



Digest Paper

1,3-Diyne chemistry: synthesis and derivations

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ABSTRACT

Conjugated diynes have attracted more and more attention not only for their unique rod like structures and wide existence in nature product, but also the abundant properties and derivations of them. Although oxidative dimerization of alkynes or Cadiot–Chodkiewicz reactions were the main pathway and have achieved great success in the synthesis of diynes, oxidative cross coupling, FBW rearrangement as well as diyne metathesis emerged rapidly recently. Moreover, diynes could be precursors of basic heterocycles, which represented an emerging research area. This Letter will cover the recent progresses in the synthesis and further derivations of diynes.

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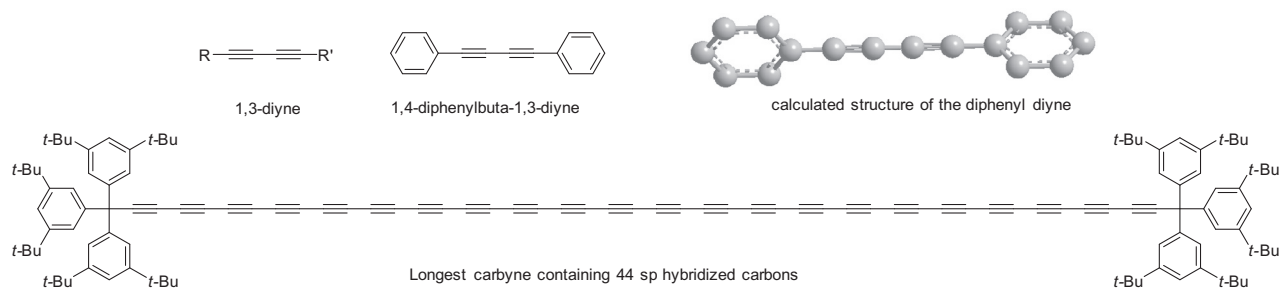
Introduction

1,3-Diynes (referred to as diynes hereinafter) are a kind of conjugated diynes with unique structures (Scheme 1). They have a

rod-like molecular shape with high rigidness. Chauvin and Lepetit have a detailed review on the theoretical studies on acetylenic scaffolds.¹ Tykwinski et al. have prepared a series of 1,3-diynes and derivated polyynes (also known as carbyne) and characterized their structures using the methods including Raman, IR, XRD, etc.² In most cases, the four carbon atoms in diynes are arranged linearly, although longer chains containing 8 or more linked *sp* hybridized carbon atoms may be slightly bent.³ The reported longest carbyne is also shown in Scheme 1.

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Scheme 1. Rigid structure of 1,3-diyne.

Because of the rigid structure, diynes are easy to stack in crystal cells and form a needle-like crystalline solid. This instinct characterization means diynes could be easily recrystallized and purified from other byproducts. More importantly, diynes are thermally and moisture stable. Although highly unsaturated, the conjugation of the carbon atoms provided extra stability. According to the authors' experience, pure diynes could be prepared and stored under normal conditions, and remain the same for years. This advantage has made the diynes as one of the most easily handled organic architectures.

On the other side, the highly unsaturated carbon chains could also exhibit fascinating reaction properties under special conditions. It is known that 1,3-diynes could undergo polymerization upon the irradiation of UV light. This reaction could lead to the cross-linking between different carbon chains and has been widely used in material field.⁴

Moreover, diynes could be attacked by nucleophiles such as amines, alcohols, and sulfides. For example, diynes could react with water, primary amines, hydroxylamines, or hydrogen sulfide to form 5-membered heterocycles like furans,⁵ pyrazoles,⁶ pyrroles,^{5b,7} isoxazoles,⁸ and thiophenes.^{5a,9} Diynes could be also oxidized to form complex structures, which were used as the precursor of some organic dyes like indigo.¹⁰

The unusual structure, relative stability, and abundant potential reactivity have together made the diynes as important building blocks in organic synthesis and material science. More and more reports have emerged to discuss the synthesis and application of diynes recently. There have also been a few reviews on the nature of occurrence of diynes, synthesis of acetylenic scaffolds, and reactivity of alkynes. However, few reviews concerning the synthetic pathways as well as the applications of this magic structure were published. As a witness of the rapid development of diyne chemistry in the recent decades, this review would summarize the synthetic pathways of diynes, as well as their further derivations.

Synthesis of diynes

Diynes could be divided into two kinds: symmetrical or unsymmetrical, according to the substituent groups linked to both sides of the buta-1,3-diyne structure. While earlier reports focused on the synthesis of symmetrical diynes, the unsymmetrical diynes were much more common in nature and have attracted more and more attention in the recent years.

