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HETEROCYCLE FORMATION FROM ZIRCONACYCLES

Lishan Zhou, Masamichi Yamanaka,[#] Ken-ichiro Kanno, and Tamotsu Takahashi*

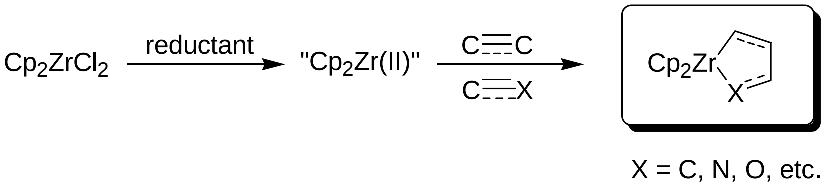
Catalysis Research Center, Hokkaido University and SORST, Japan Science and Technology Agency (JST), Kita-ku, Sapporo 001-0021, Japan
[#]Department of Chemistry, Faculty of Science, Shizuoka University, 836 Ohya, Suruga-ku, Shizuoka 422-8529, Japan

Abstract – Zirconium-mediated synthetic methods of a series of heterocyclic compounds were reviewed. Discussion was focused on the reactions including the other metals, such as Cu, Ni, Li, and so on. These enable us to synthesize a series of heterocycles having N, O, Si, S, Sn, etc. in the ring skeletons. The key point of the reaction is transmetalation from Zr to the other employed metals, which have a crucial role for reactivity and selectivity of the reaction.

1. INTRODUCTION

Heterocycles have been very important compounds not only in medicinal chemistry but also in material science. Development of novel reactions and useful reagents for heterocycle formation is an important activity in organic chemistry. For synthetic chemists, transition metal catalyzed or mediated cyclization is one of the most important methods for construction of heterocyclic skeletons.[1]

Zirconocene complexes are very useful in organic synthesis, in particular because of their high reactivity toward a series of organic unsaturated compounds, such as alkynes, alkenes, aldehydes, ketones, nitriles, and so on.[2] Among them, low-valent zirconium species, $Cp_2Zr(II)$ shows outstanding advantage for the formation of various zirconacycles in high yields via oxidative cyclization with unsaturated compounds (Scheme 1). The resulting zirconacycles can be subjected for further transformation to produce a variety

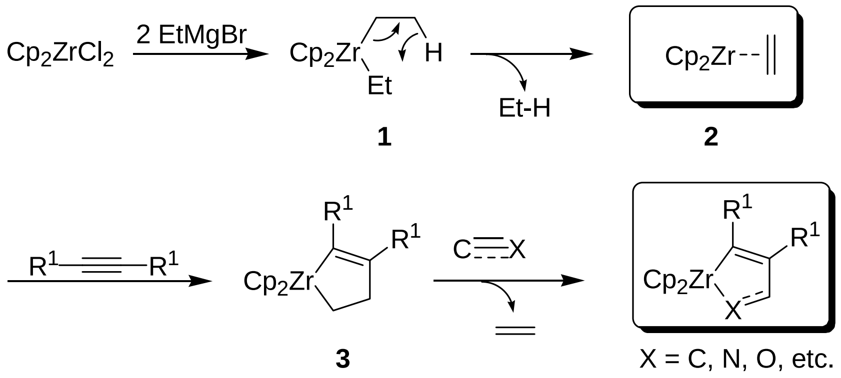


Scheme 1

Dedicated to Professor Ryoji Noyori on the occasion of his 70th birthday.

of organic compounds.

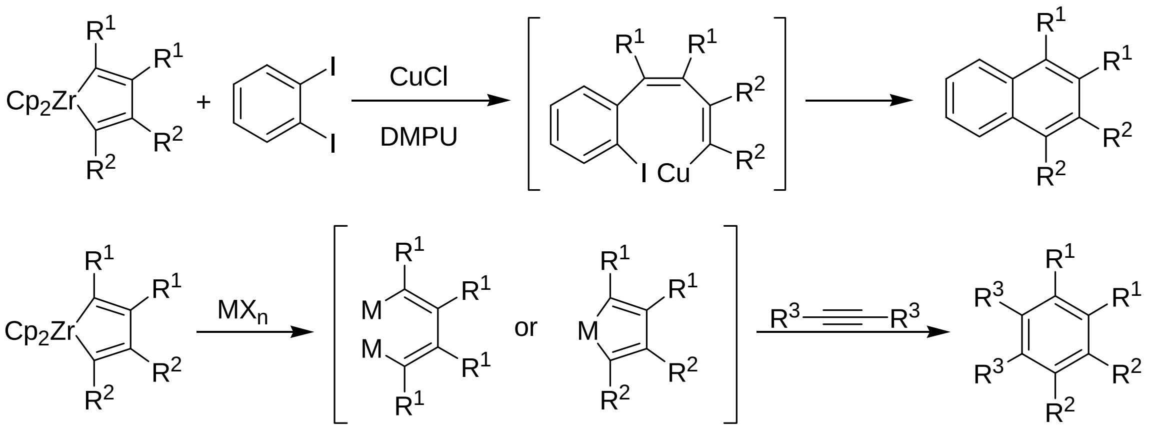
So far, various transition-metal-mediated cyclization reactions of a series of unsaturated substrates have been developed.[1] A crucial drawback to be overcome, however, is selective formation of *unsymmetrical* metalacycles from two different unsaturated components because it is very often accompanied with undesirable formation of *symmetrical* metalacycles from homocoupling of one of the substrates. As shown in Scheme 2, zirconocene(ethylene) complex **2** provides a fine solution for the problem.[3]



Scheme 2

Zirconocene(ethylene) complex **2** has unique advantage for construction of unsymmetrical metalacycles from two different unsaturated substrates. Firstly, zirconocene(ethylene) complex **2** can be easily generated in situ from zirconocene diethyl (**1**) via intramolecular *β*-hydrogen abstraction. When it is formed in the presence of an alkyne, the corresponding zirconacyclopentene **3** is produced. Secondly, the zirconacycle can react with the second unsaturated component to afford the desired unsymmetrical zirconacycle with high pair-selectivity. In contrast, the same reaction does not proceed with zirconocene(1-butene) complex (Negishi reagent: generated from zirconocene dibutyl)[4] because dissociation of 1-butene from the zirconium center is much faster than that of ethylene to produce symmetrical zirconacycles via homo-coupling of the same component.

The applicability of zirconacycles toward organic synthesis can be widen via transmetalation into the other metals such as Cu, Ni, Li, Mg, Al, and so on.[2h,i,p,q] The transmetalation strategy is highly effective



Scheme 3

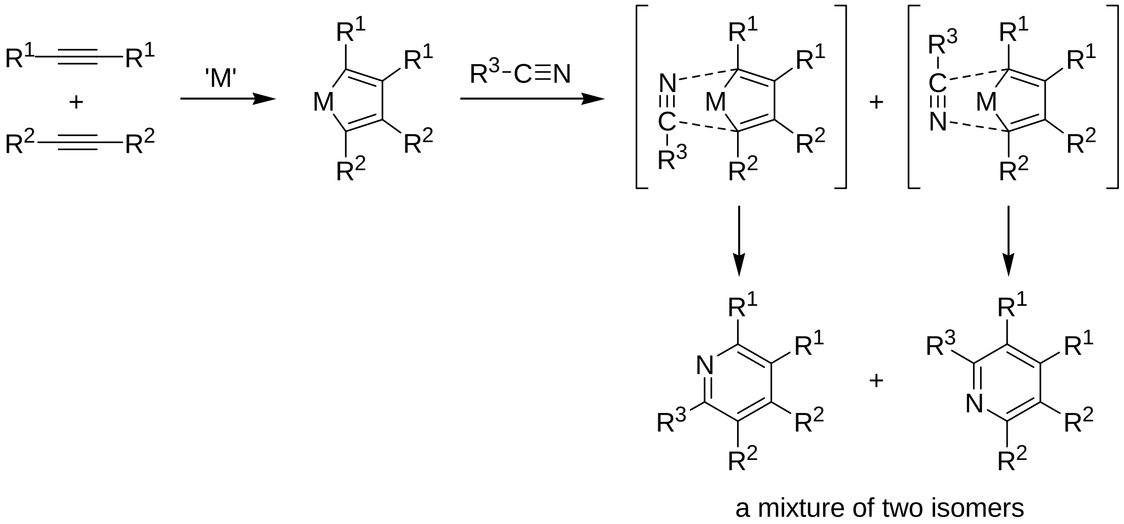
for the cycloaddition reactions with zirconacycles. For example, coupling reaction of *o*-diiodobenzene with zirconacyclopentadiene could proceed efficiently in the presence of CuCl.[5] And also, cycloaddition reactions of zirconacyclopentadienes with alkynes to afford highly-substituted benzenes [6] were mediated by Cu or Ni salts as shown in Scheme 3.

In the zirconium-mediated reactions shown above, heteroatom-containing substrates are also applicable and it enables us to synthesize a series of heterocyclic compounds. For instance, when nitriles or carbonyl compounds are employed for the reactions with zirconacyclopentenes, the corresponding aza- or oxazirconacycles can be produced, and the subsequent cycloaddition affords the corresponding N- or O-containing heterocycles. On the other hand, cycloaddition of zirconacyclopentadienes with heteroatom components also produces the corresponding heterocycles. Along with the strategy, a series of heterocycles containing nitrogen, oxygen, silicon, tin, sulfur, and so on have been synthesized as described in the following sections.

