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Elimination Strategy for Aromatic Acetylenes

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Contents

1. Introduction

Aromatic acetylenes are capable of giving rise to unique structures as well as electronic properties due to their skeletal persistency and rich π electrons.[1] Traditionally, the coupling of terminal acetylenes has been the most common method to build such frameworks.[2] The Sonogashira reaction is perhaps the most popular;[3] it is very versatile yet suffers from a few drawbacks. Somewhat chemically labile terminal acetylenes must be used, the homocoupling of which results in diyne byproducts. The products are contaminated by residues of transition-metal catalysts and occasionally difficult-to-remove colored impurities. Alternatively, elimination reactions can be employed. The elimination of substituted carbon−carbon double or even single bonds is a traditional mode of generating carbon−carbon triple bonds. Many classical elimination protocols are employable for constructing molecular architectures of structural interest. Moreover, newer elimination reactions also have been emerging to satisfy the needs generated by the increased sophistication of molecular designs. Since the Sonogashira protocol has already been documented elsewhere, elimination-based syntheses of aromatic acetylenes are the subject of this review to show the usefulness of this old but still growing methodology. In the next section the general features of elimination processes are summarized; their applications to furnish structurally complex or interesting aromatic acetylenes will be described in the subsequent section. It should be noted that this review deals with β-elimination only. Although α-elimination of geminal dihalides also gives rise to acetylenes, this reaction involves the rearrangement of

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Junzo Otera was born in Hyogo, Japan, in 1943. He received his undergraduate as well as graduate education at Osaka University. Immediately after earning his Ph.D. degree in 1971 he became a research chemist in Central Research Laboratories of Kuraray Co. In 1979 he moved to Okayama University of Science as Associate Professor and has been Full Professor since 1986. In the meantime, he has served as a visiting professor at many universities in Japan, the United States, France, Spain, and Australia. Since 2005 he has had a chair at Hunan University in China as a Chief Scientist. His research interests are focused on aromatic acetylene chemistry, Lewis acid catalysts, and green chemistry.

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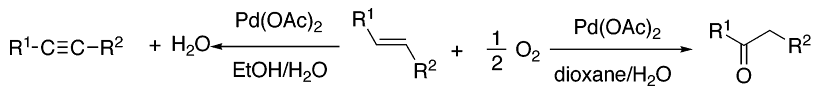
Scheme 1

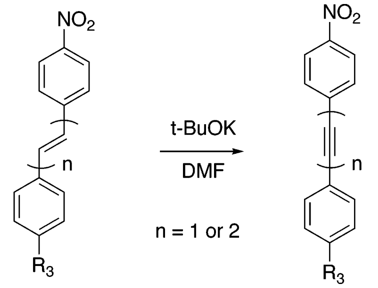


intermediary carbenes, and thus, elimination is not the key step leading to acetylenic bonds.[4,5]

2. Elimination Reactions

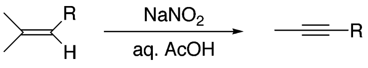
2.1. Simple Alkenes

As described later, alkynes are usually derived from functionalized alkenes, yet nonactivated carbon−carbon double bonds have been converted into the corresponding triple bonds on occasion. Dehydrogenation can be effected in the presence of oxygen by use of $Pd(OAc)_2$ immobilized on oligo-*p*-phenyleneterephthalamide in 70% aq. $HClO_4$/EtOH/H_2O (Scheme 1).[6] The reaction is not always selective because a ketone is formed as a byproduct in some cases. 1,2-Diarylethenes and 1,4-diaryl-1,3-butadienes underwent dehydrogenation upon treatment with t-BuOK in DMF under air (eq 1).[7]



(1)

A novel formal elimination of a CH_4 unit occurred when isopropylidene moieties were treated with $NaNO_2$ in AcOH/H_2O (eq 2).[8] Thus, various terpenylalkanolamines were converted into ethylidyne *N*-nitroso compounds.



(2)

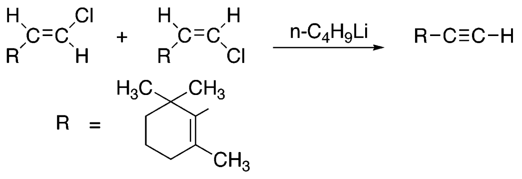
2.2. Haloalkenes

1,2-Dehydrohalogenation of haloalkenes is one of the most classical and popular ways to generate acetylenic bonds. The simplest is treatment of haloalkenes (mostly bromoalkenes) with a base. A variety of bases are employable, the relevant references on this issue have already been covered in the handbook by Larock,[9] and only fundamental aspects are mentioned herein. *β*-Bromostyrene was lithiated by BuLi to give phenylethynyllithium (Scheme 2).[10] A similar reaction occurred with a chloro olefin derived by the Wittig reaction of chloromethylene triphenylphosphorane (eq 3).[11] 1,4-Dehydrobromination is also feasible. Thus, a bromo-1,2,3-triene was transformed into a diyne upon treatment with $BnMe_3NOMe$ (eq 4).[12]

Scheme 2

$$C_6H_5CH{=}CHBr \;+\; n\text{-}C_4H_9Li \longrightarrow C_6H_5C{\equiv}CH$$

$$\xrightarrow{[n\text{-}C_4H_9Li]} C_6H_5C{\equiv}CLi \xrightarrow{CO_2,\ H^+} C_6H_5C{\equiv}CCO_2H$$



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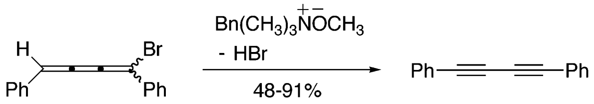
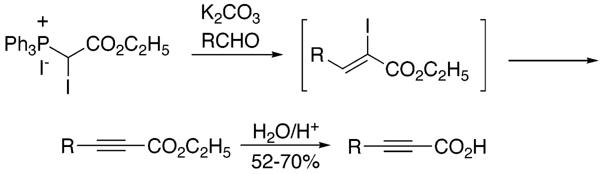
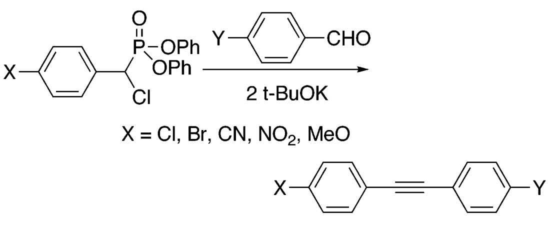


(4)

Wittig reactions of α-chloroarylmethylphosphonates were followed by dehydrochlorination to furnish aromatic acetylenes in one pot (eq 5).[13] Analogously, α-iodomethylene triphenylphosphoranes were used for the synthesis of propiolic acids (Scheme 3)[14] and acetylenic ketones (Scheme 4).[15] 1-Aryl-3,3,3-trifluoropropynes were obtained from 1-chloro-1-(trifluoromethyl)alkenes, which were available by reaction between aldehydes and 1,1,1-trichloro-2,2,2-trifluoroethane in the presence of zinc powder and acetic anhydride (eq 6).[16] Acetylenic sulfones were accessible by dehydrochlorination of α-sulfonyl chloroalkenes (eq 7).[17]

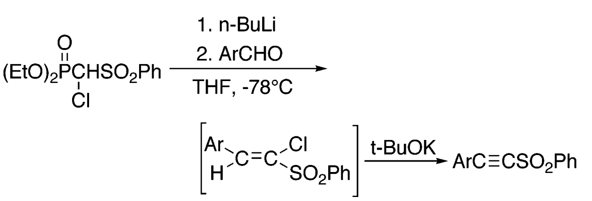
Scheme 3





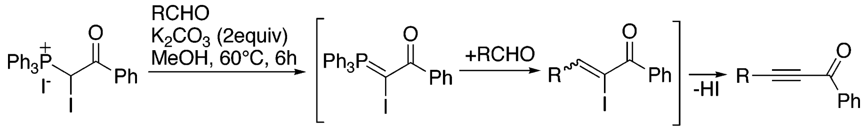
(5)

$$ArCHO + CCl_3CF_3 \xrightarrow{Zn/Ac_2O} ArCH{=}CClCF_3 \xrightarrow[t\text{-}BuOH]{t\text{-}BuONa} ArC{\equiv}CCF_3 \qquad (6)$$

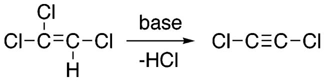


(7)

Scheme 4



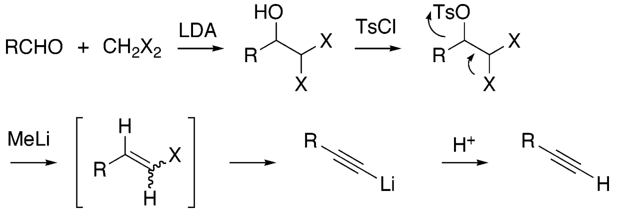
Dehydrochlorination of trichloroethylene is an important means to access chemically labile dichloroacetylene under basic conditions (eq 8). Hence, various bases were employed: KOH in ethylene glycol,[18a] $LiN(SiMe_3)_2$,[18b] $PhCH_2NEt_3{}^+Cl^-$,[18c] KOH/MeOH,[18d] etc.

