博士学位論文

Pd 触媒による α-ヒドロキシケトン誘導体の C－O 結合切断を鍵とした脱炭酸型アルキニル化反応

藪田 明優

北海道大学大学院生命科学院
生命科学専攻　生命医薬科学コース
精密合成化学研究室

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略語表

本論文中で以下の略語を使った。

Ac	;	acetyl
Ar	;	aryl
B	;	base
Bn	;	benzyl
BrettPhos	;	dicyclohexyl(2',4',6'-triisopropyl-3,6-dimethoxy-[1,1'-biphenyl]-2-yl)phosphine
Bu	;	butyl
Cat.	;	catalyst
CN	;	cyanide
Cp	;	cyclopentadienyl
CPME	;	cyclopentyl methyl ether
COD	;	1,5-cyclooctadiene
Cy	;	cyclohexyl
CyJohnPhos	;	(2-biphenyl)dicyclohexylphosphine
DAIBAL-H	;	diisobutyl aluminium hydride
dba	;	dibenzylideneacetone
DCC	;	*N*,*N*'-dicyclohexyl carbodiimide
dcpf	;	1,1’-bis(dicyclohexylphosphino)ferrocene
dcpp	;	1,3-bis(dicyclohexylphosphino)propane
DDQ	;	2,3-dichloro-5,6-dicyano-p-benzoquinone
DIAD	;	diisopropyl azodicarboxylate
DIPEA	;	*N*,*N*-diisopropylethylamine
DMA	;	*N*,*N*-dimethylacetamide
DMAP	;	4-dimethylaminopyridine
dmdba	;	3,5,3’,5’-dimethoxydibenzylideneacetone
DME	;	1,2-dimethoxyethane
DMP	;	Dess-Martin periodinane
DMF	;	*N*,*N*-dimethylformamide

DMSO	;	dimethyl sulfoxide
dppe	;	1,2-bis(diphenylphosphino)ethane
dppf	;	1,1’-bis(diphenyllphosphino)ferrocene
dppp	;	1,3-bis(diphenylphosphino)propane
E	;	electrophile
EPhos	;	dicyclohexyl(3-isopropoxy-2’,4’,6,7-triisopropyl-[1,1’-biphenyl]-2-yl)phosphane
ESI-MS	;	electrospray ionization mass spectrometry
Et	;	ethyl
eq	;	equivalent
EWG	;	electron-withdrawing group
GC	;	gas chromatography
h	;	hour(s)
HMBC	;	heteronuclear multiple-bond correlation spectroscopy
HMQC	;	heteronuclear multiple quantum correlation
JohnPhos	;	2-(di-*tert*-butylphosphino)biphenyl
i	;	iso
LDA	;	lithium diisopropylamide
LHMDS	;	lithium bis(trimethylsilyl)amide
M	;	metal
m	;	meta
m-CPBA	;	*m*-chloroperoxybenzoic acid
Me	;	methyl
min	;	minute(s)
n	;	normal
N.D.	;	not detected
NMR	;	nuclear magnetic resonance
°C	;	degree Celsius
o	;	ortho
p	;	para
Ph	;	phenyl

Piv	;	pivaloyl
PMB	;	*p*-methoxybenzyl
Pr	;	propyl
R	;	alkyl group or heteroatom
rec.	;	recovered
rt	;	room temperature
RuPhos	;	dicyclohexyl(2’,6’-diisopropoxy-[1,1’-biphenyl]-2-yl)phosphine
SM	;	starting material
t	;	tertiary
TBAF	;	tetrabutylammonium fluoride
TBAI	;	tetrabutylammonium iodide
^{t}BuBrettPhos	;	[3,6-dimethoxy-2’,4’,6’-tris(1-methylethyl) [1,1’-biphenyl]-2-yl]bis(1,1-dimethylethyl)phosphine
^{t}BuMePhos	;	2-di-*tert*-butylphosphino-2’-methylbiphenyl
TBS	;	*tert*-butyldimethylsilyl
temp.	;	temperature
Tf	;	trifluoromethylsulfonyl
THF	;	tetrahydrofuran
THP	;	2-tetrahydropyranyl
TIPS	;	triisopropylsilyl
TLC	;	thin-layer chromatography
TMS	;	trimethylsilyl
Tol	;	tolyl
Ts	;	toluenesulfonyl
UV	;	ultraviolet
XantPhos	;	4,5-bis(diphenylphosphino)-9,9-dimethylxanthene
XPhos	;	2-dicyclohexylphosphino-2’,4’,6’-triisopropylbiphenyl

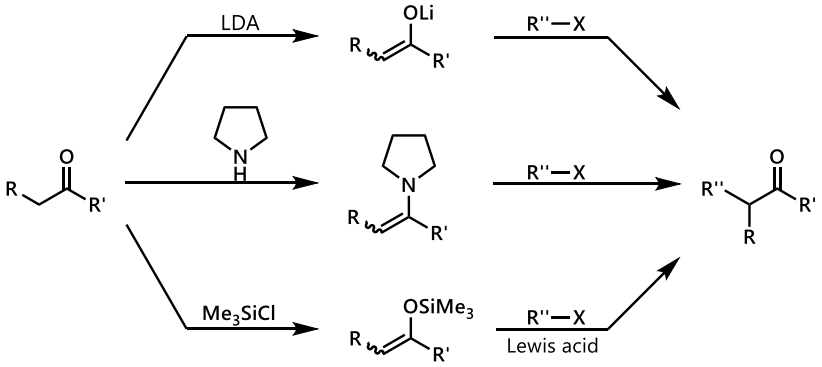
目次

序論

有機化合物は炭素を基本骨格とした物質であり、それらの用途は医薬品や機能性材料など多岐にわたっている。そのため、様々なニーズに応じて有機化合物を合成する上で C－C 結合形成反応の開発は重要であり、古くから有機合成化学における中心課題として研究されている。最近でも 2021 年の List、MacMillan の有機触媒を用いた不斉Ｃ－Ｃ結合形成反応に対してノーベル化学賞が与えられており、Ｃ－Ｃ結合形成反応の開発はいまだに有機合成化学において重要な研究分野である。これまでの反応開発の長い歴史の中でも、特にカルボニル化合物の α 位における C－C 結合形成は、aldol 反応などに代表されるように分子骨格構築の重要な方法論となっている。

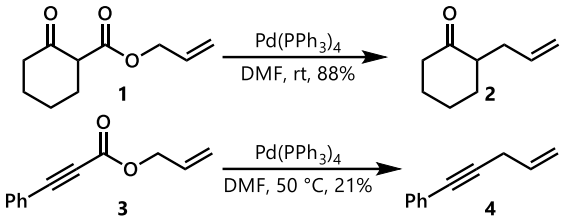
一般に、カルボニル化合物の α 位におけるＣ－Ｃ結合形成反応はエノラートやエノラート等価体を用いる手法が広く用いられている(Scheme 1)[1)]。中でも LDA などの塩基とカルボニル化合物から簡便に調製できるリチウムエノラートは、反応性も高く、様々な求電子剤との反応により、α 位での新たな C－C 結合の形成が可能になる。また、ケトンと第二級アミンを反応させることで調製されるエナミンは、ハロゲン化アルキルなどの求電子剤と反応させた後、加水分解することで対応するケトンの α 位置換体が得られる。エナミンを用いた α 位のアルキル化では、1)エノラートを発生させるための強塩基を用いる必要がない、2)一般に熱力学的に安定なエナミンが調製されるため、ケトンと強塩基からは調製しにくい熱力学的エノラート等価体として利用できる、などの利点がある。また、シリルエノールエーテルは、ルイス酸存在下、様々な求電子剤と反応し、カルボニル化合物の α 位に官能基を導入することができる。しかしながら、これらのエノラートまたはエノラート等価体を用いた α 位官能基化反応は、通常 sp^3 炭素上での求核置換反応であるため、sp^2 および sp 炭素の導入は、一般に困難であることが知られている。

Scheme 1. α-Alkylation of enolate



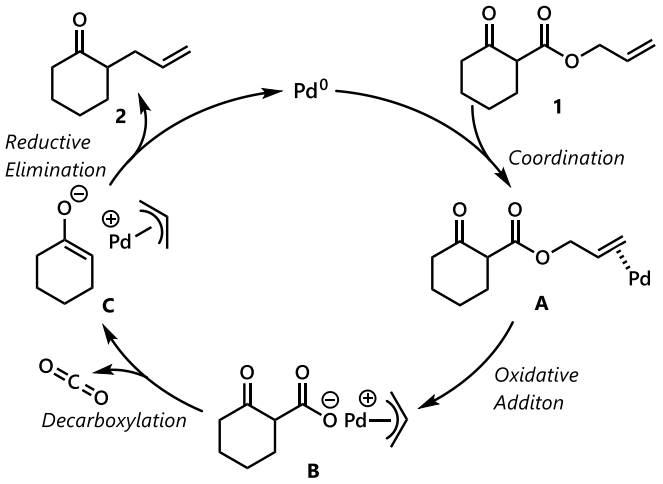
一方、エノラートまたはエノラート等価体の調製を要しないカルボニル基の α 位官能基化反応としては、Pd 触媒による β-ケトエステルの脱炭酸型カップリングも有用な手段の一つである [2)]。1980 年に三枝らは、β-ケトエステル **1** やプロピオール酸エステル **3** を基質に用いた最初の分子内脱炭酸型カップリングを報告した(Scheme 2)[2d)]。

Scheme 2. Decarboxylative allylation



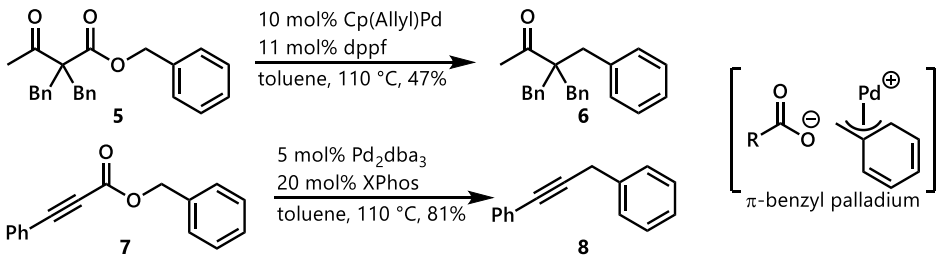
この反応では、アリル位の C–O 結合が Pd 触媒に酸化的付加し、Pd 中間体 **B** となり、**B** からの脱炭酸が起こり、π-アリル Pd 中間体 **C** が生成する。中間体 **C** の Pd 上のエノラート部と π-アリル部で還元的脱離が進行することで、α-アリル化体 **2** が得られる（Scheme 3）。C–O 結合の反結合性軌道が隣接する二重結合の π 結合と重なり合うことで S_N2' による酸化的付加が可能となっている。

Scheme 3. Decarboxylative allylation mechanism



また、同様の機構で分子内脱炭酸型ベンジル化が進行することも報告されている(Scheme 4)[3)]。この反応においても、ベンジル位 C－O 結合が Pd に酸化的付加し生じる π-ベンジル Pd 中間体を経由し、脱炭酸型カップリングが進行する。

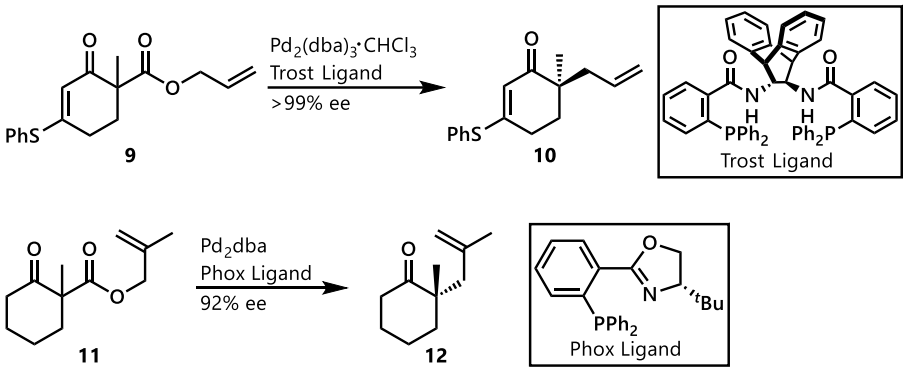
Scheme 4. Pd catalyzed decarboxylative benzylation



このように Pd 触媒による β-ケトエステルの脱炭酸を伴うカップリング反応は、1) 基質合成が容易、2) 副生成物が二酸化炭素のみ、3) 中性条件で反応が進行する等、既存のケトンの α 位アルキル化反応と比較して、多くの利点を有する。また、これらの反応は触媒的不斉反応にも展開されている(Scheme 5)[4)]。2006 年に Trost らは環状ビニロガスチオエステル **9** に対して自身が開発した配位子を用いることで高い不斉収率で脱炭酸型アリル化が進行することを見出した [4b)]。また、Stolz らに

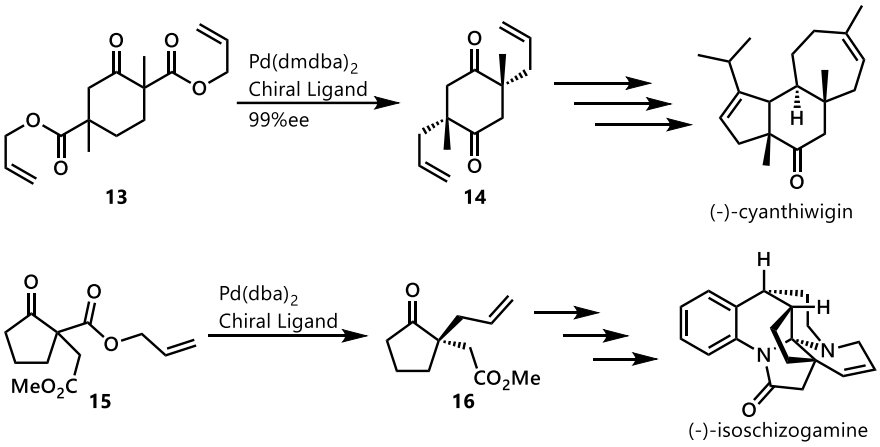
よって、Phox 型配位子が不斉脱炭酸型アリル化反応に有効であることを明らかにし、基質適用範囲はより広範なものとなった [4c)]。

Scheme 5. Enantioselective decarboxylative allylation



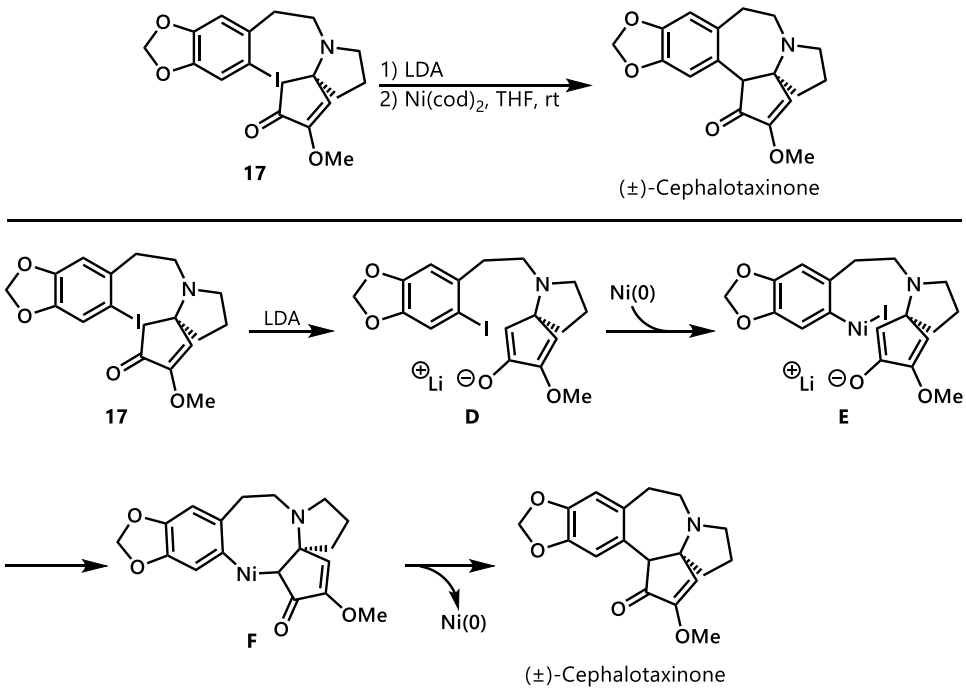
これらの触媒的不斉反応は、全合成における鍵反応としても用いられている(Scheme 6)。Stoltz らはダブル脱炭酸アリル化反応によって合成中間体 **14** を高い不斉収率で得たのち数工程で(-)-cyanthiwigin を合成した [4h)]。Zhu らは不斉脱炭酸型アリル化を利用し、(-)-isoschizogamine の合成を達成している [4i)]。このように、β-ケトエステルの脱炭酸を伴う触媒的不斉カップリング反応は有用性の高い反応であるが、Pd 触媒に基質の C–O 結合が酸化的付加することが必要であり、そのため α 位のアリル化とベンジル化に反応が制限される。したがって、本反応ではカルボニル化合物の α 位に sp^2 および sp 炭素を導入するのは困難である。

Scheme 6. Total synthesis with enantioselective decarboxylative allylations



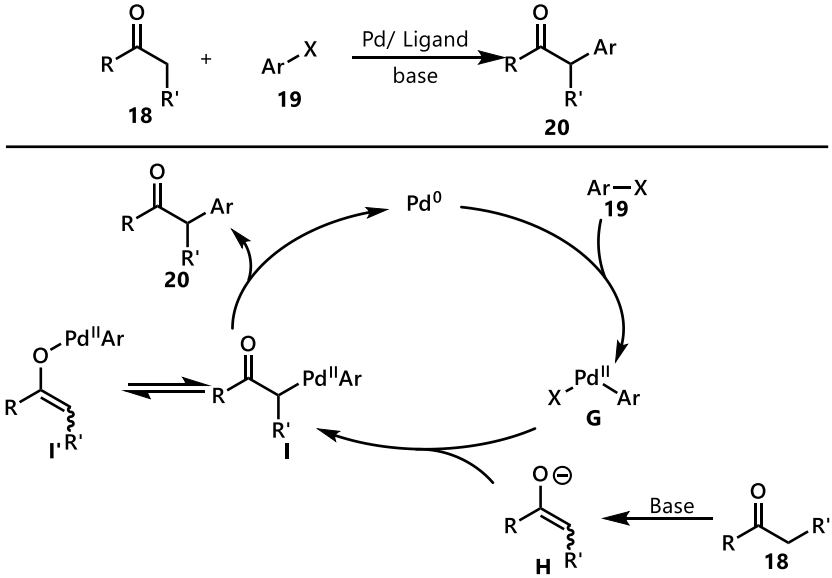
一方、カルボニル基の α 位に sp^2 炭素を導入する反応として、遷移金属触媒によるハロゲン化アリールと金属エノラートとのカップリング反応が古くから研究されてきた [5)]。1975 年に Semmelhack らは、(±)-Cephalotaxinone の全合成の鍵工程として、アリール Ni 種とエノラートとのカップリング反応をはじめて報告した(Scheme 7)[5b)]。この反応では、基質のヨウ化アリール部が Ni(0)に酸化的付加して生成したアリール Ni 錯体 **E** が、塩基によって生成したリチウムエノラートとトランスメタル化、続いて還元的脱離することで閉環する。

Scheme 7. Synthesis of (±)-cephalotaxinone with Ni(0) promoted α-arylation



その後、1990 年代後半になって三浦 [5c]、Buchwald[5d]、Hartwig[5e]らがそれぞれ Pd 触媒を用いたケトンの α 位アリール化を報告した（Scheme 8）。カルボニル化合物と強塩基から系内にて発生させたエノラートを求核剤とし、ヨウ化アリールもしくは臭化アリールとカップリングさせることで、ベンジルケトンが得られる。本反応では、ハロゲン化アリール **19** が Pd(0)に酸化的付加し、アリール Pd 錯体 **G** が生成する。この錯体がエノラート **H** とトランスメタル化することによって Pd エノラート **I(I')**を形成し、続く還元的脱離によってアリール化体 **20** が得られる。

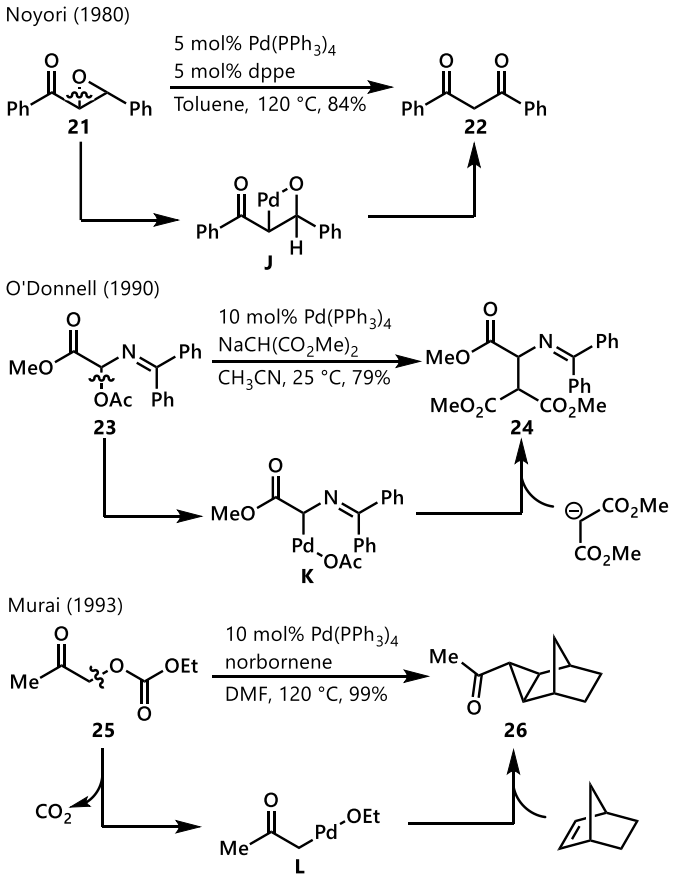
Scheme 8. Pd catalyzed α-arylation of ketones



α位アリール化はケトンだけでなくアルデヒド、エステル、アミドにも適用可能であり、不斉配位子を用いた不斉アリール化反応にも展開されている。またそれぞれの反応においてNi触媒を用いた反応も開発されている[5g)]。これらの反応はα位のビニル化反応へも展開されており、多様なsp^2炭素を導入する手法として確立されている[5j)]。しかしながら、カルボニルのα位にsp炭素を導入する方法としては確立されていない。

ところで、ヒドロキシケトン誘導体のα位C−O結合は、Pd触媒に酸化的付加し、Pdエノラートを与えることが知られている(Scheme 9)[6)]。例えば、野依らはα,β-エポキシケトン **21** に対してPd触媒を作用させると酸化的付加が進行し、生じたPdエノラート **J** のβ水素脱離によって1,3-ジケトン **22** が生成することを報告している[6a)]。O'Donnellらはヘミアミナール誘導体 **23** のα位C−O結合の酸化的付加によって生じたPdエノラート **K** に対して、ジメチルマロネートの求核付加反応が進行することを見出している[6c)]。また村井らはカルボナート **25** のPdへの酸化的付加続く脱炭酸により生じるPdエノラート **L** とノルボルネンとの反応により、シクロプロパン **26** が生成することを報告している[6d)]。このように、α位C−O結合の酸化的付加により直接Pdエノラートが生じることは知られているものの、カルボニル化合物のα位官能基化反応に利用された例は限られる。

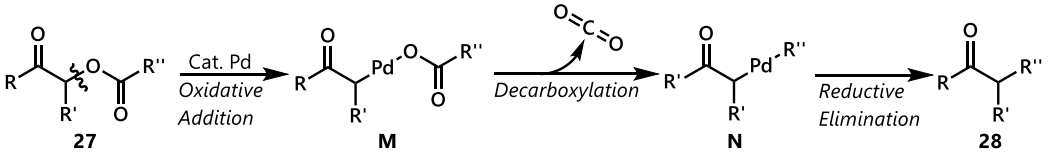
Scheme 9. Formation of Pd enolate with αC–O scission



そこで著者は、上記のようなα位C−O結合のPd触媒への酸化的付加の過程で生じるPdエノラートに注目し、新たなケトンのα位官能基化反応を開発すべく研究に着手した(Scheme 10)。すなわちα位にアシル基を持つ基質 **27** とPd触媒を反応させると、**27** の酸化的付加によりPdエノラート

M が生成すると考えられる。この Pd 中間体 **M** から、脱炭酸が起こり、続いて還元的脱離が進行するならば、α 位が官能基化されたカルボニル化合物 **28** が得られる。もし本反応が進行すれば、従来の α 位官能基化では達成困難なアルキニル基を含む、様々な官能基が導入できるものと期待した。

Scheme 10. α-Functionalization of ketone with αC–O scission



以下に本論文の概略を示す。

Pd 触媒による α-ヒドロキシケトン誘導体の C－O 結合切断を鍵とした脱炭酸型ケトンの α 位アルキニル化反応の開発に成功した(第一章)[7]。また、本反応の鍵中間体である Pd エノラート **M** に相当する中間体の単離に成功し、反応機構に関する考察を行った。さらに、分子内に不飽和結合を有するヒドロキシケトン誘導体を用いて反応を検討したところ、Pd エノラートへのアレンの挿入を伴う環化反応を見出した(第二章)[8]。また、DFT 計算を用いて本反応の反応機構の考察を行った。これらの研究の詳細について以下順に記載する。

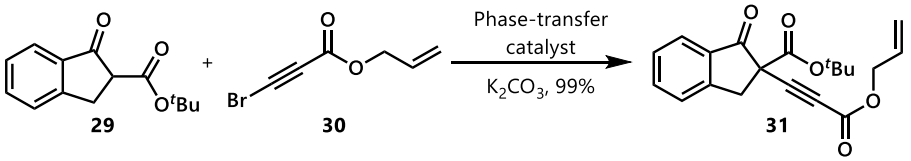
第一章　Pd 触媒による脱炭酸を伴う ケトンの α 位アルキニル化反応の開発

第一節　研究背景

これまで報告されているカルボニル基の α 位へのアルキニル基（sp 炭素）の導入反応の例を以下に概観する。

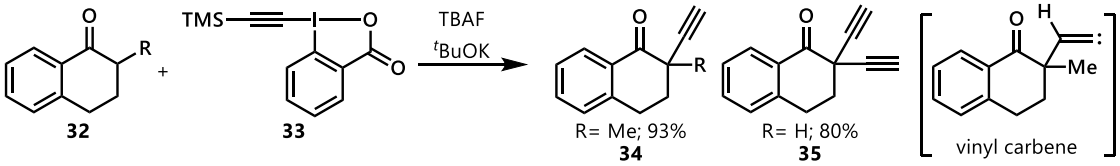
エノラートを求核剤としたカルボニル化合物の α 位アルキニル化の例としては、相間移動触媒の存在下、β-ケトエステルとハロゲン化アルキニルとの反応による α位アルキニル化反応が報告されている [9]。この反応は、電子求引性基を有するハロゲン化アルキニルへの 1,4-付加，引き続く 1,2-脱離反応によって反応が進行するため、電子求引性基を有するアルキンのみに基質が限定され、また β-ケトエステルのような活性化されたカルボニル化合物を基質に用いる必要がある（Scheme 11）。

Scheme 11. α-Alkynylation of carbonyl compound with haloalkynyl



カルボニル化合物のアルキニル求電子剤として超原子価ヨウ素 **33** を用いると、ビニルカルベンの転位を経由してケトンの α 位アルキニル化が進行することが知られている（Scheme 12）[10]。しかしながら、ケトンの α 位に置換基を持たない基質ではモノアルキニル化では反応が停止せず、2 つのアルキニル基が導入されたジイン **35** が生成物となる。また、超原子価ヨウ素の調製にも複数の工程を必要とする。

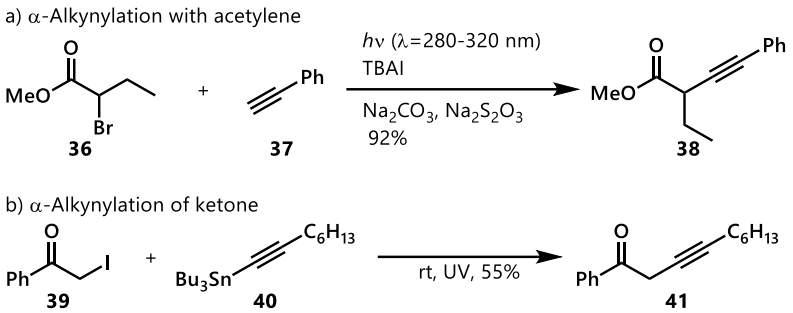
Scheme 12. α-Alkynylation of carbonyl compound with hypervalent iodine



一方、α-ハロカルボニル化合物に対してアルキンを反応させる α位アルキニル化反応も報告されている [11]。例えば、α-ハロカルボニル化合物とフェニルアセチレンの光照射下におけるアルキニル化反応では、光照射によって α 位 C–ハロゲン結合を均等開裂することによって α 位にラジカルが生じ、これが末端アルキンと反応することでアルキニル化が進行する（Scheme 13a）[11a]。この反応は、ラジカルとの反応性が低いエステルとアミドに基質は限られている。唯一、ケトンでの反応例は安田、馬場らによっ

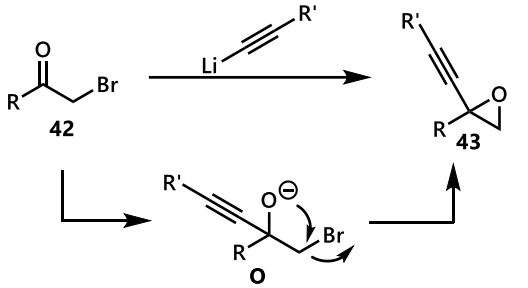
て報告されているが、毒性の高いスズ求核剤と紫外線照射が必要である（Scheme 13b）[11b)]。

Scheme 13. α-Alkynylation of α-halocarbonyl compound



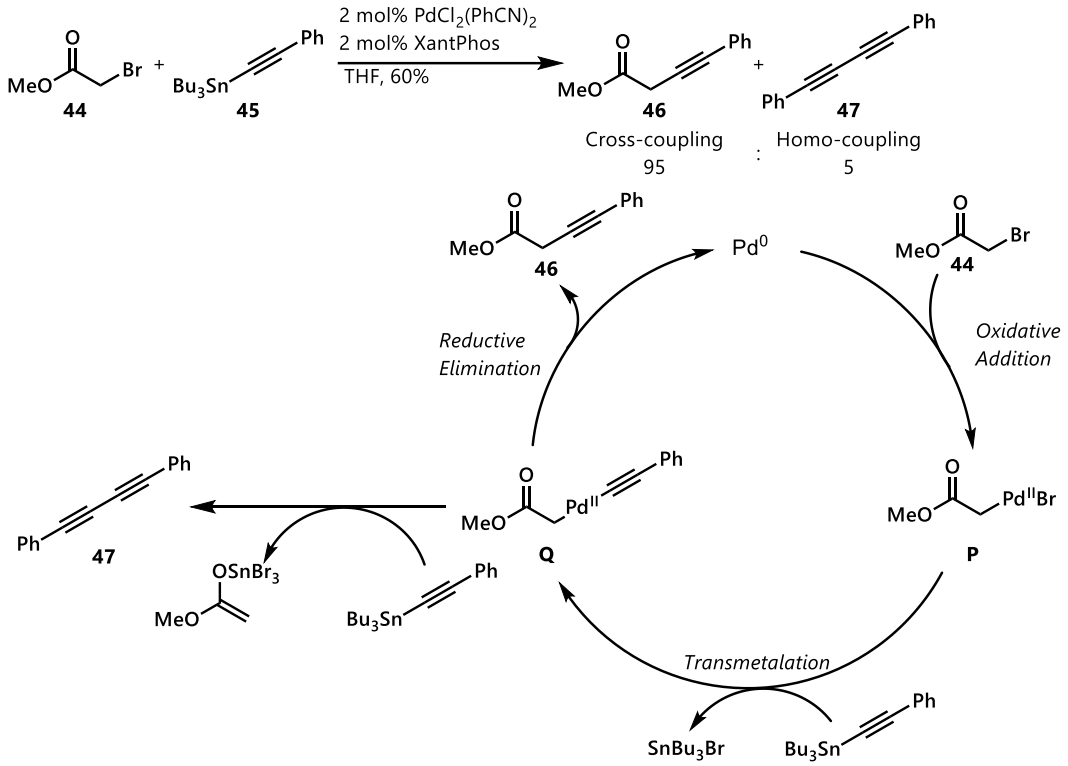
一般に、α-ハロカルボニル化合物にアセチリドを求核剤として反応させた場合は、カルボニル基への付加反応や α 水素の脱プロトン化が併発することが知られている [12)]。例えば、α-ハロケトン **42** とアセチリド求核剤との反応では、カルボニル基が求核攻撃を受け、生じたアルコキシド **O** が C–ハロゲン結合と S_Ni 反応することでエポキシド **43** が生成する (Scheme 14)。従って、カルボニル化合物の α 位アルキニル化反応では中性条件および求核力の高いアセチリドを用いない反応設計が求められる。

Scheme 14. Formation epoxide from α-halo ketone



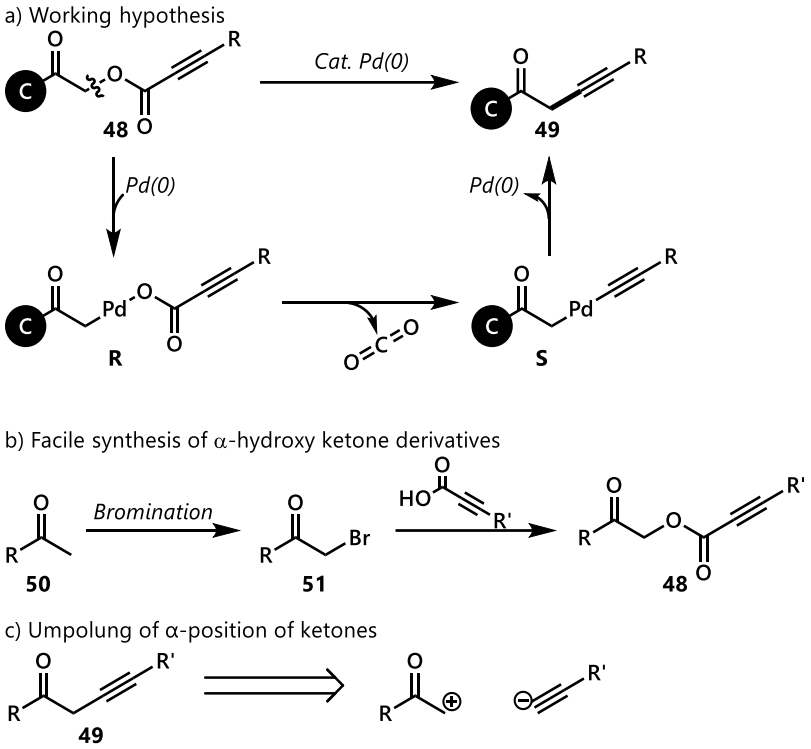
このような背景のもと、遷移金属触媒を用いた α-ハロカルボニル化合物とアルキニル求核剤との反応も報告されている(Scheme 15)[13)]。この反応は、α-ハロカルボニル化合物 **44** の Pd への酸化的付加によって生じた Pd エノラート **P** とアルキニル求核剤 **45** とのトランスメタル化、続く還元的脱離によって α-アルキニルカルボニル化合物 **46** が生成する。この反応では中性条件にてトランスメタル化が進行するアルキニルスズや強い求核性を持たないホウ素試薬を用いることでカルボニル基への付加反応や α 水素の脱プロトン化を抑制している。しかしながら、ホモカップリング体[*1] が副生する点や、基質として α-ハロケトンの適用ができないことが、未だ課題として残されている。

Scheme 15. α-Alkynylation of carbonyl compound for cross-coupling strategy



そこで、著者は、脱炭酸型カップリング反応がケトンの α 位アルキニル化に有効な手法になると考えた(Scheme 16a)。すなわちプロピオール酸エステル **48** の α 位 C–O 結合の Pd 触媒への酸化的付加が進行すれば、Pd エノラート **R** が生成し、続く脱炭酸と還元的脱離によって α-アルキニルケトン **49** が得られると想定した。この反応が想定した機構で進行するならば、塩基を用いることなく系内でアセチリドが発生し、またカップリングさせるユニットは酸化的付加した時点で Pd に結合しているため、適切な配位子を選択することで副反応を防ぎつつ、還元的脱離を促進することが可能であると考えた。またこのヒドロキシケトン誘導体 **48** はケトンの α 位臭素化、続く求核置換反応によって容易に合成が可能である(Scheme 16b)。本反応は、本来、求核性を示すカルボニル基の α 炭素に対して求核剤を結合させる、いわゆる極性転換反応として捉えることもでき、分子変換をより柔軟かつ幅広く行えるようにする優れた合成戦略の一つになり得る(Scheme 16c)。このような想定をもとに種々条件検討を行った結果、脱炭酸型カップリングによって α-アルキニルケトンが高収率で得られることを見出した。

Scheme 16. Decarboxylative alkynylation of ketone (This Work)



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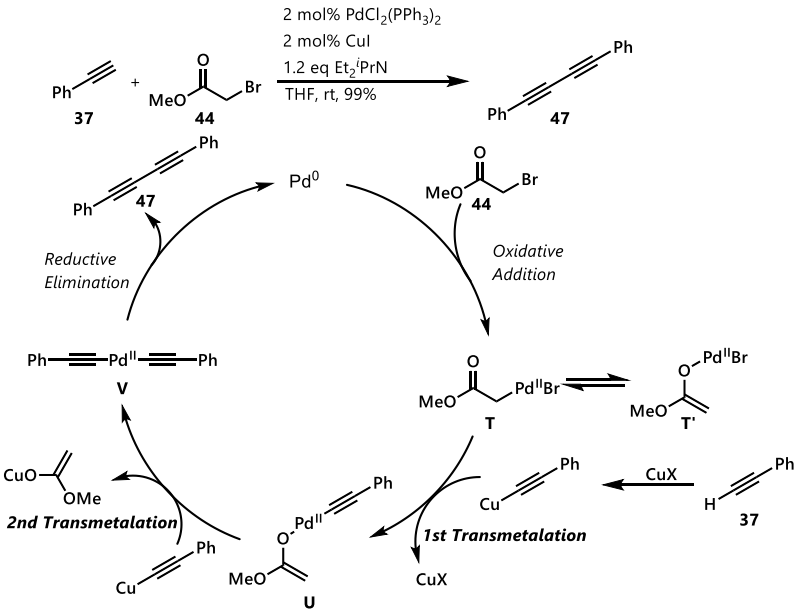
*1 α-ハロカルボニル化合物と求核剤との遷移金属触媒を用いた反応でのホモカップリングは α 位 C–金属結合の分極が大きいために連続したトランスメタル化によって進行する [14)]。2002 年に Zhang らは α-ハロエステル存在下、アルキニル銅とのホモカップリングが進行することを報告している(Scheme 17)[14a)]。このホモカップリングの想定反応機構では α-ハロエステルが Pd(0) に酸化的付加することで Pd エノラート **T**(または **T'**)が生成する。続く二度のトランスメタル化で Pd 中間体 **V** を経由し、還元的脱離によってホモカップリング体が生成する。Pd エノラートは二つの共鳴構造を取ることが可能であり、*O*-エノラート **U** を介して二度目のトランスメタル化が進行すると考えられている。反応を通して α-ハロエステル **44** は酸化剤として作用している。α-ハロエステルや α-ハロアミドの場合には適切な配位子や求核剤を選択することで、クロスカップリング選択的に進行する手法が開発されているものの、α-ハロケトンの場合にはエステルやアミドと比較して、α 位 C–金属結合の分極がより大きいため、ホモカップリングの併発の抑制が困難である。そこでアルキニル求核剤を用いないケトンの直接的な α 位アルキニル化反応の開発が求められる。

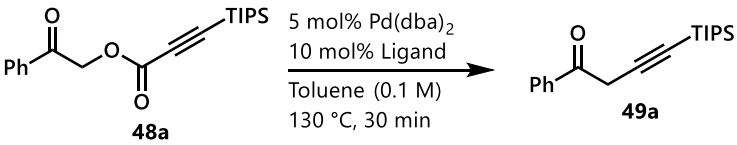
Scheme 17. Homo-couplimg of alkynes



第二節　Pd 触媒による脱炭酸を伴うケトンの α 位アルキニル化反応の検討

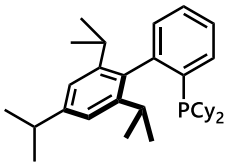
モデル基質としてプロピオール酸フェナシル **48a** を用いて、反応条件の初期検討として、まず配位子の検討を行った(Table 1)。5 mol%の $Pd(dba)_2$ と 10 mol%の XPhos 配位子存在下、トルエン溶媒中、加熱還流することで α-アルキニルケトン **49a** を収率 56%で得た(entry 1)。このことから Pd 触媒によるケトンの α 位 C−O 結合切断は可能であることが示唆された。この結果をもとに更なる配位子検討を行ったが、XPhos 配位子を用いた際の収率を超える配位子を見つけることは出来なかった。トリアルキルホスフィンまたは二座配位子を用いた際には全く反応が進行せず、原料を回収するのみであった(entries 2-8)。次に XPhos 配位子に構造が類似した配位子を用いて反応を検討した。XPhos 配位子のビアリール部分を持たないジシクロヘキシルフェニルホスフィンを用いた場合には原料を回収するのみであった(entry 9)。これに対し、ビアリール骨格を有する配位子を用いた場合には原料の消費を確認できた(entries 10-14)。特に 2,4,6-トリイソプロピルフェニル基をビアリール部分に有する BrettPhos の場合には α-アルキニルケトン **49a** を収率 24%で与えた。本反応においてビアリール骨格部分の置換基は収率に大きく影響し、より嵩高いアリール基を有する配位子を用いた方が良い収率を与える傾向にあった。以上の結果から、以降の検討は XPhos を配位子として用いることとした。

Table 1. Ligand screening[a]

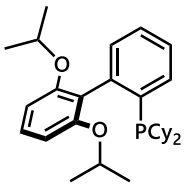


entry	Ligand	rec. **48a** (%)[c]	**49a** (%)[c]
1	XPhos	N.D.	56
2[b]	P^nBu_3	98	N.D.
3[b]	PCy_3	97	N.D.
4[b]	P^tBu_3	99<	N.D.
5[b]	dppe (5 mol%)	99<	N.D.
6[b]	dcpp (5 mol%)	99<	N.D.
7[b]	dppp (5 mol%)	90	N.D.
8	^{t}BuXantPhos (5 mol%)	94	N.D.
9	$PPhCy_2$	97	N.D.
10[b]	RuPhos	44	9
11	^{t}BuXPhos	77	N.D.
12[b]	BrettPhos	N.D.	24
13	JohnPhos	12	N.D.
14	CyJohnPhos	42	N.D.

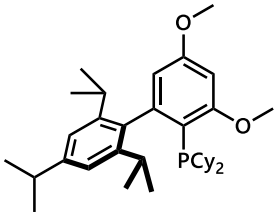
[a] Reactions were performed using $Pd(dba)_2$ (5 mol %, 0.005 mmol), ligand (10 mol%, 0.01 mmol), compoud **48a** (0.1 mmol, 1 eq) in toluene (1.0 mL). [b] 0.5 ml of toluene were used. [c] Yields were determined by ^{1}H NMR.



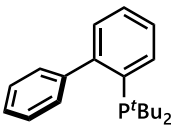
XPhos



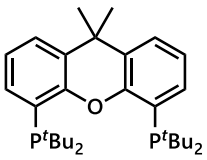
RuPhos



BrettPhos



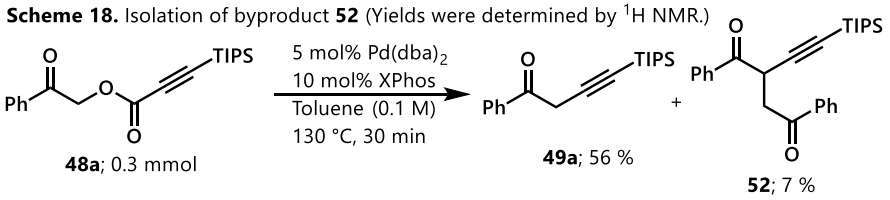
JohnPhos



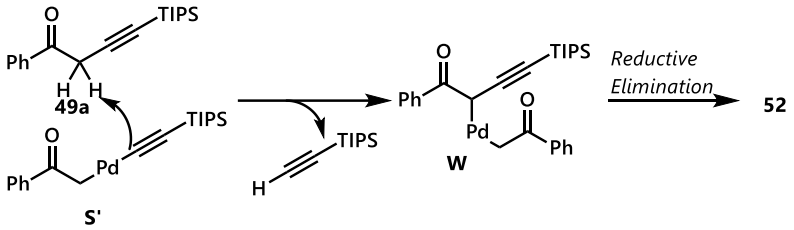
^{t}BuXantphos

上記の検討において目的物は得られたものの、その収率が中程度であったことから、系中で生成する副生成物の単離を行い、HMBC、HMQC、ESI-MS を用いて、その構造を精査したところ、1,4-ジケトン **52** が収率 7%で生成していることを確認した(Scheme 18)。この副生成物は、反応中間体である Pd アセチリド **S'**が生成物である α-アルキニルケトン **49a** から α 水素を引き抜くことで、アセチレンの遊離とともに中間体 **W** が生成し、**W** からの還元的脱離によって生成したと考えられる(Scheme 19)。

Scheme 18. Isolation of byproduct **52** (Yields were determined by ^{1}H NMR.)

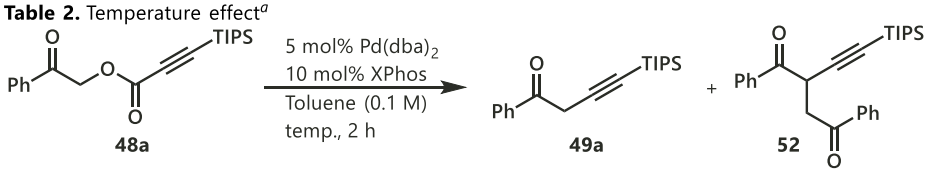


Scheme 19. Possible pathway forming **52**



この副生成物を抑制するべく、反応温度を検討した(Table 2)。反応温度が 70 ℃の時には、未反応の原料が残り、目的物は 3%得られたのみであった(entry 2)。また反応温度が 90 ℃または 110 ℃の場合では、原料は消失したものの、収率の向上は見られず、低収率にとどまった(entries 3,4)。このことから反応温度を低下させても、副生成物の生成は抑制されず、目的生成物の収率のみが低下することが明らかになった。

Table 2. Temperature effect[a]



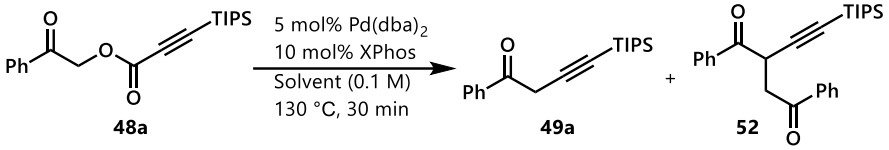
entry	temp. (°C)	rec. **48a** (%)[b]	**49a** (%)[b]	**52** (%)[b]
1	130	N.D.	56[c]	7
2	70	77	3	1
3	90	N.D.	17	6
4	110	N.D.	22	6

[a] Reactions were performed using Pd(dba)$_2$ (5 mol %, 0.005 mmol), ligand (10 mol%, 0.01 mmol), compoud **48a** (0.1 mmol, 1 eq) in toluene (1.0 mL). [b] Yields were determined by ^{1}H NMR.

反応温度 130 ℃にて XPhos 配位子を用いた反応条件下、密閉容器を用いて溶媒検討を行った(Table 3)。トルエン同様に無極性溶媒である *m*-キシレン、メシチレン、ベン

ゼンを用いても収率に向上は見られなかった(entries 2-4)。またアミド系溶媒やニトリル系溶媒などの極性溶媒またはプロトン性溶媒では大きく収率が低下する結果となった(entry 5-10)。おそらく溶媒効果によって反応中間体である Pd カルボキシラート同士での交換などが進行し、目的の反応が阻害されたと考えられる(Scheme 20)。エーテル系溶媒である 1,4-ジオキサンを溶媒として用いた際にはトルエンとほぼ同程度の収率で目的物を得ることができた(entry 11)。

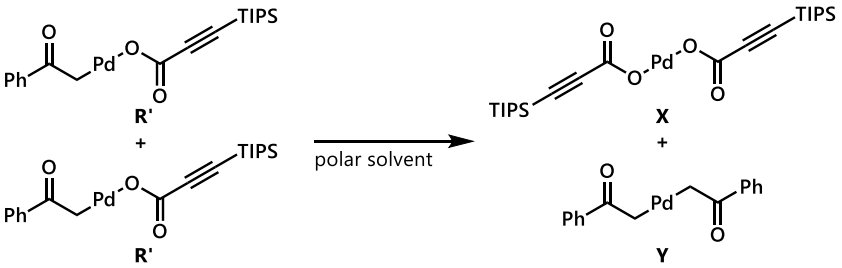
Table 3. Solvent screening[a]



entry	Solvent	rec. **49a** (%)[b]	**49a** (%)[b]	**52** (%)[b]
1	Toluene	N.D.	56	7
2	*m*-Xylene	N.D.	42	6
3	Mesitylene	N.D.	30	3
4	Benzene	N.D.	39	3
5	DMF	N.D.	6	N.D.
6	DMA	N.D.	15	N.D.
7	^{i}PrCN	N.D.	15	N.D.
8	PhCN	N.D.	19	N.D.
9	$PhCF_3$	N.D.	9	3
10	^{i}BuOH	N.D.	19	N.D.
11	1,4-Dioxane	N.D.	54	7

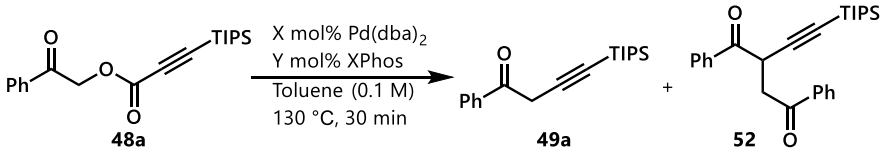
[a] Reactions were performed using $Pd(dba)_2$ (5 mol %, 0.005 mmol), XPhos (10 mol%, 0.10 mmol), compoud **48a** (0.1 mmol, 1 eq) in solvent (1.0 mL).[b] Yields were determined by ^{1}H NMR.

Scheme 20. Scrambling of Pd carboxylate



次に Pd と XPhos 配位子の量比を検討した(Table 4)。Pd に対して等量の XPhos 配位子を用いたときは収率の向上は見られなかった(entry 2)。一方、Pd に対して 4 倍量の XPhos 配位子を用いたとき、収率は 73%まで向上した(entry 3)。そこで Pd と XPhos 配位子の比を 1:4 に固定し、Pd 触媒の低減を検討した(entries 4-6)。2.5 mol%の Pd 触媒を用いた際には 5 mol%とほぼ同様の収率である 76%で目的物を与えたが、1.0 mol%の Pd 触媒を用いた際には反応時間を延ばしても反応は終了せず、原料が残る結果となった。また対照実験として Pd 触媒を加えずに反応を行ったところ原料を回収するのみであったため Pd 触媒が反応に関与していることが分かった(entry 7)。Pd に対して過剰量の配位子を加えることによる収率の向上は、130 ℃の高温条件において活性種である Pd(0)錯体の分解を防ぐとともに還元的脱離を促進する効果があると考えられる。また XPhos 配位子は高価な配位子であるため、比較的安価なホスフィン配位子を併用することでそのホスフィン配位子が Pd の分解を防ぐ効果を担うことができると考え、いくつかの配位子を検討した(entries 8,9)。しかし予想に反して目的の反応は全く進行しなくなり、原料を回収するのみであった。この結果を踏まえ、Pd 触媒を 2.5 mol%、XPhos 配位子を 10 mol%を用いて今後の検討を行うこととした。

Table 4. Pd/Ligand ratio[a]

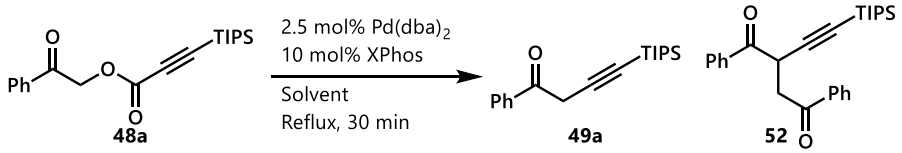


entry	X (mol%)	Y (mol%)	rec. **48a** (%)[b]	**49a** (%)[b]	**52** (%)[b]
1	5	10	N.D.	56	7
2	5	5	N.D.	52	6
3	5	20	N.D.	73	6
4	2.5	10	N.D.	76	6
5	1	4	46	45	3
6[c]	1	4	46	42	3
7	0	10	100	N.D.	N.D.
8	5	10 mol% XPhos 10 mol% PPh_3	99	N.D.	N.D.
9	5	10 mol% XPhos 10 mol% PCy_3	92	N.D.	N.D.

[a] Reactions were performed using $Pd(dba)_2$ (5 mol %, 0.005 mmol), XPhos (10 mol%, 0.10 mmol), compoud **48a** (0.1 mmol, 1 eq) in toluene (1.0 mL). [b] Yields were determined by ^{1}H NMR. [c] Reaction time was 9 h.