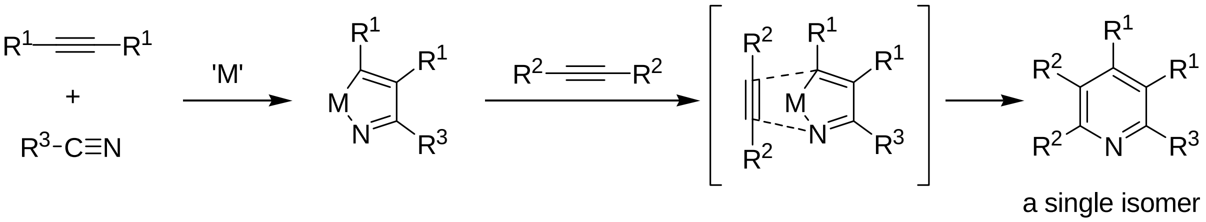
In this article, discussion is focused on zirconium-mediated synthesis of heterocyclic compounds via transmetalation to other metals. Although there are many examples of heterocycle formations, especially via direct reactions of zirconacycles with halides of main group elements,[7,8] we would like to emphasize the cooperative effects between zirconium and the other metal species. For the same reason, reactions of zirconium-based reagents with heteroatom-tethered enynes or diynes to produce the corresponding heterocyclic compounds[9] were also precluded.

2. FORMATION OF NITROGEN-CONTAINING HETEROCYCLES FROM ZIRCONACYCLES

Syntheses of nitrogen containing six-membered ring compounds represented by pyridine derivatives have been paid much attention for long decades. Cocycloaddition of two alkynes and one nitrile mediated or



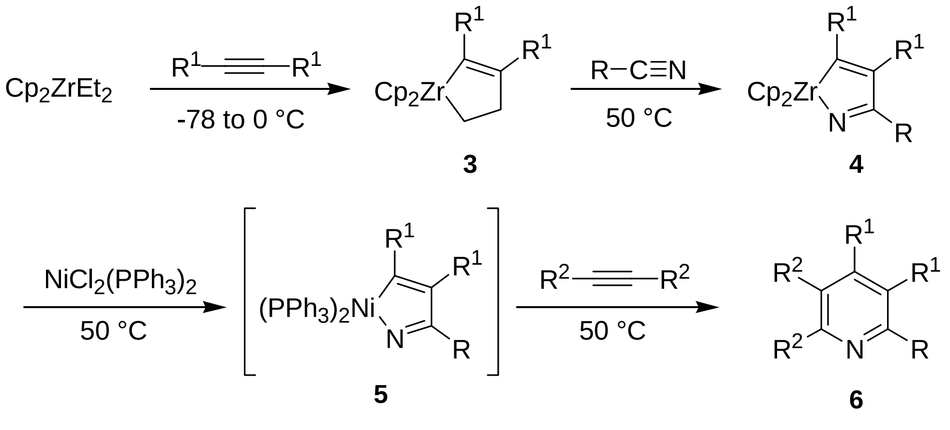
Scheme 4



Scheme 5

catalyzed by transition metal complex is one of the simplest synthetic pathways to construct pyridine framework. There is a critical problem, however, as regards the selectivity in the intermolecular coupling of two different alkynes and a nitrile resulting from the reaction mechanism via metalacyclopentadiene. The reaction between metalacyclopentadiene prepared from two different alkynes and a nitrile affords a mixture of two regioisomers due to the orientation of the nitrile (Scheme 4). Changing reaction order of those three components i. e. the reaction of azametalacyclopentadiene with alkyne would solve the selectivity problem essentially (Scheme 5).

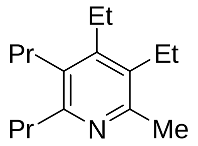
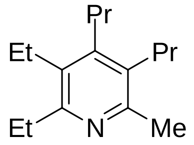
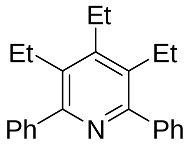
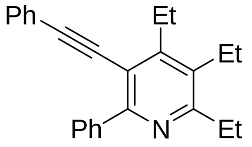
Selective coupling of an alkyne and nitrile using Cp_2ZrEt_2 afforded the corresponding azazirconacyclopentadiene **4**.[3] Reaction of the azazirconacyclopentadiene **4** with the second alkyne in the presence of Ni(II) complex gave the corresponding pyridine derivative as a single isomer[6a,10] (Scheme 6). The results of selective pyridine formation from two different alkynes and a nitrile are summarized in Table 1. The reaction of azazirconacyclopentadiene prepared from 3-hexyne and acetonitrile with 4-octyne gave **6a** in 86% yield. On the other hand, the reaction of azazirconacyclopentadiene prepared from 4-octyne and acetonitrile with 3-hexyne gave **6b** in 58% yield. Pyridine formation via azazirconacyclopentadiene could synthesize **6a** or **6b** selectively by changing addition order of alkynes. Using unsymmetrical alkynes such as 1-phenyl-1-butyne or diphenylbutadiyne as the second alkynes, the coupling reactions with azazirconacyclopentadiene proceeded regioselectively and gave single isomers of the corresponding pyridines **6c** and **6d**, respectively.



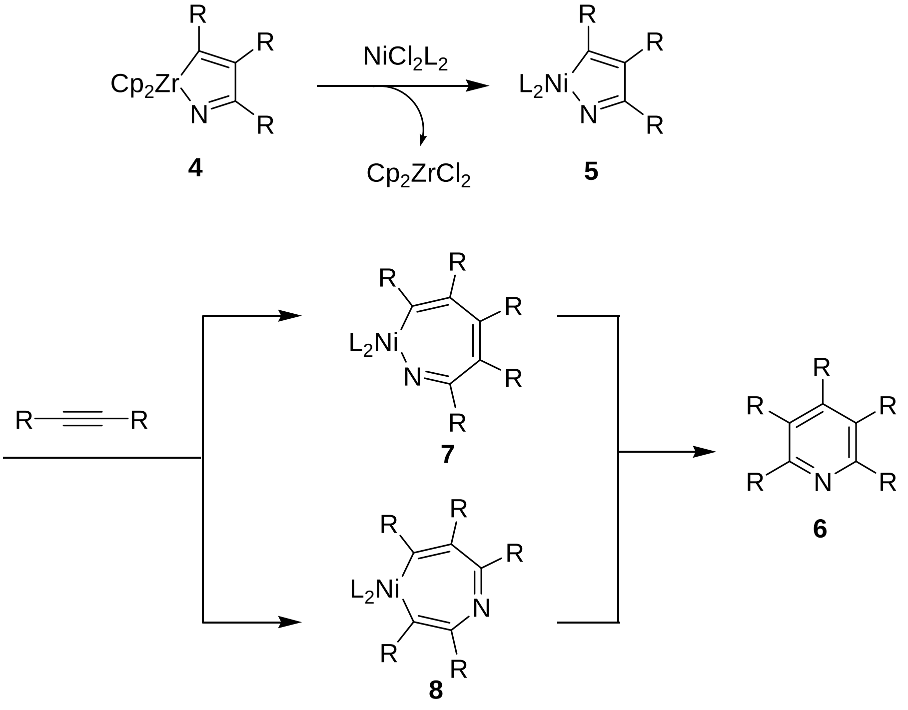
Scheme 6

The reaction mechanism is supposed as shown in Scheme 7. Transmetalation of azazirconacyclopentadiene **4** and $NiCl_2(PPh_3)_2$ takes place at first. Then second alkyne is inserted to the

Table 1. Formation of Pyridine Derivatives

entry	first Alkyne	nitrile	second Alkyne	product	yield (%)[a]
1	Et—≡—Et	MeCN	Pr—≡—Pr	 **6a**	86(66)
2	Pr—≡—Pr	MeCN	Et—≡—Et	 **6b**	58(41)
3	Et—≡—Et	PhCN	Ph—≡—Et	 **6c**	64(53)
4	Et—≡—Et	EtCN	Ph—≡—≡—Ph	 **6d**	75(44)

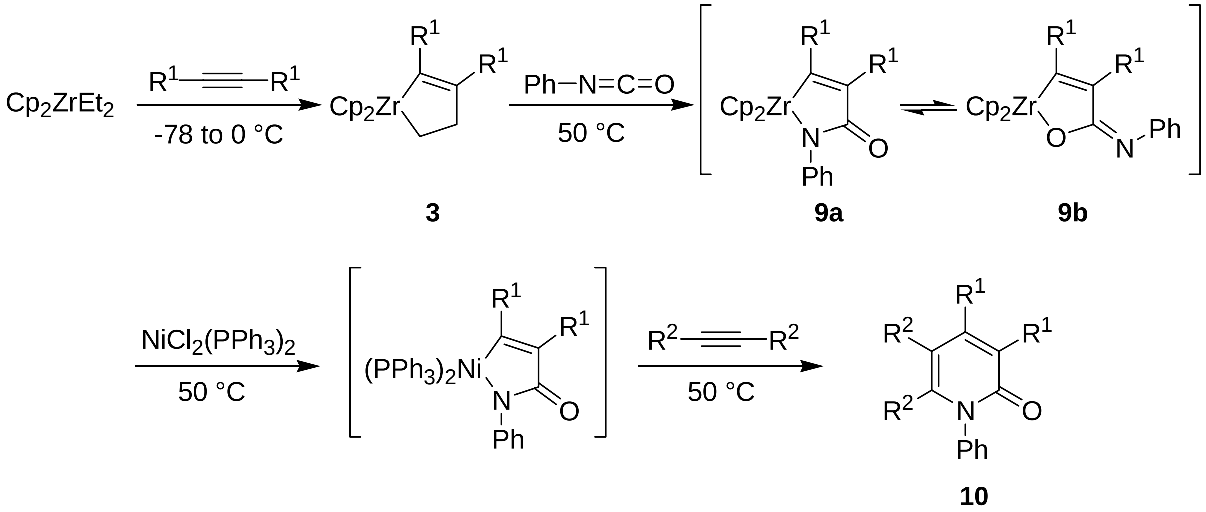
[a] GC yields. Isolated yields are given in parentheses.