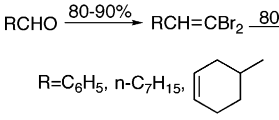


$$Cl{-}\overset{Cl}{C}{=}\underset{H}{C}{-}Cl \xrightarrow[-HCl]{base} Cl{-}C{\equiv}C{-}Cl \qquad (8)$$

Dehydrobromination of *gem*-dibromoalkenes is a very useful method to obtain terminal acetylenes (eq 9).[19] Treatment of aldehydes with CBr_4/PPh_3 affords the desired *gem*-dibromoalkenes, which are converted to acetylenes upon exposure to BuLi. Unfavorable side reactions can be suppressed by addition of Et_3N.[20] Dihalotosylates, prepared by addition of dihalomethyllithium to aldehydes followed by tosylation, may be directly transformed into acetylenes by reaction with MeLi (Scheme 5).[21] This process was modified using the trichloromethyl anion generated from trichloroacetic acid (Scheme 6).[22]

Scheme 5





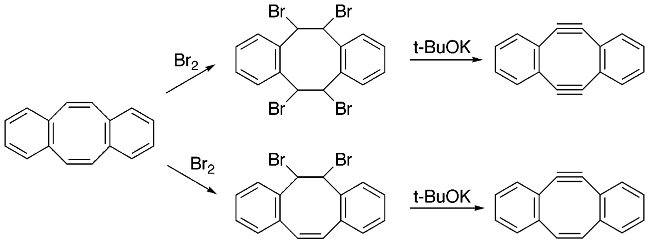
$$RCHO \xrightarrow{80\text{-}90\%} RCH{=}CBr_2 \xrightarrow{80\text{-}95\%} RC{\equiv}CH \text{ or } RC{\equiv}CR' \qquad (9)$$

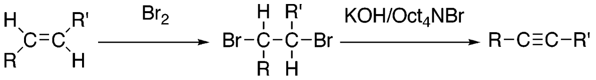
$R{=}C_6H_5$, $n\text{-}C_7H_{15}$,

2.3. Dihaloalkanes

Double dehydrobromination of alkanes with vicinal bromines is a more versatile alternative to dehydrobromination of haloalkenes because the dibromides are readily accessible by bromination of alkenes. A variety of acetylenes were prepared by treatment of 1,2-dibromoolefins with KOH under phase-transfer conditions (eq 10).[23] This method was also applied to cyclic compounds. For example, cyclooctatetraene derivatives were transformed into diene−diyne and triene−yne (Scheme 7).[24] This type of reaction found a number of applications for producing compounds of structural interest and will be discussed later in greater detail.

Scheme 7

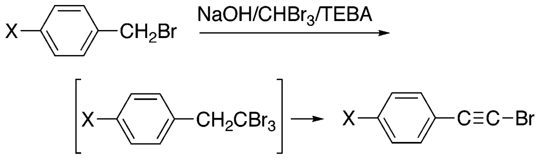




(10)

R = aryl, alkyl; R' = aryl, H

Reaction of benzyl bromide with $CHBr_3$/NaOH/TEBA affords bromo acetylenes in one pot (eq 11).[25] The reaction proceeds via 1,1,1-tribromo-2-arylethane intermediates. Treatment of 1,1-dichloro-1,2-diarylethanes with KOH in alcohol gives the corresponding acetylenes (eq 12).[26] These results indicate that polyhaloalkanes substituted at geminal positions also serve as precursors for acetylenes.



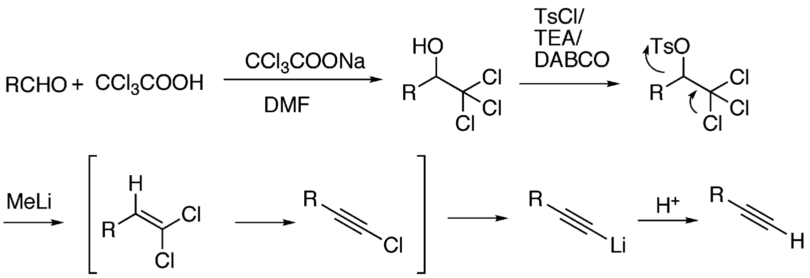
(11)

$$XC_6H_4CH_2CCl_2Ph \xrightarrow[alcohol]{KOH} XC_6H_4C{\equiv}CPh \qquad (12)$$

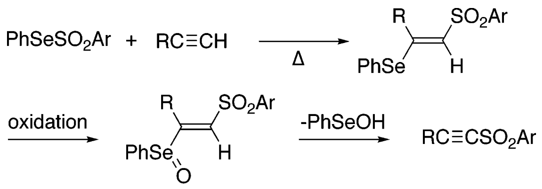
2.4. Heteroatom-Substituted Alkenes and Their Equivalents

Alkenes substituted with various heteroatom functional groups can undergo elimination. The well-known *syn*-

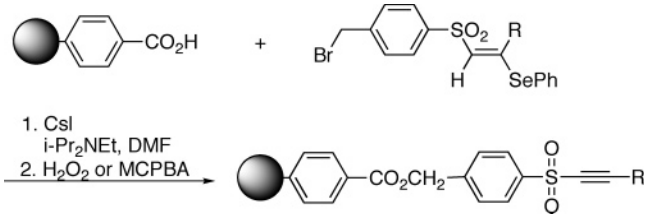
Scheme 6



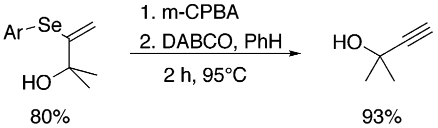
Scheme 8



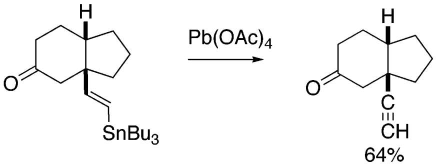
Scheme 9



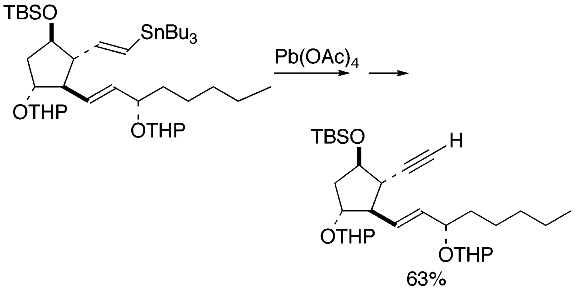
elimination of selenoxides was utilized for the conversion of alkenes into alkynes (eq 13).[27] This method was applied to the synthesis of acetylenic sulfones (Scheme 8),[28] and the precursors, β-selenosulfones, were attached to solid supports to give immobilized acetylenic sulfones (Scheme 9).[29] Elimination of vinylstannanes by use of $Pb(OAc)_4$ affords terminal acetylenes (eqs 14 and 15).[30]



(13)



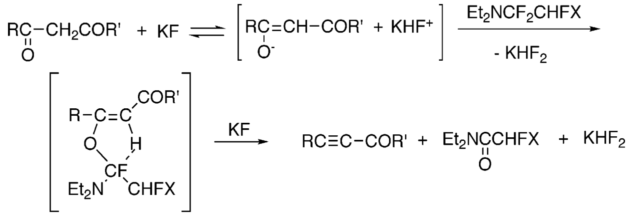
(14)

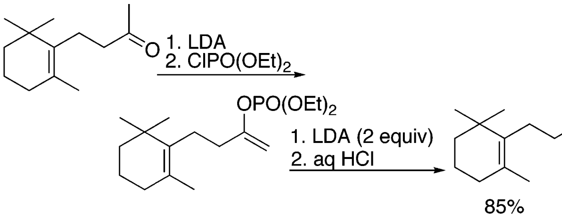


(15)

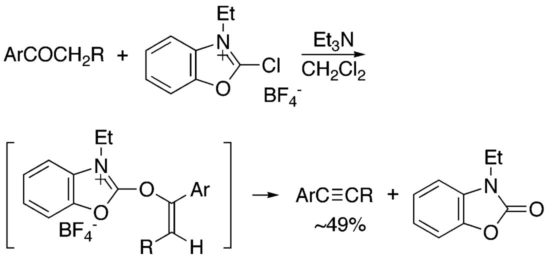
Elimination of enol ethers can be employed for acetylene synthesis. In particular, enol phosphates smoothly undergo elimination with LDA, offering a convenient means for the conversion of methyl ketones into terminal acetylenes (eq 16).[31] This protocol has found numerous applications[32] but failed to afford internal acetylenes when higher alkyl ketones were subjected to the same conditions (Scheme 10).[33] Allenes were produced as the major products except in the case of cyclododecyne. Reaction of aryl ketones and 2-chloro-3-ethylbenzoxazolium tetrafluoroborate in the presence of Et_3N furnished acetylenes directly (eq 17).[34] This reaction is applicable to both terminal and internal acetylenes, and formation of enolate intermediates plays a key role. Use of Et_2NCF_2CHFX ($X = Cl$ or CF_3) in combination with KF generated enolates which spontaneously underwent elimination to furnish acetylenic ketones (Scheme 11).[35]

Scheme 11



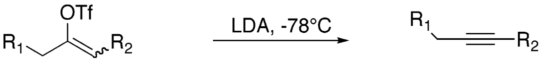


(16)



(17)

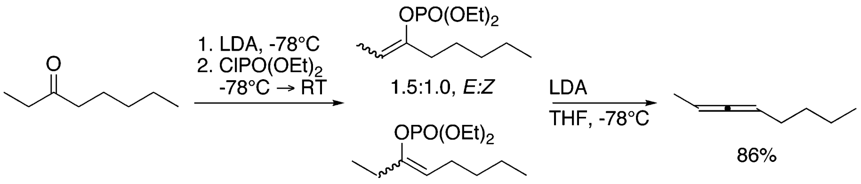
Vinyl triflates are also useful compounds for the synthesis of acetylenes. Thus, treatment of these compounds with LDA gave internal acetylenes in reasonable yields (eq 18).[36] Alkenyl triflates with a 1,2,3-benzotriazolyl group at the vicinal position underwent elimination to give the corresponding acetylenes, which were further derivatized by lithium and magnesium reagents (Scheme 12).[37]



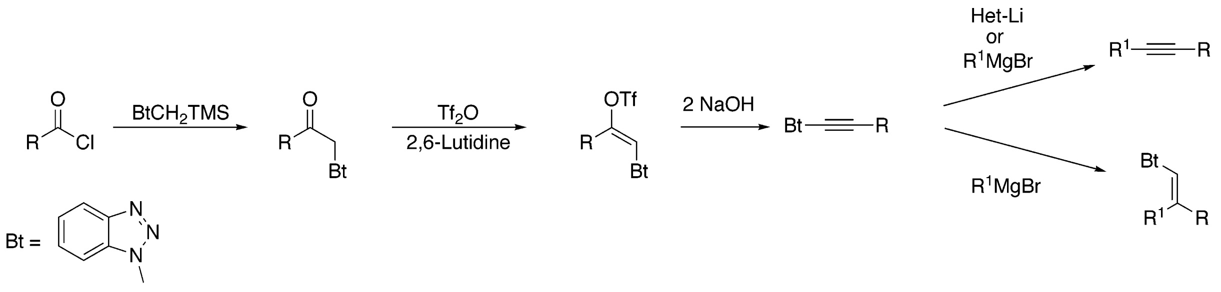
(18)