これまで述べてきた検討では、0.1 mmol スケールかつ密閉容器を用いて反応を行なっていた。そこで次に、有機合成への利用を考え、スケールアップへの対応が容易である還流管を接続した反応容器を用いて、0.3 mmol スケールで反応を行った。その結果、単離収率が 61%まで低下した(Table 5 entry 2)。反応容器やスケールの変更によって反応系内の温度や圧力を再現できなった可能性を考え、反応濃度と溶媒を再検討した。その結果、0.05 M の濃度まで希釈したところ、収率はわずかに向上した(entry 3)。またより高沸点な溶媒である *m*-キシレンを用いて加熱還流条件下で反応を行ったところ、目的物の収率は 84%に向上した(entry 4)。また、本反応条件下では、反応は 10 分で終了し、高収率で目的物を与えることがわかった(entry 5)。以上の検討から、Pd 触媒を 2.5 mol%、XPhos 配位子を 10 mol%用い、*m*-キシレン中で加熱還流を行う条件を最適条件とし、次に基質適用範囲の検討を行うこととした

Table 5. Concentration effect[a]



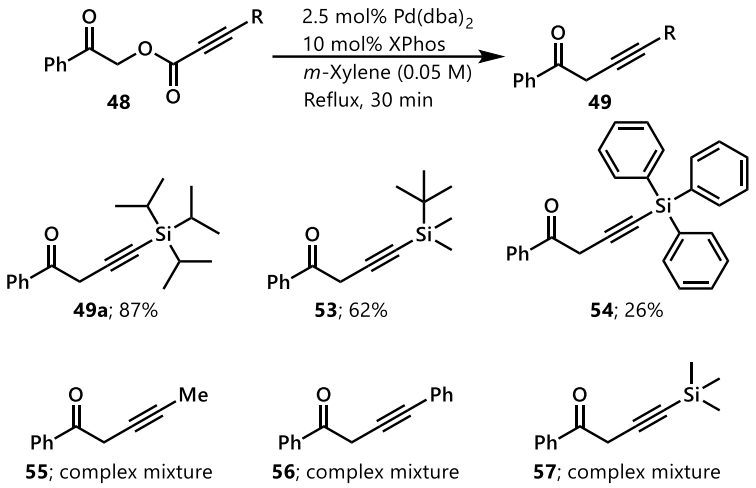
entry	Solvent	Yield (%)[b] 49a	52	
1	Toluene (0.1 M)	76[c]	6[c]	0.1 mmol scale
2	Toluene (0.1 M)	61	12	0.3 mmol scale
3	Toluene (0.05 M)	69	10	
4	*m*-Xylene (0.05 M)	84	3	
5[d]	*m*-Xylene (0.05 M)	87	6	

[a] The reaction was conducted at 0.3 mmol scale. [b] Isolated yield. [c] Yields were determined by ^{1}H NMR. [d] Reaction time was 10 min.

第三節　基質適用範囲の検討

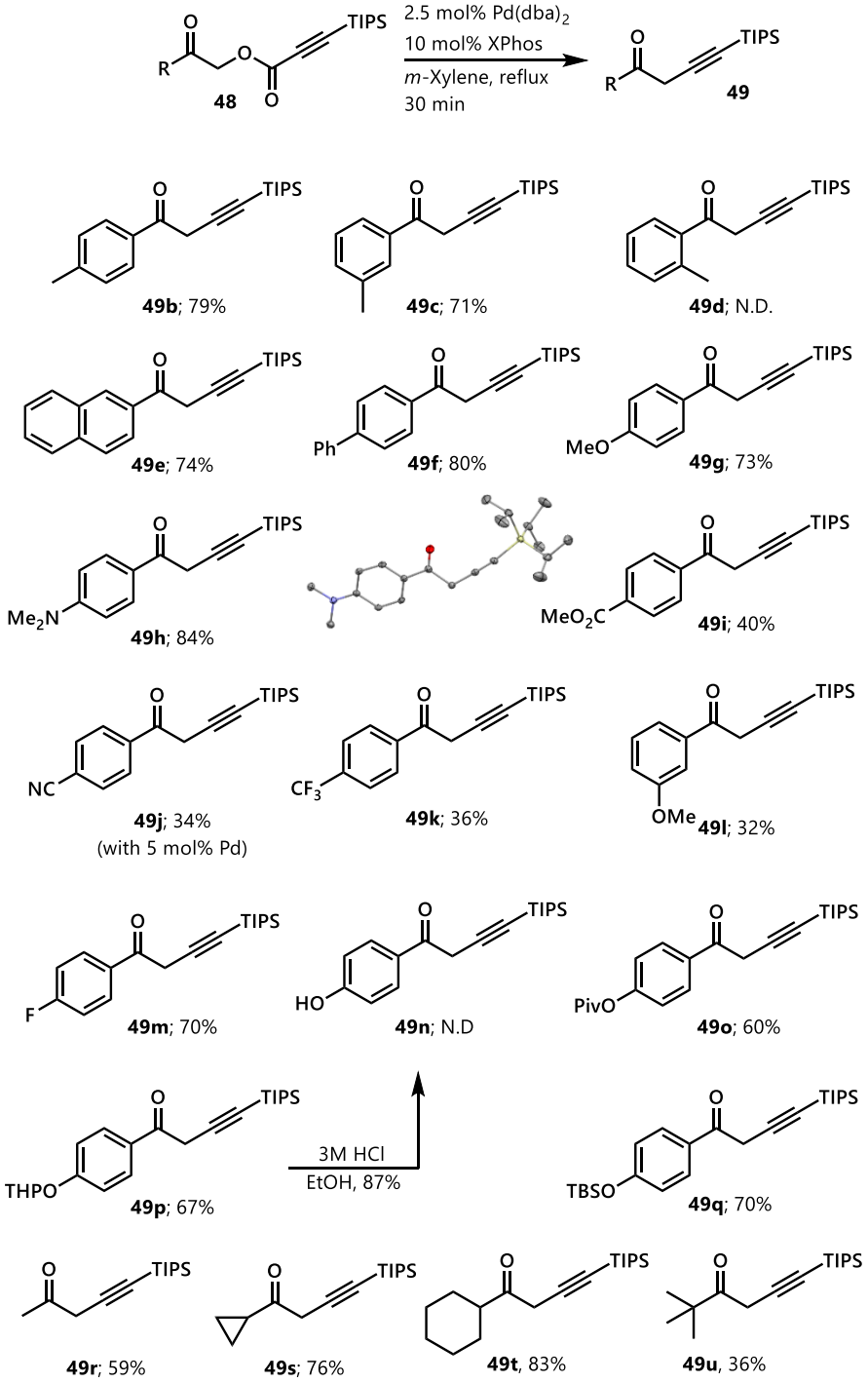
基質適用範囲の検討を行うにあたり、まずアルキン末端の置換基の反応への影響を検証した(Table 6)。ケイ素上に嵩高い置換基を持つ TIPS 基、TBS 基、トリフェニルシリル基では反応が進行し、それぞれ 87%、62%、26%の収率で目的の α-アルキニルケトンを与えた。一方、メチル基やフェニル基、及びケイ素上にメチル基を持つ TMS 基の場合、目的物は得られず、複雑な混合物を与えるのみであった[*2]。

Table 6. Effect of alkyne substituents



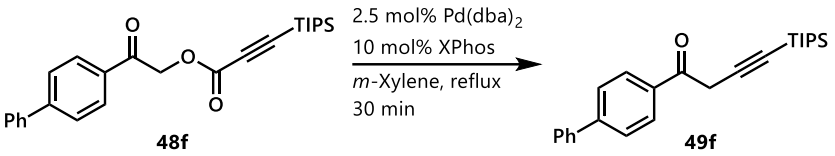
そこで、最も高い収率が得られた TIPS 基をアルキン末端に持つ基質を用いて、ケトン部分の基質適用範囲の検討を行った(Table 7)。まず芳香環上の置換基の位置の影響を検証した。化合物 **48b** と **48c** のようにパラ位もしくはメタ位にメチル基を有する基質の場合には良い収率で目的の α-アルキニルケトンを与えた。一方で化合物 **48d** のようにオルト位にメチル基を有する基質の場合、反応は進行せず、出発原料を回収するのみであった。また化合物 **48e** と **48f** のようにナフタレン環もしくはビフェニル基を有する基質ではそれぞれ収率 74%、80%で目的物を与えた。次に芳香環上の置換基による電子的影響について検証した。パラ位に電子供与基であるメトキシ基もしくは *N,N*-ジメチルアミノ基を有する芳香環の基質では効率よく反応が進行し、目的の α-アルキニルケトン **49g** と **49h** をそれぞれ収率 73%、84%にて得た。化合物 **49h** は単結晶が得られたため、X 線結晶構造解析によってその構造を確認することができた。一方で電子求引基を有する **48i**、**48j**、**48k**、**48l** では低収率にとどまっている。ハロゲンを含む化合物にも反応の適用を試みた結果、塩素化体や臭素化体の場合には目的物は得られなかったが、フッ素化体 **48m** を基質に用いた際には脱ハロゲン化せずに反応が進行した。そして無保護フェノール誘導体 **48n** の水酸基に対する官能基許容性はなく、目的物を得ることは出来なかった。そこでフェノール部分をピバロイル、テトラヒドロピラン、TBS で保護した基質 **48o**、**48p**、**48q** を用いて反応を検討した結果、それぞれ良い収率で目的物を与えた。テトラヒドロピラン保護されたフェノール誘導体 **49p** は酸性条件下で脱保護することで **49n** を収率 87%で得た。最後に脂肪族ケトンについても検討した。第一級、第二級、第三級の脂肪族ケトン **48r**、**48s**、**48t**、**48u** においてプロピオール酸と α 炭素の結合部位で選択的にアルキニル化が進行し、目的物を得ることができた。第二級脂肪族ケトン **48s** と **48t** では特に高収率で目的物を与え、またシクロプロパンが開環することはなかった。

Table 7. Substrate scope



基質 **48f** を用いて、反応のスケールアップを検討した(Table 8)。スケールを大きくするにつれて収率の低下が見られ、5 mmol スケールでは収率 66%まで下がる結果となった。Table 2 に示してあるように、Pd 触媒存在下、130 ℃を下回る温度の時に基質の分解が観測されているため、スケールを大きくするにつれて反応溶液の昇温速度が遅くなり、その間に基質の分解が進行したことが考えられた。そこで基質 **48f** のみの *m*-キシレン溶液の加熱還流を事前に行い、そこに Pd/XPhos 触媒の *m*-キシレン溶液を加えたが、収率の向上は見られなかった。

Table 8. Scale-up of decarboxylative alknylation



0.3 mmol scale ; 80%
2 mmol scale ; 73%
5 mmol scale ; 66%

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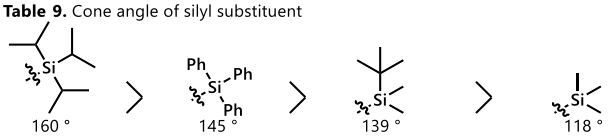
*2 ケイ素上に嵩高い置換基を持つ場合にのみ反応が進行したことから、それぞれのシリル基において嵩高さの指標となるコーンアングルを比較した(Table 9)[15)]。最もコーンアングルの大きい TIPS 基を有する場合に最もよい収率で目的物を与えたが、嵩高いシリル基はアルキン部の Pd への配位を妨げることにより、アルキン部が関与する副反応を防ぐ働きがあると考えられる。一方、TBS 基よりもトリフェニルシリル基はコーンアングルが大きいが、実際の実験では TBS 基を有する基質の方が収率よく目的物を与えたことから、アルキン末端の反応への影響は置換基の立体的な嵩高さによるものだけではないことが示唆される。

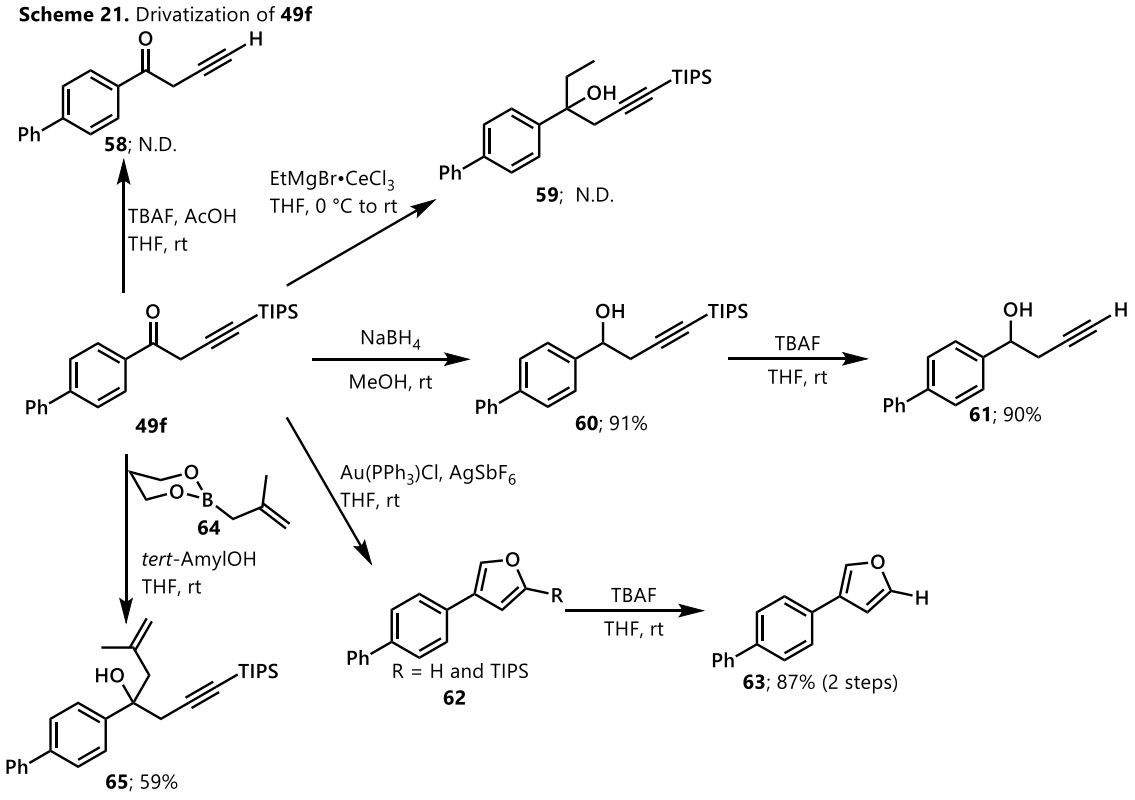
Table 9. Cone angle of silyl substituent



第四節　α-アルキニルケトンの誘導体化

合成した **49f** を用いて、α-アルキニルケトンの誘導体化を検討した(Scheme 21)。まず **49f** を TBAF で処理することで TIPS が脱保護された化合物 **58** の合成を試みたが、複雑な混合物を得るのみであった。Grignard 反応によってアルコール **59** を合成しようとしたが目的物は得られず、複雑な混合物を得るのみであった。これらの反応が進行しない理由として、塩基性条件において α-アルキニルケトンが分解していることが考えられたため、中性条件で進行する分子変換を検討した。**49f** を水素化ホウ素ナトリウムで処理するとケト基に対して選択的に還元が進行し、ホモプロパルギルアルコール **60** が収率 91%で得られた。得られたホモプロパルギルアルコール **60** を TBAF で処理することで TIPS 基の脱保護は円滑に進行し、化合物 **61** が収率 90%で得られた。カチオン性金触媒存在下、α-アルキニルケトン **49f** から環化異性化によってフランとシリルフランの混合物 **62** が生成した。その混合物を TBAF で処理することでフラン **63** が収率 87%で得られた[16]。アリルボロン酸エステル **64** によってエンイン **65** を収率 59%で得た[17]。このように，条件を適切に選択することにより合成した α-アルキニルケトンは多種多様な反応に用いることが可能であり、有用な合成中間体であると言える。

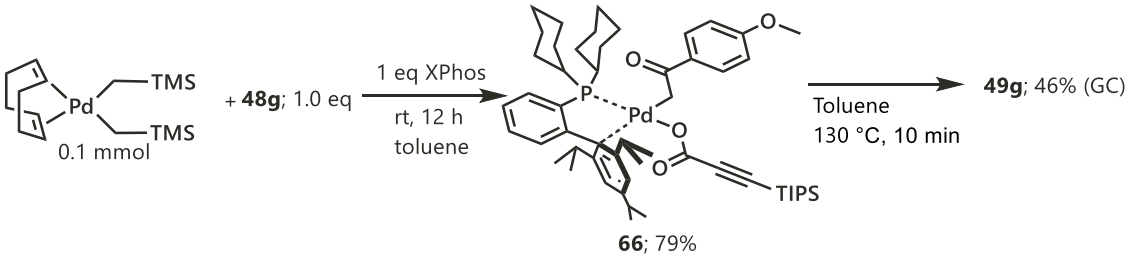
Scheme 21. Drivatization of **49f**



第五節　反応機構の探索

本反応の鍵となる Pd 中間体を錯体として単離することで、構造化学的な解析と反応機構に関する知見が得られると考え、Pd(0)/リン錯体前駆体である $Pd(cod)(CH_2TMS)_2$ を量論量用いた反応を検討した [18]。**48g** と XPhos のトルエン溶液に $Pd(cod)(CH_2TMS)_2$ を室温で加えたところ、Pd エノラート **66** が収率 79%で得られた(Scheme 22)。

Scheme 22. Generation of Pd enolate complex **66** and heating Pd enolate complex **66**



X 線結晶構造解析によって得られた Pd 中間体錯体 **66** の ORTEP 図を Figure 1 に示した。Pd エノラート **66** の構造的特徴は、Pd(II)に典型的な平面 4 配位構造であり、配位座のうちひとつは XPhos のビアリール骨格のイプソ位によって η^1 で占有されている点である。XPhos に代表されるビアリール骨格を有する Buchwald 配位子では配位座の一つがビアリール骨格のイプソ位によって η^1 で占有されていることが知られており、それらと同様な構造を形成している [19]。ケトン部分の C=O 結合距離は 1.24 Å であり、一般的なケトンの C=O 結合距離の 1.21 Å に近い値を示していることから α 炭素と Pd が結合している *C*-エノラートの状態を取っていることが示された。

得られた Pd エノラートをトルエン溶媒中、130 ℃に加熱することで収率 46%にて α-アルキニルケトン **49g** の生成を確認した。このことから Pd エノラート **66** が本反応の中間体である可能性が示唆された。また、これらの実験結果から、Pd(0)への基質の C－O 結合の酸化的付加は室温で進行し、かつ室温下では脱カルボキシル化は進行しないことが明らかとなった。このことから本反応の律速段階は、脱炭酸の過程あるいはその後の還元的脱離の過程であると推測される。

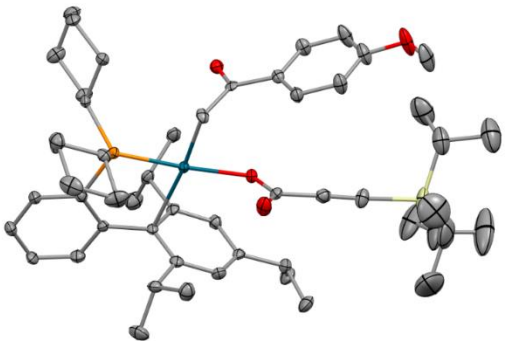
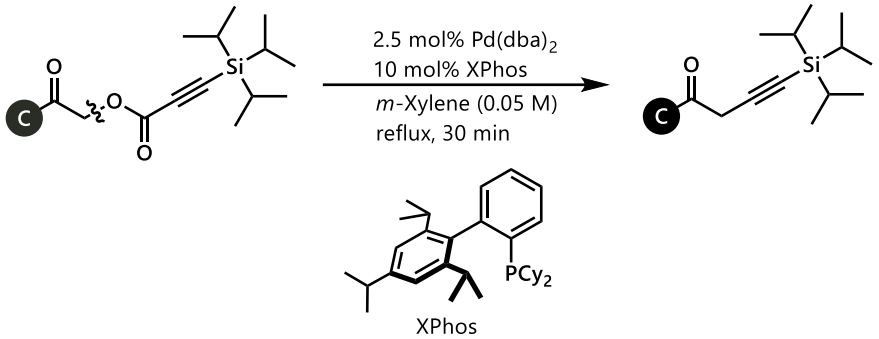


Figure 1. Crystal structure of **66**

結語

本研究では脱炭酸型カップリングによるケトンの α 位アルキニル化反応の開発に成功した[*3]。2.5 mol%の Pd 触媒、10 mol%の XPhos 配位子存在下、*m*-キシレン溶媒中、プロピオール酸エステル誘導体を加熱還流することによって α-アルキニルケトンが良い収率で得られることを見出した。アルキン末端の置換基の嵩高さは反応に大きく関与し、TIPS 基をアルキン末端に導入した場合に最もよい収率で α 位アルキニル化が進行する。基質適用範囲に関しては芳香族ケトンだけでなく脂肪族ケトンでも効率よく反応が進行し、目的物を与えた。本反応で得られた α-アルキニルケトンは、中性条件で多様な分子変換が可能であった。本反応では α 位 C–O 結合切断による Pd エノラート生成が重要な過程であり、Pd エノラート錯体の合成およびその X 線結晶構造解析を行い、その構造を解析するとともに、加熱することで Pd エノラート錯体から生成物が得られることも確認した[7)]。

Scheme 23. Palladium catalyzed decarboxylative α-alkynylation of ketone



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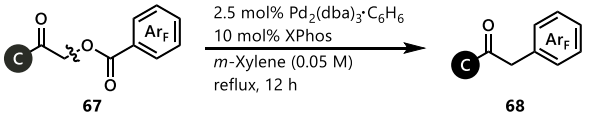
[*3] 尚、当研究室ではフルオロアリール安息香酸誘導体 **67** を基質として用いることで、ケトンの α 位にフルオロアリール基も導入できることを明らかにしている(Scheme 24)[20)]。

Scheme 24. Palladium catalyzed decarboxylative α-polyfluoroarylation of ketones

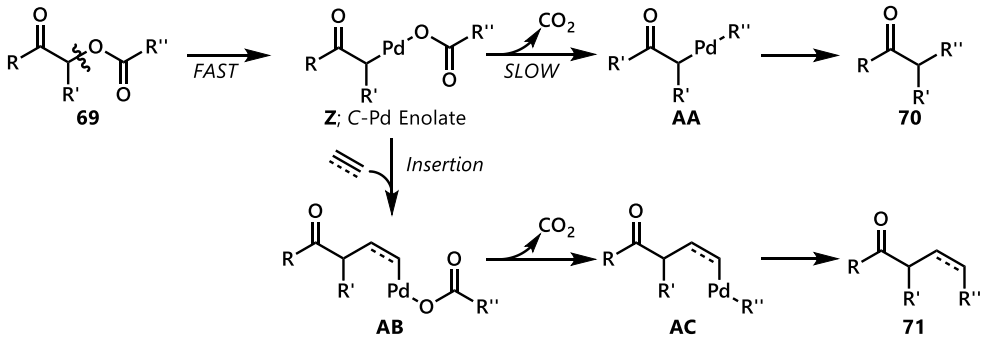


第二章　Pd 触媒による C－O 結合切断を鍵としたアレンの挿入を伴う脱炭酸型環化アルキニル化反応の開発

第一節　研究背景

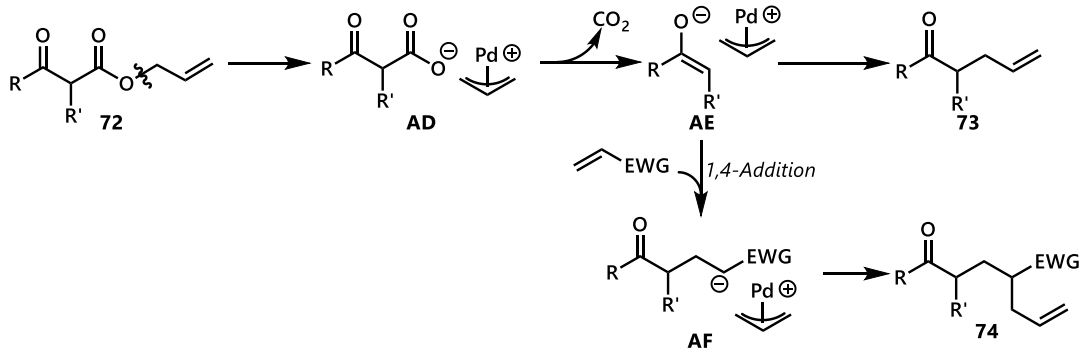
前章で述べたように、α-ヒドロキシケトン誘導体 **69** に Pd を作用させると酸化的付加が進行し、Pd エノラート **Z** が生成することを明らかにした(Scheme 25)。また、酸化的付加は室温下でも速やかに進行するのに対し、それ以降のプロセスには加熱が必要であることがわかった。そこで著者は、反応系内に他の多重結合が存在すれば、**Z** の Pd－C 結合への挿入反応が進行し、脱炭酸を経由して二つの C－C 結合が形成できると考えた。

Scheme 25. Addition of α-position of ketone to multiple bonds



ところで、従来の脱炭酸型 α 位アルキル化反応のプロセスを利用した多重結合の挿入反応は既に報告されている(Scheme 26)[21]。しかしながら、この反応では、π-アリル Pd 中間体 **AE** 生成後にエノラートの求核性を利用し、多重結合と反応する形式のため、利用できる多重結合は Michael 反応受容型のものに限られている。一方、著者が計画した反応(Scheme 25)では、中間体 **Z** において、α 炭素と Pd との結合が *C*-エノラートの状態であることが X 線結晶構造解析からも明らかであり、活性化されていない多重結合に対しても通常の挿入反応が進行することが期待される。

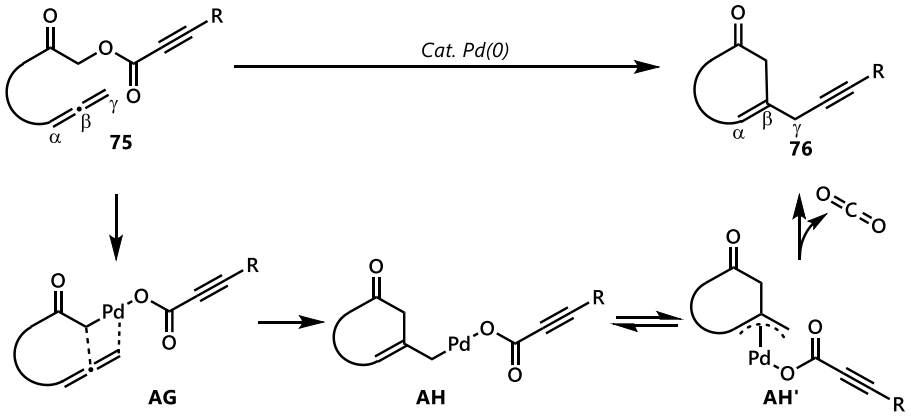
Scheme 26. Decarboxylative Michael addition and allylation



そこで著者は、挿入する多重結合としてアレンを選択し、基質 **75** と Pd 触媒との環化反応を検討することとした(Scheme 27)。アレンは集積型二重結合の一つであり、他の多重結合よりも反応性が

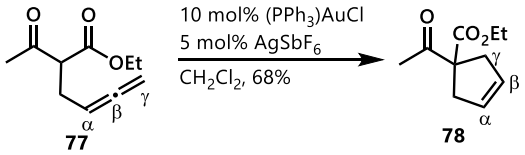
高いため、Pd エノラート中間体の Pd－C 結合に挿入反応が起こることを期待した[*4, 5]。すなわち、本反応では C－O 結合が Pd に酸化的付加し、Pd エノラート **AG** が生成し、続いて立体的に空いているアレンの末端二重結合が挿入することで Pd 中間体 **AH** となる。この中間体は π-アリル Pd 中間体 **AH'** との間で平衡状態になるため、比較的安定な中間体と考えられ、これら中間体から脱炭酸、引き続く還元的脱離が進行するならば、環状ケトン **76** が生成するものと考えた。本反応で生成する環状ケトン **76** は、スキップエンイン構造を持つ β,γ-不飽和ケトンであり、共役エンインあるいは共役ケトンにオレフィン部分が異性化する可能性がある。したがって、従来法での合成は比較的困難であると考えられるが、本反応では中性条件で反応が進行するため、このような分子の構築が可能であると期待される。

Scheme 27. Pd catalyzed decarboxylative cycloalkynylation of allene

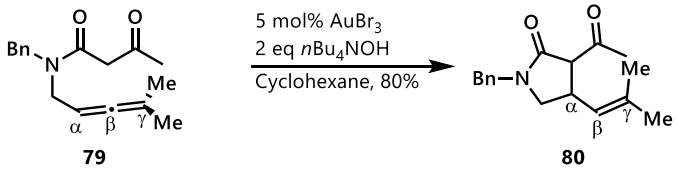


ところで、カルボニル化合物の α 位におけるアレンとの C－C 結合形成反応による環化反応は数多く報告されている[22-25]。例えば、Au 触媒による Conia-ene 型反応では炭素鎖やアレン上の置換基によって反応の選択性が異なる。2008 年、Ma らは側鎖にアレンを持つ化合物と Au 触媒との反応において、カルボニル化合物の α 炭素とアレン γ 位で C–C 結合が生成することを報告している(Scheme 28a)[24b]。また、2012 年に Poli らは γ 位に二つの置換基を持つアレン **79** を基質とすると、アレンの α 位で反応が進行することを見出している(Scheme 28b)[24c]。

Scheme 28. Au(I)-catalyzed addition onto allene
a) γ-Selective cyclization
Ma(2008)

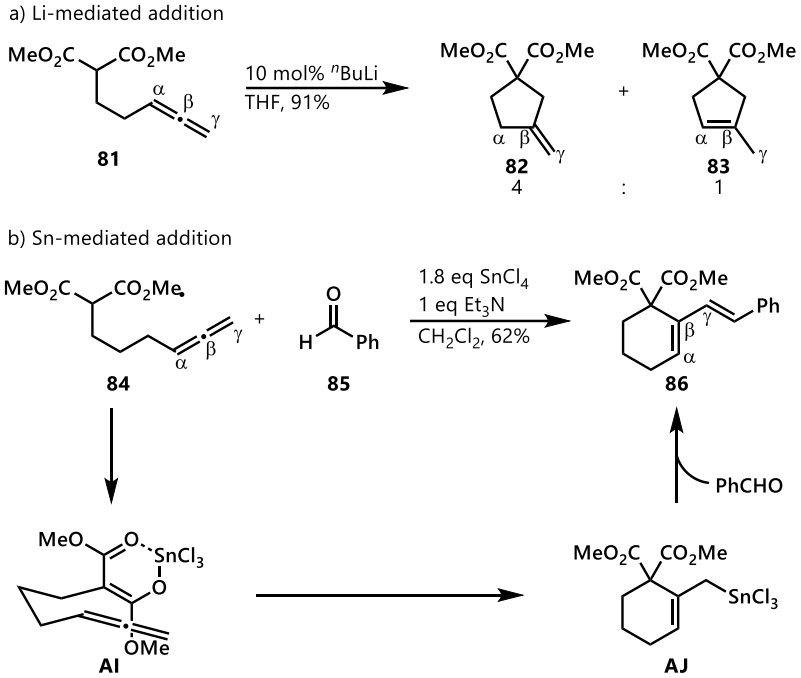


b) α-Selective cyclization
Poli(2012)



一方、カルボニル化合物のα位とアレンの中心炭素(β位)でC－C結合形成反応もいくつか報告されている(Scheme 29)[25)]。例えば、アレニルエステル **81** に触媒量の *n*-ブチルリチウムを作用させると、アレンの中心炭素において新たなC－C結合が形成される(Scheme 29a)[25a)]。また四塩化スズを用いることでスズエノラート **AI** を経由し、同様にアレンの中心炭素への付加反応が進行する(Scheme 29b)[25c)]。しかしながら、これらの反応はいずれも活性メチンのアレンへの求核付加が鍵となる反応であり、単純なカルボニル化合物のα位とアレンの中心炭素でのC－C結合形成反応は報告されていない。

Scheme 29. β-Selective cycloaddition onto allene

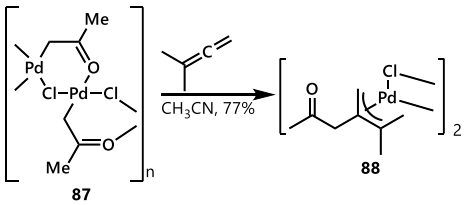


そこで著者は、Scheme 27 に示すように、分子内にアレンを導入したα-ヒドロキシケトン誘導体 **75** と Pd 触媒との反応を検討した。その結果、カルボニル化合物のα位とアレンのβ位で新たな C–C 結合が形成される環化アルキニル化反応の開発に成功した。また、計算科学を用いてその過程を解析したので、その詳細について述べる。

****

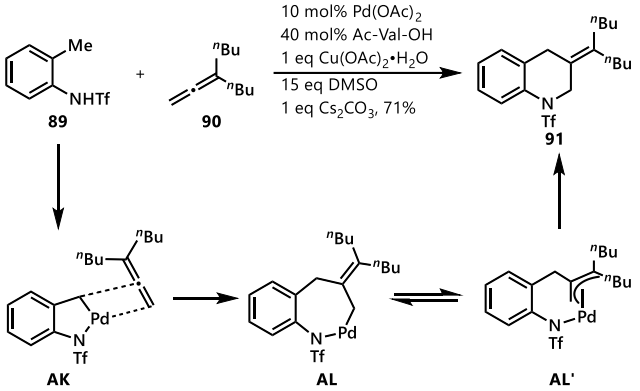
*4 錯体化学においては、Pd エノラート錯体 **87** と、アレンが反応して、π-アリル Pd 錯体 **88** が生成することが報告されている(Scheme 30)[26)]。この反応では、**87** の Pd－C 結合にアレンが挿入し、カルボニル化合物のα位とアレンの中心炭素(β位)でC－C結合が形成されている。このことからC－Pd結合を有する Pd エノラートでは、アレンの中心炭素に挿入反応が進行するものと考えられる。

Scheme 30. Insertion of Pd-enolate to allene



[*5]Gulías らは Pd 触媒によるベンジル C－H 活性化を利用したキノリン合成を報告している(Scheme 31)[27]。この反応では、Pd 中間体 **AK** にアレンの挿入が起こり、π-アリル Pd 中間体 **AL'** となることで、反応中間体の安定化される。最後に、**AL'** から還元的脱離が進行し、環化体 **91** を与える。アレン以外にも、挿入する多重結合として、ジフェニルアセチレンやアクリル酸エチルが検討されているが、これらを用いた場合には全く目的の生成物は得られていない。このように、Pd－C 結合への多重結合の挿入反応において、アレンのみが適用可能な反応が報告されている。

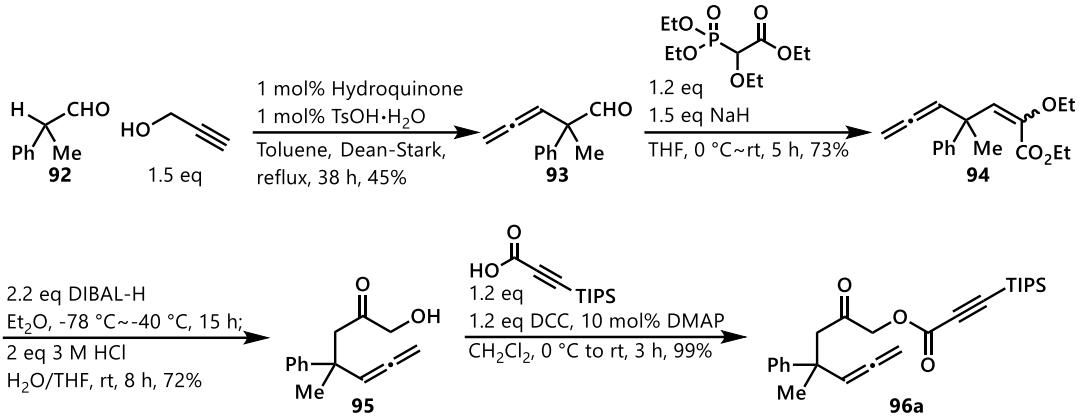
Scheme 31. Pd-catalyzed cycloaddition involving the activation of C(sp^3)–H Bonds



第二節　Pd 触媒による C－O 結合切断を鍵としたアレンの挿入を伴う脱炭酸型環化アルキニル化反応の検討

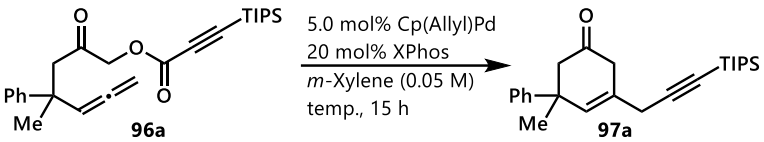
まず分子内にアレニル基を有する基質 **96a** を以下に示す方法で合成した(Scheme 32)。プロパルギル Claisen 転位によってアレニルアルデヒド **93** を合成した。続く Horner-Wadsworth-Emmons 反応によってビニルエーテル **94** とし、DAIBAL 還元続く加水分解によってヒドロキシケトン **95** を得た。その後、DCC 縮合によって基質 **96a** を合成した。

Scheme 32. Synthesis of compound **96a**



合成した化合物 **96a** を用いて脱炭酸型ケトンの α 位アルキニル化反応での反応条件(Table 5 entry 5)を参考に 5 mol%の Cp(Allyl)Pd と 20 mol%の XPhos 配位子存在下、*m*-キシレン溶媒中、反応温度を検討した(Table 10)[*6]。その結果、反応温度を 100 ℃以上にすると目的のシクロヘキセノンの生成が痕跡量ながら確認された。

Table 10. Temperature effect[a]



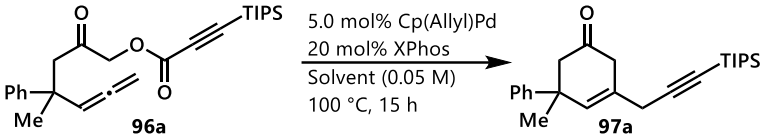
entry	temp. (C°)	Rec. **96a** (%)[b]	**97a** (%)[b]
1	Reflux	N.D.	Trace
2	120	N.D.	Trace
3	100	35	Trace
4	80	55	N.D.

[a] Reactions were performed using Cp(Allyl)Pd (5 mol %, 0.005 mmol), XPhos (20 mol%, 0.02 mmol), compoud **96a** (0.1 mmol, 1 eq) in *m*-Xylene (2.0 mL). [b] Yields were determined by ^{1}H NMR.

反応温度 100 ℃にて XPhos 配位子を用いて、溶媒検討を行った(Table 11)。*m*-キシレン同様に非極性溶媒であるトルエンを用いると、わずかに収率の向上が見られた(entry 2)。一方、脱炭酸型ケトンの α 位アルキニル化反応の際と同様にアミド系溶媒やニトリル系溶媒などの極性溶媒では大きく収率が低下する結果となった(entries 4-6)。CPME、THF、DME などのエーテル構造を有する溶媒で反応を行うと、収率が大きく改善された(entries 8-10)。特に DME では、**96a** の収率が 35%と最もよ

い値を示した。また XPhos 配位子を 10 mol%まで低減させても収率の低下は見られなかった(entry 11)。

Table 11. Solvent effect[a]

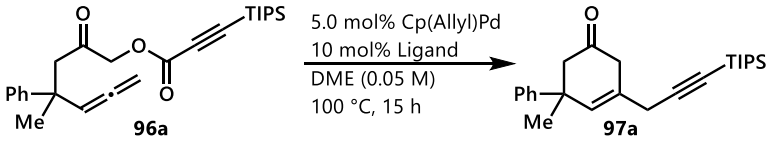


entry	Solvent	Rec. **96a** (%)[b]	**97a** (%)[b]	
1	*m*-Xylene	35	Trace	
2	Toluene	32	8	
3	$PhCF_3$	74	N.D.	
4	DMSO	N.D.	N.D.	
5	DMF	N.D.	trace	
6	CH_3CN	N.D.	N.D.	
7	1,4-Dioxane	N.D.	trace	
8	CPME	N.D.	26	
9	THF	N.D.	30	
10	DME	N.D.	35	
11[c]	DME	N.D.	34	XPhos 10 mol%

[a] Reactions were performed using Cp(Allyl)Pd (5 mol %, 0.005 mmol), XPhos (20 mol%, 0.02 mmol), compoud **96a** (0.1 mmol, 1 eq) in solvent (2.0 mL). [b] Yields were determined by ^{1}H NMR. [c] 0.01 mmol of XPhos was used.

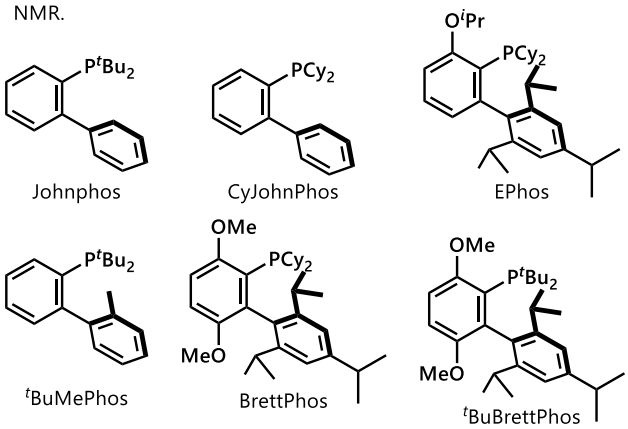
反応溶媒として DME を用い、配位子のスクリーニングを行った(Table 12)。様々な単座または二座のホスフィン配位子を用いた際には全く反応が進行しなかった(entries 1-7)。一方、Buchwald 型配位子を用いた際には目的物を得ることができた。JohnPhos を用いた際には 36%で目的物が得られたが、リン上がシクロヘキシルである CyJohnPhos では 2%にとどまった(entry 8 vs entry 9)。また JohnPhos に類似した配位子である ^{t}BuMePhos を用いた場合には収率 19%にとどまった(entry 10)。続いてビフェニル部分に 2,4,6-トリイソプロピルフェニル基を有する EPhos について検討した結果、収率 19%であった(entry 11)。一方で BrettPhos を用いた結果、これまでで最もよい収率である 47%で目的物が得られた(entry 12)。しかしリン上を ^{t}Bu 基とした場合には目的物が得られず、複雑な混合物を与えるのみであった(entry 13)。このようにビフェニル部分の骨格とリン上の置換基のどちらかに嵩高い置換基を有する配位子に良い収率で目的物を与える傾向にあった。BrettPhos 配位子は特異的に *C*-異性体 **AM** と O-異性体 **AM'**が平衡状態で存在することが知られている(Scheme 33)[28)]。*O*-異性体 **AM'**の際に Pd 中心が立体的に空くため、アレン部位は Pd に近づきやすくなり、会合機構による配位子交換が促進され、結果的に挿入反応が進行しやすくなり、収率が向上したものと考えられる。以上の結果に基づき、これ以降の検討では BrettPhos を配位子として用いることとした。

Table 12. Ligand screening[a]

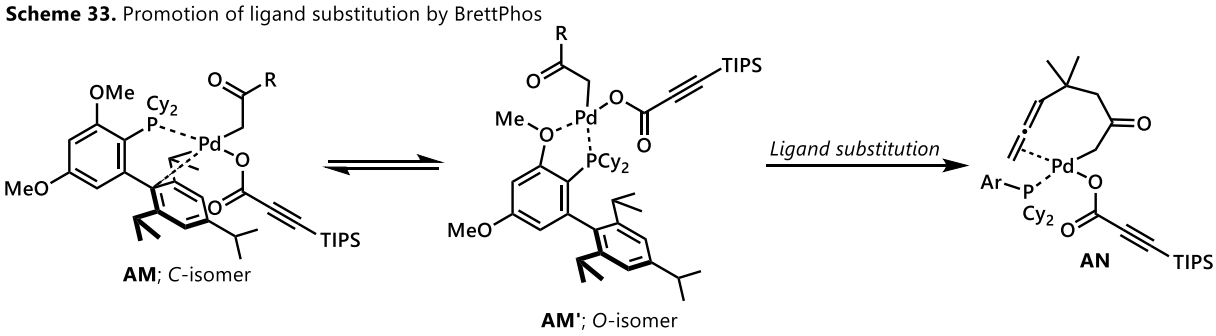


entry	Ligand	Rec. **96a** (%)[b]	**97a** (%)[b]
1	XPhos	N.D.	34
2	PPh_3	73	4
3	PCy_3	78	N.D.
4	P^tBu_3	27	N.D.
5	P(*o*-tol)$_3$	47	N.D.
6	dcpe (5 mol%)	42	N.D.
7	XantPhos (5 mol%)	N.D.	N.D.
8	JohnPhos	N.D.	36
9	CyJohnPhos	N.D.	2
10	^{t}BuMePhos	N.D.	19
11	EPhos	N.D.	19
12	BrettPhos	N.D.	47
13	^{t}BuBrettPhos	N.D.	N.D.

[a] Reactions were performed using Cp(Allyl)Pd (5 mol %, 0.005 mmol), Ligand (10 mol%, 0.01 mmol), compoud **96a** (0.1 mmol, 1 eq) in DME (2.0 mL). [b] Yields were determined by ^{1}H NMR.

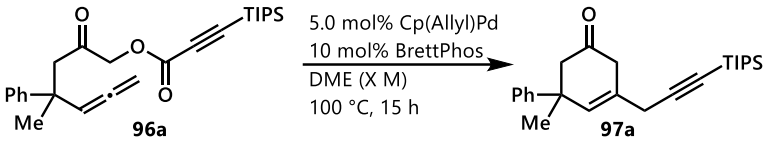


Scheme 33. Promotion of ligand substitution by BrettPhos



本反応において、分子間反応などの副反応により収率が中程度に留まっていると考え、反応溶液の濃度について検討した(Table 13)。その結果、0.02M まで希釈させると収率が向上し、65%で目的物が得られた(entry 2)。さらに 0.01 M まで希釈すると収率 71%まで向上した(entry 3)。この条件を最適条件として基質適用範囲の検討を行った。

Table 13. Concentration effect[a]



Entry	DME (M)	Rec. **96a** (%)[b]	**97a** (%)[b]
1	0.05	N.D.	47
2	0.02	N.D.	65
3	0.01	N.D.	78(71[c])

[a] Reactions were performed using Cp(Allyl)Pd (5 mol %, 0.005 mmol), Ligand (10 mol%, 0.01 mmol), compoud **96a** (0.1 mmol, 1 eq) in DME (2, 5 or 10 mL). [b] Yields were determined by ^{1}H NMR. [c] Isolated yield.

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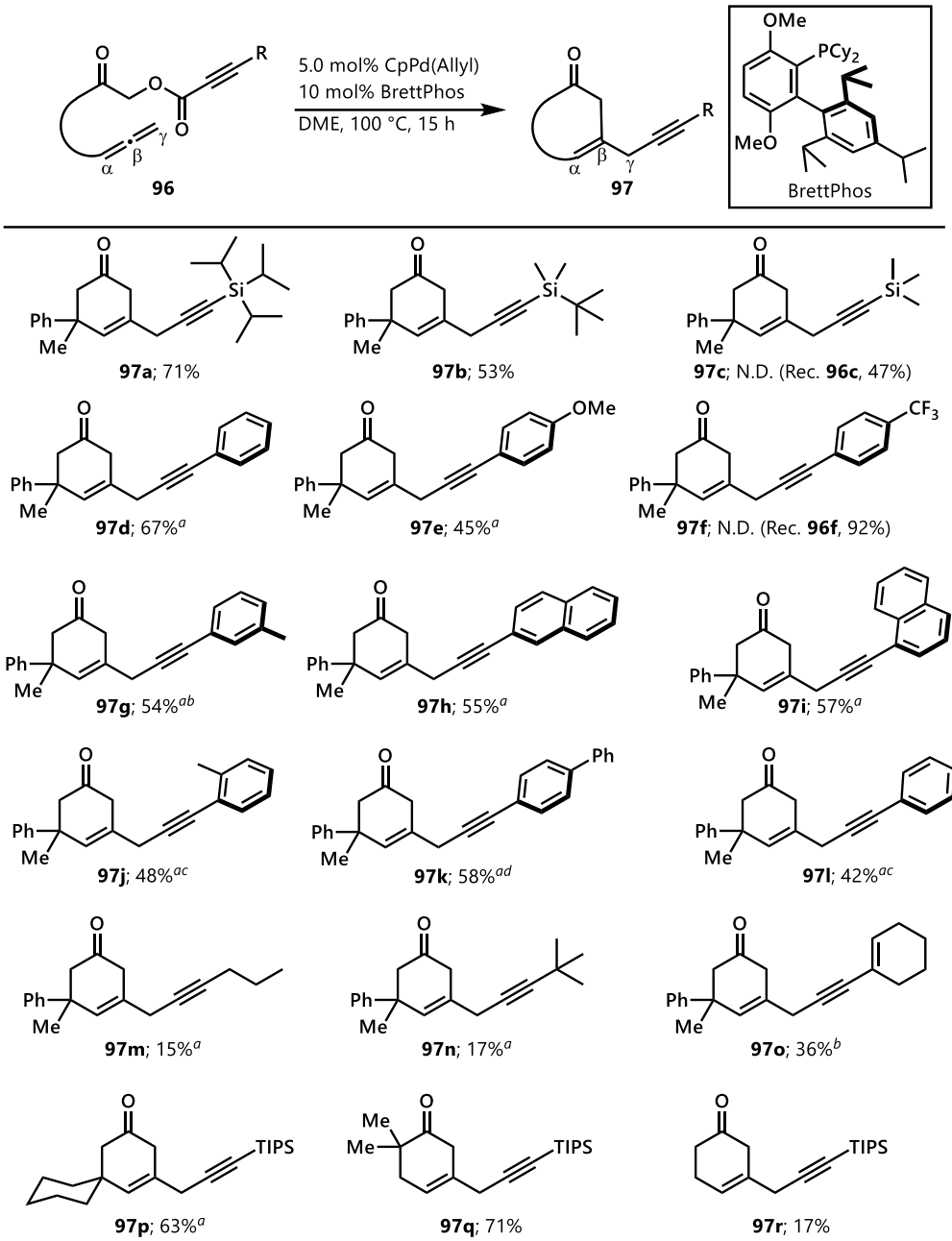
[*6] 第 1 章の「Pd 触媒による脱炭酸を伴うケトンの α 位アルキニル化反応」では Pd 源として $Pd(dba)_2$ を使用していたが、本反応系では目的物 **97a** と Pd 錯体の配位子である dba が精製の際に分離困難であったため、Cp(Allyl)Pd を Pd 源として使用した。

第三節　基質適用範囲の検討

アルキン末端及びケトカルボニル基とアレンの間に様々な置換基を導入して本反応の基質の適用範囲を調べることにした(Table 14)[*7]。まず、アルキン末端のケイ素上の置換基について検討した。TBS 基をアルキン末端に有する基質 **96b** では収率 53%と中程度の収率で目的物が得られた。一方でアルキン末端に TMS 基を有する基質 **96c** では目的の反応は進行せず、原料を回収するのみであった。副生成物は確認できていないものの、おそらく系中で TMS 基が脱離し、Pd アセチリドとなることで反応が停止したのではないかと考えている。つぎにアルキン末端に芳香環を有する基質について検討した。化合物 **96d**、**96e** のようなフェニル基、アニシル基を有する基質では目的の反応が進行し、それぞれ 67%、45%で環化体が得られた。一方で電子求引基であるトリフルオロメチル基が芳香環上にある基質 **96f** では、目的物が得られず、原料を回収した。*m*-トリル基、*o*-トリル基、ナフチル基、ビフェニル基でも目的の反応が進行し、中程度の収率で目的物を得られた(**96g-96k**)。1,3-ベンゾジオキソールのような 2 置換の芳香環を持つ基質 **96l** を用いても収率 42%で目的物が得られた。続いてアルキン末端に *n*-プロピル基、*t*-ブチル基、ビニル基を導入した基質 **96m-96o** について検討したが、収率はそれぞれ 15%、17%、36%と低収率にとどまった。基質のケトカルボニル基とアレンの間の置換基の反応への影響について検討した。その結果、2 位と 3 位に置換基がある基質 **96p**[*8]、**96q**[*9] の反応ではそれぞれ良い収率で目的物を得られたが、置換基を持たない基質 **96r**[*10] の環化反応は低収率にとどまった。本反応が効率よく進行するためには、Thorpe-Ingold 効果を利用することが必要であると考えられる。

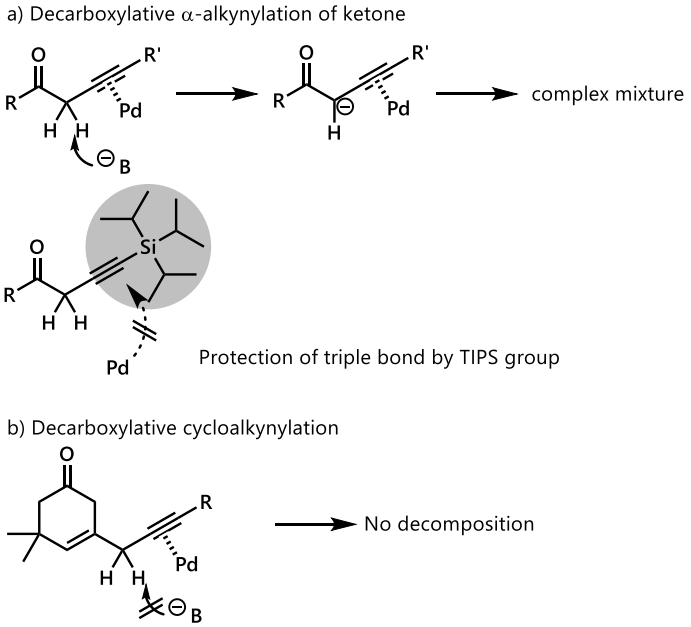
Table 14. Substrate scope



[a] Reaction temperature was 120 °C. [b] Reaction time was 36 h. [c] Reaction time was 34 h.
[d] Reaction time was 32 h.

