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Recent Topics of Cp*RuCl-Catalyzed Annulation Reactions

Yoshihiko Yamamoto

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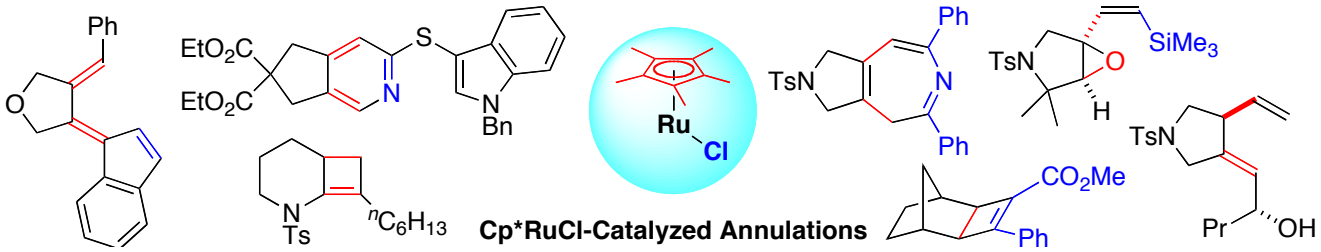

Cp*RuCl-Catalyzed Annulations

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Recent Topics of Cp*RuCl-Catalyzed Annulation Reactions

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ABSTRACT

A wide variety of annulation reactions have been developed using Cp*RuCl(cod) and related complexes as precatalysts. This digest highlights recent progress in Cp*RuCl-catalyzed annulation reactions. State-of-the-art examples are outlined as follows: [2 + 2 + 2] cycloadditions, [2 + 2] cycloadditions, cyclizations of enynes, and other annulation reactions.

Contents

Introduction

Transition-metal (TM)-catalyzed annulation reactions are efficient methods to construct complex cyclic structures from acyclic unsaturated starting materials.[1] Accordingly, countless TM catalysts have been developed and applied to the synthesis of diverse complex molecules, including natural products and functional materials. Among them, Cp*RuCl(cod) (**1a**, Cp* = η^5-pentamethylcyclopentadienyl, cod = 1,5-cyclooctadiene) has been utilized as a precatalyst for various annulation reactions such as [*l* + *m* + *n*] cycloadditions, cycloisomerizations of α,ω-enynes and dienes, and azide-alkyne cycloadditions among others.[2] In this digest, catalytic annulation reactions using Cp*RuCl as the catalyst will be discussed. The latest reports published from 2013 to 2017 are included. Because the focus of this digest is the novelty of each catalytic transformation, typical examples rather than complete reaction scopes are discussed. For comprehensive information on the relevant studies, see previously published reviews.[2]

Cp*RuCl(cod) and Related Ruthenium Complexes

Three-legged, piano-stool-type ruthenium complex **1a** can be prepared from $RuCl_3$•$3H_2O$ and Cp*H in two steps via oligomeric Ru(III) complex $[Cp^*RuCl_2]_n$ (**1b**), as shown in Scheme 1.[3] It was recently reported that the preparation of **1b** could be facilitated by microwave heating.[4] Complexes **1a** and **1b** are now commercially available from major suppliers such as Sigma-Aldrich. Ruthenium(II) complex **1a** has several ligands, which differently contribute to the catalytic behavior of **1a**. The bulky Cp* ligand regulates the access of reacting molecules to the coordination sphere. In addition, the electron-donor ability of Cp* facilitates the oxidative coupling of unsaturated molecules on the Cp*RuCl fragment.[5] The chlorine ligand also affects the catalytic performance of **1a**, as the π-donor chlorine ligand destabilizes the *d*π electrons of the d^6 Ru(II) center, enhancing ligand exchange reactions. The chlorine ligand induces steric effects on the coordination environment as well. Moreover, a most recent study revealed that the chlorine ligand determines the selectivity in catalytic coupling reactions by forming hydrogen bonds with hydroxyl groups on the reacting molecules.[6] Accordingly, **1a** generally exhibits different catalytic activities than related cationic complex $[Cp^*Ru(MeCN)_3]PF_6$ (**1c**).[7] 1,5-Cyclooctadiene (cod) is a temporal supporting ligand (actor ligand), which dissociates in solution to create two vacant sites for the coordination of reacting molecules. Thus, cod is not necessary for catalytic reactions, and a tetrameric complex,

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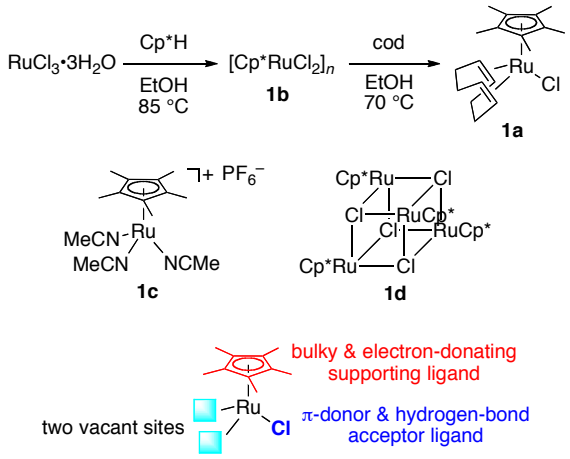
[Cp*RuCl]$_4$ (**1d**), can be used in place of **1a** as a source of the Cp*RuCl fragment.[8]

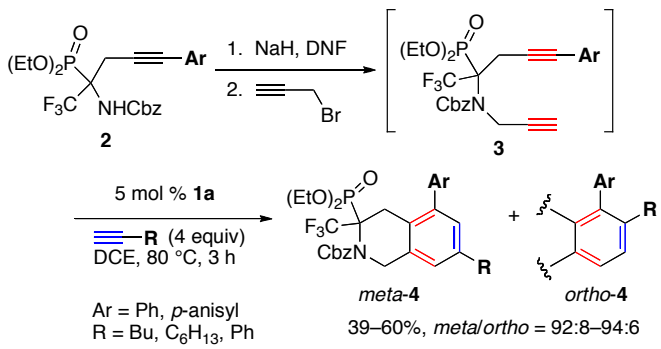


Scheme 1. Preparation and coordination environment of ruthenium complex **1a**.