Reductive elimination of alkenes with vicinal heteroatom functional groups is also a versatile approach. Fluorinated alkene phosphonates derived from fluorinated alkanoyl chloride and triethyl phosphite were converted into fluoroalkylacetylenes upon treatment with TBAF (eq 19).[38] β-Arylsulfinyl alkenyl phosphates or triflates were transformed into acetylenes by action of t-BuLi (eq 20).[39] Use of the

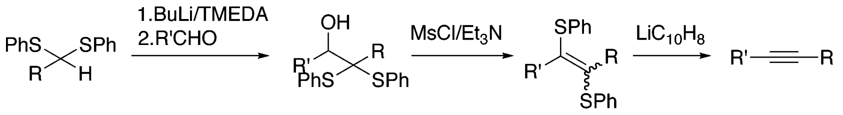
Scheme 10



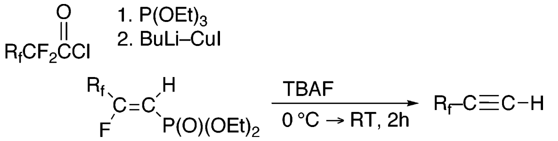
Scheme 12



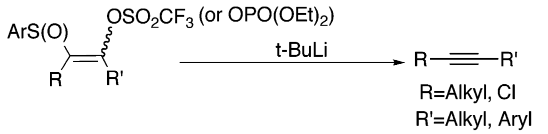
Scheme 13



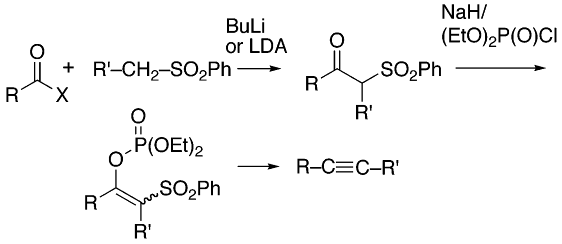
sulfonyl analogues is more flexible because these substrates are readily available from sulfonyl ketones (eq 21).[40] Alkene disulfides, available from dithioacetals and aldehydes, were reduced to acetylenes with lithium naphthalenide (Scheme 13).[41] Norbornyne was generated by reaction of β-silylnorbornenyl iodonium salt with TBAF (Scheme 14).[42] This highly reactive acetylene was trapped with 2,3-dihydropyran. Adducts obtained from $LiC(TMS)_3$ and arylnitriles eliminated $LiN(TMS)_2$ upon heating in refluxing benzene to yield the corresponding acetylenes (eq 22).[43]



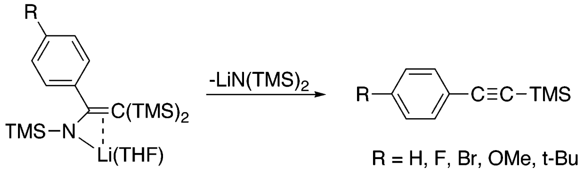
(19)



(20)

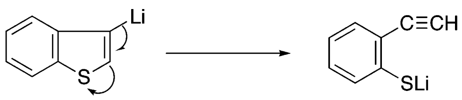


(21)



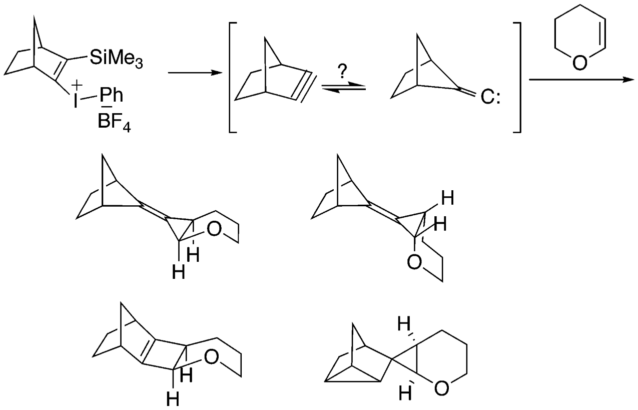
(22)

Intramolecular elimination of 3-lithiobenzothiophene provided *o*-ethynylthiophenol derivatives (eq 23).[44]

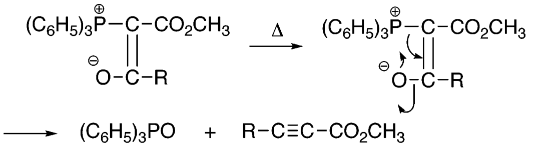


(23)

Scheme 14

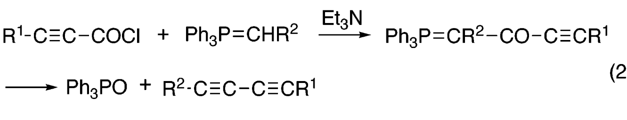


Acetylenic esters were prepared by taking advantage of the strong extrusion power of phosphine oxide from oxo-ylides (eq 24).[45] This methodology was applied to the synthesis of diynes (eq 25),[46] perfluorophenyl- and trifluoromethylacetylenes (Scheme 15),[47,48] ethynyl ethers (Scheme 16),[49] and ethynyl phosphonium salts (Scheme 17).[50] The protocol was modified by the use of triflates, which underwent elimination by exposure to sodium amalgam (Scheme 18).[51]



$$(C_6H_5)_3\overset{\oplus}{P}-C(=C(-O^{\ominus})-R)-CO_2CH_3 \xrightarrow{\Delta} (C_6H_5)_3PO + R-C\equiv C-CO_2CH_3$$

(24)

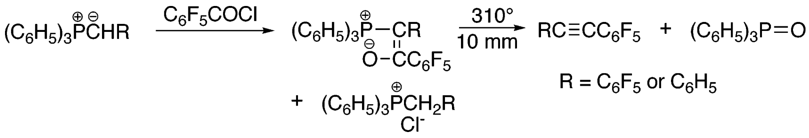


$$R^1\text{-}C\equiv C-COCl + Ph_3P=CHR^2 \xrightarrow{Et_3N} Ph_3P=CR^2-CO-C\equiv CR^1 \longrightarrow Ph_3PO + R^2\text{-}C\equiv C-C\equiv CR^1$$

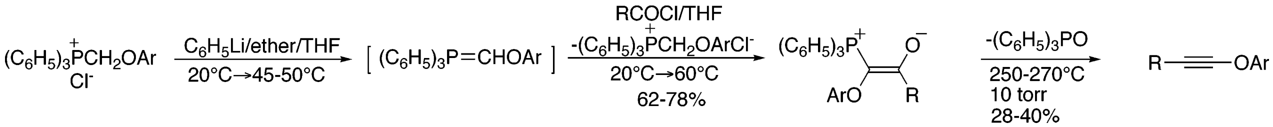
(25)

Oxidation of 1,2-bis(hydrazone)s, which are obtained from the corresponding α-diketones, furnishes the corresponding acetylenes (eq 26).[52] When α,β-epoxy ketones were combined with tosylhydrazine, acetylenes were produced in one pot (Scheme 19).[53] The reaction proceeds via a hydrazone intermediate. The tosylhydrazone of benzoin acetate or benzoate was converted into diphenylacetylene upon treatment with a base (eq 27).[54] The mesyloxy (eq 28)[55] and

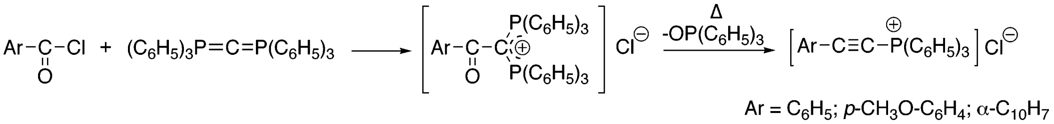
Scheme 15



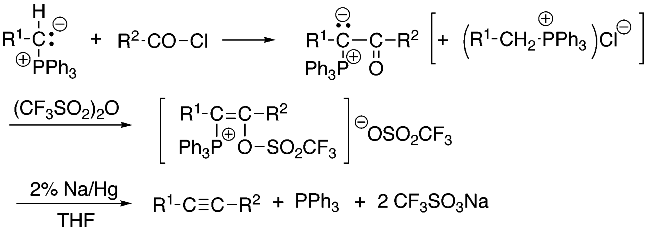
Scheme 16



Scheme 17



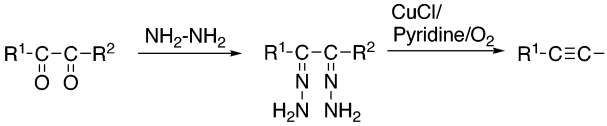
Scheme 18



methylthio (Scheme 20)[56] groups at the β-position of the hydrazone also act as leaving groups.

2.5. Double Elimination of Nucleophilic Addition Products

Nucleophilic addition, such as aldol reaction, produces 1,2-substituted motifs. Double elimination of the resulting functions can lead to carbon−carbon triple bonds. A highly versatile double-elimination protocol was developed by taking advantage of sulfone anion chemistry (Scheme 21).[57] An α-sulfonyl carbanion underwent addition to aldehydes, and the resulting aldolates were trapped with acetic anhydride, dihydropyran, TMSCl, or $ClP(O)(OEt)_2$. Exposure of this intermediate to a base such as t-BuOK, LDA, or LiHMDS led to acetylenes. Later, these steps were integrated into a one-pot procedure (Scheme 22).[58] Thus, the initial aldolates were trapped by TMSCl or $ClP(O)(OEt)_2$, and additional base was added to this reaction mixture to provide acetylenes without isolation of the intermediates. Elimination was also combined with the Peterson reaction (Scheme 23).[59] This protocol was applied to the synthesis of a variety of aromatic acetylenes, which will be one of the main subjects of the next section.