Synthesis of symmetrical diynes

Symmetrical diynes could be generated simply from the oxidative coupling of the corresponding terminal alkynes (or their derivations such as alkynyl metallic reagents or 1-halo-alkynes), as shown in Scheme 2. Theoretically, pathways directly from alkynes are more easy-handling with better atom efficiency than other methods, and hence much more widely used. In most cases, copper was employed either as a catalyst or additive. Since Glaser had reported the earliest example, and followed modifications made by Eglinton and Hay, this copper mediated oxidative coupling of terminal alkynes is generally called Glaser–Eglinton–Hay coupling. Besides this name reaction, other methods have offered an alternative possible synthetic route by replacing the alkynes with derivations of alkynes, and have shown certain advantages in some cases.

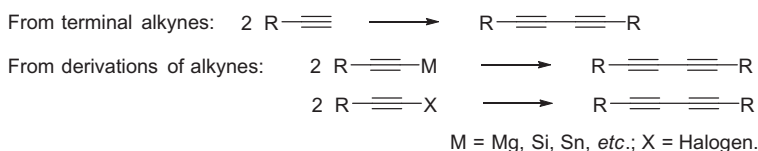
The oxidative Glaser–Eglinton–Hay coupling

Symmetrical diynes are the earliest diynes prepared in laboratories. The first report was published in 1869 by Carl Glaser.¹⁰ In this Letter, phenylacetylene reacted with cuprous chloride to form a phenylacetylidene, and this yellow insoluble solid could dimerize to form the 1,4-diphenylbuta-1,3-diyne in the presence of oxygen smoothly (Scheme 3).

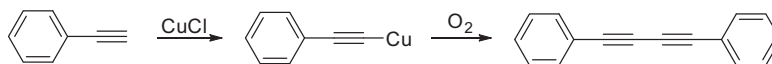
Glaser coupling of terminal alkynes could achieve the diynes with moderate yields. This could be partially due to the instability of the copper acetylidene, the intermediate of the process. On the other hand, for those aromatic ethynyl compounds, good yields were observed, while for a broader scope of aliphatic alkynes, the Glaser coupling failed to give satisfactory results.

The modification of Glaser coupling was then carried out. Additives such as ammonium salts were introduced and in some cases improved the efficiency.¹¹ In 1956, Eglinton and Galbraith found that stoichiometric or excess $\text{Cu}(\text{OAc})_2$ in methanolic pyridine could accelerate the dimerization of alkynes.¹² Later, Hay had found that pyridine served also as ligand in this process. Using this method, Hay prepared the polymer containing the diyne group¹³ (Scheme 4).

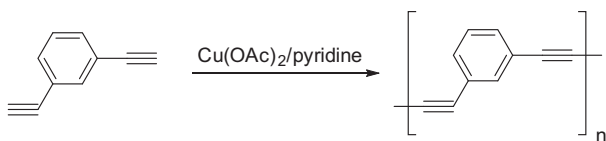
In 1962, Hay had found that some amines could be a better ligand for this process.¹⁴ TMEDA (*N,N,N',N'*-tetramethylethylenediamine) was proved to be suitable in the dimerization of terminal alkynes. In this procedure, only a catalytic amount of CuCl was needed, and good yields of diynes were obtained. Better solubility of the $\text{Cu}(\text{I})$ –TMEDA complex was considered to improve the reaction rate.



Scheme 2. Methods to symmetric diynes.



Scheme 3. Glaser's dimerization of phenylacetylene.

Scheme 4. Polymerization of *m*-diethynylbenzene by Hay.

Using this Cu mediated dimerization of terminal alkynes, a variety of diynes and macrocycles¹⁵ containing diene structure were synthesized. Detailed reviews could be found in Diederich's publication^{10,16} and Li's textbook on name reactions.¹⁷ Selected examples are listed in Scheme 5.

Modifications of Glaser–Eglinton–Hay coupling reactions

The Glaser–Eglinton–Hay coupling has represented the classic pathways to symmetric diynes in a long time. However, the modification of this process has not been static. In this new century, many synthetic scientists have contributed to this reaction. New catalytic system, oxidants, as well as new solvents were introduced.

The introduction of other metal catalysts could improve the efficiency in some cases. The commonly used co-catalysts were Palladium, Gold, and Nickel. Besides the catalytic systems, oxidants could also vary from oxygen in the air to other organic/inorganic reagents. Stefani et al. have reviewed the homocoupling of alkynes in 2010,¹⁸ and Table 1 here shows some selected catalytic systems apart from that.¹⁹

It is noteworthy that one of the applications of alkyne oxidative coupling reactions is the synthesis of polymers bearing the diene group. This represented a new research field and the polymers could found potential usages in material science research. Readers

could refer to Tang's review²⁰ and find more typical examples therein.

