), 124.3, 117.5, 103.3, 78.2, 71.9, 56.0, 53.1, 52.9, 52.3, 31.0, 28.2, 22.9; IR (neat) 1738, 1724 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{24}H_{23}O_6$ 407.1495; Found 407.1487.



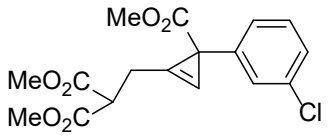
S4k

This compound was prepared in the same manner as described for **S4b** using alkyne **S5**[9] and the corresponding diazo ester[10] instead of **S3** and **S2** in 46% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for S4k:** orange oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.17 (dt, *J* = 9.2, 2.8 Hz, 2H), 6.83 (dt, *J* = 9.2, 2.8 Hz, 2H), 6.79 (t, *J* = 1.2 Hz, 1H), 3.79 (s, 3H), 3.72 (t, *J* = 7.2 Hz, 1H), 3.72 (s, 3H), 3.69 (s, 3H), 3.67 (s, 3H), 3.23–3.18 (m, 1H), 3.18–3.13 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.3, 168.3 (2C), 158.1, 133.0, 129.1 (2C), 117.9, 113.4 (2C), 100.0, 55.2, 52.8 (2C), 52.0, 49.3, 32.5, 24.0; IR (neat) 1737 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{18}H_{24}NO_7$ 366.1553; Found 366.1578.



4-18k

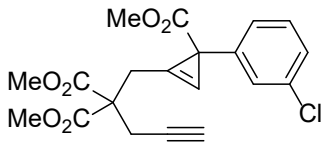
This compound was prepared in the same manner as described for **4-18b** using **S4k** instead of **S4b** in 66% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-18k:** orange oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 6.82 (s, 1H), 3.79 (s, 3H), 3.74 (s, 3H), 3.67 (s, 3H), 3.67 (s, 3H), 3.42 (d, *J* = 17.2 Hz, 1H), 3.35 (d, *J* = 17.2 Hz, 1H), 2.98 (dd, *J* = 17.2, 2.8 Hz, 1H), 2.92 (dd, *J* = 17.2, 2.8 Hz, 1H), 2.02 (t, *J* = 2.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.2, 169.2, 169.1, 158.1, 133.0, 129.2 (2C), 116.3, 113.4 (2C), 101.5, 78.3, 71.8, 55.7, 55.1, 53.1, 53.0, 52.0, 31.8, 27.6, 22.8; IR (neat) 1239, 1720, 1713 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{21}H_{23}O_7$ 387.1444; Found 387.1453.



S4l

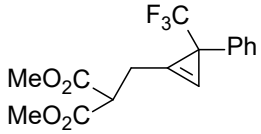
This compound was prepared in the same manner as described for **S4b** using alkyne **S5**[9] and the corresponding diazo ester[11] instead of **S3** and **S2** in 78% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for S4l:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.24–7.15 (m, 4H), 6.78 (s, 1H), 3.73 (s, 3H), 3.694 (s, 3H), 3.690 (t, *J* = 7.2 Hz, 1H), 3.68 (s, 3H), 3.23–3.12 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.1, 168.0 (2C), 142.8, 133.5, 129.0, 128.0, 126.3,

126.2, 117.0, 99.1, 52.6 (2C), 51.8, 48.9, 32.5, 23.7; IR (neat) 1734 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{17}H_{18}O_6Cl$ 353.0792; Found 353.0809.



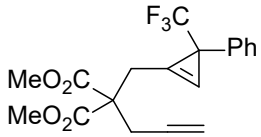
4-18l

This compound was prepared in the same manner as described for **4-18b** using **S4l** instead of **S4b** in 67% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-18l:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.24–7.15 (m, 4H), 6.80 (t, *J* = 1.2 Hz, 1H), 3.75 (s, 3H), 3.69 (s, 3H), 3.68 (s, 3H), 3.40 (dd, *J* = 17.2, 1.2 Hz, 1H), 3.36 (dd, *J* = 17.2, 1.2 Hz, 1H), 2.98 (dd, *J* = 17.2, 2.4 Hz, 1H), 2.93 (dd, *J* = 17.2, 2.4 Hz, 1H), 2.03 (t, *J* = 2.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.3, 169.09, 169.07, 142.9, 133.8, 129.3, 128.3, 126.6, 126.4, 115.8, 100.8, 78.1, 72.0, 55.6, 53.14, 53.07, 52.1, 32.1, 27.6, 22.9; IR (neat) 1738 1723 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{20}H_{23}NO_6Cl$ 408.1214; Found 408.1213.



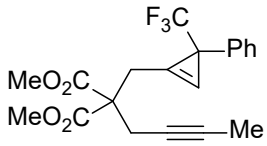
S6

This compound was prepared in the same manner as described for **S4b** using alkyne **S5**[9] and the corresponding diazo compound[12] instead of **S3** and **S2** in 54% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for S6:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34–7.24 (m, 5H), 6.85 (t, *J* = 1.2 Hz, 1H), 3.73 (t, *J* = 7.6 Hz, 1H), 3.72 (s, 3H), 3.69 (s, 3H), 3.18 (dd, *J* = 7.6, 1.2 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.22, 168.16, 138.0, 128.4, 127.7 (2C), 127.5 (2C), 126.3 (q, *J* = 279 Hz), 117.5 (q, *J* = 2.9 Hz), 100.3 (q, *J* = 2.8 Hz), 52.8 (2C), 49.3, 31.9 (q, *J* = 35.7 Hz), 23.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ –65.8; IR (neat) 1739 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{16}H_{19}NO_4F_3$ 346.1266; Found 346.1272.



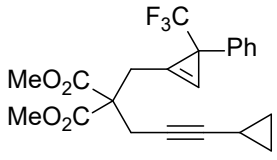
4-18w

This compound was prepared in the same manner as described for **4-18b** using **S6** instead of **S4b** in 88% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-18w:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34–7.23 (m, 5H), 6.85–6.84 (m, 1H), 3.73 (s, 3H), 3.66 (s, 3H), 3.42 (dd, *J* = 17.2, 1.6 Hz, 1H), 3.35 (dd, *J* = 17.2, 1.6 Hz, 1H), 2.99 (dd, *J* = 17.2, 2.4 Hz, 1H), 2.93 (dd, *J* = 17.2, 2.4 Hz, 1H), 2.02 (t, *J* = 2.4 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.80, 169.79, 138.6, 129.1, 128.3 (2C), 127.9 (2C), 127.0 (q, *J* = 279 Hz), 117.1 (q, *J* = 1.9 Hz), 101.6 (q, *J* = 2.9 Hz), 78.5, 72.8, 56.4, 53.8, 53.7, 31.6 (q, *J* = 35.7 Hz), 28.2, 23.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ –65.9 ;IR (neat) 1740 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{19}H_{21}NO_4F_3$ 384.1423; Found 384.1417.



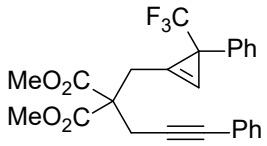
4-18o

This compound was prepared in the same manner as described for **4-18b** using **S6** and 1-bromo-2-butyne instead of **S4b** and propargyl bromide in 83% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-18o:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.36–7.23 (m, 5H), 6.81–6.80 (m, 1H), 3.72 (s, 3H), 3.65 (s, 3H), 3.39 (dd, *J* = 17.2, 1.6 Hz, 1H), 3.33 (dd, *J* = 17.2, 1.6 Hz, 1H), 2.97–2.85 (m, 2H), 1.71 (t, *J* = 2.4 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.5 (2C), 138.1, 128.3, 127.6 (2C), 127.1 (2C), 126.0 (q, *J* = 279 Hz), 116.4 (q, *J* = 1.9 Hz), 100.5 (q, *J* = 2.8 Hz), 79.7, 72.4, 56.0, 53.0, 52.9, 30.8 (q, *J* = 35.7 Hz), 27.5, 23.4, 3.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ –65.9; IR (neat) 1740 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{20}H_{23}NO_4F_3$ 398.1579; Found 398.1569.



4-18p

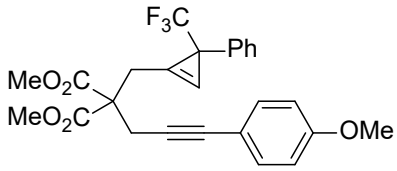
This compound was prepared in the same manner as described for **4-18b** using **S6** and the corresponding alkyl bromide[13] instead of **S4b** and propargyl bromide in 83% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-18p:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34–7.24 (m, 5H), 6.81–6.80 (m, 1H), 3.71 (s, 3H), 3.65 (s, 3H), 3.37 (dd, *J* = 18.0, 1.6 Hz, 1H), 3.31 (dd, *J* = 18.0, 1.6 Hz, 1H), 2.93 (dd, *J* = 17.6, 2.0 Hz, 1H), 2.87 (dd, *J* = 17.6, 2.0 Hz, 1H), 1.16–1.08 (m, 1H), 0.70 (dd, *J* = 7.2, 4.0 Hz, 1H), 0.67 (dd, *J* = 7.2, 4.0 Hz, 1H), 0.53 (dd, *J* = 7.2, 4.0 Hz, 1H), 0.51 (dd, *J* = 7.2, 4.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.4 (2C), 138.1, 128.4, 127.5 (2C), 127.2 (2C), 126.3 (q, *J* = 278 Hz), 116.3 (q, *J* = 2.9 Hz), 100.5 (q, *J* = 2.9 Hz), 87.6, 68.5, 56.1, 53.0, 52.9, 30.8 (q, *J* = 35.7 Hz), 27.5, 23.3, 8.1 (2C), –0.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ –65.9; IR (neat) 1740 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{22}H_{22}O_4F_3$ 407.1470; Found 407.1460.



4-18s

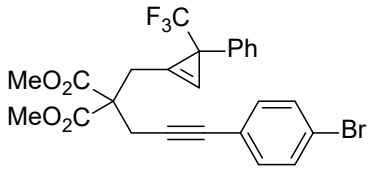
This compound was prepared in the same manner as described for **4-18b** using **S6** and the corresponding alkyl bromide[13] instead of **S4b** and propargyl bromide in 58% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-18s:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32–7.21 (m, 10H), 6.86–6.85 (m, 1H), 3.74 (s, 3H), 3.68 (s, 3H), 3.48 (dd, *J* = 18.0, 1.6 Hz, 1H), 3.43 (dd, *J* = 18.0, 1.6 Hz, 1H), 3.22 (d, *J* = 17.6 Hz, 1H), 3.17 (d, *J* = 17.6 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.3 (2C), 138.0, 131.6 (2C), 128.4 (2C), 128.2 (2C), 127.5 (2C), 126.3 (q, *J* = 278 Hz), 127.2 (2C), 122.7, 116.3 (q, *J* = 2.9 Hz), 100.8 (q, *J* = 2.9 Hz), 84.2, 83.1, 56.0, 53.1, 53.0,

30.9 (q, J = 35.6 Hz), 27.7, 23.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ –65.9; IR (neat) 1739 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{25}H_{25}NO_4F_3$ 460.1736; Found 460.1734.



4-18t

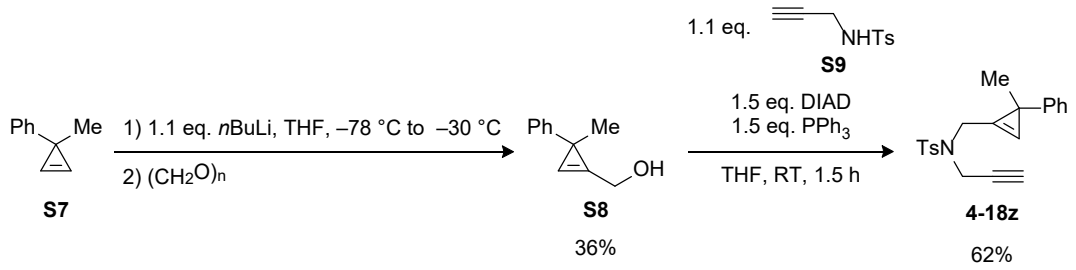
This compound was prepared in the same manner as described for **4-18b** using **S6** and the corresponding alkyl bromide[14] instead of **S4b** and propargyl bromide in 70% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-18t:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32–7.22 (m, 7H), 6.86 (s, 1H), 6.78 (d, J = 8.0 Hz, 2H), 3.77 (s, 3H), 3.74 (s, 3H), 3.68 (s, 3H), 3.47 (d, J = 18.0 Hz, 1H), 3.42 (d, J = 18.0 Hz, 1H), 3.20 (d, J = 18.0 Hz, 1H), 3.15 (d, J = 18.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.3 (2C), 159.5, 138.0, 133.0 (2C), 128.4, 127.5 (2C), 127.2 (2C), 126.3 (q, J = 279 Hz), 116.3 (q, J = 1.9 Hz), 114.9, 113.8 (2C), 100.8 (q, J = 1.9 Hz), 84.0, 81.5, 56.1, 55.2, 53.05, 53.00, 30.9 (q, J = 35.7 Hz), 27.7, 23.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ –65.9; IR (neat) 1739 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{26}H_{27}NO_5F_3$ 490.1841; Found 490.1853.

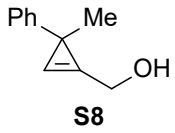


4-18v

This compound was prepared in the same manner as described for **4-18b** using **S6** and the corresponding alkyl bromide[15] instead of **S4b** and propargyl bromide in 27% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-18v:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.40 (dt, J = 8.8, 2.0 Hz, 2H), 7.30–7.24 (m, 5H), 7.14 (dt, J = 8.8, 2.0 Hz, 2H), 6.87–6.86 (m, 1H), 3.76 (s, 3H), 3.70 (s, 3H), 3.46 (dd, J = 17.8, 1.6 Hz, 1H), 3.39 (dd, J = 17.8, 1.6 Hz, 1H), 3.20 (d, J = 17.8 Hz, 1H), 3.14 (d, J = 17.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.2 (2C), 137.9, 133.1 (2C), 131.5 (2C), 128.4, 127.6 (2C), 127.3 (2C), 126.2 (q, J = 278 Hz), 122.4, 121.7, 116.3 (q, J = 1.9 Hz), 100.9 (q, J = 1.9 Hz), 84.4, 83.2, 55.9, 53.2, 53.1, 31.0 (q, J = 35.7 Hz), 27.7, 23.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ –65.9; IR (neat) 1739 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{25}H_{24}NO_4BrF_3$ 538.0841; Found 538.0869.

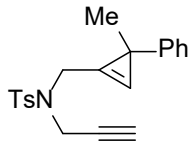
Synthesis and characterization of 4-18z





S8

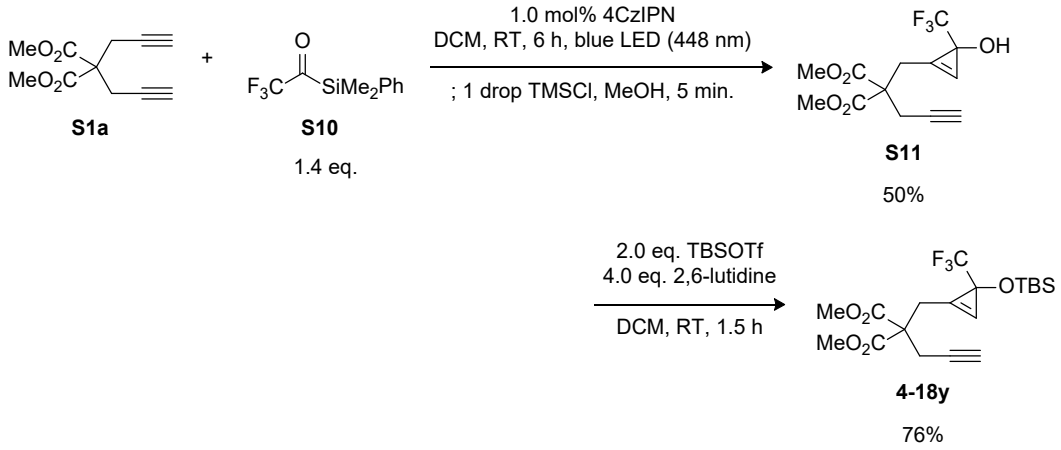
To a solution of **S7**[16] (405 mg, 3.12 mmol) in dry THF (5.0 mL) was added ^{n}BuLi (2.20 mL, 1.60 M in hexane) at –78 °C under Ar atmosphere. The reaction mixture was stirred at –30 °C for 1 h. To this reaction mixture was added paraformaldehyde (251 mg, 8.36 mmol) at –78 °C and stirring was continued for 4 h at room temperature. The reaction was quenched with water. The aqueous phase was extracted with Et_2O. The combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in vacuo, the obtained crude product was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to afford **S8** (179 mg, 36%). **Analytical data for S8:** colorless liquid; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34–7.26 (m, 2H), 7.23–7.21 (m, 2H), 7.15 (tt, *J* = 7.2, 1.6 Hz, 1H), 7.04 (s, 1H), 4.67 (s, 2H), 1.64 (s, 3H); ^{13}C-NMR (100 MHz, $CHCl_3$) δ 149.4, 128.6 (2C), 126.8, 126.5 (2C), 125.7, 108.3, 58.1, 26.8, 24.8; IR (neat) 3431 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{11}H_{16}NO$ 178.1232; Found 178.1222.