第 1 章の「Pd 触媒による脱炭酸を伴うケトンの α 位アルキニル化反応」ではアルキン末端は嵩高いシリル基のみしか導入できなかったものの、本反応ではシリル基以外にもアリール基、アルキル基、ビニル基でも反応が進行した。第 1 章では、目的物である α-アルキニルケトンの三重結合が Pd へ配位することで、ケトンの α 水素の酸性度が上がり、ケトンの α 水素の脱プロトン化によってエノラートが生じて様々な副反応が進行してしまうと考えた(Scheme 34a)。一方、本反応の生成物においても三重結合が Pd に配位することが考えられるものの、先の反応とは異なり、アリル位及びプロパルギル位に位置する炭素上の水素の酸性度はカルボニル基の α 水素ほど高くはないと考えられ、本反応では分解や副反応を引き起こすほどの影響を与えなかったと推測される(Scheme 34b)。また本反応では比較的安定な π-アリル Pd 中間体を経由することで、脱炭酸の過程および還元的脱離の過程が促進され、嵩高いシリル基以外にもアリール基、アルキル基、ビニル基でも反応が進行したとも考えられる。

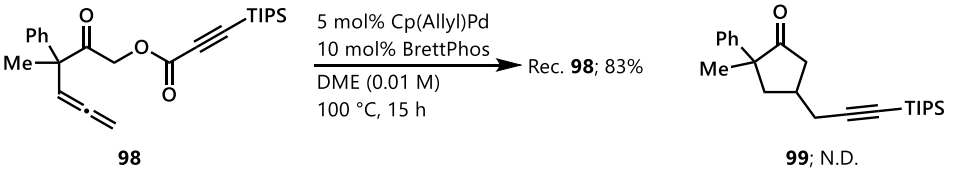
Scheme 34. Expected pathway of the product decomposition



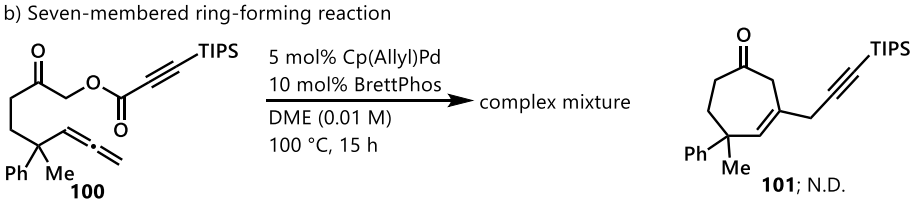
本反応を利用して、6 員環以外の環構築を検討した(Scheme 35)。すなわち、5 員環形成反応の場合には、目的物は得られず、原料 **98** を回収するのみであった(Scheme 35a)[*11]。一方、7 員環形成反応では、複雑な混合物を与えるのみであった(Scheme 35b)[*12]。以上の結果から、本反応では、6 員環のみが効率よく構築できることが明らかになった。

Scheme 35. Carbon chain length effect

a) Five-membered ring-forming reaction



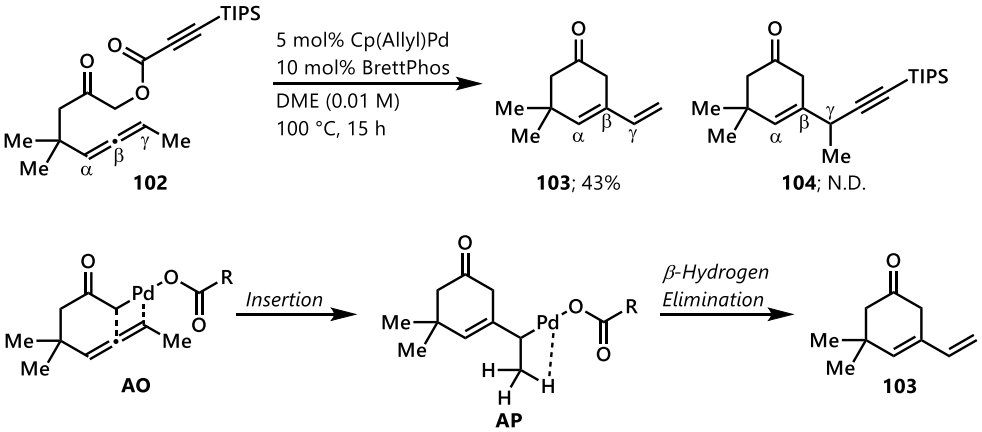
b) Seven-membered ring-forming reaction



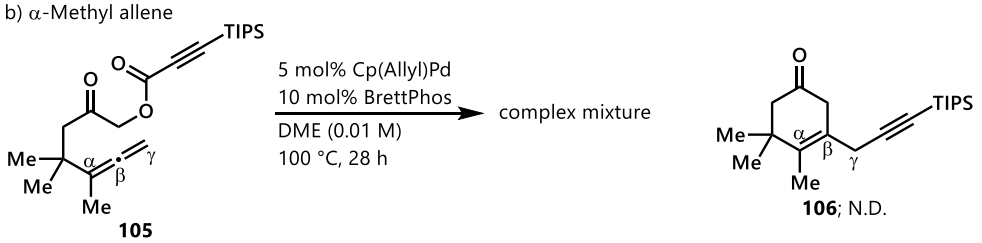
アレン上の置換基の影響についても検討した(Scheme 36)。アレンの γ 位にメチル基を有する基質 **102** では目的物 **104** は得られず、化合物 **103** が 43%生成した(Scheme 36a)[*13]。この化合物 **103** は酸化的付加によって生じた Pd エノラート **AO** からアレンの二重結合に挿入したのちに、β 水素脱離が優先して起こり生成したものと考えられる。またアレンの α 位にメチル基を有する基質 **105** の場合、目的物は得られず、複雑な混合物を与えるのみであった(Scheme 36b)[*14]。おそらくアレンの α 位炭素上のメチル基およびアレン隣接炭素上のメチル基の立体障害により、アレンの挿入反応が起こらず、複雑な混合物を与えたものと考えている。

Scheme 36. Reactions of allenes containing methyl substituents

a) γ-Methyl allene



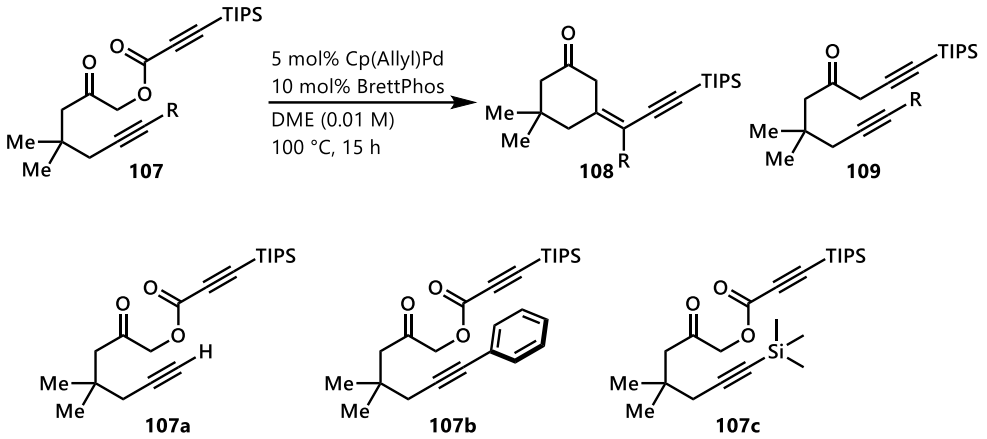
b) α-Methyl allene



アルキンの挿入反応についても検討した(Table 15)。末端アルキンを有する基質 **107a** を用いた場合には、反応が進行せず、原料を回収するのみであった[*15]。おそらくアルキン末端の脱プロトン化が進行し、Pd アセチリドとなることで Pd 触媒が失活したものと考えられる。一方、アルキン末端

にフェニル基 **107b**[*16] および TMS 基 **107c**[*17] を有する基質の場合にも、環化反応は進行せず、α-アルキニルケトン **109** が生成した。本反応では、Pd 中間体 **AQ** にアルキンが挿入する際、アルキン上の置換基と立体障害が生じる。したがって、Pd 中間体 **AQ** から直接脱炭酸、つづく還元的脱離により **109** を与えたものと考えられる。

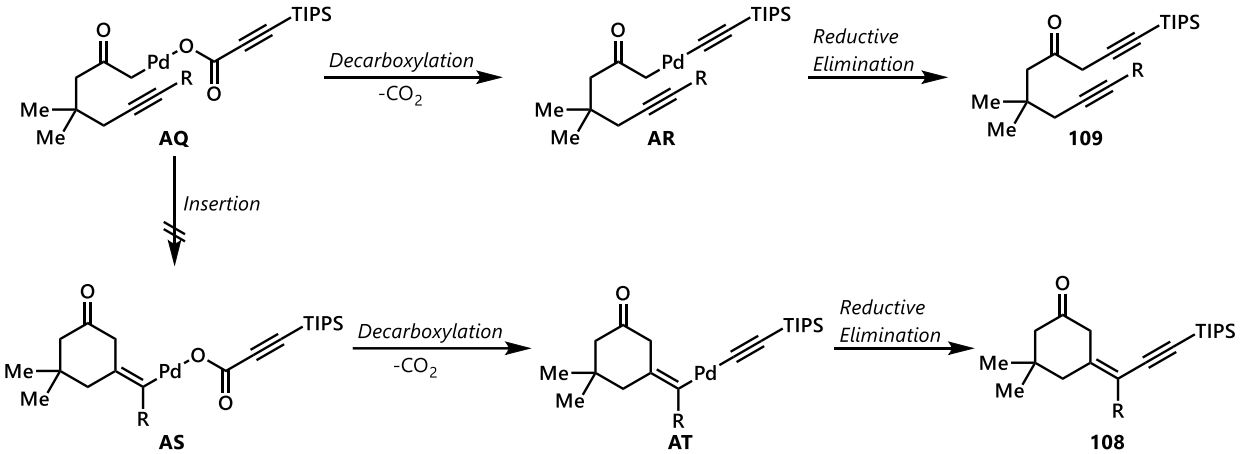
Table 15. Addition of α-position of ketone to triple bonds



Rec. **107a**;100%
108a;N.D.
109a;N.D.

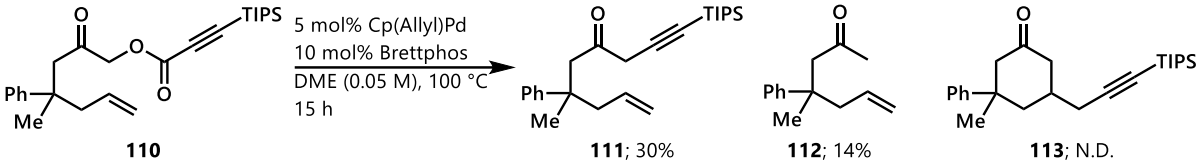
Rec. **107b**; N.D.
108b; N.D.
109b; 61%

Rec. **107c**; N.D.
108c; N.D.
109c; 54%



アルケンへの挿入を伴う環化反応も検討した(Scheme 37)*[18]。基質 **110** を用いて反応を検討したが、アルキンの反応(Table 15)と同様に環化反応は進行せず、α-アルキニルケトン **111** および反応中間体のプロトン化体である化合物 **112** が生成するのみであった。

Scheme 37. Addition of α-position of ketone to alkene



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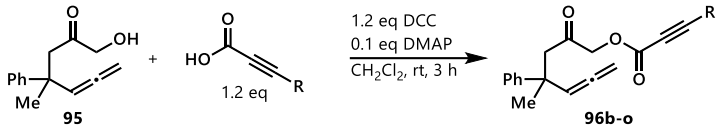
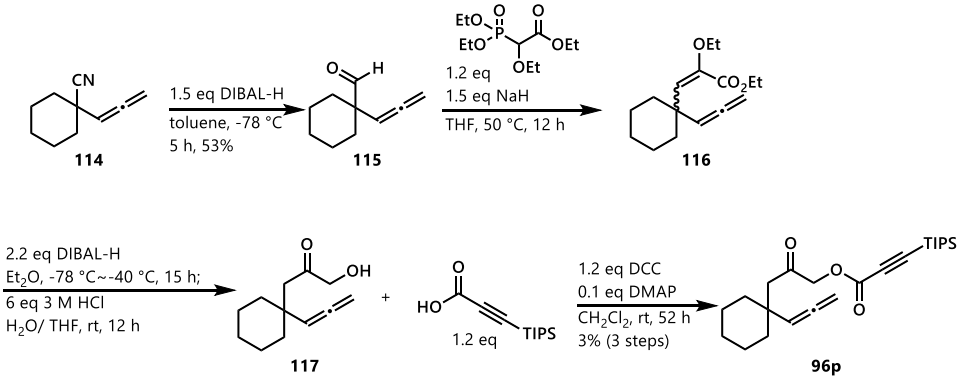
*7 基質 **96b-o** は以下のように合成した(Scheme 38)。α-ヒドロキシケトン **95** と対応するプロピオール酸との DCC 縮合によって合成した。

Scheme 38. Synthesis of substrate **96b-o**



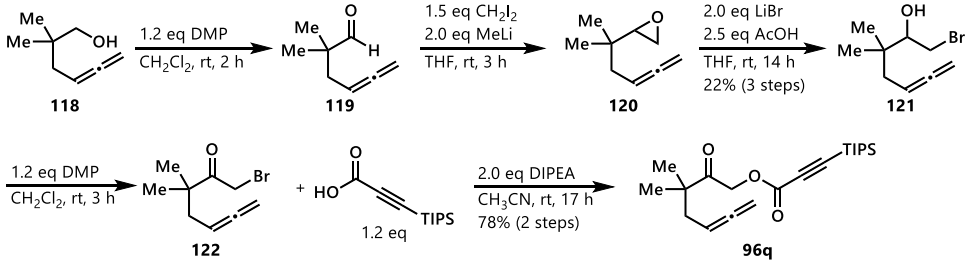
*8 基質 **96p** は以下のように合成した(Scheme 39)。文献既知のアレニルニトリル **114**[29]の DIBAL 還元によってアレニルアルデヒド **115** を合成し、続く Horner-Wadsworth-Emmons 反応によってビニルエーテル **116** とし、DAIBAL 還元続く、加水分解によって α-ヒドロキシケトン **117** を得た。その後、DCC 縮合によって基質 **96p** を合成した。

Scheme 39. Synthesis of substrate **96p**



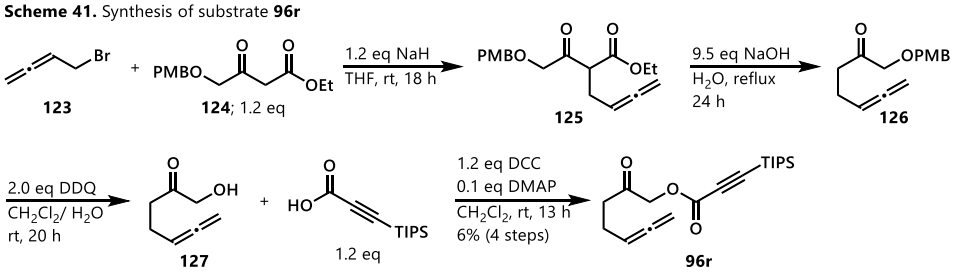
*9 基質 **96q** は以下のように合成した(Scheme 40)。文献既知のアレニルアルコール **118**[30]に対して Dess-Martin 酸化によってアレニルアルデヒド **119** を合成した。その後、ジヨードメタンを用いたエポキシ化続く，臭化リチウムのエポキシドの開環によってブロモヒドリン **121** を得た。得られたブロモヒドリンから Dess-Martin 酸化、続く求核置換反応によって基質 **96q** を合成した。

Scheme 40. Synthesis of substrate **96q**



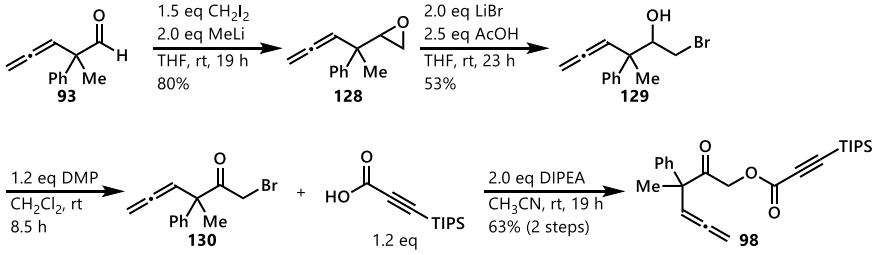
*10 基質 **96r** は以下のように合成した(Scheme 41)。アレニルブロミド **123** と β-ケトエステル **124** とのアルキル化、加水分解、脱炭酸によってケトン **126** を合成した。その後、PMB 基の脱保護を行った後、DCC 縮合によって基質 **96r** を合成した。

Scheme 41. Synthesis of substrate **96r**



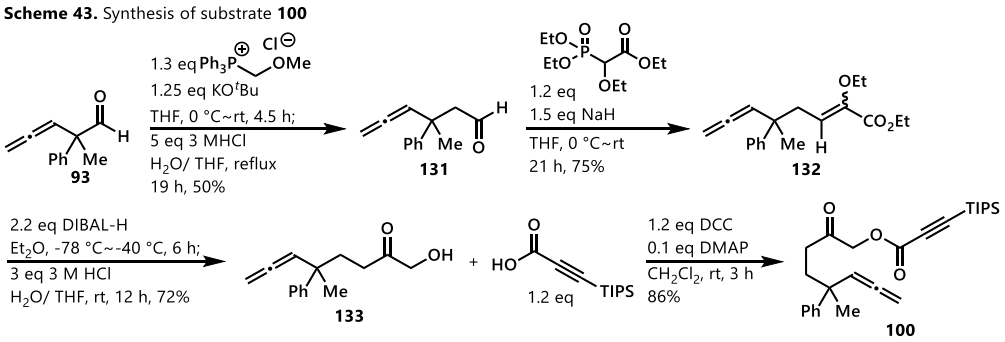
*11 基質 **98** は以下のように合成した(Scheme 42)。アレニルアルデヒドとジヨウドメタンとの反応によりエポキシド **128** を合成し、臭化リチウムのエポキシドの開環によってブロモヒドリン **129** を得た。ブロモヒドリン **130** から Dess-Martin 酸化、続く求核置換反応によって基質 **98** を合成した。

Scheme 42. Synthesis of substrate **98**



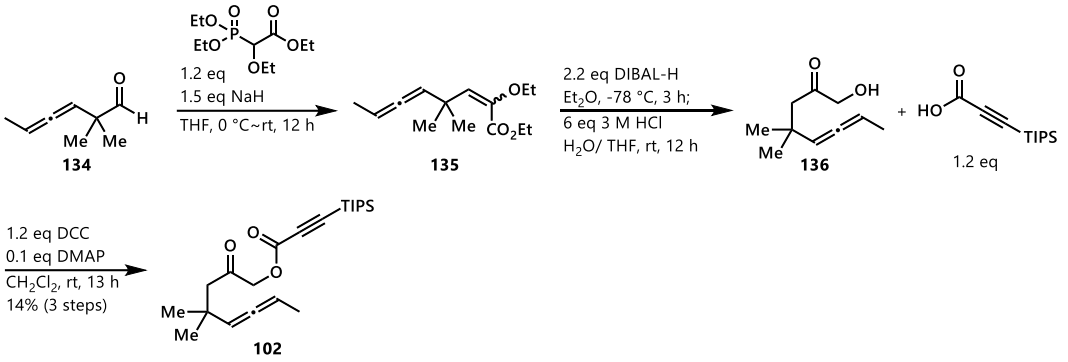
*12 基質 **100** は以下のように合成した(Scheme 43)。アレニルアルデヒド **93** から Wittig 反応の増炭反応によりアレニルアルデヒド **131** を合成し、続く Horner-Wadsworth-Emmons 反応によってビニルエーテル **132** を得た。その後、DAIBAL 還元、続く加水分解によってヒドロキシケトン **133** を合成し、DCC 縮合によって基質 **100** を合成した。

Scheme 43. Synthesis of substrate **100**



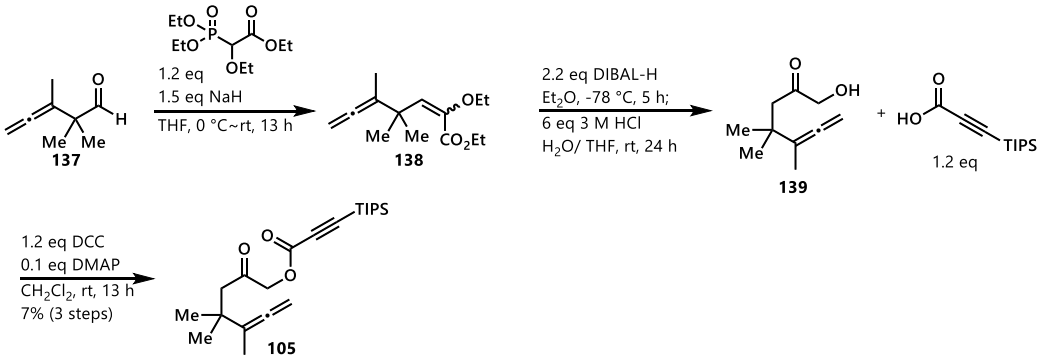
*13 基質 **102** は以下のように合成した(Scheme 44)。文献既知のアレニルアルデヒド **134**[31)]に対して Horner-Wadsworth-Emmons 反応によってビニルエーテル **135** とし、DAIBAL 還元、続く加水分解によってヒドロキシケトン **136** を得た。その後、DCC 縮合によって基質 **102** を合成した。

Scheme 44. Synthesis of substrate **102**



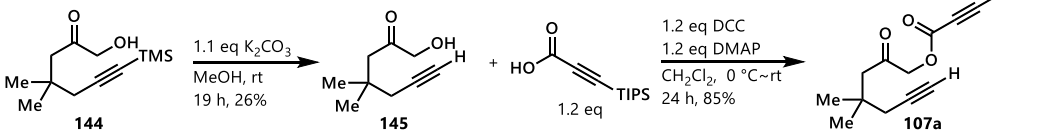
*14 基質 **105** は以下のように合成した(Scheme 45)。文献既知のアレニルアルデヒド **137**[32)]に対して Horner-Wadsworth-Emmons 反応によってビニルエーテル **138** とし、DAIBAL 還元、続く加水分解によってヒドロキシケトン **139** を得た。その後、DCC 縮合によって基質 **105** を合成した。

Scheme 45. Synthesis of substrate **105**



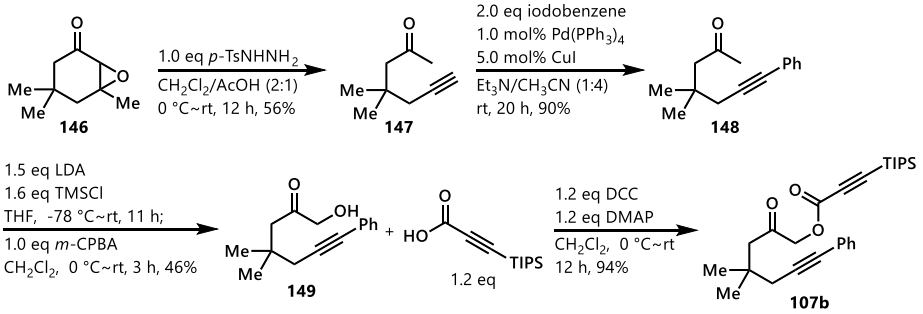
*15 基質 **107a** は以下のように合成した(Scheme 46)。文献既知のヒドロキシケトン **144**[33)]を炭酸カリウムにより脱保護を行い、末端アルキン **145** を得たのち、DCC 縮合によって基質 **107a** を合成した。

Scheme 46. Synthesis of substrate **107a**



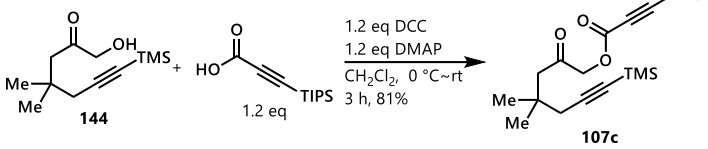
*16 基質 **107b** は以下のように合成した(Scheme 47)。イソホロンオキシドから Eschenmoser-Tanabe 開裂反応によりアルキニルケトン **148** を合成し、薗頭カップリングによってアルキン末端に Ph 基を導入した。その後、Rubottom 酸化によってヒドロキシケトン **149** を合成し、DCC 縮合によって基質 **107b** を合成した。

Scheme 47. Synthesis of substrate **107b**



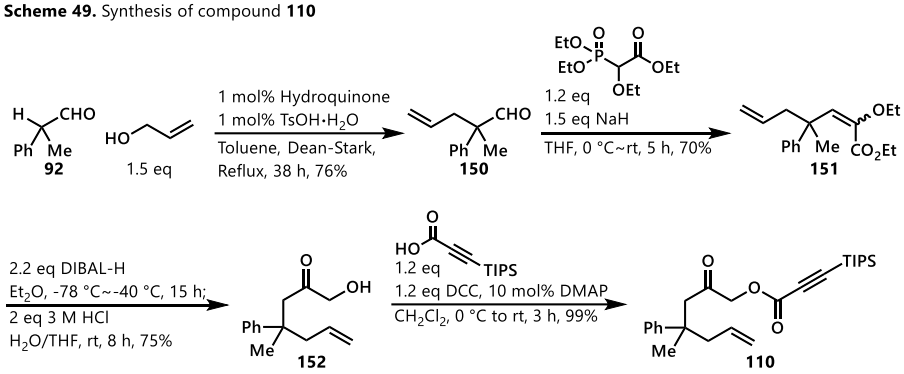
*17 基質 **107c** は以下のように合成した(Scheme 48)。文献既知のヒドロキシケトン **144**[33]とプロピオール酸とのDCC 縮合によって基質 **107c** を合成した。

Scheme 48. Synthesis of substrate **107c**



*18 基質 **110** を以下に示す方法で合成した(Scheme 49)。Claisen 転位によってアレニルアルデヒド **150** を合成した。続く Horner-Wadsworth-Emmons 反応によってビニルエーテル **151** とし、DAIBAL 還元続く加水分解によってヒドロキシケトン **152** を得た。その後、DCC 縮合によって基質 **110** を合成した。

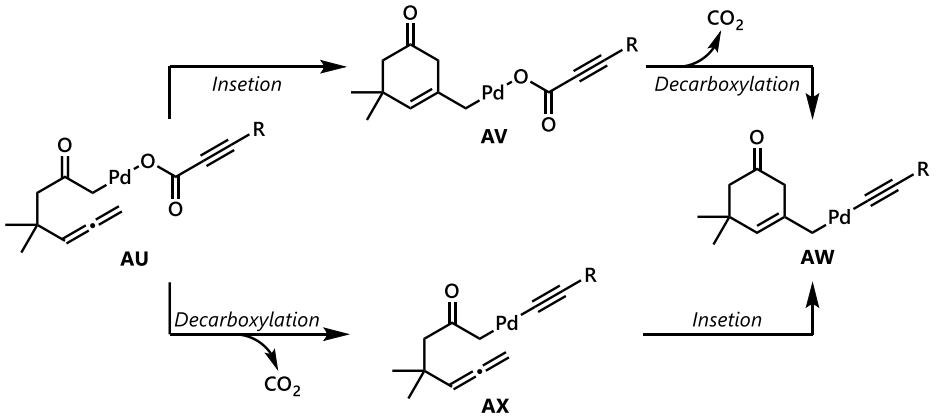
Scheme 49. Synthesis of compound **110**



第四節　DFT 計算を用いた反応機構の考察

本反応では、Pd(0)錯体に基質が酸化的付加し、中間体 **AU** を与える(Scheme 50)。Scheme 27 に示した想定反応機構では、この中間体 **AU** の Pd－C 結合に側鎖のアレンが挿入し、脱炭酸を経て環化体 **97** を与えると考えていた。一方、中間体 **AU** において、最初に脱炭酸が起こり、中間体 **AX** を与え、続いてアレンが挿入し、環化体 **97** を与える経路も考えられる。そこで、これら二つの経路のどちらが優先するのか明らかにするべく、DFT 計算を用い反応機構に関する考察を行うこととした。計算にはモデル化合物として **96'**、モデル配位子として **153** を用いたが、**153** と類似構造である Johnphos でも反応が進行している(Table 12 entry 8)ことから挿入反応および脱炭酸の過程を定性的に十分説明できると考えられる。これらモデル化合物 **96'**およびモデル配位子 **153** を用いて B3LYP/6-31G(d)(LANL2DZ for Pd)により中間体及び遷移状態を求め、得られた各構造の最適化を更に M06/6-311+G(d,p,)(SDD for Pd)によって行った(Figure 2)。先述の通り、Pd(0)錯体への基質の酸化的付加は室温でも十分に進行することがわかっているため、本 DFT 計算では酸化的付加によって生じた Pd 錯体 **I** からの反応経路を探索することとし、Pd 錯体 **I** の初期構造は Figure 1 に示した X 線構造解析の結果を参考に設定した。Pd 錯体 **I** に対してアレン末端の二重結合が挿入すると、遷移状態 $TS_{I\text{-}II}$ を経由して、中間体 **II** を与えるが、この際の活性化エネルギーは 15.7 kcal/mol であった。一方、Pd 錯体 **I** から Pd エノラート **III** へと異性化した後、6 員環遷移状態($TS_{III\text{-}IV}$)を経由し、C(sp^3)－C(sp^2)結合が形成される経路も考えられるが、この際の活性化エネルギーは 35.0 kcal/mol であることから、本反応では酸化的付加の後に、アレン末端の二重結合が Pd－C(sp^3)結合に挿入する経路が有利であると考えられる。また、Pd 錯体 **I** においてアレンと反応する前に脱炭酸が進行する経路も考えられるが、この過程の遷移状態 $TS_{I\text{-}V}$ の活性化エネルギーは 19.0 kcal/mol と比較的高い値を示した。したがって、本反応では、Pd 錯体 **I** を形成した後、末端アレンの Pd－C(sp^3)結合への挿入が起こり、その後、脱炭酸、続く還元的脱離を経て反応が進行する経路が最も有利であると示唆された。最後に、環化後の経路についても DFT 計算を用い、本反応機構の一連の反応経路について確認した。すなわち、Pd 中間体 **II** からは遷移状態 $\mathbf{TS_{II\text{-}VII}}$ を経て、脱炭酸が進行するが、この際の活性化エネルギーは 13.7kcal/mol と比較的容易に反応が進行すると考えられる。また中間体 **VIII** から還元的脱離によって最終生成物となるが、この過程の活性化エネルギーは 21.5 kcal/mol であった。

Scheme 50. Expected pathway of cyclization



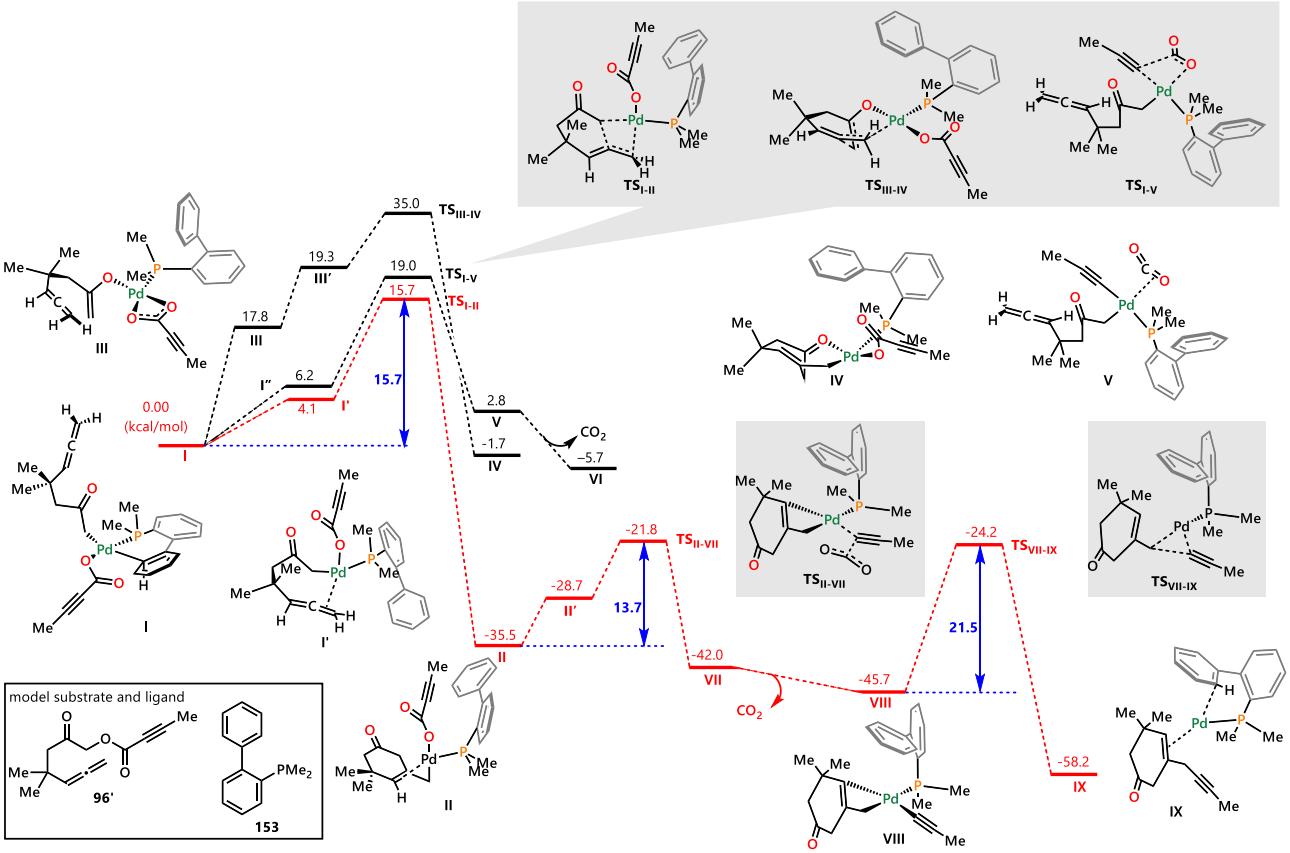


Figure 2. Reaction profile with proposed structures of Intermediates based on DFT calculations M06/6-311+G(d,p,)(SDD for Pd)(Solvent = THF)//B3LYP/6-31G(d)(LANL2DZ for Pd)

本反応では、中間体 **AU**(Scheme 50)においてアレンが挿入する際、その向きや位置の違いによって様々な環状化合物を与える可能性があるが、6 員環化合物 **97** のみを選択的に与えている。そこで、6 員環化合物 **97** を選択的に与える理由に関して、DFT 計算を用いてさらに考察することにした(Figure 3)。アレンの 2 つの二重結合が Pd－C(sp^3) 結合へと挿入するには、1) 6-exo-dig(β 炭素への攻撃)、2) 5-exo-trig(α 炭素への攻撃)、3) 7-endo-trig(γ 炭素への攻撃)の 3 つの経路が考えられる。先に述べたように(Figure 2)、6 員環化合物 **97** を与える 6-exo-dig 環化では、遷移状態(**$TS_{I\text{-}II}$**)を経由して反応が進行し、その活性化エネルギーは 15.7 kcal/mol であった。一方、5-exo-trig 環化及び 7-endo-trig 環化で反応が進行する際、それぞれ **$TS_{I\text{-}II\_5mem}$** 及び **$TS_{I\text{-}II\_7mem}$** の遷移状態を経由することが示唆された。**$TS_{I\text{-}II\_5mem}$** を経由する際の活性化エネルギーは 17.3 kcal/mol、一方、**$TS_{I\text{-}II\_7mem}$** を経由する際のエネルギーは>45 kcal/mol と見積もられた。これらの結果は、本反応において選択的に 6 員環化合物 **97** が生成するという実験結果に一致している。尚、これらの遷移状態における活性化エネルギーの違いは、次のように説明できる。**$TS_{I\text{-}II\_5mem}$** では、ケトンの α 位(C^1)がアレンの α 位(C^5)へ付加する際に Pd と C^8 が近づくことで、立体障害が生じる。加えて 5 員環形成によって生じる H^1 と H^5 との水素同士での立体障害はより活性化エネルギーが高く見積もられたと考えられる。一方、**$TS_{I\text{-}II\_7mem}$** では、Pd と C^8 メチル基の間のアリルひずみおよび環状ひずみが生じることで大きな活性化エネルギーが必要となる。一方、**$TS_{I\text{-}II}$** はアレンの直線的である構造的特徴により、C－C 結合形成の際、立体の影響が小さくなる。立体的な影響により 5-exo-trig 環化および 7-endo-trig 環化によって生じるアルケニル Pd 種よりも 6-exo-dig 環化による生じるアルキル Pd 種の形成が優先される。

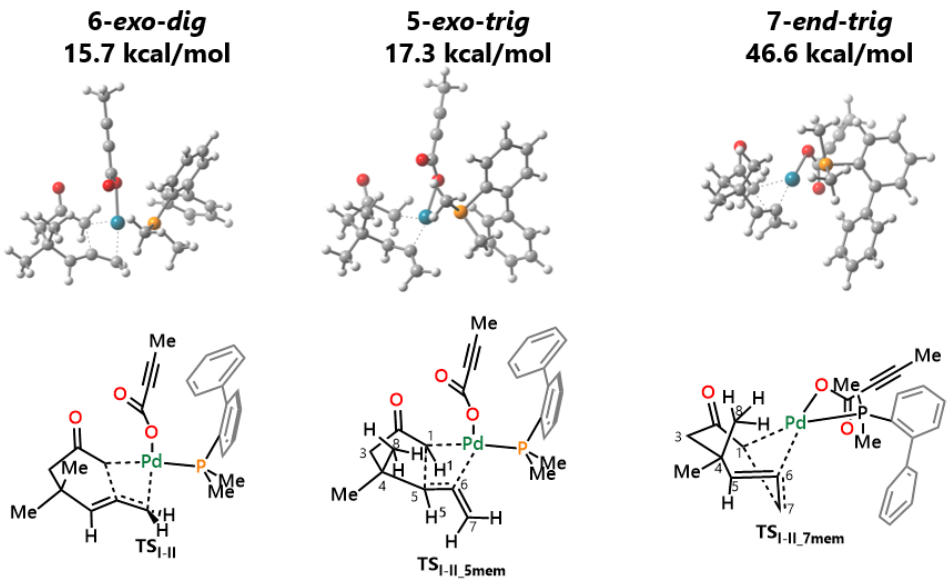
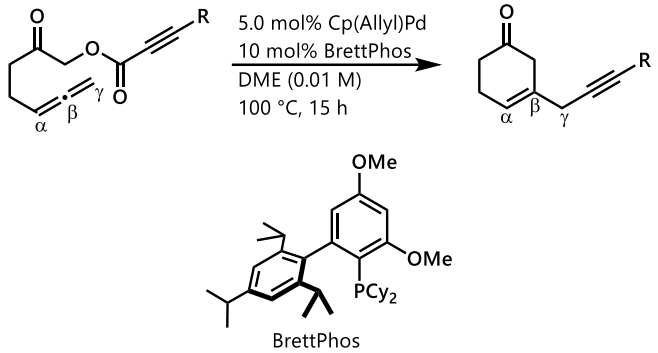


Figure 3. Proposed Structures of Transition States in the Formation of a 5-, 6-, or 7-Membered Product Based on DFT Calculations

結語

本研究では α 位 C–O 結合の酸化的付加によって生じる Pd 中間体に着目し、アレンの挿入を経由する環化アルキニル化反応によりシクロヘキセノン骨格の構築に成功した[*19]。5 mol%の Cp(Allyl)Pd、10 mol%の BrettPhos 配位子存在下、1,2-ジメトキシエタン溶媒中、100 ℃で加熱することで最もよい収率で目的の環化体が得られることを見出した。本環化反応では、新しい C－C 結合がカルボニル基の α 炭素とアレンの β 炭素との間に形成され、アルキニル基の γ 炭素への移動とともに、さまざまなシクロヘキサノン誘導体が生成できる。酸化的付加によって生じた Pd エノラートがアレンの β 炭素へ移動挿入が優先するメカニズムであることが DFT 計算によって示唆された [8)]。

Scheme 51. Pd catalyzed decarboxylative cycloalkynylation of allenes



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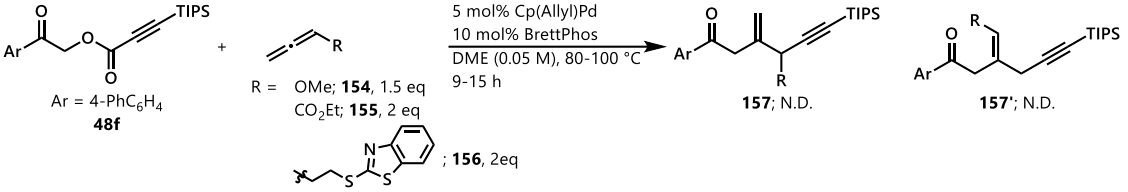
*19 アレンやアルケンをカップリングパートナーとした分子間反応の検討を行った。アルコキシアレン **154**、共役アレニルエステル **155**、アルキルアレン **156** をカップリングパートナーとした場合には目的のカップリング体は得られず、複雑な混合物を与えるのみか原料 **48f** を回収するのみであった(Scheme 52)。

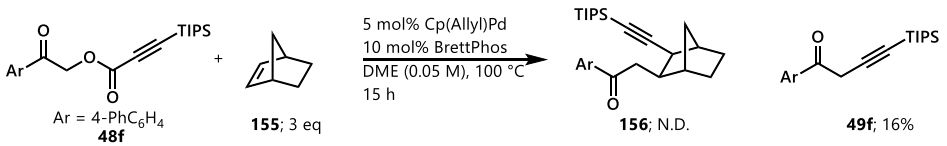
Scheme 52. Insertion of allenes



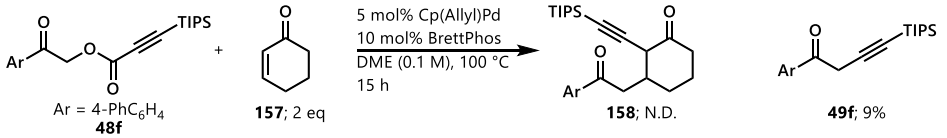
またアルケンをカップリングパートナーとした反応では、ノルボルネン、エノンについて検討を行ったが、カップリング体は得られず、α-アルキニルケトン **49f** が得られるのみであった(Scheme 53)。

Scheme 53. Insertion of alkenes

a) Norbornene



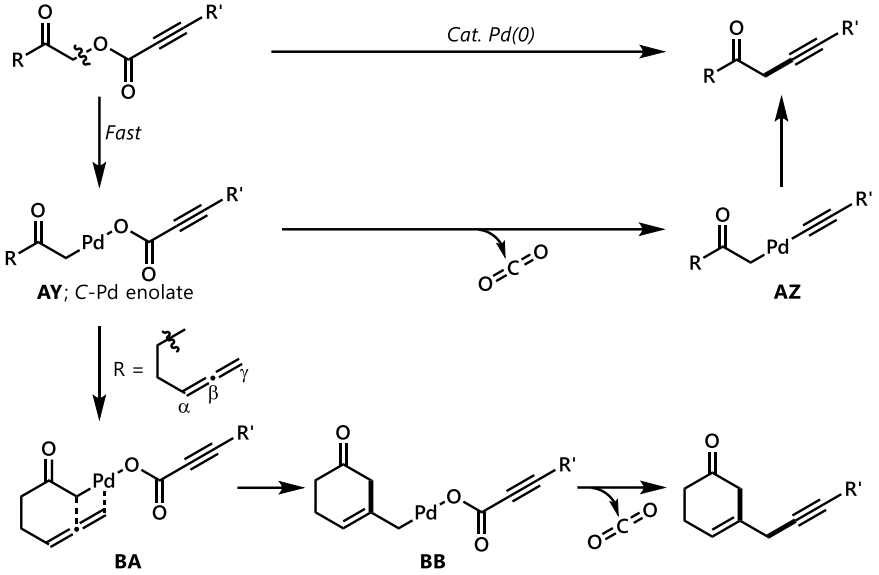
b) Enone



総括

著者は、従来の脱炭酸型アルキル化では困難であったカルボニル基の脱炭酸型 α 位官能基化反応を見出した。すなわち、従来の脱炭酸型アルキル化反応ではアリル化、ベンジル化に限られていたが、ケトンの α 位 C－O 結合切断によって生じる C－Pd エノラートに注目することで、脱炭酸型アルキニル化を達成できた。また、ケトンの α 位 C－O 結合が Pd 錯体に酸化的付加によって生じた Pd エノラート **AY** からの脱炭酸が遅いことを利用して、不活性な多重結合の挿入を伴う新しい環化反応を開発した。

Scheme 54. Pd catalyzed decarboxylative alkynylation of α-hydroxyketone derivatives by C-O bond cleavage



実験の部

General Information

All reactions were performed under an atmosphere of nitrogen unless otherwise stated. Acetonitrile and THF were purified under nitrogen using The Ultimate Solvent System (Glass Counter Inc.). Toluene, *m*-xylene, 1,4-dioxane and 1,2-dimethoxyethane were distilled from Na/benzophenone ketyl and stored under nitrogen. All other reagents were purchased from commercial source and used as received. Column chromatography was performed on silica gel (Wakogel® FC-40, neutral, 20-40 μm, FUJIFILM Wako Chemical Corporation) with the indicated solvents as an eluent. Analytical thin-layer chromatography was performed on Silica gel 60 $PF_{254\alpha}$ (Merck).

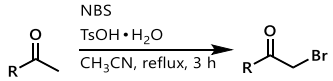
^{1}H NMR spectroscopy was recorded on JEOL ECA500 (500 MHz), ECX400P, ECS400 or ECP400 (400 MHz) NMR spectrometer. Chemical shifts are reported in ppm from the solvent resonance as an internal standard ($CDCl_3$: δ= 7.26 ppm). NMR data are reported as follows: chemical shifts, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet, br: broad signal), coupling constant (Hz), and integration. ^{13}C NMR spectroscopy was recorded on JEOL ECA500 (125 MHz), ECX400P, ECS400, or ECP400 (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from the internal reference ($CDCl_3$: δ= 77.00 ppm). Mass spectra were obtained on JEOL JMS-T100GCv mass spectrometer.

Experimental Details

第一章　Pd 触媒による脱炭酸を伴うケトンの α 位アルキニル化反応の開発

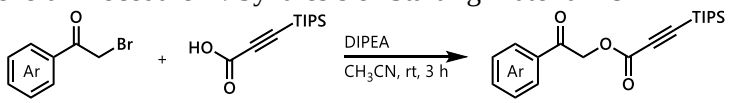
Synthesis of Starting Materials

General Procedure A: Synthesis of Bromoketones



A literature procedure was applied.[1] A two-necked flask was charged with methylketone (2.0 mmol). The flask was equipped with a condenser and nitrogen balloon. Then, anhydrous MeCN (12 mL), TsOH•H_2O (516 mg, 3.0 mmol) was loaded. To the stirring solution was added *N*-bromosuccinimide solution in MeCN (383 mg, 2.15 mmol in 12 mL MeCN) dropwise. The mixture was refluxed for 3 h. The progress of the reaction was monitored by means of TLC analysis. The reaction mixture was cooled to room temperature and then evaporated. The resulting liquid was dissolved in 50 mL EtOAc. The solution was washed with water and brine (15 mL each). The organic layer was dehydrated with Na_2SO_4 and then purified by column chromatography to afford bromoketone.

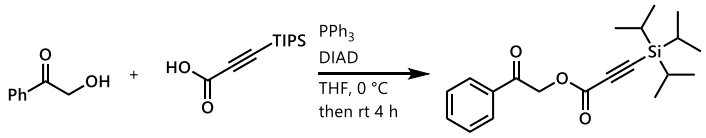
General Procedure B: Synthesis of Starting Material **48**



3-(Triisoprosilyl)propiolic acid was prepared according to a literature procedure.[2]

Phenacyl bromide and 3-(Triisoprosilyl)propiolic acid (1.1 equiv.) was dissolved in MeCN (0.1 M). To the solution was added *N*,*N*-diisopropylethylamine (2 equiv.) dropwise with stirring. The solution was stirred for 3 h (monitored by TLC) at room temperature and then evaporated. The residue was purified by column chromatography to afford the desired product.

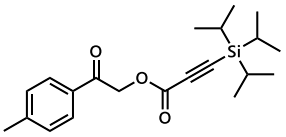
48a



48a; 74%

In a flask containing a stirring bar, 3-(triisoprosilyl)propiolic acid (680 mg, 3 mmol), 2-hydroxyacetophenone (commercially available, 449 mg, 3.3 mmol) and PPh_3 (449 mg, 3.3 mmol) was dissolved in THF (20 mL). To the solution was added diisopropyl azodicarboxylate (0.47 mL, 3.3 mmol) dropwise with stirring at 0 °C. The solution was stirred for 4 h (monitored by TLC) at room temperature. Aqueous NH_4Cl were added at room temperature, and the mixture was extracted with EtOAc three times. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. It was then purified by silica gel column chromatography (hexane/AcOEt, 20:1), affording 857 mg of compound **48a** as a white solid (74%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.90-7.92 (m, 2H), 7.61 (m, 1H), 7.50 (m, 2H), 5.42 (s, 2H), 1.09-1.18 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 190.84, 152.11, 134.01, 133.91, 128.89, 127.76, 95.81, 93.33, 66.84, 18.42, 10.91. HRMS (EI) calcd.for $C_{17}H_{21}O_3Si$ [M-^{i}Pr]$^+$ *m/z* 301.1260, found 301.1251.

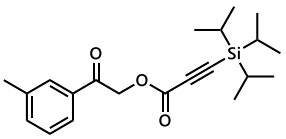
48b



Corresponding phenacyl bromide was purchased from commercial source (TCI).

By following general procedure B, the reaction of corresponding phenacyl bromide (426 mg, 2.0 mmol) with 3-(Triisoprosilyl)propiolic acid (589 mg, 1.3 mmol) in the presence of diisopropylethylamine (0.45 mL, 2.6 mmol) in 6 mL MeCN delivered 717 mg of compound **48b** as white solid (100%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.81 (d, J = 8.1 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 5.39 (s, 2H), 2.42 (s, 3H), 1.09-1.18 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 190.44, 152.18, 145.02, 131.45, 129.57, 127.87, 95.87, 93.23, 66.80, 21.76, 18.44, 10.93. HRMS (EI) calcd.for $C_{18}H_{23}O_3Si$ [M-^{i}Pr]$^+$ *m/z* 315.1416, found 315.1417

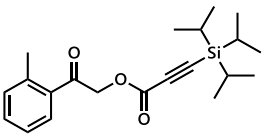
48c



Corresponding phenacyl bromide was prepared according to literature procedure.[1]

By following general procedure B, the reaction of corresponding phenacyl bromide (351 mg, 1.65 mmol) with 3-(Triisoprosilyl)propiolic acid (410 mg, 1.81 mmol) in the presence of diisopropylethylamine (0.32 mL, 1.81 mmol) in 4.5 mL MeCN delivered 302 mg of compound **48c** as white solid (51%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.71 (d, J = 12.1 Hz, 2H), 7.36-7.44 (m, 2H), 5.40 (s, 2H), 2.42 (s, 3H), 1.10-1.18 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 191.01, 152.14, 138.80, 134.78, 133.96, 128.74, 128.27, 124.93, 95.86, 93.27, 66.91, 21.31, 18.42, 10.92. HRMS (EI) calcd.for $C_{18}H_{23}O_3Si$ [M-^{i}Pr]$^+$ *m/z* 315.1416, found 315.1417.

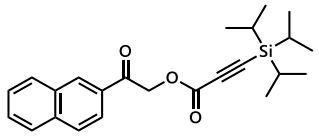
48d



Corresponding phenacyl bromide was prepared by following general procedure A. The spectrum data matched to that of literature.[3]

By following general procedure B, the reaction of corresponding phenacyl bromide (215 mg, 1.0 mmol) with 3-(Triisoprosilyl)propiolic acid (249 mg, 1.1 mmol) in the presence of diisopropylethylamine (0.35 mL, 2 mmol) in 10 mL MeCN delivered 314.3 mg of compound **48d** as colorless liquid (88%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.58-7.60 (m, 1H), 7.40-7.44 (m, 1H), 7.27 (m, 2H), 5.25 (s, 2H), 2.52 (s, 3H), 1.11 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 194.25, 152.14, 139.27, 133.95, 132.68, 132.31, 128.04, 125.78, 95.82, 93.25, 68.01, 21.19, 18.43, 10.92. HRMS (EI) calcd. for $C_{18}H_{23}O_3Si$ [M-^{i}Pr]$^+$ *m/z* 315.1416, found 315.1417.

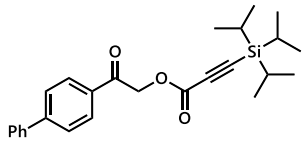
48e



Corresponding phenacyl bromide was purchased from commercial source (TCI).

By following general procedure B, the reaction of corresponding phenacyl bromide (249 mg, 1.0 mmol) with 3-(Triisoprosilyl)propiolic acid (249 mg, 1.1 mmol) in the presence of diisopropylethylamine (0.35 mL, 2 mmol) in 10 mL MeCN delivered 399 mg of compound **48e** as white solid (quant.). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.42 (s, 1H), 7.88-7.99 (m, 4H), 7.58-7.66 (m, 2H), 5.56 (s, 2H), 1.05-1.19 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 191.01, 152.14, 138.80, 134.78, 133.96, 128.74, 128.27, 124.93, 95.86, 93.27, 66.91, 21.31, 18.42, 10.92. HRMS (EI) calcd.for $C_{24}H_{30}O_3Si$ $[M]^+$ *m/z* 394.1964, found 394.1964.

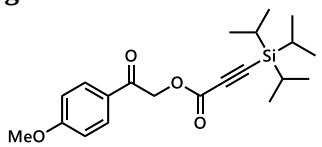
48f



Corresponding phenacyl bromide was purchased from commercial source (TCI).