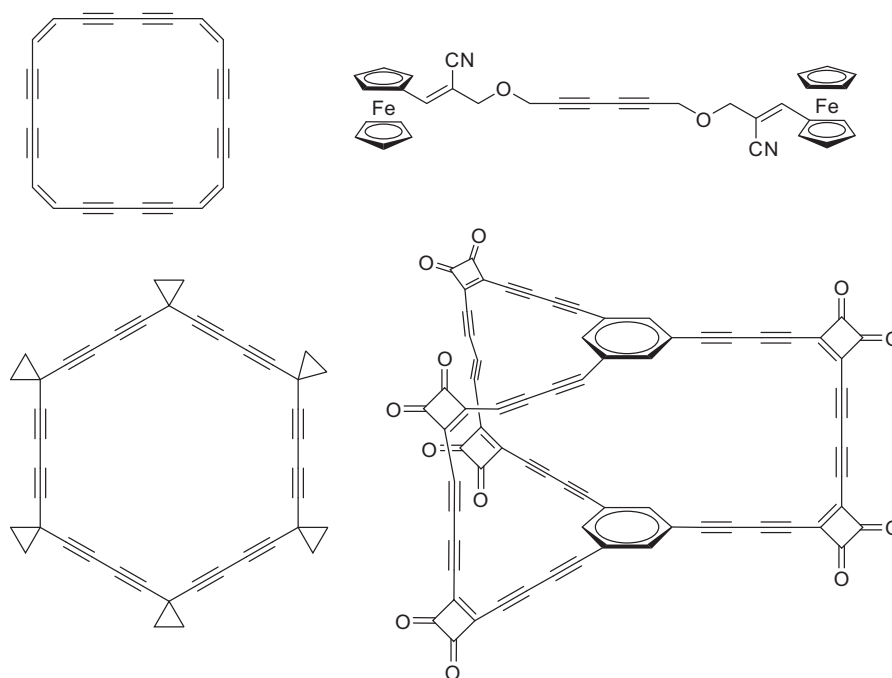
Oxidative coupling from alkyne derivatives

It is generally supposed that in Cu mediated systems, the copper(I) acetylides are active intermediates.^{10,17,21} The copper acetylides, as well as other metallic acetylides, could be recognized as the alkyne derivatives, and they have also been used in the synthesis of diynes.

Mori and co-workers had reported that alkynylsilanes could undergo dimerization in the presence of CuCl in DMF smoothly.²² Zhang and co-workers used the alkynyltin but only observed low yield.^{19a} Kukukawa and co-workers had developed this method using organic oxidants.²³ However, the highly toxic tin had limited their applications. Oh et al. found that alkynyltriisopropoxyborates could undergo homocoupling, though only moderate yields were observed.²⁴ Another alkynyl borate example was reported later by Paixão and Stefani, in which alkynyltrifluoroborates were employed.²⁵ Later, Stefani had proved that alkynyltellurides could also be dimerized to diynes.²⁶ Cahiez et al. reported some Manganese or Iron catalyzed examples from alkynyl Grignard Reagents.²⁷ The protocol had proved to be efficient to both aromatic and aliphatic alkynes, and good functional group tolerance was also observed.

Although all these alkynyl reagents are generated from the corresponding terminal alkynes, the utility of them could in some cases show better stability under oxidative atmosphere. Table 2 has listed the differences of these processes. Comparison of yields for phenylacetylene and aliphatic alkynes is listed in the table.

Another oxidative system to yield the symmetric diynes could be the oxidation of dialkynylalkylborates.²⁸ It is noteworthy that unsymmetric diynes could also be formed in satisfactory yields when the two alkynyl substituents were different.²⁹



Scheme 5. Typical products from the Glaser–Eglinton–Hay coupling.

Table 1
Different catalytic systems in the oxidative coupling of terminal alkynes

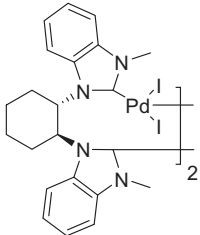
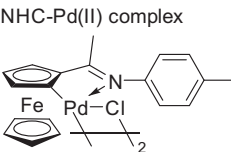
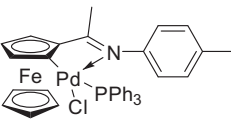
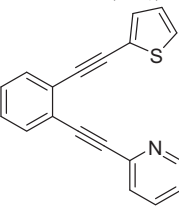
| Year | Authors | Catalytic systems | Comments | Ref. no. |
|------|----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|----------|
| 2002 | Zhang and co-workers | $\text{PdCl}_2(\text{PPh}_3)_2$, CuI, $\text{BrCH}_2\text{COOEt}$ as oxidant | Palladium enolate as the intermediate, and double transmetalation was proposed | 19a |
| 2006 | Xi and co-workers | 3.5 mol % $\text{Pd}(\text{PPh}_3)_4$, 0.5 mol % CuI, <i>p</i> -chloranil as oxidant. | For aromatic 1-alkynes only | 19b |
| 2006 | Shi | 0.5 mol % NHC-Pd(II), 3.0 mol % CuI, $\text{BnNHC}_2\text{H}_4\text{OH}$, O_2 | Aromatic alkynes showed obvious higher yields than aliphatic alkynes | 19c |
| | |  <p>NHC-Pd(II) complex</p>  | | |
| 2007 | Wu | | Aromatic alkynes showed obvious higher yields than aliphatic alkynes | 19d |
| | |  | | |
| 2008 | Mizuno | Monomeric dicopper-substituted silicotungstate | Broad substrate scope, catalyst could be recycled | 19e |
| 2009 | Beifuss | 2 mol % CuCl, 1.5 mol % ligand, base, O_2 | Influence of bases and ligands were investigated | 19f |
| 2009 | Tsai | 0.0001–1 mol % cationic 2,2'-bipyridyl palladium(II)/CuI system and 1 mol % CuI | Reusable catalyst, low Pd loading, water as solvent | 19g |
| 2009 | Lee, Oberhauser | NHC-Pd catalyst | Much better performance was obtained by aromatic alkynes | 19h |
| 2009 | Pale, Sommer | 10–30 mol % copper-zeolite | Morphology of the zeolite would affect the yields | 19i |
| 2009 | Radivoy | Copper nanoparticles | Neither Palladium nor ligand was needed | 19j |
| 2010 | Chen | 3 mol % CuCl_2 , Et_3N , air | Solvent free | 19k |
| 2011 | Jia | 5 mol % CuCl, in DMSO, 90 °C | Base-, ligand-, Pd-free, electron-rich aromatic alkynes perform better | 19l |
| 2013 | Sonoda | 2 mol % $\text{PdCl}_2(\text{PPh}_3)_2$, ligand | Moderate to good yields were obtained. <i>Trans</i> -spanning ligands were proved to be effective | 19m |
| | |  | | |