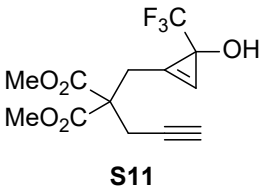


4-18z

To a solution of **S8** (98.0 mg, 0.61 mmol) and **S9** (146 mg, 0.70 mmol) in dry THF (2.0 mL) was added PPh_3 (265 mg, 1.01 mmol) and DIAD (226 mg, 1.19 mmol) at 0 °C under Ar atmosphere. The reaction mixture was stirred at room temperature for 1.5 h. The resultant mixture was concentrated in vacuo. The obtained crude product was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to afford **4-18z** (131 mg, 62%). **Analytical data for 4-18z:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.29–7.24 (m, 4H), 7.15–7.12 (m, 3H), 6.86 (s, 1H), 4.41 (s, 2H), 4.20 (dd, *J* = 18.0, 2.4 Hz, 1H), 4.13 (dd, *J* = 18.0, 2.4 Hz, 1H), 2.42 (s, 3H), 2.05 (t, *J* = 2.4 Hz, 1H), 1.55 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.0, 143.7, 135.6, 129.5 (2C), 127.8 (2C), 127.6 (2C), 125.8 (2C), 125.1, 121.5, 109.8, 76.2, 74.1, 41.8, 36.4, 25.4, 23.6, 21.4; IR (neat) 1350, 1161 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{21}H_{25}N_2O_2S$ 369.1637; Found 369.1661.

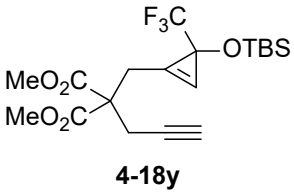
Synthesis and characterization of 4-18y





S11

S11 was synthesized under the modified conditions, referring to the previous report.[17] 4CzIPN (5.52 mg, 0.0070 mmol), **S1a** (146 mg, 0.70 mmol) and **S10** (146 mg, 1.0 mmol) were dissolved in degassed dry DCM (3.0 mL) under Ar atmosphere. A LED lamp (PER-AMP available from Techno Sigma) was put into the reaction mixture in the Schlenk tube, and the reaction mixture was stirred at room temperature under irradiation. After stirring for 6 h, TMSCl (1 drop) and MeOH (2.0 mL) was added, and the mixture was stirred at room temperature for 5 min. The reaction mixture was quenched with H_2O and extracted with DCM. The organic phase was combined and washed with brine, dried over Na_2SO_4, concentrated in vacuo. The residue was then purified by a silica gel column chromatography (Hexane/EtOAc = 5:1) to give **S11** (108 mg, 50%). **Analytical data for S11:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.06 (s, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.43 (d, J = 16.4 Hz, 1H), 3.30 (s, 1H), 3.27 (d, J = 16.4 Hz, 1H), 2.94 (dd, J = 17.6, 2.8 Hz, 1H), 2.86 (dd, J = 17.6, 2.8 Hz, 1H), 2.09 (t, J = 2.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.2, 169.3, 124.1 (q, J = 278 Hz), 122.2 (q, J = 2.8 Hz), 109.5 (q, J = 2.8 Hz), 77.7, 72.3, 55.6, 54.1 (q, J = 40.5 Hz), 53.4, 53.3, 28.2, 23.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ –74.5; IR (neat) 3445 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{13}H_{17}NO_5F_3$ 324.1059; Found 324.1087.

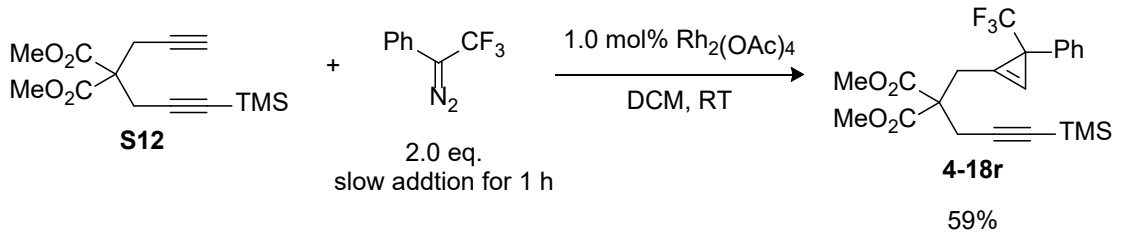


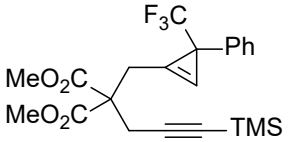
4-18y

To a solution of **S11** (83.4 g, 0.27 mmol) and 2,6-lutidine (120 μL, 0.50 mmol) in dry DCM (5.0 mL) was added TBSOTf (120 μL, 1.00 mmol) at 0 °C, and the mixture was allowed to warm to room temperature. After being stirred at room temperature for 1.5 h, the reaction was quenched with water and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 20:1) and distillation (50 °C, 0.2

mmHg) to furnish **4-18y** (86.3 mg, 76%). **Analytical data for 4-18y:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.92–6.91 (m, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 3.34 (dd, *J* = 17.2 Hz, 1.6 Hz, 1H), 3.29 (dd, *J* = 17.2, 1.6 Hz, 1H), 2.96 (dd, *J* = 17.2, 1.6 Hz, 1H), 2.91 (dd, *J* = 17.2, 1.6 Hz, 1H), 2.01 (t, *J* = 1.6 Hz, 1H), 0.82 (s, 9H), 0.06 (s, 3H), –0.03 (s, 3H); ^{13}C-NMR (100 MHz, $CHCl_3$) δ 169.1 (2C), 124.0 (q, *J* = 279 Hz), 124.9 (q, *J* = 2.9 Hz), 109.7 (q, *J* = 2.8 Hz), 77.9, 72.1, 55.4, 55.2 (q, *J* = 41.4 Hz), 53.2, 53.1, 27.3, 25.4 (3C), 22.9, 17.7, –4.08, –4.11; ^{19}F NMR (376 MHz, $CDCl_3$) δ –73.1; IR (neat) 1743 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{19}H_{31}NO_5F_3Si$ 438.1924; Found 438.1942.

Synthesis and characterization of 4-18r

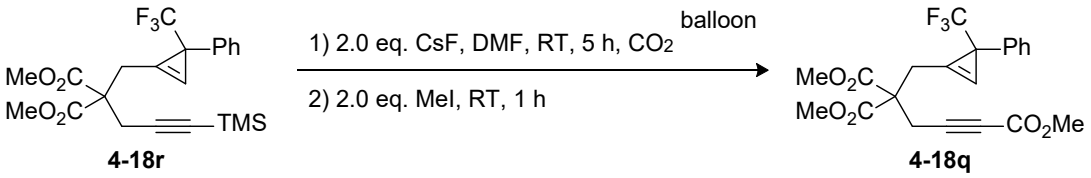


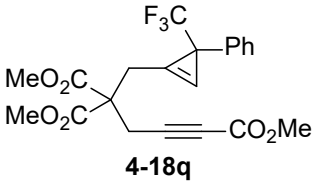


4-18r

To a 50 mL two-necked flask was added dry DCM (5.0 mL), $Rh_2(OAc)_4$ (4.4 mg, 0.010 mmol) and **S12**[18] (293 mg, 1.10 mmol) under Ar atmosphere. The homogeneous green solution was stirred at room temperature for 5 min. A solution of a corresponding diazo compound[12] (410 mg, 2.20 mmol) in dry DCM (2.0 mL) was added to the reaction mixture over 1 h using a syringe pump. After completion of the addition, the reaction mixture was additionally stirred at room temperature for 30 min. The solvent was removed under reduced pressure. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 20:1) and distillation (90 °C, 0.2 mmHg) to furnish **4-18r** (284 mg, 59%). **Analytical data for 4-18r:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34–7.24 (m, 5H), 6.82–6.81 (m, 1H), 3.73 (s, 3H), 3.67 (s, 3H), 3.41 (dd, *J* = 18.4, 1.2 Hz, 1H), 3.34 (dd, *J* = 18.4, 1.2 Hz, 1H), 3.02 (d, *J* = 17.2 Hz, 1H), 2.95 (d, *J* = 17.2 Hz, 1H), 0.10 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.2 (2C), 138.0, 128.4, 127.5 (2C), 127.2 (2C), 126.3 (q, *J* = 278 Hz), 116.3 (q, *J* = 1.9 Hz), 100.8 (q, *J* = 2.9 Hz), 100.1, 89.2, 56.0, 53.1, 53.0, 30.8 (q, *J* = 34.7 Hz), 27.5, 24.3, –0.2 (3C); ^{19}F NMR (376 MHz, $CDCl_3$) δ –66.0; IR (neat) 1741 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{22}H_{29}NO_4F_3Si$ 456.1818; Found 456.1835.

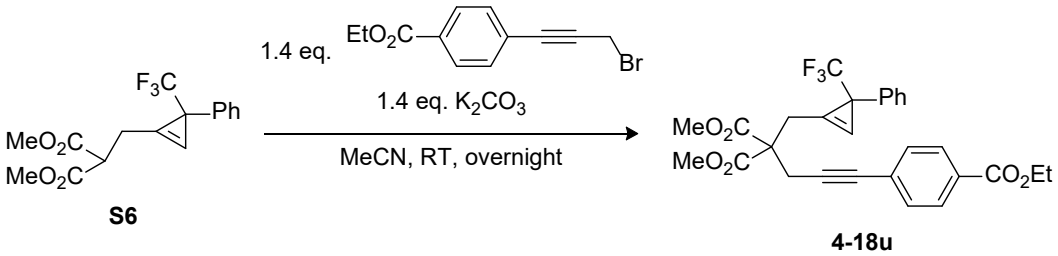
Synthesis and characterization of 4-18q

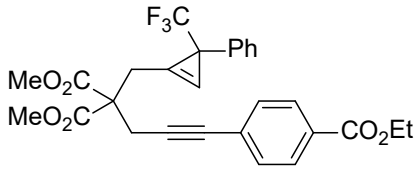




4-18q was synthesized under the modified conditions, referring to the previous report.[19] In a flask, CsF (105 mg, 0.60 mmol) was heated under vacuum at 120 °C for 2 h. The flask was filled with CO_2 gas (balloon) and then with dry DMF (1.0 mL). To the resultant suspension was added **4-18r** (134 g, 0.30 mmol) at room temperature. The reaction mixture was stirred at room temperature for 5 h. After addition of methyl iodide (22.0 μL, 0.60 mmol), the stirring was continued at room temperature for another 1 h. The reaction was quenched with sat. aq. NH_4Cl and the whole mixture was extracted with EtOAc. The combined organic layer was washed with water, brine, and dried over $MgSO_4$. After concentration in vacuo, the crude material was purified by flash column chromatography on silica gel (Hexane/EtOAc = 10:1) to yield **1r** (66.0 mg, 52%). **Analytical data for 4-18q:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35–7.24 (m, 5H), 6.89–6.88 (m, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 3.69 (s, 3H), 3.42 (dd, *J* = 18.0, 1.2 Hz, 1H), 3.35 (dd, *J* = 18.0, 1.2 Hz, 1H), 3.12 (d, *J* = 18.0 Hz, 1H), 3.06 (d, *J* = 18.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 168.6 (2C), 153.4, 137.7, 128.4, 127.5 (2C), 127.3 (2C), 126.2 (q, *J* = 278 Hz), 116.1 (q, *J* = 1.9 Hz), 101.5 (q, *J* = 2.9 Hz), 82.4, 75.8, 55.4, 53.35, 53.30, 52.7, 31.1 (q, *J* = 35.7 Hz), 27.8, 23.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ –66.0; IR (neat) 1741, 1719 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{21}H_{23}NO_6F_3$ 442.1478; Found 442.1483.

Synthesis and characterization of 4-18u

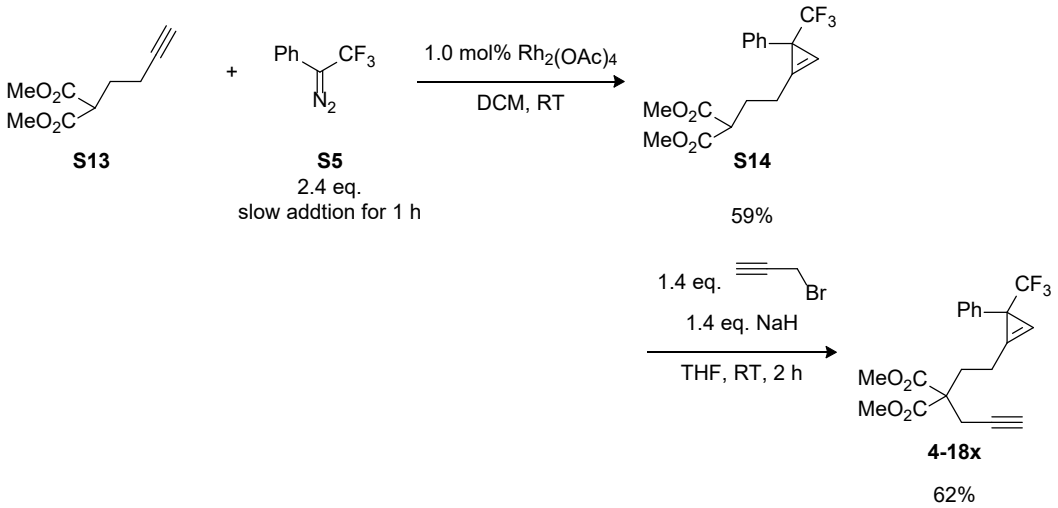


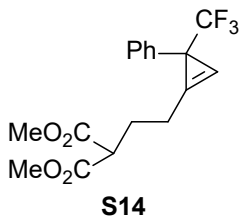


4-18u

To a 10 mL flask was added dry MeCN (2.0 mL), **S6** (197 mg, 0.60 mmol), the corresponding alkyl bromide[15] (267 mg, 1.0 mmol) and K_2CO_3 (138 mg, 1.0 mmol) under Ar atmosphere. The resulting solution was stirred at room temperature overnight. Water was added and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 20:1) to furnish **4-18u** (223 mg, 72%). **Analytical data for 4-18u:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.8 Hz, 2H), 7.35–7.24 (m, 7H), 6.90–6.89 (m, 1H), 4.36 (q, *J* = 7.2 Hz, 2H), 3.76 (s, 3H), 3.70 (s, 3H), 3.49 (dd, *J* = 18.4, 1.2 Hz, 1H), 3.42 (dd, *J* = 18.4, 1.2 Hz, 1H), 3.25 (d, *J* = 18.4 Hz, 1H), 3.19 (d, *J* = 18.4 Hz, 1H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.3 (2C), 166.1, 138.0, 131.7 (2C), 130.0, 129.4 (2C), 128.5, 127.7 (2C), 127.4 (2C), 126.4 (q, *J* = 278 Hz), 116.5, 101.1, 86.5, 83.7, 61.2, 56.1, 53.3, 53.2, 31.1 (q, *J* = 35.7 Hz), 27.9, 24.1, 14.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ –65.9; IR (neat) 1741, 1720 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{28}H_{29}NO_6F_3$ 532.1947; Found 532.1970.

Synthesis and characterization of 4-18x

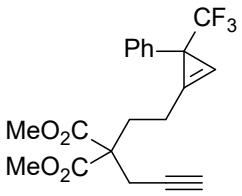




S14

To a 20 mL two-necked flask was added dry DCM (5.0 mL), $Rh_2(OAc)_4$ (4.7 mg, 0.010 mmol) and **S13**[20] (128 mg, 0.70 mmol) under Ar atmosphere. The homogeneous green solution was stirred at room temperature for 5 min. A solution of **S5**[9] (202 mg, 1.09 mmol) in dry DCM (2.0 mL) was added to the reaction mixture over 1 h using a syringe pump. After completion of the addition, the reaction mixture was additionally stirred at room temperature for 30 min. The solvent was removed under reduced pressure. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 10:1) to furnish

S14 (112 mg, 59%). **Analytical data for S14:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.34–7.24 (m, 5H), 6.82 (s, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.42 (t, *J* = 7.6 Hz, 1H), 2.64 (t, *J* = 7.6 Hz, 2H), 2.29–2.19 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.2 (2C), 138.3, 128.4, 127.6 (2C), 127.1 (2C), 126.5 (q, *J* = 278 Hz) 119.4 (q, *J* = 1.9 Hz), 98.9 (q, *J* = 2.9 Hz), 52.69, 52.67, 50.5, 31.6 (q, *J* = 35.7 Hz), 25.8, 22.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ –65.6; IR (neat) 1734 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{17}H_{21}F_3NO_4$ 360.1423; Found 360.1401.