Scheme 7

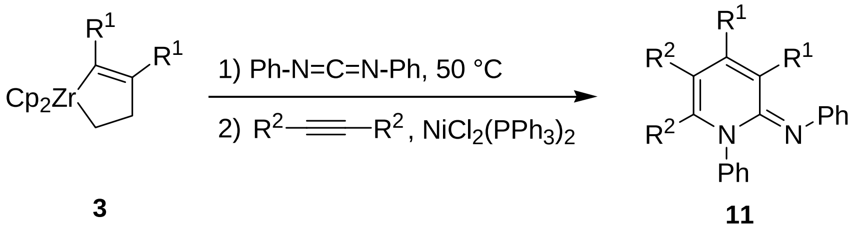
azanickelacyclopentadiene **5**. There are two pathways for insertion of the alkyne into azanickelacyclopentadiene to produce azanickelacycloheptatrienes **7**, **or** **8**. Intramolecular reductive coupling of **7** or **8** affords the pyridine derivative **6** as products.

The addition-order-dependent selective coupling reactions can be applied for other nitrogen containing heterocyclic compounds (Scheme 8).[10b] Reaction of zirconacyclopentenes and isocyanates gave azazirconacyclopentenones and its isomers (**9a** and **9b**).[11] Coupling reaction of azazirconacyclopentenone with second alkyne in the presence of $NiCl_2(PPh_3)_2$ afforded pyridone derivative **10** as a product. Even though using two different alkynes, the reaction proceeded selectively and provided a product as a single isomer. Selected examples were shown in part of Table 2.



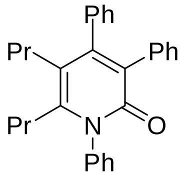
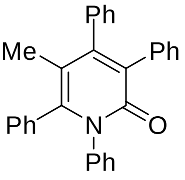
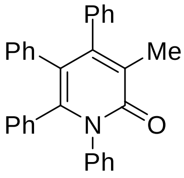
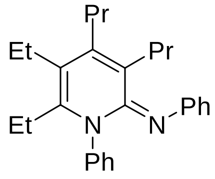
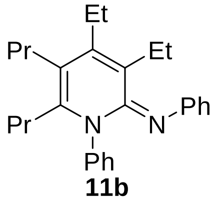
Scheme 8

When unsymmetrically substituted alkyne such as 1-phenyl-1-propyne was used as the first or for the second alkyne, the reaction proceeded regioselectively and only one regioisomer was obtained as a product (**10b** or **10c**). Iminopyridine derivatives **11** were also synthesized by using the similar procedure. A carbodiimide derivative was employed for the reaction instead of phenylisocyanate (Scheme 9). In this reaction, iminopyridine derivative was formed as a single isomer. In part of Table 2 are given some typical examples. Formation of regioisomers constructed from 4-octyne, 3-hexyne and a carbodiimide is controlled by changing the addition-order of alkynes and **11a** and **11b** were selectively synthesized selectively.



Scheme 9

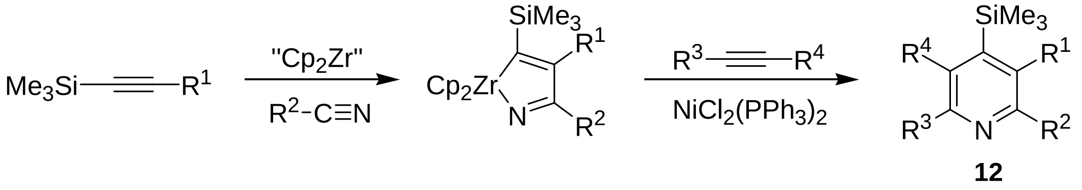
Table 2. Formation of Pyridone and Iminopyridine Derivatives

entry	First Alkyne	Isocyanate or carbodiimide	Second Alkyne	Product	Yield (%)[a]
1	Ph—≡—Ph	Ph−N=C=O	Pr—≡—Pr	 **10a**	72(61)
2	Ph—≡—Ph	Ph−N=C=O	Ph—≡—Me	 **10b**	(56)
3	Ph—≡—Me	Ph−N=C=O	Ph—≡—Ph	 **10c**	(65)
4	Pr—≡—Pr	Ph−N=C=N−Ph	Et—≡—Et	 **11a**	(56)
5	Et—≡—Et	Ph−N=C=N−Ph	Pr—≡—Pr	 **11b**	(69)

[a] GC yields. Isolated yields are given in parentheses.

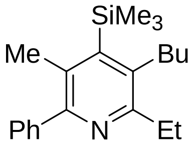
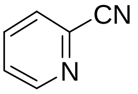
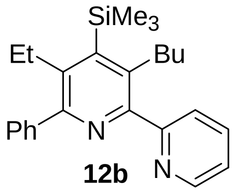
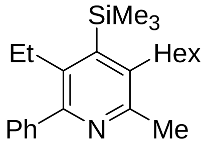
Combination of the addition-order-dependent selective coupling procedure and functional-group-dependent selective coupling of unsymmetrical alkynes could provide pyridine derivatives with five different substituents selectively (Scheme 10).[10b] Silyl-substituted unsymmetrical alkynes and nitriles afford azazirconacyclopentadienes with complete regioselectivity.[3,11] Phenyl and alkyl substituted unsymmetrical alkynes react with azanickelacyclopentadienes selectively as described above. Selected examples were shown in Table 3.

Coupling reaction of 1-trimethylsilyl-1-hexyne as the first alkyne, propionitrile and 1-phenyl-1-propyne as the second alkyne proceeded to give pyridine derivative **12a** with five different substituents as a single



Scheme 10

Table 3. Regioselective Formation of Pentasubstituted Pyridine Derivatives

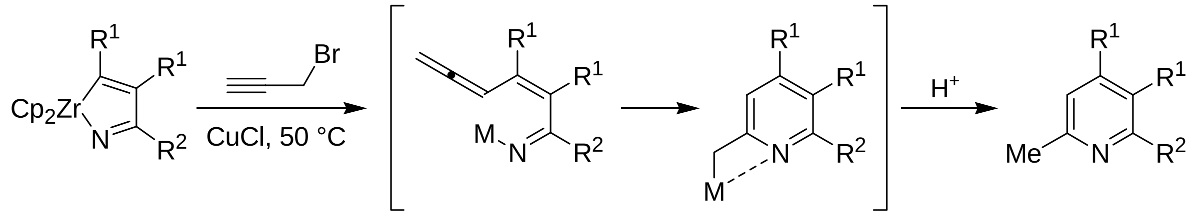
entry	first alkyne	nitrile	second alkyne	product	yield (%)[a]
1	Me_3Si—≡—Bu	EtCN	Ph—≡—Me	 **12a**	77(52)
2	Me_3Si—≡—Bu		Ph—≡—Et	 **12b**	62(49)
3	Me_3Si—≡—Hex	MeCN	Ph—≡—Et	 **12c**	69(59)

[a] GC yields. Isolated yields are given in parentheses.

isomer in 77% yield. Using pyridine substituted nitrile gave bipyridine derivative (**12b**) as a product. It is noteworthy that no regioisomers were obtained in all cases.

Tetrasubstituted pyridine derivatives **14** could be formed by the reaction of azazirconacyclopentadiene **4** with propargyl bromide in the presence of CuCl (Scheme 11).[10b] Two different bonds of azazirconacyclopentadiene such as the Zr-C and the Zr-N bonds are reactive for the regioselective reactions. The sp^2 carbon attached to zirconium in the zirconacycle transmetalates from zirconium to copper and then reacts with propargyl bromide. Allenic intermediate **13** is converted to pyridine derivative **14** via intramolecular cyclization. In Table 4 are given some typical examples. Pyridine derivatives are formed with complete regioselectivity and substituents are introduced to the 2, 3, 4, and 6 positions of pyridine framework. All different substituted pyridine derivatives including hydrogen (**14c**) were formed as a single isomer using triethylsilylphenylethyne, propionitrile and propargyl bromide.