[2 + 2 + 2] Cycloadditions

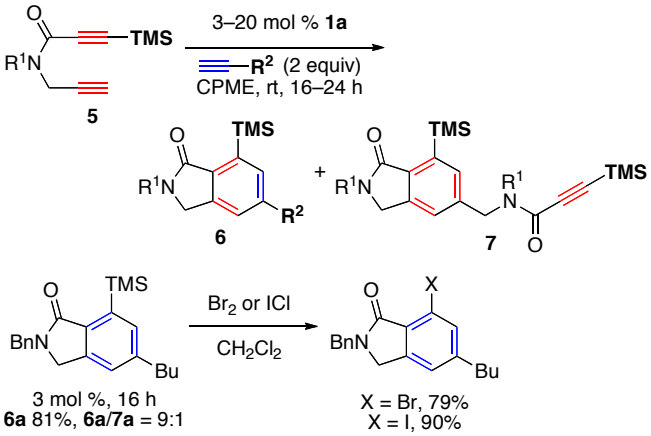
Ruthenium complex **1a** is one of the most efficient and versatile precatalysts for [2 + 2 + 2] alkyne cycloadditions and related cocycloadditions.[2d] Notably, **1a** catalyzes the cycloadditions of 1,6- and 1,7-diynes with monoalkynes with wide functional group compatibility. Notably, synthetically useful C–B and C–X (X = I and Br) bonds are preserved during these catalytic reactions. When unsymmetrical diynes are used as substrates, the regioselectivity is mainly governed by the sterics of the diyne terminal substituents. By taking advantage of these features, Cp*RuCl-catalyzed [2 + 2 + 2] cycloadditions have been applied to the synthesis of biologically interesting molecules.

Osipov and coworkers employed Cp*RuCl-catalyzed [2 + 2 + 2] cycloaddition for the synthesis of CF_3-substituted tetrahydroisoquinoline-3-phosphonates (Scheme 2).[9] Unsymmetrical 1,7-diynes **3**, which were prepared by the propargylation of **2**, were directly subjected to the cycloaddition with terminal alkynes in the presence of **1a** (5 mol %) in 1,2-dichloroethane (DCE) at 80 °C. As a result, the expected isoquinoline derivatives **4** were obtained in 39–60% yields; phosphonate, trifluoromethyl, and carbamate groups were tolurated. High *meta*/*ortho* ratios of 92:8–94:6 were observed, owing to the aryl terminal groups on the diyne substrates. In this example, the 2G Grubbs catalyst improved the yield and regioselectivity.



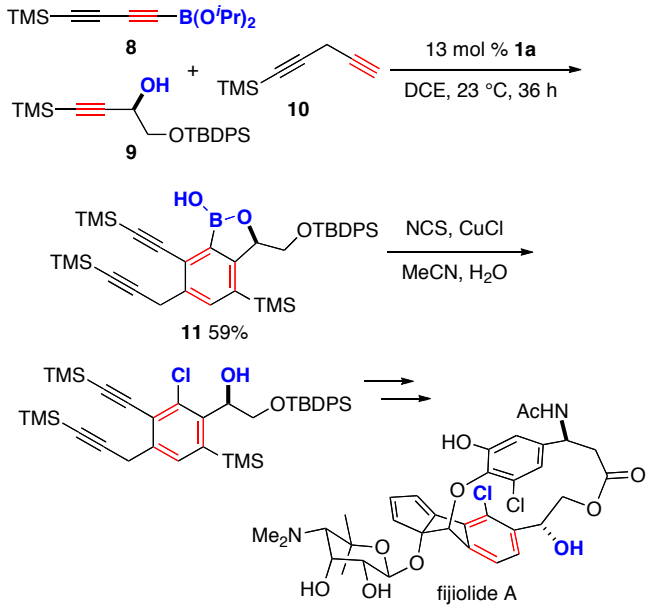
Scheme 2. Synthesis of CF_3-substituted tetrahydroisoquinoline-3-phosphonates **4**.

Sheppard and coworkers revisited the previously reported Cp*RuCl-catalyzed cycloaddition for the synthesis of isoindolinones under industrially compatible conditions (Scheme 3).[10] TMS-substituted diynes **5** bearing amide tethers were subjected to the [2 + 2 + 2] cycloaddition with diverse monoalkynes. In place of DCE, less toxic cyclopentyl methyl ether (CPME) was used as a solvent. The desired isoindolinones **6** were obtained as single regioisomers owing to the synergistic directing effect of the bulky TMS and internal carbonyl groups.[11] However, the loading amount of the terminal alkyne was suppressed to 2 equivalents, resulting in the unfavorable formation of dimers **7**. Nevertheless, cycloadduct **6a** was obtained in 81% yield with a **6a**/**7a** ratio of 9:1. Importantly, the TMS group could be replaced with bromine or iodine, which are useful synthetic handles for subsequent transformations. Kotora and coworkers also reported the synthesis of cyclopropyl-substituted phthalans and phthalides via the Cp*RuCl-catalyzed [2 + 2 + 2] cycloaddition of diynes bearing cyclopropyl terminal groups.[12]



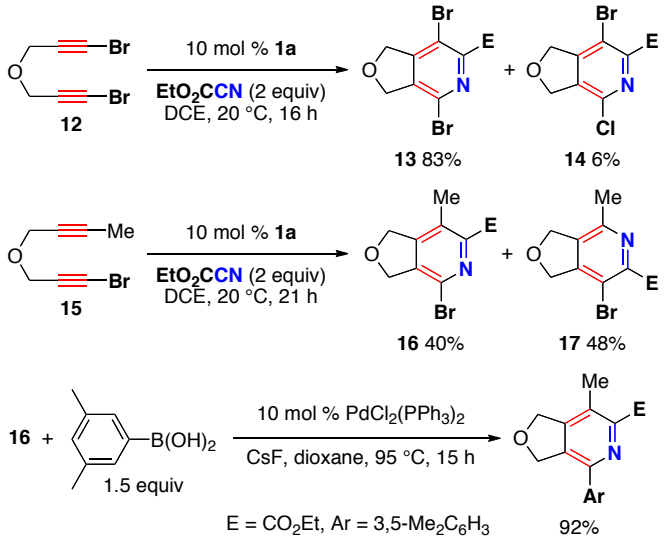
Scheme 3. Synthesis of isoindolinones **6**.