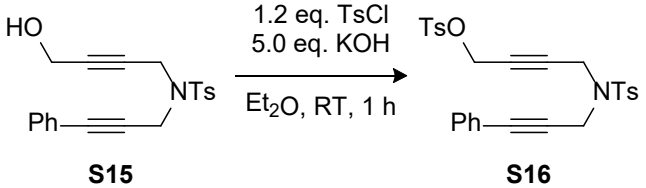


4-18x

To a solution of **S14** (137 mg, 0.40 mmol) in dry THF (2.0 mL) was added NaH (60% dispersion in mineral oil, 24.3 mg, 0.80 mmol) at 0 °C under Ar atmosphere. The reaction mixture was stirred at room temperature for 10 min. To this reaction mixture was added propargyl bromide (100 μL, 1.33 mmol) and stirring was continued for 2 h at room temperature. The reaction was quenched with water. The aqueous phase was extracted with Et_2O. The combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in vacuo, the obtained crude product was purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to afford **4-18x** (94.1 mg, 62%). **Analytical data for 4-18x:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35–7.23 (m, 5H), 6.80–6.79 (m, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 2.86 (d, *J* = 2.8 Hz, 2H), 2.57–2.52 (m, 2H), 2.49–2.34 (m, 2H), 2.03 (t, *J* = 2.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.1 (2C), 138.5, 128.4, 127.8 (2C), 127.1 (2C), 126.6 (q, *J* = 278 Hz), 119.9 (q, *J* = 1.9 Hz), 98.7 (q, *J* = 2.9 Hz), 78.1, 71.9, 56.3, 53.0 (2C), 31.9 (q, *J* = 35.7 Hz), 29.5, 23.3, 19.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ –65.8; IR (neat) 1734 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{20}H_{23}F_3NO_4$ 398.1579; Found 398.1586.

4. Synthesis and Characterization of Cyclopropenediynes 4-23

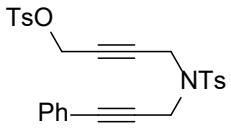
Synthesis and characterization of S16



S15 **S16**

46%

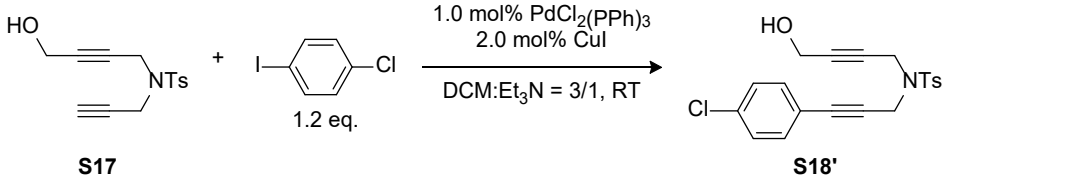
To a dry Et_2O solution (10 mL) of **S15**[21] (1.46 g, 4.1 mmol) and *p*-toluenesulfonyl chloride (830 mg, 4.4 mmol) was added KOH (1.21 g, 21 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 1 h. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 5:1) to furnish **S16** (957



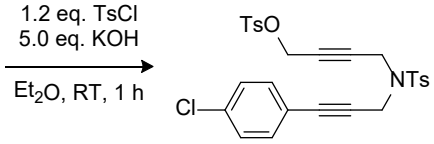
S16

mg, 46%) as a colorless oil. **Analytical data for S16:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.30–7.24 (m, 5H), 7.16 (d, *J* = 8.0 Hz, 2H), 4.57 (s, 2H), 4.23 (s, 2H), 4.10 (s, 2H), 2.44 (s, 3H), 2.37 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 145.2, 144.0, 134.8, 132.7, 131.4 (2C), 129.8 (2C), 129.5 (2C), 128.5, 128.1 (2C), 127.9 (2C), 127.7 (2C), 121.8, 85.9, 82.0, 80.9, 77.4, 57.4, 37.2, 36.5, 21.5, 21.3; IR (neat) 1351, 1176, 1163 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{27}H_{25}NNaO_5S_2$ 532.1030, found 532.1017.

Synthesis and characterization of S18–S20

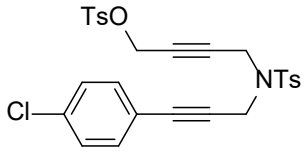


S17 **S18'**



S18

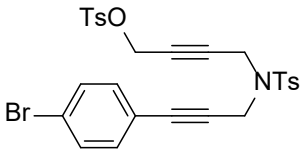
46% (2 steps)



S18

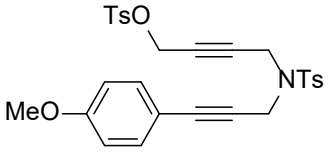
To a solution of **S17**[21] (565 mg, 2.0 mmol) and 1-chloro-4-iodobenzene (572 g, 2.4 mmol) in DCM (6.0 mL) and Et_3N (3.0 mL) was added $PdCl_2(PPh_3)_2$ (27.6 mg, 0.020 mmol) and CuI (16.2 mg, 0.040 mmol). Insoluble materials were filtered off through a pad of Celite®, and the filtrate was concentrated in vacuo. The obtained crude product was purified by silica gel column chromatography (Hexane/EtOAc = 2:1) to give **S18'**, which was used for the next reaction without detailed identification. To a dry Et_2O solution (3.0 mL) of **S18'** (216 mg, 0.56 mmol) and *p*-toluenesulfonyl chloride (128 mg, 0.67 mmol) was added KOH (157 g, 2.80 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 1 h. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 5:1) to furnish **S18** (957 mg, 46%, 2steps). **Analytical data for S18:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.24 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.09 (dt, *J* = 8.0, 2.0 Hz, 2H), 4.56 (t, *J* = 1.6 Hz, 2H), 4.23 (s, 2H), 4.11 (t, *J* = 1.6 Hz, 2H), 2.45 (s, 3H), 2.38 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 145.2, 144.0, 134.8, 134.5, 132.7 (2C),

129.8 (2C), 129.5 (2C), 128.4 (2C), 127.8 (2C), 127.7 (2C), 120.3, 84.7, 82.1, 81.9, 77.5, 57.4, 37.2, 36.6, 21.5, 21.3, One Csp^2 signal is missing due to overlapping.; IR (neat) 1351, 1176, 1163 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{27}H_{24}ClNNaO_5S_2$ 565.0630, found 565.0616.



S19

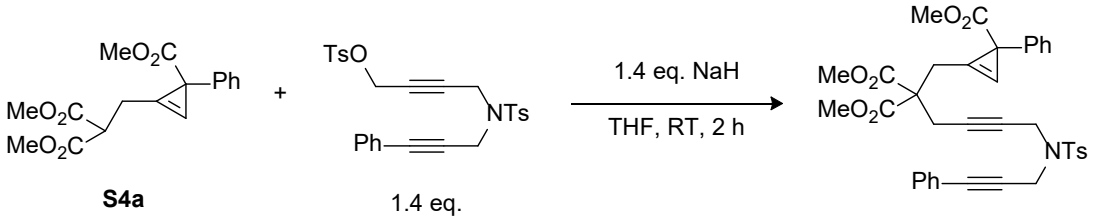
This compound was prepared in the same manner as described for **S18** using 1-bromo-4-iodobenzene instead of 1-chloro-4-iodobenzene in 57% yield (2 steps). **Analytical data for S19:** brown oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.78 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.70 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.40 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.03 (dt, *J* = 8.0, 2.0 Hz, 2H), 4.56 (t, *J* = 1.6 Hz, 2H), 4.23 (s, 2H), 4.11 (t, *J* = 1.6 Hz, 2H), 2.45 (s, 3H), 2.38 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 145.3, 144.1, 134.9, 132.9 (2C), 132.7, 131.4 (2C), 129.8 (2C), 129.5 (2C), 127.9 (2C), 127.8 (2C), 122.8, 120.8, 84.8, 82.3, 82.0, 77.5, 57.4, 37.2, 36.6, 21.6, 21.4; IR (neat) 1351, 1175, 1163 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{27}H_{24}BrNNaO_5S_2$ 609.0171, found 609.0184.



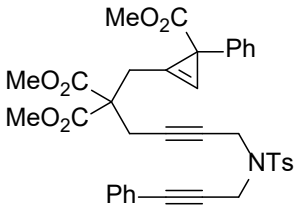
S20

This compound was prepared in the same manner as described for **S18** using 4-iodoanisole instead of 1-chloro-4-iodobenzene in 78% yield (2 steps). **Analytical data for S20:** pale-brown oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.78 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.70 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.11 (dt, *J* = 8.0, 2.0 Hz, 2H), 6.78 (dt, *J* = 8.0, 2.0 Hz, 2H), 4.57 (t, *J* = 1.6 Hz, 2H), 4.21 (s, 2H), 4.10 (t, *J* = 1.6 Hz, 2H), 3.80 (s, 3H), 2.45 (s, 3H), 2.38 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 159.7, 145.2, 144.0, 134.9, 132.9 (2C), 132.8, 129.8 (2C), 129.5 (2C), 127.9 (2C), 127.7 (2C), 113.8, 113.7 (2C), 85.9, 82.1, 79.5, 77.3, 57.5, 55.2, 37.3, 36.4, 21.5, 21.3; IR (neat) 1351, 1175, 1163 cm^{-1}; HRMS (ESI) *m/z* $[M+Na]^+$ calcd for $C_{28}H_{27}NNaO_6S_2$ 561.1171, found 561.1186.

Synthesis and characterization of 4-23a–d

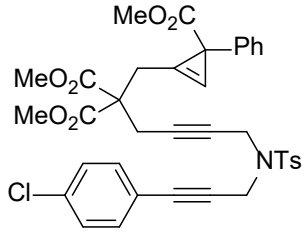


S4a 1.4 eq. **S16** **4-23a** 51%



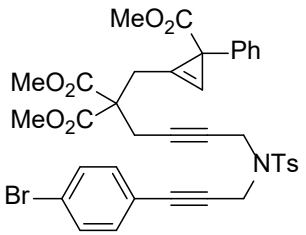
4-23a

To a solution of **S4a** (191 mg, 0.60 mmol) in dry THF (2.0 mL) was added NaH (60% dispersion in mineral oil, 36.9 mg, 0.82 mmol) at 0 °C under Ar atmosphere. The reaction mixture was stirred at room temperature for 10 min. To this reaction mixture was added **S16** (406 mg, 0.80 mmol) and stirring was continued for 2 h at room temperature. The reaction was quenched with water. The aqueous phase was extracted with Et_2O. The combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in vacuo, the obtained crude product was purified by silica gel column chromatography (hexane/AcOEt 5:1) to afford **4-23a** (201 mg, 51%). **Analytical data for 4-23a:** pale-yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.31–7.18 (m, 10H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.79 (s, 1H), 4.29 (s, 2H), 4.09 (t, *J* = 2.0 Hz, 2H), 3.71 (s, 3H), 3.65 (s, 3H), 3.63 (s, 3H), 3.32 (d, *J* = 17.6 Hz, 1H), 3.26 (d, *J* = 17.6 Hz, 1H), 2.91 (dt, *J* = 17.6, 2.0 Hz, 1H), 2.85 (dt, *J* = 17.6, 2.0 Hz, 1H), 2.34 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.6, 169.9 (2C), 144.5, 141.4, 135.8, 132.2 (2C), 130.3 (2C), 129.2, 128.82 (2C), 128.76 (2C), 128.5 (2C), 127.2, 122.8, 116.9, 102.0, 86.4, 81.9, 81.0, 76.9, 56.4, 53.8, 53.7, 52.7, 37.5, 37.4, 33.2, 28.5, 23.9, 22.1, Two C*sp*^{2} signals are missing due to overlapping.; IR (neat) 1738, 1720 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{37}H_{35}NNaO_8S$ 677.1975; Found 677.1977.



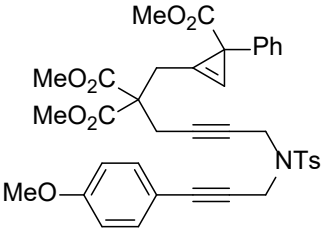
4-23b

This compound was prepared in the same manner as described for **4-23a** using **S18** instead of **S16** in 76% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 5:1). **Analytical data for 4-23b:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.30–7.20 (m, 9H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.79 (s, 1H), 4.27 (s, 2H), 4.08 (s, 2H), 3.71 (s, 3H), 3.66 (s, 3H), 3.63 (s, 3H), 3.31 (d, *J* = 17.2 Hz, 1H), 3.24 (d, *J* = 17.2 Hz, 1H), 2.90 (d, *J* = 17.2 Hz, 1H), 2.84 (d, *J* = 17.2 Hz, 1H), 2.36 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.7, 169.0 (2C), 143.7, 140.6, 134.9, 134.3, 132.7 (2C), 129.4 (2C), 128.3 (2C), 127.9 (2C), 127.7 (2C), 126.4 (2C), 120.4, 115.9, 101.1, 84.4, 82.2, 80.3, 76.0, 55.5, 53.0, 52.9, 51.9, 36.6, 32.3, 27.6, 23.0, 21.2, Two C*sp*^{2} signals and one C*sp*^{3} signal are missing due to overlapping.; IR (neat) 1738, 1720 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{37}H_{34}ClNNaO_8S$ 712.1562; Found 712.1561.



4-23c

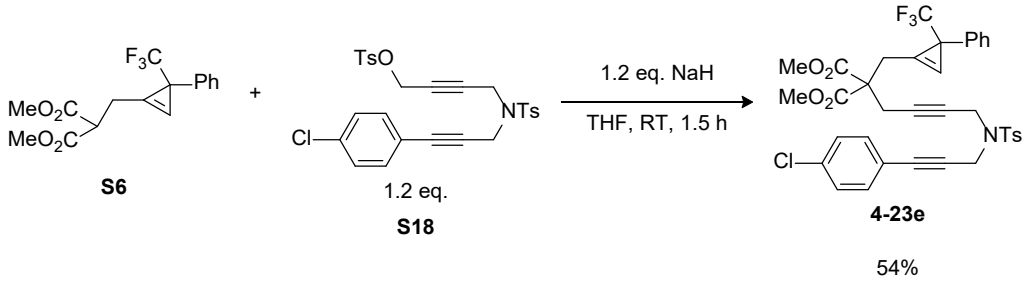
This compound was prepared in the same manner as described for **4-23a** using **S19** instead of **S16** in 85% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 5:1). **Analytical data for 4-23c:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.38 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.30–7.19 (m, 7H), 7.01 (dt, *J* = 8.0, 2.0 Hz, 2H), 6.79 (s, 1H), 4.26 (s, 2H), 4.08 (s, 2H), 3.71 (s, 3H), 3.66 (s, 3H), 3.63 (s, 3H), 3.31 (dd, *J* = 17.2, 1.2 Hz, 1H), 3.24 (dd, *J* = 17.2, 1.2 Hz, 1H), 2.90 (dt, *J* = 17.2, 1.2 Hz, 1H), 2.84 (dt, *J* = 17.2, 1.2 Hz, 1H), 2.36 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.0, 169.3 (2C), 144.0, 140.9, 135.2, 133.1 (2C), 131.5 (2C), 129.7 (2C), 128.2 (2C), 128.0 (2C), 126.7, 122.9, 121.1, 116.2, 101.4, 84.8, 82.7, 80.6, 76.3, 55.9, 53.3, 53.2, 52.2, 36.9, 32.6, 27.9, 23.3, 21.6, Two C*sp*^{2} and one C*sp*^{3} signals are missing due to overlapping.; IR (neat) 1738, 1720 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{37}H_{34}BrNNaO_8S$ 758.1024; Found 758.1029.