By following general procedure B, the reaction of corresponding phenacyl bromide (275 mg, 1.0 mmol) with 3-(Triisoprosilyl)propiolic acid (272 mg, 1.2 mmol) in the presence of diisopropylethylamine (0.35 mL, 2 mmol) in 10 mL MeCN delivered 391 mg of compound **48f** as a white solid (93%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.98-8.00 (m, 2H), 7.70-7.72 (m, 2H), 7.62-7.64 (m, 2H), 7.42-7.50 (m, 3H), 5.45 (s, 2H), 1.11-1.19 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 190.45, 152.15, 146.69, 139.52, 132.56, 128.99, 128.45, 128.37, 127.48, 127.24, 95.82, 93.37, 66.87, 18.43, 10.91. HRMS (EI) calcd.for $C_{23}H_{25}O_3Si$ $[M-^{i}Pr]^+$ *m/z* 377.1573, found 377.1573.

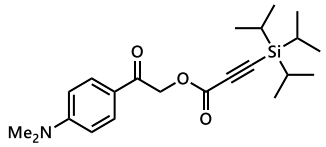
48g



Corresponding phenacyl bromide was purchased from commercial source (TCI).

By following general procedure B, the reaction of corresponding phenacyl bromide (458 mg, 2 mmol) with 3-(Triisoprosilyl)propiolic acid (589 mg, 2.6 mmol) in the presence of diisopropylethylamine (0.45 mL, 2.6 mmol) in 10 mL MeCN delivered 385 mg of compound **48g** as white solid (51%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.88-7.90 (m, 2H), 6.94-6.97 (m, 2H), 5.37 (s, 2H), 3.88 (s, 3H), 1.09-1.18 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 189.32, 164.13, 152.21, 130.10, 126.97, 114.08, 95.93, 93.16, 66.62, 55.52, 18.42, 10.94. HRMS (EI) calcd.for $C_{18}H_{23}O_4Si$ $[M-^{i}Pr]^+$ *m/z* 331.1366, found 331.1354.

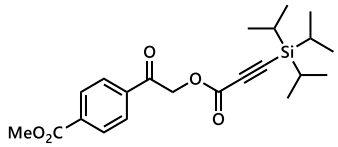
48h



Corresponding phenacyl bromide was prepared according to literature procedure.[4]

By following general procedure B, the reaction of corresponding phenacyl bromide (242 mg, 1.0 mmol) with 3-(Triisoprosilyl)propiolic acid (249 mg, 1.1 mmol) in the presence of diisopropylethylamine (0.35 mL, 2 mmol) in 10 mL MeCN delivered 142.6 mg of compound **48h** as white solid (37%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.80-7.82 (m, 2H), 6.64-6.66 (m, 2H), 5.35 (s, 2H), 3.07 (s, 6H), 1.12 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 188.48, 153.85, 152.38, 129.98, 121.82, 110.75, 96.19, 92.72, 66.52, 39.98, 18.45, 10.97. HRMS (EI) calcd.for $C_{22}H_{33}NO_3Si$ $[M]^+$ *m/z* 387.2230, found 387.2216.

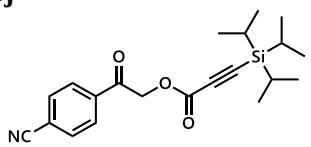
48i



Corresponding phenacyl bromide was prepared according to literature procedure.[5]

By following general procedure B, the reaction of corresponding phenacyl bromide (165 mg, 0.64 mmol) with 3-(Triisoprosilyl)propiolic acid (158.5 mg, 0.7 mmol) in the presence of diisopropylethylamine (0.22 mL, 1.28 mmol) in 6.4 mL MeCN delivered 207.9 mg of compound **48i** as white solid (81%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.15-8.17 (m, 2H), 7.96-7.98 (m, 2H), 5.41 (s, 2H), 3.96 (s, 3H), 1.12 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 190.58, 165.99, 152.35, 137.10, 134.61, 130.09, 127.77, 95.67, 93.86, 67.04, 52.58, 18.54, 10.93. HRMS (EI) calcd.for $C_{19}H_{23}O_5Si$ [M-^{i}Pr]$^{+}$ *m/z* 359.1315, found 359.1315.

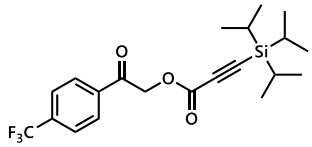
48j



Corresponding phenacyl bromide was purchased from commercial source (TCI).

By following general procedure B, the reaction of corresponding phenacyl bromide (220 mg, 1 mmol) with 3-(Triisoprosilyl)propiolic acid (249 mg, 1.1 mmol) in the presence of diisopropylethylamine (0.35 mL, 2 mmol) in 10 mL MeCN delivered 339 mg of compound **48j** as white solid (92%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.02-8.00 (m, 2H), 7.82-7.80 (m, 2H), 5.38 (s, 2H), 1.15-1.11 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 190.09, 151.90, 136.88, 132.74, 128.30, 117.57, 117.28, 95.43, 94.21, 66.77, 18.40, 10.90. HRMS (EI) calcd.for $C_{18}H_{20}O_3Si$ [M-^{i}Pr]$^{+}$ *m/z* 326.1212, found 326.1212.

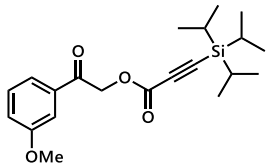
48k



Corresponding phenacyl bromide was prepared by following general procedure A (79%). The spectrum data matched to that of literature.[6]

By following general procedure B, the reaction of corresponding phenacyl bromide (208 mg, 0.78 mmol) with 3-(Triisoprosilyl)propiolic acid (192 mg, 0.85 mmol) in the presence of diisopropylethylamine (0.27 mL, 1.56 mmol) in 7.8 mL MeCN delivered 309.1 mg of compound **48k** as white solid (96%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.03 (d, J = 8.1 Hz, 2H), 7.77 (d, J = 8.1 Hz, 2H), 5.40 (s, 2H), 1.12 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 190.45, 152.09, 136.75, 135.37 (q, J = 32.5 Hz), 128.33, 126.10 (q, J = 2.9 Hz), 123.44 (q, J = 274 Hz), 95.66, 94.12, 66.93, 18.52, 11.04. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): −63.19. HRMS (EI) calcd.for $C_{18}H_{20}F_3O_3Si$ [M-^{i}Pr]$^{+}$ *m/z* 369.1134, found 369.1136.

48l



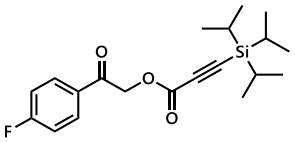
Corresponding phenacyl bromide was prepared by following general procedure A (69%).

The spectrum data matched to that of literature.[7]

By following general procedure B, the reaction of corresponding phenacyl bromide (490 mg, 2.1 mmol) with 3-(Triisoprosilyl)propiolic acid (530 mg, 2.3 mmol) in the presence of diisopropylethylamine (0.73 mL, 4.2 mmol) in 20 mL MeCN delivered 779 mg of compound **48l** as colorless oil (99%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.42-7.45 (m, 2H), 7.42-7.38 (m, 1H), 7.15-7.17 (m, 1H), 5.40 (s, 2H), 3.86 (s, 3H), 1.10-1.19 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 190.75, 160.01, 152.12, 135.24, 129.88, 120.56, 120.16, 112.06,

95.86, 93.36, 66.92, 55.45, 18.42, 10.95. HRMS (EI) calcd.for $C_{18}H_{23}O_4Si$ [M-^{i}Pr]$^+$ *m/z* 331.1366, found 331.1366.

48m

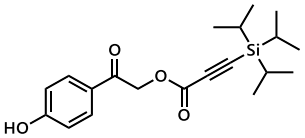


Corresponding phenacyl bromide was prepared by following general procedure A (61%).

The spectrum data matched to that of literature.[6]

By following general procedure B, the reaction of corresponding phenacyl bromide (132.2 mg, 0.61 mmol) with 3-(Triisoprosilyl)propiolic acid (152 mg, 0.67 mmol) in the presence of diisopropylethylamine (0.21 mL, 1.2 mmol) in 6.1 mL MeCN delivered 192.2 mg of compound **48m** as colorless liquid (87%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.93-7.98 (m, 2H), 7.15-7.20 (m, 2H), 5.37 (s, 2H), 1.12 (d, J = 8.2 Hz, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 189.46, 166.25 (d, J = 251.9 Hz), 152.10, 130.55 (d, J = 9.6 Hz), 116.19 (d, J = 22.0 Hz), 95.74, 93.66, 66.65, 18.45, 10.96. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): −102.92. HRMS (EI) calcd.for $C_{17}H_{20}FO_3Si$ [M-^{i}Pr]$^+$ *m/z* 319.1166, found 319.1166.

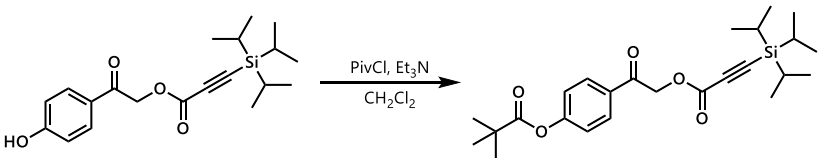
48n



Corresponding phenacyl bromide was purchased from commercial source (TCI).

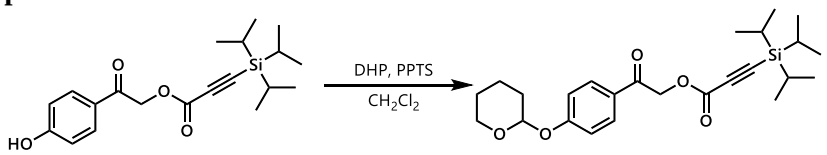
By following general procedure B, the reaction of corresponding phenacyl bromide (215 mg, 0.61 mmol) with 3-(Triisoprosilyl)propiolic acid (249 mg, 1.1 mmol) in the presence of diisopropylethylamine (0.35 mL, 2 mmol) in 10 mL MeCN delivered 204 mg of compound **48n** as white solid (57%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.83-7.51 (m, 2H), 6.91-6.89 (m, 2H), 5.38 (s, 2H), 1.06-1.16 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 189.68, 161.28, 152.51, 130.45, 126.67, 115.79, 95.72, 93.83, 66.68, 18.41, 10.92. HRMS (EI) calcd.for $C_{17}H_{21}O_4Si$ [M-^{i}Pr]$^+$ *m/z* 317.1209, found 317.1197.

48o



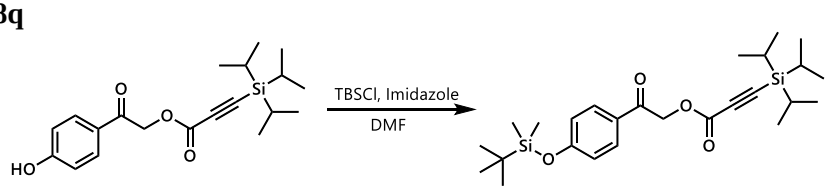
Phenacyl propionate **48n** (360 mg, 1 mmol) was dissolved in CH_2Cl_2 (10 mL). To the solution was added pivaloyl chloride (0.14 mL, 1.2 mmol) and triethylamine (0.17 mL, 1.2 mmol) dropwise with stirring at 0 ℃. The solution was stirred for 15 h (monitored by TLC) at room temperature and then evaporated. The residue was purified by column chromatography to afford compound **48o** as white solid (330 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.96-7.94 (m, 2H), 7.21-7.19 (m, 2H), 5.39 (s, 2H), 1.37 (s, 9H), 1.10-1.18 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 189.76, 176.36, 155.58, 152.11, 131.35, 129.42, 122.15, 95.79, 93.51, 66.72, 39.23, 27.04, 18.44, 10.95. HRMS (EI) calcd.for $C_{22}H_{29}O_5Si$ [M-^{i}Pr]$^+$ *m/z* 401.1784, found 401.1784.

48p



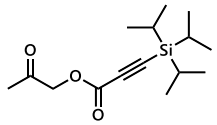
Phenacyl propionate **48n** (360 mg, 1 mmol) and pyridinium *p*-toluenesulfonate (12.6 mg, 0.05 mmol) were dissolved in CH_2Cl_2 (5 mL). To the solution was added 3,4-dihydro-2*H*-pyran (0.14 mL, 1.5 mmol) dropwise with stirring. Saturated aqueous $NaHCO_3$ were added at room temperature, and the mixture was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over Na_2SO_4, and removed under reduced pressure. The residue was purified by column chromatography to afford compound **48p** as white solid (417 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.90-7.86 (m, 2H), 7.13-7.09 (m, 2H), 5.53 (t, J = 2.9 Hz, 1H), 5.37 (s, 2H), 3.80-3.86 (m, 1H), 3.60-3.64 (m, 1H), 1.86-2.01 (m, 3H), 1.58-1.73 (m, 3H), 1.07-1.20 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 189.42, 161.68, 152.21, 129.94, 127.55, 116.30, 96.05, 95.95, 93.15, 66.65, 62.01, 30.01, 24.99, 18.44, 18.38, 10.96. HRMS (ESI) calcd.for $C_{25}H_{36}O_5NaSi$ $[M+Na]^+$ *m/z* 467.2230, found 467.2224.

48q



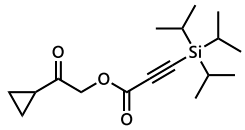
Phenacyl propionate **48n** (360 mg, 1 mmol) was dissolved in DMF (10 mL). To the solution was added *tert*-butyldimethylsilyl chloride (200 mg, 1.3 mmol) and imidazole (280 mg, 4 mmol) with stirring at 0 ℃. The mixture was extracted with EtOAc three times. The combined organic layer was washed with brine, dried over Na_2SO_4, and removed under reduced pressure. The residue was purified by column chromatography to afford compound **48q** as colorless oil (437 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.82-7.86 (m, 2H), 6.88-6.91 (m, 2H), 5.36 (s, 2H), 1.10-1.18 (m, 21H), 0.99 (s, 9H), 0.24 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 189.41, 161.03, 152.18, 130.02, 127.51, 120.25, 95.94, 93.11, 66.63, 25.53, 18.42, 18.22, 10.95, −4.41. HRMS (EI) calcd.for $C_{26}H_{42}O_4Si_2$ $[M]^+$ *m/z* 474.2622, found 474.2622.

48r



By following general procedure B, the reaction of bromoacetone (134 mg, 1 mmol, purchased from FUJIFILM Wako) with 3-(Triisoprosilyl)propiolic acid (249 mg, 1.1 mmol) in the presence of diisopropylethylamine (0.35 mL, 2 mmol) in 10 mL MeCN delivered 271 mg of compound **48r** as white solid (92%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.71 (s, 2H), 2.19 (s, 3H), 1.09-1.17 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 200.63, 151.96, 95.63, 93.66, 69.01, 26.11, 18.41, 10.92. HRMS (EI) calcd.for $C_{12}H_{19}O_3Si$ $[M-^iPr]^+$ *m/z* 239.3660, found 239.1104.

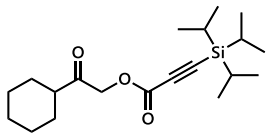
48s



Corresponding bromoketone was prepared according to literature procedure.[8] The spectrum data matched to that of literature.[9]

By following general procedure B, the reaction of bromomethyl cyclopropyl ketone (163 mg, 1 mmol) with 3-(Triisoprosilyl)propiolic acid (249 mg, 1.1 mmol) in the presence of diisopropylethylamine (0.35 mL, 2 mmol) in 10 mL MeCN delivered 85 mg of compound **48s** as colorless liquid (28%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.89 (s, 2H), 1.94-1.99 (m, 1H), 0.95-1.16 (m, 25H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 202.79, 152.11, 95.85, 93.46, 69.23, 18.52, 17.31, 11.73, 11.02. HRMS (EI) calcd.for $C_{14}H_{21}O_3Si$ $[M-^{i}Pr]^+$ *m/z* 265.1260, found 265.1260.

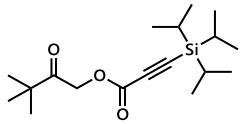
48t



Corresponding bromoketone was prepared according to literature procedure.[8]

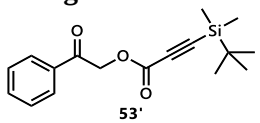
By following general procedure B, the reaction of bromomethyl cyclohexyl ketone (678 mg, 3.31 mmol) with 3-(Triisoprosilyl)propiolic acid (823 mg, 3.63 mmol) in the presence of diisopropylethylamine (1.15 mL, 6.62 mmol) in 30 mL MeCN delivered 378 mg of compound **48t** as yellow liquid (33%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.80 (s, 2H), 2.40-2.46 (m, 1H), 1.66-1.86 (m, 5H), 0.93-1.44 (m, 26H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 205.18, 152.01, 95.83, 93.23, 67.48, 47.32, 28.09, 25.63, 25.42, 21.01, 18.42, 10.93. HRMS (EI) calcd.for $C_{17}H_{27}O_3Si$ $[M-^{i}Pr]^+$ *m/z* 307.1729, found 307.1730.

48u



By following general procedure B, the reaction of 1-bromo-3,3-dimethyl-2-butanone (purchased from TCI, 358 mg, 2.0 mmol) with 3-(Triisoprosilyl)propiolic acid (498 mg, 2.2 mmol) in the presence of diisopropylethylamine (0.7 mL, 4 mmol) in 20 mL MeCN delivered 363.3 mg of compound **48u** as colorless waxy solid (56%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 4.95 (s, 2H), 1.21 (s, 9H), 1.11 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 206.52, 152.19, 95.81, 92.98, 65.32, 42.86, 26.14, 18.43, 10.94. HRMS (EI) calcd.for $C_{15}H_{25}O_3Si$ $[M-^{i}Pr]^+$ *m/z* 281.1573, found 281.1573.

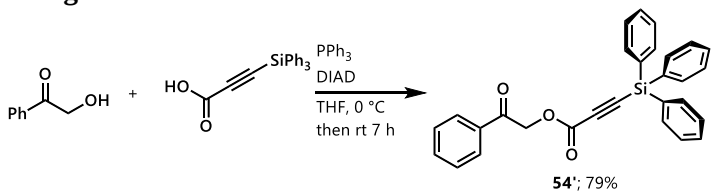
Starting material of 53



3-(*tert*-butyldimetheylsilyl)propiolic acid was prepared according to the literature procedure.[10]

3-(*tert*-butyldimetheylsilyl)propiolic acid (995 mg) was dissolved in H_2O (4 mL). To the solution was added 10% NaOH aq. (2 mL, 5.1 mmol) dropwise with stirring. The solution was stirred for 10 min at room temperature. To the mixture were added the solution of phenacyl bromide (995 mg, 5 mmol) in EtOH (8 mL). The mixture was refluxed for 4 h and then evaporated. The residue was purified by column chromatography to afford compound **53'** as white solid (934 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.90-7.92 (m, 2H), 7.60-7.64 (m, 1H), 7.48-7.52 (m, 2H), 5.42 (s, 2H), 0.98 (s, 9H), 0.20 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 190.68, 152.04, 134.00, 133.79, 128.86, 127.71, 94.62, 94.46, 66.84, 25.87, 16.46, -5.33. HRMS (EI) calcd.for $C_{13}H_{13}O_3Si$ [M-^{t}Bu]$^+$ *m/z* 245.0634, found 245.0626.

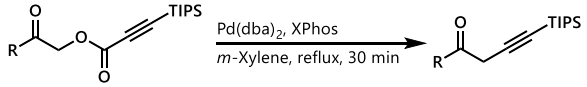
Starting material of 54



3-(triphenylsilyl)propiolic acid was prepared in an analogous manner of TBS derivatives by following a literature method.[10] A crude product was used without further purification. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 11.00 (s, 1H), 7.65-7.67 (m, 6H), 7.36-7.44 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 135.73, 131.37, 130.59, 128.32.

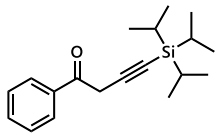
3-(Triphenylsilyl)propiolic acid (1.7 g, 4 mmol), 2-hydroxyacetophenone (540 mg, 4 mmol) and PPh_3 (1.31 g, 5 mmol) were dissolved in THF (30 mL). To the solution was added diisopropyl azodicarboxylate (0.71 mL, 5 mmol) dropwise with stirring at 0 °C. The solution was stirred for 7 h (monitored by TLC) at room temperature. Sat. NH_4Cl was added at room temperature, and the mixture was extracted with EtOAc three times. The combined organic layer was washed with brine, dried over Na_2SO_4, and removed under reduced pressure. The residue was purified by column chromatography to afford compound **54'** as white solid (1.41 g, 79%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.91-7.94 (m, 2H), 7.61-7.68 (m, 7H), 7.46-7.52 (m, 5H), 7.39-7.43 (m, 6H), 5.46 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 190.57, 151.98, 135.64, 134.08, 133.81, 131.14, 130.50, 128.92, 128.20, 127.77, 97.16, 90.88, 67.05 HRMS (ESI) calcd.for $C_{29}H_{22}O_3NaSi$ [M+Na]$^+$ *m/z* 469.1236, found 469.1230.

General Procedure C: Decarboxylative Alkynylation



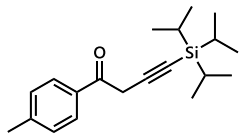
In a flask, starting material **48**, $Pd(dba)_2$ (2.5 mol%) and XPhos (10 mol%) were dissolved in *m*-xylene (0.05 M). The solution was refluxed for 30 min under nitrogen and then evaporated. The residue was purified by column chromatography to afford desired product.

49a



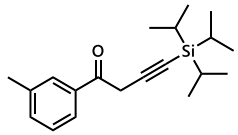
By following general procedure C, the reaction of corresponding phenacyl propionate (103.4 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 76 mg of compound **49a** as yellow oil (84%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.03-8.05 (m, 2H), 7.55-7.59 (m, 1H), 7.44-7.48 (m, 2H), 3.88 (s, 2H), 0.94-1.07 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 193.23, 135.24, 133.41, 128.84, 128.48, 100.05, 86.88, 32.30, 18.47, 11.13. HRMS (EI) calcd.for $C_{19}H_{28}OSi$ $[M]^+$ *m/z* 319.1909, found 319.1901.

49b



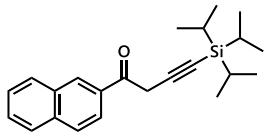
By following general procedure C, the reaction of corresponding phenacyl propionate (107.6 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 75 mg of compound **49b** as yellow oil (79%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.93 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 3.84 (s, 2H), 2.40 (s, 3H), 1.02-1.02 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 192.80, 144.25, 132.85, 129.15, 128.94, 100.30, 86.55, 32.19, 21.64, 18.48, 11.15, 10.86. HRMS (EI) calcd.for $C_{20}H_{30}OSi$ $[M]^+$ *m/z* 314.2066, found 314.2059.

49c



By following general procedure, the reaction of corresponding phenacyl propionate (107.6 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-Xylene delivered 67 mg of compound **49c** as yellow oil (71%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.82-7.85 (m, 2H), 7.31-7.38 (m, 2H), 3.85 (s, 2H), 2.39 (s, 3H), 0.97-1.06 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 193.32, 138.20, 135.28, 134.14, 129.37, 128.34, 126.02, 100.24, 86.67, 32.33, 21.22, 18.45, 11.12. HRMS (EI) calcd.for $C_{20}H_{30}OSi$ $[M]^+$ *m/z* 314.2066, found 314.2057.

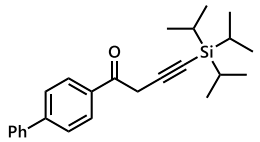
49e



By following general procedure C, the reaction of corresponding phenacyl propionate (118.4 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 78 mg of compound **49e** as yellow oil (74%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.62 (s, 1H), 8.06-8.08 (m, 1H), 7.86-7.95 (m, 3H), 7.55-7.63 (m, 2H), 4.00 (s, 2H), 0.95-1.17 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$,

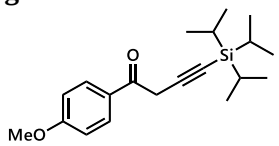
rt, δ/ppm): 193.09, 135.68, 132.55, 132.33, 130.92, 129.57, 128.61, 128.36, 127.73, 126.74, 124.18, 100.25, 86.93, 32.43, 18.47, 11.11. HRMS (EI) calcd.for $C_{23}H_{30}OSi$ $[M]^+$ *m/z* 350.2066, found 350.2054.

49f



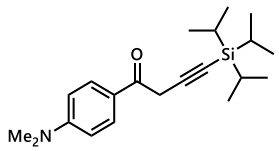
By following general procedure C, the reaction of corresponding phenacyl propionate (126.3 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 90 mg of compound **49f** as yellow oil (80%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.11-8.13 (m, 2H), 7.67-7.69 (m, 2H), 7.62-7.64 (m, 2H), 7.46-7.50 (m, 2H), 7.41-7.43 (m, 1H), 3.90 (s, 2H), 1.02-1.14 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 192.87, 146.07, 139.81, 134.03, 129.47, 128.95, 128.28, 127.26, 127.13, 100.15, 86.96, 32.41, 18.50, 11.17. HRMS (EI) calcd.for $C_{22}H_{25}OSi$ $[M-^iPr]^+$ *m/z* 333.1675, found 337.1671.

49g



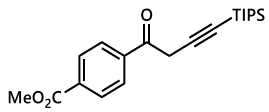
By following general procedure C, the reaction of corresponding phenacyl propionate (112.3 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 72 mg of compound **49g** as yellow oil (73%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.00-8.02 (m, 2H), 6.89-6.92 (m, 2H), 3.85 (s, 3H), 3.80 (s, 2H), 1.01-1.10 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 191.68, 163.67, 131.16, 128.30, 113.60, 100.52, 86.39, 55.40, 32.03, 18.46, 11.12. HRMS (EI) calcd.for $C_{20}H_{30}O_2Si$ $[M]^+$ *m/z* 330.2015, found 330.2001.

49h



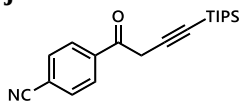
By following general procedure C, the reaction of corresponding phenacyl propionate (113.3 mg, 0.292 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 84 mg of compound **49h** as a yellow solid (84%). X-ray quality orange crystals were obtained by freezing a saturated hexane solution of **49h** at −30 ˚C. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.90-7.94 (m, 2H), 6.59-6.62 (m, 2H), 3.76 (s, 2H), 3.03 (s, 6H), 0.98-1.06 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 191.06, 153.48, 131.03, 123.22, 110.44, 101.41, 85.50, 39.91, 31.65, 18.51, 11.16. HRMS (EI) calcd.for $C_{21}H_{33}NOSi$ $[M]^+$ *m/z* 343.2331, found 343.2331. Crystallographic data: M = 687.17, yellow, block, monoclinic, P-1 (#2), a = 8.5598(5) Å, b = 13.7308(7) Å, c = 18.0870(8) Å, α = 75.225(5)˚, β = 85.888(6)˚, γ = 88.512(6)˚ V = 2050.16(18) Å^3, Z = 4, D_{calc} = 1.113 g/cm^3, T = −140 ºC, $R_1(wR_2)$ = 0.0822 (0.224).

49i



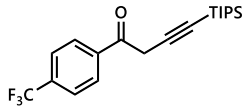
By following general procedure C, the reaction of corresponding phenacyl propionate (96.2 mg, 0.239 mmol) in the presence of $Pd(dba)_2$ (3.4 mg, 0.00597 mmol) and XPhos (11.3 mg, 0.0239 mmol) in 4.8 mL *m*-xylene delivered 34 mg of compound **49i** as yellow oil (40%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.10-8.13 (m, 4H), 3.95 (s, 3H), 3.89 (s, 2H), 0.97-1.01 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 192.74, 166.13, 138.47, 134.12, 129.70, 128.78, 99.37, 87.58, 52.48, 32.59, 18.47, 11.11. HRMS (EI) calcd.for $C_{21}H_{30}O_3Si$ $[M]^+$ *m/z* 358.1964, found 358.1957.

49j



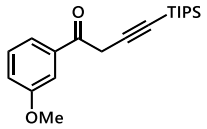
By following general procedure C, the reaction of corresponding phenacyl propionate (110.9 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (8.6 mg, 0.015 mmol) and XPhos (28.6 mg,0.06 mmol) in 6 mL *m*-xylene delivered 33 mg of compound **49j** as yellow oil (34%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.14 (d, J = 8.4 Hz, 2H), 7.77 (d, J = 8.4 Hz, 2H), 3.88 (s, 2H), 0.98-0.99 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 191.96, 138.20, 132.35, 129.33, 117.82, 116.66, 98.82, 88.28, 32.59, 18.45, 11.09. HRMS (ESI) calcd.for $C_{20}H_{27}NNaOSi$ $[M+Na]^+$ *m/z* 348.1760, found 348.1759.

49k



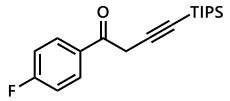
By following general procedure C, the reaction of corresponding phenacyl propionate (123.8 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 40 mg of compound **49k** as yellow oil (34%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.15 (d, J = 8.1 Hz, 2H), 7.73 (d, J = 8.1 Hz, 2H), 3.89 (s, 2H), 0.97-1.03 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 192.43, 137.97, 134.71 (q, J = 30.5 Hz), 129.23, 125.60, 125.57, 99.19, 87.92, 32.63, 18.45, 11.12. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): −63.11. HRMS (EI) calcd.for $C_{17}H_{20}F_3OSi$ $[M-^iPr]^+$ *m/z* 325.1236, found 325.1234.

49l



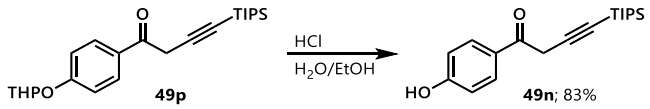
By following general procedure C, the reaction of corresponding phenacyl propionate (125 mg, 0.334 mmol) in the presence of $Pd(dba)_2$ (4.8 mg, 0.0083 mmol) and XPhos (15.9 mg, 0.0334 mmol) in 6.6 mL *m*-xylene delivered 35 mg of compound **49l** as yellow oil (34%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.62-7.64 (m, 1H), 7.54-7.54 (m, 1H), 7.34-7.38 (m, 1H), 7.10-7.13 (m, 1H), 3.87 (s, 2H), 3.85 (s, 3H), 1.02-1.17 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 193.01, 159.77, 136.67, 129.47, 121.57, 120.11, 112.76, 100.02, 86.82, 55.41, 32.36, 18.49, 11.17. HRMS (EI) calcd.for $C_{20}H_{30}OSi$ $[M]^+$ *m/z* 330.2015, found 330.2015.

49m



By following general procedure C, the reaction of corresponding phenacyl propionate (108.8 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-Xylene delivered 67 mg of compound **49m** as yellow oil (70%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.07-8.11 (m, 2H), 7.11-7.15 (m, 2H), 3.84 (s, 2H), 0.98-1.04 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 191.71, 165.89 (d, J = 255.6 Hz), 131.69, 131.59, 115.65 (d, J = 22.5 Hz), 99.80, 87.24, 32.37, 18.48, 11.13. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): −104.26. HRMS (EI) calcd.for $C_{17}H_{20}FO_3Si$ $[M-^iPr]^+$ *m/z* 275.1267, found 275.1267.

49n

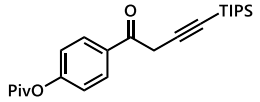


By following general procedure C, the desired compound **49n** was not obtained at all.

An ethanol solution of **49p** (75 mg, 0.187 mmol) was added 3M aqueous HCl (0.1 mL, 0.3 mmol) and the mixture was stirred for 3 h at room temperature. The mixture was neutralized with 1 M aqueous Na_2CO_3 (5 mL) and extracted with $CHCl_3$ three times. The combined organic layer was dried over Na_2SO_4 and volatiles were removed under reduced pressure. The residue was purified by column chromatography to afford compound **49n**

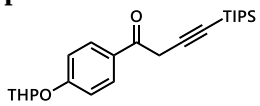
as white solid (49 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.99 (d, J = 8.4 Hz, 2H), 6.91 (d, J = 8.4 Hz, 2H), 3.84 (s, 2H), 1.01-1.10 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 192.84, 161.03, 131.68, 128.03, 115.43, 100.18, 86.76, 32.04, 18.49, 11.15. HRMS (EI) calcd.for $C_{16}H_{21}O_2Si$ [M-^{i}Pr]$^{+}$ *m/z* 273.1311, found 273.1311.

49o



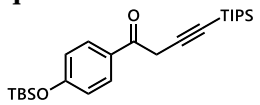
By following general procedure C, the reaction of corresponding phenacyl propionate (133.4 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 72 mg of compound **49o** as yellow oil (60%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.06-8.08 (m, 2H), 7.14-7.16 (m, 2H), 3.86 (s, 2H), 1.36 (s, 9H), 0.87-1.05 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 191.91, 176.34, 155.12, 132.64, 130.41, 121.64, 99.80, 86.99, 39.16, 32.26, 27.00, 18.48, 11.12. HRMS (EI) calcd.for $C_{21}H_{29}O_3Si$ [M-^{i}Pr]$^{+}$ *m/z* 357.1886, found 357.1886.

49p



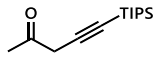
By following general procedure C, the reaction of corresponding phenacyl propionate (133.4 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-Xylene delivered 81 mg of compound **49p** as yellow oil (67%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.98-8.01 (m, 2H), 7.05-7.08 (m, 2H), 5.51 (t, J = 2.9 Hz, 1H), 3.80-3.86 (m, 3H), 3.58-3.63 (m, 1H), 1.85-2.00 (m, 3H), 1.58-1.72 (m, 3H), 0.94-1.06 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 191.84, 161.17, 130.99, 128.86, 115.82, 100.50, 95.91, 86.42, 61.91, 32.08, 29.99, 24.98, 18.48, 18.37, 11.12. HRMS (ESI) calcd.for $C_{24}H_{36}NaO_3Si$ [M+Na]$^{+}$ *m/z* 423.2331, found 423.2341.

49q



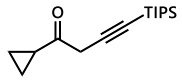
By following general procedure C, the reaction of corresponding phenacyl propionate (142.4 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 91 mg of compound **49q** as yellow oil (70%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.96-7.98 (m, 2H), 6.85-6.87 (m, 2H), 3.80 (s, 2H), 1.01 (s, 21H), 0.98 (s, 9H), 0.23 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 191.85, 160.53, 131.18, 128.85, 119.87, 100.59, 86.51, 32.15, 25.55, 18.49, 18.23, 11.17, -4.42. HRMS (EI) calcd.for $C_{25}H_{42}O_2Si_2$ [M]$^{+}$ *m/z* 430.2723, found 430.2723.

49r



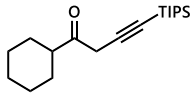
By following general procedure C, the reaction of corresponding propionate (84.7 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-Xylene delivered 42 mg of compound **49r** as yellow oil (59%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 3.28 (s, 2H), 2.33 (s, 3H), 1.07-1.09 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 202.75, 100.15, 85.90, 36.14, 28.53, 18.54, 11.20. HRMS (EI) calcd.for $C_{11}H_{19}OSi$ [M-^{i}Pr]$^{+}$ *m/z* 195.1205, found 195.1205.

49s



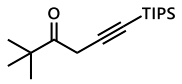
By following general procedure C, the reaction of corresponding propionate (76 mg, 0.25 mmol) in the presence of $Pd(dba)_2$ (3.5 mg, 0.0062 mmol) and XPhos (11.4 mg, 0.025 mmol) in 5 mL *m*-Xylene delivered 50 mg of compound **49s** as yellow oil (76%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 3.42 (s, 2H), 2.33-2.39 (m, 1H), 1.05-1.10 (m, 24H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 204.55, 100.24, 85.76, 36.08, 19.06, 18.54, 11.88, 11.18. HRMS (EI) calcd.for $C_{13}H_{21}OSi$ $[M-^iPr]^+$ *m/z* 221.1362, found 221.1362.

49t



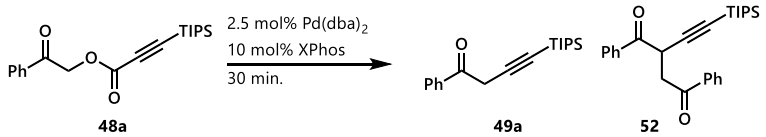
By following general procedure C, the reaction of corresponding propionate (105.2 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 76 mg of compound **49t** as yellow oil (83%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 3.32 (s, 2H), 2.82-2.88 (m, 1H), 1.66-1.94 (m, 5H), 1.20-1.35 (m, 5H), 0.99-1.09 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 207.75, 100.35, 85.40, 48.51, 34.01, 28.38, 25.77, 25.55, 18.57, 11.20. HRMS (EI) calcd.for $C_{16}H_{27}OSi$ $[M-^iPr]^+$ *m/z* 263.1831, found 263.1831.

49u



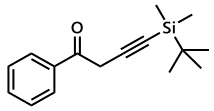
By following general procedure C, the reaction of corresponding propionate (97.4 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 30 mg of compound **49u** as yellow oil (36%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 3.47 (s, 2H), 1.20 (s, 9H), 1.02-1.07 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 208.42, 100.28, 85.14, 44.58, 30.13, 26.60, 18.56, 11.20. HRMS (EI) calcd.for $C_{14}H_{25}OSi$ $[M-^iPr]^+$ *m/z* 237.1675, found 237.1675.

52



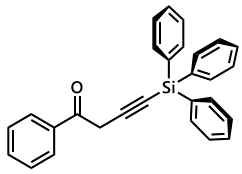
In a flask, starting material **48a** (103.4 mg, 0.3 mmol), $Pd(dba)_2$ (2.5 mol%) and XPhos (10 mol%) were dissolved in toluene (0.05 M). The solution was refluxed for 30 min and then evaporated. The residue was purified by column chromatography to afford **52**(9 mg, 7%).^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.15-8.17 (m, 2H), 8.02-8.04 (m, 2H), 7.56-7.61 (m, 2H), 7.46-7.52 (m, 4H), 4.93 (dd, J = 9.7, 3.7 Hz, 1H), 4.04 (dd, J = 17.8, 9.7 Hz, 1H), 3.35 (dd, J = 17.8, 3.7 Hz, 1H), 0.88-1.09 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 197.15, 193.98, 136.33, 135.20, 133.34, 133.32, 129.20, 128.59, 128.37, 128.23, 104.01, 87.26, 39.82, 36.28, 18.43, 11.04. HRMS (EI) calcd.for C27H34O2Si $[M]^+$ *m/z* 418.2328, found 418.2311.

53



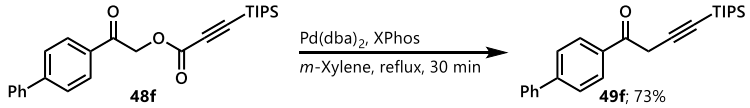
By following general procedure C, the reaction of corresponding phenacyl propionate (90.7 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 47 mg of compound **53** as yellow oil (61%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.01-8.03 (m, 2H), 7.56-7.58 (m, 1H), 7.45-7.48 (m, 2H), 3.87 (s, 2H), 0.88 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 193.00, 135.32, 133.48, 128.74, 128.54, 98.95, 88.83, 32.13, 25.95, 16.52, -4.75. HRMS (EI) calcd.for $C_{16}H_{22}OSi$ $[M]^+$ *m/z* 258.1440, found 258.1432.

54



By following general procedure C, the reaction of corresponding phenacyl propionate (133.8 mg, 0.3 mmol) in the presence of $Pd(dba)_2$ (4.3 mg, 0.0075 mmol) and XPhos (14.3 mg, 0.03 mmol) in 6 mL *m*-xylene delivered 32 mg of compound **54** as yellow oil (26%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 8.05-8.08 (m, 2H), 7.60-7.67 (m, 7H), 7.33-7.50 (m, 11H), 4.04 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 192.49, 135.47, 135.28, 133.60, 133.33, 129.86, 128.84, 128.65, 127.90, 103.33, 85.80, 32.49. HRMS (ESI) calcd.for $C_{29}H_{22}O_3Si$ $[M+Na]^+$ *m/z* 469.1236, found 469.1230.

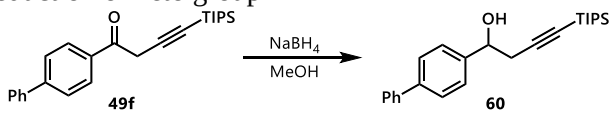
Table 8: 2 mmol Scale Reaction



Phenacyl propionate **48f** (841 mg, 2 mmol) was dissolved in *m*-xylene (38 mL). The solution was refluxed for 5 min. To the mixture was added the *m*-xylene (2 mL) of $Pd(dba)_2$ (28.1 mg, 0.05 mmol) and XPhos (95.3 mg, 0.2 mmol) at this temperature and then refluxed for further 30 min. Volatiles were removed under reduced pressure. The residue was purified by column chromatography to afford desired product **49f** (549 mg, 73%).

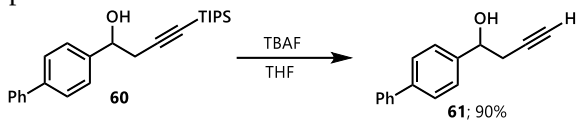
Scheme 21: Derivatization of **49f**

Reduction of keto group



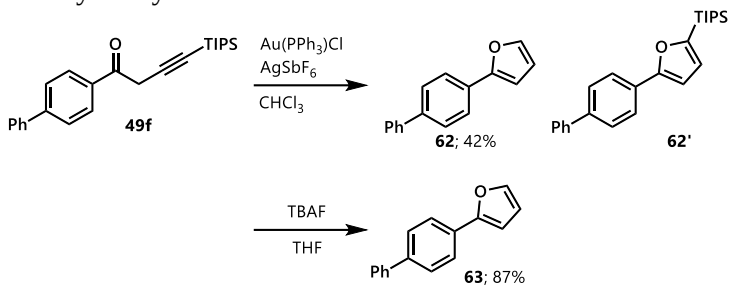
In a round-bottomed flask equipped with a stirring bar, **49f** (113 mg, 0.3 mmol) and $NaBH_4$ (13.6 mg, 0.36 mmol) were mixed in MeOH (3 mL). The solution was stirred for 4 h (monitored by TLC) at room temperature. The mixture was extracted with EtOAc three times. The combined organic layer was washed with brine, dried over Na_2SO_4, and removed under reduced pressure. It was then purified by silica gel column chromatography, affording 103 mg of compound **60** as white solid (91%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.58-7.62 (m, 4H), 7.45-7.50 (m, 4H), 7.36-7.39 (m, 1H), 4.92 (t, J = 6.5 Hz, 1H), 2.79 (d, J = 6.5 Hz, 2H), 2.57 (s, 1H), 1.04-1.11 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 141.48, 140.87, 140.72, 128.72, 127.23, 127.09, 127.06, 126.28, 104.22, 84.04, 72.14, 30.94, 18.55, 11.15. HRMS (EI) calcd.for $C_{25}H_{33}Si$ $[M-OH]^+$ *m/z* 361.2352, found 361.2301.

Deprotection of TIPS



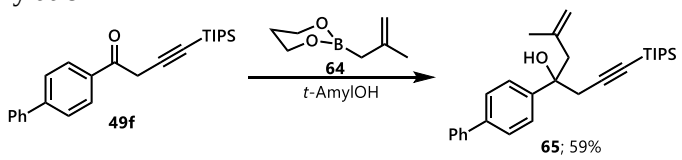
Alcohol **60** (80 mg, 0.21 mmol) was dissolved in THF (3 mL). To the solution was added 1 M THF solution of TBAF (0.23 mmL, 0.23 mmol) dropwise at 0 °C. The mixture was stirred for 2.5 h at room temperature and was quenched with water. The mixture was extracted with EtOAc three times. The combined organic layer was washed with brine, dried over Na_2SO_4, and removed under reduced pressure. Purification by silica gel column chromatography delivered 42 mg of compound **61** as white solid (90%). The spectrum data matched to that of literature.[13]

Au-catalyzed cyclization



In a round-bottomed flask equipped with a stirring bar, **49f** (113 mg, 0.3 mmol), $Au(PPh_3)Cl$ (29.7 mg, 0.06 mmol) and $AgSbF_6$ (20.6 mg, 0.06 mmol) were dissolved in $CHCl_3$ (dried over MS4A, and bubbled with N_2 stream, 3 mL). The solution was stirred for 3 h (monitored by TLC) at 50 °C and then evaporated. The residue was purified by column chromatography to afford 28 mg of **62** (42%). According to NMR analysis, another fraction would be TIPS-furan **62**' judged by characteristic signals at 6.77 ppm and 6.71 ppm (each signal was a 1H doublet with a coupling constant of 3.3 Hz that resembles to 2-phenyl-5-(triisopropylsilyl)furan showing the same signal pattern at 6.65 ppm and 6.73 ppm),[14] though this fraction was contaminated by inseparable TIPS-containing by-product(s). The residue was dissolved in THF (3 mL). To the solution was added 1 M THF solution of TBAF (0.66 mmL, 0.66 mmol) dropwise at 0 °C. The mixture was stirred for 6 h at room temperature and was quenched with water. The mixture was extracted with EtOAc three times. The combined organic layer was washed with brine, dried over Na_2SO_4, and removed under reduced pressure. Purification by silica gel column chromatography delivered 58 mg of compound **63** as white solid (87%). The spectrum data matched to that of literature.[15]

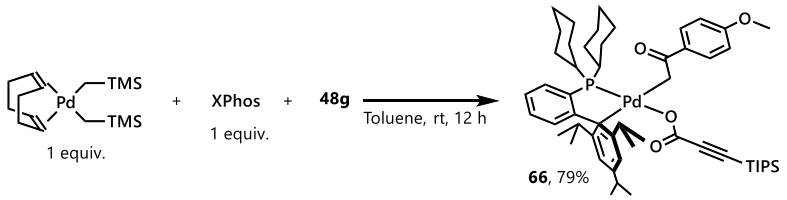
Allylation



To a dry flask were charged **49f** (56 mg, 0.15 mmol), **64** (48 mg, 0.34 mmol) and *tert*-amylalcohol (32 μL, 0.3 mmol) under nitrogen. The resulting mixture was stirred under nitrogen at room temperature for 27 h. Purification of the reaction mixture by column chromatography on silica gel gave desired product **65** as a yellow oil (38 mg, 59%). ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.59-7.61 (m, 2H), 7.55 (s, 4H), 7.42-7.46 (m, 2H), 7.34-7.36 (m, 1H), 4.89 (s, 1H), 4.74 (s, 1H), 2.86 (d, J = 1.4 Hz, 2H), 2.73 (d, J = 6.8 Hz, 2H), 2.67 (s, 1H), 1.55 (s, 3H), 0.97-1.03 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 144.42, 141.99, 140.89, 139.63, 128.69, 127.14, 127.02, 126.66, 125.81, 115.71, 104.32, 84.69, 74.79, 49.27, 34.92, 24.31, 18.53, 11.15. HRMS (EI) calcd.for $[M-H_2O]^+$ *m/z* 414.2743, found 414.2738.

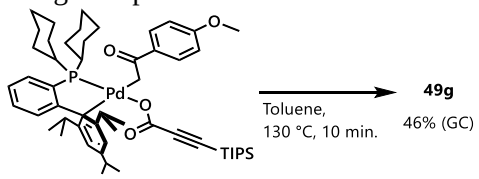
Scheme 22: Palladium Enolate Complex

Synthesis of Palladium Enolate **66**



In a glove box, a vial equipped with a stirrer bar was charged with XPhos (95.4 mg, 0.20 mmol) and **48g** (74.9 mg, 0.20 mmol). The solids were dissolved in 2 mL of toluene under vigorous stirring. Then, to the clear solution was added Pd(cod)($CH_2TMS)_2$ (57.2 mg, 0.20 mmol) in one portion. The gold reaction mixture was stirred for 12 h at room temperature. Then the resulting orange solution was transferred to a peer-shaped flask with toluene rinse (2 mL×2). The solution was evaporated in vacuo to leave an orange oil. Addition of hexane/evaporation sequence was repeated 10 times to remove cyclooctadiene and $TMSCH_2CH_2TMS$ azeotropically. The resultant orange powder was washed with hexane three times (first washing was bright orange, but second and third ones were pale yellow) to give yellow powder (150.69 mg, 79%). Recrystallization for X-ray analysis was achieved by cooling the solution of **66** in $PhCF_3$/pentane (ca 1:4) at −35 °C for several days. ^{1}H NMR (500 MHz, Toluene-d_8, −30 °C, δ/ppm): 8.44 (s, 2H), 6.86-7.24 (m, overlapping with solvent signal), 6.60 (s, 1H), 3.72 (s, 2H), 3.53 (s, 1H), 3.32 (s, 3H), 3.20 (s, 1H), 2.47 (d, J = 61.9 Hz, 4H), 2.09 (s, overlapping with solvent signal), 0.83-1.72 (m). ^{13}C NMR (125 MHz, Toluene-d_8, −30 °C, δ/ppm): 199.52, 162.33, 157.13, 155.04, 149.85, 146.96, 146.81, 135.69, 135.41, 132.35, 131.53, 131.30, 129.91, 126.60, 124.07, 123.06, 112.77, 105.90, 105.84, 77.91, 54.17, 35.00, 33.65, 31.46, 29.19, 28.24, 27.17, 27.09, 27.00, 25.94, 25.85, 23.80, 23.45, 18.55, 16.14, 11.20 (complexity due to P-C coupling). ^{31}P NMR (202 MHz, Toluene-d_8, −30 °C, δ/ppm): 36.31. Crystallographic data: M = 957.63, yellow, block, monoclinic, $P2_1/c$ (#14), a = 107586(4) Å, b = 30.2721(10) Å, c = 17.3424(6) Å, β = 92.621(7) °, V = 5642.2(3) Å^3, Z = 4, D_{calc} = 1.127 g/cm^3, T = −140 ºC, $R_1(wR_2)$ = 0.0626 (0.1804). Elemental Analysis: The product would be partially contaminated with solvent which was observed by X-ray crystallography but was not fully characterized. Calc. C, 67.72; H, 8.31; O, 6.68; P, 3.23; Pd, 11.11; Si, 2.93, found C, 69.43; H, 8.53.

Heating Complex **66**

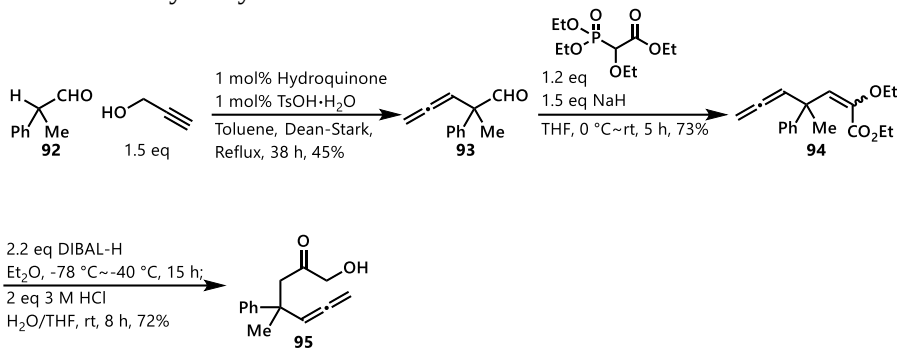


In a glove box, a vial charged with Pd complex **66** (9.6 mg, 0.01 mmol) and magnetic stirrer bar was added toluene (0.1 mL) and the vial was tightly capped. The vial was quickly removed from the glove box and was heated with preheated metal bath at 130 °C for 10 min to give black solution. To the mixture was added *n*-eicosane as an internal standard and the solution was analyzed by GC to indicate formation of **49g** in 46% yield.

第二章　Pd 触媒による C－O 結合切断を鍵としたアレンの挿入を伴う脱炭酸型環化アルキニル化反応の開発

Synthesis of Starting Material

Synthesis of α-Hydroxy Ketone **95**



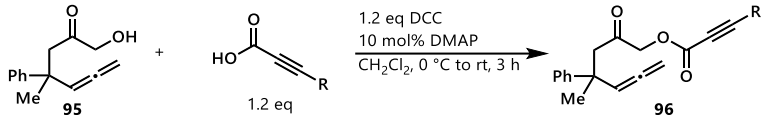
A 300-ml round bottomed flask was charged 2-phenylpropionaldehyde (6.71 g, 50 mmol), 2-butyn-l-ol (4.2 g, 75 mmol), TsOH•H_2O (95 mg, 0.5 mmol) and hydroquinone (55 mg, 0.5 mmol). The flask was equipped with a condenser, a Dean-Stark water separator and nitrogen balloon. Then, anhydrous toluene (50 mL) was loaded. The solution was heated under reflux for 36 h and then evaporated. The residue was purified by column chromatography (eluent: Hexane/EtOAc = 50:1), affording 3.05 g of β-allenyl aldehyde **93**[16] as a brown oil (35%). IR (neat): 1725, 1445, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 9.55 (s, 1H), 7.41-7.38 (m, 2H), 7.32-7.29 (m, 3H), 5.58 (t, J = 6.9 Hz, 1H), 4.95-4.93 (m, 2H), 1.54 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.4, 198.9, 140.1, 128.9, 127.5, 127.3, 92.6, 78.5, 54.3, 20.9. LRMS (EI) *m/z* 172 [M^+], 153, 143.