Table 2
Oxidative homo-coupling of alkyne derivatives to form diynes

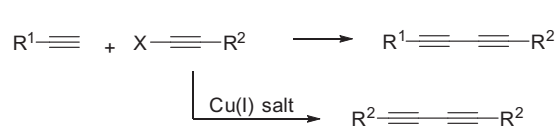
| Year | Authors | Alkyne derivatives | Reaction conditions | Yields (%) for | | Ref. |
|------|------------------------|---------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------|------------------|------|
| | | | | Ph—C≡C— | Aliphatic alkyne | |
| 2000 | Mori and co-workers | R—C≡C—SiMe ₃ | Stoichiometric CuCl, DMF, 60 °C, 3–12 h | >99 | 80 | 22 |
| 2002 | Zhang and co-workers | R—C≡C—SnBu ₃ | 5 mol % PdCl ₂ (PPh ₃) ₂ , PhCHBrCOOMe, THF, 3 days | 20 | — | 19a |
| 2004 | Oh et al. | [R—C≡C—B(O <i>i</i> Pr) ₃] [−] Li ⁺ | 5 mol % Pd(OAc) ₂ /DPEPhos, 10 mol % CuI, THF, 60 °C | 93 | 87 | 24 |
| 2007 | Cahiez et al. | R—C≡C—MgCl | 5 mol % MnCl ₂ ·2LiCl, dry air, THF, rt, 45 min | 89 | 91 | 27 |
| 2008 | Paixão, Stefani et al. | R—C≡C—BF ₃ k | 10 mol % Cu(OAc) ₂ , DMSO, 60 °C, 6 h | 97 | 86–88 | 25 |
| 2009 | Stefani et al. | R—C≡C—T <i>en</i> Bu | 8 mol % PdCl ₂ , AgOAc, MeOH, Ultrasonic | 85 | 75–87 | 26 |

| entry | substrate | X | product | yield (%) |
|-------|-----------|----|---------|-----------|
| 1 | | Br | | 94 |
| 2 | | I | | 97 |
| 3 | | Br | | 83 |
| 4 | | I | | 90 |
| 5 | | I | | 85 |
| 6 | | I | | 73 |
| 7 | | I | | 86 |
| 8 | | Br | | 72 |
| 9 | | I | | 75 |
| 10 | | Br | | 89 |
| 11 | | I | | 93 |

Scheme 6. Dienes from haloalkynes.

Reductive coupling to form symmetric diynes

Besides oxidative coupling, diynes could also be prepared by reductive coupling reactions from the alkynyl halides. However, few reports were published using this protocol. Lee and co-workers



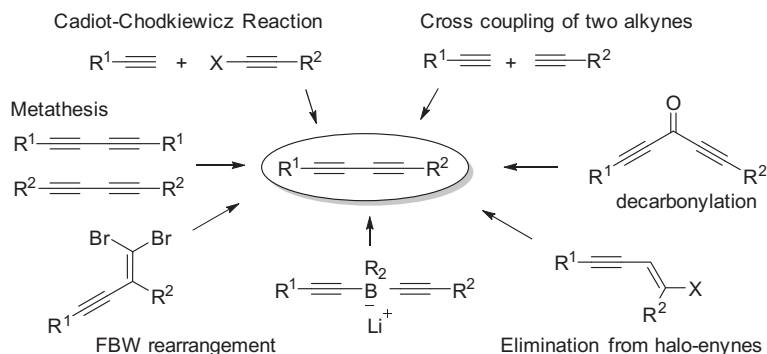
Scheme 8. Side reactions of the Cadiot–Chodkiewicz reactions.

have reported the diyne synthesis from reductive coupling of 1-iodoalkynes using palladium catalysts.³⁰ Jiang et al. have prepared a variety of symmetric diynes from the bromoalkynes or iodoalkynes under the reduction of potassium iodide,³¹ as shown in **Scheme 6**. The procedure was free from transition metals or bases, and moderate to high yields were achieved. The authors had also investigated the cross-coupling between two different haloalkynes, and statistical distributions of mixed diynes were obtained as was expected.