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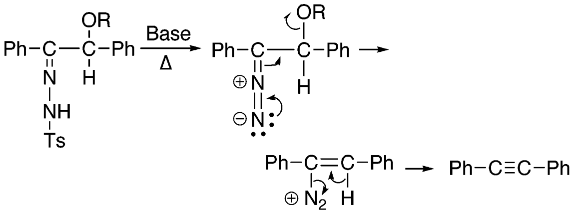
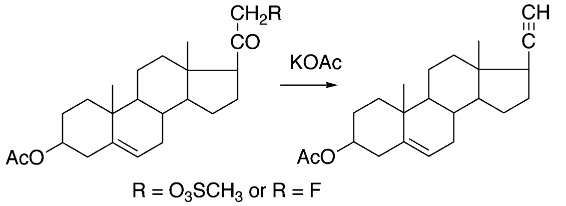


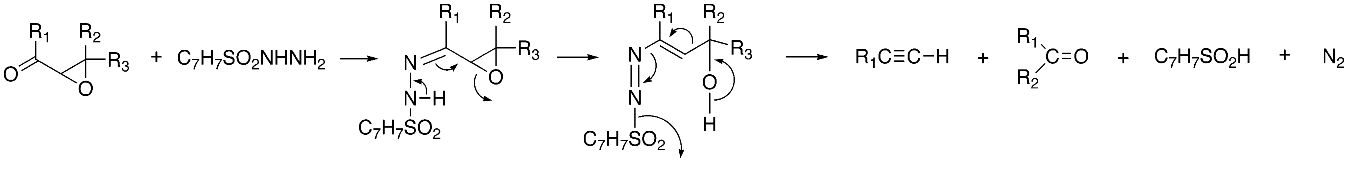
(27)



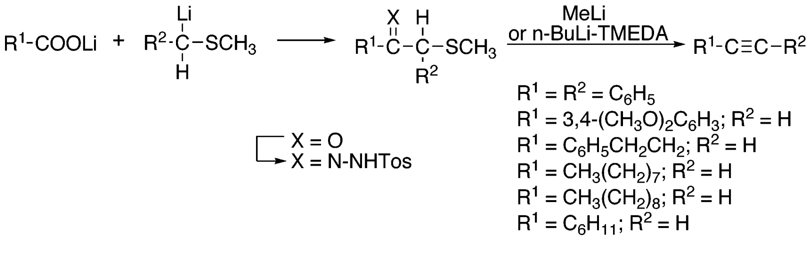
(28)

Reaction of 1-arylmethylbenzotriazole with imines in the presence of t-BuOK furnished diaryl acetylenes (Scheme

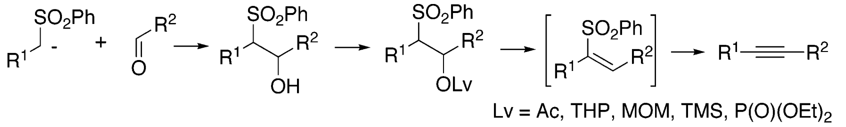
Scheme 19



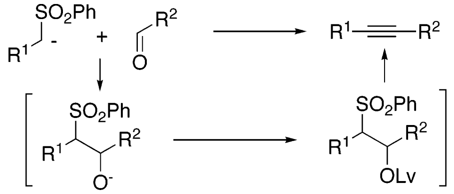
Scheme 20



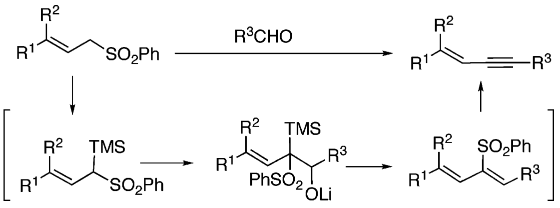
Scheme 21



Scheme 22



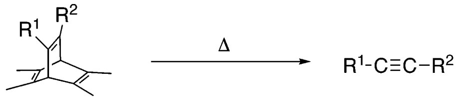
Scheme 23



24).[60] The reaction proceeds by elimination of aniline followed by benzotriazole. Esters can also be utilized as electrophiles in place of the imines.[61]

2.6. Fused Cyclic Compounds

Cycloelimination of annulated rings is another effective means to increase the degree of unsaturation. Release of ring strain of cyclic hydrocarbons is exploited as a driving force for this type of reaction. The ketene/anthracene adducts were thus transformed into acetylene/anthracene adducts, which provided acetylenes upon flash vacuum pyrolysis (eq 29).[62] Photochemical $[2 + 2]$ cycloreversion of indan adducts releases polyynes (eq 30).[63] The same technology was employed for the generation of cyclic polyynes (Scheme 25).[64]



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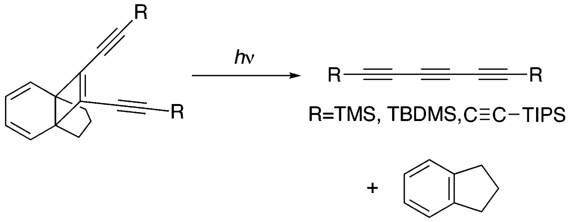
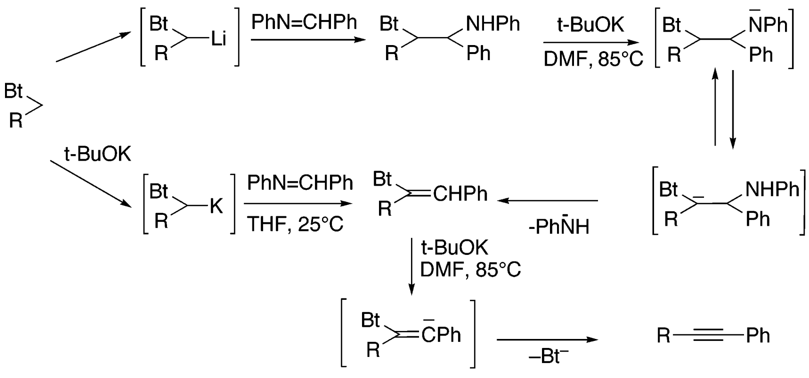


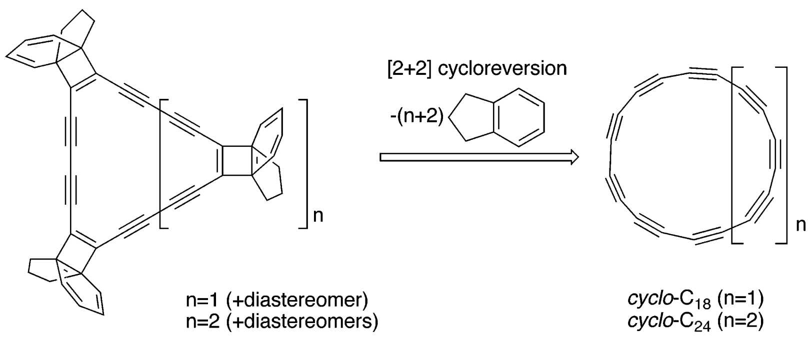
(30)

Decarbonylation of ketene adducts is also an effective route. Thus, solution-spray flash vacuum pyrolysis of cyclobutenediones led to polyynes (eqs 31 and 32).[65] This subject was summarized in a review article.[66] A cyclopropenone unit is also a suitable precursor. By means of UV,[67a−e] ultrafast laser irradiation,[67f] or thermolysis in the presence of alumina,[67g] various diarylacetylenes and even aliphatic acetylenes were accessible (eq 33).[67] Ethynol, which is considered as a possible constituent of flames, planetary atmospheres, and interstellar clouds, was generated by photolysis of 3-hydroxycyclobutene-1,2-dione (Scheme 26).[68]

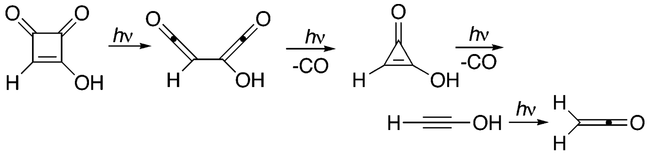
Scheme 24



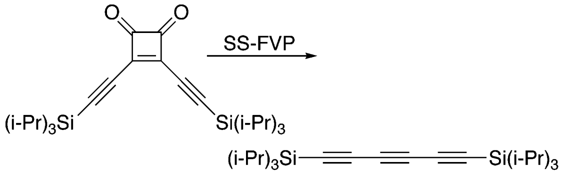
Scheme 25



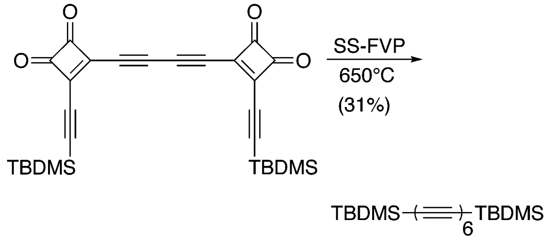
Scheme 26



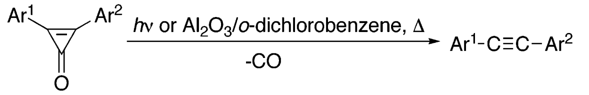
Heteroatom-substituted acetylenes were obtained by gas-phase pyrolysis of the corresponding cyclobutane-1,2-dione precursors (eq 34).[69]



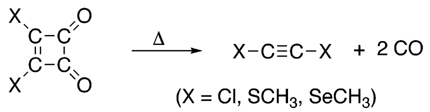
(31)



(32)



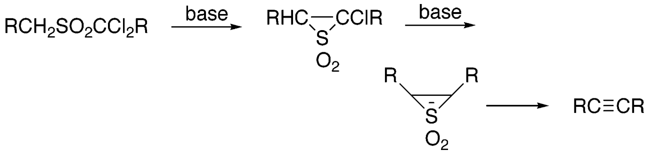
(33)



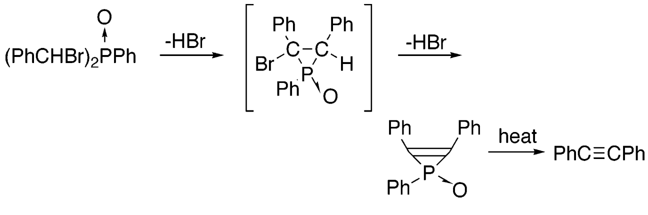
(34)

The Ramberg−Bäcklund reaction is known to create unsaturation. Disubstituted thiirene dioxides which were prepared from α,α-dichlorosulfones were used for the synthesis of acetylenes (Scheme 27).[70] Use of sulfides in place of sulfones gave acetylenes by the action of Ph_3P and t-BuOK in THF (eq 35).[71] Triphenylphosphiren oxide underwent a similar reaction to give diphenylacetylene (Scheme 28).[72] Pyrolysis of 4,5-dicyano-1,3-dithiol-2-one furnished dicyanoacetylene in 57% yield (Scheme 29).[73]