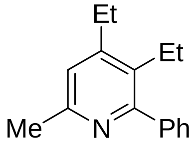
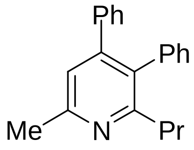
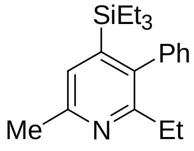
A reaction of $Cp_2Zr(II)$ species with an alkyne and an isocyanate produces the corresponding aza- or oxazirconacycle **15** as shown in Scheme 12. Zirconacycle **15** can be used for the synthesis of



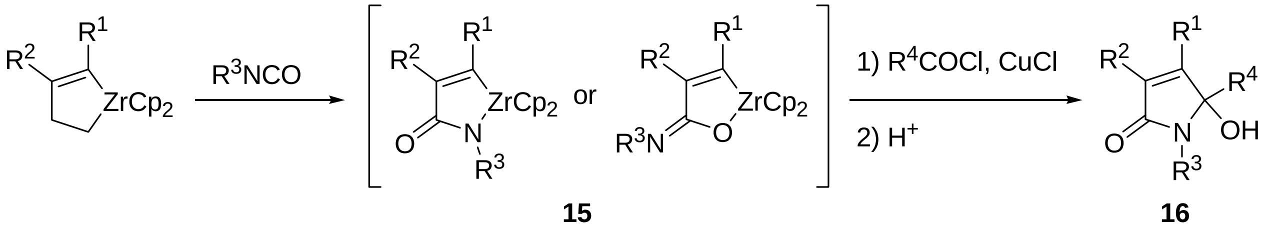
4 **13** **14**

Scheme 11

Table 4. Regioselective Formation of Tetrasubstituted Pyridine Derivatives

entry	first alkyne	nitrile	product	yield (%)[a]
1	Et—≡—Et	PhCN	 **14a**	98(77)
2	Ph—≡—Ph	PrCN	 **14b**	66(57)
3	Et_3Si—≡—Ph	EtCN	 **14c**	94(81)

[a] GC yields. Isolated yields are given in parentheses.

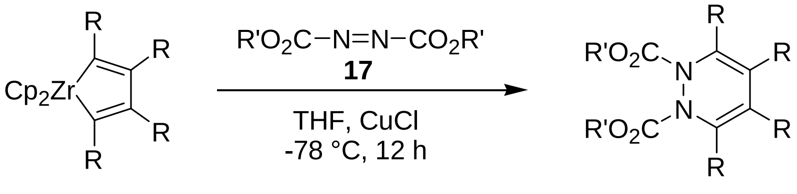


15 **16**

Scheme 12

5-hydroxypyrrol-2(5*H*)-ones **16** by the reaction with acyl halides in the presence of CuCl.[12]

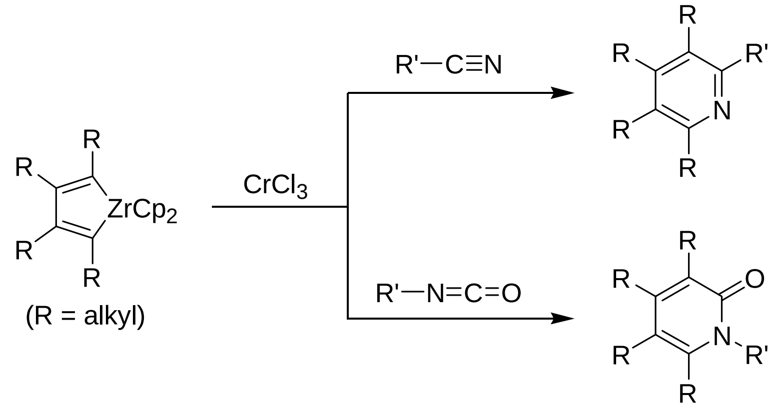
Formation of substituted dihydropyridazines was achieved by the reaction of zirconacyclopentadiene with azodicarboxylate **17** (Scheme 13).[13] Although so many examples of the formation of five-membered heterocycles from zirconacyclopentadienes have been reported,[7,8] six-membered heterocyclic compound formation is very limited from zirconacyclopentadienes. In this case, CuCl was the most effective as the additive to be transmetalated from the zirconacycles. When zirconacycles was treated with 2 equiv of azodicarboxylate and 2 equiv of CuCl at -78 °C and stirred for 12 h, the corresponding dihydropyridazines **18** were formed in good yields.



18

Scheme 13

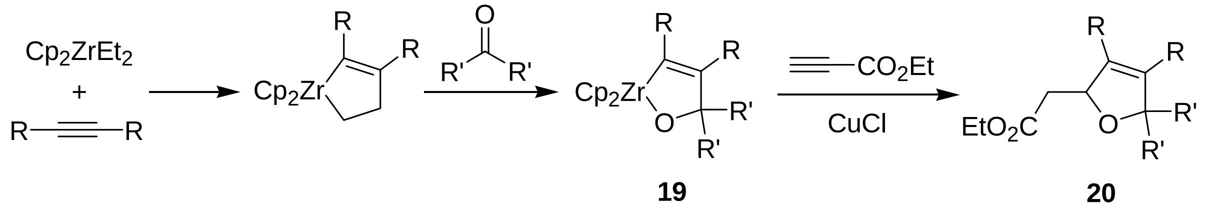
Transmetalation from zirconacyclopentadienes to chromium is also applicable for nitrogen-containing 6-membered heterocycles. It was found that alkyl-substituted zirconacyclopentadienes were treated with nitriles and isocyanates to afford pyridines and pyridones, respectively, in good yields (Scheme 14).[14] It is reasonable to assume that the reaction proceeds via the corresponding chromacyclopentadiene as an intermediate. In the reaction mixture, formation of Cp_2ZrCl_2 was detected. This fact suggests that transmetalation from zirconacyclopentadienes to Cr proceeded. The similar cycloaddition reaction of the intermediary chromacycles with alkynes was reported.[15]



Scheme 14

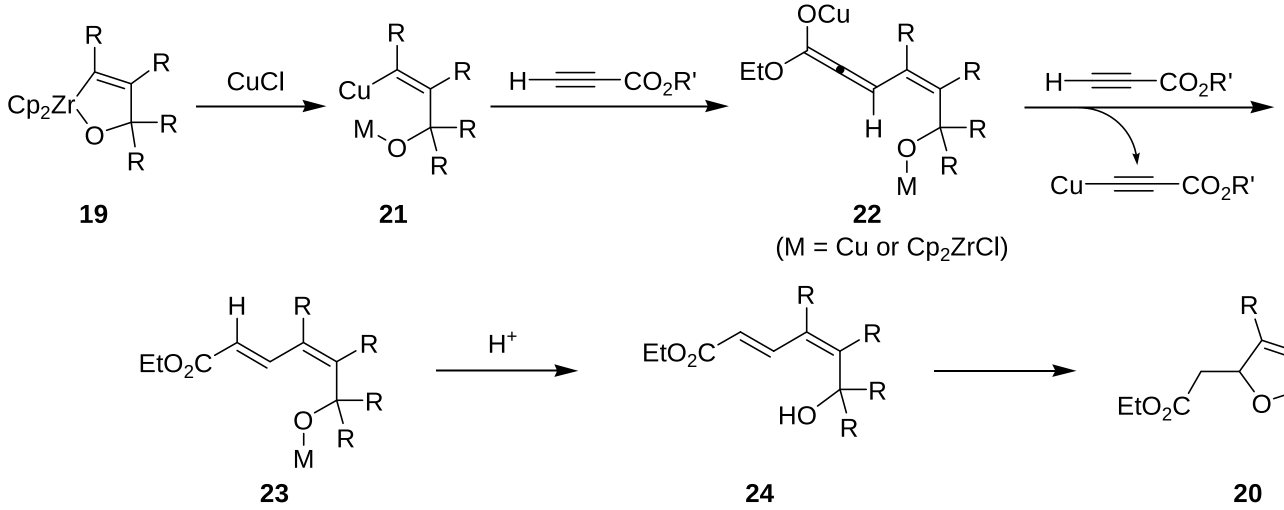
3. FORMATION OF OXYGEN-CONTAINING HETEROCYCLES FROM ZIRCONACYCLES

Oxazirconacyclopentenes **19** can be prepared conveniently by the reaction of zirconacyclopentenes with ketones,[3d,16] and they were applied for the preparation of oxygen-containing heterocycles. As shown in Scheme 15, the reactions of **19** with ethyl propynoate in the presence of CuCl produced the corresponding 2,5-dihydrofurans **20** via 1,1-addition of zirconacycle to propynoate ester.[17] It is interesting that the reaction of zirconacyclopentadienes to propynoates proceeds in 1,1-cycloaddition manner to afford the corresponding cyclopentadienes.[18] This is in sharp contrast to that the most of the cycloadditions of zirconacycles proceed in 1,2-cycloaddition manner.[6,9e,10] The existence of CuCl was essential for the reaction, and no cyclization proceeds without CuCl. To obtain the product in high yield, 2 equivalents of ethyl propynoates were necessary. When substituted propynoates (internal alkynes) was employed, no reaction took place.



Scheme 15

The following reaction mechanism can be proposed for the formation of dihydrofurans (Scheme 16). In the first step the Zr-C bond of **19** is transmetalated to the Cu-C bond to give **21**. Alkenyl copper moiety of **21** adds to the triple bond of propynoate to give enolate **22**. Enolate **22** is hydrolyzed by acidic hydrogen of another molecule of propynoate to give open-chain intermediate **23**, which was detected by NMR measurement of the reaction mixture (R = Et). Hydrolysis with HCl gives alcohol **24** that undergoes intramolecular cyclization reaction to afford a dihydrofuran derivative **20**.