To a suspension of 60% sodium hydride (702 mg, 17.6 mmol) in anhydrous THF (30 mL), Phosphonoacetate (3.78 g, 14.1 mmol) in THF (60 mL) was added at 0 °C, and the reaction mixture was stirred at 0 °C for 1 h. To the solution was added aldehyde **93** (2.02 g, 11.7 mmol) in dry THF (30 mL) at 0 °C. The reaction mixture was stirred at roo for 12 h. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $NaSO_4$, and evaporated under reduced pressure. The residue was then purified by silica gel column chromatography (hexane/AcOEt, 30:1) to yield 2.064 g of desired compound **94** as a yellow oil, which was the mixture of *E*/*Z* isomers (73%). IR (neat): 2978, 1954, 1719, 1642, 847, 764, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.41-7.36 (m, 2H), 7.31-7.24 (m, 2H), 7.21-7.13 (m, 1H), 6.50 (s, 0.3H), 5.69 (td, J = 6.6, 2.3 Hz, 1H), 5.27 (s, 0.7H), 4.90-4.86 (m, 2H), 4.23 (q, J = 7.2 Hz, 0.7H), 3.83-3.72 (m, 2H), 3.62-3.42 (m, 1.3H), 1.60 (s, 1H), 1.55 (s, 2H), 1.37-1.30 (m, 3H), 1.05 (t, J = 7.1 Hz, 2H), 0.95 (t, J = 6.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 207.1, 207.0, 164.4, 164.3, 147.8, 147.6, 145.0, 132.9, 128.0, 127.9, 126.5, 126.2, 125.9, 116.1, 99.8, 98.6, 78.1, 77.9, 66.9, 64.1, 61.0, 61.0, 43.0, 42.3, 30.5, 27.6, 14.9, 14.5, 14.2, 13.6 (two carbons missing). LRMS(EI) *m/z* 285 [$(M-H)^+$], 271, 143.

To a stirred solution of ester **94** (2.06 g, 7.19 mmol) in dry Et_2O (22 mL), DIBAL-H (15.8 mL of a 1 M solution in toluene, 15.8 mmol) was added under N_2 at -78 °C. The reaction mixture was stirred at -40 °C for 12 h. A saturated aqueous solution of potassium sodium tartrate tetrahydrate (30 mL) was added to the reaction mixture, and it was left to stir for several hours until the organic and aqueous layers had completely separated. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude as a yellow oil, which was used without further purification in the next step. To a stirred solution of the crude alcohol in THF (32 mL) was added HCl (16 mL of a 3 M solution in H_2O, 48 mmol) at room temperature. After 24 h, the reaction mixture was quenched by saturated solution of $NaHCO_3$ (30 mL). The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was then purified by silica gel column chromatography (hexane/AcOEt, 5:1) to yield 1.192 g of desired compound **95** as a yellow oil (77%). IR (neat): 3469, 3057, 2969, 1955, 1719, 1038, 835 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.37-7.31 (m, 4H), 7.25-7.21 (m, 1H), 5.49 (t, J = 6.6 Hz, 1H), 4.95-4.89 (m, 2H), 3.99 (dd, J = 19.2, 4.6 Hz, 1H), 3.75 (dd, J = 19.2, 4.6 Hz, 1H), 2.94 (t, J = 4.8 Hz, 1H), 2.88 (d, J = 15.1 Hz,

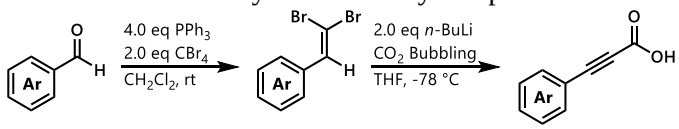
1H), 2.82 (d, J = 15.1 Hz, 1H), 1.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.0, 206.6, 145.8, 128.5, 126.7, 126.0, 99.4, 78.4, 69.3, 49.8, 40.9, 26.7. LRMS(EI) *m/z* 216 [M^+], 201, 185.

General Procedure D: Synthesis of α-Acyloxy Ketones



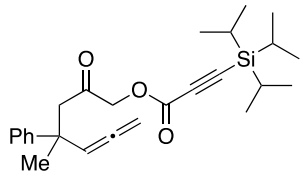
α-Hydroxy ketone (1 eq) and 3-(triisoprosilyl)propiolic acid (1.2 eq) were dissolved in CH_2Cl_2 (0.25 M). To the solution were added *N*,*N'*-dicyclohexylcarbodiimide (1.2 eq) and 4-dimethylaminopyridine (10 mol%) with stirring at 0 °C. After a further 5 min at 0 °C, the ice bath was removed, and the reaction mixture was stirred for 3 h at room temperature (monitored by TLC). The precipitate was removed by filtration over a pad of Celite. Then the filtrate was evaporated. The residue was purified by column chromatography to afford desired product.

General Procedure E: Synthesis of Aryl Propiolic acids[17]



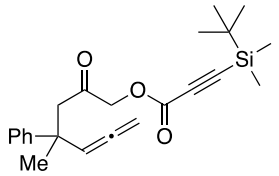
TriphenylPhosphine (20 mmol) was added to a solution of carbon tetrabromide (10 mmol) in dry dichloromethane (50 mL). Upon addition of aldehyde (5 mmol), the solution slowly faded away. The reaction mixture was stirred at ambient temperature until the completion of the reaction. After removal of solvent, the residue was repeatedly triturated with hexane and hexane solution was concentrated. Finally, the mixture was subjected to column chromatography to afford the (2,2-dibromovinyl) arene. A solution of (2,2-dibromovinyl)arene (6 mmol) in10 mL of dry THF at −78 °C was treated with a solution of *n*-BuLi in hexane (1.56 M, 7.5 mL, 12 mmol) under nitrogen atmosphere. After stirring for 1 h at −78 °C, the reaction mixture was warmed to 25 °C during 1 h, and cooled to −78 °C. Carbon dioxide was bubbled through the solution for 30 min at −78 °C, and the mixture was allowed to warm gradually to room temperature. The mixture was poured into water, and diethyl ether was added to it. The aqueous layer was separated and washed further with ethyl acetate. The aqueous part was acidified with 3 M HCl and extracted with diethyl ether three times. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. Evaporation of solvent afforded pure arylpropiolic acid.

96a



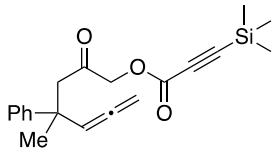
By following general procedure D, the reaction of α-hydroxy ketone (1.08 mg, 5.0 mmol) with the corresponding propiolic acid[18] (1.36 g, 6.0 mmol) in the presence of *N*,*N'*-dicyclohexylcarbodiimide (1.24 g, 6.0 mmmol) and 4-dimethylaminopyridine (61 mg, 0.5 mmol) in 20 mL CH_2Cl_2 delivered 2.14 g of compound **96a** as a colorless liquid (100%). IR (neat): 2944, 2866, 2173, 1956, 1717, 1221 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.39-7.31 (m, 4H), 7.24-7.21 (m, 1H), 5.49 (t, J = 6.6 Hz, 1H), 4.96-4.88 (m, 2H), 4.48 (d, J = 16.5 Hz, 1H), 4.25 (d, J = 16.9 Hz, 1H), 2.92 (d, J = 15.1 Hz, 1H), 2.86 (d, J = 15.1 Hz, 1H), 1.57 (s, 3H), 1.16-1.07 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.6, 200.6, 151.8, 146.0, 128.4, 126.7, 126.1, 99.4, 95.7, 93.2, 78.4, 69.4, 50.1, 40.8, 26.5, 18.4, 10.9. HRMS (EI) calcd. for $C_{26}H_{36}O_3Si$ [M^+] *m/z* 424.2434, found 424.2437.

96b



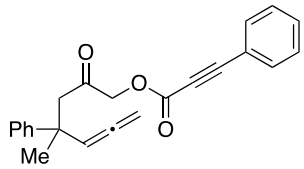
By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid[19] (221 mg, 1.2 mmol) in the presence of *N*,*N*'-dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 355 mg of compound **96b** as a colorless liquid (93%). IR (neat): 3059, 2930, 2176, 1955, 1715, 1223 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.39-7.31 (m, 4H), 7.24-7.22 (m, 1H), 5.48 (t, J = 6.6 Hz, 1H), 4.91 (dd, J = 6.4, 5.0 Hz, 2H), 4.49 (d, J = 16.9 Hz, 1H), 4.24 (d, J = 16.5 Hz, 1H), 2.91 (d, J = 15.1 Hz, 1H), 2.84 (d, J = 15.1 Hz, 1H), 1.57 (s, 3H), 0.96 (s, 9H), 0.17 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.6, 200.4, 151.8, 145.9, 128.5, 126.7, 126.1, 99.4, 94.6, 94.4, 78.4, 69.5, 50.1, 40.8, 26.4, 25.9, 16.5, -5.3. HRMS (ESI) calcd. for $C_{23}H_{30}NaO_3Si$ [$(M+Na)^+$] *m/z* 405.1862, found 406.1867.

96c



By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid[20] (170 mg, 1.2 mmol) in the presence of *N*,*N*'-dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 102 mg of compound **96c** as a colorless liquid (30%). IR (neat): 2965, 2177, 1955, 1715, 1223 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.39-7.31 (m, 4H), 7.22 (tt, J = 7.1, 1.7 Hz, 1H), 5.48 (t, J = 6.8 Hz, 1H), 4.96-4.87 (m, 2H), 4.50 (d, J = 16.8 Hz, 1H), 4.23 (d, J = 16.8 Hz, 1H), 2.90 (d, J = 15.0 Hz, 1H), 2.84 (d, J = 15.4 Hz, 1H), 1.57 (s, 3H), 0.23 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.6, 200.3, 151.8, 145.9, 128.5, 126.7, 126.1, 99.4, 95.9, 93.6, 78.4, 69.5, 50.1, 40.9, 26.4, -1.0. HRMS (EI) calcd. $C_{20}H_{24}NaO_3Si$ for [M^+] *m/z* 363.1392, found 364.1403.

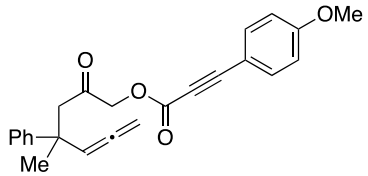
96d



Corresponding propiolic acid was purchased from commercial source (TCI).

By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid (175 mg, 1.2 mmol) in the presence of *N*,*N*'-dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 273 mg of compound **96d** as a colorless liquid (79%). IR (nujol): 2923, 2853, 2220, 1735, 1694, 1172 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.46-7.44 (m, 2H), 7.34-7.30 (m, 1H), 7.28-7.19 (m, 6H), 7.13-7.09 (m, 1H), 5.38 (t, J = 6.6 Hz, 1H), 4.84-4.76 (m, 2H), 4.44 (d, J = 16.9 Hz, 1H), 4.17 (d, J = 16.5 Hz, 1H), 2.81 (d, J = 15.1 Hz, 1H), 2.75 (d, J = 15.1 Hz, 1H), 1.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.6, 200.5, 152.9, 145.9, 133.0, 130.8, 128.6, 128.5, 126.7, 126.1, 119.3, 99.4, 87.8, 79.8, 78.4, 69.6, 50.1, 40.9, 26.5. HRMS (EI) calcd. for $C_{22}H_{17}O_3$ [$(M-Me)^+$] *m/z* 329.1178, found 329.1170.

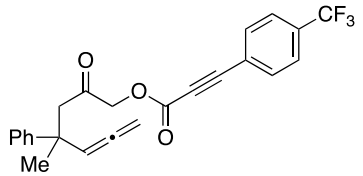
96e



Corresponding propiolic acid was prepared according to general procedure E. The spectrum data of the propiolic acid matched to that of literature.[21]

By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid (211 mg, 1.2 mmol) in the presence of *N,N'*-dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 230 mg of compound **96e** as a white solid (61%). IR (nujol): 2923, 2214, 1715, 1602, 1291, 1157 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.53 (d, J = 8.2 Hz, 2H), 7.40-7.32 (m, 4H), 7.23 (t, J = 7.3 Hz, 1H), 6.88 (d, J = 8.2 Hz, 2H), 5.51 (t, J = 6.6 Hz, 1H), 4.96-4.88 (m, 2H), 4.56 (d, J = 16.9 Hz, 1H), 4.29 (d, J = 16.9 Hz, 1H), 3.84 (s, 3H), 2.93 (d, J = 15.1 Hz, 1H), 2.88 (d, J = 15.1 Hz, 1H), 1.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.7, 200.8, 161.7, 153.2, 146.0, 135.1, 128.5, 126.7, 126.1, 114.3, 111.1, 99.4, 88.8, 79.3, 78.4, 69.5, 55.4, 50.1, 40.9, 26.5. HRMS (EI) calcd. for $C_{23}H_{19}O_4$ [(M-Me)$^+$] *m/z* 359.1283, found 359.1274.

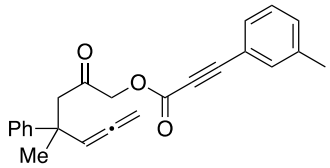
96f



Corresponding propiolic acid was prepared according to general procedure E. The spectrum data of the propiolic acid matched to that of literature.[21]

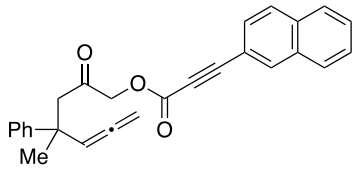
By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid (221 mg, 1.2 mmol) in the presence of *N,N'*-dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 324 mg of compound **96f** as a pale yellow oil (79%). IR (neat): 3250, 2971, 2933, 2233, 1955, 1715, 1616, 1290, 1174 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.68 (d, J = 8.2 Hz, 2H), 7.64 (d, J = 8.2 Hz, 2H), 7.41-7.33 (m, 4H), 7.26-7.22 (m, 1H), 5.51 (t, J = 6.6 Hz, 1H), 4.98-4.89 (m, 2H), 4.59 (d, J = 16.5 Hz, 1H), 4.31 (d, J = 16.9 Hz, 1H), 2.93 (d, J = 14.6 Hz, 1H), 2.87 (d, J = 14.6 Hz, 1H), 1.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.7, 200.2, 152.4, 145.9, 133.2, 132.4, 128.5, 126.7, 126.1, 125.5, 123.5, 123.2, 99.4, 85.4, 81.4, 78.5, 69.7, 50.2, 40.9, 26.4. ^{19}F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): δ -63.1. HRMS (ESI) calcd. for $C_{24}H_{19}F_3NaO_3$ [(M+Na)$^+$] *m/z* 435.1184, found 435.1171.

96g



By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid[20] (192 mg, 1.2 mmol) in the presence of *N,N'*-dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 324 mg of compound **96g** as a colorless oil (90%). IR (neat): 3057, 2928, 2211, 1955, 1714, 1298, 1213, 1156 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.41-7.32 (m, 6H), 7.27-7.21 (m, 4H), 5.51 (t, J = 6.6 Hz, 1H), 4.93 (ddd, J = 16.6, 10.1, 6.2 Hz, 2H), 4.56 (d, J = 16.9 Hz, 1H), 4.30 (d, J = 16.5 Hz, 1H), 2.93 (d, J = 15.1 Hz, 1H), 2.94 (d, J = 15.1 Hz, 1H), 2.88 (d, J = 15.1 Hz, 1H), 2.34 (s, 3H), 1.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.7, 200.6, 153.0, 146.0, 138.4, 133.6, 131.8, 130.2, 128.5, 126.7, 126.1, 119.1, 99.4, 88.2, 79.5, 78.4, 69.6, 50.2, 40.9, 26.5, 21.1 One aromatic carbon is missing probably due to overlapping. HRMS (ESI) calcd. for $C_{24}H_{22}NaO_3$ [(M+Na)$^+$] *m/z* 381.1467, found 381.1449.

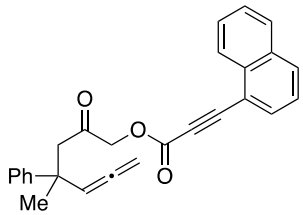
96h



Corresponding propiolic acid was prepared according to general procedure E. The spectrum data of the propiolic acid matched to that of literature.[23]

By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid (235 mg, 1.2 mmol) in the presence of *N*,*N*'-dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 331 mg of compound **96h** as a yellow oil (84%).IR (neat): 3057, 2931, 2220, 1955, 1713, 1236, 1202 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 8.15 (s, 1H), 7.85-7.81 (m, 3H), 7.58-7.53 (m, 3H), 7.42-7.39 (m, 2H), 7.35 (td, J = 6.7, 2.0 Hz, 2H), 7.27-7.23 (m, 1H), 5.52 (t, J = 6.6 Hz, 1H), 4.98-4.90 (m, 2H), 4.60 (d, J = 16.9 Hz, 1H), 4.32 (d, J = 16.5 Hz, 1H), 2.95 (d, J = 14.6 Hz, 1H), 2.89 (d, J = 15.1 Hz, 1H), 1.60 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.7, 200.6, 152.9, 146.0, 134.5, 133.9, 132.6, 128.5, 128.4, 128.2, 128.2, 128.0, 127.9, 127.0, 126.7, 126.1, 116.5, 99.4, 88.3, 80.0, 78.4, 69.7, 50.2, 40.9, 26.5. HRMS (ESI) calcd. for $C_{27}H_{22}NaO_3$ [$(M+Na)^+$] *m/z* 417.1467, found 417.1450.

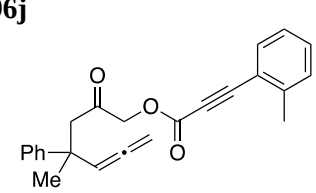
96i



Corresponding propiolic acid was prepared according to general procedure E. The spectrum data of the propiolic acid matched to that of literature.[24]

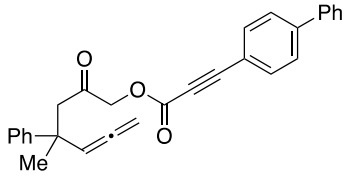
By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid (235 mg, 1.2 mmol) in the presence of *N*,*N*'-dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 291 mg of compound **96i** as a colorless liquid (74%). IR (neat): 3058, 2929, 2217, 1955, 1714, 1253 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm):δ 8.32 (d, J = 7.8 Hz, 1H), 7.96 (d, J = 8.7 Hz, 1H), 7.89-7.84 (m, 2H), 7.62-7.56 (m, 2H), 7.49-7.41 (m, 3H), 7.38-7.34 (m, 2H), 7.26-7.25 (m, 1H), 5.52 (t, J = 6.6 Hz, 1H), 4.96-4.93 (m, 2H), 4.62 (d, J = 16.9 Hz, 1H), 4.36 (d, J = 16.5 Hz, 1H), 2.97 (d, J = 15.1 Hz, 1H), 2.91 (d, J = 15.1 Hz, 1H), 1.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.7, 200.6, 153.0, 146.0, 133.6, 133.3, 133.0, 131.6, 128.5, 128.5, 127.7, 126.9, 126.7, 126.2, 125.7, 125.1, 116.9, 99.4, 86.2, 84.4, 78.5, 69.7, 50.2, 40.9, 26.5. HRMS (EI) calcd. for $C_{27}H_{22}O_3$ [M^+] *m/z* 394.1569, found 394.1562.

96j



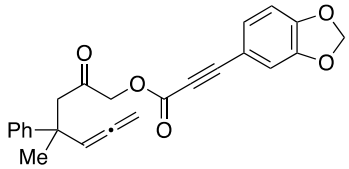
By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid[21] (192 mg, 1.2 mmol) in the presence of *N*,*N*'-dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 331 mg of compound **96j** as a colorless oil (92%). IR (neat): 3059, 2928, 2221, 1955, 1714, 1182 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.53 (d, J = 7.8 Hz, 1H), 7.41-7.39 (m, 2H), 7.36-7.32 (m, 3H), 7.25-7.22 (m, 2H), 7.18 (t, J = 7.5 Hz, 1H), 5.51 (t, J = 6.6 Hz, 1H), 4.95-4.91 (m, 2H), 4.57 (d, J = 16.9 Hz, 1H), 4.31 (d, J = 16.9 Hz, 1H), 2.94 (d, J = 15.1 Hz, 1H), 2.89 (d, J = 15.1 Hz, 1H), 2.48 (s, 3H), 1.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.7, 200.7, 153.0, 146.0, 142.4, 133.5, 130.8, 129.8, 128.5, 126.7, 126.1, 125.8, 119.2, 99.4, 86.9, 83.5, 78.4, 69.6, 50.2, 40.9, 26.5, 20.5. HRMS (EI) calcd. for $C_{24}H_{22}O_3$ [M^+] *m/z* 358.1569, found 358.1558.

96k



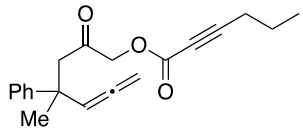
By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid[22] (211 mg, 1.2 mmol) in the presence of *N*,*N*'-dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 161 mg of compound **96k** as a white solid (38%). IR (nujol): 2928, 2222, 1952, 1739, 1702, 1292, 1171 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.66-7.58 (m, 6H), 7.48-7.33 (m, 7H), 7.31-7.22 (m, 1H), 5.51 (t, J = 6.8 Hz, 1H), 4.98-4.89 (m, 2H), 4.58 (d, J = 16.8 Hz, 1H), 4.31 (d, J = 16.8 Hz, 1H), 2.94 (d, J = 15.0 Hz, 1H), 2.88 (d, J = 15.0 Hz, 1H), 1.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.7, 200.6, 152.9, 146.0, 143.7, 139.8, 133.6, 129.0, 128.5, 128.2, 127.3, 127.1, 126.7, 126.2, 118.1, 99.4, 87.9, 80.4, 78.5, 69.6, 50.2, 40.9, 26.5. HRMS (EI) calcd. for $C_{29}H_{24}O_3$ [M^+] *m/z* 420.1725, found 420.1717.

96l



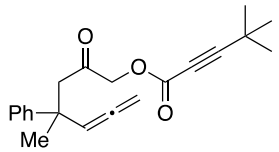
By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid[22] (229 mg, 1.2 mmol) in the presence of *N*,*N*'-dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 200 mg of compound **96l** as a colorless oil (59%). IR (neat): 2969, 2925, 2211, 1955, 1714, 1233 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.40-7.38 (m, 2H), 7.36-7.32 (m, 2H), 7.25-7.21 (m, 1H), 7.15 (dd, J = 8.0, 1.6 Hz, 1H), 6.99 (d, J = 1.4 Hz, 1H), 6.79 (d, J = 8.2 Hz, 1H), 6.01 (s, 2H), 5.50 (t, J = 6.6 Hz, 1H), 4.97-4.88 (m, 2H), 4.55 (d, J = 16.5 Hz, 1H), 4.29 (d, J = 16.9 Hz, 1H), 2.93 (d, J = 15.1 Hz, 1H), 2.87 (d, J = 15.1 Hz, 1H), 1.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm):δ 206.6, 200.6, 153.0, 150.2, 147.6, 146.0, 129.0, 128.5, 126.7, 126.1, 112.5, 112.3, 108.7, 101.8, 99.4, 88.4, 78.8, 78.4, 69.5, 50.1, 40.9, 26.5. HRMS (EI) calcd. for $C_{24}H_{20}O_5$ [M^+] *m/z* 388.1311, found 388.1306.

96m



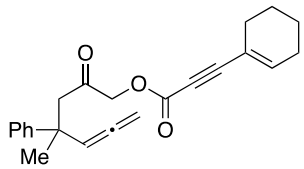
By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid[24,25] (135 mg, 1.2 mmol) in the presence of *N*,*N*'-dicyclohexylcarbodiimide (248 mg, 1.2 mmol,) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 288 mg of compound **96m** as a colorless liquid (93%). IR (neat): 2967, 2875, 2239, 1955, 1717, 1635, 1246 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.39-7.31 (m, 4H), 7.24-7.21 (m, 1H), 5.49 (t, J = 6.6 Hz, 1H), 4.95-4.87 (m, 2H), 4.49 (d, J = 16.5 Hz, 1H), 4.23 (d, J = 16.9 Hz, 1H), 2.90 (d, J = 15.1 Hz, 1H), 2.84 (d, J = 15.1 Hz, 1H), 2.31 (t, J = 7.1 Hz, 2H), 1.65-1.58 (m, 2H), 1.57 (s, 3H), 1.00 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.7, 200.7, 152.7, 146.0, 128.5, 126.7, 126.1, 99.4, 91.3, 78.4, 72.4, 69.4, 50.1, 40.9, 26.5, 21.0, 20.7, 13.4. HRMS (EI) calcd. for $C_{19}H_{19}O_3$ [$(M-Me)^+$] *m/z* 295.1334, found 295.1333.

96n



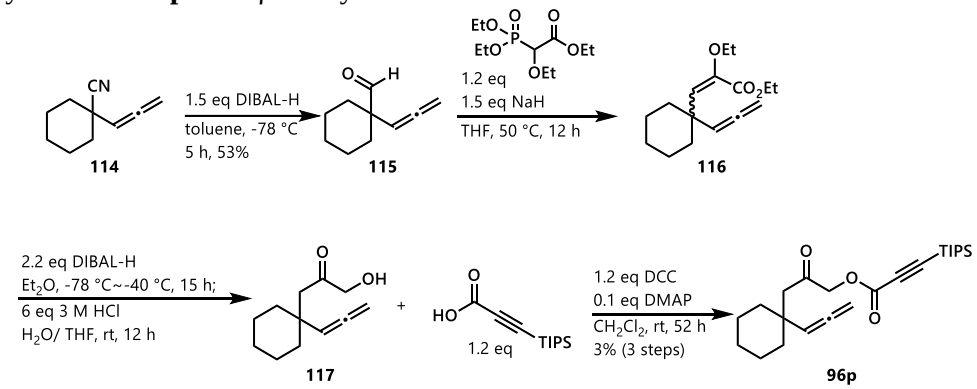
By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid[24] (144 mg, 1.2 mmol) in the presence of *N*,*N*'-dicyclohexylcarbodiimide (248 mg, 1.2 mmol,) and 4-dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 299 mg of compound **96n** as a pale yellow liquid (92%). IR (neat): 2972, 2932, 2241, 1955, 1715, 1221 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.39-7.31 (m, 4H), 7.24-7.22 (m, 1H), 5.49 (t, J = 6.6 Hz, 1H), 4.93-4.90 (m, 2H), 4.49 (d, J = 16.9 Hz, 1H), 4.23 (d, J = 16.9 Hz, 1H), 2.90 (d, J = 15.1 Hz, 1H), 2.84 (d, J = 15.1 Hz, 1H), 1.57 (s, 3H), 1.27 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.7, 200.7, 152.9, 146.0, 128.5, 126.7, 126.1, 99.4, 98.3, 78.4, 77.3, 77.0, 76.7, 71.0, 69.4, 50.1, 40.8, 29.9, 27.6, 26.5. HRMS (EI) calcd. for $C_{20}H_{21}O_3$ [M^+-Me] *m/z* 309.1491, found 309.1485.

96o



By following general procedure D, the reaction of α-hydroxy ketone (216 mg, 1.0 mmol) with the corresponding propiolic acid[26]. (180 mg, 1.2 mmol) in the presence of *N*,*N*'-dicyclohexylcarbodiimide (248 mg, 1.2 mmol,) and 4-Dimethylaminopyridine (12 mg, 0.1 mmol) in 4 mL CH_2Cl_2 delivered 292 mg of compound **96o** as pale yellow liquid (84%). IR (neat): 2933, 2207, 1955, 1714, 1257cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.39-7.31 (m, 4H), 7.24-7.20 (m, 1H), 6.47-6.45 (m, 1H), 5.49 (t, J = 6.6 Hz, 1H), 4.95-4.87 (m, 2H), 4.50 (d, J = 16.9 Hz, 1H), 4.24 (d, J = 16.9 Hz, 1H), 2.90 (d, J = 15.1 Hz, 1H), 2.85 (d, J = 15.1 Hz, 1H), 2.16-2.14 (m, 4H), 1.66-1.58 (m, 4H), 1.57 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.6, 200.8, 153.2, 146.0, 142.8, 128.4, 126.6, 126.1, 118.3, 99.4, 90.2, 78.4, 77.8, 69.5, 50.1, 40.8, 28.0, 26.5, 26.0, 21.8, 21.0. HRMS (EI) calcd. for $C_{23}H_{24}O_3$ [M^+] *m/z* 348.1725, found 348.1729.

Synthesis of **96p** from β-allenyl nitrile

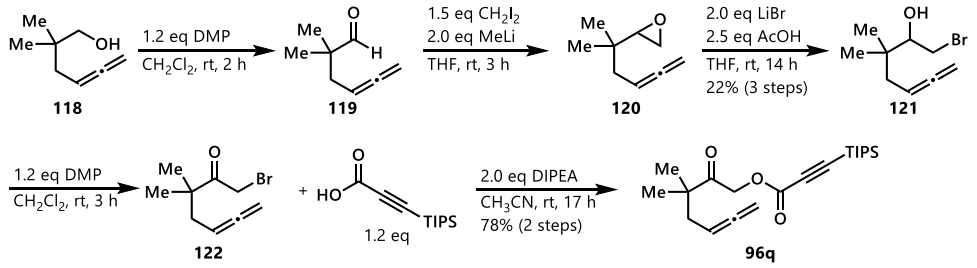


To a stirred solution of allenyl nitrile **114**[13] (155 mg, 1.05 mmol) in dry toluene (3.5 mL), DIBAL-H (1.58 mL of a 1 M solution in toluene, 1.58 mmol) was added under N_2 at -78 °C. After 5 h, a saturated aqueous solution of potassium sodium tartrate tetrahydrate was added to the reaction mixture, and it was left to stir for several hours until the organic and aqueous layers had completely separated. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. Then, the residue was purified by silica gel column chromatography (hexane/AcOEt, 20:1) to yield 84 mg of desired compound **115** as a brown oil (53%). IR (neat): 2927, 2853, 1725, 1449, 841 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 9.32 (s, 1H), 4.95-4.92 (m, 1H), 4.88-4.86 (m, 2H), 1.87-0.83 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 209.1, 202.4, 92.3, 77.8, 50.0, 30.7, 25.7, 22.3. LRMS (EI) *m/z* 150 [M^+], 149, 121, 111.

To a suspension of 60% sodium hydride (238 mg, 5.96 mmol) in anhydrous THF (13 mL), Phosphonoacetate (1.28 g, 4.76 mmol) in THF (26 mL) was added at 0 °C and the reaction mixture was stirred at the same temperature for 1 h. To the solution was added aldehyde **115** (596 mg, 3.97 mmol) in dry THF (13 mL) at the same temperature. The reaction mixture was stirred at 50 °C for 3 h. The mixture was extracted with Et_2O three

times. The combined organic layer was washed with brine, dried over $NaSO_4$, and evaporated under reduced pressure. Then, the resideu was roughly purified by silica gel column chromatography (hexane/AcOEt, 20:1) to the desired compound **116** as a yellow oil, which was used without further purification in the next step. To a stirred solution of the crude ester **116** in dry Et_2O (6.8 mL), DIBAL-H (2.91 mL of a 1 M solution in toluene, 2.97 mmol) was added under N_2 at -78 °C. After 8 h, a saturated aqueous solution of potassium sodium tartrate tetrahydrate was added to the mixture, and it was left to stir for several hours until the organic and aqueous layers had completely separated. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude product as a yellow oil, which was used without further purification in the next step. To a stirred solution of the crude alcohol in THF (6.8 mL) was added HCl (2.7 mL of a 3 M solution in H_2O, 8.1 mmol) at room temperature. After 4 h, the reaction mixture was quenched by saturated aqueous solution of $NaHCO_3$ (30 mL). The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. Then, the residue was roughly purified by silica gel column chromatography (hexane/AcOEt, 5:1) to yield desired compound **117** as a pale-yellow oil. It was used without further purification in the next step. The crude α-hydroxy ketone **117** and 3-(triisoprosilyl)propiolic acid (139 mg, 0.61 mmol) were dissolved in CH_2Cl_2 (2.0 mL). To the solution were added *N*,*N'*-dicyclohexylcarbodiimide (126 mg, 0.61 mmol) and 4-dimethylaminopyridine (6.1 mg, 0.05 mmol) with stirring at 0 °C. After a further 5 min at 0 °C, the ice bath was removed, and the reaction mixture was stirred for 52 h at room temperature. The precipitate was removed by filtration over a pad of Celite. Then the filtrate was evaporated. The residue was then purified by silica gel column chromatography (hexane/AcOEt, 20:1) to yield 193 mg of desired compound **96p** as a yellow oil (3%, 3steps). IR (neat): 2930, 2865, 2172, 2119, 1954, 1716, 1662, 1212 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 5.15 (t, J = 6.8 Hz, 1H), 4.79 (d, J = 6.8 Hz, 2H), 4.69 (s, 2H), 2.45 (s, 2H), 1.71-1.63 (m, 2H), 1.53-1.39 (m, 6H), 1.28-1.21 (m, 1H), 1.13-1.09 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm):δ 207.4, 201.1, 151.9, 97.1, 95.8, 93.2, 77.2, 70.0, 37.7, 36.5, 33.1, 25.8, 22.2, 18.4, 10.9. HRMS (ESI) calcd. $C_{24}H_{38}NaO_3Si$ for [(M+Na)$^+$] *m/z* 425.2488, found 425.2474.

Synthesis of **96q** from ε-allyl alchol

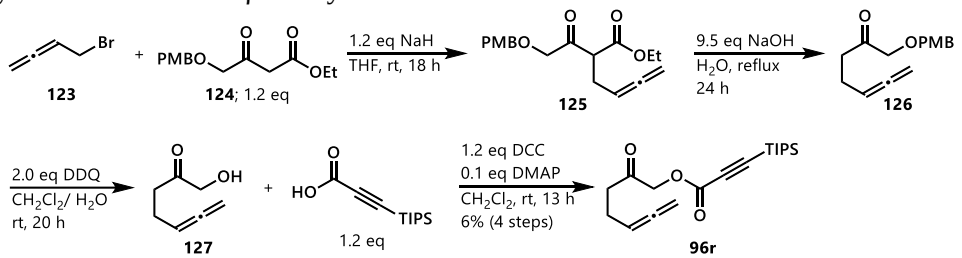


The alcohol **118**[25] (402 mg, 3.18 mmol) was dissolved in in anhydrous CH_2Cl_2 (30 mL) under N_2. To the solution was added DMP (1.62 g, 3.82 mmol) at 0 °C. The ice bath was removed. The reaction mixture was stirred for 2 h at room temperature. The reaction mixture was quenched by saturated aqueous solution of $NaHCO_3$ and $Na_2S_2O_3$. The mixture was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude as a yellow oil, which was used without further purification in the next step. To a solution of the crude aldehyde **119** and CH_2I_2 (0.36 mL, 4.29 mmol) in THF (12 mL), methyllithium (1.15 M in Et_2O, 5.0 mL, 5.72 mmol) was added at 0 °C under Ar. After 30 min, the reaction mixture was stirred for 3 h at room temperature. The reaction mixture was quenched by H_2O. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude as a yellow oil, which was used without further purification in the next step. To a solution of the crude epoxide **120** and LiBr (392 mg, 4.51 mmol) in THF (23 mL), acetic acid (0.32 mL, 5.65 mmol) was added at room temperature. The reaction mixture was stirred for 14 h at the same temperature. The reaction mixture was quenched by saturated aqueous solution of $NaHCO_3$. The mixture was extracted with AcOEt three times. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was then purified by silica gel column chromatography (hexane/AcOEt, 1:20) to yield 154 mg of desired compound **121** as a colorless oil (22%, 3 steps). IR (neat): 3466, 2962, 1954, 1469, 1073, 842 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, rt, δ/ppm):δ 5.10-5.04 (m, 1H), 4.67-4.65 (m, 2H), 3.69 (dd, J = 10.3, 1.8 Hz, 1H), 3.64 (d, J = 10.3 Hz, 1H), 3.39 (t, J = 10.3 Hz, 1H), 2.26 (d, J = 3.0 Hz, 1H), 2.19-2.14 (m, 1H), 2.01-1.95 (m, 1H), 0.96 (s, 3H), 0.94 (s, 3H).

^{13}C NMR (126 MHz,, $CDCl_3$, rt, δ/ppm): δ 209.8, 85.5, 77.5, 73.9, 38.9, 38.6, 38.2, 23.1, 22.5. LRMS (CI) *m/z* 218 [M^+], 125, 139.

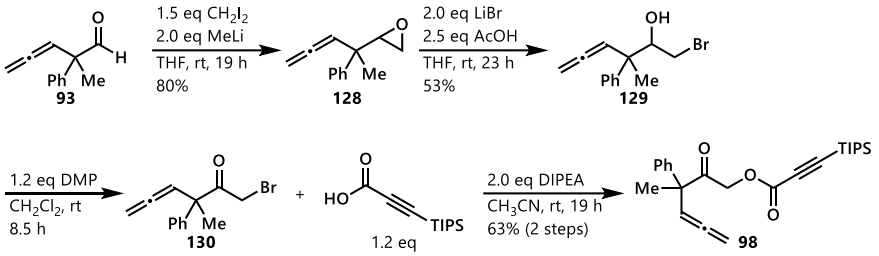
The alcohol **121** (154 mg, 0.70 mmol) was dissolved in in anhydrous CH_2Cl_2 (7 mL) under N_2. To the solution was added DMP (357 g, 0.84 mmol) at 0 °C. The ice bath was removed. The reaction mixture was stirred for 3 h at room temperature. The reaction mixture was quenched by saturated aqueous solution of $NaHCO_3$ and $Na_2S_2O_3$. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude as a yellow oil, which was used without further purification in the next step. The crude acyl bromide **122** and 3-(triisoprosilyl)propiolic acid (179 mg, 0.66 mmol) were dissolved in MeCN (2.6 mL). To the solution was added *N*,*N*-diisopropylethylamine (0.23 mL, 1.32 mmol). The solution was stirred for 17 h at room temperature and then evaporated. The residue was then purified by silica gel column chromatography (hexane/AcOEt, 50:1) to yield 198 mg of desired compound **96q** as a colorless oil (78%, 2 steps). IR (neat): 2945, 2867, 2173, 1956, 1715, 1220 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 5.02-4.97 (m, 1H), 4.94 (s, 2H), 4.69 (td, J = 4.5, 2.1 Hz, 2H), 2.26 (td, J = 5.1, 2.6 Hz, 2H), 1.21 (s, 6H), 1.18-1.07 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 209.9, 205.7, 152.1, 95.9, 93.0, 85.1, 74.7, 66.0, 46.7, 38.7, 23.9, 18.4, 10.9. HRMS (ESI) calcd. for $C_{21}H_{34}NaO_3Si$ [$(M+Na)^+$] *m/z* 385.2175, found 386.2182.

Synthesis of **96r** from β-allenyl bromide



To a suspension of 55% sodium hydride (160 mg, 3.6 mmol) in anhydrous THF (3 mL), β-keto ester **124** (960 mg, 3.60 mmol) in THF (3 mL) was added at 0 °C, and the reaction mixture was stirred at 0 °C for 30 min. To the solution was added allenyl bromide **123**[28] (400 mg, 3.0 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 18 h. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. Then, the residue was roughly purified by silica gel column chromatography (hexane/AcOEt, 10:1~5:1) to yield 281 mg of desired compound **125** as a yellow oil, which was used without further purification in the next step. To a solution of the crude β-keto ester **125** in H_2O (9.0 mL) was added NaOH (334 mg, 8.36 mmol) at room temperature. The reaction mixture was heated under reflux for 24 h. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. Then, the residue was roughly purified by silica gel column chromatography (hexane/AcOEt, 5:1) to yield 84 mg of desired compound **126** as a pale yellow oil, which was used without further purification in the next step. To a solution of the crude PMB ether **126** in CH_2Cl_2/H_2O (10:1, 3.7 mL), DDQ (154 mg, 0.68 mmol) was added at 0 °C. The reaction mixture was stirred at room temperature for 20 h. The reaction mixture was quenched by saturated aqueous solution of $NaHCO_3$. The mixture was extracted with CH_2Cl_2 three times. The combined organic layer was dried over $MgSO_4$ and evaporated under reduced pressure to give the crude as a pale yellow oil. Then, the residue was roughly purified by silica gel column chromatography (hexane/AcOEt, 4:1) to yield 51 mg of desired compound **127** as pale yellow oil, which was used without further purification in the next step. The crude α-hydroxy ketone **127** and 3-(triisoprosilyl)propiolic acid (109 mg, 0.48 mmol) were dissolved in CH_2Cl_2 (1.6 mL). To the solution were added *N*,*N*'-dicyclohexylcarbodiimide (99 mg, 0.48 mmol) and 4-dimethylaminopyridine (5 mg, 0.04 mmol) with stirring at 0 °C. After a further 5 min at 0 °C, the ice bath was removed. The reaction mixture was stirred for 11 h at room temperature. The precipitate was removed by filtration over a pad of Celite. Then the filtrate was evaporated, and the residue was then purified by silica gel column chromatography (hexane/AcOEt, 50:1) to yield 59 mg of desired compound **96r** as a yellow oil (6%, 4 steps). IR (neat): 2945, 2867, 2173, 1956, 1718, 1219 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 5.21-5.15 (m, 1H), 4.75-4.69 (m, 4H), 2.59 (t, J = 7.1 Hz, 2H), 2.35-2.28 (m, 2H), 1.15-1.05 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.3, 202.0, 152.0, 95.7, 93.5, 88.7, 76.5, 68.8, 37.4, 21.1, 18.4, 10.9. HRMS (ESI) calcd. for $C_{19}H_{30}NaO_3Si$ [$(M+Na)^+$] *m/z* 357.1862, found 357.1865.

Synthesis of **98** from β-allenyl aldehyde

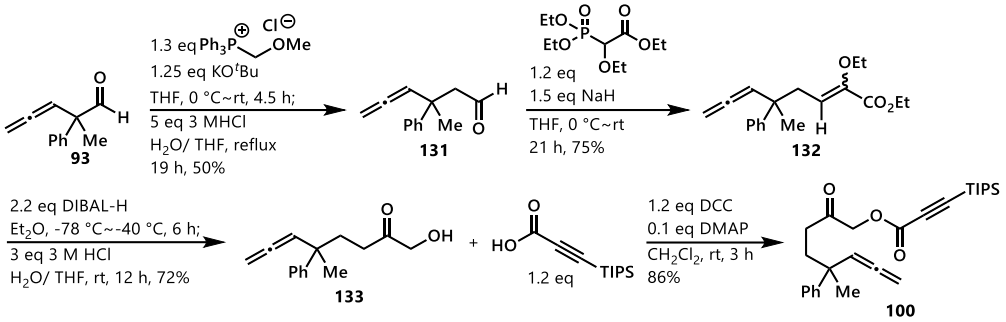


To a solution aldehyde **93** (1.3 g, 7.5 mmol) and CH_2I_2 (0.91 mL, 11.3 mmol) in THF (30 mL), methyllithium (1.16 M in Et_2O, 12.9 mL, 15.0 mmol) was added at 0 ° C under Ar. After 30 min, the reaction mixture was stirred for 19 h at room temperature. The reaction mixture was quenched by H_2O. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure It was then purified by silica gel column chromatography (hexane/AcOEt, 1:20) to yield 1.119 g of desired compound **128** as red oil (80%, diastereomer mixture).IR (neat): 2978, 1955, 1723, 1494, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.48-7.44 (m, 2H), 7.36-7.32 (m, 2H), 7.27-7.23 (m, 1H), 5.37-5.33 (m, 1H), 4.89-4.81 (m, 2H), 3.27 (dd, J = 4.1, 2.7 Hz, 0.4H), 3.19 (dd, J = 4.1, 2.7 Hz, 0.6H), 2.76 (dd, J = 5.0, 4.1 Hz, 1H), 2.63 (dd, J = 5.9, 3.2 Hz, 1H), 1.40 (s, 1H), 1.39 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 207.7, 128.3, 128.2, 126.9, 126.7, 95.8, 95.4, 77.5, 58.4, 58.3, 44.3, 22.4, 22.3. LRMS (EI) *m/z* 185 [$(M-H)^+$], 171, 143, 77.

To a solution epoxide **128** (1.12 g, 6.01 mmmol) and LiBr (1.04 g, 12.02 mmol) in THF (60 mL), acetic acid (0.86 mL, 15.03 mmol) was added dropwise at room temperature. The reaction mixture was stirred for 23 hr at same temperature. The reaction mixture was quenched by saturated solution of $NaHCO_3$. The mixture was extracted with AcOEt three times. The combined organic layer was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure. It was then purified by silica gel column chromatography (hexane/AcOEt, 10:1) to yield 833 mg of desired compound **129** as yellow oil (53%, diastereomer mixture). IR (neat): 3437, 3056, 1671, 1496, 701 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.44-7.40 (m, 2H), 7.38-7.33 (m, 2H), 7.28-7.24 (m, 1H), 5.59 (t, J = 6.6 Hz, 0.4H), 5.49 (t, J = 6.9 Hz, 0.6H), 4.96-4.86 (m, 2H), 4.22 (dd, J = 10.5, 1.8 Hz, 0.4H), 4.14 (dd, J = 10.5, 1.8 Hz, 0.6H), 3.63 (dd, J = 10.5, 1.8 Hz, 0.6H), 3.47 (dd, J = 10.5, 1.8 Hz, 0.4H), 3.30-3.25 (m, 1H), 1.49 (s, 1.8H), 1.45 (s, 1.2H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 207.7, 207.5, 128.6, 127.0, 126.9, 126.8, 95.9, 95.8, 78.6, 78.0, 77.9, 77.3, 47.1, 36.9, 22.2, 21.5. LRMS (EI) *m/z* 266 [M^+], 251, 143.

The alcohol **129** (154 mg, 0.70 mmol) was dissolved in in anhydrous CH_2Cl_2 (7 mL) under N_2. To the solution was added DMP (357 g, 0.84 mmol) at 0 °C. The ice bath is removed. The reaction mixture was stirred for 3 hr at room temperature. The reaction mixture was quenched by saturated solution of $NaHCO_3$ and $Na_2S_2O_3$. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. It was then roughly purified by silica gel column chromatography (hexane/AcOEt, 10:1) to yield desired compound **130**, which was used without further purification in the next step. Crude α-bromo ketone **130** and 3-(Triisoprosilyl)propiolic acid (649 mg, 2.87 mmol) was dissolved in MeCN (8.0 mL). To the solution was added *N*,*N*-diisopropylethylamine (0.83 mL, 4.78 mmol) dropwise with stirring. The solution was stirred for 19 h at room temperature and then evaporated. It was then purified by silica gel column chromatography (hexane/AcOEt, 10:1) to yield 810 mg of desired compound **98** as colorless oil (63%, 2 steps). IR (neat): 2944, 2866, 2173, 1955, 1717, 1220 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.39-7.35 (m, 2H), 7.33-7.27 (m, 3H), 5.74 (t, J = 6.8 Hz, 1H), 4.93 (d, J = 6.8 Hz, 2H), 4.84 (d, J = 16.8 Hz, 1H), 4.72 (d, J = 16.8 Hz, 1H), 1.59 (s, 3H), 1.16-1.06 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.2, 201.7, 151.9, 141.7, 129.0, 127.6, 126.7, 95.8, 93.8, 93.1, 78.8, 77.3, 77.0, 76.7, 66.3, 54.6, 24.0, 18.4, 11.0. HRMS (ESI) calcd. $C_{25}H_{34}NaO_3Si$ for [$(M+Na)^+$] *m/z* 433.2175, found 433.2163.

Synthesis of **100** from β-allenyl aldehyde



To (Methoxymethyl)triphenylphosphonium Chloride (2.67 g, 7.8 mmol) in THF (3 mL), KO^{t}Bu (841 mg, 7.5 mmol) in anhydrous THF (3 mL) was added at 0 °C dropwise and the reaction mixture was stirred at 0 °C for 1 h. aldehyde **93** (1.03 g, 6.0 mmol) was then added in dry THF (3 mL) at 0 °C. The reaction mixture was stirred at rt for 4.5 h. The mixture was evaporated under reduced pressure and diluted with hexane. The precipitate was removed by filtration over a pad of Celite. Then the filtrate was evaporated under reduced pressure to give the crude as a yellow oil, which was used without further purification in the next step. To a stirred solution of crude vinyl methyl ether in THF (20mL), HCl (10 mL of a 3 M solution in H_2O, 30 mmol) was added at rt. After 21 h, the reaction mixture was quenched by saturated solution of $NaHCO_3$ (30 mL). The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by column chromatography (eluent: Hexane/EtOAc = 20:1), affording 560 g of desired compound **131** as yellow oil (50%). IR (neat): 2967, 1954, 1703, 1072, 1028 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 9.63 (d, J = 2.3 Hz, 1H), 7.41-7.32 (m, 4H), 7.29-7.22 (m, 1H), 5.50 (t, J = 6.9 Hz, 1H), 4.95-4.92 (m, 2H), 2.80-2.78 (m, 2H), 1.57 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 206.9, 202.6, 146.0, 128.6, 126.7, 126.1, 99.0, 78.6, 54.0, 40.1, 27.5. LRMS (EI) *m/z* 186 [M$^+$], 171, 143.

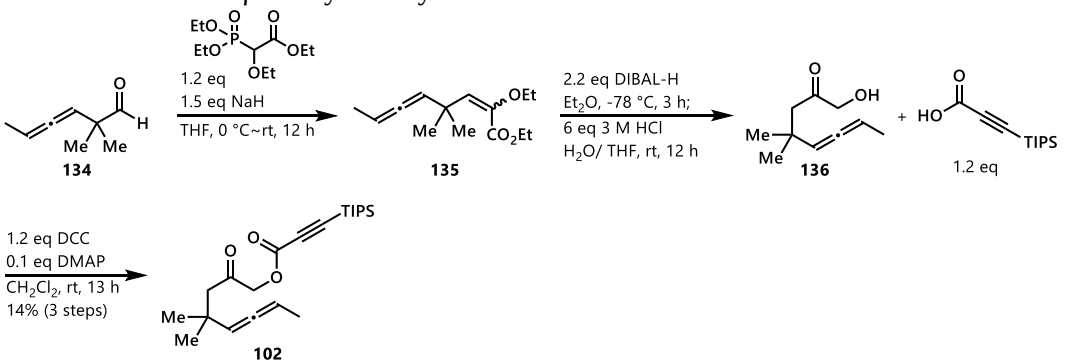
To a suspension of 60% sodium hydride (180 mg, 4.5 mmol) in anhydrous THF (18 mL), Phosphonoacetate (966 mg, 3.6 mmol) in THF (9 mL) was added dropwise at 0 °C and the reaction mixture was stirred at 0 °C for 1 h. To the solution was added aldehyde **131** (560 mg, 3.0 mmol) in dry THF (9 mL) at same temperature. The reaction mixture was stirred at rt for 21 h. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $NaSO_4$, and evaporated under reduced pressure. It was then purified by silica gel column chromatography (hexane/AcOEt, 20:1) to yield 672 mg of desired compound **132** as yellow oil which were mixture of E/Z isomers (75%). IR (neat): 2978, 1954, 1721, 1643, 1240, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.40-7.37 (m, 2H), 7.34-7.29 (m, 2H), 7.22-7.18 (m, 1H), 6.15 (t, J = 7.4 Hz, 0.4H), 5.42-5.37 (m, 1H), 5.05 (t, J = 7.4 Hz, 0.6H), 4.88-4.84 (m, 2H), 4.26 (q, J = 7.2 Hz, 1.2H), 4.19 (q, J = 7.0 Hz, 0.8H), 3.81-3.72 (m, 0.8H), 3.62 (q, J = 6.9 Hz, 1.2H), 2.89-3.03 (m, 1.2H), 2.77-2.66 (m, 0.8H), 1.42 (s, 1.2H), 1.40 (s, 1.8H), 1.34 (t, J = 7.0 Hz, 1.8H), 1.30-1.25 (m, 4.2H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 207.1, 163.9, 147.1, 147.1, 145.9, 128.2, 128.2, 126.5, 126.3, 126.2, 126.1, 125.1, 112.5, 99.4, 77.6, 77.3, 77.0, 76.7, 67.8, 64.2, 60.9, 60.8, 42.2, 41.7, 38.6, 38.0, 26.6, 26.4, 15.4, 14.4, 14.2. LRMS (EI) *m/z* 300 [M$^+$], 271, 227.

To a stirred solution of ester **132** (672 mg, 2.23 mmol) in dry Et_2O (6.8 mL), DIBAL-H (4.9 mL of a 1 M solution in toluene, 4.9 mmol) was added under N_2 at -78 °C. After 6 h, a saturated solution of potassium sodium tartrate tetrahydrate (10 mL) was added the mixture was left to stir for several hours until the organic and aqueous layers had completely separated. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude as a yellow oil, which was used without further purification in the next step. To a stirred solution of crude alcohol in THF (4 mL) was added HCl (2 mL of a 3 M solution in H_2O, 6 mmol) at rt. After 12 h, the reaction mixture was quenched by saturated solution of $NaHCO_3$ (30 mL). The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. It was then purified by silica gel column chromatography (hexane/AcOEt, 3:1) to yield 369 mg of desired compound **133** as pale yellow oil (72%). IR (neat): 3443, 2969, 1954, 1719, 1287, 700 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.37-7.30 (m, 4H), 7.20-7.24 (m, 1H), 5.36 (t, J = 6.6 Hz, 1H), 4.88 (d, J = 6.9 Hz, 2H), 4.12 (s, 2H), 3.02 (s, 1H), 2.27 (t, J = 7.8 Hz, 2H), 2.19-2.05 (m, 2H), 1.41 (s, 3H). ^{13}C NMR (100

MHz, $CDCl_3$, rt, δ/ppm): δ 209.5, 206.9, 146.4, 128.4, 126.4, 126.3, 99.0, 77.7, 68.0, 41.4, 35.1, 34.3, 26.7. LRMS (EI) *m/z* 230 [M^+], 199, 171.