Scheme 27

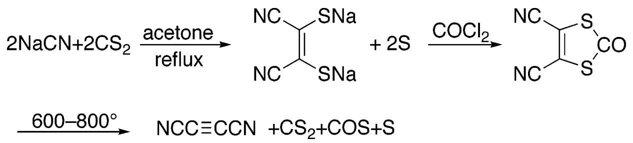


Scheme 28



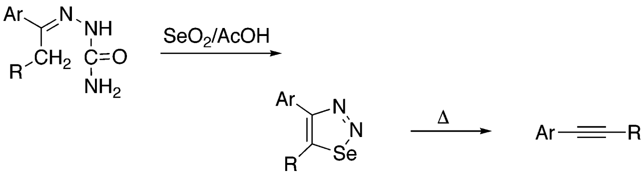
$$\mathrm{ArCH_2SCCl_2Ar} \xrightarrow{\mathrm{Ph_3P/t\text{-}BuOK}} \mathrm{ArC{\equiv}CAr} \quad (35)$$

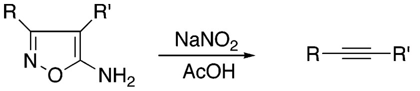
Scheme 29



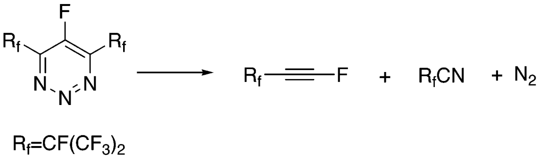
Thermolysis of 1,2,3-selenadiazoles provides acetylenes (Schemes 30 and 31).[74] This protocol is employed widely for the synthesis of acetylenes and will be described later in more detail. Diazotization of 5-aminoisoxazoles that bear at least one electron-withdrawing group by reaction with sodium nitrite in $AcOH/H_2O$ affords substituted acetylenes (eq 36).[75] Vacuum pyrolysis of perfluoroalkyl-1,2,3-triazine gave a fluoroalkyne (eq 37).[76] Treatment of isoxazol-5-ones derived from β-keto esters and hydroxylamine with sodium nitrite and ferrous sulfate in aqueous acetic acid affords the corresponding acetylenes in moderate to good yields (Scheme 32).[77] A review on this subject has appeared.[78] Alkynyl oxime ethers were prepared by exposure of α-chloro oximes to LDA (Scheme 33).[79] This reaction probably involves azacyclobutadiene intermediates. It should be noted that a review dealing with thermal and photochemical nitrogen-cycloelimination is available.[80]

Scheme 30





(36)

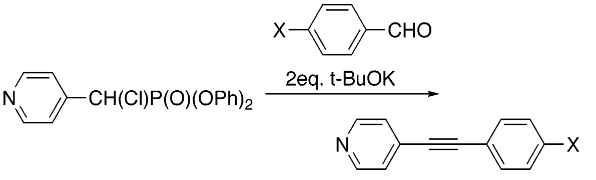


(37)

3. Aromatic Acetylenes through Elimination

3.1. From Haloalkenes

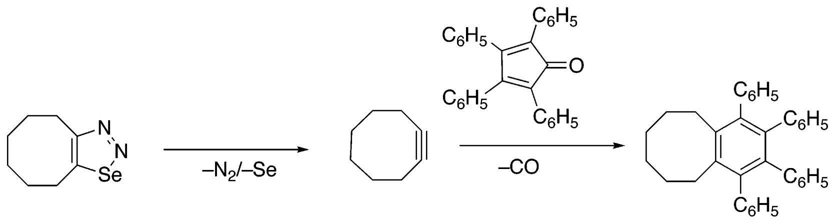
Dehydrochlorination of chloroalkene **1** followed by silylation was employed to synthesize bis(diyne) **2** in quantitative yield (Scheme 34).[81] The same reaction with **3** yielded **4**, which was transformed into tetrayne **5** (Scheme 35). The α-chloroarylmethylphosphonate protocol described in section 2.2 was further extended to pyridine derivatives (eq 38).[82]



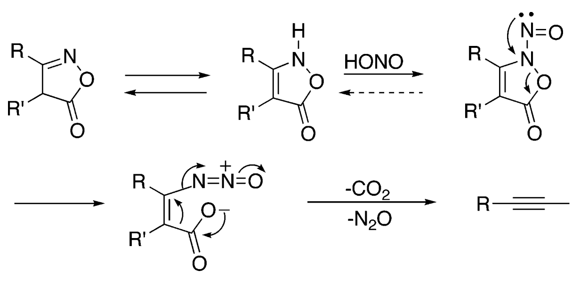
(38)

The potential of the dehydrobromination protocol can be exemplified by making reference to the synthesis of cyclooctapolyene derivatives, although these compounds are not aromatic. Treatment of bromocyclooctatetraene with t-BuOK in ether generated the corresponding acetylene **6**,

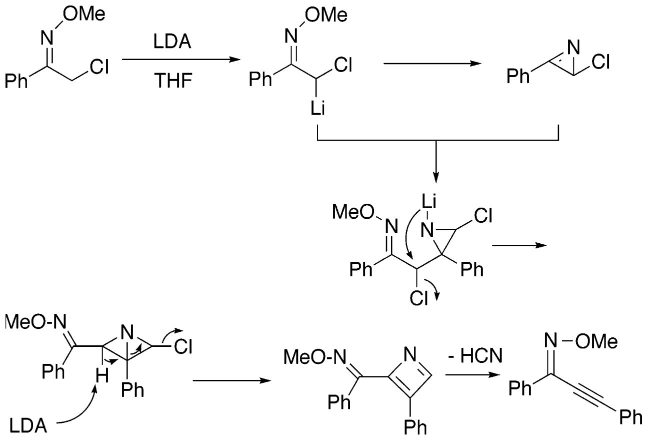
Scheme 31



Scheme 32



Scheme 33



which was derivatized to various compounds (Scheme 36).[83] Bromination of cyclooctadiene furnished a mixture of diastereomers of the corresponding tetrabromide (Scheme 37).[84] Treatment of this compound with t-BuOK yielded two isomeric dibromides, which were transformed into yne–bromide **7** upon treatment with t-BuOK/18-crown-6. Further reaction for a prolonged time afforded diyne **8**, which was finally converted into cyclooctatetraene. Reaction of **7** with tetraphenylcyclopentadienone (TPCP) afforded adduct **9**, dehydrobromination of which led to acetylene **10** (Scheme 38). Reaction of this compound with TPCP gave **11**, which could also be directly obtained from **8**.

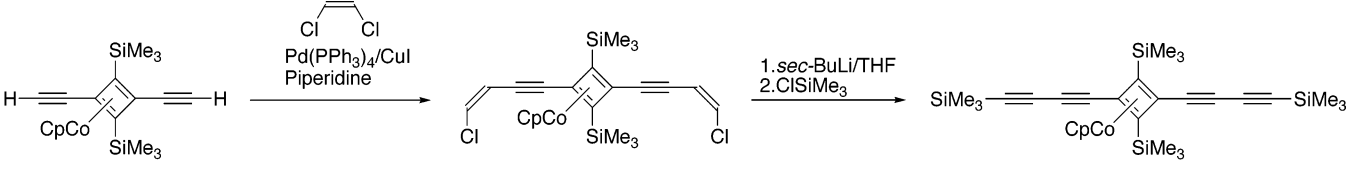
3.2. From *gem*-Dibromoalkenes

Generation of a terminal alkyne unit from *gem*-dibromoalkenes (Corey–Fuchs protocol) has been widely used. Diederich made use of this method for constructing tetraethynylethene frameworks. For example, a free *trans*-enediyne unit **12** was successfully obtained by simultaneous conversion of bis(*gem*-dibromoalkene) (Scheme 39).[85] On the basis of this technology, various enediynes with a free trans or cis unit were synthesized. A free *cis*-enediyne building block with TIPS-terminated ethynyl groups was trimerized to hexaethynylhexadehydro[18]annulene **13** (Scheme 40).[86] On the other hand, the trans counterpart was transformed into conjugated carbon rods with a persilylethynylated polytriacetylene backbone (Scheme 41).[87] Tetraethynylethenes bearing electron-donating and -withdrawing groups were prepared.[88] Tetrabromide **14** was transformed into dibromide **15** by treating with LDA followed by TMSCl (Scheme 42). This dibromide was treated with LDA to give mono-deprotected **16**, which was converted into trans donor–acceptor-substituted chromophores **17** and **18**. Irradiation at λ = 366 nm induced the isomerization of **17** into **19**. Treatment of **14** with LDA followed by Bu_3SnCl afforded bis(stannyl)enediyne **20** (Scheme 43).[89] Coupling of this compound with (*R*)-**21** provided optically active photochemical switch (*R*,*R*)-**22**. By use of **16** another type of photoswitchable tetraethynylethenes **23** and **24** were synthesized in which reversible conversions take place between the dihydroazulene and vinylheptafulvene structures upon photoirradiation (Scheme 44).[90]

The geminal dibromoalkene unit was used for generating unsymmetrically substituted hexaethynylbenzene **25**, which was transformed into carbon network **26** (Scheme 45).[91]

Spirocyclopropanated oligocyclic diacetylenes are of interest because the HOMOs of the cyclopropane ring are close in energy to the π MOs of an acetylene unit, resulting in