Yamamoto and coworkers previously reported the pair- and regio-selective [2 + 2 + 2] cycloaddition of alkynylboronates, propargylic alcohols, and third terminal alkynes using **1a** as a precatalyst.[13] The cyclotrimerization of these three unsymmerical alkynes proceeded via 1,6-diynes temporally connected through a B–O linkage, affording boraphthalides as single regioisomers. Moreover, the boryl substituent of the cycloadduct could be utilized for subsequent transformations such as Suzuki–Miyaura coupling and palladium-catalyzed cyclocarbonylation. Heinz and Cramer applied the Cp*RuCl-catalyzed cyclotrimerization using a B–O temporal tether to the total synthesis of biologically active natural product fijiolide A (Scheme 4).[14] They accomplished the pair- and regio-selective cyclotrimerization of 1,3-diynylboronate **8**, optically active propargylic alcohol **9**, and 1,4-diyne **10** to obtain highly substituted boraphthalide **11** in 59% yield, even though a high catalyst loading and long reaction time were required. The TMS-substituted alkyne moieties, which are critical for the second strategic TM-mediated cycloaddition, were preserved under the reaction conditions. Subsequently, the temporal boron tether was cleaved with the concomitant conversion of the boryl group to a chloride, which is required for the tricyclic aromatic core of fijiolide A.



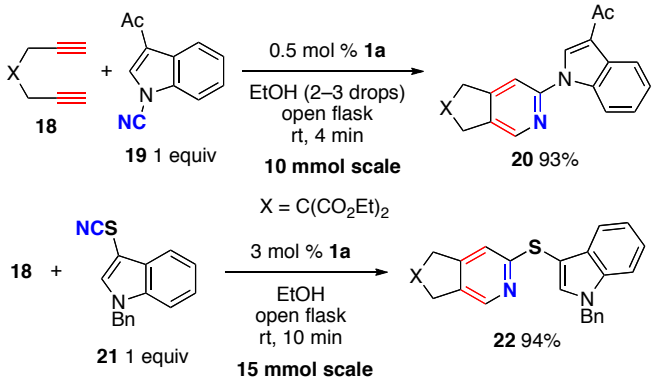
Scheme 4. Total synthesis of biologically active natural product fijiolide A.

The [2 + 2 + 2] cocyclotrimerization of alkynes with nitriles is a powerful approach towards substituted pyridines.[15] The Cp*RuCl-catalyzed cycloaddition of diynes with nitriles bearing electron-withdrawing or coordinating groups affords fused pyridines with good chemo- and regio-selectivity.[2d] Lamaty, Kotora, and coworkers investigated the cycloaddition of halodiynes with activated nitriles.[16] Dibromodiyne **12** underwent the cycloaddition with ethyl cyanoformate in the presence of **1a** (10 mol %) in DCE at 20 °C, affording the desired dibromopyridine **13** in 83% yield along with a trace amount of monochlorinated side product **14** (Scheme 5). When unsymmetrical bromodiyne **15** was used as a substrate, regioisomers **16** and **17** were formed in an almost 1:1 ratio. The Suzuki–Miyaura coupling of the obtained bromopyridines demonstrated the synthetic utility of this method.



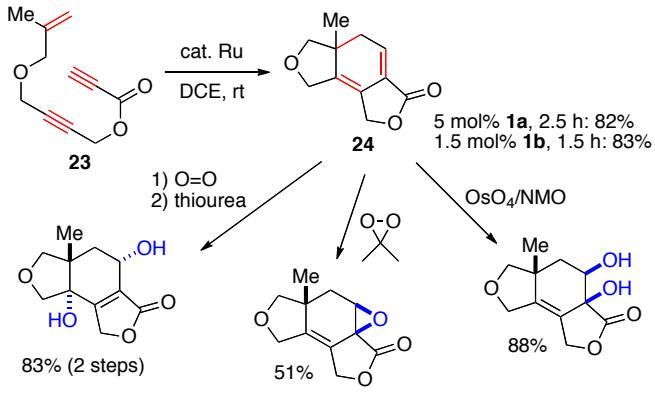
Scheme 5. Cycloaddition of bromodiynes **12** and **15** with ethyl cyanoformate.

Owing to the pharmaceutical importance of indoles bearing *N*-(2-pyridyl) or 3-(2-thiopyridyl) moieties, Chowdhury and Goswami investigated the [2 + 2 + 2] cycloadditions of 1,6-diynes with *N*-cyanoindoles and 3-thiocyanatoindoles (Scheme 6).[17] Representative examples are shown in Scheme 6. In the presence of **1a** (0.5 mol %), 1,6-diyne **18** reacted with *N*-cyanoindole **19** in EtOH at room temperature for 4 min, affording *N*-(2-pyridyl)indole **20** in 93% yield. The reaction of **18** with 3-thiocyanatoindole **21** was also conducted in the presence of **1a** (3 mol %) in EtOH at room temperature for 10 min to afford 3-(2-thiopyridyl)indole **22** in 94% yield. Notably, these reactions could be performed in 10–15 mmol scales in open flasks.



Scheme 6. Synthesis of *N*-(2-pyridyl)indole **21** and 3-(2-thiopyridyl)indole **23**.