Synthesis of unsymmetric diynes

Unsymmetric diynes are more important and more challenging in synthesis other than symmetric diynes. Typically, there are several pathways to form this structure. Simply by mixing two different terminal alkynes together in an oxidative atmosphere a mixture of diynes could be obtained. However, the yields of different products are mainly based on statistical distribution. Lack of chemoselectivity had inhibited the application of this method. One alternative method is the iodine oxidized dialkynyldialkylborates with different alkynyl substituents.²⁹

The most efficient and widely used method till now is the Cadiot–Chodkiewicz coupling reaction³² and its modifications, which requires a 1-haloalkyne as the electrophile and another terminal alkyne as the nucleophile. Another pathway to unsymmetric



Scheme 7. Different pathways to form the unsymmetric diynes.

diynes is the Fritsch–Buttenberg–Wiechell (FBW) rearrangement,³³ and these methods are usually used to prepare the long whole *Csp*-carbon chains. Elimination from halo-enynes could also generate the diynes.³⁴ Other methods include the oxidation of dialkynylalkylborates²⁹ mentioned in section 2.1.3, decarbonylation of diyrones,³⁵ and metathesis of symmetric diynes.³⁶ Scheme 7 has listed these different pathways.

Cadiot–Chodkiewicz coupling and modifications

Since Cadiot and Chodkiewicz's first report on the copper catalyzed cross coupling of 1-haloalkynes and terminal alkynes in the 1950s, this procedure had been the major synthetic route to the unsymmetric diynes over the past half-century. The advantages of these coupling reactions include the relatively high yields, low cost of catalyst, wide substrate scope, and mild conditions. There are so many reports focusing on the total synthesis of naturally occurring diynes that have used the Cadiot–Chodkiewicz coupling as the key step.³⁷ However, though powerful in many cases, there are also some disadvantages. They often suffer from relatively poor selectivity and yield a considerable amount of homocoupling byproducts, especially for those bulky alkynes, or the case that when the electronic properties of the substituents attached to the haloalkynes and the terminal alkynes are similar (Scheme 8).

Kurth and Schore co-workers had utilized the polymer supported haloalkynes in the Cadiot–Chodkiewicz couplings to prevent the homocoupling of the haloalkynes.³⁸ Though lower yields were observed, the side products were effectively inhibited (Scheme 9).

Another improvement was made by Jiang,³⁹ who has used the supercritical CO₂ as the reaction medium and NaOAc as the base instead of the organic amine. Moderate to high yields were

obtained, and the hydroxyl group in haloalkynes was found to be crucial in this protocol. In a recent report Wang⁴⁰ et al. have used CuI and tris(*o*-tolyl)phosphine and yielded the unsymmetric diynes in good yields.

To further improve the efficiency of the Cadiot–Chodkiewicz coupling, Palladium catalysts were employed together with Cu(I) salts. Potts, Wityak, and Alami et al. have reported the Palladium catalyst in the coupling of haloalkynes and terminal alkynes respectively.⁴¹ The mechanism of the palladium–copper catalyzed cross coupling reaction of haloalkynes and terminal alkynes was investigated by our team,⁴² and the proposed pathways in this process are shown in Scheme 10. A phosphine–olefin ligand was proved to accelerate the path A by in situ IR spectra. In a recent report also from our team,⁴³ the loading of the Palladium and copper could be less than 0.01 mol % and 0.2 mol %. The TON of this system could be up to 350,000. Palladium nanoparticles were proposed to be the catalytic center by kinetic studies.

Fritsch–Buttenberg–Wiechell (FBW) rearrangement

Fritsch–Buttenberg–Wiechell (FBW) rearrangement reactions are named after Paul Ernst Moritz Fritsch, Wilhelm Paul Buttenberg, and Heinrich G. Wiechell. This type of reactions could generate alkynes from 1,1-dihaloolefins under low temperatures, as shown in Scheme 11. In the case that either R¹ or R² was the alkynyl group, the product could be unsymmetric diyne.⁴⁴ Triynes or even longer polyynes chains could be obtained through this transformation when both R¹ and R² were alkynyl groups.