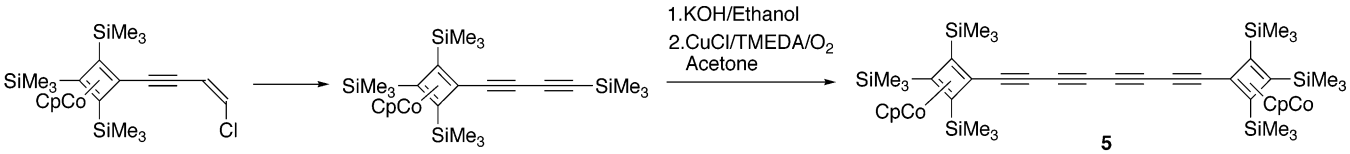
Scheme 34



1

2

Scheme 35

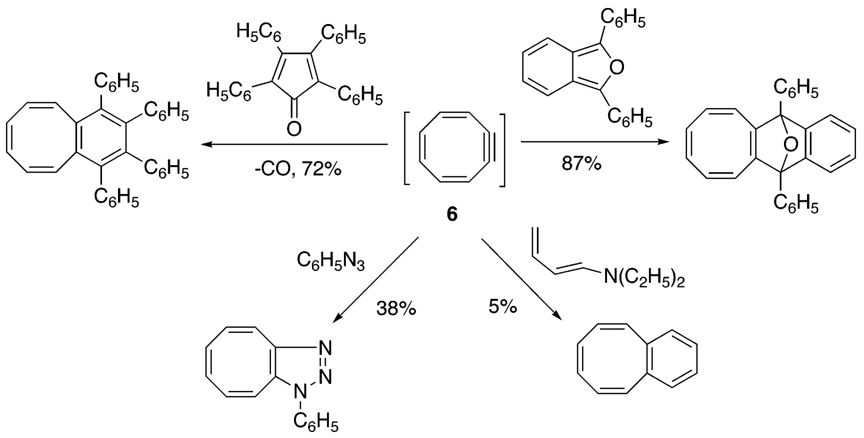


3

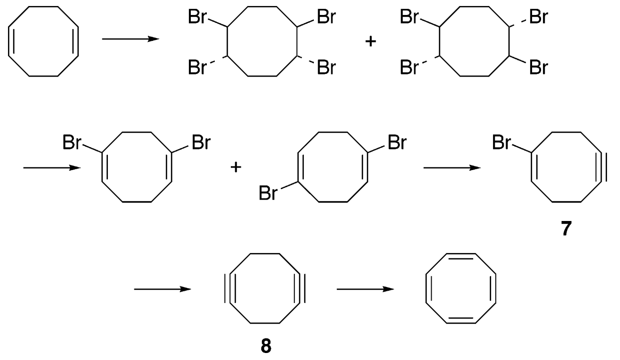
4

5

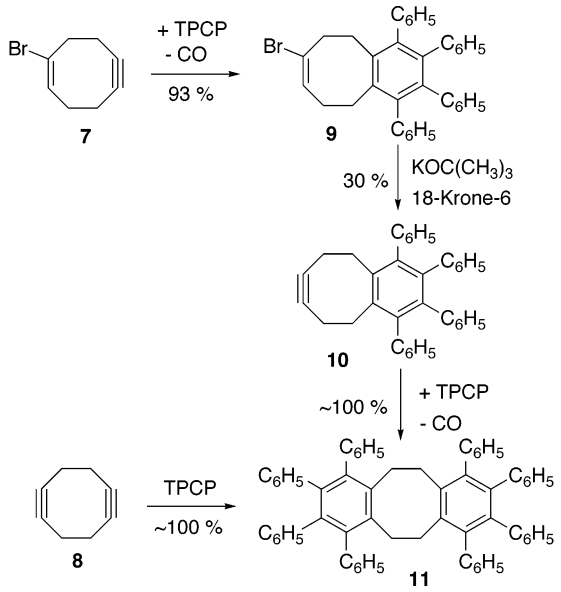
Scheme 36



Scheme 37



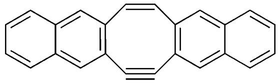
Scheme 38



strong conjugation. In the de Meijere−Scott procedure, simple dehydrobromination of geminal dibromoalkene played a key role. As shown in Scheme 46, exposure of dibromide **27** to t-BuOK furnished monobromo diethynylcyclopropane **28** and **29**.[92] These building blocks were coupled to give precursors **30**, which were finally converted into the desired cyclic acetylenes **31**. A similar strategy was applied to synthesis of pentayne **32** (Scheme 47).[93]

3.3. From *vic*-Dibromoalkanes

As described in section 2.3, Wong and Sondheimer prepared *sym*-dibenzo-1,5-cyclooctadiene-3,7-diyne (**33**) and *sym*-dibenzo-1,3,5-cyclooctatrien-7-yne (**34**) with recourse to the double-dehydrobromination process.[24] By the same procedures, Wong synthesized dinaphtho **35**,[94] benzo/naphtho **36**,[94] and benzo/phenanthro **37**[95] analogues. He then developed a rich cyclooctene chemistry by making use of these strained acetylenes.[96] Reaction of dichloroketene with **33** or **34** provided adducts **38** or **39**, which was converted into cyclobutendione **40** or **41** upon hydrolysis (Scheme 48).[97,98] 1,3-Dipolar cycloaddition of **34** with phenyl azide furnished triazole **42**.[98] These bent acetylenes underwent smooth Diels−Alder reaction with benzofuran and 1,3-diphenylisobenzofuran.[94,98,99] Deoxygenation of the resulting adducts



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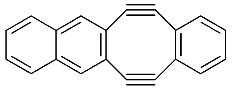

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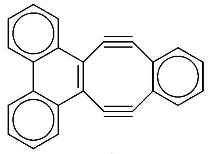
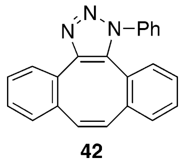
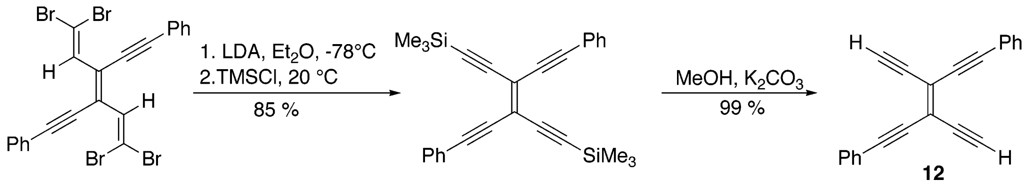


37

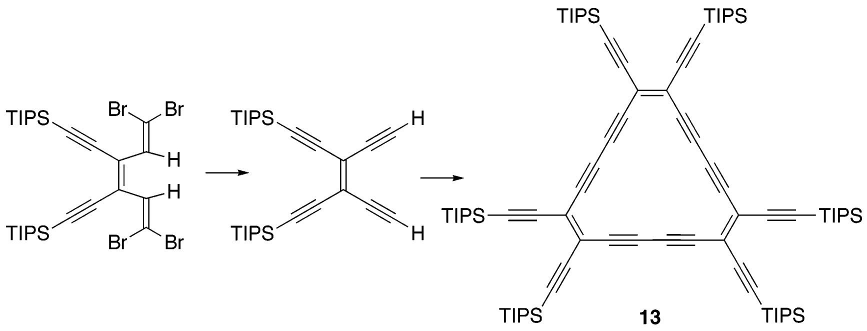


42

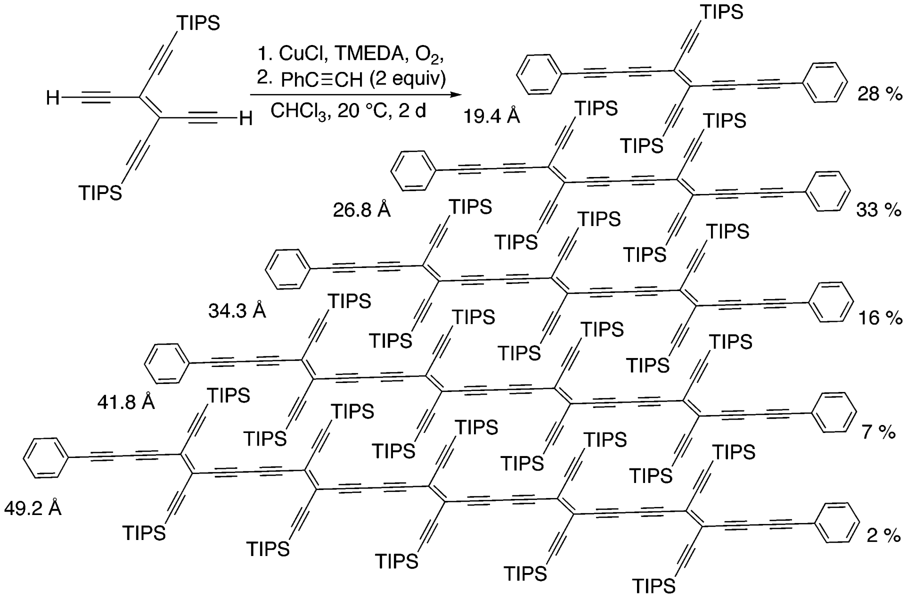
Scheme 39



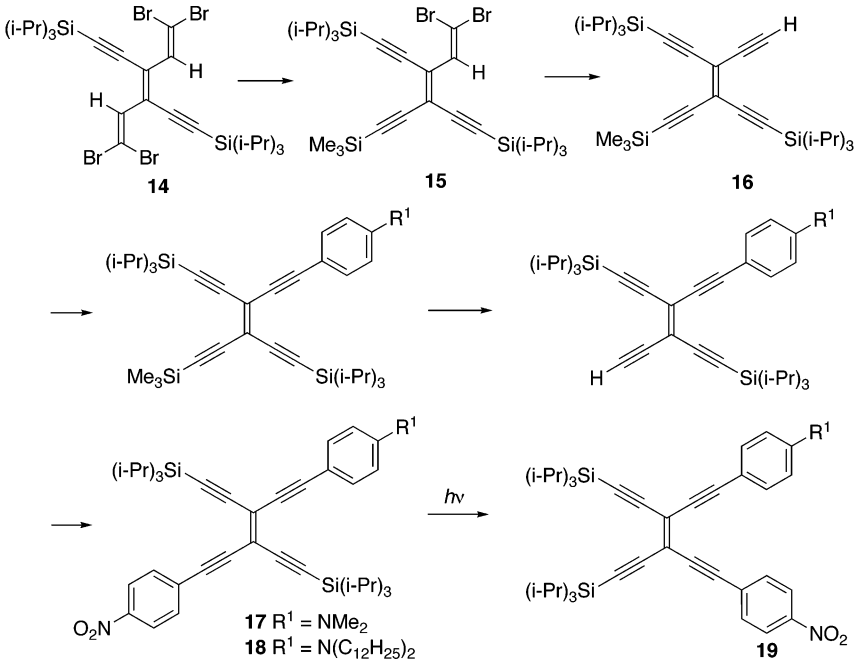
Scheme 40



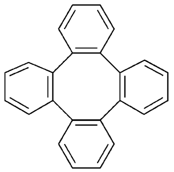
Scheme 41



Scheme 42



with low-valent titanium induced aromatization. As a result of combining cyclooctene building blocks and benzofurans, a variety of benzo-fused tetraphenylenes **43**−**48** were synthesized. Cyclopropenation of **33** was reported by German workers (Scheme 49).[100] Thus, reaction of **33** with diazomethane furnished bis-3*H*-pyrazolene **49**, photolysis of which effected stepwise dinitrogen elimination to afford dibenzo[*a*,*e*]dicyclopropa[*c*,*g*]cyclooctenes **50**. The