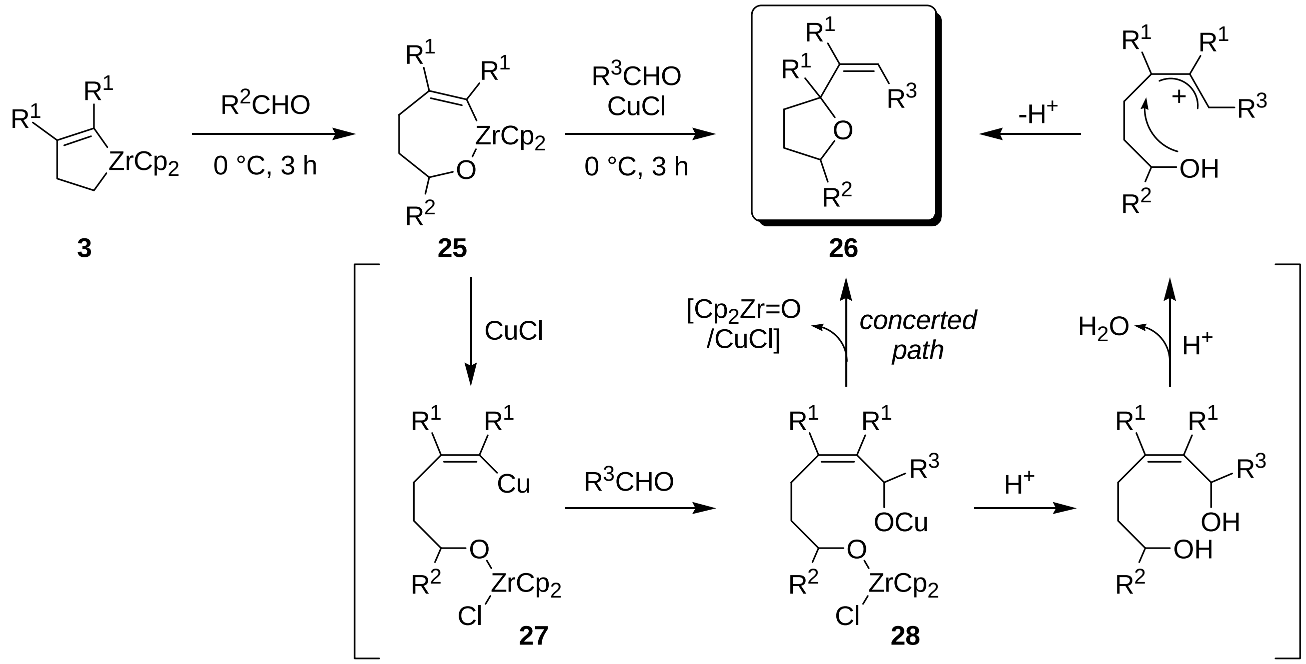


Scheme 16

One-pot synthesis of tetrahydrofuran derivatives via oxazirconacycles was reported (Scheme 17).[19] A reaction of zirconacyclopentene **3** with an aldehyde at 0 °C affords the corresponding oxazirconacycloheptene **25**. In the presence of CuCl, 7- membered zirconacycle **25** reacts with another aldehyde to afford the corresponding alkenyltetrahydrofuran **26** in a good yield after hydrolysis. Since zirconacyclopentene **3** can be prepared from an alkyne and ethylene, the formation of **26** is regarded as selective four-component coupling reaction mediated by zirconium.

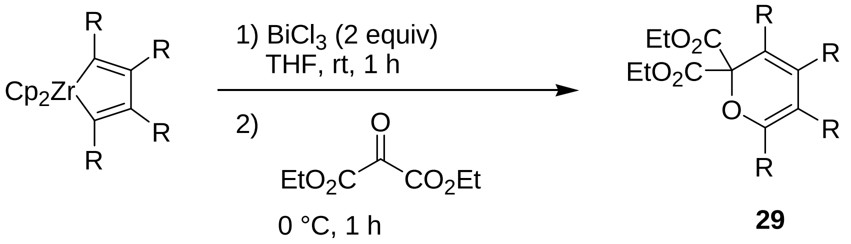
It is highly probable that the reaction of zirconacycle **25** with CuCl produces alkenylcopper **27** via transmetalation from Zr to Cu. Addition reaction of **27** to the second aldehyde affords **28**. The subsequent hydrolysis may cause ring closing by attacking of the hydroxy group toward the allylic alcohol moiety in 5-*exo-trig* manner. The NMR monitoring of the reaction mixture, however, indicated the possibility of the other mechanism, because the formation of **26** was observed without hydrolysis.

This observation suggests the direct pathway from **28** to **26** by the concerted elimination of [Cp_2Zr=O·CuCl].



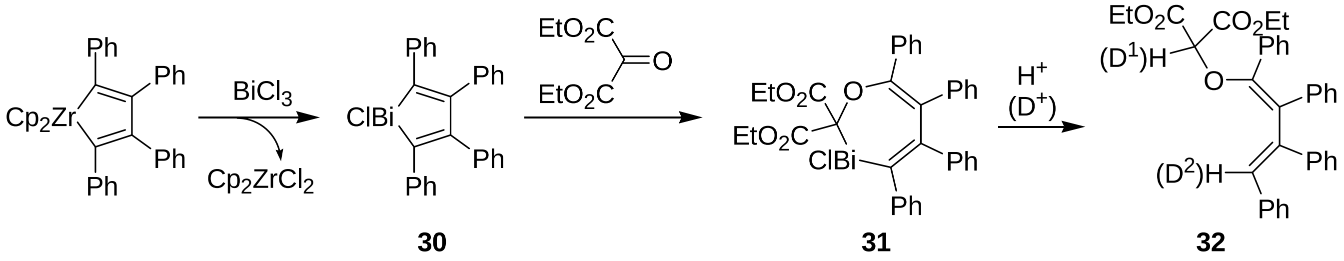
Scheme 17

Transmetalation to bismuth enables us to convert zirconacyclopentadienes into 6-membered heterocyclic compounds via cycloaddition to C=O, C=N, and N=N bonds.[13] Reaction of zirconacyclopentadienes with diethyl ketomalonate gave *α*-pyrans **29** in excellent yields in the presence of $BiCl_3$ as shown in Scheme 18. For the pyran formation, $BiCl_3$ gave the best result among the other metal halides.



Scheme 18

The intermediacy of the bismole is very likely in the pyran formation because it have been known that a reaction of a zirconacyclopentadiene with $BiCl_3$ afforded a 1-chlorobismole **30** (Scheme 19).[7] Insertion of ketomalonate into the Bi-C bond would produce the 7-membered oxabismacycle **31**, followed by



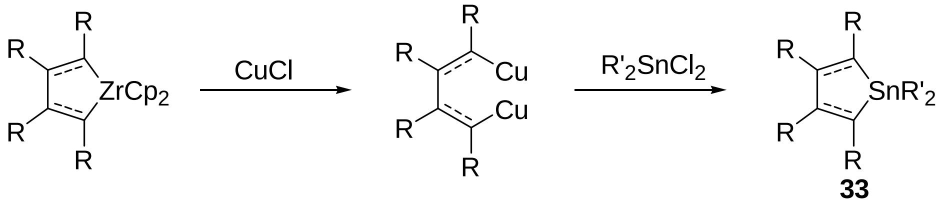
Scheme 19

elimination of bismuth chloride to afford the pyran **29**. The reaction with tetraphenylzirconacycle **17** afforded a dienolic ether **32** instead of the expected pyran, and dideuterated **32** was obtained after deuterolysis with d-contents D^1=50%, D^2>98%. This result supported the formation of 7-membered oxabismacycle **32** as an intermediate. In addition, the double incorporation of deuterium in **32** indicated that the sense of the insertion of C=O bond of ketomalonate is such that the C-O bond was formed rather than the Bi-O bond.

4. FORMATION OF STANNOLES FROM ZIRCONACYCLES

Fagan, Nugent and co-workers have reported a versatile synthesis of heterocycles of main group elements via "metalacycle transfer" of the carbon fragment from a 5-membered zirconacycle to a main group halide.[7] However, this method is strongly affected by steric factor of the substituents on zirconacycles.[8k] Although, a reaction of tin(IV) chloride with tetramethylzirconacyclopentadiene afforded the corresponding stannole in excellent yield, no reaction took place in the reaction with tetraethylzirconacycle.

The critical limitation was eliminated by a simple addition of a catalytic amount of CuCl in the reaction system (Scheme 20).[20] There have been so many examples for the CuCl-promoted reactions of organozirconium species via transmetalation.[2,21] The effect of addition of CuCl was also remarkable on the reaction of zirconacycles with tin chlorides. Using this methods, symmetrical and unsymmetrical stannacycles **33** such as stannacyclopentanes, -cyclopentenes, and -cyclopentadienes were efficiently prepared from the corresponding zirconacycles in high yields.