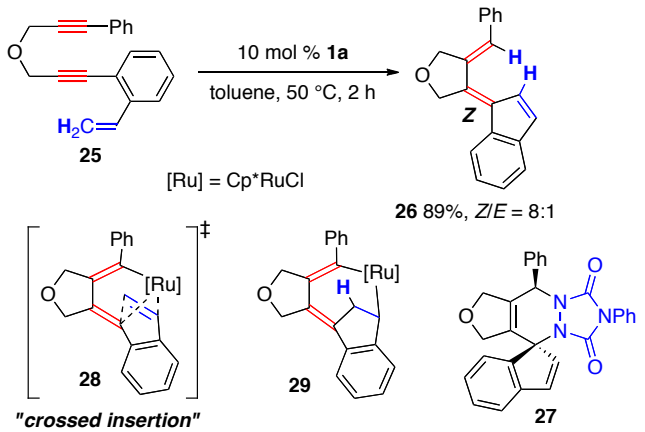
The fully intramolecular [2 + 2 + 2] cycloaddition of triynes is a powerful method to construct tricyclic benzenes with strict chemo- and regio-selectivity. Similarly, the fully intramolecular [2 + 2 + 2] cycloaddition of enediynes is also attractive because the expected cyclohexadiene products can be further transformed. Nevertheless, the Cp*RuCl-catalyzed enediyne cyclization is underdeveloped owing to the facile isomerization and aromatization of the resulting cyclohexadienes.[18] Shibuya and coworkers studied the [2 + 2 + 2] cyclization of 1,6,11-enediyne **23** bearing 1,1-disubstituted alkene and ester-tethered diyne moieties (Scheme 7).[19] In the presence of **1a** (5 mol %), **23** underwent cyclization at room temperature for 2.5 h, affording the expected lactone-fused cyclohxeadiene **24** in 82% yield. Moreover, the same reaction was complete within 1.5 h when oligomeric complex **1b** (1.5 mol %) was used as a precatalyst. For regio- and stereo-selective transformations of the central cyclohexadiene, several diastereoselective oxygenation methods were applied to **24**.



Scheme 7. Cyclization of enediyne **23** and subsequent oxygenations of the resultant cyclohexadiene **24**.

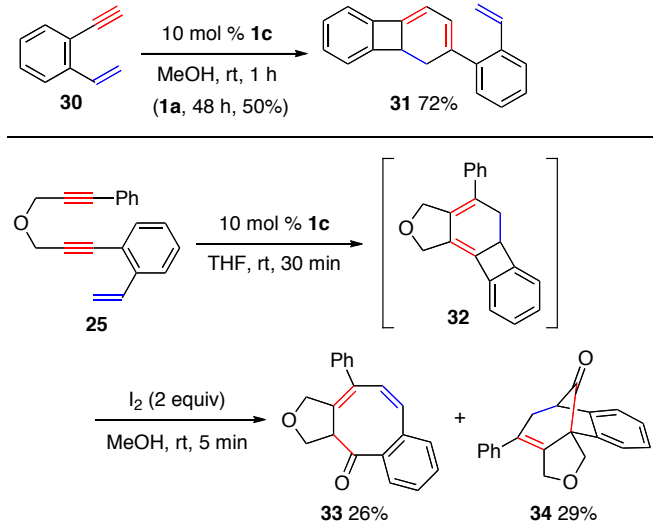
An unusual cycloisomerization involving indenylidene formation was observed when the cyclization of 1,5,10-enediyne **25** bearing a styryl terminus was performed using **1a**, as shown in Scheme 8.[20] In the presence of **1a** (10 mol %), **25** was heated in toluene at 50 °C for 2 h, affording cycloisomerization product **26** in 89% yield with a *Z*/*E* ratio of 8:1. The stereochemistry of the major isomer was confirmed by X-ray crystallography of **27**,

which was obtained by the Diels–Alder reaction of (*Z*)-**26** and *N*-phenyltriazolinedione. On the basis of density functional theory (DFT) calculations, it was proposed that the cycloisomerization proceeded via an unprecedented "crossed insertion" of the styryl alkene into the adjacent Ru–C bond of a ruthenacyclopentadiene intermediate (transition state **28**) and subsequent H transfer in the resulting ruthenacycle intermediate **29**.



Scheme 8. Indenylidene-forming cycloisomerization of enediyne **25**.

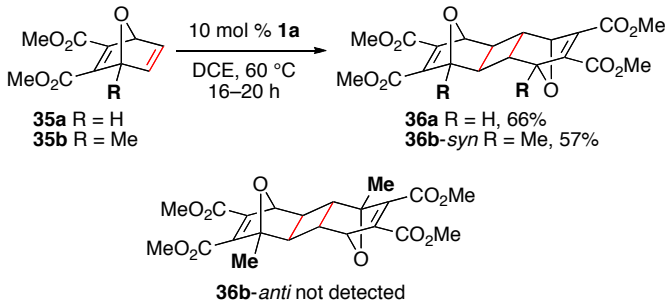
Esteruelas, Saá, and coworkers discovered that the [2 + 2 + 2] cyclodimerization of *o*-ethynylstyrene **30** produced dihydrobiphenylene derivative **31** (Scheme 9).[21] In this fascinating transformation, cationic complex **1c** is a superior precatalyst than **1a**. Cross [2 + 2 + 2] cycloadditions of **30** with arylalkynes are also possible, even though excess amounts of arylalkynes are required. In stark contrast, the corresponding dihydrobiphenylene derivative **32** was not detected when enediyne **25** was treated with **1a** in MeOH, even though a cationic species Cp*Ru$^+$ should be generated in protic solvents.[22] When **25** was treated with **1c** (10 mol %) in THF at room temperature, the reaction was complete within 30 min. Although the formation of **32** was confirmed by NMR, its isolation was hampered by its instability. Thus, crude **32** was subjected to aromatization using I_2 in MeOH at room temperature for 5 min, affording unexpected oxidative ring-expansion products **33** and **34** in 26% and 29% yields, respectively. Moreover, the one-pot reaction of **25** was conducted with *N*-iodosuccinimide (NIS) instead of I_2, resulting in the selective formation of bridged ketone **34** in 64% yield.



Scheme 9. Cyclodimerization of *o*-ethynylstyrene **30** and [2 + 2 + 2] cyclization of enediyne **25** and subsequent oxidative ring expansion.