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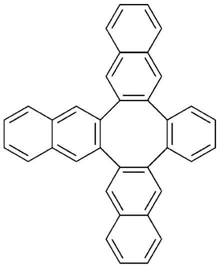

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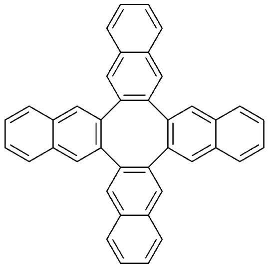

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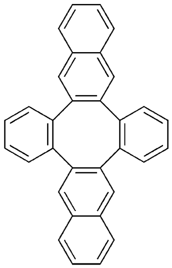
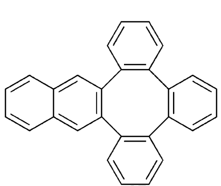


47



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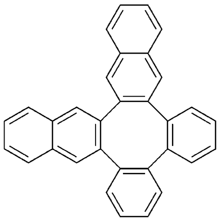
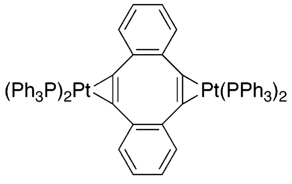


48

platinum analogue **51** was prepared by reaction of **33** and $Pt(CH_2{=}CH_2)(PPh_3)_2$.[101]

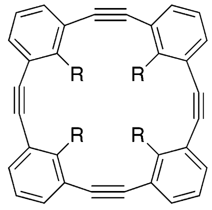


51

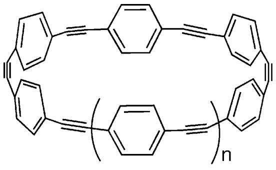
Bromination *o*-divinylbenzene gave tetrabromide **52** (Scheme 50).[102] Exposure of this compound to t-BuOK in BuOH provided dibromide **53**. Further clean elimination failed, but reaction with t-BuOK in benzene furnished diethynylbenzene **54**. Another route involving monobromide **55** was also established.[103]

The double-dehydrobromination method was applied to the synthesis of a number of larger cyclic compounds. The trimer of phenylacetylene **57** was obtained by treatment of tetrabromide **56**, which was derived from bis-ylide and *o*-phthaldehyde (Scheme 51).[104] A similar strategy was employed for the synthesis of tolanophanes (Scheme 52)[104] and tetradehydrocyclodecabiphenylenes (Scheme 53).[105]

Kawase and Oda synthesized cyclic phenylene ethynylenes. The smallest members of [2.*n*]metacyclophene-*n*-ynes were obtained according to a sequence of McMurry coupling−bromination−dehydrobromination (Schemes 54 and 55).[106,107] A tetrayne derivative with methoxy groups **58** proved to be a good ionophore for alkali metals except for Cs^+.[108] Metacyclophane-bearing biphenyl units were also prepared (Scheme 56).[109] This compound exists as a dl/*meso* equilibrium mixture in solution. Using an analogous strategy, [2.*n*]paracyclophane-*n*-ynes ([*n*]CPPA) **59** were synthesized.[110] [6]CPPA gave an inclusion complex with hexamethylbenzene, while [8]CPPA accommodated four toluene

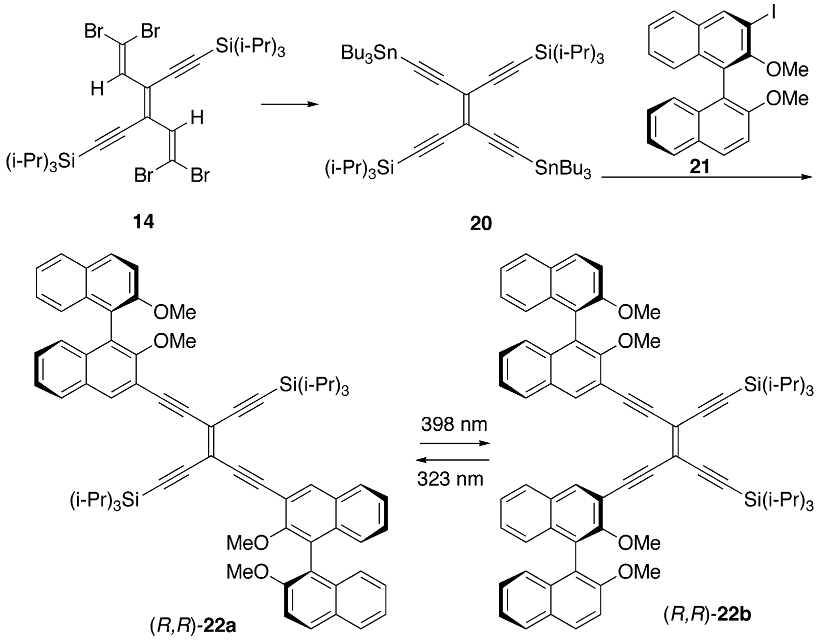


58 R = OMe or H

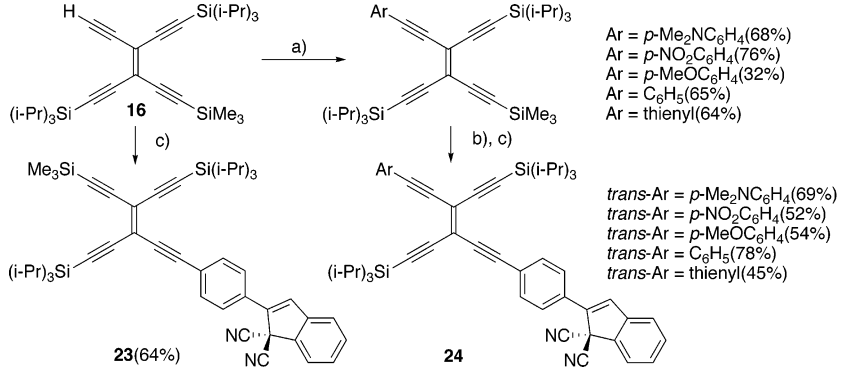


59 n = 1, 2, 3, 4

Scheme 43

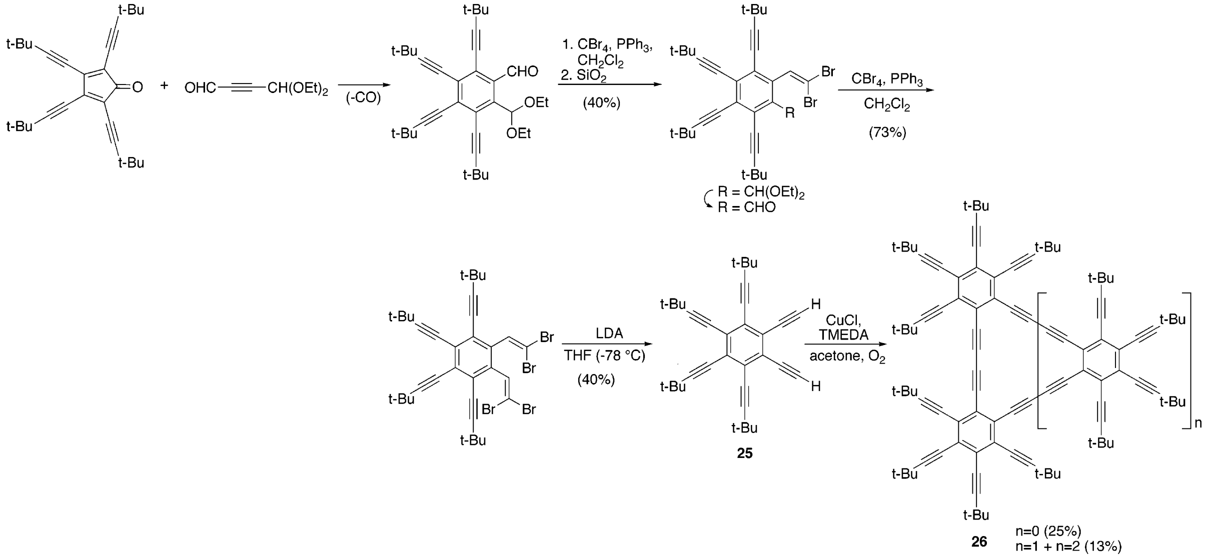


Scheme 44[a]

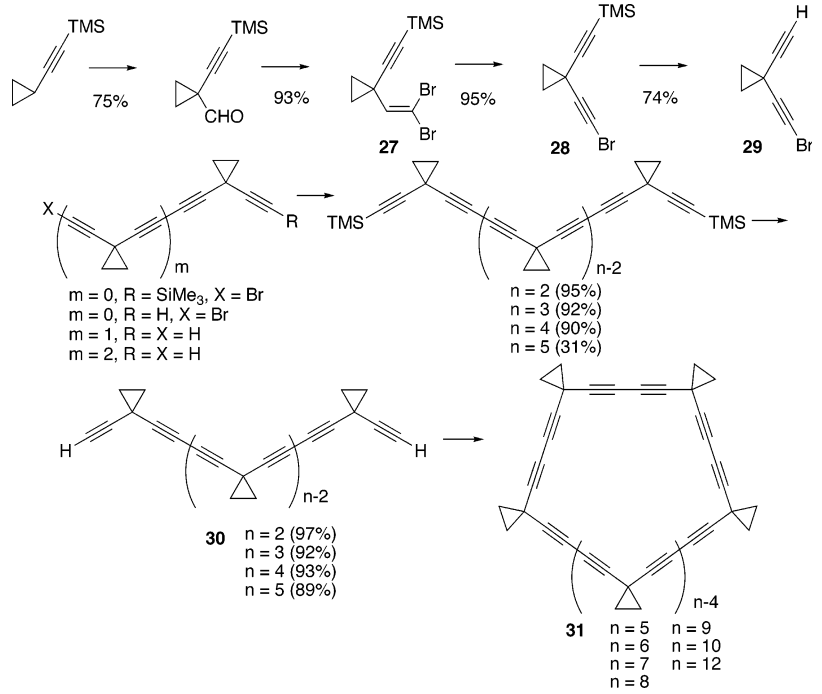


[a] Reaction conditions: (a) $[PdCl_2(PPh_3)_2$, CuI, Bu_4NBr, $(i\text{-}Pr)_2NH$, THF, 4-Me_2N-C_6H_4I or 4-O_2N-C_6H_4I or 4-MeO-C_6H_4I or PhI or iodothiophene, 20 °C, 45 min to 15 h. (b) K_2CO_3, MeOH, THF, 20 °C, 60−90 min. (c) $[PdCl_2(PPh_3)_2]$, CuI, Bu_4NBr, $(i\text{-}Pr)_2NH$, THF, 20 °C, 1−17 h. All steps were usually performed in the dark to prevent trans → cis isomerization.