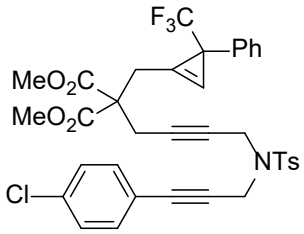


4-23d

This compound was prepared in the same manner as described for **4-23a** using **S20** instead of **S16** in 32% yield. This compound was purified by silica gel column chromatography (Hexane/EtOAc = 5:1). **Analytical data for 4-23d:** orange oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.30–7.18 (m, 9H), 7.09 (dt, *J* = 8.8, 2.4 Hz, 2H), 6.79 (s, 1H), 6.76 (dt, *J* = 8.8, 2.4 Hz, 2H), 4.27 (s, 2H), 4.08 (t, *J* = 1.2 Hz, 2H), 3.79 (s, 3H), 3.71 (s, 3H), 3.66 (s, 3H), 3.63 (s, 3H), 3.32 (dd, *J* = 17.2, 1.2 Hz, 1H), 3.26 (dd, *J* = 17.2, 1.2 Hz, 1H), 2.91 (dt, *J* = 17.2, 2.0 Hz, 1H), 2.84 (dt, *J* = 17.2, 2.0 Hz, 1H), 2.36 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.6, 169.9 (2C), 160.4, 144.4, 141.5, 135.9, 133.8 (2C), 130.2 (2C), 128.8 (2C), 128.6 (2C), 127.2 (2C), 116.9, 114.9, 114.5 (2C), 102.0, 86.4, 80.9, 80.5, 77.0, 56.5, 56.0, 53.8, 53.7, 52.8, 37.6, 37.3, 33.2, 28.5, 23.9, 22.2, One C*sp*^{2} signal is missing due to overlapping.; IR (neat) 1738, 1720 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{38}H_{37}NNaO_9S$ 706.2087; Found 706.2073.

Synthesis and characterization of 4-23e

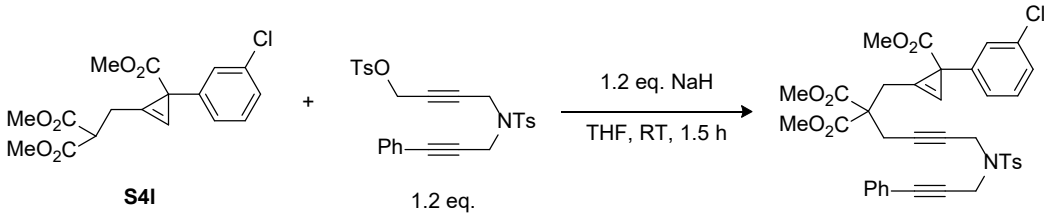


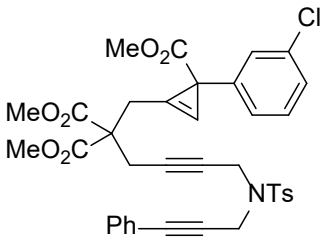


4-23e

To a solution of **S6** (191 mg, 0.60 mmol) in dry THF (2.0 mL) was added NaH (60% dispersion in mineral oil, 32.4 mg, 0.80 mmol) at 0 °C under Ar atmosphere. The reaction mixture was stirred at room temperature for 10 min. To this reaction mixture was added **S18** (434 mg, 0.80 mmol) and stirring was continued for 1.5 h at room temperature. The reaction was quenched with water. The aqueous phase was extracted with Et_2O. The combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in vacuo, the obtained crude product was purified by silica gel column chromatography (Hexane/EtOAc 5:1) to afford **4-23e** (228 mg, 54%). **Analytical data for 4-23e:** orange oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.0 Hz, 2H), 7.35–7.21 (m, 9H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.80–6.79 (m, 1H), 4.24 (s, 2H), 4.09 (s, 2H), 3.70 (s, 3H), 3.64 (s, 3H), 3.30 (dd, *J* = 17.2, 1.2 Hz, 1H), 3.22 (dd, *J* = 17.2, 1.2 Hz, 1H), 2.90 (dt, *J* = 17.2, 2.0 Hz, 1H), 2.84 (dt, *J* = 17.2, 2.0 Hz, 1H), 2.35 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.6 (2C), 144.5, 138.3, 135.6, 135.1, 133.4 (2C), 130.2 (2C), 129.1 (2C), 129.0 (2C), 128.4 (2C), 128.1 (2C), 127.9, 126.8 (q, *J* = 279 Hz), 121.1, 116.9 (q, *J* = 2.9 Hz), 101.4 (q, *J* = 2.9 Hz), 85.2, 82.9, 80.6, 77.0, 56.2, 53.7, 53.6, 37.33, 37.26, 31.5 (q, *J* = 35.7 Hz), 28.1, 23.8, 22.0, Two C*sp*^{2} signals are missing due to overlapping.; ^{19}F NMR (376 MHz, $CDCl_3$) δ –65.8; IR (neat) 1739 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{36}H_{31}ClF_3NNaO_6S$ 720.1410; Found 720.1400.

Synthesis and characterization of 4-23f

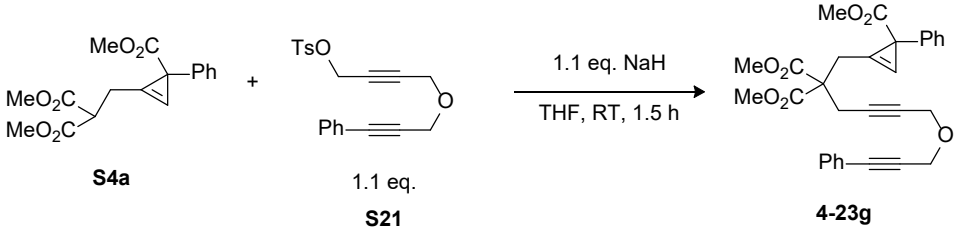


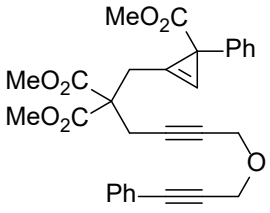


4-23f

To a solution of **S4l** (142 mg, 0.40 mmol) in dry THF (2.0 mL) was added NaH (60% dispersion in mineral oil, 20.3 mg, 0.50 mmol) at 0 °C under Ar atmosphere. The reaction mixture was stirred at room temperature for 10 min. To this reaction mixture was added **S16** (253 mg, 0.50 mmol) and stirring was continued for 1.5 h at room temperature. The reaction was quenched with water. The aqueous phase was extracted with Et_2O. The combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in vacuo, the obtained crude product was purified by silica gel column chromatography (Hexane/EtOAc = 5:1) to afford **4-23f** (135 mg, 49%). **Analytical data for 4-23f:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.31–7.16 (m, 8H), 7.14–7.11 (m, 3H), 6.76 (s, 1H), 4.31 (s, 2H), 4.10 (t, *J* = 1.6 Hz, 2H), 3.72 (s, 3H), 3.66 (s, 6H), 3.30 (dd, *J* = 17.2, 1.6 Hz, 1H), 3.25 (dd, *J* = 17.2, 1.6 Hz, 1H), 2.91 (dt, *J* = 17.2, 2.0 Hz, 1H), 2.85 (dt, *J* = 17.2, 2.0 Hz, 1H), 2.34 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.9, 169.8 (2C), 144.5, 143.6, 135.7, 134.5, 132.2 (2C), 130.2 (2C), 130.0, 129.1, 128.9, 128.8 (2C), 128.5 (2C), 127.4, 127.0, 122.7, 116.5, 101.5, 86.4, 81.8, 80.8, 77.1, 56.3, 53.84, 53.78, 52.8, 37.5, 37.4, 32.8, 28.3, 23.9, 22.1; IR (neat) 1738, 1723 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{37}H_{34}ClNNaO_8S$ 712.1549; Found 712.1554.

Synthesis and characterization of 4-23g



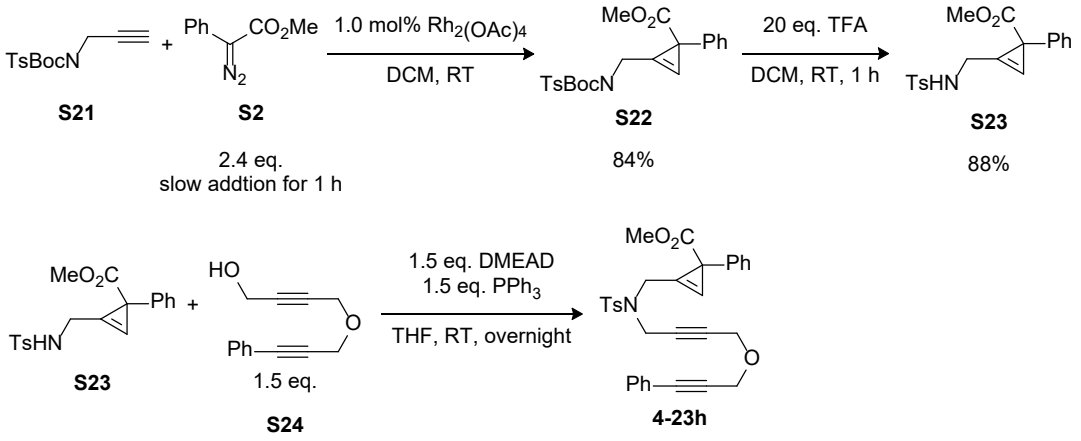


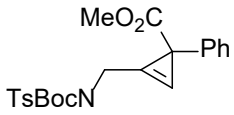
4-23g

To a solution of **S4a** (388 mg, 1.12 mmol) in dry THF (2.0 mL) was added NaH (60% dispersion in mineral oil, 54.4 mg, 1.34 mmol) at 0 °C under Ar atmosphere. The reaction mixture was stirred at room temperature for 10 min. To this reaction mixture was added **S21**[22] (476 mg, 1.34 mmol) and stirring was continued for 1.5 h at room temperature. The reaction was quenched with water. The aqueous phase was extracted with Et_2O. The combined organic layer was washed with brine and dried over $MgSO_4$. After concentration in vacuo, the obtained crude product was purified by silica gel column chromatography (hexane/AcOEt 5:1) to afford **4-23g** (403 mg, 60%). **Analytical data for 4-23g:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.45–7.43 (m, 2H), 7.33–7.23 (m, 7H), 7.22–7.18 (m, 1H), 6.83 (t, *J* = 1.2 Hz, 1H), 4.38 (s, 2H), 4.24 (t, *J* = 2.0 Hz, 2H), 3.74 (s, 3H),

3.67 (s, 3H), 3.66 (s, 3H), 3.42 (dd, J = 17.4, 1.2 Hz, 1H), 3.36 (dd, J = 17.4, 1.2 Hz, 1H), 3.05 (dt, J = 17.4, 2.0 Hz, 1H), 2.99 (dt, J = 17.4, 2.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.1, 169.4 (2C), 141.0, 131.9 (2C), 128.7, 128.4 (2C), 128.3 (2C), 128.2 (2C), 126.6, 122.6, 116.3, 101.4, 86.8, 84.5, 81.5, 79.1, 57.0, 56.8, 56.0, 53.3, 53.1, 52.1, 32.6, 28.0, 23.4; IR (neat) 1739, 1721 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{30}H_{28}NaO_7$ 523.1733; Found 523.1730.

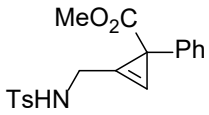
Synthesis and characterization of 4-23h





S22

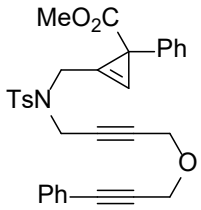
To a 50 mL two-necked flask was added dry DCM (15 mL), $Rh_2(OAc)_4$ (13.3 mg, 0.020 mmol) and **S21**[23] (928 mg, 3.0 mmol) under Ar atmosphere. The homogeneous green solution was stirred at room temperature for 5 min. A solution of **S2** (1.26 g, 7.2 mmol) in dry DCM (2.0 mL) was added to the reaction mixture over 1 h using a syringe pump. After completion of the addition, the reaction mixture was additionally stirred at room temperature for 1 h. The solvent was removed under reduced pressure. The residue was purified by a silica gel column chromatography (Hexane/EtOAc = 5:1) to furnish **S22** (1.15 g, 84%). **Analytical data for S22:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.76 (dt, J = 8.4, 2.0 Hz, 2H), 7.28–7.19 (m, 7H), 6.88 (t, J = 1.2 Hz, 1H), 5.06 (dd, J = 17.6, 1.2 Hz, 1H), 4.97 (dd, J = 17.6, 1.2 Hz, 1H), 3.66 (s, 3H), 2.43 (s, 3H), 1.30 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.1, 151.0, 145.1, 141.1, 137.3, 129.9 (2C), 129.0 (2C), 128.9 (2C), 128.8 (2C), 127.3, 117.8, 102.2, 85.5, 52.8, 42.0, 35.4, 28.4 (3C), 22.3; IR (neat) 1724 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{24}H_{31}N_2O_6S$ 475.1903; Found 475.1879.



S23

To a 100 mL flask was added **S22** (1.37 g, 3.0 mmol) followed by DCM (10 mL). TFA (4.6 mL, 60.0 mmol) was added to the solution. After being stirred at room temperature for 2 h under Ar atmosphere, the reaction mixture was diluted with water and extracted with EtOAc. The organic layer was washed with sat. aq. $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was

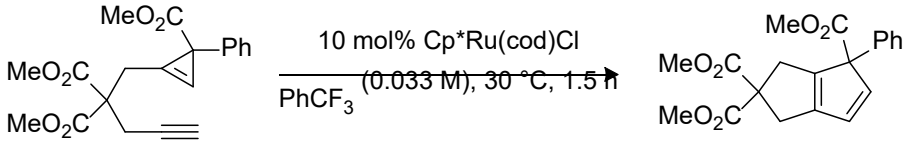
purified by silica gel column chromatography (Hexane/EtOAc = 5:1) to furnish **S23** (944 mg, 88%). **Analytical data for S23:** yellow oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.28–7.19 (m, 5H), 7.09 (dt, *J* = 8.0, 1.2 Hz, 2H), 6.66 (t, *J* = 1.6 Hz, 1H), 5.18 (t, *J* = 6.0 Hz, 1H), 4.18 (dd, *J* = 6.0, 1.6 Hz, 2H), 3.66 (s, 3H), 2.42 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.1, 143.7, 139.9, 136.7, 129.7 (2C), 128.2 (2C), 128.0 (2C), 127.2 (2C), 126.8, 117.2, 101.2, 52.4, 38.4, 34.3, 21.5; IR (neat) 3267, 1718, 1161 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{19}H_{20}NO_4S$ 358.1113; Found 358.1105.



4-23h

To a solution of **S23** (72.0 mg, 0.20 mmol), **S24**[22] (63.0 mg, 0.30 mmol) and PPh_3 (78.7 mg, 0.30 mmol) in THF (1.0 ml) was added bis(2-methoxyethyl) azodicarboxylate (105 mg, 0.49 mmol). The mixture was stirred at room temperature overnight and concentrated in vacuo. The residue was purified by silica gel column chromatography (Hexane/EtOAc = 5:1) to furnish **4-23h** (45.0 mg, 44%). **Analytical data for 4-23h:** colorless oil; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.71 (dt, *J* = 8.4, 2.0 Hz, 2H), 7.45–7.41 (m, 2H), 7.35–7.27 (m, 7H), 7.24–7.20 (m, 3H), 6.82 (t, *J* = 1.2 Hz, 1H), 4.52 (dd, *J* = 17.6, 1.2 Hz, 1H), 4.45 (dd, *J* = 17.6, 1.2 Hz, 1H), 4.23 (s, 2H), 4.18 (dt, *J* = 17.6, 2.0 Hz, 1H), 4.13 (dt, *J* = 17.6, 2.0 Hz, 1H), 4.05 (t, *J* = 2.0 Hz, 2H), 3.68 (s, 3H), 2.40 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.7, 144.0, 140.1, 135.7, 131.7, 129.6, 128.7, 128.4, 128.2, 127.8, 126.8, 122.3, 115.9, 102.7, 86.9, 84.0, 81.4, 79.3, 57.1, 56.4, 52.3, 41.7, 37.0, 33.9, 21.5, One C*sp*^{2} signal is missing due to overlapping.; IR (neat) 1719 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{32}H_{29}NNaO_5S$ 563.1658; Found 563.1642.

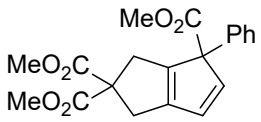
5. Representative Procedure for the Ruthenium-Catalyzed Cycloisomerization of 4-18



4-18a **4-20a**

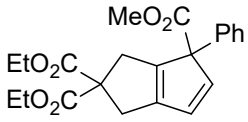
Cp*Ru(cod)Cl (3.80 mg, 0.0100 mmol) was dissolved in degassed $PhCF_3$ (3.0 mL) under Ar atmosphere. To the resulting mixture was added **4-18a** (35.6 mg, 0.100 mmol). After stirring at 30 °C for 1.5 h, the resulting solution was concentrated. The crude was then purified by silica gel column chromatography (Hexane/EtOAc = 10:1) to give **4-20a** (28.1 mg, 79%) as a yellow oil.