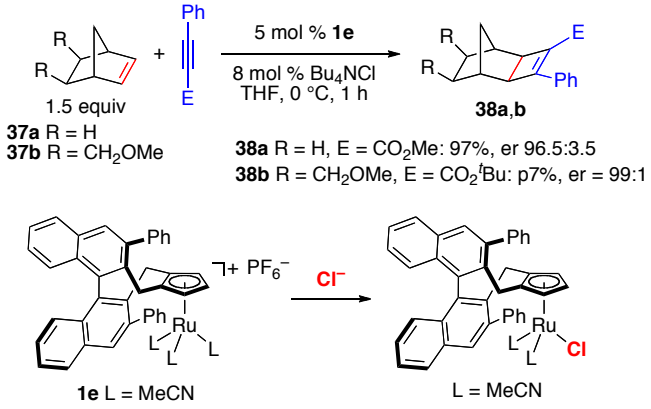
[2 + 2] Cycloadditions

Cp*RuCl(cod) is an excellent precatalyst for the [2 + 2] cycloadditions of norbornenes with alkynes to afford cyclobutenes.[23] In contrast to previous examples, Jack and Tam revealed that in the absence of an alkyne, 7-oxabicyclo[2.2.1]hepta-2,5-dicarboxylates underwent [2 + 2] dimerization (Scheme 10).[24] In the presence of **1a** (10 mol %), **35a** was heated in DCE at 60 °C for 16–20 h, stereoselectively affording *exo-trans-exo* product **36a** in 66% yield. When unsymmetrical alkene **35b** bearing a methyl group at the C1 position was used as the substrate, cycloadducts **36b**-*syn* and **36b**-*anti* were the expected products. Nevertheless, only **36b**-*syn* was obtained in 57% yield, even though **36b**-*syn* should be less stable than **36b**-*anti* because of the unfavorable steric interactions between the two methyl groups.



Scheme 10. [2 + 2] Cyclodimerization of oxanorbornadienes **35**.

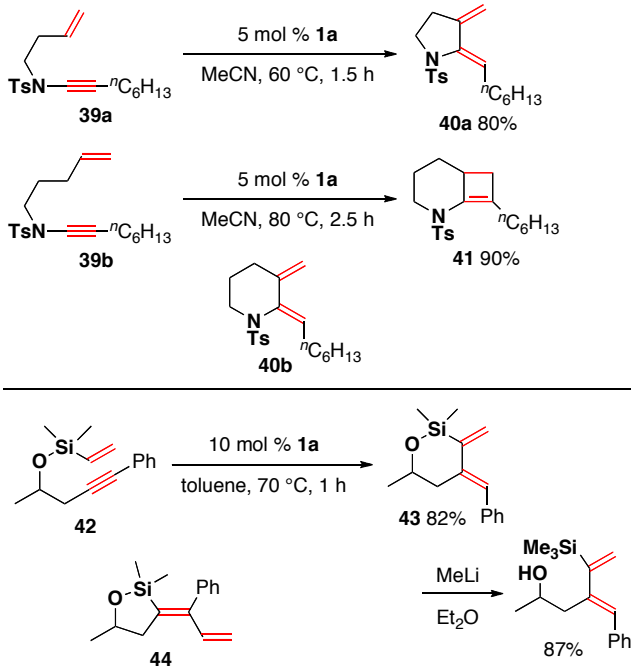
Villeneuve and Tam previously reported the diastereoselective [2 + 2] cycloaddition of norbornenes with unsymmetrical alkynes bearing chiral auxiliaries.[23b] Recently, the catalytic asymmetric [2 + 2] cycloaddition of norbornenes with phenylpropiolates was accomplished using optically active catalyst **1e** (Scheme 11).[25] Kossler and Cramer conducted the reaction of norbornene (**37a**) with ethyl phenylpropiolate in the presence of **1e** (5 mol %) and Bu_4NCl (8 mol %) in THF at 0 °C for 1 h. As a result, [2 + 2] cycloadduct **38a** was obtained in 97% yield with an enantiomer ratio (er) of 96.5:3.5. The highest er of 99:1 was observed in the reaction of norbornene derivative **37b** with *tert*-butyl phenylpropiolate. In this reaction, cationic complex **1e** reacted with Bu_4NCl to generate a neutral chlororuthenium catalyst, which is an optically active analog of **1a**.



Scheme 11. Asymmetric [2 + 2] cycloaddition of norbornenes **37** with phenylpropiolates.

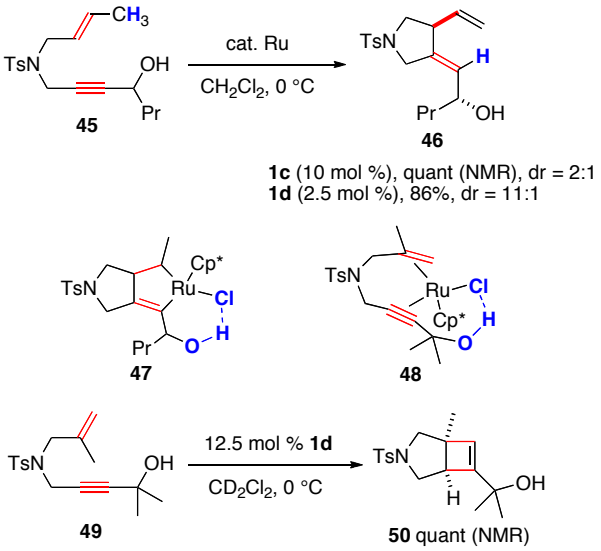
Cyclizations of Enynes

The Cp*RuCl-catalyzed cycloisomerizations of α,ω-enynes are efficient entries into functionalized cyclic compounds.[26] Therefore, the scope of Cp*RuCl-catalyzed enyne cycloisomerizations was expanded to enyne substrates that are previously underinvestigated. For instance, Anderson and coworkers demonstrated that **1a** is an efficient precatalyst for the cycloisomerization of enynamides leading to nitrogen heterocycles.[27] As a typical example, 1,6-enyne **39a** underwent cycloisomerization in the presence of **1a** (5 mol %) in MeCN at 60 °C for 1.5 h, affording exocyclic diene **40a** in 80% yield (Scheme 12). This cycloisomerization was also achieved using a palladium catalyst. Notably, intramolecular [2 + 2] cycloaddition product **41** was obtained in 90% yield when 1,7-enyne **39b** was subjected to the Cp*RuCl-catalyzed conditions at 80 °C. This result was in stark contrast to the fact that the palladium-catalyzed conditions converted **39b** into the corresponding exocyclic diene **40b** via normal cycloisomerization. In contrast to 1,7-enynamide **39b**, silicon-tethered 1,7-enyne **42** underwent normal cycloisomerization to afford exocyclic diene **43** (Scheme 12).[28] Clark and coworkers previously reported that in the presence of a different ruthenium catalyst, the cycloisomerization of **42** afforded **44** as a major product along with **43**.[29] Notably, **43** was obtained as the sole product when **1a** was used in toluene at 70 °C. The obtained cycloisomerization products could be converted into the corresponding acyclic dienylsilanes via Si–O bond cleavage.