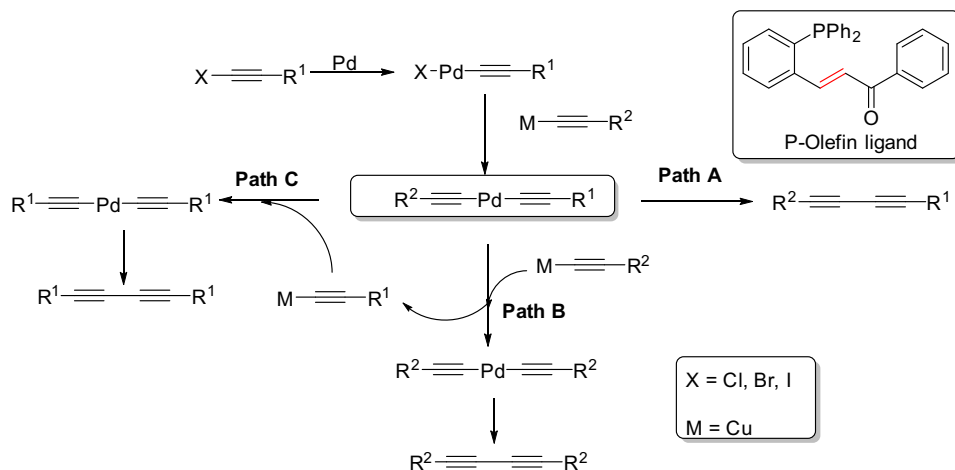
Due to the low temperature in FBW process, this method is widely applied in the synthesis of polyynes with bulky groups, which may be unstable in higher temperatures. Tykwinski and co-worker have done a great work in this field and prepared a

$$\text{R}-\text{C}\equiv\text{C}-\text{X} + \text{C}\equiv\text{C}-\text{Hex} \longrightarrow \text{R}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{Hex} + \text{R}-\text{C}\equiv\text{C}-\text{C}\equiv\text{C}-\text{R}$$

cross-coupled product homocoupling product

| entry | Alkyne (● = 2% crosslinked polystyrene backbone) | cross-coupled product (%) | homocoupling product (%) |
|-------|--------------------------------------------------|---------------------------|--------------------------|
| 1 | | 97 | trace |
| 2 | | 69 | 0 |
| 3 | | 93 | trace |
| 4 | | 81 | 0 |
| 5 | | 95 | trace |
| 6 | | 84 | 0 |
| 7 | | 66 | 34 |
| 8 | | 71 | 0 |
| 9 | | 37 | 15 |
| 10 | | 34 | 0 |
| 11 | | 40 | 18 |
| 12 | | 36 | trace |

Scheme 9. Polymer based haloalkynes in Cadiot–Chodkiewicz coupling.

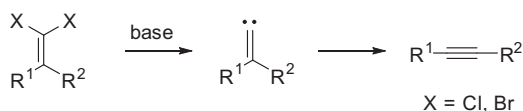


Scheme 10. Proposed pathways in palladium mediated Cadiot–Chodkiewicz coupling.

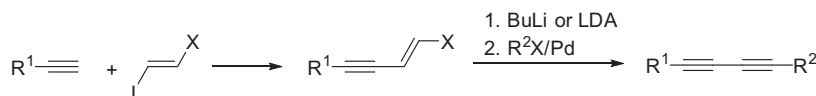
plenty of symmetric or unsymmetric diynes and polyynes through this rearrangement. For a detailed review, readers could refer to a publication in 2010 and references therein.⁴⁵ However, since strong bases such as butyllithium were used, the tolerance of functional group is usually poor for this method. In most cases, the substituent groups at the end of the diynes or polyynes were silyl, phenyl, aryl, or alkyl groups without active H atom. Moreover, the relatively long synthetic steps would be another problem. These disadvantages had limited the application of FBW rearrangement in a wider application range.

Unsymmetric diynes directly from two different terminal alkynes

Although Cadiot–Chodkiewicz reactions have achieved great success, the unstable 1-haloalkynes had limited the application scope of this reaction. Cross coupling directly from two different terminal alkynes could be the most efficient pathways to form the unsymmetric diynes. However, the lack of selectivity often leads to a mixture of the possible diyne products under the classic Glaser–Eglinton–Hay conditions by simply mixing two different alkynes. Although complex products were obtained, this method could be potentially useful if the mixtures were easy to be isolated, or one of the starting alkynes was in large excess. There are also some achievements recently that could solve the problem in some cases. Lei and co-workers have reported a nickel catalyzed oxidative coupling reaction between two different terminal alkynes.⁴⁶ In this process, oxygen was employed as the sole oxidant, and 20 mol % of TMEDA was used as the ligand. Although 5 times excess of one alkyne was required, this process has represented a potential pathway to unsymmetric diynes. Several reports emerged



Scheme 11. FBW rearrangement.



Scheme 12. Negishi's protocol to unsymmetric diynes based on elimination.

since then, but the requirement of excess of one alkyne had still limited the application scope.