6. Characterization of Fused Cyclopentadienes 4-20



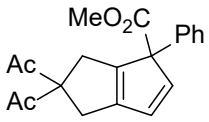
4-20a

According to the representative procedure, **4-20a** was obtained in 79% yield as a yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20a:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33–7.23 (m, 3H), 7.21–7.18 (m, 2H), 6.66 (d, *J* = 5.2 Hz, 1H), 6.32 (d, *J* = 5.2 Hz, 1H), 3.77 (s, 3H), 3.73 (s, 3H), 3.72 (s, 3H), 3.29 (d, *J* = 17.2 Hz, 1H), 3.24 (dt, *J* = 17.2, 2.0 Hz, 1H), 3.14 (dt, *J* = 17.2, 2.0 Hz, 1H), 3.12 (d, *J* = 17.2 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.4, 172.1, 170.7, 148.4, 146.3, 143.4, 136.7, 129.0 (2C), 128.3, 127.5, 126.3 (2C), 67.4, 64.3, 53.01, 53.04, 52.8, 37.3, 36.7; IR (neat) 1733 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{20}H_{24}NO_6$ 374.1604; Found 374.1620.



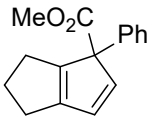
4-20b

According to the representative procedure, **4-20b** was obtained in 76% yield as a yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20b:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32–7.24 (m, 3H), 7.23–7.19 (m, 2H), 6.65 (d, *J* = 5.6 Hz, 1H), 6.32 (d, *J* = 5.6 Hz, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.73 (s, 3H), 3.31–3.20 (m, 2H), 3.15–3.10 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.6, 172.2, 171.3, 149.0, 147.0, 144.0, 137.3, 129.5 (2C), 128.9, 128.1, 126.9 (2C), 67.9, 65.0, 62.3 (2C), 53.3, 37.7, 37.1, 14.7, 14.6; IR (neat) 1731 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{22}H_{28}NO_6$ 402.1917; Found 402.1930.



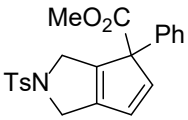
4-20c

According to the representative procedure, **4-20c** was obtained in 75% yield as a yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20c:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33–7.24 (m, 3H), 7.18–7.15 (m, 2H), 6.67 (d, *J* = 5.6 Hz, 1H), 6.36 (d, *J* = 5.6 Hz, 1H), 3.74 (s, 3H), 3.19 (d, *J* = 17.2 Hz, 1H), 3.10 (dt, *J* = 17.2, 2.4 Hz, 1H), 3.03 (dt, *J* = 17.2, 2.4 Hz, 1H), 2.97 (d, *J* = 17.2 Hz, 1H), 2.19 (s, 3H), 2.07 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 204.9, 204.4, 170.6, 148.9, 145.8, 142.9, 136.4, 128.9 (2C), 128.8, 127.5, 126.0 (2C), 78.8, 67.3, 52.7, 33.8, 33.2, 26.4, 26.3; IR (neat) 1729, 1699 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{20}H_{24}NO_4$ 342.1705; Found 342.1704.



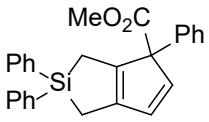
4-20d

The reaction was performed at 100 °C and **4-20d** was obtained in 35% yield as a yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-20d:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32–7.19 (m, 5H), 6.64 (d, *J* = 5.2 Hz, 1H), 6.41 (d, *J* = 5.2 Hz, 1H), 3.72 (s, 3H), 2.62–2.59 (m, 1H), 2.50–2.26 (m, 5H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.6, 152.7, 149.5, 142.1, 137.7, 129.8, 128.8 (2C), 127.3, 126.4 (2C), 66.9, 52.6, 28.3, 28.1, 28.0; IR (neat) 1730 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{16}H_{20}NO_2$ 258.1494; Found 258.1476.



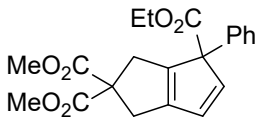
4-20e

According to the representative procedure, **4-20e** was obtained in 49% yield as a pale-yellow amorphas solid after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20e:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.31–7.25 (m, 5H), 7.05–7.02 (m, 2H), 6.69 (d, *J* = 5.6 Hz, 1H), 6.30 (d, *J* = 5.6 Hz, 1H), 4.47–4.41 (m, 1H), 4.33–4.19 (m, 3H), 3.69 (s, 3H), 2.42 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 169.6, 145.6, 143.6, 143.4, 135.3, 134.4, 129.7 (2C), 129.0 (2C), 127.8, 127.3 (2C), 126.4, 125.8 (2C), 67.5, 52.8, 51.8, 51.0, 21.5, One C*sp*^{2} signal is missing due to overlapping.; IR (neat) 1730 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{22}H_{25}N_2O_4S$ 413.1535; Found 413.1556.



4-20f

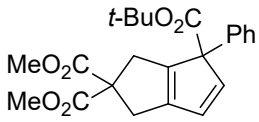
The reaction was performed at 100 °C and **4-20f** was obtained in 45% yield as a pale-yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 50:1). **Analytical data for 4-20f:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.6 Hz, 2H), 7.45–7.23 (m, 11H), 7.14 (d, *J* = 7.6 Hz, 2H), 6.64 (d, *J* = 5.6 Hz, 1H), 6.48 (d, *J* = 5.6 Hz, 1H), 3.73 (s, 3H), 2.18 (d, *J* = 18.8 Hz, 1H), 2.04 (s, 2H), 1.79 (d, *J* = 18.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.7, 150.3, 145.0, 140.5, 137.6, 135.9, 135.7, 134.70 (2C), 134.66 (2C), 133.9, 129.8, 129.7, 128.8 (2C), 128.09 (2C), 128.05 (2C), 127.2, 126.5 (2C), 69.9, 52.5, 14.6, 13.3; IR (neat) 1729 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{27}H_{28}NO_2Si$ 426.1889; Found 426.1881.



4-20g

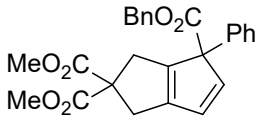
According to the representative procedure, **4-20g** was obtained in 65% yield as a yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20g:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32–7.24 (m, 3H), 7.20–7.19 (m, 2H), 6.66 (d, *J* = 5.2 Hz, 1H), 6.32 (d, *J* = 5.2 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.76 (s, 3H), 3.72 (s, 3H), 3.34–3.22 (m, 2H), 3.16–3.09 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.0, 172.7, 170.7, 149.1, 146.7, 144.2, 137.4, 129.5 (2C), 128.8,

128.0, 126.8 (2C), 68.0, 64.9, 62.2, 53.6 (2C), 38.0, 37.3, 14.7; IR (neat) 1733 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{21}H_{23}O_6$ 371.1495; Found 371.1486.



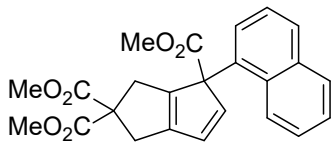
4-20h

According to the representative procedure, **4-20h** was obtained in 56% yield as a yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20h:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31–7.19 (m, 5H), 6.62 (d, *J* = 5.2 Hz, 1H), 6.29 (d, *J* = 5.2 Hz, 1H), 3.76 (s, 3H), 3.72 (s, 3H), 3.32 (d, *J* = 17.2 Hz, 1H), 3.23 (d, *J* = 17.2, 1H), 3.15 (dt, *J* = 17.2, 2.4 Hz, 1H), 3.08 (d, *J* = 17.2 Hz, 1H), 1.44 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.3, 172.1, 169.0, 148.5, 145.7, 143.8, 137.2, 128.7 (2C), 127.8, 127.1, 126.1 (2C), 81.9, 68.2, 64.2, 52.9 (2C), 37.4, 36.6, 27.9 (3C); IR (neat) 1736 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{23}H_{30}NO_6$ 416.2073; Found 416.2086.



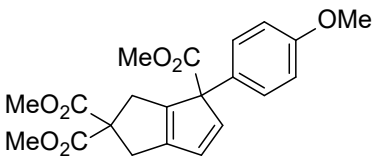
2i

According to the representative procedure, **4-20i** was obtained in 58% yield as a yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20i:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35–7.31 (m, 3H), 7.30–7.23 (m, 5H), 7.17–7.15 (m, 2H), 6.68 (d, *J* = 5.6 Hz, 1H), 6.33 (d, *J* = 5.6 Hz, 1H), 5.17 (s, 2H), 3.71 (s, 6H), 3.25 (dd, *J* = 15.6, 1.6 Hz, 2H), 3.11 (dd, *J* = 15.6, 1.6 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.0, 172.6, 170.6, 149.0, 146.9, 144.0, 137.2, 136.3, 129.5 (2C), 129.2 (2C), 129.0, 128.8, 128.7 (2C), 128.1, 126.9 (2C), 68.0, 67.8 (2C), 64.9, 53.6, 37.9, 37.3; IR (neat) 1733 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{26}H_{28}NO_6$ 450.1917; Found 450.1941.



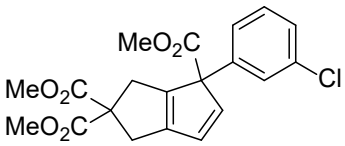
4-20j

According to the representative procedure, **4-20j** was obtained in 60% yield as a brown amorphas solid after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20j:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.0 Hz, 1H), 7.88 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.79 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.54–7.45 (m, 2H), 7.40–7.34 (m, 2H), 6.88 (d, *J* = 5.6 Hz, 1H), 6.46 (d, *J* = 5.6 Hz, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 3.66 (s, 3H), 3.38–3.29 (m, 1H), 3.22–3.17 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.4, 172.3, 171.9, 147.7, 147.5, 142.7, 134.2, 133.2, 132.0, 129.5, 129.4, 128.8, 126.3, 125.7, 125.5, 123.6, 123.4, 67.3, 64.0, 53.0 (2C), 52.9, 37.7, 36.6; IR (neat) 1732 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{24}H_{26}NO_6$ 424.1760; Found 424.1753.



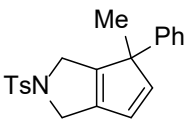
4-20k

According to the representative procedure, **4-20k** was obtained in 67% yield as a brown amorphous solid after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20k:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.14 (dt, *J* = 8.8, 2.4 Hz, 2H), 6.83 (dt, *J* = 8.8, 2.4 Hz, 2H), 6.64 (d, *J* = 5.2 Hz, 1H), 6.30 (d, *J* = 5.2 Hz, 1H), 3.774 (s, 3H), 3.766 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H), 3.34–3.22 (m, 2H), 3.17–3.10 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.3, 172.0, 170.8, 158.8, 148.4, 145.9, 143.5, 128.5, 127.9, 127.3 (2C), 114.2 (2C), 66.5, 64.2, 55.2, 52.9 (2C), 52.6, 37.2, 36.6; IR (neat) 1733, 1252 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{21}H_{23}O_7$ 387.1444; Found 387.1435.



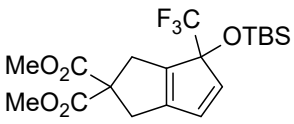
4-20l

According to the representative procedure, **4-20l** was obtained in 79% yield as a brown oil after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20l:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.24–7.22 (m, 2H), 7.18–7.18 (m, 1H), 7.13–7.08 (m, 1H), 6.61 (d, *J* = 5.6 Hz, 1H), 6.34 (d, *J* = 5.6 Hz, 1H), 3.77 (s, 3H), 3.74 (s, 3H), 3.74 (s, 3H), 3.28–3.23 (m, 2H), 3.16–3.09 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.2, 171.8, 170.1, 147.9, 146.8, 142.8, 138.5, 134.6, 130.0, 128.7, 127.6, 126.3, 124.6, 66.7, 64.2, 53.0, 52.9, 52.8, 37.0, 36.5; IR (neat) 1734 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{20}H_{23}NO_6Cl$ 408.1214; Found 408.1212.



4-20z

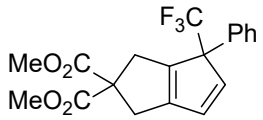
According to the representative procedure, **4-20z** was obtained in 70% yield as a brown amorphas solid after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20z:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.24–7.17 (m, 3H), 7.02 (dd, *J* = 8.0, 1.6 Hz, 2H), 6.53 (d, *J* = 5.2 Hz, 1H), 6.18 (d, *J* = 5.2 Hz, 1H), 4.33–4.26 (m, 2H), 4.25–4.17 (m, 1H), 4.08 (td, *J* = 14.0, 4.4 Hz, 1H), 2.42 (s, 3H), 1.47 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 151.8, 151.2, 143.3, 140.7, 139.5, 134.7, 129.8 (2C), 128.7 (2C), 127.3 (2C), 126.8, 125.6 (2C), 123.5, 55.9, 51.1, 50.7, 21.5, 20.1; IR (neat) 1344, 1163 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{21}H_{25}N_2O_2S$ 369.1637; Found 369.1627.



4-20y

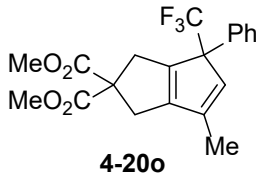
The reaction was performed using 20 mol% Cp*Ru(cod)Cl at 100 °C and **4-20y** was obtained in 74% yield as a colorless oil after purification by silica gel column chromatography (Hexane/EtOAc = 50:1). **Analytical data for 4-20y:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.36 (d, *J* = 5.2 Hz, 1H), 6.19 (d, *J* = 5.2 Hz, 1H), 3.76 (s, 3H), 3.75 (s, 3H),

3.19 (d, J = 18.8 Hz, 1H), 3.11 (s, 2H), 3.06 (d, J = 18.8 Hz, 1H), 0.88 (s, 9H), 0.04 (s, 3H), –0.06 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.9, 171.6, 149.0, 144.8, 138.2, 132.2, 124.2 (q, J = 285 Hz), 83.3 (q, J = 30.8 Hz), 64.0, 53.02, 52.98, 36.6, 35.9, 25.4 (3C), 18.1, –3.4, –4.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ –79.1; IR (neat) 1740 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{19}H_{31}NO_5F_3Si$ 438.1924; Found 438.1920.



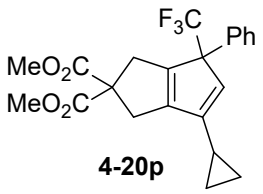
4-20w

The reaction was performed at 100 °C and **4-20w** was obtained in 94% yield as a pale-yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-20w:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.45–7.43 (m, 2H), 7.37–7.31 (m, 3H), 6.65 (d, J = 5.6 Hz, 1H), 6.46 (d, J = 5.6 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 3.35 (d, J = 18.0 Hz, 1H), 3.27 (dt, J = 16.0, 1.6 Hz, 1H), 3.25 (d, J = 18.0 Hz, 1H), 3.13 (dt, J = 16.0, 1.6 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.6, 172.3, 149.8, 146.7, 140.6, 133.2, 131.7, 129.3, 128.9 (2C), 128.7 (2C), 126.2 (q, J = 284 Hz), 65.1, 64.5 (q, J = 27.0 Hz), 53.74, 53.69, 38.2, 37.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ –68.9; IR (neat) 1738 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{19}H_{21}NO_4F_3$ 384.1423; Found 250.384.1420.



4-20o

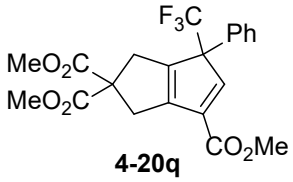
The reaction was performed at 100 °C and **4-20o** was obtained in 89% yield as a pale-yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-20o:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 7.2 Hz, 2H), 7.36–7.28 (m, 3H), 6.25 (d, J = 1.6 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 3.38 (d, J = 17.2 Hz, 1H), 3.27 (d, J = 17.2 Hz 1H), 3.22 (d, J = 17.2 1H), 3.10 (d, J = 17.2 Hz, 1H), 1.94 (d, J = 1.6 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.0, 171.7, 151.1, 145.3, 141.1, 133.3, 133.2, 128.5, 128.1 (2C), 128.0 (2C), 125.7 (q, J = 284 Hz), 64.5 (q, J = 27.0 Hz), 64.2, 53.12, 53.07, 38.0, 35.4, 14.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ –69.3; IR (neat) 1738 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{20}H_{23}NO_4F_3$ 398.1579; Found 398.1588.