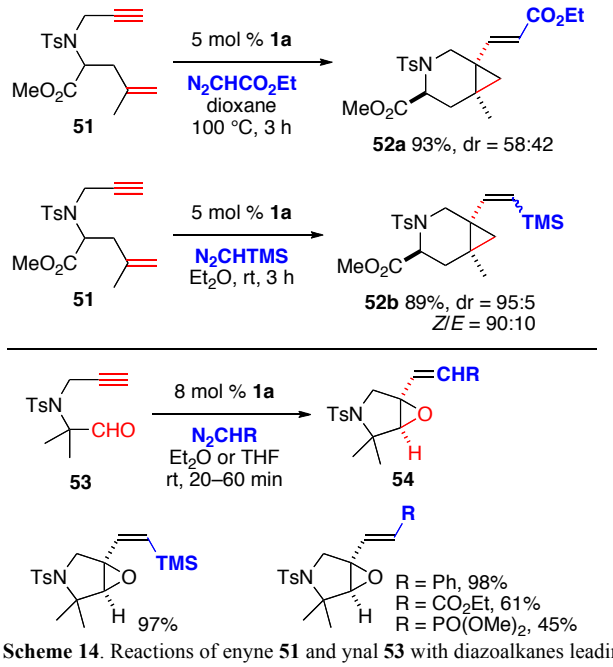
Scheme 12. Cycloisomerizations of enynamides **39a,b** and silicon-tethered 1,7-enyne **42**.

Fürstner and coworkers investigated the diastereoselectivity of the Alder-ene-type cycloisomerization of 1,6-enyne **45** bearing a propargylic alcohol moiety (Scheme 13).[30] When cationic complex **1c** was used as a precatalyst, the diastereoselectivity was moderate (2:1), even though **46** was quantitatively formed. In stark contrast, the use of tetrameric complex **1d** resulted in a significant increase in the diastereoselectivity (11:1). This result was ascribed to the intramolecular hydrogen bond formation between the chloro ligand and hydroxyl group (see **47**). A similar hydrogen bonding interaction was revealed by X-ray crystallography of complex **48**, which was derived from **1d** and enyne **49**. The catalytic transformation of **49** into fused cyclobutene **50** was also reported.



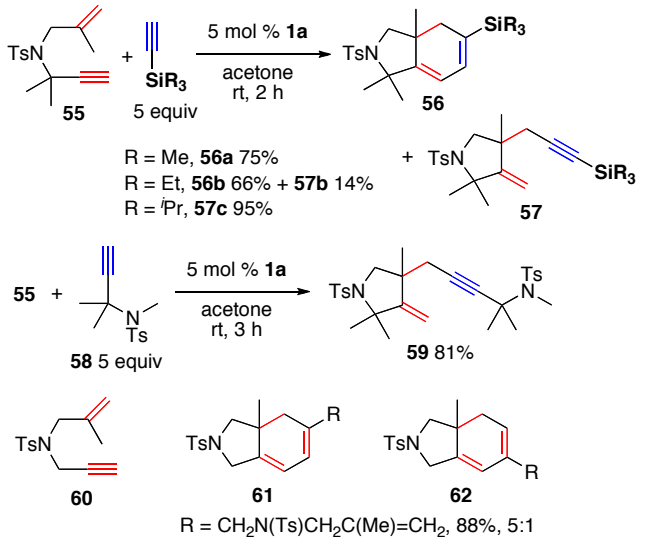
Scheme 13. Diastereoselective Alder-ene-type cycloisomerization of 1,6-enyne **45**.

Dérien, Dixneuf, and coworkers previously reported the cyclocoupling of enynes with diazoalkanes, leading to bicyclo[3.1.0]hexane derivatives.[31] Dérien and coworkers extended this method to the synthesis of cyclic α-amino ester derivatives (Scheme 14).[32] In the presence of **1a** (5 mol %), 1,7-enyne **51** and ethyl diazoacetate were heated in dioxane at 100 °C for 3 h, affording bicyclic α-amino ester **52a** in 93% yield. Although the *E* configuration was observed for the acrylate moiety, the diastereomeric ratio was not high (58:42). On the other hand, the reaction of **51** with (trimethylsilyl)diazomethane in ether at room temperature afforded **52b** in 89% yield with a dr of 95:5 and *Z*/*E* ratio of 90:10. The Saá group also developed the cyclization of alkynals with diazoalkanes, leading to epoxypyrrolidines (Scheme 14).[33] When (trimethylsilyl)diazomethane was used, alkynal **53** was converted into (*Z*)-**54** in 97% yield. (*E*)-**54** were obtained from **53** and diazoalkanes bearing phenyl, ester, and phosphonate groups.



Scheme 14. Reactions of enyne **51** and ynal **53** with diazoalkanes leading to bicyclic compounds.