α-Hydroxy ketone **133** (230 mg, 1 mmol) and 3-(Triisoprosilyl)propiolic acid (272 mg, 1.2 mmol) was dissolved in CH_2Cl_2 (4 mL). To the solution was added N,N'-Dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-Dimethylaminopyridine (12 mg, 0.1 mmol) with stirring at 0 °C. After a further 5 min at 0 °C, the ice bath is removed and the reaction mixture is stirred for 3 hr at room temperature (monitored by TLC). The precipitate was removed by filtration over a pad of Celite. Then the filtrate was evaporated. It was then purified by silica gel column chromatography (hexane/AcOEt, 20:1) to yield 375 mg of desired compound **100** as colorless oil (86%). IR (neat): 2944, 2867, 2173, 1954, 1718, 1231 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.37-7.30 (m, 4H), 7.23-7.19 (m, 1H), 5.35 (t, J = 6.6 Hz, 1H), 4.87 (d, J = 6.4 Hz, 2H), 4.61 (s, 2H), 2.31 (t, J = 7.8 Hz, 2H), 2.17-2.02 (m, 2H), 1.40 (s, 3H), 1.17-1.07 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 207.0, 202.7, 151.9, 146.6, 128.3, 126.3, 99.0, 95.7, 93.5, 77.6, 68.6, 41.3, 34.7, 34.6, 26.7, 18.4, 10.9. HRMS (ESI) calcd. for $C_{27}H_{38}NaO_3Si$ [$(M+Na)^+$] *m/z* 461.2488, found 461.2475.

Synthesis of **102** from β-allenyl aldehyde

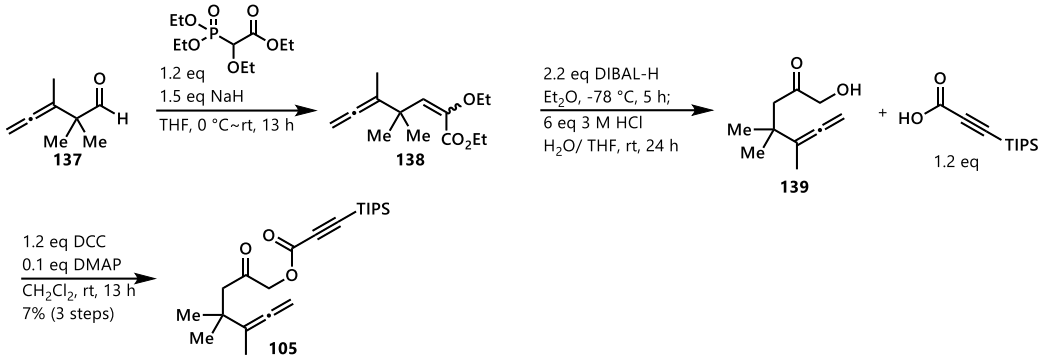


To a suspension of 60% sodium hydride (600 mg, 15 mmol) in anhydrous THF (30 mL), phosphonoacetate (3.49 g, 13 mmol) in THF (60 mL) was added dropwise at 0 °C and the reaction mixture was stirred at same temperature for 1 h. To the solution was added aldehyde **134**[29] (1.24 mg, 10 mmol) in dry THF (30 mL) at same temperature. The reaction mixture was stirred at room temperature for 12 h. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $NaSO_4$, and evaporated under reduced pressure. Then, it was roughly purified by silica gel column chromatography (hexane/AcOEt, 50:1~20:1) to the desired compound **135** as a yellow oil, which was used without further purification in the next step. To a stirred solution of crude ester **135** in dry Et_2O (6.3 mL), DIBAL-H (4.62 mL of a 1 M solution in toluene, 4.62 mmol) was added under N_2 at -78 °C. After 3 h, a saturated solution of potassium sodium tartrate tetrahydrate was added the mixture was left to stir for several hours until the organic and aqueous layers had completely separated. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude as a yellow oil, which was used without further purification in the next step. To a stirred solution of crude alcohol in THF (4.2 mL) was added HCl (2.1 mL of a 3 M solution in H_2O, 6.3 mmol) at rt. After 12 h, the reaction mixture was quenched by saturated solution of $NaHCO_3$. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. Then, it was purified by silica gel column chromatography (hexane/AcOEt, 5:1) to yield 244 mg of desired compound **136** as pale yellow oil (14%, 2 steps). IR (neat): 3465, 2962, 1961, 1718, 1055 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 5.20-5.07 (m, 2H), 4.19 (s, 2H), 3.16 (s, 1H), 2.41 (s, 2H), 1.64 (dd, J = 7.2, 3.2 Hz, 3H), 1.14 (s, 3H), 1.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.6, 202.4, 99.9, 88.5, 69.6, 50.0, 34.6, 28.5, 28.4, 14.5. LRMS (EI) *m/z* 168 [M+], 137, 109.

α-Hydroxy ketone **136** (168 mg, 1.00 mmol) and 3-(Triisoprosilyl)propiolic acid (271 mg, 1.20 mmol) was dissolved in CH_2Cl_2 (4.0 mL). To the solution was added N,N'-Dicyclohexylcarbodiimide (248 mg, 1.20 mmol) and 4-Dimethylaminopyridine (12 mg, 0.10 mmol) with stirring at 0 °C. After a further 5 min at 0 °C, the ice bath was removed and the reaction mixture is stirred for 13 hr at room temperature. The precipitate was removed by filtration over a pad of Celite. Then the filtrate was evaporated. It was then purified by silica gel column chromatography (hexane/AcOEt, 20:1) to yield 368 mg of desired compound **102** as colorless oil (98%). IR (neat): 2944, 2867, 2173, 1716, 1221 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 5.21-5.11 (m, 2H), 4.69

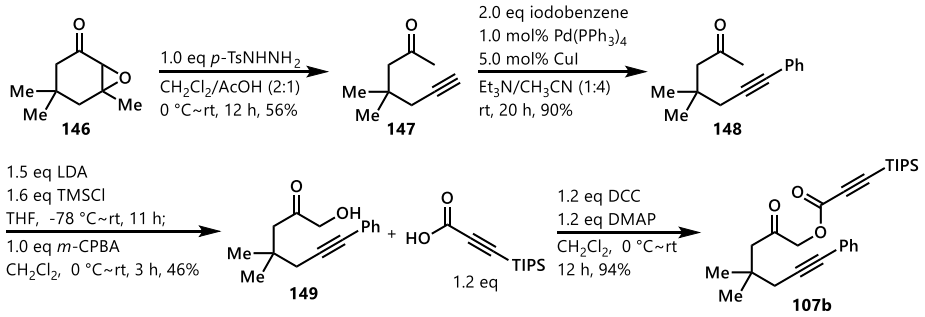
(s, 2H), 2.43 (s, 2H), 1.65 (dd, J = 7.1, 3.4 Hz, 3H), 1.14 (s, 6H), 1.13-1.06 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 202.4, 201.2, 151.9, 100.1, 95.8, 93.3, 88.5, 69.7, 50.2, 34.5, 28.3, 28.3, 18.4, 14.5, 10.9. HRMS (ESI) calcd. for $C_{22}H_{36}NaO_3Si$ [$(M+Na)^+$] *m/z* 399.2331, found 399.2319.

Synthesis of **105** from β-allenyl aldehyde



To a suspension of 60% sodium hydride (600 mg, 15 mmol) in anhydrous THF (30 mL), phosphonoacetate (3.49 g, 13 mmol) in THF (60 mL) was added dropwise at 0 °C and the reaction mixture was stirred at same temperature for 1 h. To the solution was added aldehyde **137**[16] (1.24 mg, 10 mmol) in dry THF (30 mL) at same temperature. The reaction mixture was stirred at room temperature for 13 h. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $NaSO_4$, and evaporated under reduced pressure. Then, it was roughly purified by silica gel column chromatography (hexane/AcOEt, 20:1) to the desired compound **138** as a yellow oil, which was used without further purification in the next step. To a stirred solution of crude ester **138** in dry Et_2O (9.0 mL), DIBAL-H (6.00 mL of a 1 M solution in toluene, 6.00 mmol) was added under N_2 at -78 °C. After 5 h, a saturated solution of potassium sodium tartrate tetrahydrate was added the mixture was left to stir for several hours until the organic and aqueous layers had completely separated. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude as a yellow oil, which was used without further purification in the next step. To a stirred solution of crude alcohol in THF (5.4 mL) was added HCl (2.7 mL of a 3 M solution in H_2O, 8.1 mmol) at rt. After 24 h, the reaction mixture was quenched by saturated solution of $NaHCO_3$. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. Then, it was roughly purified by silica gel column chromatography (hexane/AcOEt, 10:1~5:1) to yield desired compound **139** as pale yellow oil, which was used without further purification in the next step. α-hydroxy ketone **139** (91 mg, 0.54 mmol) and 3-(Triisoprosilyl)propiolic acid (147 mg, 0.65 mmol) was dissolved in CH_2Cl_2 (2.0 mL). To the solution was added N,N'-Dicyclohexylcarbodiimide (134 mg, 0.65 mmol) and 4-Dimethylaminopyridine (6 mg, 0.05 mmol) with stirring at 0 °C. After a further 5 min at 0 °C, the ice bath was removed and the reaction mixture is stirred for 15 hr at room temperature. The precipitate was removed by filtration over a pad of Celite. Then the filtrate was evaporated. It was then purified by silica gel column chromatography (hexane/AcOEt, 50:1) to yield 99 mg of desired compound **105** as pale yellow oil (7%, 3 steps).

Synthesis of **107b** from Isophorone Oxide



To a stirred solution of Isophorone Oxide (2.31 g, 15 mmol) in dry CH_2Cl_2/AcOH (2:1, 22.5 mL) was added *p*-$TsNHNH_2$ (2.79 g, 15 mmol) in CH_2Cl_2/AcOH (2:1, 22.5 mL) under N_2 at -20 °C. the reaction mixture was

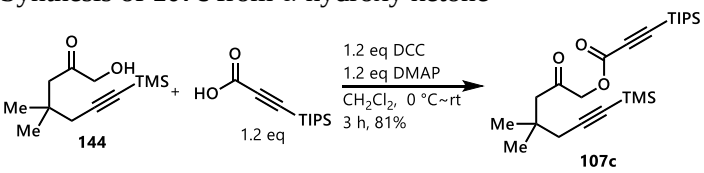
stirred at 0 °C for 1 h. The reaction mixture was stirred at rt for 12 h. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by column chromatography (eluent: Hexane/EtOAc = 10:1), affording 1.16 g of desired compound **146** as colorless liquid (56%). The ^{1}H NMR spectrum of the product matched to that of literature.[30]

To a stirred solution of ketone **147** (1.16 g, 8.38 mmol) in dry CH_3CN (22.4 mL) was added Et_3N (28 mL), Iodobenzene (1.9 mL, 3.42 g, 16.8 mmol), $Pd(PPh_3)_4$ (97 mg, 0.084 mmol) and CuI (80 mg, 0.42 mmol) under N_2. the reaction mixture was stirred at room temperature for 20 h. The precipitate was removed by filtration over a pad of Celite. Then the filtrate was evaporated. It was then purified by silica gel column chromatography (hexane/AcOEt, 10:1) to yield 1.61 g of desired compound **148** as colorless oil (86%). IR (neat): 2959, 1714, 1442, 692 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.40-7.37 (m, 2H), 7.29-7.25 (m, 3H), 2.52 (s, 2H), 2.45 (s, 2H), 2.15 (s, 3H), 1.13 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm):δ 208.4, 131.5, 128.2, 127.6, 123.8, 87.8, 82.7, 52.6, 33.9, 32.3, 32.2, 27.2. LRMS(EI) *m/z* 214 [M$^+$], 199, 157.

To a stirred solution of diisopropylamine (0.63 mL, 455 mg, 4.5 mmol) in dry THF (20 mL) was added MeLi (3.8 mL of a 1.2 M solution in toluene, 4.5 mmol) under N_2 at -78 °C. The reaction mixture was stirred at same temperature for 30 min. To the solution was added ketone **148** (643 mg, 3.0 mmol) in THF (10 mL) and stirred at -78 °C for 30 min. To the mixture was added TMSCl (0.61 mL, 520 mg, 4.8 mmol) at -78 °C and stirred at rt for 11 h. The reaction mixture was quenched by saturated solution of $NaHCO_3$. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure to give the crude as a yellow oil, which was used without further purification in the next step. To a stirred solution of the crude silyl enol ether in CH_2Cl_2 (10 mL) was added *m*-CPBA (518 mg, 3.0 mmol) at 0 °C. The reaction mixture was stirred at rt for 3 h. The reaction mixture was quenched by saturated solution of $Na_2S_2O_3$. The mixture was extracted with Et_2O three times. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated under reduced pressure. It was then purified by silica gel column chromatography (eluent; hexane/AcOEt, 5:1~2:1) to yield 320 mg of desired compound **149** as white oil (46%). IR (neat): 3467, 2961, 1719, 1442, 692 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 7.41-7.38 (m, 2H), 7.29 (t, J = 3.2 Hz, 3H), 4.24 (s, 2H), 2.49 (s, 2H), 2.47 (s, 2H), 1.17 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 209.0, 131.5, 128.3, 127.8, 123.6, 87.2, 83.2, 69.6, 47.6, 34.3, 32.6, 27.4. LRMS (EI) *m/z* 230 [M$^+$], 213, 199.

α-Hydroxy ketone **149** (320 mg, 1.39 mmol) and 3-(Triisoprosilyl)propiolic acid (377 mg, 1.67 mmol) was dissolved in CH_2Cl_2 (5.6 mL). To the solution was added N,N'-Dicyclohexylcarbodiimide (345 mg, 1.67 mmol) and 4-Dimethylaminopyridine (17 mg, 0.14 mmol) with stirring at 0 °C. After a further 5 min at 0 °C, the ice bath is removed and the reaction mixture is stirred for 12 hr at room temperature (monitored by TLC). The precipitate was removed by filtration over a pad of Celite. Then the filtrate was evaporated. It was then purified by silica gel column chromatography (hexane/AcOEt, 20:1) to yield 571 mg of desired compound **107b** as colorless oil (94%). IR (neat): 2945, 2867, 2173, 1716, 1221, 680 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.41-7.39 (m, 2H), 7.30-7.27 (m, 3H), 4.74 (s, 2H), 2.50 (s, 2H), 2.48 (s, 2H), 1.17 (s, 6H), 1.13-1.09 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 201.5, 151.9, 131.5, 128.2, 127.7, 123.6, 95.7, 93.4, 87.3, 83.1, 69.7, 47.6, 34.3, 32.4, 27.3, 18.4, 10.9. HRMS (ESI) calcd. for $C_{27}H_{38}NaO_3Si$ [(M+Na)$^+$] *m/z* 461.2488, found 461.2475.

Synthesis of **107c** from α-hydroxy ketone

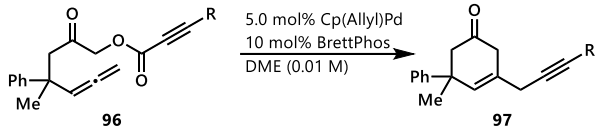


α-Hydroxy ketone **144**[31] (226 mg, 1 mmol) and 3-(Triisoprosilyl)propiolic acid (272 mg, 1.2 mmol) was dissolved in CH_2Cl_2 (4 mL). To the solution was added N,N'-Dicyclohexylcarbodiimide (248 mg, 1.2 mmol) and 4-Dimethylaminopyridine (12 mg, 0.1 mmol) with stirring at 0 °C. After a further 5 min at 0 °C, the ice bath is removed and the reaction mixture is stirred for 3 hr at room temperature (monitored by TLC). The precipitate was removed by filtration over a pad of Celite. Then the filtrate was evaporated. It was then purified by silica gel column chromatography (hexane/AcOEt, 20:1) to yield 353 mg of desired compound **107c** as colorless oil (81%). IR (neat): 2959, 2867, 2173, 1718, 1221, 680 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 4.71 (s, 2H), 2.43 (s, 2H), 2.27 (s, 2H), 1.13-1.09 (m, 22H), 0.16 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, rt,

δ/ppm): δ 201.5, 151.9, 104.5, 95.8, 93.3, 87.4, 69.7, 47.4, 33.8, 32.8, 27.2, 18.4, 10.9, 0.1. HRMS (ESI) calcd. for $C_{24}H_{42}NaO_3Si_2$ [(M+Na)$^+$] *m/z* 457.2570, found 457.2560.

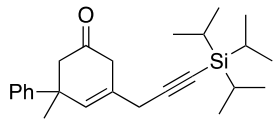
Palladium-Catalyzed Decarboxylative Cyclization of α-Acyloxyketones Having an Allene Moiety in the Tether

General Procedure F: Palladium-Catalyzed Decarboxylative Cyclization



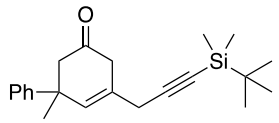
In a sealed tube, starting material **96**, (Cp)Pd(Allyl) (5.0 mol%) and BrettPhos (10 mol%) were dissolved in 1,2-dimethoxymethane (0.01 M). The solution was heated at 100 °C or 120 °C for 15~36 h under nitrogen and then evaporated. The residue was purified by column chromatography to afford desired product.

97a



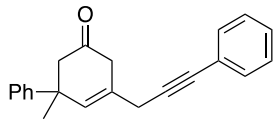
By following general procedure F, the reaction of the corresponding propionate (41.1mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 100 °C delivered 27 mg of compound **97a** as a yellow oil (71%). IR (neat): 2942, 2864 2173, 1719, 1683, 1233 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.31-7.29 (m, 4H), 7.22-7.19 (m, 1H), 6.15 (s, 1H), 3.08 (s, 2H), 2.88 (s, 2H), 2.81 (d, J = 13.9 Hz, 1H), 2.58 (d, J = 13.9 Hz, 1H), 1.48 (s, 3H), 1.10-1.05 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.7, 146.7, 132.4, 130.1, 128.5, 126.5, 125.6, 104.0, 83.9, 53.9, 43.1, 41.9, 29.0, 27.5, 18.6, 11.2. HRMS (EI) calcd. for $C_{25}H_{36}OSi$ [M$^+$] *m/z* 380.2535, found 380.2528.

97b



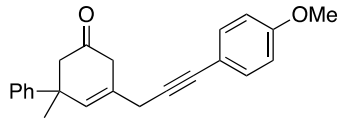
By following general procedure F, the reaction of the corresponding propionate (38.3 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 100 °C delivered 18 mg of compound **97b** as a yellow oil (53%). IR (neat): 2928, 2856, 2173, 1941, 1868, 1718, 1250 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.31-7.30 (m, 4H), 7.23-7.18 (m, 1H), 6.11 (s, 1H), 3.06 (s, 2H), 2.88 (s, 2H), 2.81 (d, J = 14.2 Hz, 1H), 2.58 (d, J = 14.2 Hz, 1H), 1.48 (s, 3H), 0.94 (s, 9H), 0.11 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.5, 146.8, 132.4, 129.9, 128.6, 126.5, 125.6, 103.0, 86.2, 53.9, 43.1, 41.8, 28.9, 27.4, 26.1, 16.5, -4.5. HRMS (EI) calcd. for $C_{22}H_{30}OSi$ [M$^+$] *m/z* 338.2066, found 380.2064.

97d



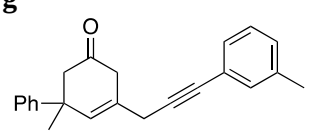
By following general procedure F, the reaction of the corresponding propionate (34.4 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 120 °C delivered 20 mg of compound **97d** as a yellow oil (67%). IR (neat): 3057, 2964, 1716, 1277 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.43-7.41 (m, 2H), 7.33-7.29 (m, 7H), 7.22-7.21 (m, 1H), 6.12 (s, 1H), 3.26 (s, 2H), 2.97 (s, 2H), 2.83 (d, J = 13.7 Hz, 1H), 2.60 (d, J = 13.7 Hz, 1H), 1.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.7, 146.8, 132.4, 131.6, 130.1, 128.6, 128.3, 128.0, 126.5, 125.6, 123.3, 85.6, 83.5, 54.0, 43.2, 41.9, 28.8, 27.1. HRMS (EI) calcd. for $C_{22}H_{20}O$ [M$^+$] *m/z* 300.1514, found 300.1509.

97e



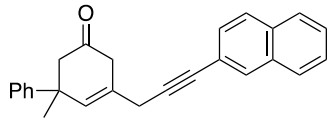
By following general procedure F, the reaction of the corresponding propionate (37.4 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 120 °C delivered 15 mg of compound **97e** as a yellow oil (45%). IR (neat): 2963, 2930, 1716, 1604, 1248 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.37-7.32 (m, 6H), 7.22 (q, J = 4.6 Hz, 1H), 6.83 (d, J = 7.6 Hz, 2H), 6.11 (s, 1H), 3.81 (s, 3H), 3.24 (s, 2H), 2.96 (s, 2H), 2.83 (d, J = 13.9 Hz, 1H), 2.59 (d, J = 13.9 Hz, 1H), 1.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.8, 159.3, 146.8, 133.0, 132.2, 130.3, 128.6, 126.5, 125.7, 115.4, 113.9, 84.0, 83.2, 55.3, 54.0, 43.3, 41.9, 28.8, 27.1. HRMS (EI) calcd. for $C_{23}H_{22}O_2$ [M^+] *m/z* 330.1620, found 330.1626.

97g



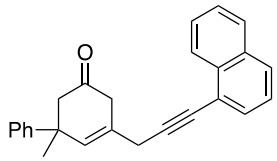
By following general procedure F, the reaction of the corresponding propionate (35.8 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 120 °C delivered 17 mg of compound **97g** as a yellow oil (54%). IR (neat): 3056, 2964, 2920, 1716, 1601, 1279 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.33-7.29 (m, 4H), 7.25-7.17 (m, 4H), 7.11 (d, J = 6.8 Hz, 1H), 6.12 (s, 1H), 3.25 (s, 2H), 2.97 (s, 2H), 2.83 (d, J = 13.6 Hz, 1H), 2.60 (d, J = 13.6 Hz, 1H), 2.33 (s, 3H), 1.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.6, 146.8, 137.9, 132.4, 132.2, 130.1, 128.9, 128.6, 128.6, 128.2, 126.5, 125.7, 123.1, 85.2, 83.6, 54.0, 43.3, 41.8, 28.8, 27.1, 21.2. HRMS (EI) calcd. for $C_{23}H_{22}O$ [M^+] *m/z* 314.1671, found 314.1662.

97h



By following general procedure F, the reaction of the corresponding propionate (39.4 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 120 °C delivered 20 mg of compound **97h** as a yellow oil (57%). IR (neat): 3056, 2964, 1715, 1234 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.94 (s, 1H), 7.82-7.76 (m, 3H), 7.51-7.46 (m, 3H), 7.36-7.31 (m, 4H), 7.23 (td, J = 5.7, 2.9 Hz, 1H), 6.16 (s, 1H), 3.31 (s, 2H), 3.01 (s, 2H), 2.85 (d, J = 14.0 Hz, 1H), 2.62 (d, J = 14.0 Hz, 1H), 1.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.5, 146.8, 133.0, 132.7, 132.5, 131.3, 130.1, 128.6, 128.5, 127.9, 127.7, 127.6, 126.5, 126.5, 125.7, 120.6, 86.0, 83.8, 54.0, 43.3, 41.9, 28.9, 27.2(one aromatic carbon missing). HRMS (EI) calcd. for $C_{26}H_{22}O$ [M^+] *m/z* 350.1671, found 350.1661.

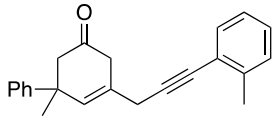
97i



By following general procedure F, the reaction of the corresponding propionate (39.4 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 120 °C delivered 20 mg of compound **97i** as a yellow oil (57%). IR (neat): 3061, 2964, 2250, 1932, 1715, 1231 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm):δ 8.34-8.31 (m, 1H), 7.86-7.81 (m, 2H), 7.67-7.65 (m, 1H), 7.56-7.49 (m, 2H), 7.44-7.40 (m, 1H), 7.38-7.31 (m, 4H), 7.25-7.21 (m, 1H), 6.26 (s, 1H),

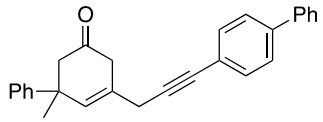
3.42 (s, 2H), 3.04 (s, 2H), 2.87 (d, J = 14.2 Hz, 1H), 2.63 (d, J = 13.7 Hz, 1H), 1.54 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.5, 146.8, 133.4, 133.2, 132.6, 130.3, 130.1, 128.6, 128.4, 128.3, 126.7, 126.5, 126.3, 126.0, 125.7, 125.2, 121.0, 90.6, 81.6, 53.9, 43.3, 42.0, 28.9, 27.4. HRMS (ESI) calcd. $C_{26}H_{22}NaO$ for [M$^+$] *m/z* 373.1568, found 373.1557.

97j



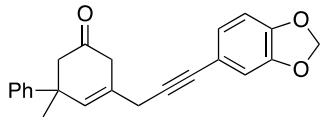
By following general procedure F, the reaction of the corresponding propionate (35.8 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 120 °C delivered 15 mg of compound **97j** as a yellow oil (48%). IR (neat): 3059, 2965, 1717, 1276 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.39 (d, J = 7.3 Hz, 1H), 7.33-7.32 (m, 4H), 7.23-7.19 (m, 3H), 7.13 (dd, J = 8.0, 3.0 Hz, 1H), 6.17 (s, 1H), 3.30 (s, 2H), 2.97 (s, 2H), 2.84 (d, J = 14.2 Hz, 1H), 2.60 (d, J = 14.2 Hz, 1H), 2.42 (s, 3H), 1.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.5, 146.8, 140.0, 132.4, 131.9, 130.2, 129.4, 128.6, 128.0, 126.5, 125.6, 125.5, 123.1, 89.5, 82.4, 54.0, 43.2, 41.9, 28.9, 27.2, 20.8. HRMS (EI) calcd. for $C_{23}H_{22}O$ [M$^+$] *m/z* 314.1671, found 314.1667.

97k



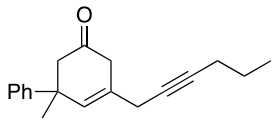
By following general procedure F, the reaction of the corresponding propionate (42.0 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 120 °C delivered 17 mg of compound **97k** as a yellow oil (45%). IR (neat): 3057, 3029, 2964, 1715, 1233 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.60-7.54 (m, 4H), 7.51-7.43 (m, 5H), 7.38-7.30 (m, 4H), 7.24-7.21 (m, 1H), 6.15 (s, 1H), 3.28 (s, 2H), 2.99 (s, 2H), 2.85 (d, J = 14.2 Hz, 1H), 2.61 (d, J = 14.2 Hz, 1H), 1.52 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.5, 146.8, 140.8, 140.4, 132.4, 132.0, 130.1, 128.8, 128.6, 127.6, 127.0, 127.0, 126.5, 125.7, 122.2, 86.3, 83.3, 54.0, 43.3, 41.9, 28.9, 27.2. HRMS (EI) calcd. for $C_{28}H_{24}O$ [M$^+$] *m/z* 376.1827, found 376.1810.

97l



By following general procedure F, the reaction of the corresponding propionate (38.8 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 120 °C delivered 20 mg of compound **102l** as a yellow oil (58%). IR (neat): 2965, 2899, 1717, 1601, 1213 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.33-7.30 (m, 4H), 7.22 (q, J = 4.3 Hz, 1H), 6.94 (dd, J = 8.0, 1.6 Hz, 1H), 6.87 (d, J = 1.8 Hz, 1H), 6.74 (d, J = 7.8 Hz, 1H), 6.10 (s, 1H), 5.96 (s, 2H), 3.22 (s, 2H), 2.95 (s, 2H), 2.83 (d, J = 13.7 Hz, 1H), 2.59 (d, J = 13.7 Hz, 1H), 1.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm):δ 208.6, 147.6, 147.4, 146.8, 132.3, 130.2, 128.6, 126.5, 126.0, 125.7, 116.6, 111.6, 108.4, 101.2, 83.9, 83.2, 54.0, 43.3, 41.9, 28.8, 27.0. HRMS (EI) calcd. for $C_{23}H_{20}O_3$ [M$^+$] *m/z* 344.1412, found 344.1402.

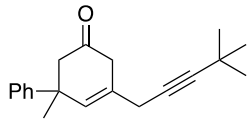
97m



By following general procedure F, the reaction of the corresponding propionate (31.0 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-

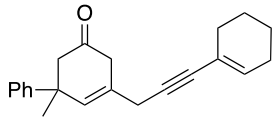
dimethoxyethane at 120 °C delivered 4 mg of compound **97m** as a yellow oil (15%). IR (neat): 2963, 2930, 2872, 1716, 1275 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.32-7.29 (m, 4H), 7.21 (q, J = 4.6 Hz, 1H), 6.04 (s, 1H), 2.99 (d, J = 1.4 Hz, 2H), 2.89 (s, 2H), 2.80 (d, J = 13.7 Hz, 1H), 2.57 (d, J = 14.2 Hz, 1H), 2.19-2.15 (m, 2H), 1.54-1.50 (m, 2H), 1.48 (s, 3H), 0.98 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.9, 146.9, 131.7, 130.9, 128.5, 126.5, 125.7, 83.4, 75.9, 54.0, 43.2, 41.8, 28.9, 26.5, 22.4, 20.8, 13.5. HRMS (EI) calcd. for $C_{19}H_{22}O$ [M^+] *m/z* 266.1671, found 266.1662.

97n



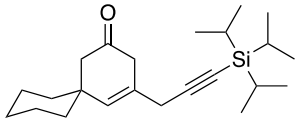
By following general procedure F, the reaction of the corresponding propionate (31.0 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 120 °C delivered 5 mg of compound **97n** as a yellow oil (17%). IR (neat): 2955, 2917, 1659, 1592, 1070 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.32-7.30 (m, 4H), 7.23-7.20 (m, 1H), 6.05 (s, 1H), 2.98 (s, 2H), 2.87 (s, 2H), 2.80 (d, J = 13.7 Hz, 1H), 2.58 (d, J = 13.7 Hz, 1H), 1.49 (s, 3H), 1.22 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 209.0, 147.0, 131.7, 131.0, 128.5, 126.5, 125.6, 92.3, 74.3, 54.0, 43.1, 41.8, 31.2, 28.9, 27.5, 26.3. HRMS (ESI) calcd. for $C_{20}H_{24}NaO$ [$(M+Na)^+$] *m/z* 303.1725, found 303.1712.

97o



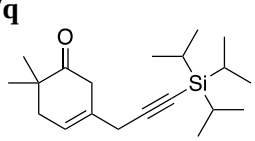
By following general procedure F, the reaction of the corresponding propionate (31.0 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 100 °C delivered 11 mg of compound **97o** as a yellow oil (36%). IR (neat): 3055, 3024, 2930, 2861, 1716, 1268 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.35-7.29 (m, 4H), 7.23-7.19 (m, 1H), 6.07-6.06 (m, 1H), 6.04 (s, 1H), 3.13 (s, 2H), 2.90 (s, 2H), 2.80 (d, J = 14.2 Hz, 1H), 2.57 (d, J = 14.2 Hz, 1H), 2.13-2.07 (m, 4H), 1.65-1.57 (m, 4H), 1.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 208.7, 146.9, 134.2, 132.0, 130.5, 128.6, 126.5, 125.7, 120.6, 85.3, 82.6, 54.0, 43.2, 41.8, 29.4, 28.8, 27.0, 25.6, 22.3, 21.5. HRMS (ESI) calcd. for $C_{22}H_{24}NaO$ [$(M+Na)^+$] *m/z* 327.1725, found 327.1715.

97p



By following general procedure F, the reaction of the corresponding propionate (33.4 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 120 °C delivered 24 mg of compound **97p** as a yellow oil (63%). IR (neat): 2927, 2863, 2174, 1719, 1462, 1020 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 6.06 (s, 1H), 2.99 (s, 2H), 2.83 (s, 2H), 2.37 (s, 2H), 1.56-1.37 (m, 8H), 1.34-1.22 (m, 2H), 1.11-1.03 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 210.0, 131.9, 128.7, 104.3, 83.7, 51.5, 42.5, 39.0, 37.8, 27.4, 25.6, 21.7, 18.6, 11.3. HRMS (ESI) calcd. for $C_{23}H_{38}NaOSi$ [$(M+Na)^+$] *m/z* 381.2590, found 381.2578.

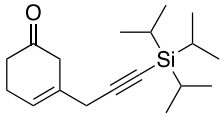
97q



By following general procedure F, the reaction of the corresponding propionate (36.3 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 100 °C delivered 23 mg of compound **97q** as a yellow oil (71%). IR (neat): 2942, 2865,

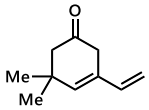
2172, 1717 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, rt, δ/ppm): δ 5.76 (br, 1H), 2.98 (s, 2H), 2.93 (s, 2H), 2.28-2.27 (m, 2H), 1.13 (s, 6H), 1.07-1.05 (m, 21H). ^{13}C NMR (126 MHz, $CDCl_3$, rt, δ/ppm): δ 213.4, 130.6, 121.1, 104.3, 83.2, 43.4, 40.7, 40.3, 27.4, 24.2, 18.6, 11.2. HRMS (ESI) calcd. for $C_{20}H_{34}NaOSi$ [(M+Na)$^+$] *m/z* 341.2277, found 341.2272.

97r



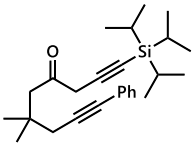
By following general procedure F, the reaction of the corresponding propionate (33.4 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 100 °C delivered 5 mg of compound **102r** as a yellow oil (17%). IR (neat): 2942, 2864, 2173, 1720, 1463, 1019 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 5.94 (t, J = 1.6 Hz, 1H), 3.00 (s, 2H), 2.88 (s, 2H), 2.47 (br, 4H), 1.09-1.07 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$, rt, δ/ppm): δ 209.9, 131.2, 122.3, 104.1, 83.5, 42.6, 38.3, 27.5, 24.8, 18.6, 11.3. HRMS (ESI) calcd. for $C_{18}H_{30}NaOSi$ [(M+Na)$^+$] *m/z* 313.1964, found 313.1956.

103



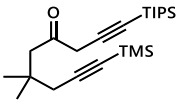
By following general procedure F, the reaction of the corresponding propionate (37.6 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 100 °C delivered compound **103** as a yellow oil (43%). It was not purified, and yields was determined by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm) δ 6.39 (dd, J = 17.4, 11.0 Hz, 1H), 5.76 (s, 1H), 5.08-5.03 (m, 2H), 2.94 (s, 2H), 2.38 (s, 2H), 1.78-1.62 (m, 2H), dimethyl group was not assigned.

109b



By following general procedure F, the reaction of corresponding propionate (43.9 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and BrettPhos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane at 100 °C delivered 24 mg of compound **109b** as yellow oil (61%). IR (neat): 2944, 2866, 1713, 1464, 1240, 883 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): δ 7.39-7.37 (m, 2H), 7.27-7.25 (m, 3H), 3.29 (s, 2H), 2.79 (s, 2H), 2.49 (s, 2H), 1.15 (s, 6H), 1.10-1.01 (m, 21H). ^{13}C NMR (126 MHz, $CDCl_3$, rt, δ/ppm): δ 203.6, 131.5, 128.2, 127.6, 123.8, 100.3, 87.7, 86.0, 82.8, 50.0, 37.1, 33.9, 32.2, 27.1, 18.6, 11.2. HRMS (ESI) calcd. for $C_{26}H_{38}NaOSi$ [(M+Na)$^+$] *m/z* 417.2590, found 417.2575

109c



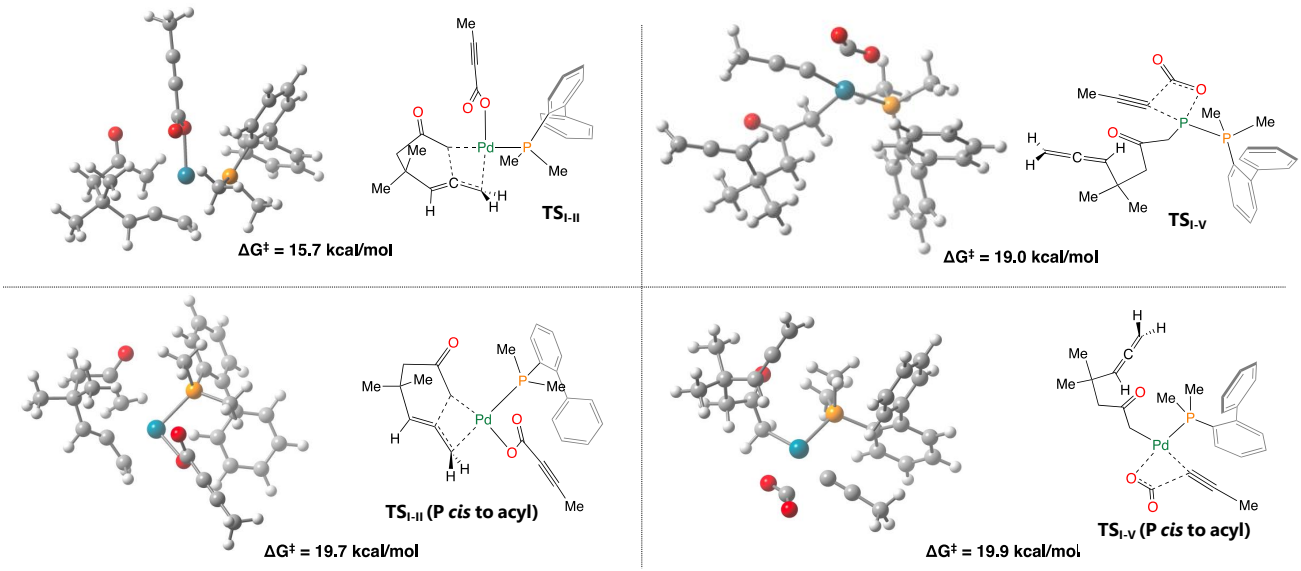
By following general procedure F, the reaction of corresponding propionate (43.5 mg, 0.1 mmol) in the presence of (Cp)Pd(Allyl) (1.1 mg, 0.005 mmol) and Brettphos (5.4 mg, 0.01 mmol) in 10 mL 1,2-dimethoxyethane delivered 21 mg of compound **109c** as yellow oil (54%). IR (neat): 2959, 2866, 2174, 1724, 1464, 1249 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$, rt, δ/ppm): δ 3.28 (s, 2H), 2.71 (s, 2H), 2.30 (s, 2H), 1.09-1.08 (m, 21H), 0.14 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$, rt, δ/ppm): δ 203.6, 104.9, 100.3, 86.8, 85.9, 50.0, 37.0, 33.4, 32.4, 27.0, 18.6, 11.2, 0.1. HRMS (ESI) calcd. for $C_{23}H_{42}NaOSi_2$ [(M+Na)$^+$] *m/z* 413.2672, found 413.2658.

Computational Studies of the Reaction

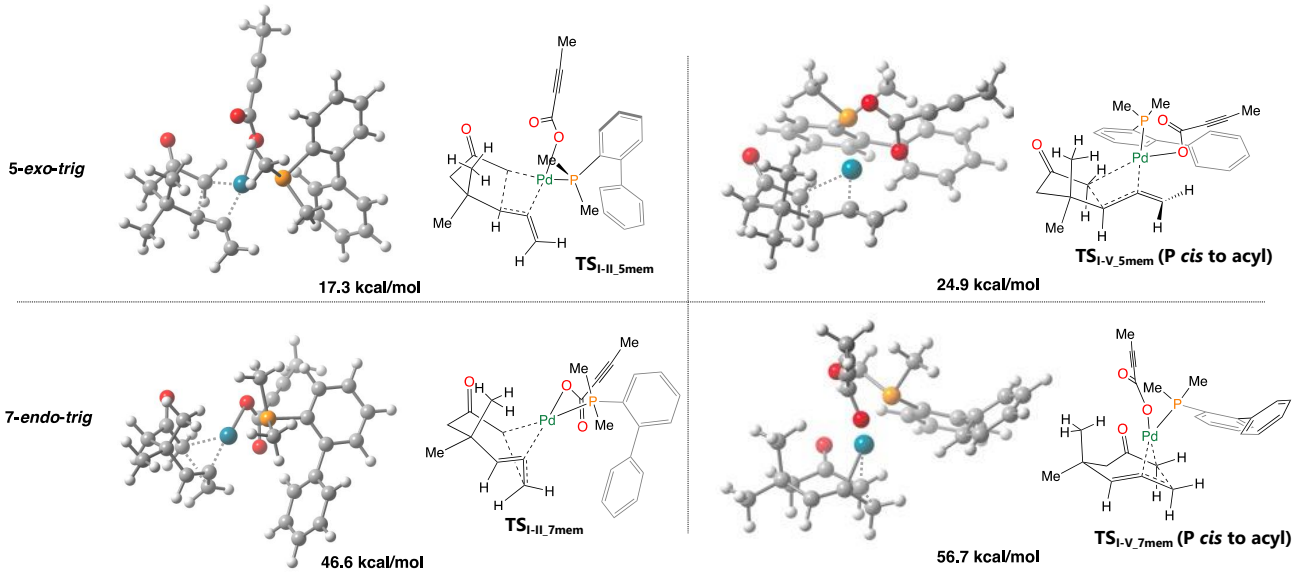
General computational details

All calculation reported in the present study were carried out using density functional theory with the B3LYP or M06-2x functional, as implemented in the Gaussian 16, Revision C. 01. For ease, a model complexes X were used instead of Y and the structures of them are described in Figure SX. Geometry optimization calculations were performed at the B3LYP/BS1 level of the theory under the condition of tight SCF convergence criteria (scf=tight) with an ultrafine integration grid (int=(grid=ultrafine)). BS1 refers to the basis sets employed, which were LANL2DZ for Pd atom and 6-31G(d) basis sets for all other atoms. After optimization of structures, frequency calculations were performed at the same level of the theory to confirm that the obtained structure were either a stationary point (no imaginary frequencies) or a transition state (one imaginary frequency). The IRC calculations were performed for each transition state structure to confirm the transition state connects the reaction pathway between the starting materials and the products. Thermal corrections to the Gibbs energy at 373K (100 °C) were calculated by frequency calculation. Single-point energy calculation were performed for all optimized geometries at the M06-2x/BS2 level of theory with solvents effects simulated by a polarizable continuum model (PCM) solvation model (THF). BS2 refers to the basis sets employed, which were SDD pseudopotential for Pd atom and 6-311+G(d,p) basis sets for all other atoms.

Key transition structures (insertion vs. decarboxylation) and their energies

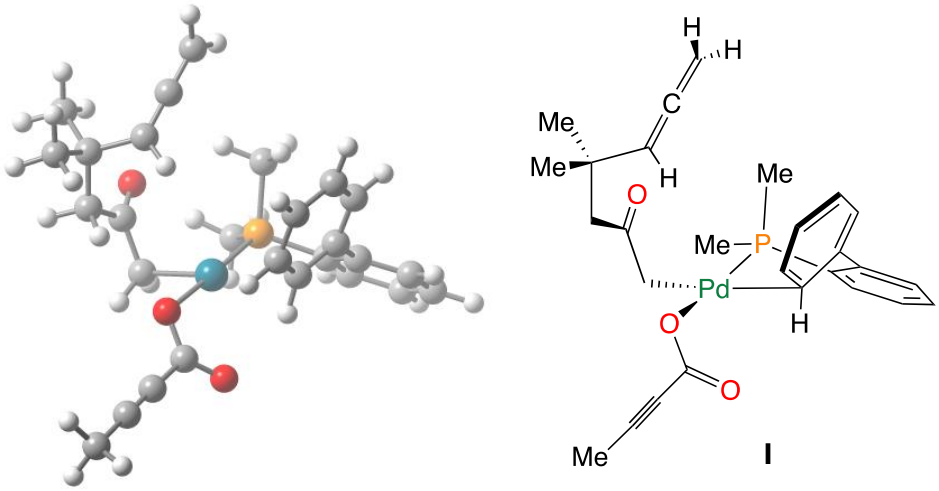


Key transition structures (regioselectivity) and their energies



Detailed information for calculated structures

I



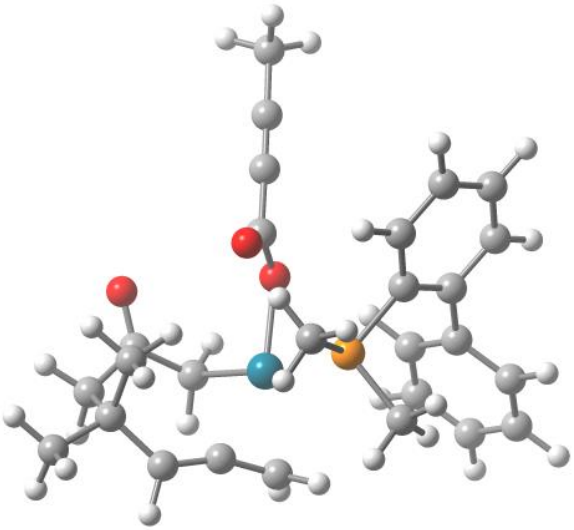
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.85097703
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 342.77
Entropy [cal/mol•K]: 233.737

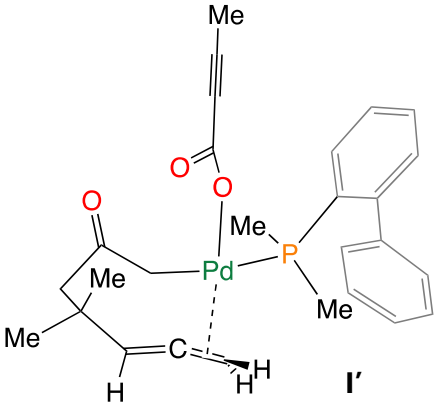
Pd	0.08754400	0.52511800	-0.62803400
P	-1.59836600	-0.97486100	-1.08771700
C	1.87349700	-1.41925100	-1.70495400
C	-1.72876900	-1.63161300	-2.80064500
C	-1.48549000	-2.52328300	-0.09241600
C	-3.24815500	-0.25036900	-0.69519500
C	3.17902300	-1.25223600	-0.92757600
O	1.36815200	-2.51980900	-1.93577800
H	-0.79369100	-2.16595700	-2.99270500
H	-1.83836500	-0.82124300	-3.52679800

H	-2.56736900	-2.32872700	-2.89630300
H	-2.32449400	-3.19037500	-0.31823600
H	-0.54041100	-3.00889100	-0.35355100
H	-1.47999300	-2.28631700	0.97336800
C	-4.29615300	-0.29341100	-1.62754700
C	-3.47922100	0.33727600	0.57183900
C	3.52946300	-2.30649600	0.15728800
H	3.98489000	-1.24499800	-1.67939500
H	3.17827200	-0.24921900	-0.48365500
C	-5.55888900	0.21125100	-1.31617800
H	-4.13536000	-0.72714000	-2.60849200
C	-4.76032600	0.81763900	0.87667900
C	-2.40521300	0.45440600	1.60191800
C	2.41062900	-2.33585800	1.19751000
C	-5.79434800	0.76078000	-0.05713200
H	-6.35365200	0.16924000	-2.05558800
H	-4.93261600	1.26257200	1.85268800
C	-1.32083300	1.33989600	1.42418000
C	-2.47905700	-0.29676000	2.78355100
C	1.82514600	-3.40149100	1.68203200
H	2.10969200	-1.36013800	1.58710700
H	-6.77512100	1.15334100	0.19627400
C	-0.32233100	1.43581400	2.40537400
H	-1.30878700	2.05075900	0.59173900
C	-1.48002400	-0.19618800	3.75457500
H	-3.31662400	-0.97294500	2.93334300
C	1.23895800	-4.46267900	2.17575900
C	-0.39514900	0.66250000	3.56443000
H	0.50373800	2.12136500	2.25184700
H	-1.54853100	-0.79488700	4.65895500
H	0.33532500	-4.87747200	1.73169500
H	1.63416400	-4.98225800	3.04745500
H	0.38122400	0.73746000	4.32037900
C	2.34478300	4.07089800	-0.20348100
C	1.27770900	3.08504300	-0.35346500
C	3.20567300	4.91490600	-0.08437200
O	1.67083900	1.85199000	-0.22443600
O	0.11443000	3.45165800	-0.57010200
C	4.23992000	5.93462300	0.05356300
H	5.15641400	5.52372100	0.49438700
H	4.50168100	6.35873700	-0.92380500
H	3.90037500	6.76107900	0.68999800
C	1.25299300	-0.15937800	-2.20236100
H	1.94622800	0.67463000	-2.31276900
H	0.63570800	-0.31022300	-3.08720800
C	4.81260600	-1.81766900	0.87284500
H	5.63798800	-1.71161100	0.15752700
H	4.65825900	-0.84490000	1.35485600
H	5.11843900	-2.53414700	1.64333000
C	3.79018700	-3.69360200	-0.45286800
H	2.90689600	-4.06391700	-0.97477800
H	4.61806200	-3.63770200	-1.17060500

H	4.06898400	-4.41154100	0.32666200

I'





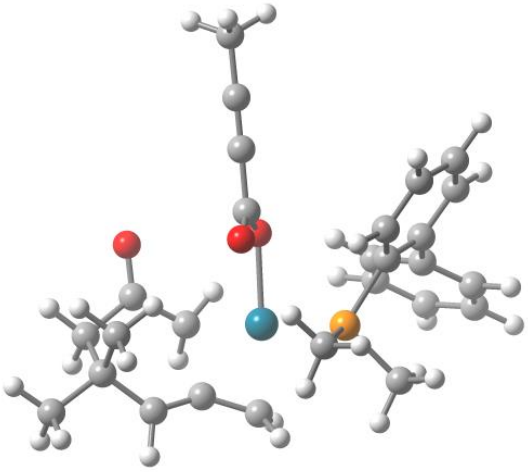
I'

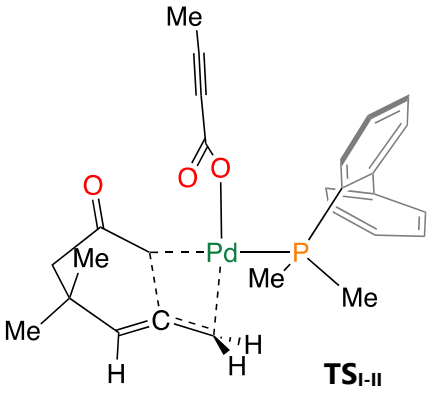
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.85039166
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 342.703
Entropy [cal/mol•K]: 223.642

Pd	0.98156100	-0.12563900	-0.50956200
P	-0.27187800	1.95729600	-0.16248200
C	2.43863600	-2.74279500	0.20589500
C	0.60654400	2.96595900	1.10667500
C	-0.37651400	3.14610300	-1.58443900
C	-2.02073900	1.84504100	0.41895400
C	3.94527900	-2.56785200	0.44641400
O	1.80713100	-3.48890500	0.94075200
H	1.60355800	3.19440300	0.71467400
H	0.72441000	2.35685700	2.00518000
H	0.09034100	3.90464800	1.33375400
H	-0.92604100	4.04727600	-1.29325900
H	0.63290500	3.43787800	-1.89094300
H	-0.87896100	2.68034900	-2.43435200
C	-2.31814500	2.22580600	1.73714800
C	-3.07573000	1.42272600	-0.42848300
C	4.44652100	-1.14861800	0.85145800
H	4.20397400	-3.26922900	1.24688800
H	4.48435800	-2.87876100	-0.46009100
C	-3.62997200	2.24221400	2.20920600
H	-1.51888800	2.50260500	2.41371700
C	-4.39084800	1.47186800	0.05883800
C	-2.87389900	0.89054200	-1.81144500
C	4.21949200	-0.17959000	-0.30656300
C	-4.67385900	1.88078200	1.36093100
H	-3.82842400	2.53785600	3.23549600
H	-5.19674800	1.15228600	-0.59605600

C	-2.20964600	-0.33093100	-2.01403700
C	-3.41479600	1.56081000	-2.92097200
C	3.11888800	0.23407000	-0.89994600
H	5.12821100	0.21189500	-0.77273100
H	-5.70171400	1.89688500	1.71309000
C	-2.07476800	-0.85302300	-3.30310700
H	-1.82780400	-0.87737900	-1.15612100
C	-3.27183200	1.03904800	-4.20795700
H	-3.94194200	2.49981900	-2.77093900
C	2.37034100	0.87002800	-1.85430800
C	-2.59792200	-0.16912300	-4.40263400
H	-1.57004700	-1.80547100	-3.44306100
H	-3.69039200	1.57396100	-5.05659300
H	2.22151700	0.41050000	-2.83169100
H	2.22492000	1.94555700	-1.81460300
H	-2.49188500	-0.57950800	-5.40340100
C	-1.36481100	-1.67528000	2.70280700
C	-0.45578200	-0.86411900	1.89944600
C	-2.09673700	-2.33334400	3.40894300
O	0.21950100	0.02683200	2.43631600
O	-0.45164800	-1.16728400	0.63590700
C	-2.97586200	-3.13856100	4.25032600
H	-3.98821200	-3.19000500	3.83060600
H	-2.60122300	-4.16641000	4.33188200
H	-3.05233700	-2.72919700	5.26518100
C	1.77862600	-2.06326400	-0.94995200
H	2.41387700	-1.98613900	-1.83461200
H	0.82341100	-2.54540500	-1.16672600
C	5.97013700	-1.23528000	1.09923500
H	6.18738400	-1.93490400	1.91327500
H	6.50487400	-1.58033400	0.20553000
H	6.37527300	-0.25577000	1.38116100
C	3.75892700	-0.67588300	2.14877700
H	2.67447500	-0.57713600	2.04254200
H	3.95586700	-1.39227100	2.95520400
H	4.15562500	0.29847100	2.45763400