4-20p

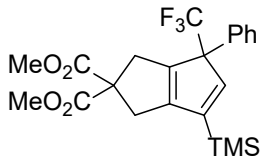
The reaction was performed using 20 mol% Cp*Ru(cod)Cl at 100 °C and **4-20p** was obtained in 99% yield as a yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-20p:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.6 Hz, 2H), 7.35–7.27 (m, 3H), 6.14 (s, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 3.32 (d, J = 17.2 Hz, 1H), 3.23 (dt, J = 17.2, 1.6 Hz, 1H), 3.21 (d, J = 17.2 Hz, 1H), 3.10 (dt, J = 17.2, 1.6 Hz, 1H), 1.60–1.53 (m, 1H), 0.86–0.80 (m, 2H), 0.65–0.58 (m, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.9, 171.6, 149.2, 148.0, 146.0, 133.4, 129.8, 128.5, 128.0 (2C), 127.9 (2C), 125.7 (q, J = 283 Hz), 64.1, 62.3 (q, J = 27.0

Hz), 53.05, 53.01, 37.3, 35.8, 10.2, 7.3, 7.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ –69.1; IR (neat) 1737 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{22}H_{22}O_4F_3$ 407.1470; Found 407.1455.



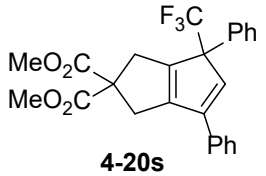
4-20q

The reaction was performed with 20 mol% Cp*Ru(cod)Cl at 150 °C using a sealed tube and **4-20q** was obtained in 65% yield as a yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20q:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.45–7.43 (m, 2H), 7.39 (s, 1H), 7.38–7.34 (m, 3H), 3.81 (s, 3H), 3.79 (s, 3H), 3.76 (s, 3H), 3.49 (dt, *J* = 18.0, 2.4 Hz, 1H), 3.39 (dt, *J* = 18.0, 2.4 Hz, 1H), 3.37–3.32 (m, 1H), 3.28–3.23 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.9, 171.5, 163.1, 146.94, 146.85, 136.6, 131.1, 128.9, 128.7 (2C), 128.1 (2C), 124.9 (q, *J* = 284 Hz), 63.8, 63.7 (q, *J* = 27.9 Hz), 53.11, 53.09, 52.0, 37.7, 36.8, One C*sp*^{2} signal is missing due to overlapping.; ^{19}F NMR (376 MHz, $CDCl_3$) δ –68.4; IR (neat) 1737 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{21}H_{23}NO_6F_3$ 442.1478; Found 442.1469.



4-20r

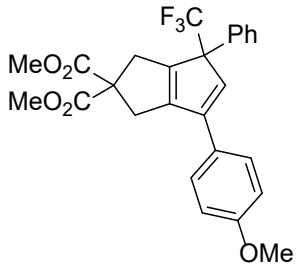
The reaction was performed with 20 mol% Cp*Ru(cod)Cl at 150 °C using a sealed tube and **4-20r** was obtained in 87% yield as a pale-yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-20r:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.42–7.39 (m, 2H), 7.37–7.30 (m, 3H), 6.73 (s, 1H), 3.78 (s, 3H), 3.75 (s, 3H), 3.32 (dd, *J* = 16.0, 2.4 Hz, 1H), 3.28–3.20 (m, 2H), 3.16–3.11 (m, 1H), 0.18 (s, 9H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.1, 171.7, 152.5, 147.8, 145.6, 145.1, 132.8, 128.6, 127.99 (2C), 127.96 (2C), 125.5 (q, *J* = 284 Hz), 65.0 (q, *J* = 27.0 Hz), 64.5, 53.04, 53.01, 37.0, 36.8, –1.5 (3C); ^{19}F NMR (376 MHz, $CDCl_3$) δ –68.6; IR (neat) 1738 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{22}H_{29}NO_4F_3Si$ 456.1818; Found 456.1809.



4-20s

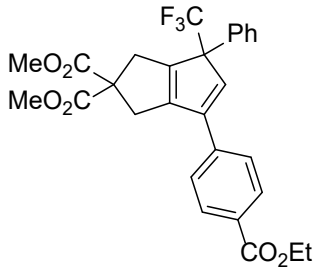
The reaction was performed with 20 mol% Cp*Ru(cod)Cl at 150 °C using a sealed tube and **4-20s** was obtained in 74% yield as a pale-yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-20s:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.2 Hz, 2H), 7.49 (d, *J* = 7.2 Hz, 2H), 7.40–7.29 (m, 6H), 6.79 (s, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 3.56 (d, *J* = 17.2 Hz, 1H), 3.47 (d, *J* = 17.2 Hz, 1H), 3.39 (d, *J* = 17.2 Hz, 1H), 3.31 (d, *J* = 17.2 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.9, 171.6, 148.5, 147.3, 144.3, 133.6, 132.9, 132.7, 128.7, 128.5 (2C), 128.2 (2C), 128.0 (2C), 126.4 (2C), 125.6 (q, *J* = 285 Hz), 64.1, 62.8 (q, *J* = 27.0 Hz), 53.1 (2C), 37.5, 37.3, One C*sp*^{2} signal is missing due to overlapping.; ^{19}F NMR (376 MHz, $CDCl_3$) δ –68.6; IR (neat) 1738 cm^{-1}; HRMS

(DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{25}H_{25}NO_4F_3$ 460.1736; Found 460.1728.



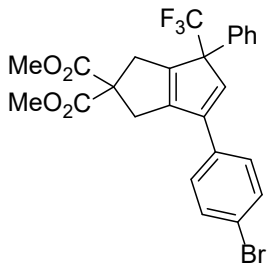
4-20t

The reaction was performed at 60 °C and **4-20t** was obtained in 84% yield as a pale-yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20t:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.49–7.45 (m, 4H), 7.37–7.29 (m, 3H), 6.89 (dt, *J* = 8.0 , 1.2 Hz, 2H), 6.67 (s, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.76 (s, 3H), 3.55 (d, *J* = 17.2, 1H), 3.46 (d, *J* = 17.2 Hz, 1H), 3.37 (d, *J* = 17.2 Hz, 1H), 3.30 (d, *J* = 17.2 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.9, 171.6, 159.8, 148.6, 147.2, 143.6, 133.1, 130.7, 128.7, 128.1 (2C), 128.0 (2C), 127.8 (2C), 126.3, 125.7 (q, *J* = 285 Hz), 114.1 (2C), 64.2, 62.6 (q, *J* = 27.0 Hz), 55.3, 53.13, 53.09, 37.6, 37.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ –68.6; IR (neat) 1736 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{24}O_5F_3$ 473.1576; Found 473.1548.



4-20u

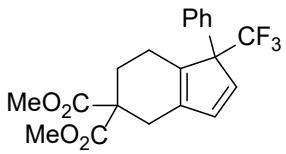
The reaction was performed with 20 mol% Cp*Ru(cod)Cl at 150 °C using a sealed tube and **4-20u** was obtained in 82% yield as a pale-yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 10:1). **Analytical data for 4-20u:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.04 (dt, *J* = 8.0, 1.6 Hz, 2H), 7.58 (dt, *J* = 8.0, 1.6 Hz, 2H), 7.50–7.48 (m, 2H), 7.39–7.33 (m, 3H), 6.90 (s, 1H), 4.39 (q, *J* = 7.2 Hz, 2H), 3.81 (s, 3H), 3.77 (s, 3H), 3.58 (d, *J* = 17.2 Hz, 1H), 3.46 (d, *J* = 17.2 Hz, 1H), 3.42 (d, *J* = 17.2 Hz, 1H), 3.32 (d, *J* = 17.2 Hz, 1H), 1.41 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.8, 171.4, 166.1, 148.0, 147.8, 143.5, 137.8, 134.7, 132.5, 130.2, 130.0 (2C), 128.8 (2C), 128.3, 128.0 (2C), 126.3 (2C), 125.4 (q, *J* = 285 Hz), 64.1, 63.0 (q, *J* = 27.9 Hz), 61.1, 53.2, 53.1, 37.5, 37.3, 14.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ –68.5; IR (neat) 1737, 1716 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{28}H_{29}NO_6F_3$ 532.1947; Found 532.1969.



4-20v

The reaction was performed with 20 mol% Cp*Ru(cod)Cl using a sealed tube at 150 °C and **4-20v** was obtained in 76% yield as a pale-yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-20v:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50–7.47 (m, 4H), 7.40–7.31 (m, 5H), 6.80 (s, 1H), 3.80 (s, 3H), 3.76 (s, 3H), 3.53 (d, *J* = 18.0 Hz, 1H), 3.43 (d, *J* = 18.0 Hz, 1H), 3.39 (d, *J* = 18.0 Hz, 1H), 3.31 (d, *J* = 18.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.8, 171.4, 148.0, 147.7, 143.3, 133.2, 132.6, 132.5, 131.9 (2C), 128.8 (2C), 128.3, 127.98

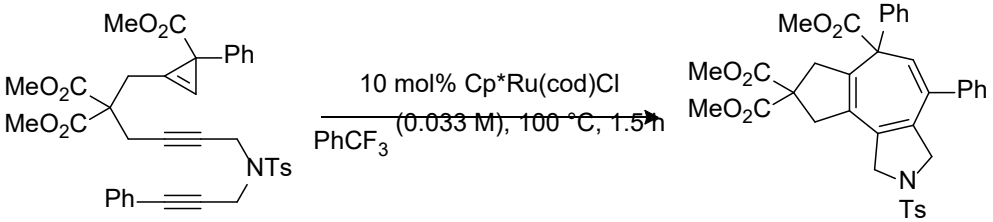
(2C), 127.95 (2C), 125.5 (q, J = 284 Hz), 122.5, 64.1, 62.9 (q, J = 27.0 Hz), 53.2, 53.1, 37.4, 37.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ –68.6; IR (neat) 1736 cm^{-1}; HRMS (DART) *m/z*: $[M + H]^+$ Calcd for $C_{25}H_{21}O_4BrF_3$ 521.0575; Found 521.0599.



4-20x

The reaction was performed with 20 mol% Cp*Ru(cod)Cl at 150 °C using a sealed tube and **4-20x** was obtained in 76% yield as a yellow oil after purification by silica gel column chromatography (Hexane/EtOAc = 20:1). **Analytical data for 4-20x:** δ 7.33–7.25 (m, 3H), 7.21–7.19 (m, 2H), 6.42 (d, J = 5.2 Hz, 1H), 6.40 (d, J = 5.2 Hz, 1H), 3.74 (s, 3H), 3.70 (s, 3H), 3.08–2.74 (m, 2H), 2.36–2.29 (m, 2H), 2.24–2.17 (m, 1H), 2.12–2.04 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.6, 171.4, 140.7, 139.5, 137.1, 135.5, 132.8, 128.8, 127.6 (2C), 126.7 (2C), 126.0 (q, J = 284 Hz), 68.1 (q, J = 26.0 Hz), 53.6, 52.8, 52.7, 30.4, 28.3, 20.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ –66.4; IR (neat) 1735 cm^{-1}; HRMS (DART) *m/z*: $[M + NH_4]^+$ Calcd for $C_{20}H_{23}F_3NO_4$ 398.1579; Found 398.1600.

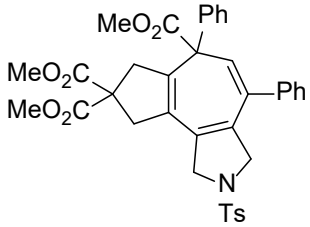
7. Representative Procedure for the Ruthenium-Catalyzed Cycloisomerization of 4-23



4-23a **4-24a**

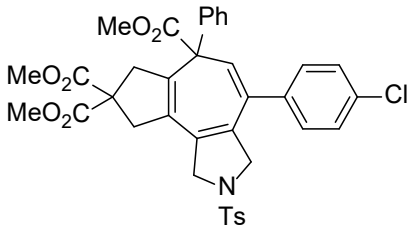
Cp*Ru(cod)Cl (3.80 mg, 0.0100 mmol) was dissolved in degassed $PhCF_3$ (3.0 mL) under Ar atmosphere. To the resulting mixture was added **4-23a** (65.4 mg, 0.100 mmol). After stirring at 100 °C for 1.5 h, the resulting solution was concentrated. The crude was then purified by a silica gel column chromatography (Hexane/EtOAc = 5:1) and reprecipitation (Et_2O/Hexane) to give **4-24a** (30.1 mg, 46%).

8. Characterization of Fused Cycloheptatriene 4-24



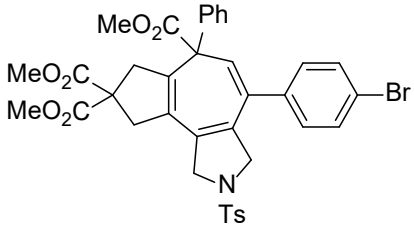
4-24a

According to the representative procedure, **4-24a** was obtained in 46% yield as a pale-yellow amorphous solid after purification by silica gel column chromatography (Hexane/EtOAc = 5:1) and reprecipitation (Et_2O/Hexane). **Analytical data for 4-24a:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.34–7.33 (m, 3H), 7.29–7.26 (m, 2H), 7.19–7.17 (m, 2H), 7.04–6.95 (m, 5H), 6.11 (s, 1H), 4.35 (dd, *J* = 14.0, 4.0 Hz, 1H), 4.17 (dd, *J* = 14.0, 4.0 Hz, 1H), 3.92 (dt, *J* = 14.0 Hz, 1H), 3.80 (s, 3H), 3.71 (s, 3H), 3.61 (s, 3H), 3.57 (d, *J* = 14.0 Hz, 1H), 3.33 (d, *J* = 18.0 Hz, 1H), 3.28 (s, 2H), 3.04 (d, *J* = 18.0 Hz, 1H), 2.47 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.0, 172.0, 171.4, 143.4, 140.1, 139.4, 135.1, 133.6, 133.1, 129.7 (2C), 128.7 (2C), 128.4 (2C), 128.0, 127.4 (2C), 127.24 (2C), 127.16 (2C), 127.0, 123.4, 58.3, 55.5, 55.4, 55.2, 53.2, 53.1, 52.7, 42.9, 40.5, 21.6, Three C*sp*^{2} signals are missing due to overlapping.; IR (KBr) 1736 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{37}H_{35}NNaO_8S$ 678.1939; Found 678.1946.



4-24b

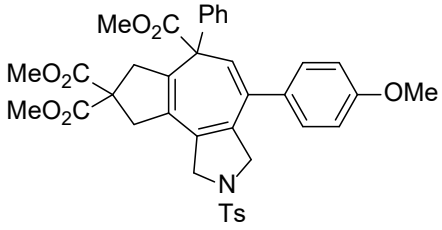
According to the representative procedure, **4-24b** was obtained in 63% yield as a white amorphous solid after purification by silica gel column chromatography (Hexane/EtOAc = 5:1) and reprecipitation (Et_2O/Hexane). **Analytical data for 4-24b:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.01–6.95 (m, 5H), 6.10 (s, 1H), 4.34 (dd, *J* = 14.0, 3.6 Hz, 1H), 4.12 (dt, *J* = 14.0, 3.6 Hz, 1H), 3.92 (dt, *J* = 14.0, 3.6 Hz, 1H), 3.80 (s, 3H), 3.71 (s, 3H), 3.61 (s, 3H), 3.55 (dd, *J* = 14.0, 3.6 Hz, 1H), 3.33 (d, *J* = 18.4 Hz, 1H), 3.28 (s, 2H), 3.03 (d, *J* = 18.4 Hz, 1H), 2.47 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.9, 172.0, 171.3, 143.5, 139.9, 137.8, 134.0, 133.6, 133.2, 133.1, 130.0, 129.7 (2C), 128.8 (2C), 128.6, 127.4 (2C), 127.3 (2C), 127.10, 127.08 (2C), 124.0, 58.2, 55.6, 55.3, 55.1, 53.2, 53.1, 52.8, 42.9, 40.5, 21.6, Three C*sp*^{2} signals are missing due to overlapping.; IR (KBr) 1736 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{37}H_{34}ClNNaO_8S$ 710.1591; Found 710.1572.