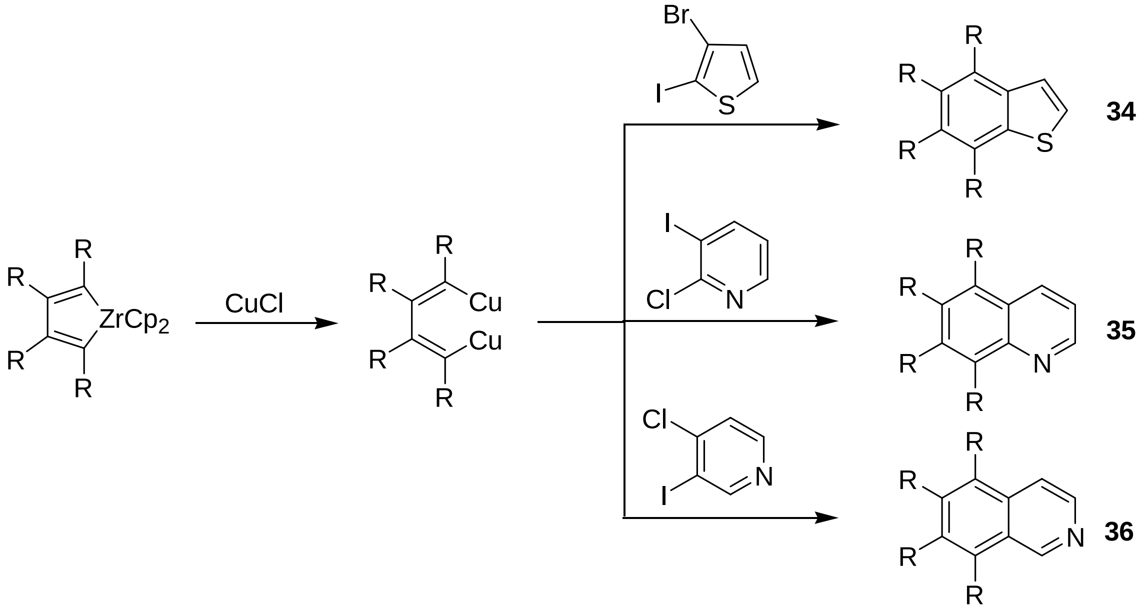
33

Scheme 20

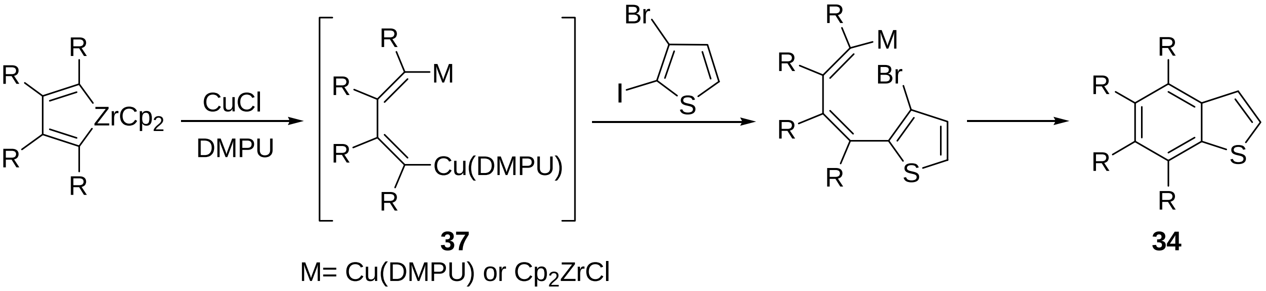
The positive effect was explained by the transmetalation from Zr to Cu, and the resulting organocopper species reacted with tin chloride. The similar promoting effect was observed in the reaction of zirconacycles with chlorophosphines.[22]

5. FORMATION OF FUSED-HETEROCYCLIC AROMATICS FROM ZIRCONACYCLES

Copper-mediated intermolecular coupling reaction of zirconacycles with dihalogenated heteroaromatic compounds is applicable for synthesis of fused aromatic heterocycles.[5] Zirconacyclopentadiene reacted with 2-iodo-3-bromothiophene in the presence of 2 equiv of CuCl and DMPU at 50 °C to afford the corresponding benzothiophenes **34**. When 2-chloro-3-iodopyridine, and 4-chloro-3-iodopyridine were used, the corresponding substituted quinolines **35** and isoquinolines **36** were obtained in high yields, respectively (Scheme 21). Some typical examples of heterocycles formation are given in Table 5.



Scheme 21



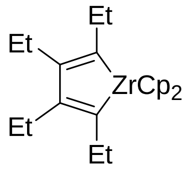
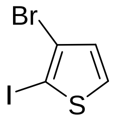
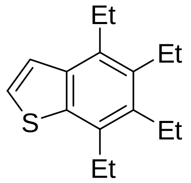
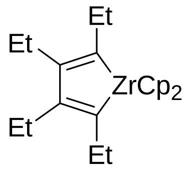
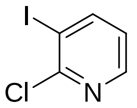
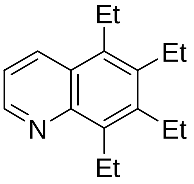
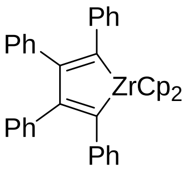
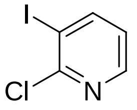
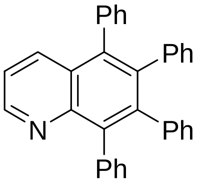
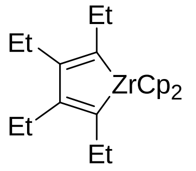
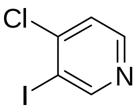
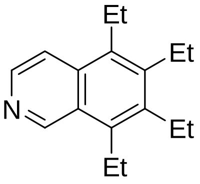
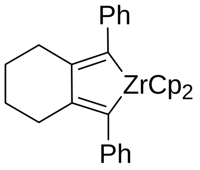
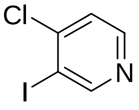
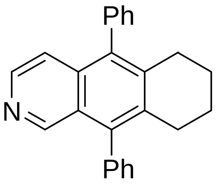
Scheme 22

A plausible mechanism of the coupling reaction was shown in Scheme 22. The first step is transmetalation of the Zr-C bond to Cu-C bond affording organocopper derivative **37**. It is a rate-determining step. Aryl iodide is essential for the first intermolecular coupling step. For the following intramolecular coupling step, bromide is reactive enough. By this method, the substituents can be conveniently introduced into extended aromatic rings.

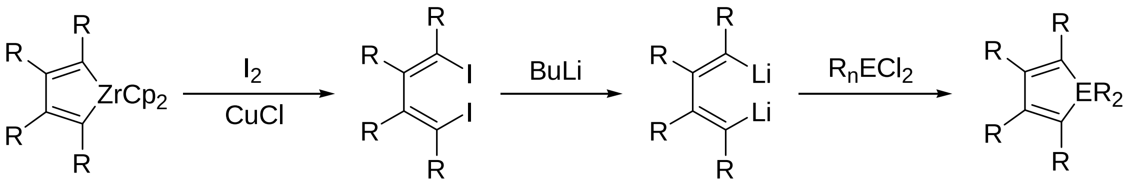
6. FORMATION OF HETEROCYCLES WITH LITHIATED BUTADIENES

Lithiated butadienes, including 1,4-dilithio-1,3-butadienes and 1-lithio-1,3-butadienes, are potentially attractive and useful building blocks for the preparation of not only carbocycles[23] but also heterocycles as shown below. Lithiobutadienes are easily prepared from zirconacyclopentadienes by iodination-lithiation sequence. So far, thus generated dilithiobutadienes were used for the reactions with a series of metal halides to produce the corresponding metalacyclopentadienes (Scheme 23).[20,24]

Table 5. Reaction of Zirconacyclopenradienes with Heteroaryl Dihalides

entry	zirconacyclopentadiene	heteroaryl dihalide	product	yield (%)[a]
1				32 (29)
2				85 (81)
3				- (35)
4				- (65)
5				- (42)

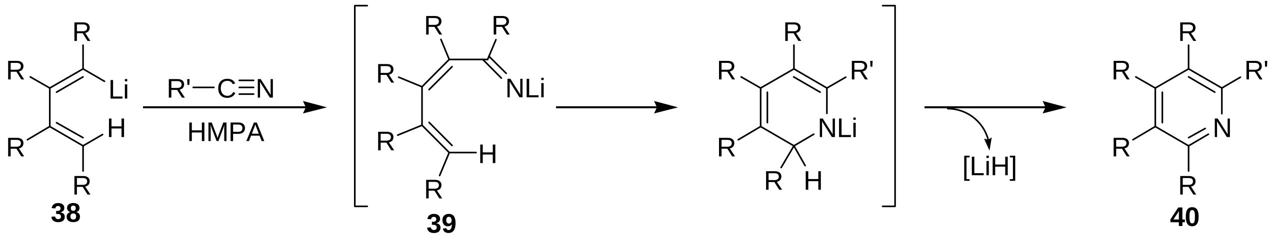
[a] GC yields. Isolated yields were given in parentheses.



Scheme 23

Recently, interesting and novel reactions have been reported using 1,4-dilithio-1,3-butadienes[25,26] and 1-lithio-1,3-butadienes[26,27] with a series of organic substrates. The lithium reagent showed unprecedented reaction patterns during these reactions. Several reactions of them can provide nitrogen- or oxygen-containing heterocycles as shown below.

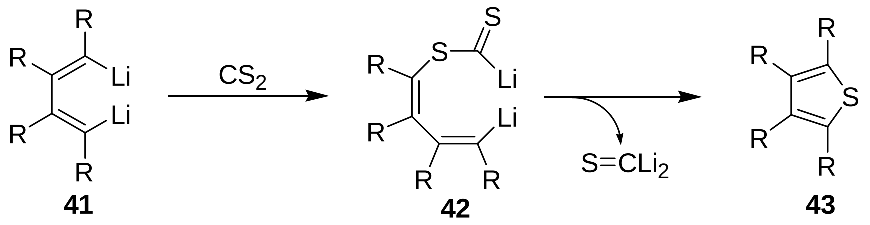
A novel and useful method for the synthesis of pyridine derivatives was reported using lithiated butadienes as substrates.[26] Lithiobutadienes **38** are treated with nitriles in the presence of HMPA at room temperature for 1 h to give the substituted pyridines in excellent yields (Scheme 24). When 2-cyanopyridine is used, 2,2'-bipyridines are obtained in good to excellent yields. The butadienylketimine **39** is the key intermediate of the reaction. Although the ketimine was alternatively generated by the reaction of lithiobutadienes with copper cyanide, the same pyridine **40** was obtained,[28] and this result supported the present mechanism.