Other methods to unsymmetric diynes

Negishi et al. had developed a tandem protocol by combining Palladium catalyzed coupling of terminal alkynes and 1,2-dihaloalkenes with subsequent base-induced elimination to afford the conjugated unsymmetric diynes,^{34,47} shown in Scheme 12. This method could reach high yields under mild conditions. Eneynes, also widely existing in nature, were also achieved conveniently. Like the FBW protocol, this method also suffered from the long synthetic steps and the limited functional group tolerance.

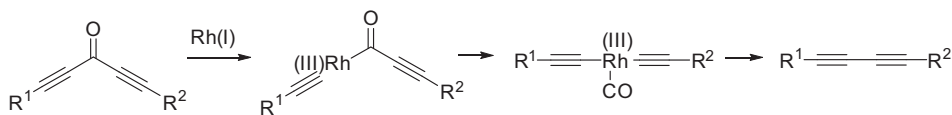
C–C bond cleavage could be utilized to construct unsymmetric diynes. Dong et al. have reported the Rh(I)-catalyzed decarbonylation of diynes to form the unsymmetric diynes via C–C activation, shown in Scheme 13.

Another example was the alkyne cross-metathesis, which represented a new route to unsymmetric diynes. Tamm and co-workers have reported a tungsten benzylidyne complex catalyzed metathetic conversion between diynes to give the unsymmetric diynes recently.³⁶ This method could start from the readily available symmetric diynes under room temperature. Scheme 14 has shown the transformation and the structure of the tungsten benzylidyne complex. High selectivity was achieved with 4 equivalent excess of one diyne. The authors have proved that the reaction time was also crucial to the yield of the product. Degradation of the product could be observed for prolonged period.

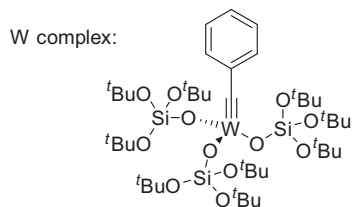
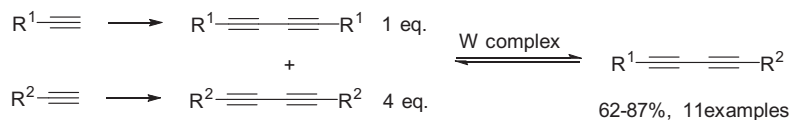
Although excess of one initial diyne was necessary to achieve the selectivity, and column chromatography was required to isolate the unsymmetric product from the diyne mixture, this method had shown another possibility in the synthesis of the unsymmetric diynes.

Heterocycles from diynes

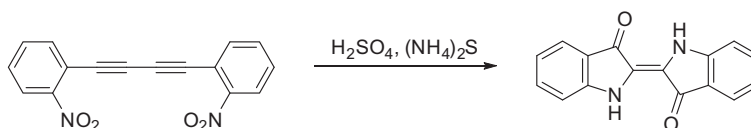
The derivation of the diynes could be dated to 1882, by Baeyer who oxidized the diyne to indigo,¹⁰ shown in Scheme 15. Indigo



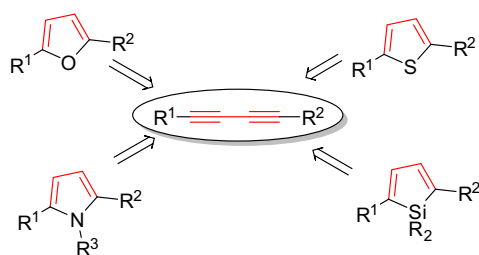
Scheme 13. Diyne synthesis from decarbonylation of diyones.



Scheme 14. Diyne cross-metathesis to prepare unsymmetric diyne.



Scheme 15. Indigo from diyne by Baeyer.



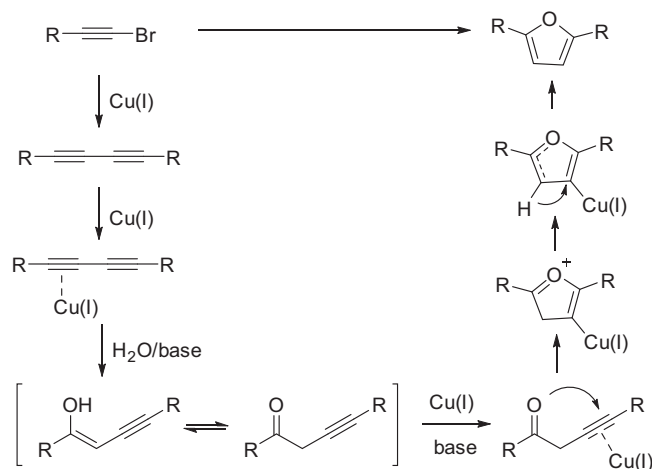
Scheme 16. Heterocycles prepared from diyne.

has been used as a blue pigment, and was extracted from plants historically. It is the blue of blue jeans, and the structure could be recognized as the two heterocycles connected by a double bond.