4-24c

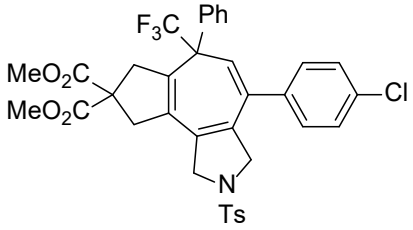
According to the representative procedure, **4-24c** was obtained in 58% yield as a white amorphous solid after purification by silica gel column chromatography (Hexane/EtOAc = 5:1). Colorless crystals (mp 241.8–243.2 °C) was obtained by recrystallization from toluene and hexane. **Analytical data for 4-24c:** ^{1}H-NMR (400 MHz,

$CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.46 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.05 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.01–6.95 (m, 5H), 6.10 (s, 1H), 4.34 (dd, *J* = 14.4, 3.6 Hz, 1H), 4.11 (dd, *J* = 14.4, 2.0 Hz, 1H), 3.92 (dt, *J* = 14.0, 3.6 Hz, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 3.61 (s, 3H), 3.56–3.52 (m, 1H), 3.33 (d, *J* = 18.0 Hz, 1H), 3.28 (s, 2H), 3.03 (d, *J* = 18.0 Hz, 1H), 2.47 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.5, 172.6, 172.0, 144.2, 140.6, 139.0, 134.7, 134.3, 133.8, 132.7, 132.2 (2C), 131.0 (2C), 130.4 (2C), 129.5, 128.1 (2C), 128.0 (2C), 127.8, 127.7 (2C), 124.6, 122.9, 58.9, 56.3, 55.9, 55.8, 53.9, 53.8, 53.5, 43.6, 41.2, 22.3, One C*sp*^{2} signal is missing due to overlapping.; IR (KBr) 1735 cm^{-1}; HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for $C_{37}H_{34}BrNNaO_8S$ 758.1036; Found 758.1021.



4-24d

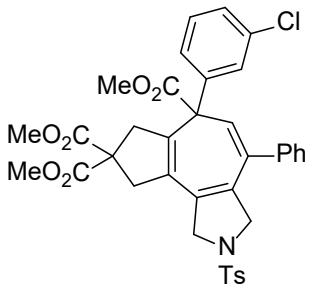
According to the representative procedure, **4-24d** was obtained in 39% yield as a pale-yellow amorphous solid after purification by silica gel column chromatography (Hexane/EtOAc = 5:1) and reprecipitation (Et_2O/Hexane). **Analytical data for 4-24d:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.12 (dt, *J* = 9.2, 2.4 Hz, 2H), 7.01–6.92 (m, 5H), 6.86 (dt, *J* = 9.2, 2.4 Hz, 2H), 6.03 (s, 1H), 4.34 (ddd, *J* = 14.0, 4.4, 2.8 Hz, 1H), 4.18 (ddd, *J* = 14.0, 4.4, 2.8 Hz, 1H), 3.90 (ddd, *J* = 14.0, 4.4, 2.8 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.71 (s, 3H), 3.60 (s, 3H), 3.58–3.53 (m, 1H), 3.32 (d, *J* = 18.0 Hz, 1H), 3.27 (s, 2H), 3.03 (d, *J* = 18.0 Hz, 1H), 2.47 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.1, 172.0, 171.4, 159.4, 143.4, 140.1, 134.6, 133.8, 133.1, 132.9, 132.0, 129.9 (2C), 129.7 (2C), 128.5, 127.4 (2C), 127.19 (2C), 127.16 (2C), 127.0, 122.00, 121.96, 113.8 (2C), 58.2, 55.5, 55.4, 55.3, 55.1, 53.2, 53.1, 52.7, 42.8, 40.5, 21.6; IR (KBr) 1736 cm^{-1}; HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for $C_{38}H_{37}NNaO_9S$ 706.2087; Found 706.2105.



4-24e

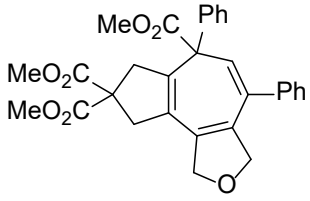
According to the representative procedure, **4-24e** was obtained in 42% yield as a brown amorphous solid after purification by silica gel column chromatography (Hexane/EtOAc = 5:1) and reprecipitation (Et_2O/Hexane). **Analytical data for 4-24e:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.43 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.34 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.13 (dt, *J* = 8.0, 2.0 Hz, 2H), 7.05 (d, *J* = 6.8 Hz, 2H), 6.96–6.91 (m, 3H), 5.80 (s, 1H), 4.33 (dd, *J* = 14.4, 2.4 Hz, 1H), 4.21 (dd, *J* = 14.4, 2.4 Hz, 1H), 3.86 (s, 3H), 3.75 (s, 3H), 3.67–3.62 (m, 2H), 3.49–3.37 (m, 2H), 3.27–3.17 (m, 2H), 2.48 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.1, 171.3, 143.5, 137.0, 136.3, 135.9,

135.8, 134.6, 134.3, 133.9, 132.9, 130.0, 129.9 (2C), 129.7 (2C), 128.8 (2C), 128.0, 127.9 (2C), 127.3 (2C), 126.8 (2C), 126.4 (q, J = 284 Hz), 123.4, 58.4, 55.4 (q, J = 25.0 Hz), 55.2, 55.1, 53.4, 53.2, 42.4, 40.2, 21.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ –71.4; IR (KBr) 1737 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{36}H_{31}ClF_3NNaO_6S$ 720.1410; Found 720.1412.



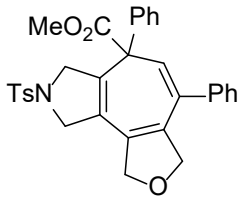
4-24f

According to the representative procedure, **4-24f** was obtained in 52% yield as a brown amorphous solid after purification by silica gel column chromatography (Hexane/EtOAc = 5:1) and reprecipitation (Et_2O/Hexane). **Analytical data for 4-24f:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.0 Hz, 2H), 7.36–7.35 (m, 3H), 7.29 (d, J = 8.0 Hz, 2H), 7.21–7.19 (m, 2H), 7.00 (s, 1H), 6.92–6.83 (m, 3H), 6.09 (s, 1H), 4.37 (dd, J = 14.4, 4.0 Hz, 1H), 4.24 (dd, J = 14.4, 4.0 Hz, 1H), 3.84–3.80 (m, 4H), 3.72 (s, 3H), 3.66 (s, 3H), 3.48 (dd, J = 14.4, 6.8 Hz, 1H), 3.36 (d, J = 18.0 Hz, 1H), 3.28 (s, 2H), 3.08 (d, J = 18.0 Hz, 1H), 2.48 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.4, 172.0, 171.2, 143.4, 142.2, 139.1, 135.4, 134.0, 133.2, 132.9, 132.8, 129.8 (2C), 128.9, 128.6 (2C), 128.5 (2C), 128.2, 128.1, 127.5, 127.4 (2C), 127.2, 125.5, 121.7, 58.4, 55.3, 55.04, 55.01, 53.3, 53.1, 53.0, 42.6, 40.4, 21.6, One Csp^2 signal is missing due to overlapping.; IR (KBr) 1737 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{37}H_{34}ClNNaO_8S$ 713.1556; Found 713.1574.



4-24g

According to the representative procedure, **4-24g** was obtained in 68% yield as a pale-yellow amorphous solid after purification by silica gel column chromatography (Hexane/EtOAc = 5:1) and reprecipitation (Et_2O/Hexane). This compound was unstable in solution and gradually decomposed. **Analytical data for 4-24g:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37–7.29 (m, 5H), 7.22–7.14 (m, 5H), 6.04 (s, 1H), 4.82 (ddd, J = 12.4, 4.8, 2.4 Hz, 1H), 4.66 (ddd, J = 12.4, 4.8, 2.4 Hz, 1H), 4.56 (dt, J = 12.4, 4.0 Hz, 1H), 4.28 (dt, J = 12.4, 4.0 Hz, 1H), 3.80 (s, 3H), 3.72 (s, 3H), 3.70 (s, 3H), 3.37–3.32 (m, 3H), 3.06 (d, J = 18.0 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.4, 172.1, 171.5, 140.5, 140.1, 135.4, 134.9, 134.6, 128.5 (2C), 128.4, 128.3 (2C), 127.7, 127.5 (4C), 127.2, 120.8, 76.0, 75.4, 58.4, 55.3, 53.1, 53.0, 52.7, 42.9, 40.5, One Csp^2 signal is missing due to overlapping.; IR (KBr) 1746, 1732 cm^{-1}; HRMS (ESI) *m/z*: $[M + Na]^+$ Calcd for $C_{30}H_{28}NaO_7$ 523.1733; Found 523.1722.

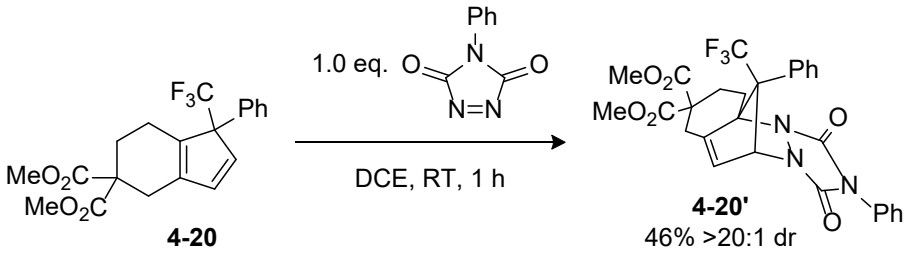


4-24h

According to the representative procedure, **4-24h** was obtained in 19% yield as a white amorphous solid after purification by silica gel column chromatography (Hexane/EtOAc = 5:1) and reprecipitation (Et_2O/Hexane). **Analytical data for 4-24h:** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.37–7.32 (m, 5H), 7.27–7.24 (m, 2H), 7.21–7.16 (m, 3H), 7.04 (dd, *J* = 8.0, 1.6 Hz, 2H), 5.99 (s, 1H), 4.74 (ddd, *J* = 12.4, 4.8, 2.4 Hz, 1H), 4.62 (ddd, *J* = 12.4, 4.8, 2.4 Hz, 1H), 4.52 (td, *J* = 12.4, 4.8 Hz, 1H), 4.42–4.28 (m, 4H), 4.09–4.04 (m, 1H), 3.68 (s, 3H), 2.39 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.6, 143.8, 139.9, 139.6, 136.7, 135.6, 134.0, 132.9, 129.9 (2C), 128.5 (2C), 128.4 (2C), 128.0, 127.9 (2C), 127.7, 127.4 (2C), 127.0 (2C), 126.4, 76.2, 75.3, 56.3, 55.4, 54.6, 53.0, 21.5, Two C*sp*^{2} signals are missing due to overlapping.; IR (KBr) 1741 cm^{-1}; HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for $C_{32}H_{29}NNaO_5S$ 562.1664; Found 562.1683.

9. Derivatization for X-Ray Diffraction Analysis

Synthesis and characterization of 4-20x'



To a solution of **4-20x** (28.9 mg, 0.076 mmol) in DCE (1.0 ml) was added 4-phenyl-1,2,4-triazoline-3,5-dione (13.3 mg, 0.076 mmol). The solution was stirred at room temperature for 1 h and concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to furnish **4-20x'** (19.3 mg, 46%) as a white solid. Colorless crystals (mp 169.9–170.9 °C) for X-ray crystallographic analysis were obtained from DCM and hexane. **Analytical data for 4-20x':** ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.57–7.56 (m, 2H), 7.45–7.38 (m, 5H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 2H), 6.24 (t, *J* = 2.8 Hz, 1H), 5.57 (d, *J* = 2.8 Hz, 1H), 3.76 (s, 6H), 3.44 (dd, *J* = 17.6, 2.8 Hz, 1H), 3.10–3.06 (m, 2H), 2.72–2.59 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 171.2, 169.8, 157.3, 157.0, 140.5, 132.8, 130.9, 129.3 (2C), 129.2, 128.7, 128.6 (2C), 128.5 (2C), 125.5 (2C), 123.7 (q, *J* = 283 Hz), 120.4, 73.1 (q, *J* = 25.0 Hz), 66.7, 53.4, 53.0, 52.6, 31.3, 27.2, 22.5, One C*sp*^{3} signal is missing; ^{19}F NMR (376 MHz, $CDCl_3$) δ –58.9; IR (KBr) 1779, 1748 cm^{-1}; HRMS (ESI) *m/z*: [M + NH_4]$^+$ Calcd for $C_{28}H_{27}F_3N_4O_5$ 556.1934; Found 556.1951.

10. X-Ray Diffraction Analysis

X-Ray Diffraction Analysis of 4-20a'

Diffraction data were collected in θ ranges specified in Table S2 at 123 K on a Rigaku R-AXIS Rapid diffractometer with graphite monochromatized Cu-Ka radiation (λ = 1.54187 Å). The Lorenz polarization absorption correction was applied. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined using the riding model. Final refinement details are compiled in Table S2.

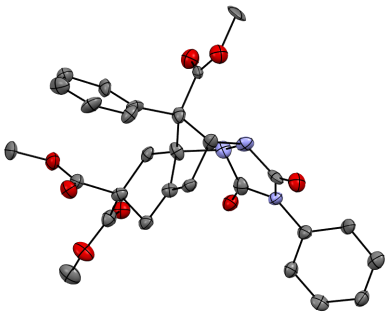


Figure S1. ORTEP plot of **4-20a'**.

Table S2. Selected crystallographic data and collection parameters for **4-20a'**.

formula	$C_{28}H_{25}N_3O_8$	μ, cm^{-1}	8.669
FW	531.52	$F(000)$	556.00
crystal system	triclinic	crystal size, mm	0.2 x 0.2 x 0.2
space group	P21/n (#14)	maximum 2θ, deg	136.3
a, Å	8.9225(8)	reflections collected	13731
b, Å	11.9144(11)	independent reflections [R(int)]	4523 [R(int) = 0.1844]
c, Å	12.3336(12)	max. and min. transmission	0.841/0.355
volume, $Å^3$	1268.4(2)	goodness-of-fit on F^2	0.667
α, °	101.917(7)	R_1 [I >2σ(I)]	0.0492
β, °	96.015(7)	R, wR_2 (all data)	0.2568, 0.0743
γ, °	92.561(7)	Weighting scheme	$R_1 = \Sigma \lvert\lvert Fo\rvert - \lvert Fc\rvert\rvert / \Sigma \lvert Fo\rvert$ $wR_2 = [\Sigma(w(Fo^2 - Fc^2)^2)/\Sigma w(Fo^2)^2]^{1/2}$
Z	2		
D (calcd), Mg m^{-3}	1.392	largest diff. peak and hole, e $Å^{-3}$	1.01 and –1.23

X-Ray Diffraction Analysis of 4-20x'

Diffraction data were collected in θ ranges specified in Table S3 at 123 K on a Rigaku R-AXIS Rapid diffractometer with graphite monochromatized Cu-Ka radiation (λ = 1.54187 Å). The Lorenz polarization absorption correction was applied. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined using the riding model. Final refinement details are compiled in Table S3. The supplementary crystallographic data for this paper (CCDC 2236991) can also be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

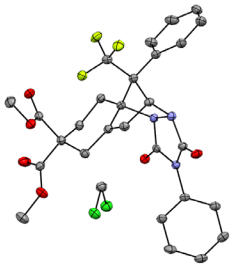


Figure S2. ORTEP plot of **4-20x'**.

Table S3. Selected crystallographic data and collection parameters for **4-20x'**.

formula	$C_{58}H_{52}Cl_4F_6N_6O_{12}$	crystal size, mm	0.2 x 0.2 x 0.1
FW	1280.88	maximum 2θ, deg	136.2
crystal system	monoclinic	reflections collected	63084
space group	P21/n (#14)	independent reflections [R(int)]	10457 [R(int) = 0.0533]
a, Å	13.1698(3)	max. and min. transmission	0.768/0.550
b, Å	18.6790(4)	goodness-of-fit on F^2	1.027
c, Å	23.4507(4)	R_1 [I >2σ(I)]	0.0723
volume, Å^3	5737.1(2)	R, wR_2 (all data)	0.1036, 0.2078
β, °	96.015(7)	Weighting scheme	$R_1 = \Sigma \lvert\lvert Fo\rvert - \lvert Fc\rvert\rvert / \Sigma \lvert Fo\rvert$ $wR_2 = [\Sigma(w(Fo^2 - Fc^2)^2)/\Sigma w(Fo^2)^2]^{1/2}$
Z	4		
D (calcd), Mg m^{-3}	1.483	largest diff. peak and hole, e Å^{-3}	0.78 and –0.99
μ, cm^{-1}	26.428		
F(000)	2640.00		

X-Ray Diffraction Analysis of 4-24c•CH_2Cl_2

Diffraction data were collected in θ ranges specified in Table S4 at 123 K on a Rigaku R-AXIS Rapid diffractometer with graphite monochromatized Cu-Ka radiation (λ = 1.54187 Å). The Lorenz polarization absorption correction was applied. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were refined using the riding model. Final refinement details are compiled in Table S4. The supplementary crystallographic data for this paper (CCDC 2236992) can also be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

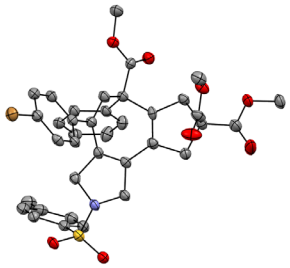


Figure S3. ORTEP plot of **4-24c**•CH_2Cl_2.