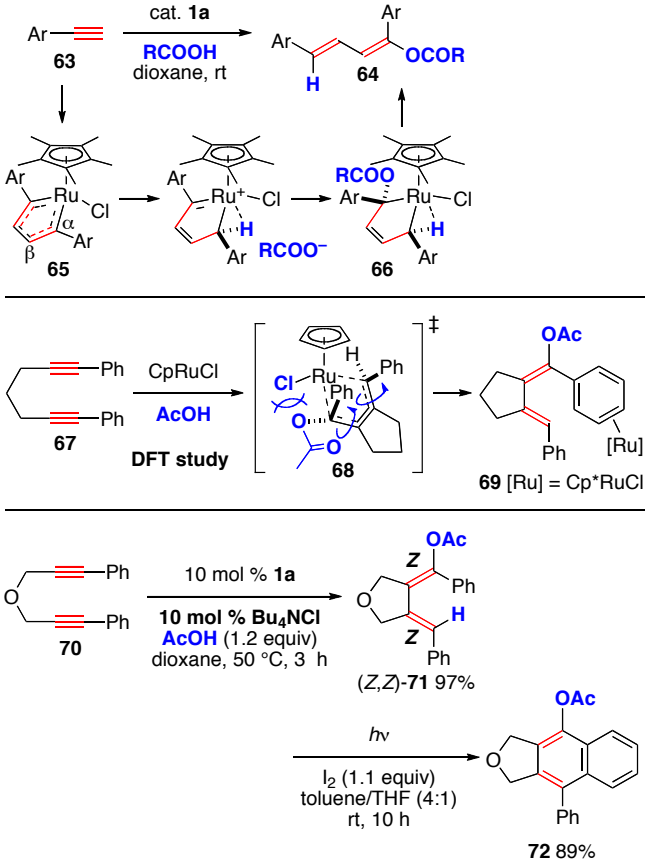
Tenaglia and coworkers discovered the unusual coupling/cyclization of 1,6-enyne **55** with silylacetylenes (Scheme 15).[34] The reaction of **55** with (trimethylsilyl)acetylene was conducted in the presence of **1a** (5 mol %) in acetone at room temperature, affording normal [2 + 2 + 2] cycloadduct **56a** in 75% yield. However, the use of bulkier (triethylsilyl)acetylene afforded alkynylated cyclization product **57b** in 14% yield along with **56b** (66%). The bulky silyl group played an important role in the selective formation of **57**; the combination of **55** with (triisopropylsilyl)acetylene produced **57c** in 95% yield as the sole product. Similarly, *N*-propargyl tosylamides such as **58** were effective terminal alkyne partners; the reaction of **55** with **58** afforded **59** in 81% yield. The propargylic tertiary centers on the enyne substrates are essential for the alkynylative cyclization, as enyne **60** afforded regioisomeric dimers **61** and **62** in a combined yield of 88% in a 5:1 ratio, even in the presence of (triisopropylsilyl)acetylene (5 equiv).



Scheme 15. Alkynylative cyclization of enyne **55** with silylacetylenes and *N*-propargylic tosylamide **58**.

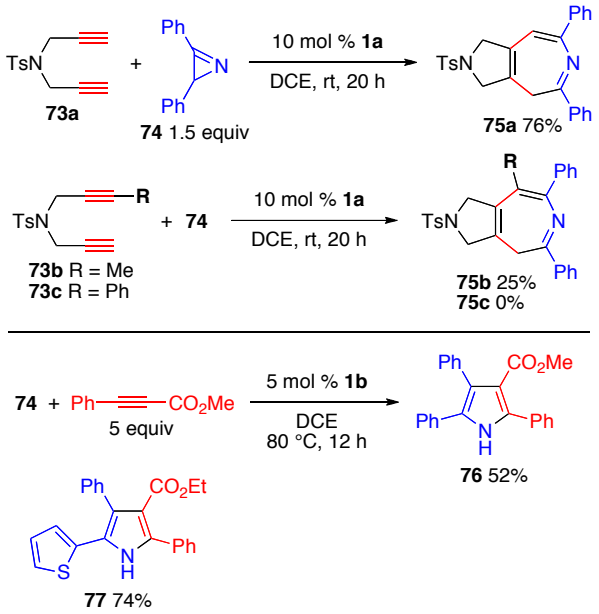
Other Annulation Reactions

The Dixneuf group reported that arylacetylenes **63** underwent carboxylative dimerization to chemo- and stereo-selectively produce (1*E*,3*E*)-1,4-diphenyl-1,3-butadienyl acetate **64** (Scheme 16).[35] This reaction was proposed to proceed via ruthenacycle intermediate **65**, which undergoes protonation at one of the α carbons by a carboxylic acid; subsequent addition of the carboxylate anion to the other α carbon generates **66**. Finally, the reductive elimination of Cp*RuCl from **66** affords **64**. Later, Yamamoto analyzed the proposed mechanism using a DFT method.[36] In his report, the carboxylative cyclization of 1,6-diyne **67** was also analyzed, and the stereoselectivity of the formation of complex **69** was ascribed to the repulsive interaction between the chlorine ligand and acetate moiety in the transition state of the final reductive elimination (see **68**). Therefore, the chlorine ligand is imperative for the stereoselective carboxylative cyclization of 1,6-diynes. In fact, the reaction of diyne **70** with acetic acid in the presence of **1a** and Bu_4NCl (10 mol % each) in dioxane at 50 °C for 3 h afforded the expected product (*Z*,*Z*)-**71** in 97% yield.[37] The addition of Bu_4NCl suppressed the dissociation of the chlorine ligand. When $AgPF_6$ was added to abstract the chlorine ligand, the stereoselectivity was completely lost. The obtained product (*Z*,*Z*)-**71** could be converted into naphthalenyl acetate in 89% yield via oxidative photocyclization. Notably, the (*Z*,*Z*)-configuration of carboxylative cyclization products is necessary for efficient photocyclization.



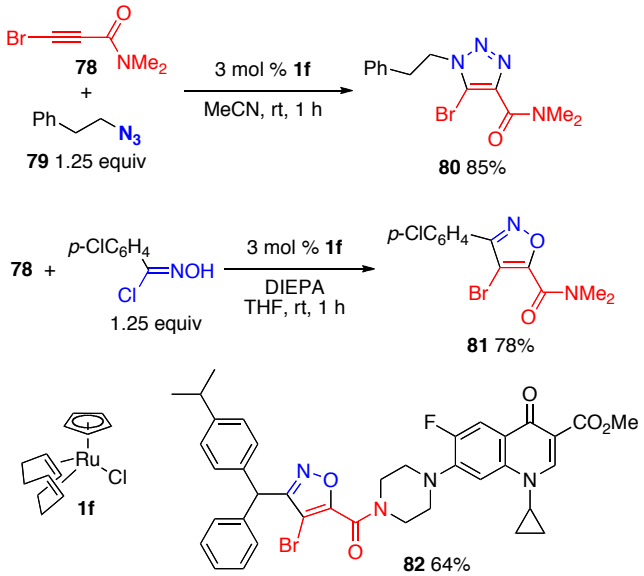
Scheme 16. Carboxylative dimerization of arylalkynes and carboxylative cyclization of 1,6-diynes.