Scheme 24

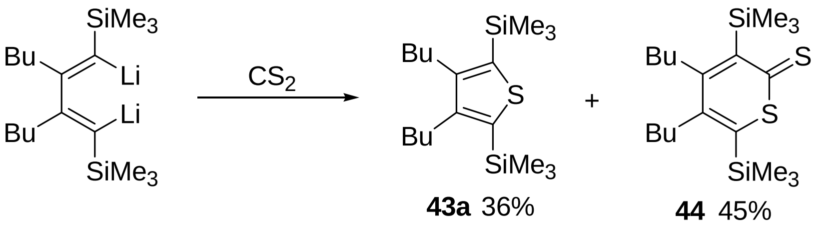
Also the same pyridine formation occurred in the reaction of nitriles with the corresponding dilithiobutadienes, but the existence of the different mechanism was indicated by the NMR observation of the reaction mixture.[26]

Although the reaction of dilithiobutadienes **41** with CO_2 afforded cyclopentadienone derivatives,[29] that with CS_2 produced sulfur-containing heterocycles.[30] In the case of CS_2, addition reaction of the C-Li bond of the dilithiobutadiene affords intermediate **42**, which causes ring-closing via thiophilic addition of the remaining C-Li bond to produce the corresponding thiophene **43** along with C-S bond cleavage (Scheme 25). Very interestingly, the substituents on the butadienyl moieties showed a remarkable influence on the reaction pattern. If the 1,4-disilyldilithiobutadiene was used, not only thiophene **43a**, but also thiopyran-2-thione **44** derivative was formed as a mixture (Scheme 26).

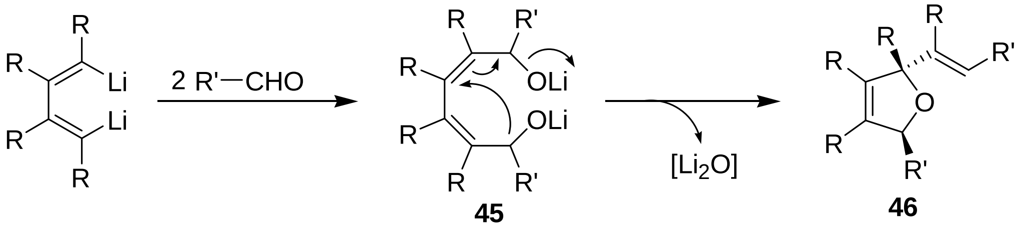


Scheme 25

By using dilithiobutadienes, formation of 2,5-dihydrofuran derivatives was reported by the reaction with aldehydes.[31] (Scheme 27). Treatment of the dilithiobutadiene with 2 equiv of aldehydes generated the corresponding dialkoxide **45** intermediate. The following intramolecular addition of one of the alkoxide and elimination of lithium oxide furnished the corresponding 2,5-dihydrofuran derivatives **46** in high yields with excellent regio- and stereoselectivities. In contrast, the reaction of 1,4-bis(bromomagnesio)butadienes with aldehydes gave cyclopentadiene derivatives instead of furans even at higher temperature.[32] Treatment with nitrosobenzene afforded pyrrole derivatives in good yields.

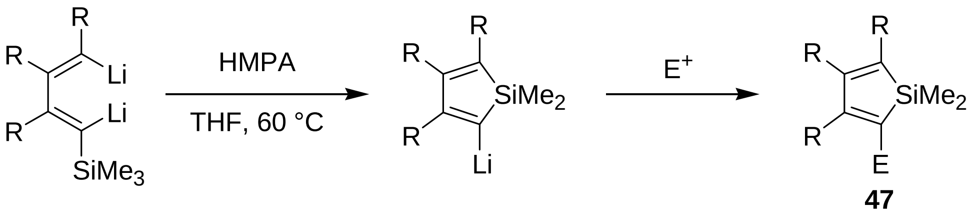


Scheme 26

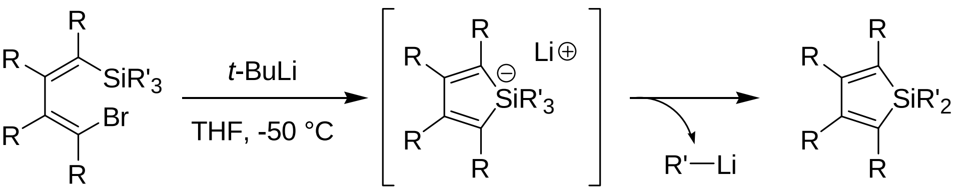


Scheme 27

Siloles are very valuable compounds for organic electronic materials due to its unique electronic character. Historically, siloles were prepared by the reaction of dilithiobutadienes with halosilanes. However, it was found that silylated dilithiobutadienes was converted into 2-lithiosiloles in high yield by simple heating of the THF solution in the presence of HMPA (Scheme 28).[33] Successive treatment with a series of electrophiles afforded a series of functionalized silole derivatives **47**. The similar reaction occurred by using 1-bromo-4-silylbutadiene as shown in Scheme 29.[34] These are very useful building blocks, which could participate further reactions to synthesize a series of substituted siloles.



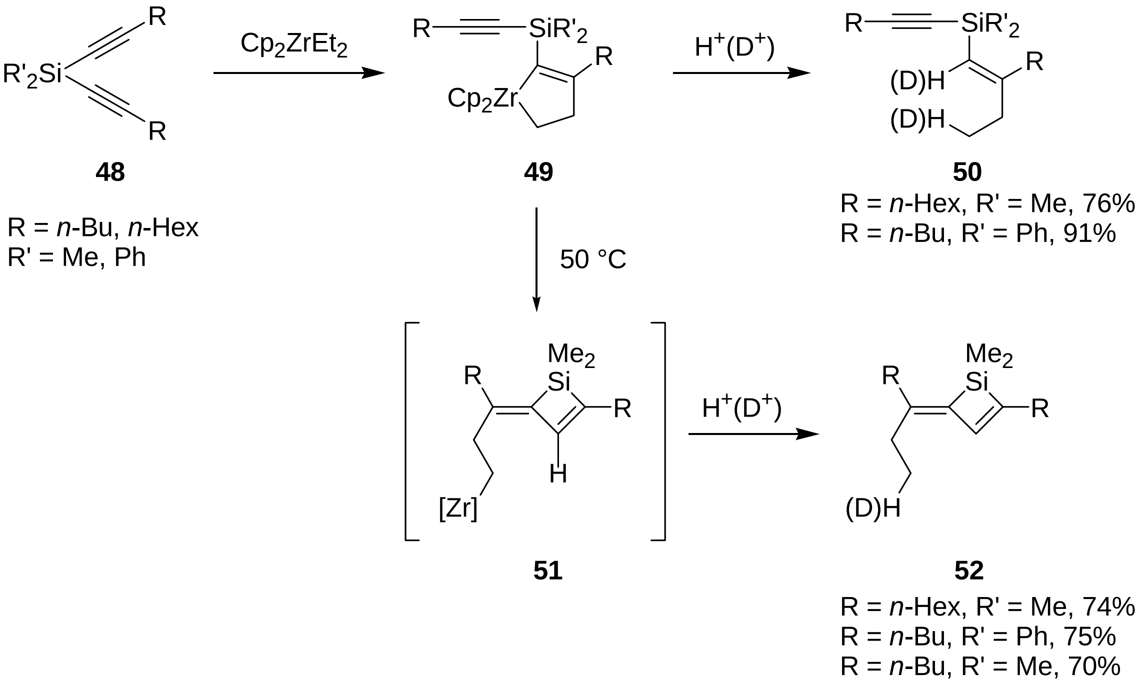
Scheme 28



Scheme 29

7. REACTIONS WITH DIALKYNYLSILANES

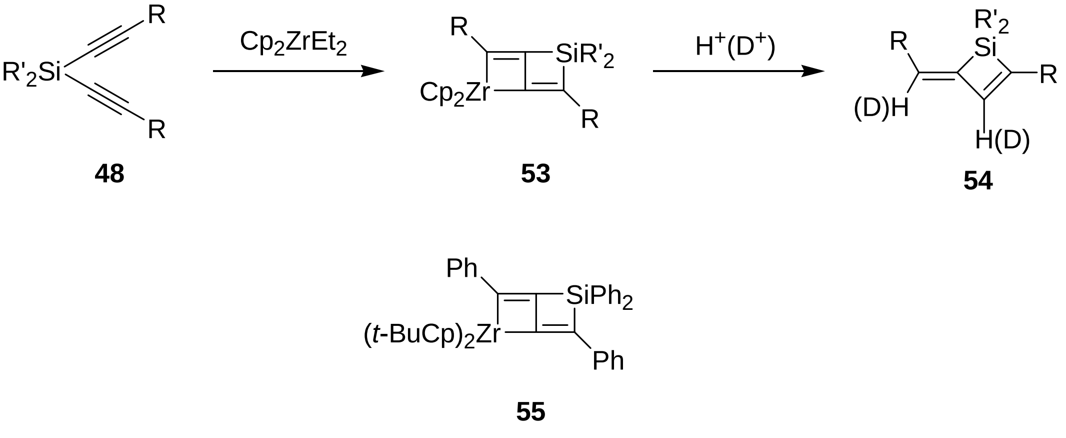
As shown in Scheme 30, when bis(alkynyl)silanes **48** (R = *n*-Bu or *n*-Hex) reacted with Cp_2ZrEt_2 at rt, the corresponding (alkynyl)silyl-substituted zirconacyclopentenes **49** were afforded in high yields.[35] Interestingly, zirconacycles **49** were converted into alkylidenesilacyclobutenes **52** by heating at 50 °C followed by hydrolysis. Deuterolysis of the heated solution, however, afforded the *mono*deuterated silacyclobutene **52-d_1**. The result suggests that occurrence of hydrogen abstraction during the silacyclobutene formation and the intermediacy of the alkylzirconium species **51**.