$TS_{I\text{-}II}$





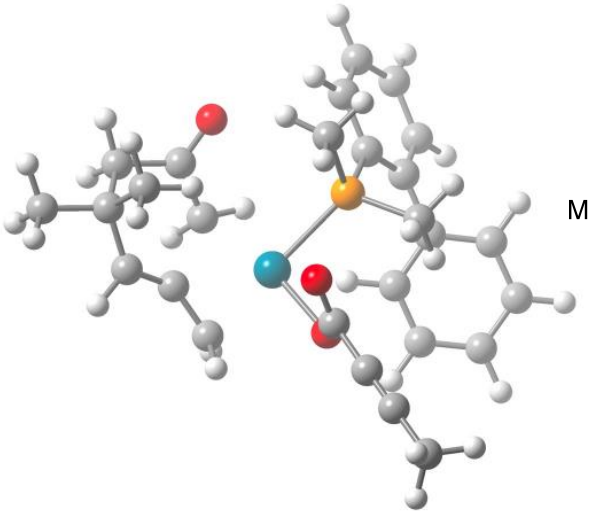
$TS_{I\text{-}II}$

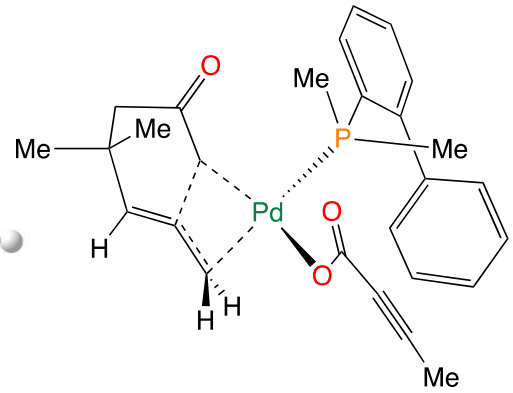
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.82270374
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 341.795
Entropy [cal/mol•K]: 222.707

Pd	-0.77227700	-0.73878200	-0.02809300
P	0.97525300	-0.69581700	1.56067200
C	-3.32349300	0.24156100	-1.70117900
C	0.27588800	-0.12775100	3.16826700
C	1.73510000	-2.31868700	2.02743200
C	2.42880900	0.39507400	1.24194500
C	-4.69996000	0.04993000	-1.08067700
O	-3.02636900	1.28607300	-2.25661200
H	-0.48319400	-0.85484300	3.47489700
H	-0.21280400	0.83532600	3.00808200
H	1.03900000	-0.05783300	3.95055700
H	2.48326500	-2.17966400	2.81498500
H	0.94909200	-2.98450300	2.39674100
H	2.20832800	-2.78295700	1.16047300
C	2.58815400	1.55290100	2.02009500
C	3.40805200	0.08156200	0.26702900
C	-4.69566700	-0.21087100	0.45201600
H	-5.28097800	0.95200000	-1.29821900
H	-5.19098600	-0.80075600	-1.57495400
C	3.71120200	2.36807000	1.88383600
H	1.82377900	1.83614100	2.73320000
C	4.54164900	0.90182600	0.16385300
C	3.29241300	-1.05978300	-0.69154500
C	-3.87364500	-1.45155300	0.76129100
C	4.70130500	2.03216500	0.96357600
H	3.80546500	3.26007600	2.49655900
H	5.29194300	0.65498100	-0.58218200
C	2.29079700	-1.06093000	-1.67666300
C	4.22799000	-2.10687300	-0.67208600
C	-2.66418200	-1.77839000	0.32191400
H	-4.34130500	-2.19730900	1.40838000
H	5.58502300	2.65463200	0.85247700
C	2.22033600	-2.10226000	-2.60533600
H	1.58990900	-0.23195900	-1.72282300
C	4.14971600	-3.14889700	-1.59782000
H	5.01398000	-2.10512100	0.07916300
C	-1.55158500	-2.59960000	0.57364800
C	3.14230100	-3.15056200	-2.56564000
H	1.44853300	-2.08426900	-3.37061800
H	4.87740600	-3.95565900	-1.56528000
H	-1.25813500	-3.35520500	-0.15621700
H	-1.32719500	-2.85035700	1.60871800
H	3.08417300	-3.95796900	-3.29085000
C	0.15797000	3.37381400	-0.78590500
C	-0.23674600	2.12141200	-0.14839300

C	0.47301000	4.43039600	-1.28707700
O	-0.63526600	2.12384800	1.02777700
O	-0.11469700	1.07825700	-0.90576400
C	0.84523100	5.69982200	-1.90188600
H	1.83339000	5.63745700	-2.37459600
H	0.12583800	5.98056600	-2.68118900
H	0.87487200	6.51343800	-1.16654800
C	-2.36250500	-0.90744100	-1.63023900
H	-2.78797800	-1.86589100	-1.92893700
H	-1.47935600	-0.68957500	-2.24231700
C	-6.15042200	-0.45580000	0.90136000
H	-6.77471500	0.41654500	0.67893400
H	-6.58705300	-1.32395700	0.39253200
H	-6.19984400	-0.63552000	1.98228300
C	-4.13264100	1.01528400	1.20769100
H	-3.09505400	1.23513100	0.93859800
H	-4.73872100	1.90353800	0.99002000
H	-4.16455800	0.84279400	2.29008900

$TS_{I\text{-}II}$ P cis to acyl



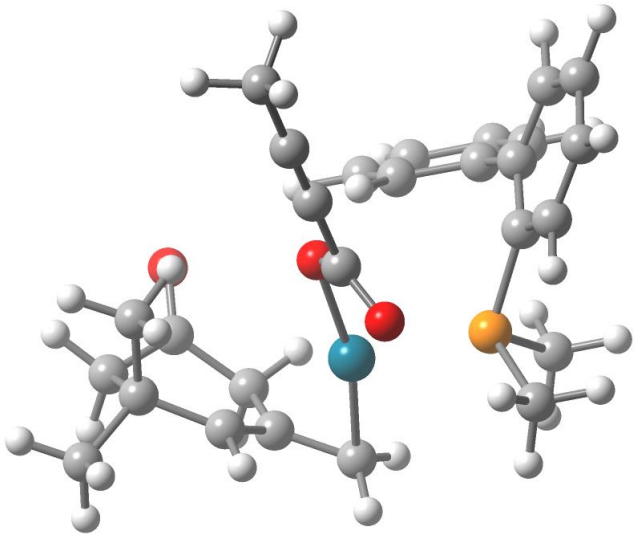


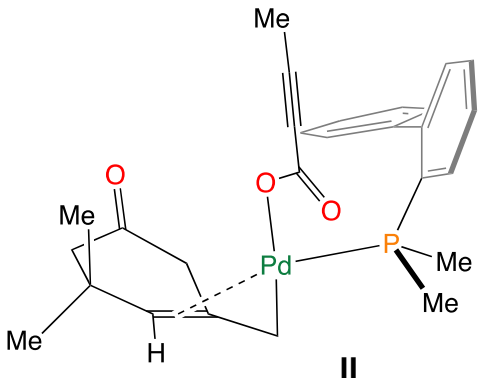
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.82270374
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 341.751
Entropy [cal/mol•K]: 225.851

Pd	0.66535300	0.48543000	-0.60584300
P	-0.63911600	-0.55563500	1.18696500
C	2.73593100	-1.97797400	-0.25225500
C	0.35507000	-0.86929900	2.70784600
C	-1.99072900	0.50644200	1.86741700
C	-1.44941400	-2.17513700	0.78572100
C	4.23712100	-1.82361800	-0.39137300
O	2.25146300	-2.57286300	0.70361100
H	0.70104200	0.11395000	3.04041500
H	1.22336600	-1.48946900	2.47840700
H	-0.24373200	-1.33973400	3.49503600

H	-2.62666000	-0.07091100	2.54590400
H	-1.50882100	1.31972400	2.41516500
H	-2.59598100	0.93195200	1.06736300
C	-0.84950200	-3.35219800	1.26716200
C	-2.63722300	-2.28433400	0.01482500
C	4.70258800	-0.35070000	-0.19081400
H	4.71380900	-2.46729300	0.35452000
H	4.55010400	-2.15355400	-1.39096700
C	-1.40945200	-4.60760600	1.03385400
H	0.07749500	-3.29326300	1.82249200
C	-3.19169000	-3.55860500	-0.19392400
C	-3.35638300	-1.12662700	-0.59665300
C	3.99435000	0.54845800	-1.18746200
C	-2.59347100	-4.71225300	0.30755800
H	-0.91874000	-5.49561100	1.42277500
H	-4.10127200	-3.63454000	-0.78333700
C	-2.73078700	-0.26725400	-1.51286700
C	-4.71185900	-0.90885100	-0.29616300
C	2.72203500	0.54461000	-1.57369300
H	4.61026500	1.30131600	-1.68265500
H	-3.04438900	-5.68316900	0.12047500
C	-3.42908100	0.79390400	-2.09049600
H	-1.68864100	-0.42664600	-1.77584700
C	-5.41245000	0.14852600	-0.87629100
H	-5.20962400	-1.56485200	0.41315000
C	1.75448000	1.33844200	-2.20016800
C	-4.77164500	1.00649700	-1.77315100
H	-2.91917000	1.45484300	-2.78534200
H	-6.45740600	0.30605500	-0.62206700
H	1.29474300	1.00776200	-3.13234200
H	1.75046800	2.41054800	-2.01836300
H	-5.31426900	1.83487500	-2.22034300
C	-0.64584900	4.24580000	0.84460400
C	-0.04717900	2.91666100	0.73365000
C	-1.12152700	5.35273400	0.97121400
O	0.65884800	2.47386100	1.64908800
O	-0.35302400	2.30556900	-0.37090300
C	-1.69622600	6.68495000	1.12511200
H	-2.72552100	6.62508200	1.50034000
H	-1.11986000	7.29158700	1.83435300
H	-1.72501200	7.22091500	0.16840100
C	1.88891100	-1.33572200	-1.30094400
H	2.24396600	-1.48263700	-2.32116000
H	0.86072600	-1.71744500	-1.24581800
C	6.22177800	-0.28643200	-0.44487800
H	6.75855400	-0.93810900	0.25352100
H	6.47050900	-0.60233800	-1.46504600
H	6.59613300	0.73469900	-0.30509400
C	4.40791600	0.12047900	1.25199800
H	3.33624100	0.11012300	1.47010700
H	4.91851900	-0.52406600	1.97844800
H	4.76109300	1.14704500	1.39849500

II



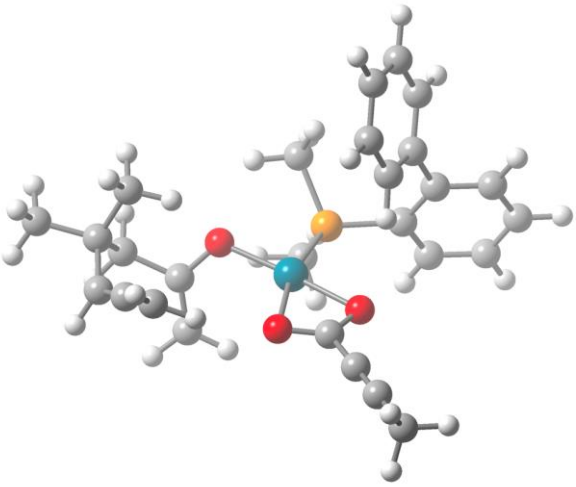


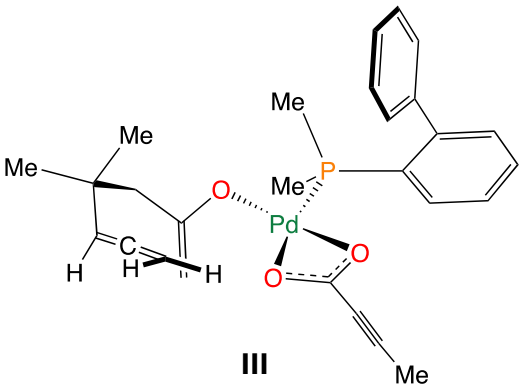
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.91488651
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 344.095
Entropy [cal/mol•K]: 225.057

Pd	0.87247200	-0.01387900	-0.50300600
P	-0.26920300	1.94431200	-0.18222700
C	2.61643400	-2.72235700	0.17613300
C	0.61605300	2.93483800	1.09325100
C	-0.35612300	3.12459200	-1.60077200
C	-2.01648600	1.82971500	0.41231500
C	4.07052900	-2.65198000	0.56050400
O	1.79903800	-3.40072700	0.76447400
H	1.61002700	3.16666600	0.69797700
H	0.73131300	2.31925400	1.98757600
H	0.09397500	3.86993700	1.32229500
H	-0.87520100	4.04268500	-1.30483300
H	0.66446800	3.36941000	-1.91073300
H	-0.87906100	2.67022400	-2.44387700
C	-2.30869600	2.21550700	1.73112100
C	-3.07721100	1.41716300	-0.43216400
C	4.51875100	-1.20414000	0.88281000
H	4.25106600	-3.31523900	1.41172100
H	4.66089200	-3.01558700	-0.29398700
C	-3.62029400	2.24229700	2.20516000
H	-1.50665200	2.48362700	2.40764700
C	-4.39083100	1.47375400	0.05794100
C	-2.87984900	0.88575600	-1.81492500
C	4.11824600	-0.27067300	-0.23560700
C	-4.66846900	1.88462000	1.36048600
H	-3.81434400	2.54006700	3.23164800
H	-5.19947800	1.15830700	-0.59549800
C	-2.21990900	-0.33769700	-2.01586300
C	-3.41607000	1.56022100	-2.92351200
C	3.05555700	-0.46080400	-1.05048500

H	4.64504300	0.68264800	-0.28841500
H	-5.69527600	1.90634500	1.71546600
C	-2.08250600	-0.85712700	-3.30505000
H	-1.83989700	-0.88361800	-1.15706100
C	-3.27131700	1.04013400	-4.21096700
H	-3.94066400	2.50061200	-2.77284700
C	2.36575000	0.62873300	-1.76789400
C	-2.59962600	-0.16927600	-4.40496700
H	-1.58034300	-1.81091200	-3.44610100
H	-3.68606200	1.57717900	-5.06007800
H	2.04969100	0.45390700	-2.79953300
H	2.78544500	1.62401400	-1.61896200
H	-2.49094500	-0.57794600	-5.40618700
C	-1.36338900	-1.68130400	2.73886000
C	-0.46154500	-0.86883100	1.93075800
C	-2.10463200	-2.34341500	3.43011300
O	0.21173600	0.03013500	2.46334800
O	-0.46284200	-1.16873000	0.67505300
C	-2.98988800	-3.14964600	4.26173900
H	-4.00017700	-3.19849000	3.83655400
H	-2.61823800	-4.17880400	4.34254800
H	-3.07203700	-2.74443700	5.27798100
C	2.31779800	-1.86358000	-1.06140200
H	2.68330800	-2.39879500	-1.95197400
H	1.22032100	-1.87598900	-1.23556200
C	6.04127300	-1.21231000	1.09469300
H	6.30946500	-1.88613300	1.91686400
H	6.56900900	-1.54769200	0.19393100
H	6.40939100	-0.21123200	1.35023200
C	3.82406700	-0.70846000	2.17990000
H	2.73435000	-0.67335100	2.08503900
H	4.07644300	-1.36528200	3.02235600
H	4.16476500	0.30328600	2.43084800

III





III

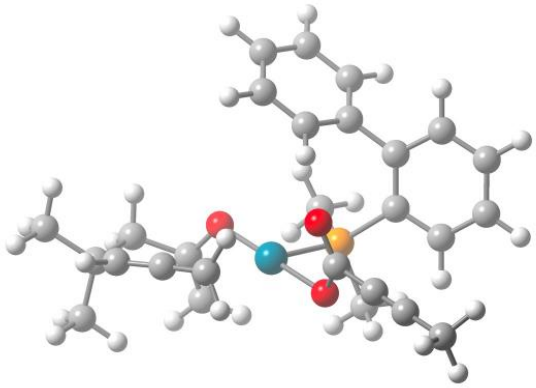
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.81560729
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 342.52

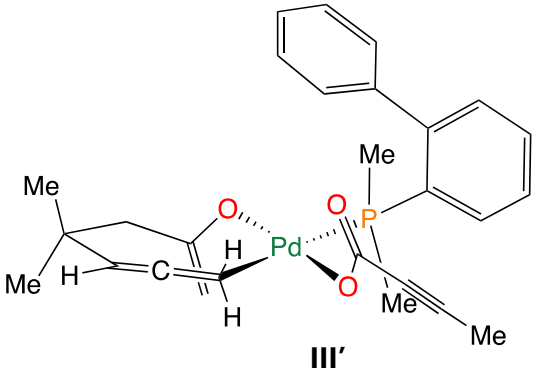
Entropy [cal/mol•K]: 234.039

Pd	0.34848800	0.27749000	-0.57516800
P	-1.13004400	-1.40098300	-0.95729500
C	2.69357700	-1.27193000	-1.28232800
C	-0.72899200	-2.18116200	-2.57584700
C	-0.92328500	-2.78937800	0.22692900
C	-2.91567500	-0.95481300	-1.03005700
C	3.84747000	-2.11835500	-0.76979000
O	1.64874000	-1.25725900	-0.43594600
H	0.31124500	-2.51164800	-2.51226000
H	-0.79332500	-1.45485400	-3.38910200
H	-1.38443200	-3.03298600	-2.78609700
H	-1.48117800	-3.66867700	-0.11189200
H	0.14907900	-2.99909800	0.25446900
H	-1.25857200	-2.50320700	1.22375100
C	-3.52474100	-0.88675300	-2.29544200
C	-3.69884000	-0.69057400	0.12274500
C	4.63852000	-1.56326100	0.46016000
H	3.46456700	-3.11312700	-0.49880300
H	4.55075700	-2.26228100	-1.59893100
C	-4.87991600	-0.59509400	-2.43786600
H	-2.94110100	-1.07051400	-3.19017800
C	-5.06638700	-0.42149500	-0.04376300
C	-3.16362500	-0.67863800	1.51799400
C	5.10850500	-0.14637900	0.14651800
C	-5.65798800	-0.37122500	-1.30422000
H	-5.32054300	-0.54987500	-3.42967900
H	-5.66333100	-0.22528200	0.84230600
C	-2.23048900	0.28663800	1.92812500
C	-3.63925300	-1.60716900	2.45880600
C	4.77523000	0.94168500	0.79233400
H	5.77005700	-0.05271900	-0.71806200
H	-6.71724600	-0.14839700	-1.39780300
C	-1.76438600	0.29975100	3.24493400
H	-1.88798800	1.03678800	1.22195400
C	-3.16982700	-1.59197500	3.77280300
H	-4.36850400	-2.35229400	2.15086600
C	4.41840900	2.03539500	1.41537200
C	-2.22611000	-0.64059200	4.16781600
H	-1.04216300	1.05284900	3.54815600
H	-3.53994000	-2.32347000	4.48630000
H	3.52970300	2.58308000	1.10607500
H	4.98628500	2.42854600	2.25767800
H	-1.85838500	-0.62886000	5.19022100
C	0.02693600	4.21297100	-0.24393200
C	0.21637800	2.78940400	-0.36082500
C	-0.12226800	5.41063800	-0.14432000
O	1.36435900	2.27200800	-0.26095600
O	-0.81299600	2.03993200	-0.56755100
C	-0.29344500	6.85283200	-0.02573900
H	0.12800700	7.22003800	0.91768100
H	0.21997700	7.37310400	-0.84326600
H	-1.35257900	7.13380700	-0.05746300

C	2.74714000	-0.65610900	-2.48165200
H	3.63974500	-0.71278500	-3.09424100
H	1.93388300	-0.03072400	-2.84012200
C	5.88669300	-2.45639000	0.64821400
H	5.59705200	-3.50382600	0.80243000
H	6.54522900	-2.41510300	-0.22834200
H	6.46648500	-2.13225300	1.51989800
C	3.79344100	-1.61223700	1.74356500
H	2.89989900	-0.99233500	1.65687700
H	3.47433900	-2.64224300	1.94575200
H	4.37995300	-1.26359200	2.60137300

III'





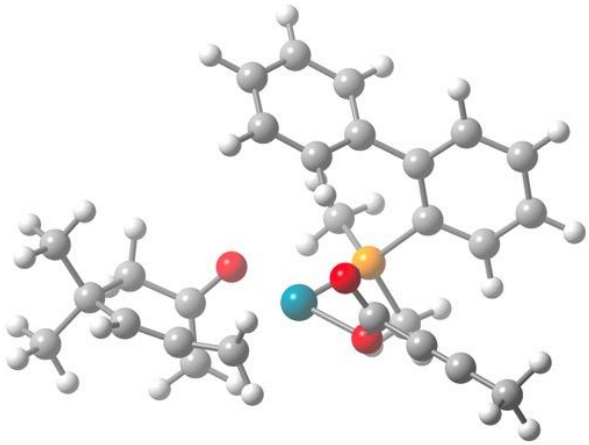
III′

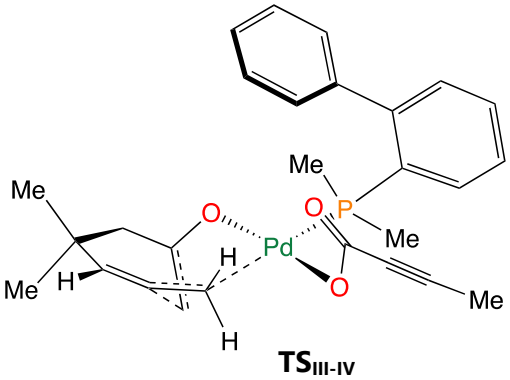
<u>M06/6-311+G(d,p) (PCM, solvent = THF)</u>
Electronic energy [Hartree]: -1741.81599972
<u>B3LYP/6-31G(d)</u>
Total thermal energy [kcal/mol]: 342.339
Entropy [cal/mol•K]: 229.684

Pd	0.53432400	-0.72457400	0.24418400
P	-0.84720500	0.49329600	1.58268700
C	3.04712200	0.40868600	1.14192300
C	-1.11017300	-0.44310200	3.14632000
C	-0.12601300	2.09157100	2.12956900
C	-2.53453000	0.83425000	0.93100600
C	4.34979200	0.75224200	0.43844100
O	1.99200500	0.65290100	0.36073500
H	-0.14626600	-0.51087700	3.65824400
H	-1.44349700	-1.45674400	2.91080000
H	-1.83279300	0.05082800	3.80423400
H	-0.83103900	2.63230800	2.76975300
H	0.79502000	1.87126500	2.67612600
H	0.13062900	2.69719100	1.26046600
C	-3.61627600	0.11820700	1.47228600
C	-2.78365700	1.80232800	-0.07412900
C	5.08828200	-0.42076000	-0.27562800
H	4.12495300	1.52691100	-0.30269000
H	5.06166700	1.18027000	1.15591400
C	-4.92677800	0.37006300	1.07068300
H	-3.44383700	-0.64773000	2.21893000
C	-4.11330500	2.05621200	-0.44392500

C	-1.71263400	2.56327700	-0.78513200
C	4.23359000	-1.27131400	-1.21964400
C	-5.17809800	1.35437800	0.11743000
H	-5.74242400	-0.20048900	1.50558100
H	-4.30010000	2.80285200	-1.21039400
C	-0.81941300	1.90475800	-1.64494200
C	-1.63373900	3.95960100	-0.65539300
C	2.97918600	-1.63459700	-1.23852600
H	4.82205300	-1.75864300	-2.00394200
H	-6.19515400	1.56629800	-0.20081500
C	0.14992800	2.63366500	-2.33754900
H	-0.90328000	0.83046600	-1.78897100
C	-0.66192500	4.68237500	-1.34791400
H	-2.33057500	4.47502500	0.00109100
C	1.75300300	-2.11757200	-1.37876700
C	0.23563800	4.01873900	-2.18827600
H	0.83641800	2.11259700	-2.99888900
H	-0.60618300	5.76160800	-1.23132800
H	1.48067600	-3.06800200	-0.92042500
H	1.03916500	-1.69504700	-2.08759800
H	0.99356300	4.58050600	-2.72780100
C	-2.66243900	-3.20935100	-0.99197700
C	-1.61038700	-2.19786300	-0.96973400
C	-3.53769500	-4.04457500	-1.05256700
O	-1.38414200	-1.50416200	-1.96625500
O	-0.97491400	-2.13907700	0.16923700
C	-4.59178600	-5.04981100	-1.13398200
H	-5.54285300	-4.59944100	-1.44398000
H	-4.33924200	-5.82234100	-1.87075700
H	-4.75282400	-5.54719900	-0.16976400
C	3.01982400	-0.06807000	2.40841800
H	3.93414200	-0.19107600	2.97802000
H	2.09379900	-0.38038200	2.88114500
C	5.70650200	-1.38807500	0.76060700
H	6.42662100	-0.85545600	1.39520100
H	4.93136400	-1.81752700	1.40089000
H	6.23829600	-2.20808300	0.26384500
C	6.22566800	0.20166600	-1.11665400
H	5.82667600	0.85549400	-1.90063200
H	6.88648600	0.80050200	-0.47939300
H	6.83598500	-0.57298300	-1.59701100

$TS_{III\text{-}IV}$



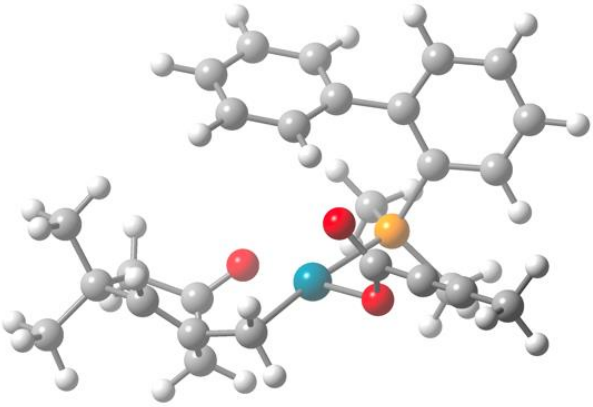


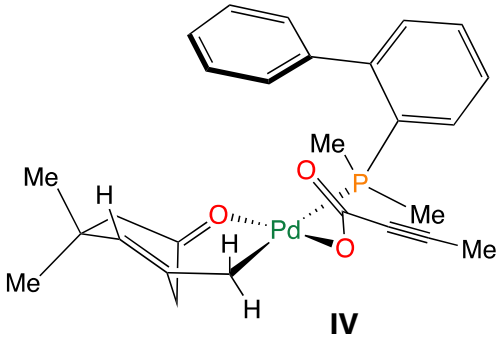
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.79603584
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 341.269
Entropy [cal/mol•K]: 226.281

Pd	0.42409900	-0.78570900	0.43310800
P	-1.03366300	0.50440700	1.65981700
C	3.09667800	-0.01038100	1.14348700
C	-1.46983500	-0.43755600	3.18170700
C	-0.29707200	2.05923900	2.31308900
C	-2.64068300	0.96173900	0.88612400
C	4.35542400	0.68625200	0.66573000
O	1.98024700	0.51537300	0.70416000
H	-0.54521600	-0.58916400	3.74684800
H	-1.86126600	-1.41892100	2.90178100
H	-2.19241600	0.09315000	3.81049500
H	-1.00709100	2.58892400	2.95687200
H	0.59868100	1.79234000	2.88021600
H	0.00450800	2.70206800	1.48532600
C	-3.81638100	0.35805400	1.36356500
C	-2.73198200	1.91021000	-0.16348500
C	5.12936900	-0.19038000	-0.39366500
H	4.05567900	1.63334200	0.20886500
H	5.02973500	0.91456300	1.49944200
C	-5.06744300	0.69907000	0.85214100
H	-3.76539800	-0.38908300	2.14680300
C	-4.00364800	2.25513600	-0.64625800
C	-1.55083400	2.56622100	-0.80335000
C	4.23977800	-1.27352100	-1.00064900
C	-5.16290200	1.66208500	-0.14979800
H	-5.95865400	0.21383300	1.24000100
H	-4.06908800	2.98633500	-1.44690700
C	-0.65465200	1.82494400	-1.59012500
C	-1.36863200	3.95415300	-0.68395400
C	3.09641500	-1.76785600	-0.57481500
H	4.62034100	-1.71840600	-1.92456700
H	-6.13159600	1.94226000	-0.55450300

C	0.41408200	2.46494100	-2.22238600
H	-0.80612200	0.75739300	-1.73054500
C	-0.29723100	4.58714600	-1.31499500
H	-2.06713200	4.53412500	-0.08556000
C	1.82668100	-2.25942900	-0.68404900
C	0.59940100	3.84126500	-2.08425800
H	1.09835100	1.87930300	-2.82993500
H	-0.16492100	5.66071000	-1.20762500
H	1.56379700	-3.19131900	-0.18521500
H	1.28421400	-2.03478100	-1.60563200
H	1.43322700	4.33319800	-2.57833400
C	-2.66823500	-3.15445300	-1.19811300
C	-1.58729300	-2.18334700	-1.05356400
C	-3.56163400	-3.95597300	-1.36144400
O	-1.17678500	-1.54838400	-2.02853400
O	-1.14116600	-2.09528600	0.17059700
C	-4.63659200	-4.92078900	-1.56626600
H	-5.54134200	-4.42757700	-1.94278300
H	-4.34683700	-5.68065800	-2.30253100
H	-4.89894000	-5.43885100	-0.63570300
C	3.21501700	-1.20889200	1.80446400
H	4.17718700	-1.53800500	2.17957800
H	2.34194900	-1.78123400	2.09836900
C	6.36577000	-0.87034700	0.24031700
H	7.06496000	-0.11776500	0.62552900
H	6.08215800	-1.53058900	1.06554100
H	6.89908700	-1.47653900	-0.50152100
C	5.60949100	0.73423200	-1.53414000
H	4.76004200	1.19618800	-2.04905000
H	6.24168300	1.53499200	-1.13160700
H	6.20010500	0.18248200	-2.27549700

IV



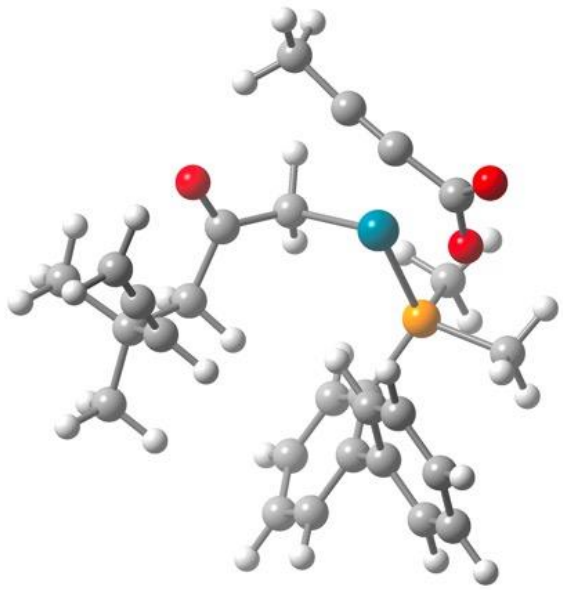


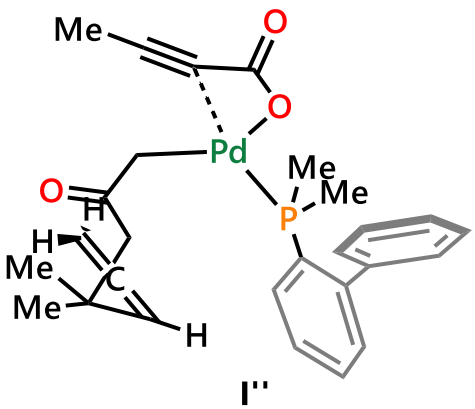
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.85874291
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 343.729
Entropy [cal/mol•K]: 225.63

Pd	0.35610200	-0.90170500	0.66439200
P	-1.30762800	0.56317700	1.67459200
C	3.15492600	0.00876200	1.22246400
C	-2.10385600	-0.40343600	3.03244800
C	-0.68010000	2.05535200	2.57499300
C	-2.71974000	1.21313400	0.67523900
C	4.36379600	0.68785000	0.63435200
O	2.02329300	0.51785000	1.21814500
H	-1.31477100	-0.68134500	3.73866000
H	-2.52034400	-1.32600100	2.61859700
H	-2.87793500	0.15569600	3.56855900
H	-1.48388000	2.57379700	3.10843800
H	0.08258500	1.72957400	3.28943900
H	-0.21171600	2.74100000	1.86560700
C	-4.03327300	0.81658900	0.97517000
C	-2.50911600	2.12614600	-0.38807600
C	4.87690800	-0.20765300	-0.58755300
H	4.08039300	1.68559800	0.29112000
H	5.15288300	0.78600800	1.39046300
C	-5.12646100	1.32345500	0.27262800
H	-4.21719100	0.10256300	1.76976800
C	-3.62323000	2.64334200	-1.06597100
C	-1.15642500	2.56786900	-0.85067800
C	3.80473600	-1.24734100	-0.92728800
C	-4.92203700	2.25176800	-0.74525300
H	-6.13030300	0.99407000	0.52661800
H	-3.45391400	3.34660400	-1.87664600
C	-0.30327100	1.67617000	-1.52171600
C	-0.76086100	3.90718000	-0.70009900
C	3.01479900	-1.82157300	0.01119600
H	3.59306100	-1.41682900	-1.98157600
H	-5.76430300	2.65989200	-1.29738200
C	0.92287700	2.12425000	-2.01937300

H	-0.60706600	0.64383100	-1.67918500
C	0.46939000	4.34677200	-1.19186800
H	-1.42379100	4.60456800	-0.19347900
C	1.66796200	-2.37369400	-0.16968100
C	1.31497200	3.45414100	-1.85471600
H	1.56411800	1.42539800	-2.55030600
H	0.76196500	5.38594200	-1.06423400
H	1.44296700	-3.25281600	0.44005800
H	1.35692400	-2.50518100	-1.20693100
H	2.26797500	3.79783900	-2.24947100
C	-2.64120200	-3.20144800	-1.23133600
C	-1.56310300	-2.23988600	-1.00498600
C	-3.53215200	-3.98942600	-1.46088200
O	-1.12540600	-1.55898800	-1.93433000
O	-1.16743200	-2.21904900	0.23833400
C	-4.60354200	-4.93830000	-1.74457300
H	-5.49272300	-4.42481200	-2.13113900
H	-4.29153000	-5.66821900	-2.50188200
H	-4.90098300	-5.49422000	-0.84688200
C	3.33922200	-1.45264700	1.46919800
H	4.35161900	-1.71911000	1.77909600
H	2.59584700	-1.85573900	2.15937600
C	6.23504100	-0.86938500	-0.25778800
H	7.00145100	-0.11188200	-0.04926600
H	6.17221300	-1.53546300	0.60901300
H	6.57649800	-1.47025400	-1.10789700
C	5.06801100	0.72177000	-1.80271800
H	4.12478400	1.20557500	-2.08000000
H	5.80458300	1.50451000	-1.58597700
H	5.42502700	0.15309900	-2.66950600

I''





I''

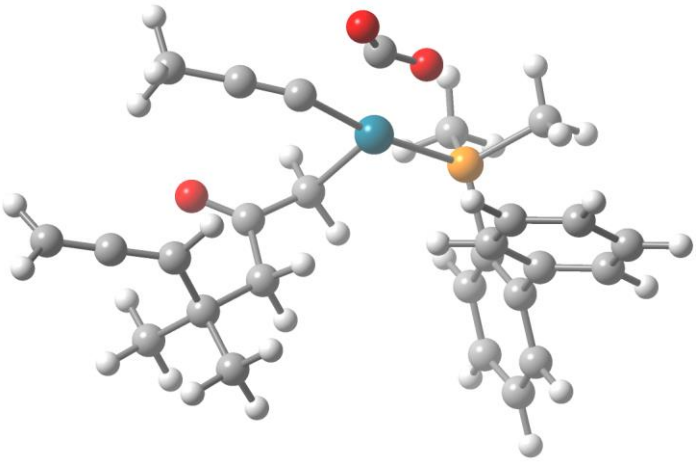
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.84718493
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 342.333

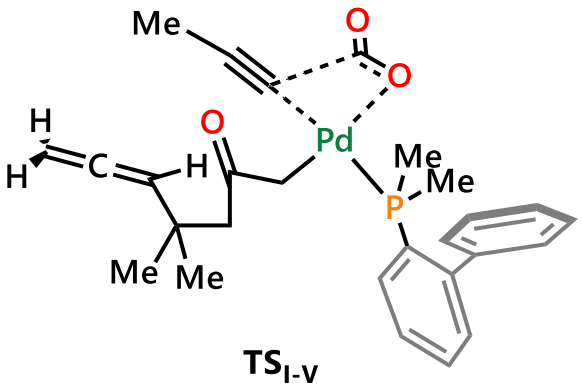
Entropy [cal/mol•K]: 230.228

Pd	0.84045400	-1.36808300	-0.75192900
P	-1.32941600	-1.20293000	-1.45315500
C	1.95910500	1.34905400	-1.13899100
C	-1.44081500	-1.59161600	-3.25543400
C	-2.35938800	-2.53799600	-0.71629000
C	-2.25354200	0.38095400	-1.24770500
C	0.96711200	2.47472500	-0.83125600
O	3.12130600	1.38689600	-0.74463800
H	-1.06916500	-2.61274800	-3.38313600
H	-0.80567600	-0.93004800	-3.84856700
H	-2.47269000	-1.53614900	-3.61777700
H	-3.39902300	-2.43963200	-1.04494900
H	-1.94641700	-3.49365600	-1.04948300
H	-2.29870500	-2.51397300	0.37046300
C	-2.42193000	1.19377600	-2.38346600
C	-2.80087700	0.81018200	-0.00936800
C	1.30376500	3.47513600	0.30722200
H	0.84341900	3.03962700	-1.76967500
H	-0.01441900	2.02143700	-0.64365000
C	-3.12446100	2.39612300	-2.32626900
H	-2.00965700	0.88532800	-3.33760600
C	-3.51964700	2.01795200	0.01808800
C	-2.68388700	0.05640700	1.27398300
C	1.39859600	2.71636400	1.62925200
C	-3.68285300	2.80749000	-1.11813500
H	-3.23669300	2.99924300	-3.22263500
H	-3.93909900	2.34354400	0.96553100
C	-1.43802800	-0.27807300	1.82645100
C	-3.84812700	-0.29616200	1.97831700
C	2.43644800	2.65685600	2.42364600
H	0.48815600	2.19313200	1.93253200
H	-4.23662500	3.73998300	-1.05536000
C	-1.35709800	-0.97030300	3.03566000
H	-0.52424800	-0.00298300	1.30857200
C	-3.76698200	-0.98389700	3.18873100
H	-4.82003400	-0.04604100	1.56083600
C	3.46904600	2.59150900	3.22368500
C	-2.52060200	-1.32656900	3.71890500
H	-0.38339000	-1.23582200	3.43557600
H	-4.67785600	-1.25907000	3.71364100
H	4.21556200	1.80558700	3.12423400
H	3.62680300	3.31976400	4.01766200
H	-2.45661400	-1.87062400	4.65692300
C	2.56736100	-2.59261400	0.33543300
C	1.48167000	-3.38322700	0.99010800
C	3.44272600	-2.00314300	-0.28591500
O	0.32599300	-3.00517800	0.52693800
O	1.72637900	-4.23972200	1.81893700
C	4.59948500	-1.39186800	-0.93199400
H	4.71347100	-1.76452900	-1.95729200
H	4.47196600	-0.30470500	-0.96292200
H	5.51194200	-1.63683400	-0.37588800

C	1.44599900	0.22943600	-1.98716900
H	0.63222000	0.56087900	-2.63785800
H	2.25167600	-0.20807400	-2.58499600
C	0.11394800	4.45849800	0.42090700
H	-0.02788200	5.00783800	-0.51857800
H	-0.82254900	3.93431400	0.64766900
H	0.29530000	5.18852000	1.21758300
C	2.58215200	4.27534400	0.00441000
H	3.45175300	3.62080900	-0.05595600
H	2.47703500	4.80489500	-0.95104600
H	2.75729300	5.02376700	0.78548100

$TS_{I\text{-}V}$



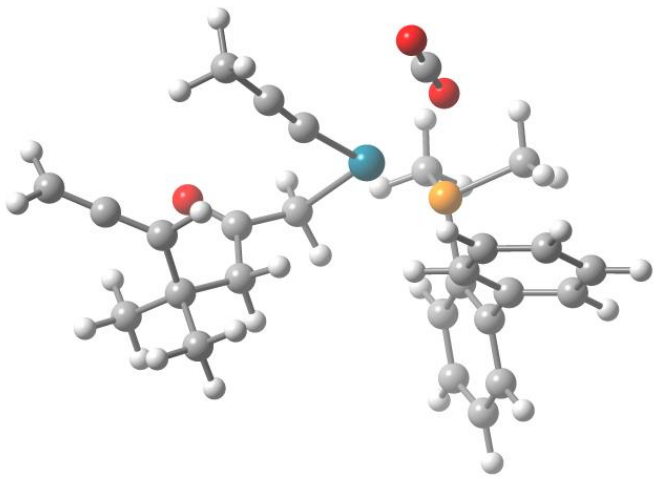


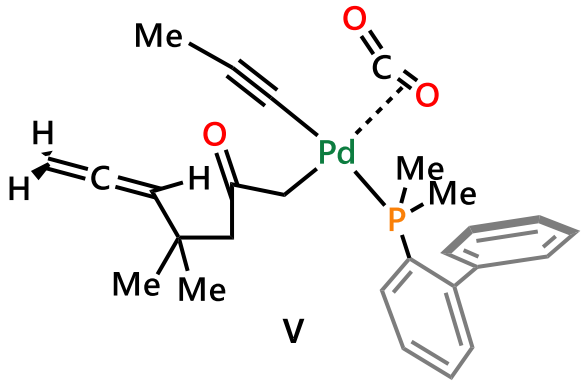
<u>M06/6-311+G(d,p) (PCM, solvent = THF)</u>
Electronic energy [Hartree]: -1741.81587804
<u>B3LYP/6-31G(d)</u>
Total thermal energy [kcal/mol]: 340.869
Entropy [cal/mol•K]: 236.77

Pd	-0.02100900	-1.10536900	0.90541500
P	2.12393700	-0.35770200	1.52071600
C	-2.16469100	1.02061100	1.09142900
C	2.26432300	-0.21972100	3.35870800
C	3.44557300	-1.59450800	1.14781000
C	2.74172800	1.26635700	0.88643400
C	-2.03557500	1.69971100	-0.27544100
O	-3.24000700	0.86941100	1.65339500
H	2.08959400	-1.21906900	3.76934100
H	1.49168600	0.44104000	3.75977200
H	3.25180100	0.13129700	3.67593500
H	4.42372300	-1.24093200	1.48985700
H	3.18944900	-2.52261700	1.66838100
H	3.48456300	-1.80262500	0.07816200
C	2.77524500	2.36043700	1.76852900
C	3.16588100	1.45866600	-0.45413200
C	-3.32595800	2.15146200	-1.00114000
H	-1.37673900	2.57205000	-0.14515700
H	-1.47324000	1.01032700	-0.92061500
C	3.23139700	3.61479300	1.36334300

H	2.45133600	2.23961300	2.79613400
C	3.64219600	2.72371300	-0.83388700
C	3.14873700	0.39201600	-1.50026800
C	-4.20678300	0.93527300	-1.28712700
C	3.67632400	3.79549000	0.05629600
H	3.24305300	4.43877700	2.07117900
H	3.96995900	2.86347900	-1.86011500
C	1.95111500	-0.21357200	-1.91089700
C	4.34478300	0.01482800	-2.13382700
C	-5.51320100	0.89557300	-1.23073700
H	-3.67654800	0.03634800	-1.60952000
H	4.04046700	4.76426300	-0.27416600
C	1.95274300	-1.18880900	-2.90972400
H	1.01363700	0.08246600	-1.44912700
C	4.34588500	-0.95900800	-3.13288400
H	5.27855900	0.47876600	-1.82671800
C	-6.81977100	0.84517000	-1.16964300
C	3.14942800	-1.56672000	-3.52104700
H	1.01629100	-1.65025200	-3.20991700
H	5.28182500	-1.24523600	-3.60523100
H	-7.33886900	0.54008800	-0.26214200
H	-7.44504300	1.10913000	-2.02148300
H	3.14958800	-2.32785300	-4.29627600
C	-1.81188000	-2.02173200	0.45032700
C	-0.61740300	-3.46203200	-0.38612900
C	-3.02916200	-2.13245700	0.61272800
O	0.48863800	-3.09847700	-0.00461100
O	-1.25189500	-4.23995100	-1.01077000
C	-4.46743300	-2.22100300	0.79578500
H	-4.74086900	-2.94929700	1.56864900
H	-4.83312900	-1.23192700	1.10356700
H	-4.97971900	-2.48992200	-0.13621800
C	-0.87124900	0.59998100	1.73739900
H	-0.13422600	1.40694400	1.65706900
H	-1.05454400	0.34442800	2.78521200
C	-2.90162800	2.74527200	-2.36759000
H	-2.21762600	3.59288100	-2.23006400
H	-2.39217000	1.99873800	-2.98929800
H	-3.77921500	3.09912800	-2.91930700
C	-4.07423900	3.22638500	-0.19432600
H	-4.38633800	2.83430700	0.77531100
H	-3.42747700	4.09798500	-0.03204100
H	-4.96462700	3.56526800	-0.73506200

V



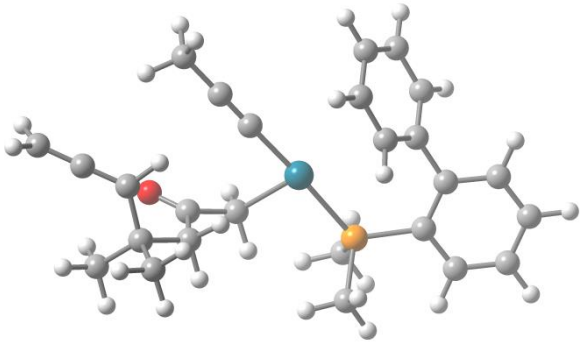


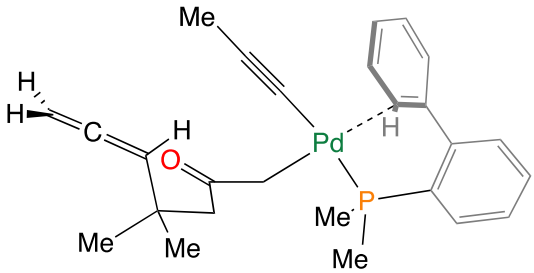
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.83829351
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 342.007
Entropy [cal/mol•K]: 245.464

Pd	0.01698100	-0.79093900	-0.99997900
P	-2.16615700	0.04655700	-1.57220700
C	2.25865500	1.31761100	-0.92523800
C	-2.23507600	0.57604400	-3.34320400
C	-3.51930000	-1.21811300	-1.53263200
C	-2.85074200	1.48976400	-0.63550700
C	2.31673900	1.66827200	0.56384700
O	3.23013200	1.36481200	-1.66076100
H	-2.00055000	-0.30395500	-3.95039700
H	-1.47249000	1.33136300	-3.55118100
H	-3.21991400	0.95761100	-3.63213600
H	-4.46930200	-0.79029700	-1.86917600
H	-3.23619300	-2.04129300	-2.19627900
H	-3.63754900	-1.61485300	-0.52292700
C	-2.98530900	2.72884300	-1.28415000
C	-3.23464600	1.39015200	0.72677200
C	3.70343100	1.91957300	1.20694200
H	1.69441900	2.56668200	0.70481500
H	1.79990500	0.86526300	1.10407500
C	-3.50311800	3.84635500	-0.62852400
H	-2.69199500	2.83273900	-2.32273400
C	-3.77510400	2.51958000	1.36071000
C	-3.10251400	0.14471300	1.54480700
C	4.54173000	0.64807800	1.10244800
C	-3.90979700	3.73910400	0.69878100
H	-3.59170100	4.78996300	-1.15958300
H	-4.07275400	2.43402800	2.40208100
C	-1.84326000	-0.38401600	1.86944800
C	-4.24835900	-0.47871500	2.06637600
C	5.79664000	0.56825800	0.74387800
H	4.02178500	-0.27223900	1.37468300

H	-4.32127100	4.59807300	1.22148700
C	-1.73505700	-1.51697300	2.67888400
H	-0.94476600	0.09852900	1.49654400
C	-4.13975200	-1.61335600	2.87186700
H	-5.22862000	-0.07342000	1.82879600
C	7.04933900	0.47340100	0.37513500
C	-2.88157500	-2.13699100	3.17905600
H	-0.75029900	-1.90509400	2.92524900
H	-5.03768800	-2.08589900	3.26107300
H	7.32456400	0.31203900	-0.66599700
H	7.86765500	0.55779100	1.08905800
H	-2.79591200	-3.01723300	3.81042100
C	1.79508700	-1.59519600	-0.61724100
C	-0.10628600	-3.92756500	-0.17644300
C	2.83511400	-2.21481900	-0.43085600
O	-0.86604300	-3.12353400	-0.57944900
O	0.58585800	-4.76931400	0.23111100
C	4.09147100	-2.93684500	-0.22823800
H	4.33163100	-3.57381100	-1.08946800
H	4.92782900	-2.23872200	-0.09356000
H	4.05256100	-3.58489000	0.65718600
C	0.88511600	1.02379300	-1.47932600
H	0.16311200	1.76607700	-1.11811100
H	0.93342100	1.01650800	-2.57159000
C	3.46947900	2.19723000	2.71251700
H	2.81885200	3.07037500	2.85281000
H	2.99651100	1.34132500	3.20986100
H	4.42117600	2.39571400	3.21763200
C	4.40758000	3.13205200	0.57518400
H	4.59035000	2.96306700	-0.48711000
H	3.78859800	4.03132700	0.68876100
H	5.36736600	3.32097200	1.06890100

VI





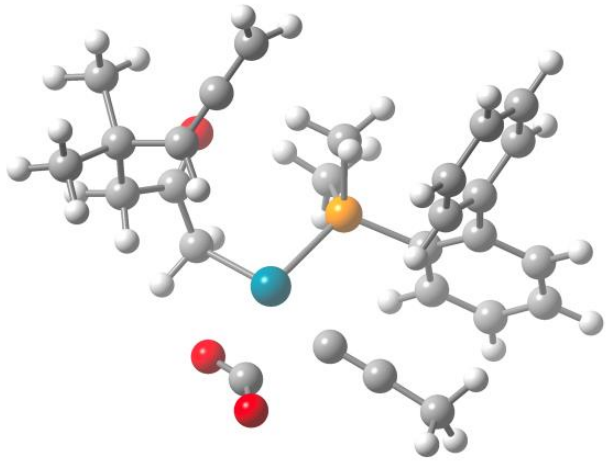
VI

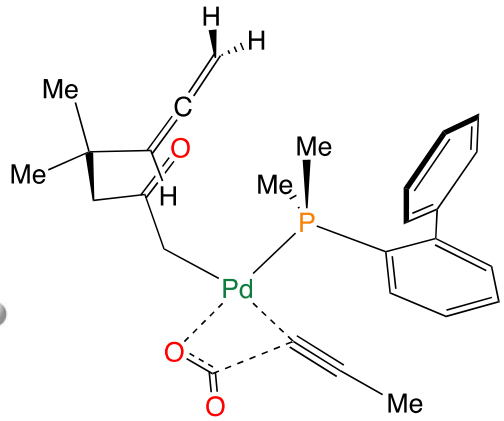
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1553.27433073
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 331.440
Entropy [cal/mol•K]: 219.911

Pd	0.19998500	0.20354400	-0.29905600
P	1.89755600	-1.49916200	-0.37635600
C	-2.59015600	-0.94650700	-0.98754000
C	1.46031100	-2.97771000	0.65311500
C	2.15850400	-2.24475500	-2.05246300
C	3.63109100	-1.11747200	0.14988700
C	-2.96154900	-1.42520000	0.41850500
O	-3.42006100	-0.62052600	-1.81928400
H	0.45936900	-3.31840300	0.37112100
H	1.43480100	-2.68838000	1.70782900
H	2.16126800	-3.80907900	0.52766300
H	2.85441700	-3.08949200	-2.02365300
H	1.19713400	-2.58350500	-2.45034900
H	2.55460600	-1.47838800	-2.72504000
C	4.56277700	-2.16635000	0.23495500
C	4.06897400	0.20637900	0.38581300
C	-4.44801100	-1.35435000	0.84643300
H	-2.61700900	-2.46858100	0.50655100
H	-2.34630800	-0.85301500	1.12331500
C	5.90079100	-1.93286900	0.54209300
H	4.24417200	-3.18756500	0.04555900
C	5.42685800	0.42609400	0.68199500
C	3.17280700	1.39584700	0.34074200
C	-4.90987700	0.10132000	0.81290500
C	6.33508100	-0.62523700	0.76281600
H	6.59769600	-2.76404500	0.60320200
H	5.75845100	1.44288000	0.87159900
C	2.04060200	1.49462300	1.18087600
C	3.49075300	2.48110300	-0.48522100
C	-6.05882500	0.54198100	0.37035600
H	-4.20092700	0.82282400	1.22354900
H	7.37558800	-0.42489500	1.00305600
C	1.25593000	2.65453300	1.17892600
H	1.84125500	0.71146900	1.90815800
C	2.70289900	3.63630000	-0.48263300
H	4.35588900	2.41623000	-1.13944800
C	-7.20150800	0.99422300	-0.08116500
C	1.58512000	3.72557600	0.34304800
H	0.39095400	2.71644300	1.82877400
H	2.96410800	4.46360700	-1.13702200
H	-7.31919600	1.31056200	-1.11649200
H	-8.08246500	1.06977400	0.55501700
H	0.96453500	4.61594400	0.33537800
C	-1.27335400	1.54291400	-0.26870800
C	-2.16570700	2.37963600	-0.28652000
C	-3.23731100	3.37482500	-0.33425400
H	-3.12053200	4.04859200	-1.19352000
H	-4.21944000	2.89345500	-0.42811200
H	-3.26170300	4.00009900	0.56885400
C	-1.12384900	-1.01372000	-1.34690600
H	-0.76507400	-2.03651200	-1.17720500
H	-0.99377500	-0.73208600	-2.39437300
C	-4.52790500	-1.83159300	2.31773700
H	-4.15045900	-2.85794700	2.41726300