Wang, Wan, and coworkers disclosed a novel [3 + 2 + 2] cycloaddition of 1,6-diynes with 2*H*-azirines.[38] In the presence of **1a** (10 mol %), diyne **73a** reacted with azirine **74** in DCE at room temperature for 20 h, affording fused azepine **75a** in 76% yield (Scheme 17). When unsymmetrical diyne **73b** bearing a methyl terminal group was used as the substrate, **75b** was obtained as a single regioisomer, albeit in a lower yield (25%). However, diyne **73c** bearing a phenyl terminal group was found to be completely unreactive. The same group also reported the [3 + 2] cycloaddition of activated alkynes with 2*H*-azirines.[39] For example, **74** reacted with excess methyl phenylpropiolate in the presence of oligomeric complex **1b** (5 mol %) in DCE at 80 °C for 12 h, affording tetra-substituted pyrrole **76** in 52% yield. Using this method, (2-thienyl)pyrrole **77** was also obtained in 74% yield.



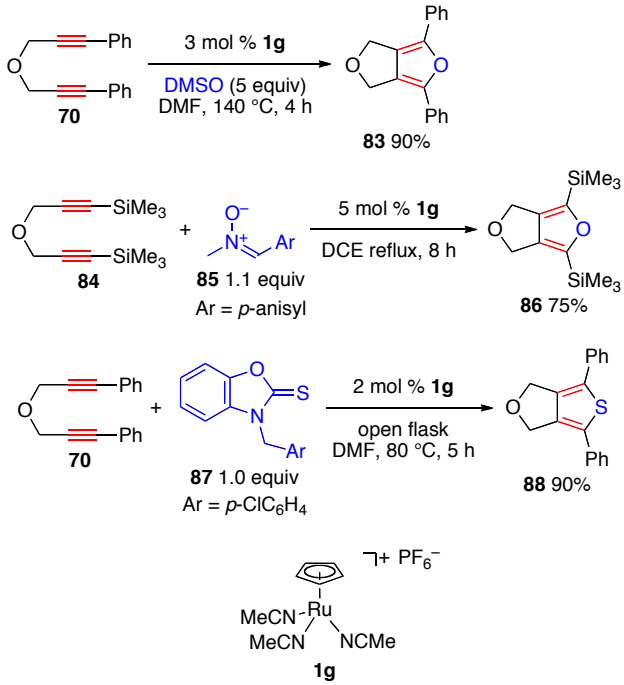
Scheme 17. [3 + 2 + 2] and [3 + 2] cycloadditions of 2*H*-azirine **74** with alkynes.

Ruthenium-catalyzed azide-alkyne [3 + 2] cycloadditions have garnered significant attention because of the regioselectivity and substrate scope, which are distinct from those of the parent copper-catalyzed click reaction.[40] Although **1a** has been conventionally employed as an efficient precatalyst for azide-alkyne cycloadditions, Fokin and coworkers reported that cyclopentadienyl complex **1f** is superior to **1a** in the cycloadditions of activated 1-haloalkynes (Scheme 18).[41] The [3 + 2] cycloaddition of 3-bromopropiolamide **78** with azide **79** proceeded in the presence of **1f** (3 mol %) in MeCN at room temperature, regioselectively affording 5-bromotriazole **80** in 85% yield. The [3 + 2] cycloaddition of **78** with an in-situ produced nitrile oxide was also efficiently catalyzed by **1f**, affording the corresponding 4-bromoisoxazole **81** in 78% yield. [3 + 2] Cycloadditions using **1f** as a precatalyst were successfully applied to the synthesis of diverse 5-bromotriazoles and 4-bromoisoxazoles, including medicinally relevant compound **82**.



Scheme 18. [3 + 2] Cycloaddition of 3-brormopropiolamide **78** with azide and nitrile oxide.

Although this digest focuses on the Cp*RuCl-catalyzed annulation reactions, closely related [2 + 2 + 1] cycloadditions of α,ω-diynes using cationic complex $[CpRu(MeCN)_3]PF_6$ (**1g**) was briefly outlined as the last topic. Yamamoto and coworkers previously demonstrated that oxygen-transfer [2 + 2 + 1] cycloaddition of 1,6-diyne **70** bearing phenyl terminal groups proceeded in the presence of a cationic complex **1g** (3 mol %) and DMSO (5 equiv) in DMF at 140 °C, affording fused furan **83** in 90% yield (Scheme 18).[42a] In this reaction, DMSO acted as the oxygen donor. When nitrone **85** (1.1 equiv) was used instead of DMSO, [2 + 2 + 1] cycloaddition proceeded with 1,6-diyne **84** bearing bulky TMS terminal groups. The reaction was complete within 8 h in the presence of **1g** (5 mol %) in DCE at reflux, affording bis(silyl)furan **86** in 75% yield.[42b] Moreover, sulfur-transfer [2 + 2 + 1] cycloaddition was recently achieved using thiocarbonyl compound **87** as the sulfur donor.[42c] In the presence of **1g** (2 mol %) and **87** (1.0 equiv), **70** underwent cycloaddition in DMF at 80 °C for 5 h, affording fused thiophene **88** in 90% yield. Notably, this reaction could be performed in an open flask.



Scheme 18. Atom-transfer [2 + 2 + 1] cycloadditions of 1,6-diynes **70** and **84**.

Conclusion

In this digest, recently reported annulation reactions using Cp*RuCl(cod) and related ruthenium complexes as precatalysts were surveyed. Conventional [2 + 2 + 2] cycloadditions and enyne cycloisomerizations have been continuously investigated to expand their applicability and improve selectivity and yields. Moreover, unconventional annulations using hitherto underinvestigated molecules such as alkynals and 2*H*-azirines have been developed to produce interesting heterocyclic compounds. As an impressive advancement in this field, asymmetric [2 + 2] cycloaddition was developed using an optically active catalyst that is closely related to Cp*RuCl complexes. Hopefully, this digest will prompt the development of novel Cp*RuCl-catalyzed transformations in the near future.

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