Table S4. Selected crystallographic data and collection parameters for **4-24c**•CH_2Cl_2.

formula	$C_{37}H_{34}BrNO_8S$	crystal size, mm	0.2 x 0.2 x 0.1
FW	732.64	maximum 2θ, deg	136.4
crystal system	monoclinic	reflections collected	37715
space group	P21/a (#14)	independent reflections [*R*(int)]	6103 [*R*(int) = 0.1698]
a, Å	9.3002(5)	max. and min. transmission	0.763/0.398
b, Å	29.7868(16)	goodness-of-fit on F^2	0.811
c, Å	12.3138(7)	R_1 [I >2σ(I)]	0.0566
volume, $Å^3$	3361.4(3)	*R*, wR_2 (all data)	0.1825, 0.1570
β, °	99.800(7)	Weighting scheme	$R_1 = \Sigma \lvert\lvert Fo\rvert - \lvert Fc\rvert\rvert / \Sigma \lvert Fo\rvert$ $wR_2 = [\Sigma(w(Fo^2 - Fc^2)^2)/\Sigma w(Fo^2)^2]^{1/2}$
Z	4		
D (calcd), Mg m^{-3}	1.448	largest diff. peak and hole, e $Å^{-3}$	0.37 and –0.52
μ, cm^{-1}	27.062		
F(000)	1512.00		

11. DFT Calculations

The Gaussian 16 program package was used for all geometry optimizations.[24] The geometries of stationary points and transition states were fully optimized by means of the Becke's three-parameter hybrid density functional method (B3LYP),[25] with a [5*s*5*p*3*d*1*f*] contracted-valence basis set with the relativistic effective core potential of Hay and Wadt (LanL2TZ(f))[26] for Ru and the 6-31G(d)[27] basis sets for other elements. The D3 version of Grimme's dispersion with Becke-Johnson damping (GD3BJ)[28] was used for empirical dispersion correction. The vibrational frequencies and thermal correction to Gibbs free energy (TCGFE) including zero-point energy were calculated at the same level of theory. The obtained structures were characterized by the number of imaginary frequencies (IF, one or zero for transition or ground states, respectively). The connectivity of each step was also confirmed by intrinsic reaction coordinate (IRC) calculation[29] from the transition states, followed by optimization of the resultant geometries. Single-point energies for geometries obtained by the above method were calculated at the same level of theory using a [6*s*5*p*3*d*2*f*1*g*] contracted-valence basis set with the Stuttgart-Dresden-Bonn energy-consistent pseudopotential (SDD)[30,31] for Ru and the 6-311++G(d,p) basis sets[32] for other elements. The GD3BJ dispersion correction (D3) was also employed for single-point energy calculations. To examine the solvent effect, the above single-point energy calculations were performed using the SMD model[33] with CH_2Cl_2 as the solvent because the ε value of CH_2Cl_2 (8.93) is similar with that of $CF_3C_6H_5$ (9.18). The obtained energies, TCGFEs, and IF are summarized in Table S5.

Table S5. Summary of theoretical calculations

Model	TCGFE/au	Energy/au	IF/cm^{-1}
A	0.311666	–1518.816555	
TS_{AB}	0.311437	–1518.804235	273.2963i
B	0.313786	–1518.825747	
TS_{BC}	0.312469	–1518.815429	105.9208i
C	0.313695	–1518.842103	
TS_{CD}	0.311721	–1518.828186	312.3936i
D	0.311908	–1518.865948	
TS_{DE}	0.311959	–1518.828084	522.8398i
E	0.316851	–1518.917799	
F	0.402072	–1712.996700	
$TS_{FF'}$	0.402885	–1712.971019	259.6258i
F'	0.401834	–1712.991407	
G	0.399441	–1712.986253	
TS_{GH}	0.397836	–1712.973725	219.6470i

H	0.400881	–1712.996135	
I	0.400067	–1713.008583	
J	0.405444	–1713.011455	
TS_{JK}	0.406368	–1713.001029	233.9083i
K	0.409516	–1713.046578	
L	0.408015	–1713.064560	
TS_{LM}	0.404060	–1713.046574	302.0477i
M	0.405903	–1713.073321	
TS_{MN}	0.405764	–1713.056675	198.8325i
N	0.408669	–1713.140201	

12. References

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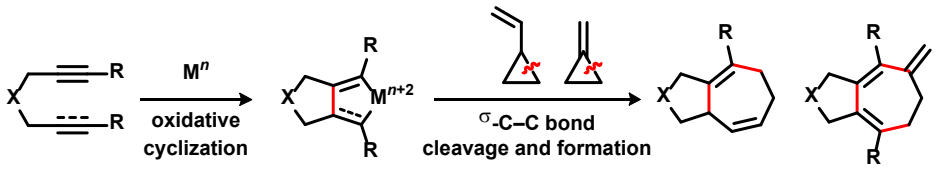
第 5 章

総括

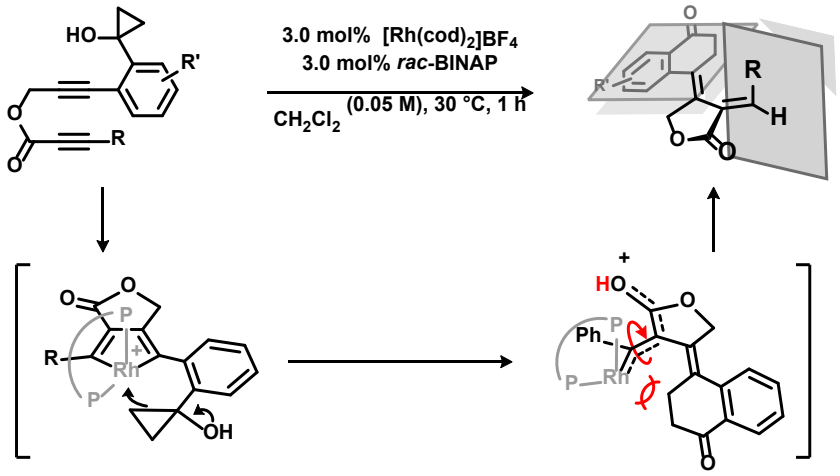
本博士学位論文研究では、シクロプロパノールとシクロプロペンを利用することで、炭素–炭素結合の新たな活性化に基づく触媒的環化異性化反応を開発し、これまで到達困難であった炭素骨格を有する分子の創出を目指した。以下に本博士学位論文を総括する。

第 1 章では、シクロプロパンの炭素–炭素結合が特異な性質を有していることやそれに起因して通常安定な炭素–炭素結合が切断されやすいことを説明した。3 炭素ビルディングブロックとしての有用性から、様々なシクロプロパン基質が設計されるとともに様々な活性化方法が開発された。シクロプロパンとアルキンやアルケンなどの不飽和分子を用いる触媒的付加環化反応では、炭素–炭素結合の切断と形成を伴って、7 員環炭素骨格を一挙に構築できるが、既存の反応は、シクロプロパンを活性化するために、隣接する π 結合を必須としていることを述べた（**Scheme 5-1**）。



Scheme 5-1 既存のシクロプロパンを用いる触媒的付加環化反応

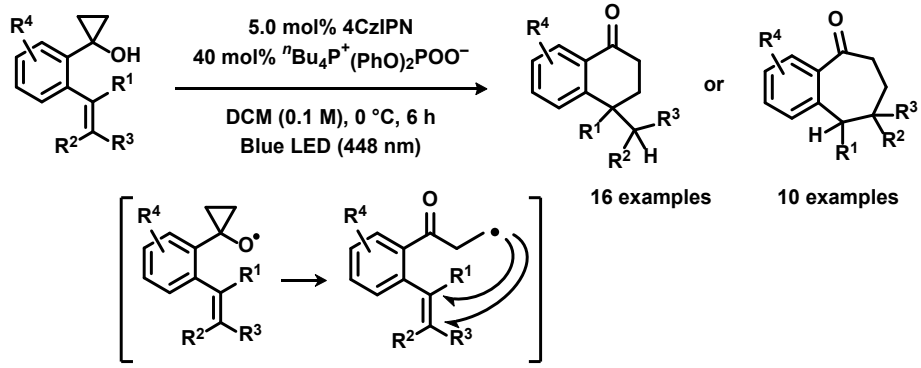
これに対して、私は、酸素電子の押し込みに起因する反応性が知られているシクロプロパノールを利用することで、隣接する π 結合の助けがなくとも、触媒的環化異性化反応にてシクロプロパンを活用できるのではないかと考えた。第 2 章では、ロジウム触媒を用いる 1,6-ジイン含有シクロプロパノールの環化異性化反応を開発したことを述べた（**Scheme 5-2**）。酸素上の電子の押し込みに起因する反応性を特徴とするシクロプロパノールをメタラサイクルの金属中心に対して適切に配置させることで、炭素–炭素結合を直接的に活性化できるのではないかと考え、1,6-ジインとシクロプロパノール部位を剛直なベンゼン環で架橋するという基質設計に至る経緯を説明した。ロジウム触媒を作用させると、1-テトラロンを含む、らせん構造を有する環外エキソジエンが得られること見出し、実験化学および計算化学の両側面から反応機構研究に取り組んだ。その結果、ロダサイクルのロジウム中心がシクロプロパノールの炭素–炭素結合を直接的に切断するという活性化様式を世界に先駆けて提案することができた。加えて、尾島–Crabtree 様のメカニズムの異性化によって生成物のらせん構造が構築されていることを明らかにした。また、本反応で得られるらせん構造を有する環外エキソジエンは、フォトクロミック化合物[1]やキラル有機触媒[2]として利用できることが知られているものの、いまだに効率的な合成法が確立されていない[1a]。本反応がらせん構造を有する環外エキソジエンの化学をさらに発展させるものと期待する。



Scheme 5-2 ロジウム触媒を用いる 1,6-ジイン含有シクロプロパノールの環化異性化反応

第 3 章では、PCET を起点とするアルケン含有シクロプロパノールの触媒的環化異性化反応の開発について述べた（**Scheme 5-3**）。1-テトラロンと 1-ベンゾスベロンなどのベンゼン縮環環状ケトンは、天然物や生理活性物質に広く見られる構造であるが、ベンジル位に置換基を有するベンゼン縮環環状ケトンのメタルフリーな触媒的合成法の開発は、いまだに発展途上である。このような背景の中、私は、プロトンと電子の移動が協奏的に起こる過程であるプロトン共役電子移動（Proton-Coupled Electron Transfer, PCET）に着目した。PCET はレドックスニュートラルで原子効率の高い分子変換反応を可能にする。

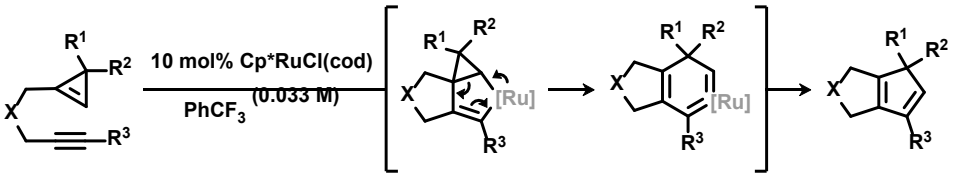
そこで、第 2 章で設計した 1,6-ジイン含有シクロプロパノールと同様にモジュラー合成可能なアルケン含有シクロプロパノール基質を設計した。PCET によってシクロプロパノールを活性化することで、不安定な第一級アルキルラジカルの発生を伴う触媒的環化異性化反応を開発できるのではないかと考えた。反応条件の検討で、本反応には有機光触媒が有効であることを見出した。その後の基質適用範囲の調査によって、基質中のアルケンの置換様式によって、第一級アルキルラジカルの分子内アルケンへのラジカル付加の位置選択性をコントロールできることが分かった。結果として、ベンジル位に多様な置換基を有する 1-テトラロンと 1-ベンゾスベロンのメタルフリーな触媒的合成法を確立することができた。



Scheme 5-3 PCET を起点とするアルケン含有シクロプロパノールの触媒的環化異性化反応

続いて、触媒的環化異性化反応においてシクロプロパンを活用するために、シクロプロペンに着目した。環内に二重結合を有するシクロプロペンは非常に反応性が高いために、遷移金属錯体の存在下で、容易にその炭素–炭素単結合が切断される。一方で、シクロプロペンの炭素–炭素二重結合を直接的かつ選択的に切断することは挑戦的な課題である。第 4 章では、ルテニウム触媒を用いるシクロプロペン-インの環化異性化反応の開発について述べた（**Scheme 5-4**）。

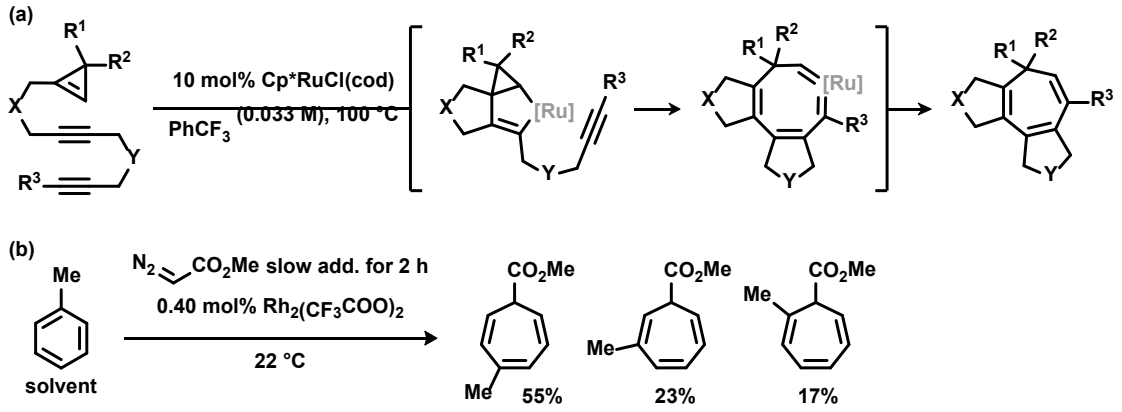
シクロプロペン中のアルケンがアルキンに似た性質を示すことを踏まえ、遷移金属錯体触媒の存在下で、二つのアルキンがメタラサイクルに変換されるのと同様に、シクロプロペンとアルキンはシクロプロパンが縮環したメタラサイクルに変換されるという考えのもと、シクロプロペン-インを設計した。この基質にルテニウム触媒を作用させると、シクロプロペンの炭素–炭素二重結合が切断され、1,2-縮環シクロペンタジエンが得られることを見出した。計算化学的手法により反応機構研究に取り組んだ結果、本反応は前例のないシクロプロペンの炭素–炭素二重結合の活性化様式を含んでいる可能性が高いことを明らかにした。すなわち、炭素–炭素 π 結合の活性化によってシクロプロパンが縮環したルテナサイクルを形成した後に、6 員環ルテニウムビスカルベノイドを与えるようにして、炭素–炭素 σ 結合の活性化によってシクロプロパンが環拡大するというものである。



Scheme 5-4 ルテニウム触媒を用いるシクロプロペン-インの環化異性化反応

また、この反応をシクロプロペン-ジインに適用すると、縮環シクロヘプタトリエンが得られることを見出した（**Scheme 5-5a**）。計算化学的手法によって、6 員環ルテニウムビスカルベノイドが形成される前に分子内アルキンの挿入が起こることが示唆された。

シクロヘプタトリエンの代表的な合成法として、Buchner 反応が挙げられる（**Scheme 5-5b**）[3]。Buchner 反応は、遷移金属錯体触媒とジアゾ化合物から調製されるメタルカルベノイドをベンゼン誘導体に反応させる脱芳香族的環拡大反応である。しかしながら、この反応は溶媒量のベンゼン誘導体を必要とし、メタルカルベノイドの挿入の位置選択性は低く、立体障害を避けるようにして進行する。そのため、本反応で得られるシクロヘプタトリエンは従来の Buchner 反応では合成困難であると考えられる。



Scheme 5-5 ルテニウム触媒を用いるシクロプロペン-ジインの環化異性化反応と Buchner 反応

以上のように、シクロプロパノールとシクロプロペンを利用することで、炭素–炭素結合の切断を伴う 3 つの触媒的環化異性化反応を開発し、これまで到達困難であった炭素骨格を有する分子の創出に成功した。今後、これらの炭素–炭素結合活性化手法が広く応用されることを期待する。

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