Heterocycles are important in organic chemistry and bioorganic chemistry. Although traditional methods to heterocycles were mainly condensation reactions, the methodology of cycloadditions from alkynes had also been developing rapidly. Recently, synthetic chemists have found new pathways to generate heterocycles from diyne directly with high atom efficiency. Synthesis of five-membered heterocycles, such as thiophenes, pyrroles, and furans, was reported from the diyne structure, shown in [Scheme 16](#).

Thiophenes and furans from diyne

Thiophenes prepared from diyne were firstly reported by Reisch and Schulte in 1960.⁴⁸ Later, Kagan and co-workers had used this method to prepare the α -thiophene oligomers in 1982.⁴⁹ By this novel method, Kagan had prepared a series of thiophene oligomers in moderate to high yields.^{9b} Potts et al. have used the gaseous H_2S as the sulfur source to react with 1,4-diphenylbuta-1,3-diyne in NaOH solution and obtained the 2,5-diphenylthiophene.^{9a} In a recent report by Zhao and

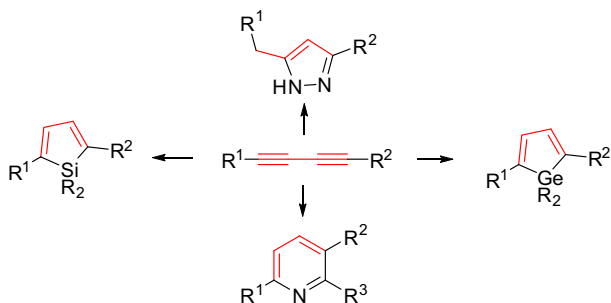


Scheme 17. Proposal mechanism for the formation of furans from diyne.

co-worker,⁵⁰ the sodium hydrosulfide, NaHS was used and had greatly improved the yields in most cases. Substrate scope was also investigated and satisfactory results were obtained for those aryl substituted diyne. Furans from diyne were much more difficult than thiophenes. Catalysts and relatively harsh conditions were typically required. Jiang et al. have reported a Cu(I) catalyzed synthesis of thiophenes and furans from diyne using 1,10-phenanthroline as ligand.^{5a} For the furan formation, the authors had proposed a mechanism, shown in [Scheme 17](#).

Pyrroles from diyne

Methods for pyrroles from the diyne could be dated to 1961, also by Reisch and Schulte.⁵¹ In this early report, five pyrroles were



Scheme 18. Other heterocycles from diynes.

prepared from the diynes and primary amines in the presence of CuCl. Chalk found that according to different reaction conditions, the diynes could give either pyrroles or pyridines in the presence of CuCl.⁵² Huerta et al. have reported the polymers with *N*-phenyl fragments from the polymers with diyne chains using this method.⁵³ Ackermann and Born have used TiCl₄ as the catalyst for the hydroamination of alkynes to form indoles, and while replacing the alkynes to diyne under the same reaction condition, they have obtained the corresponding pyrrole.⁵⁴ Gold could also show catalytic activities. Bertrand and co-workers have reported the homogeneous Au catalyst promoted hydroamination of diynes to pyrroles using ammonia under high temperatures.⁵⁵ Skrydstrup et al. had reported the Au(I)-catalyzed pyrroles or furan formation from diyne in 2010. A double hydroamination or hydration of the diynes was proved to be the mechanism.^{5b}

Fomina and Huerta had studied the mechanism of the Cu catalyzed transformation from diynes to pyrroles theoretically.⁵⁶ In this study, the Cu-stabilized carbenes were considered as the intermediates and the formation of the first intermediate was the rate determining step. The Cu catalysts were thought to decrease the activation energy of the carbene intermediate formation, from 75.0 to 50.1 kcal/mol.

Other heterocycles from diynes

Heterocycles rather than the basic five membered rings mentioned above could be achieved from the diynes. This may include siloles,⁵⁷ germoles,⁵⁸ pyrazoles,⁶ and pyridines,⁵² shown in Scheme 18. More structures as well as the mechanism were expected in this area.

Conclusion

This Letter had covered the structure, synthetic route, and derivations of the whole-carbon 1,3-diyne structure. Due to the rigid and rod-like structures of the diyne framework, this structure has attracted more and more attention not only of those organic synthetic chemists, but also the researchers in material science, natural product isolation and characterization, herbal medicine, biochemistry, etc. Diynes could be the precursors of many heterocycles, which have provided an alternative pathway to the synthesis of heterocycles.

However, this is still a fast developing research field. Challenges in this field still remain. One of these challenges could be the synthesis of unsymmetric diynes directly from different terminal alkynes, without perceptible excess of either alkyne. Other challenges would largely lie in the application aspect. Diynes could be good precursors of more heterocycles, and the mechanism study was few. On the other hand, diynes could be a suitable and particular linkage in polymers either in the main chain or in the side chains and related reports were still limited.

In a word, diynes are unique in structure, important in potential usage, widely existed in nature, and far from perfect in research.

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