H	-3.93544100	-1.18886500	2.98060700
H	-5.56498400	-1.81346300	2.67041500
C	-5.33133100	-2.26161500	-0.02633900
H	-5.29499400	-1.94643700	-1.07043000
H	-4.98975700	-3.30261000	0.04159600
H	-6.37304300	-2.22787700	0.31162200

$TS_{I\text{-}V}$ P *cis* to acyl





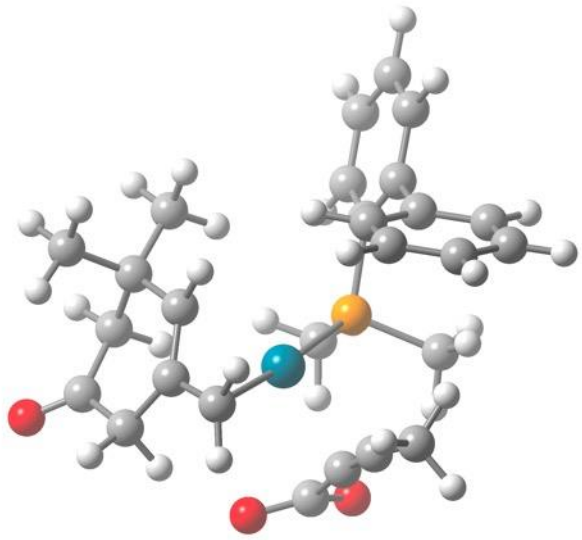
$TS_{I\text{-}V}$ P *cis* to acyl

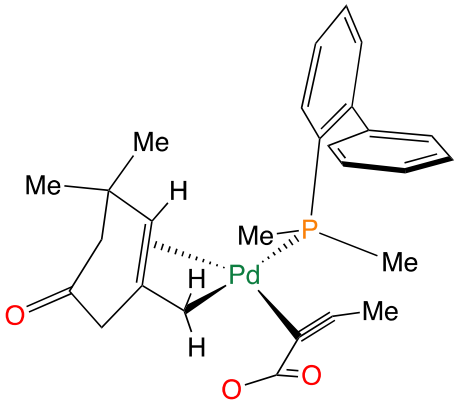
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.81785805
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 341.307
Entropy [cal/mol•K]: 232.144

Pd	-0.54814700	-1.54637600	-0.14555600
P	0.63934600	-0.04791300	-1.38496000
C	-2.92098000	-0.46283100	-1.53148600
C	0.40896100	-0.12564400	-3.21623500
C	0.11613100	1.68230000	-1.05772000
C	2.46961100	-0.25139400	-1.20324800
C	-4.07820500	-0.51840900	-0.52773200
O	-2.72041800	0.52285600	-2.24741300
H	-0.63185800	0.14322500	-3.41753500
H	0.60491000	-1.12709000	-3.60571300
H	1.08204600	0.58816200	-3.70265700
H	0.75744600	2.38873800	-1.59386000
H	-0.91064000	1.75185300	-1.43003300
H	0.12758700	1.91517900	0.00548400
C	2.97972500	-1.38857900	-1.85813700
C	3.36988300	0.60950200	-0.53221400
C	-4.58744400	0.80703300	0.10019500
H	-4.91777700	-0.99763900	-1.05660000
H	-3.79997200	-1.21564400	0.27303600
C	4.34279500	-1.66348800	-1.90054700
H	2.29552100	-2.07852600	-2.34393500
C	4.74687300	0.32369500	-0.60553500
C	2.98361800	1.79669000	0.29010400
C	-3.43765700	1.46941600	0.85676300

C	5.23646600	-0.79026900	-1.28026400
H	4.70093500	-2.54999700	-2.41617500
H	5.43553700	0.98987700	-0.09347300
C	2.23518200	1.64954500	1.46908100
C	3.44696500	3.07487500	-0.06009700
C	-3.05441600	2.71703400	0.76106400
H	-2.91924600	0.82514800	1.57185100
H	6.30560300	-0.98196500	-1.30832500
C	1.94626800	2.75844900	2.26666200
H	1.87669400	0.66517600	1.75801400
C	3.15089300	4.18329200	0.73473400
H	4.03341400	3.19873200	-0.96703900
C	-2.66616500	3.96382100	0.67415400
C	2.39900800	4.02809000	1.90100500
H	1.36674100	2.62752700	3.17655400
H	3.50825100	5.16709200	0.44221100
H	-1.89504500	4.27553900	-0.02850300
H	-3.10130900	4.74399900	1.29694000
H	2.16988100	4.88974200	2.52202200
C	0.78176200	-1.87674600	1.46734900
C	-0.82357600	-2.74487500	2.27307000
C	1.89638000	-2.03003600	1.97332900
O	-1.57361300	-2.85666200	1.30285400
O	-0.69498300	-2.93100900	3.43562200
C	3.17982700	-2.21514600	2.63462600
H	3.80890900	-2.94650400	2.11343500
H	3.73396400	-1.27021900	2.70035100
H	3.02115100	-2.57651400	3.65986500
C	-2.07291700	-1.67361300	-1.60711300
H	-2.56951900	-2.58169200	-1.25131300
H	-1.64539000	-1.81694600	-2.59970500
C	-5.67068700	0.43538800	1.14239500
H	-6.49786000	-0.10542400	0.66547700
H	-5.26446500	-0.20322800	1.93623900
H	-6.07818300	1.33833600	1.61039200
C	-5.20459900	1.74208400	-0.95305900
H	-4.46942400	2.01943000	-1.70909200
H	-6.04265300	1.24107400	-1.45340000
H	-5.59078700	2.65197200	-0.47992600

II'





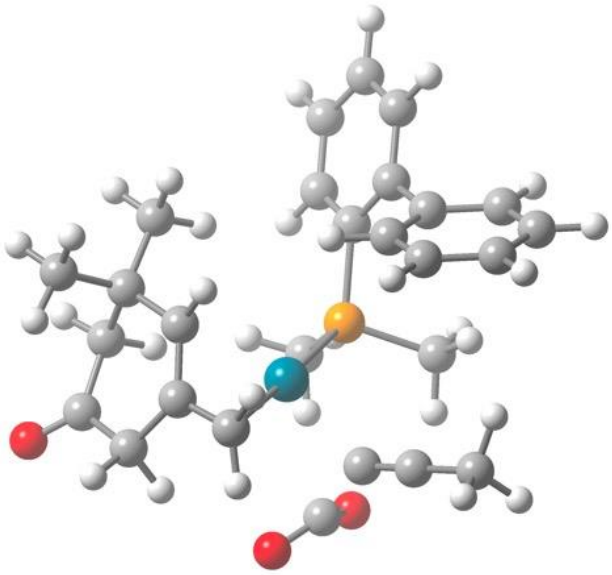
II'

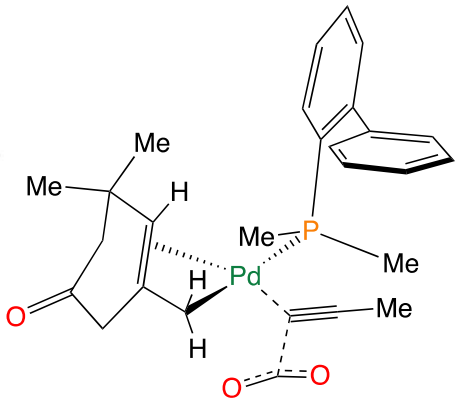
<u>M06/6-311+G(d,p) (PCM, solvent = THF)</u>
Electronic energy [Hartree]: -1741.90632517
<u>B3LYP/6-31G(d)</u>
Total thermal energy [kcal/mol]: 343.393
Entropy [cal/mol•K]: 219.132

Pd	0.66173200	-0.79501700	-0.21690600
P	-0.76808200	0.24618600	1.44885600
C	4.27232000	1.11176200	-0.31217500
C	-1.77474400	-1.00909800	2.35870500
C	0.21054900	0.96230700	2.83969100
C	-2.00274600	1.55677000	1.00138400
C	3.14929000	2.08741800	0.00176200
O	5.44658300	1.41162600	-0.22285600
H	-1.06280700	-1.67662400	2.85649500
H	-2.39985600	-1.57939800	1.66842100
H	-2.40802900	-0.51442500	3.10268300
H	-0.43962900	1.31979800	3.64528900
H	0.82812300	0.14221000	3.22453200
H	0.85697300	1.77717500	2.50317000
C	-1.96130700	2.79869000	1.65848600
C	-3.02406800	1.33449800	0.04542500
C	2.13856100	2.19206400	-1.16829300
H	2.62516600	1.72084600	0.89559800
H	3.58841200	3.06275300	0.23284800
C	-2.89790400	3.79895100	1.39765300
H	-1.18991700	2.99538100	2.39412400
C	-3.96838400	2.34554400	-0.19180900
C	-3.17546100	0.07686600	-0.75482100
C	1.64526100	0.80294900	-1.54069100
C	-3.91255400	3.57007500	0.47182300
H	-2.83394000	4.74719400	1.92415000
H	-4.75134500	2.16174500	-0.92246200
C	-4.20709900	-0.82978900	-0.46666600
C	-2.37118100	-0.15748600	-1.88114500
C	2.49558500	-0.32916000	-1.45317900

H	0.86230600	0.77817700	-2.30073100
H	-4.65386500	4.33625600	0.26255900
C	-4.42513600	-1.94550000	-1.27836700
H	-4.84596700	-0.65177300	0.39418900
C	-2.59265500	-1.26820200	-2.69778800
H	-1.59296600	0.55666900	-2.13194900
C	1.93353600	-1.57194200	-1.81229300
C	-3.62056100	-2.16567500	-2.39874300
H	-5.23131900	-2.63462300	-1.04156900
H	-1.97241500	-1.42377400	-3.57685800
H	2.47058100	-2.48939900	-1.59070000
H	1.18308500	-1.62857700	-2.59975400
H	-3.79902100	-3.02521800	-3.03915500
C	0.83984400	-2.68048400	1.07456600
C	1.79390100	-2.19233400	2.18033400
C	0.05818600	-3.21873600	0.28891500
O	1.23462700	-2.06655600	3.28732100
O	2.95501200	-1.95708400	1.79299400
C	-0.84263400	-4.01782700	-0.54179000
H	-0.97212500	-5.00827800	-0.08746200
H	-1.83104100	-3.55517800	-0.63081900
H	-0.44564200	-4.16319100	-1.55380600
C	3.83359400	-0.27884000	-0.74127100
H	4.61513900	-0.70913200	-1.37769300
H	3.76729100	-0.91326700	0.16211300
C	2.84846200	2.78203400	-2.41728100
H	3.22221600	3.78909500	-2.19778200
H	3.70142200	2.17037800	-2.73082100
H	2.15533700	2.85522900	-3.26343600
C	0.97531500	3.12002900	-0.78760600
H	0.45213200	2.76526300	0.10314900
H	1.34440800	4.13269700	-0.58780400
H	0.24125400	3.18679100	-1.60028400

$TS_{II\text{-}VII}$





$TS_{II\text{-}VII}$

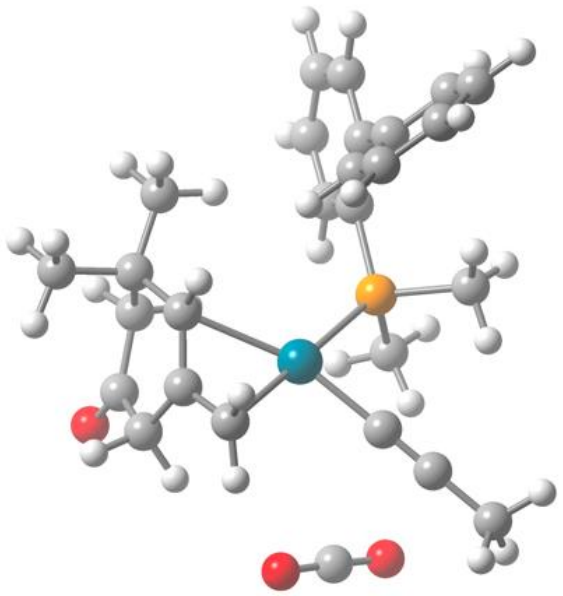
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.89532991

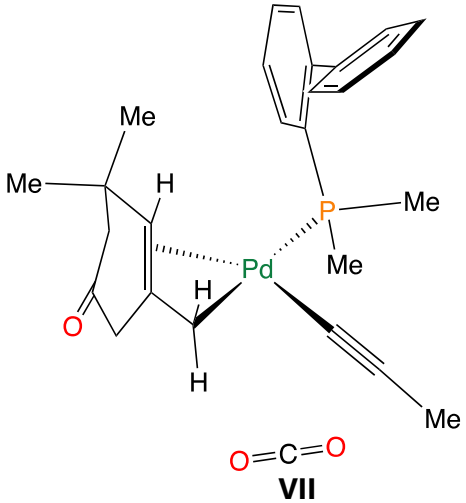
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 342.423
Entropy [cal/mol•K]: 216.521

Pd	0.72388600	-0.75852700	-0.22486000
P	-0.74419300	0.27056600	1.39990600
C	4.27954700	1.10253600	-0.00939600
C	-1.86704800	-0.95579200	2.20585500
C	0.23114100	0.83407900	2.86325800
C	-1.87160700	1.68867600	0.99876900
C	3.15340300	2.11956800	0.08667400
O	5.42042200	1.36077300	0.32029100
H	-1.22296800	-1.72131900	2.64868400
H	-2.52817200	-1.41656500	1.46986300
H	-2.46482300	-0.46724500	2.98262200
H	-0.41554100	1.18008700	3.67676400
H	0.79023100	-0.04690300	3.19599100
H	0.93860400	1.62455300	2.59906400
C	-1.69183900	2.91895800	1.65363400
C	-2.94544000	1.56267300	0.08103000
C	2.30481000	2.18805200	-1.20600200
H	2.50180800	1.81500500	0.91808500
H	3.58848900	3.09322800	0.33296500
C	-2.54220500	4.00208500	1.42887700
H	-0.88071900	3.03952700	2.36294500
C	-3.80235600	2.65682400	-0.11677500
C	-3.23987000	0.32120000	-0.70007100
C	1.82316200	0.79356100	-1.56654900
C	-3.60878800	3.86905900	0.54365100
H	-2.37226000	4.93865900	1.95276200
H	-4.62516400	2.54914600	-0.81825100
C	-4.44549900	-0.36964300	-0.49505000
C	-2.37161200	-0.13055400	-1.70570200
C	2.62532800	-0.34898900	-1.34329900
H	1.09518900	0.74510700	-2.37790100
H	-4.28440000	4.70047600	0.36278400
C	-4.76739800	-1.48988800	-1.26269100
H	-5.12922800	-0.02584700	0.27657300
C	-2.69551300	-1.24734900	-2.47875400
H	-1.45020100	0.41115700	-1.89433800
C	2.07728700	-1.60722500	-1.68730000
C	-3.89295600	-1.93207900	-2.25858900
H	-5.70354100	-2.01292400	-1.08665400
H	-2.01630500	-1.57485300	-3.26146000
H	2.56912300	-2.51458900	-1.35123000
H	1.40916600	-1.69800900	-2.54219900
H	-4.14880200	-2.79575800	-2.86664000
C	0.42687500	-2.72798600	0.60383900
C	1.59694900	-2.61920300	1.80142600
C	-0.36359000	-3.55796800	0.13942500
O	1.08741400	-2.35292700	2.88941900
O	2.72383800	-2.81965000	1.35662100
C	-1.31479700	-4.52695600	-0.38513900
H	-1.69903900	-5.16238900	0.42392000

H	-2.17727600	-4.01172500	-0.82774900
H	-0.87322100	-5.17720600	-1.15023100
C	3.90879500	-0.27941500	-0.53707100
H	4.74631600	-0.63414700	-1.15084800
H	3.84311700	-0.98151000	0.30841400
C	3.18079800	2.70829100	-2.37738900
H	3.54150600	3.72097900	-2.16088800
H	4.05535400	2.07089600	-2.54916100
H	2.60452500	2.74662700	-3.30900300
C	1.12170100	3.15015200	-1.01541200
H	0.47011300	2.83005900	-0.19834700
H	1.48092500	4.16195200	-0.79357100
H	0.51225600	3.20572200	-1.92613100

VII





<u>M06/6-311+G(d,p) (PCM, solvent = THF)</u>
Electronic energy [Hartree]: -1741.9188206
<u>B3LYP/6-31G(d)</u>
Total thermal energy [kcal/mol]: 343.486
Entropy [cal/mol•K]: 234.017

Pd	0.95552500	-0.44555800	-0.64338100
P	-0.62574200	-0.86702300	1.10732500
C	2.71039900	2.92759600	0.25527000
C	-1.39030000	-2.54953600	1.06076800
C	0.36215400	-1.00046000	2.66693000
C	-2.03002700	0.26258100	1.55947400
C	1.21781200	3.20640300	0.34565900
O	3.51225800	3.47281000	0.98931000
H	-0.56714900	-3.25989800	0.95193700
H	-2.05365200	-2.65409100	0.20189900
H	-1.94910000	-2.74682400	1.98156800
H	-0.25802300	-1.26349200	3.53044000

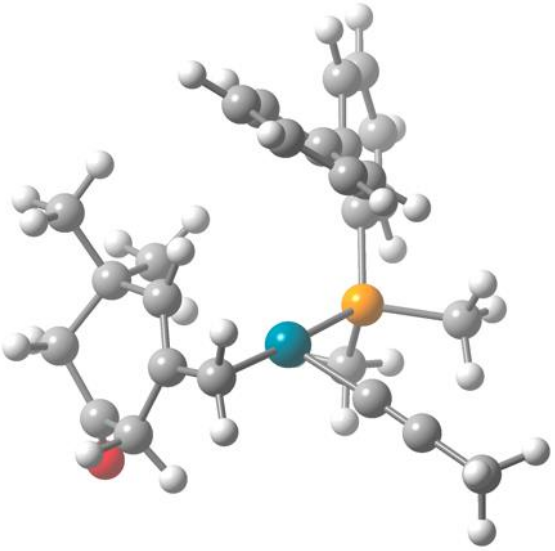
H	1.10207900	-1.78622300	2.48980100
H	0.90584800	-0.07500800	2.87486500
C	-1.86475800	1.12213200	2.66021500
C	-3.25513300	0.31311200	0.84220000
C	0.46172400	3.07113200	-0.99377800
H	0.80366900	2.47218100	1.05310000
H	1.08500600	4.19720500	0.79393700
C	-2.86792600	2.00077200	3.06852000
H	-0.93931200	1.10315800	3.22508800
C	-4.25884900	1.19323500	1.28105700
C	-3.56376900	-0.51885700	-0.35985300
C	0.80653100	1.72989700	-1.62326100
C	-4.07711600	2.03219100	2.37838700
H	-2.70231200	2.64811600	3.92528100
H	-5.19263900	1.22680000	0.72675500
C	-4.71166200	-1.32944000	-0.37001100
C	-2.76318400	-0.48079600	-1.51238300
C	2.11592200	1.22913900	-1.60909500
H	0.14080700	1.39000900	-2.41776100
H	-4.87155200	2.70750600	2.68382600
C	-5.03857500	-2.09374000	-1.49037400
H	-5.33889200	-1.37240300	0.51646300
C	-3.08989900	-1.24578700	-2.63313500
H	-1.88158800	0.15127100	-1.53131700
C	2.38146000	-0.04134500	-2.19838300
C	-4.22644200	-2.05664000	-2.62590800
H	-5.92510500	-2.72215400	-1.47360000
H	-2.45474500	-1.20482600	-3.51391100
H	3.36387200	-0.48716000	-2.08259500
H	1.82899600	-0.35181300	-3.08354100
H	-4.47765700	-2.65418400	-3.49792300
C	1.60462300	-2.33421800	-0.40917700
C	4.34973000	-1.78832600	1.33175500
C	2.01114500	-3.48030400	-0.26303500
O	3.96263200	-2.42416300	2.23405600
O	4.78623000	-1.13601700	0.46395200
C	2.49645600	-4.85118800	-0.08371400
H	2.99442700	-4.97464500	0.88737600
H	1.67777100	-5.58201700	-0.12451900
H	3.22001800	-5.13316800	-0.86008000
C	3.18869100	1.91439900	-0.78714500
H	3.85633300	2.46313000	-1.46870000
H	3.82827900	1.17902800	-0.28656800
C	0.89380900	4.20520100	-1.95991900
H	0.64308000	5.18672700	-1.53868500
H	1.97203700	4.18968100	-2.15617800
H	0.38017400	4.11097000	-2.92360900
C	-1.05185600	3.19016300	-0.75074300
H	-1.40793000	2.41969900	-0.06209900
H	-1.29936900	4.16945100	-0.32379100
H	-1.60613100	3.08903400	-1.69225900

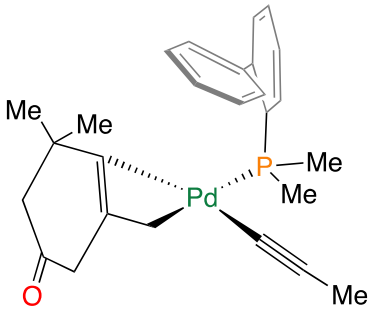
CO_2 (carbon dioxide)
M06/6-311+G(d,p) (PCM, solvent = THF)

Electronic energy [Hartree]: -188.560829811
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 8.933
Entropy [cal/mol•K]: 51.165

C	0.00000000	0.00000000	0.00000000
O	0.00000000	0.00000000	1.16930900
O	0.00000000	0.00000000	-1.16930900

VIII





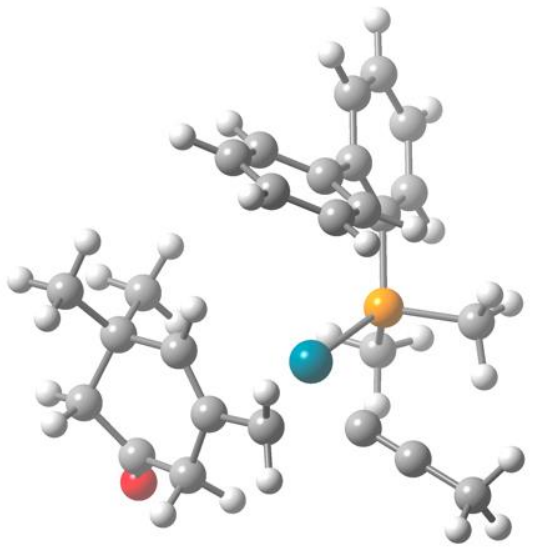
VIII

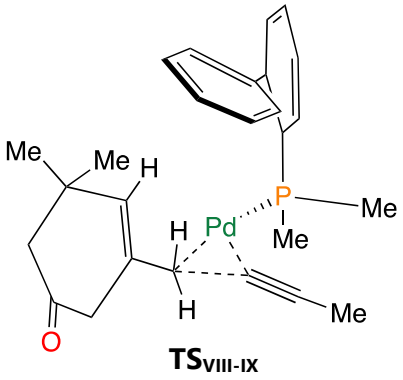
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1553.34777834
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 333.104
Entropy [cal/mol•K]: 208.268

Pd	1.01188000	0.86675900	0.07514700
P	-0.86050100	0.92905200	-1.41944100
C	3.40671000	-2.09356500	-1.14934100
C	-1.52805000	2.63006800	-1.72441200
C	-0.29712300	0.49191700	-3.13217800
C	-2.42360000	-0.05365800	-1.17540200
C	2.73985700	-3.22694000	-0.39697000
O	3.64870200	-2.12597100	-2.34083300
H	-0.68864500	3.28165200	-1.97826600
H	-1.99147200	3.02983000	-0.81942200
H	-2.26872800	2.61685100	-2.53120300
H	-1.00207900	0.79651200	-3.91256100
H	0.64842400	1.01786500	-3.29544100
H	-0.10791900	-0.58143600	-3.21341200
C	-3.15075400	-0.43064800	-2.31876300
C	-2.91356500	-0.45001200	0.09779400
C	1.38155700	-2.77942500	0.22048100
H	2.60246800	-4.07998400	-1.06810800
H	3.41272500	-3.53200400	0.41774100
C	-4.32240600	-1.18005100	-2.24058600
H	-2.79493200	-0.13983800	-3.30130900
C	-4.09979800	-1.20754500	0.15315600
C	-2.26716400	-0.13225600	1.40532000
C	1.52383800	-1.39640800	0.85779600
C	-4.79980100	-1.57350300	-0.99202400
H	-4.85424400	-1.45106100	-3.14850300
H	-4.48446800	-1.49179000	1.12826500
C	-1.90576300	1.17319500	1.77224000
C	-2.07255300	-1.16064800	2.34642600
C	2.65118600	-0.58133600	0.73776900

H	0.85216000	-1.20334100	1.69395500
H	-5.71458900	-2.15370300	-0.90694600
C	-1.35790800	1.44182000	3.02836600
H	-2.07987200	1.99564200	1.08829400
C	-1.52451700	-0.89524200	3.60112000
H	-2.34512000	-2.17915400	2.08287700
C	2.67055700	0.69140800	1.39433000
C	-1.16318600	0.40994100	3.94670700
H	-1.08470400	2.46169000	3.28253700
H	-1.38131500	-1.70759400	4.30893700
H	3.50887200	1.35915700	1.22215400
H	2.19176600	0.79452400	2.36667100
H	-0.73952000	0.62016900	4.92499300
C	1.23584500	2.85257900	-0.02402500
C	1.41196900	4.06178300	-0.08402800
C	1.62236500	5.50953900	-0.15578500
H	2.34578400	5.77475400	-0.93883000
H	0.69276100	6.05150200	-0.37877900
H	2.01114400	5.91171200	0.78955800
C	3.74494300	-0.89893500	-0.27243100
H	4.66736300	-1.13991200	0.27993100
H	3.96716700	-0.03224300	-0.90166000
C	0.98473500	-3.78619300	1.32314700
H	0.92045100	-4.80249000	0.91584400
H	1.71726500	-3.79117700	2.13882800
H	0.00769500	-3.52970400	1.74881300
C	0.29906900	-2.79668600	-0.87894900
H	0.60019800	-2.17936500	-1.73082000
H	0.13589000	-3.81942500	-1.24230400
H	-0.65175700	-2.41177100	-0.49887200

TS$_{VIII\text{-}IX}$



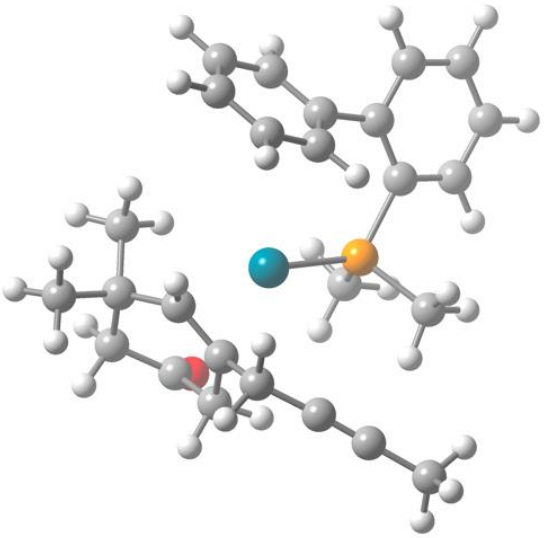


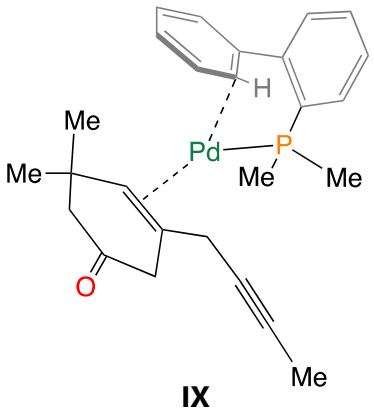
<u>M06/6-311+G(d,p) (PCM, solvent = THF)</u>
Electronic energy [Hartree]: -1553.30990001
<u>B3LYP/6-31G(d)</u>
Total thermal energy [kcal/mol]: 332.21
Entropy [cal/mol•K]: 211.885

Pd	0.65355700	0.85761800	-0.02660700
P	-1.35498800	1.14046500	-1.15401600
C	3.73935600	-1.09818100	-1.75209000
C	-2.10439200	2.81882100	-0.88580700
C	-1.06716000	1.18860900	-2.98944500
C	-2.84458800	0.03196600	-0.97843500
C	3.64442800	-2.42811600	-1.03140900
O	3.83285400	-0.99716700	-2.96073800
H	-1.32801700	3.56888100	-1.06533700
H	-2.42995000	2.92101800	0.15336400
H	-2.95998900	2.99855500	-1.54651100
H	-1.90072600	1.61039900	-3.56120900
H	-0.18191900	1.80918400	-3.15852400
H	-0.84915400	0.18157500	-3.35671400
C	-3.77439000	-0.00456000	-2.03313600
C	-3.06887200	-0.80704300	0.14420000
C	2.34958500	-2.52883200	-0.17707800
H	3.70071400	-3.24027100	-1.76262200
H	4.51309500	-2.50665400	-0.36076500
C	-4.88675100	-0.84272600	-2.01616900
H	-3.62777900	0.63267900	-2.89903800
C	-4.19622000	-1.65118700	0.14013000
C	-2.20653500	-0.86240000	1.36107600
C	2.13137100	-1.23471500	0.59267600
C	-5.09570300	-1.67874100	-0.92074800
H	-5.58085700	-0.84067400	-2.85231700
H	-4.37301600	-2.27981700	1.00820000
C	-1.88372200	0.28628100	2.10057700
C	-1.77199500	-2.10786100	1.84887900
C	2.77378000	-0.04645900	0.35138200
H	1.51189300	-1.31682300	1.48509100
H	-5.95740800	-2.33987200	-0.88541100
C	-1.15048000	0.19491700	3.28544400
H	-2.23832900	1.25659400	1.76965900
C	-1.03572600	-2.20143300	3.03005300
H	-2.01014900	-3.00826800	1.28889900
C	2.55535800	1.16706400	1.18045500
C	-0.72256200	-1.04802500	3.75450900
H	-0.92005200	1.09916900	3.84179000
H	-0.71240400	-3.17576300	3.38764700
H	3.39396000	1.85381600	1.12883800
H	2.25459300	0.96686100	2.20680600
H	-0.15757700	-1.11913100	4.68016600
C	1.35656100	2.62743200	0.72259200
C	1.36433900	3.82757400	0.97631800
C	1.36695500	5.25922300	1.27389600
H	1.36249100	5.86205400	0.35587700
H	0.48741800	5.55630700	1.86074500
H	2.25527300	5.55767100	1.84943600
C	3.71823700	0.11299200	-0.83207200
H	4.74370600	0.26622300	-0.45504800
H	3.46793700	1.00071200	-1.42192500
C	2.50082100	-3.68966100	0.83019800

H	2.68652800	-4.63628700	0.30836900
H	3.33389100	-3.51134600	1.52031500
H	1.58762000	-3.80629800	1.42596100
C	1.14303800	-2.82542200	-1.09935700
H	1.04916600	-2.06333600	-1.87961000
H	1.25684600	-3.80471500	-1.58283800
H	0.21214200	-2.82964300	-0.52306600

IX



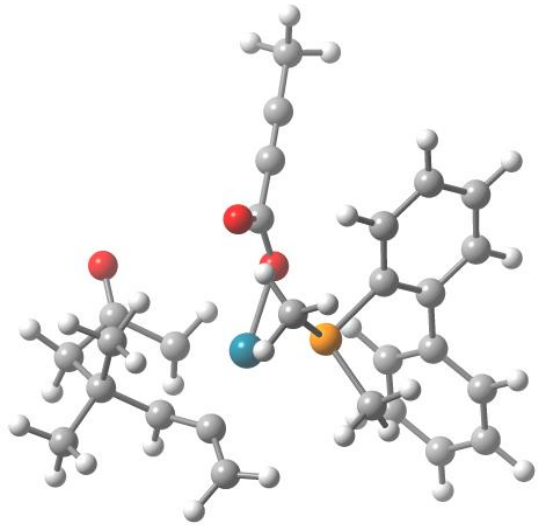


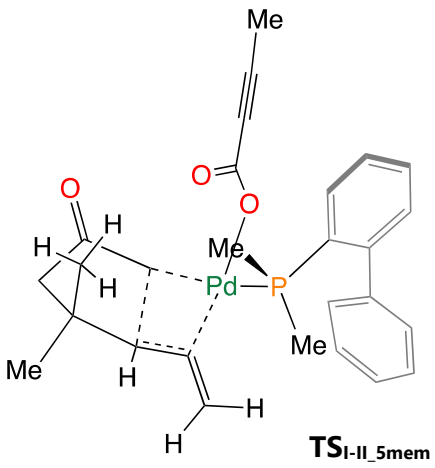
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1553.36620059
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 333.522
Entropy [cal/mol•K]: 211.653

Pd	0.52907700	-0.11700700	0.21944500
P	-1.14140200	1.32127500	-0.57473300
C	2.97628800	0.07309000	-2.03229600
C	-1.09419300	3.03620400	0.13777700
C	-0.96609200	1.66692500	-2.39178700
C	-2.95561400	0.90732500	-0.45732600
C	3.47044400	-1.35127400	-1.85599500
O	2.47693400	0.48772300	-3.06316000
H	-0.06584400	3.40035000	0.06059700
H	-1.35521500	2.99478400	1.19964000
H	-1.76872800	3.73474000	-0.37003300
H	-1.61847700	2.47631700	-2.73909700
H	0.07853100	1.91618400	-2.60148100
H	-1.20307600	0.75598600	-2.94981500
C	-3.88702800	1.82799700	-0.96880600
C	-3.43536000	-0.32296300	0.05618500
C	2.85038000	-2.09380000	-0.62880800
H	3.29612900	-1.90976700	-2.78052900
H	4.55888300	-1.28086100	-1.70967200
C	-5.25485300	1.56785300	-0.98603200
H	-3.53572800	2.77200200	-1.37634600
C	-4.82101300	-0.57440300	0.02180300

C	-2.58108600	-1.39867000	0.64413700
C	2.49961900	-1.10787500	0.49576700
C	-5.72448100	0.35233700	-0.48853400
H	-5.94502700	2.30543800	-1.38694100
H	-5.18610200	-1.51402200	0.42689300
C	-1.74884000	-1.16534400	1.75497600
C	-2.67934200	-2.70997700	0.15068500
C	2.69535200	0.27537400	0.44554600
H	2.43903500	-1.56687300	1.48443500
H	-6.78796200	0.12856000	-0.49145400
C	-1.05341000	-2.21824900	2.35828600
H	-1.69851600	-0.17166500	2.18833900
C	-1.97869900	-3.75913800	0.74857000
H	-3.31230500	-2.90502200	-0.71096500
C	2.95529400	1.04032300	1.74738400
C	-1.16702300	-3.51742500	1.85845500
H	-0.43597500	-2.01905100	3.22990500
H	-2.07279800	-4.76550300	0.34913700
H	4.03869300	0.97938500	1.95555000
H	2.45819100	0.52025400	2.57524100
H	-0.63138900	-4.33478900	2.33398400
C	2.57872200	2.45800500	1.75107300
C	2.33009300	3.64223000	1.78073300
C	2.02871200	5.07198400	1.82927900
H	0.98144400	5.27224000	1.57082200
H	2.20410600	5.48033300	2.83235600
H	2.65622000	5.63753800	1.12919200
C	3.21164500	0.94949600	-0.81522200
H	4.30061900	1.12143500	-0.71944100
H	2.74656400	1.92650100	-0.96536500
C	3.89278500	-3.09655900	-0.08251100
H	4.21233900	-3.79379900	-0.86729100
H	4.78294400	-2.57912400	0.29540800
H	3.47196200	-3.68866600	0.73950100
C	1.60568500	-2.88381000	-1.08547000
H	0.87286800	-2.22032800	-1.55776400
H	1.88488000	-3.66354200	-1.80695900
H	1.11384800	-3.36553200	-0.23326600

$TS_{I\text{-}II\_5mem}$



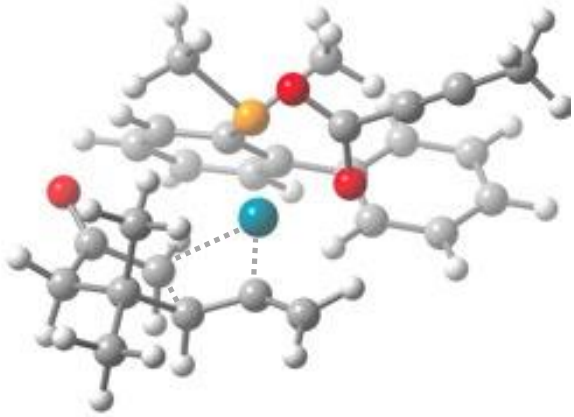


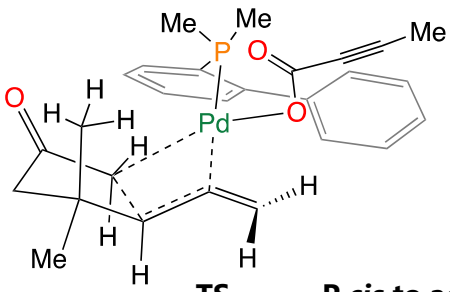
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.82768663
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 342.180
Entropy [cal/mol•K]: 224.857

Pd	-0.94875100	-0.40763500	-0.11297700
P	0.77321000	-0.81532400	1.44983500
C	-3.55672300	1.23462600	-1.43848700
C	0.18883800	-0.28439000	3.11543800
C	1.36461000	-2.53867400	1.79140000
C	2.35222300	0.10454000	1.17173600
C	-4.76776000	0.57622100	-0.79642600
O	-3.49318500	2.42848100	-1.66413900
H	-0.65205000	-0.93113200	3.38496200
H	-0.17243200	0.74345700	3.04346300
H	0.97144400	-0.37106500	3.87635300
H	2.26148600	-2.50269500	2.41800000
H	0.58856700	-3.08781000	2.32978800
H	1.59655600	-3.06317300	0.86343900
C	2.65165100	1.19426000	2.00421200
C	3.29422000	-0.28971300	0.18960100
C	-4.27872200	-0.39963400	0.29248800
H	-5.44303900	1.34100900	-0.40276300
H	-5.30924500	0.02012200	-1.57771900
C	3.87096200	1.86469800	1.90940300
H	1.92284400	1.54069300	2.72641700
C	4.52384700	0.38320600	0.12766400
C	3.04620900	-1.37062400	-0.81190700
C	-3.16233900	-1.24148200	-0.34134300
C	4.81847500	1.44766400	0.97785300
H	4.07244000	2.70818400	2.56359100
H	5.24397900	0.07525100	-0.62538200
C	2.03821500	-1.22773400	-1.77958600
C	3.86137000	-2.51370700	-0.84432200
C	-2.17159400	-1.92382800	0.41435500
H	-3.47470000	-1.75292300	-1.25001500

H	5.77527000	1.95663400	0.89830700
C	1.83860100	-2.22270000	-2.73940100
H	1.43705700	-0.32349900	-1.78573800
C	3.65625700	-3.50759100	-1.80253900
H	4.65119100	-2.62572700	-0.10559500
C	-2.13873300	-3.06168500	1.10453300
C	2.63991300	-3.36632200	-2.75063400
H	1.06005900	-2.09571700	-3.48720400
H	4.29065200	-4.39020100	-1.80924800
H	-1.24119600	-3.44076200	1.57773600
H	-3.02984200	-3.68085800	1.21092100
H	2.48089800	-4.13841800	-3.49880500
C	0.66188800	3.55283200	-0.49945300
C	0.08178300	2.31735700	0.01903200
C	1.12514800	4.59530300	-0.90644900
O	-0.39591500	2.28918700	1.16394700
O	0.13327500	1.31643100	-0.80503000
C	1.67587400	5.85163500	-1.40285300
H	0.95676900	6.35820500	-2.05859200
H	1.91763100	6.53872200	-0.58252100
H	2.59109200	5.68484400	-1.98434400
C	-2.42345600	0.29751600	-1.76350600
H	-2.66572300	-0.40880800	-2.55806700
H	-1.53649600	0.87527300	-2.03018600
C	-5.40362400	-1.37939000	0.69542600
H	-6.25672100	-0.82088800	1.09779500
H	-5.75964600	-1.96392500	-0.16171200
H	-5.06162600	-2.07497000	1.46947300
C	-3.79887700	0.37743500	1.53068900
H	-2.98922800	1.07690100	1.29300600
H	-4.63189900	0.95105600	1.95310400
H	-3.43266300	-0.30840700	2.30119300

$TS_{I\text{-}II\_5mem}$ P *cis* to acyl





$TS_{I\text{-}II\_5mem}$ P *cis* to acyl

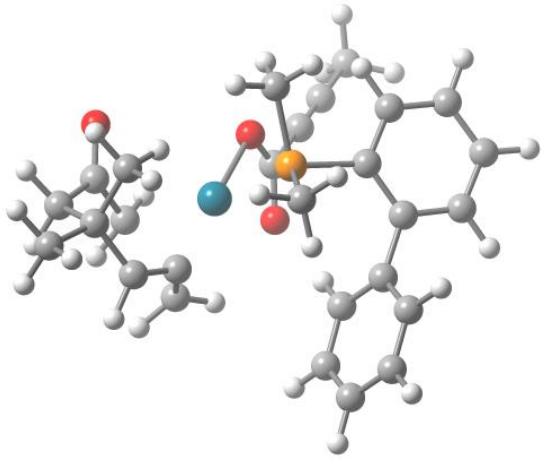
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.81642847
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 342.035
Entropy [cal/mol•K]: 226.767

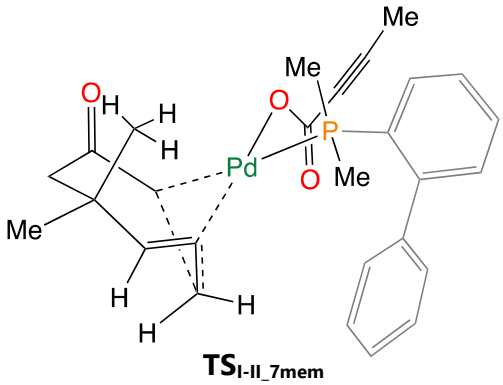
Pd	0.88956300	0.10839000	-0.37072000

P	-0.93428000	-0.29687100	1.24930200
C	2.03181800	-2.94973300	0.19268700
C	-0.21640700	-0.88316300	2.84578000
C	-1.93790900	1.14785500	1.81629200
C	-2.15536500	-1.61053300	0.77461600
C	3.50201900	-3.01448800	-0.18202600
O	1.57406100	-3.38988200	1.23474600
H	0.39313300	-0.05304100	3.21347300
H	0.43585100	-1.74437300	2.68177600
H	-0.99014200	-1.13675000	3.57839400
H	-2.74856900	0.82143900	2.47554100
H	-1.25693100	1.80331000	2.36499900
H	-2.35173600	1.69627400	0.96991200
C	-1.97011800	-2.90689600	1.28923800
C	-3.24075100	-1.38253300	-0.11337000
C	3.91847700	-1.57659200	-0.57401100
H	4.09720200	-3.41397000	0.64328200
H	3.61509600	-3.68855300	-1.04463900
C	-2.84492000	-3.94954700	0.98191300
H	-1.12509100	-3.11556400	1.93473000
C	-4.12117100	-2.44109900	-0.39030200
C	-3.51200800	-0.07719600	-0.78681700
C	2.81552500	-1.02522200	-1.50549500
C	-3.93563900	-3.71275200	0.14917400
H	-2.67116300	-4.93763500	1.39913900
H	-4.95244300	-2.25755400	-1.06552100
C	-2.55957900	0.53247600	-1.61877100
C	-4.76361200	0.54342500	-0.63673100
C	2.50527000	0.35755100	-1.55750800
H	2.76946100	-1.54506100	-2.46152800
H	-4.63066200	-4.51212700	-0.09346400
C	-2.84081000	1.73848700	-2.26200300
H	-1.58951100	0.06455100	-1.76251600
C	-5.04663800	1.74753800	-1.28177100
H	-5.50982500	0.08442000	0.00656300
C	2.97238100	1.47923600	-2.09112800
C	-4.08415100	2.35114500	-2.09428700
H	-2.08405000	2.19718400	-2.89200400
H	-6.01713900	2.21715700	-1.14411200
H	2.46122200	2.42328900	-1.92793800
H	3.88670000	1.49479800	-2.68612200
H	-4.30141400	3.29194500	-2.59268500
C	0.97793300	4.12765400	0.98519600
C	0.99758400	2.66657100	0.93918800
C	0.97456100	5.33663600	1.06201100
O	1.26253900	2.01705000	1.95902100
O	0.70415100	2.18541100	-0.23079400
C	0.97078500	6.79249900	1.15811100
H	0.14851200	7.14123200	1.79526800
H	1.90556400	7.16164800	1.59794400
H	0.85337300	7.26287300	0.17417500
C	1.22534500	-2.20322600	-0.82633800
H	1.24293500	-2.67399000	-1.80800200
H	0.17656800	-2.13930400	-0.53285500

C	5.23209600	-1.57750800	-1.38307200
H	6.04536300	-1.99314600	-0.77715700
H	5.14758100	-2.18289200	-2.29376700
H	5.51586800	-0.55924500	-1.67127700
C	4.08789500	-0.71743300	0.69080000
H	3.16591500	-0.66364700	1.28030600
H	4.87370900	-1.14373600	1.32470200
H	4.36723600	0.30805900	0.43496100

$TS_{I\text{-}II\_7mem}$



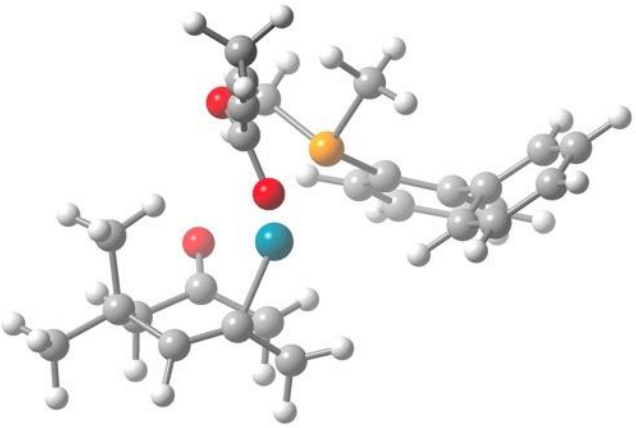


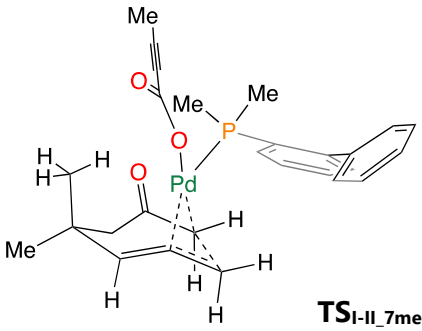
M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.77999368
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 341.624
Entropy [cal/mol•K]: 225.037

Pd	0.88097100	-0.56660800	-0.17526900
P	-0.32374900	0.50834700	1.50268200
C	3.24928600	-1.91566500	-0.29410200
C	-0.10590200	-0.48095700	3.04664600
C	0.16046000	2.20461600	2.04888600
C	-2.15783900	0.58306600	1.27669600
C	4.49020200	-1.03309400	-0.07338000
O	2.99307100	-2.79990300	0.51390900
H	0.93654400	-0.39056800	3.36400900
H	-0.30312200	-1.53341200	2.82837700
H	-0.75644400	-0.13152500	3.85512200
H	-0.46090700	2.53687100	2.88724100
H	1.20821700	2.17726400	2.36138800
H	0.06257700	2.91099400	1.22321000
C	-2.95547700	-0.32634500	1.99244300
C	-2.79315100	1.53001300	0.43648700
C	4.26895700	0.40022500	0.58094600
H	5.15018900	-1.60580000	0.58893400
H	5.01044300	-0.88398000	-1.02840800
C	-4.34714300	-0.28251900	1.92894200
H	-2.49265100	-1.08728600	2.60827000
C	-4.19571500	1.57461600	0.40779700
C	-2.06751900	2.47204900	-0.46995200
C	3.46073700	1.13156300	-0.47354200

C	-4.97267000	0.68463900	1.14606800
H	-4.93363200	-1.00270500	2.49237400
H	-4.67451700	2.30869500	-0.23417900
C	-1.41310100	1.98497400	-1.61259300
C	-2.11581300	3.85779800	-0.24931600
C	2.21848200	0.78379300	-0.85014900
H	4.06166100	1.71050300	-1.18286100
H	-6.05672100	0.73679500	1.09345400
C	-0.80671900	2.87432000	-2.50319500
H	-1.40799700	0.91483500	-1.80875300
C	-1.49921400	4.74128700	-1.13679500
H	-2.63546300	4.24028500	0.62579100
C	1.88837300	0.30554500	-2.15465700
C	-0.84122100	4.25015700	-2.26666200
H	-0.31725500	2.48978800	-3.39438100
H	-1.53892900	5.81118300	-0.94918600
H	2.65415600	0.28377100	-2.92809500
H	0.87185400	0.27082100	-2.53907500
H	-0.36786500	4.93684200	-2.96353900
C	-2.32159600	-3.24543200	-0.97990900
C	-1.29393800	-2.20480100	-0.98279300
C	-3.17543700	-4.10439400	-1.00813200
O	-1.17945600	-1.46012500	-1.97416000
O	-0.56639000	-2.15892000	0.08411300
C	-4.20311500	-5.13957400	-1.04613800
H	-4.20282700	-5.74586400	-0.13179900
H	-5.20250500	-4.70014100	-1.15649400
H	-4.04834600	-5.81677400	-1.89544300
C	2.39782400	-1.76209300	-1.54145500
H	2.99435100	-1.69471200	-2.44726500
H	1.63012200	-2.53070600	-1.62932700
C	5.65084000	1.06046300	0.74615500
H	6.29305700	0.46836900	1.40767000
H	6.16433200	1.16559100	-0.21723100
H	5.54694800	2.06086100	1.18272700
C	3.61341200	0.25904200	1.96168800
H	2.64570900	-0.24112800	1.89528700
H	4.25306200	-0.33392700	2.62556200
H	3.47169600	1.24566100	2.41795000

$TS_{I\text{-}II\_7mem}$ P *cis* to acyl





$TS_{I\text{-}II\_7mem}$ P *cis* to acyl

M06/6-311+G(d,p) (PCM, solvent = THF)
Electronic energy [Hartree]: -1741.76787402
B3LYP/6-31G(d)
Total thermal energy [kcal/mol]: 341.613
Entropy [cal/mol•K]: 224.210

Pd	0.83427900	-0.21931100	-0.42143700
P	-0.97488400	-0.05347900	1.28086000
C	1.59981100	-2.69002500	0.09830200
C	-0.39941600	-0.61834300	2.94258800
C	-1.66205400	1.60942500	1.71500000
C	-2.44065600	-1.13972100	0.92240100
C	3.11419100	-2.82625200	-0.14503500
O	1.15173600	-2.90946800	1.21913000
H	0.33825200	0.12186600	3.26174200
H	0.10097500	-1.58492400	2.86542700
H	-1.22331400	-0.67142200	3.66214000
H	-2.51088000	1.51551700	2.40005100
H	-0.84891400	2.15140900	2.20459200
H	-1.97030600	2.16145500	0.82722200
C	-2.43791600	-2.43100500	1.48318100
C	-3.53007100	-0.77138300	0.08887900
C	3.99489500	-1.55349400	-0.49907900
H	3.51254100	-3.26658800	0.77583600
H	3.25640400	-3.55674300	-0.95434100
C	-3.48634500	-3.32725400	1.27554800
H	-1.59956400	-2.74705400	2.09318400
C	-4.58571800	-1.68209500	-0.08986500
C	-3.63433300	0.53128700	-0.63415000
C	3.40560700	-1.05179100	-1.80737200
C	-4.57565100	-2.94619900	0.49541500
H	-3.44921300	-4.31382600	1.72965900
H	-5.41731200	-1.38938900	-0.72512900
C	-2.64298400	0.95308900	-1.53403400
C	-4.76910200	1.34209000	-0.46635900
C	2.14533600	-0.62085700	-1.91659800
H	3.94963400	-1.32910700	-2.71624700
H	-5.40496900	-3.62866800	0.33004300
C	-2.76979900	2.15637500	-2.22878200

H	-1.76108700	0.33700300	-1.68289200
C	-4.89923500	2.54459900	-1.16178400
H	-5.54367000	1.03256500	0.23032800
C	1.06535200	-1.20847300	-2.63270700
C	-3.89853500	2.95761100	-2.04394100
H	-1.98456500	2.46700700	-2.91262500
H	-5.78024500	3.16236800	-1.00863600
H	1.26451100	-2.01290400	-3.33954900
H	0.17771200	-0.63551300	-2.89564200
H	-3.99654400	3.89642300	-2.58207600
C	2.10914400	3.70135800	0.79346600
C	1.69441700	2.29880400	0.84437300
C	2.45646900	4.86194200	0.78641700
O	1.59304400	1.72648000	1.93910800
O	1.46496900	1.79104500	-0.32347000
C	2.87352300	6.26013900	0.77808500
H	3.25482300	6.56128100	-0.20546400
H	2.03257100	6.92059800	1.02415700
H	3.66344600	6.44512200	1.51658400
C	0.61375500	-2.49497600	-1.05747300
H	0.79267000	-3.26229100	-1.80673300
H	-0.42265800	-2.54648200	-0.72227700
C	5.43685400	-2.04388000	-0.73776900
H	5.83809900	-2.53038500	0.15802600
H	5.49057900	-2.76199500	-1.56547800
H	6.08918600	-1.19744900	-0.98138500
C	4.00054600	-0.54911500	0.66687900
H	3.00296800	-0.21079300	0.95518400
H	4.46452800	-1.00995600	1.54734400
H	4.58425400	0.33780000	0.39848900

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