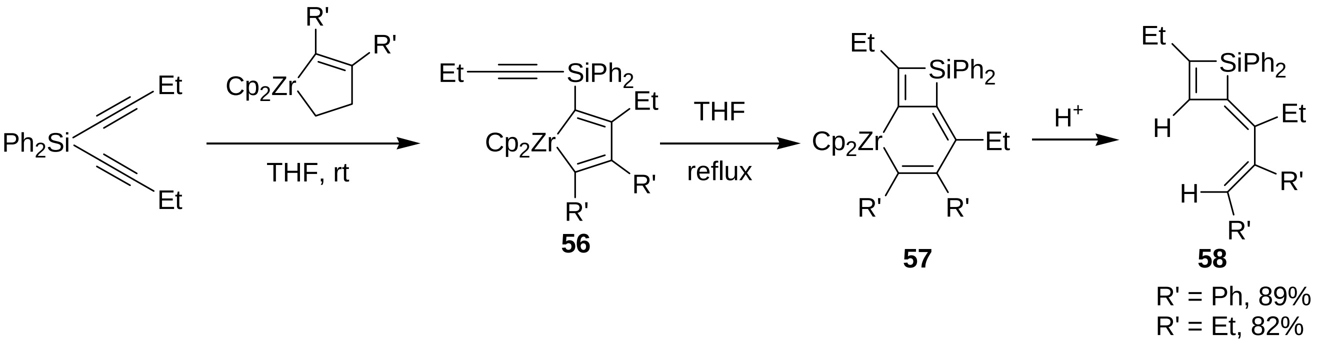
Scheme 30

It was found that the silacyclobutene formation was strongly affected by the substituents of alkynyl moieties. When the substituents of alkynyl moieties were aryl, alkenyl, or tert-butyl groups, no formation of the corresponding zirconacyclopentenes was observed under the same conditions. After hydrolysis of the reaction mixture afforded silacyclobutene derivatives **54** in high yields (Scheme 31). In contrast to **52**, silacyclobutenes **54** did not contain an ethyl group at the alkylidene moiety. Deuterolysis of the reaction mixture afforded the dideuterated compound **54-d_2**. This result suggested that the intermediate before hydrolysis has the fused ring system of zirconacyclobutene and silacyclobutene. In fact, formation of **53** (R = Ph, R' = Me) could be observed by NMR measurement, and the yield was 90%. Furthermore, the unique structure was confirmed by X-ray crystallography of the derivative **55**.

As an extension of the same type of reaction of the silylalkynyl group with zirconacycles, we investigated the reaction of zirconacyclopentadienes (Scheme 32). Zirconacyclopentadienes **56**, prepared from zirconacyclopentenes and an alkyne, were treated at reflux for 3 h to afford 1-zirconacyclohexa-2,4-diene fused with a silacyclobutene ring **57**. Hydrolysis of **57** produced silacyclobutene derivatives **58** in high yields.

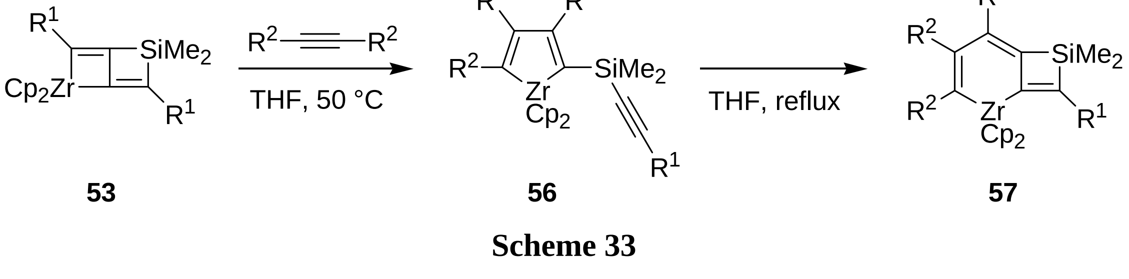


Scheme 31



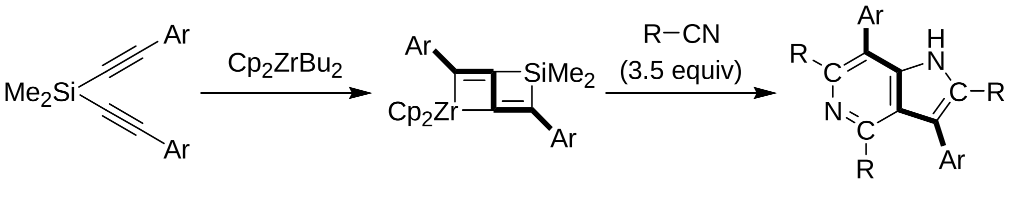
Scheme 32

The bicyclic compounds similar to **57** were obtained from the intermolecular reaction of **53** with an alkyne (Scheme 33).[36] Surprisingly, also in this case zirconacyclopentadiene **56** is observed as an intermediate. This result showed that the unusually flexible nature of the highly strained skeleton of **53**. Further reactions of **56** with a series of substrates such as alkynes, aldehydes, ketones, and isocyanates can provide various types of functionalized products in good yields.[36b,37]



Scheme 33

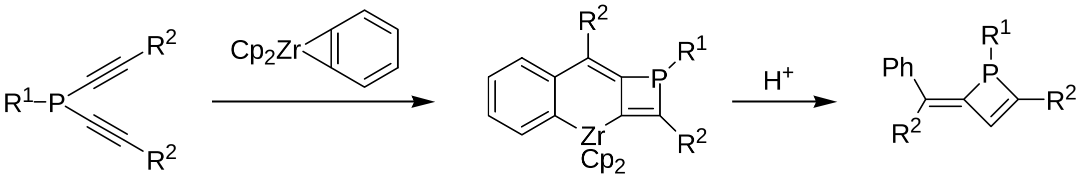
The reactions of such fused sila- and zirconacycles has been applied for the synthesis of fused aromatic heterocycles (Scheme 34). When the zirconacycles **53** reacted with nitriles, the corresponding pyrrolo[3,2-*c*]pyridines **59** were formed.[38] This indicates the unexpectedly strong effects of the alkynylsilyl groups on this unusual skeletal rearrangement of zirconacycles.



53 **59**

Scheme 34

The similar cyclobutene formation was reported using bis(alkynyl)phosphines.[39] This showed the phosphorus atom also has similar electronic effects on the zirconacycle skeletons. (Scheme 35).



Scheme 35

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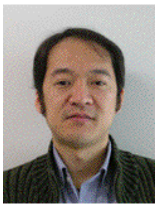
Lishan Zhou received his bachelor's degree from the Hebei University of Technology in 1996 (Tianjin, China) and Ph. D degree from Tianjin University in 2003 (Tianjin, China). Then he joined Professor Chanjuan Xi's research group at Tsinghua University-Hokkaido University Joint laboratory in Tsinghua University as a postdoctoral fellow (Beijing, China). In 2005 he moved to Professor Takahashi's group in Hokkaido University as a postdoctoral fellow (Sapporo, Japan). He was promoted to assistant professor in Hokkaido University in 2008. His current research focuses on the development of new synthetic methods mediated by zirconocene and development of acene derivatives as organic materials.

Masamichi Yamanaka received his Ph.D. under direction of Prof. Masako Nakagawa from Chiba University in 2001. He joined Takahashi's group at Hokkaido University in 2001 as a JSPS postdoctoral fellow. In late 2002, he moved to The Scripps Research Institute as a postdoctoral fellow in the laboratory of Prof. Julius Rebek, Jr. He joined Department of Chemistry at Shizuoka University as an Assistant Professor in 2004 and was promoted to an Associate Professor in 2008.



Ken-ichiro Kanno received his B. S. (1994), M. S. (1998), and Ph. D. (2001) from Tohoku University (Sendai, Japan) under the supervision of Prof. Mitsuo Kira. In 2001, he joined Prof. Takahashi's group at Hokkaido University (Sapporo, Japan) as a postdoctoral research fellow, and in 2003 he became assistant professor at the same group. His current research focuses on development of organic synthesis with organometallic reagents and application of extended *p*-conjugated molecules toward organic semiconductors.

Tamotsu Takahashi received his bachelor's and Ph. D. degree from the University of Tokyo in 1978 and 1983, respectively. He became an assistant professor at the same university in 1983. From 1984 to 1986, he joined Prof. Negishi's group at Purdue University as a postdoctoral research fellow. In 1991 he moved to Institute for Molecular Science as associate professor. In 1995, he moved to Hokkaido University as a full professor. He received the Progress Award in Synthetic Organic Chemistry, Japan in 1993 and Divisional Award (Organic Chemistry) of Chemical Society of Japan in 1998. His research covers several areas, for example, highly selective organic synthesis, development of novel reactions using organometallic compounds, carbon-carbon bond cleavage reaction, and development of organic materials such as substituted and soluble acenes as organic semiconductors.