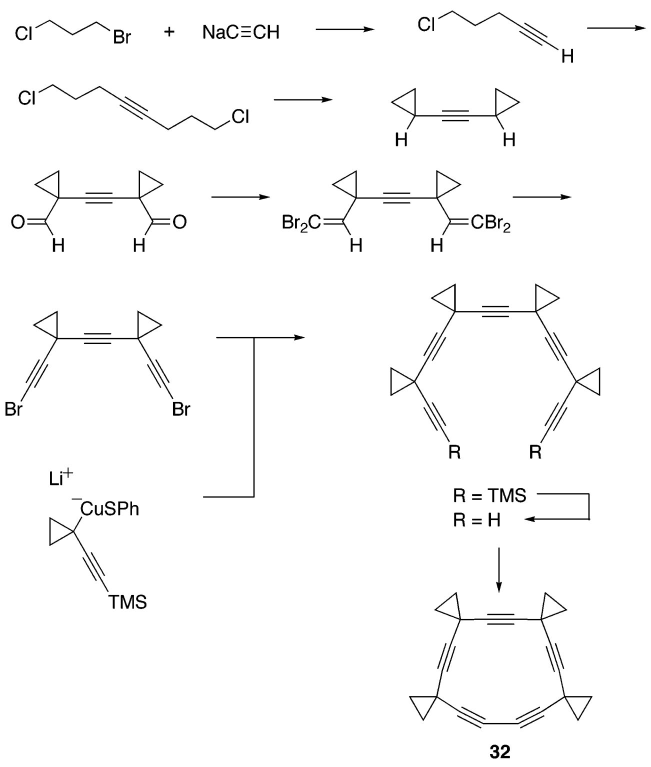
Scheme 45



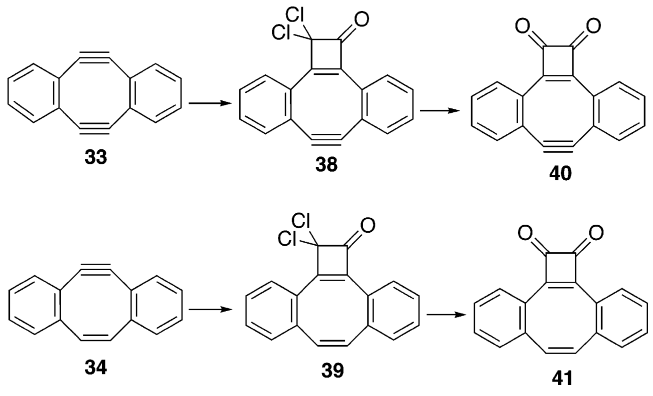
Scheme 46



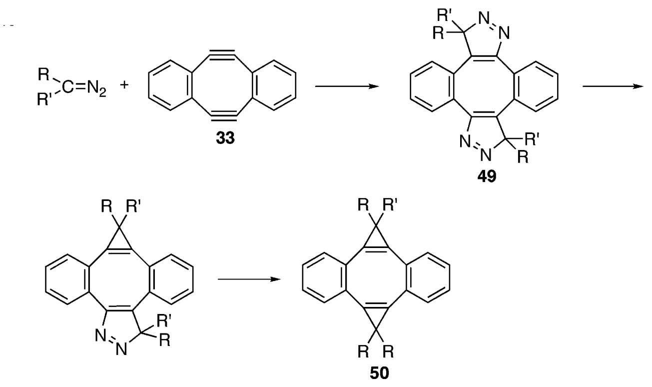
Scheme 47



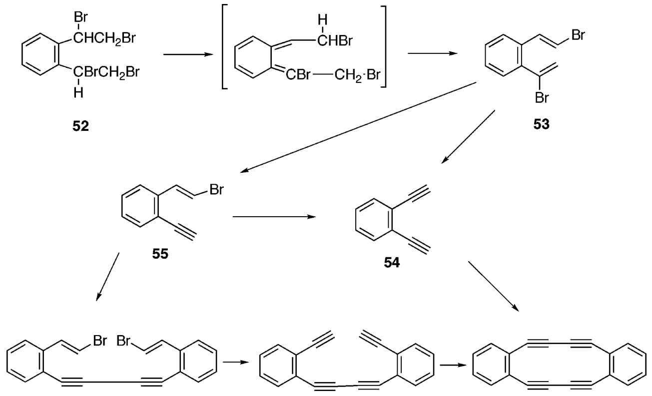
Scheme 48



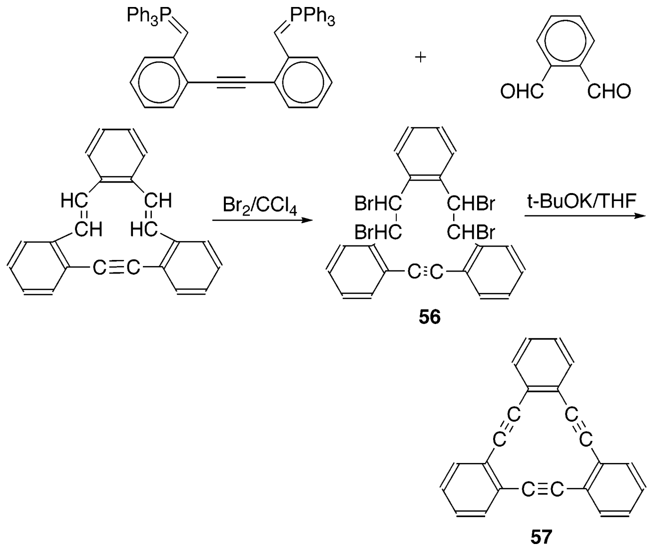
Scheme 49



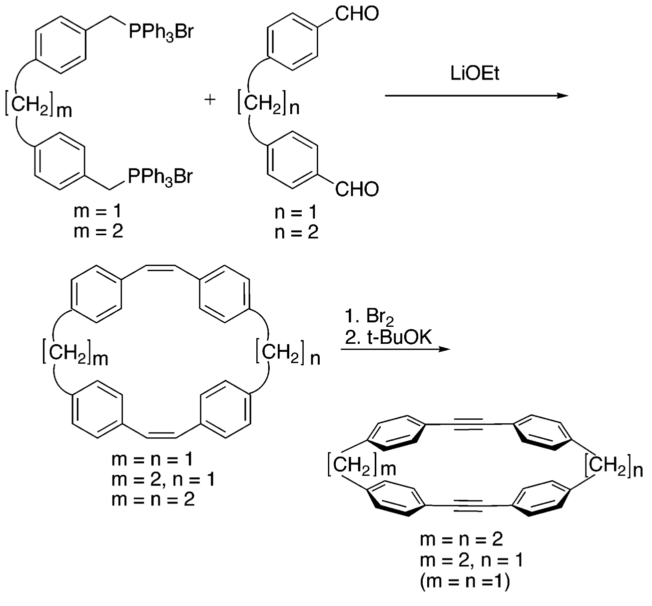
Scheme 50



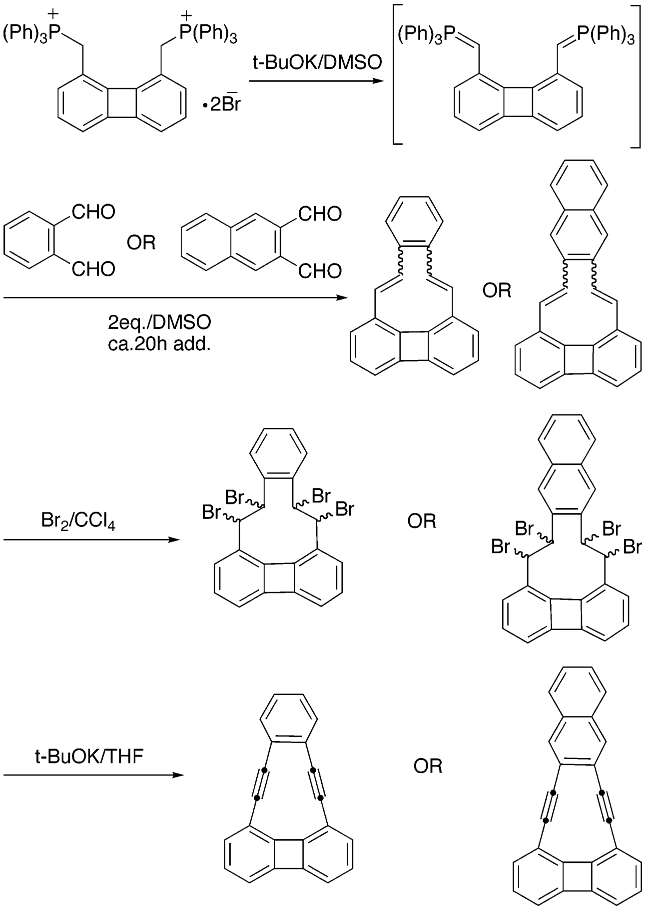
Scheme 51



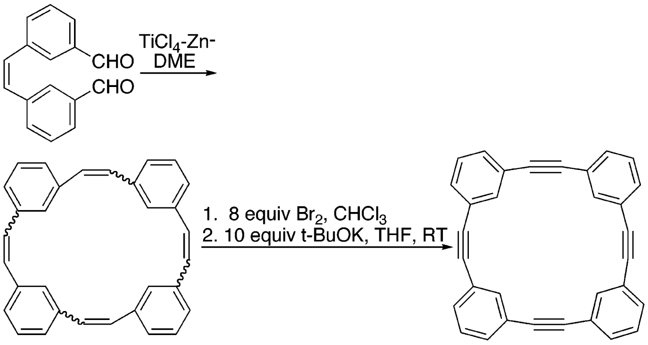
Scheme 52



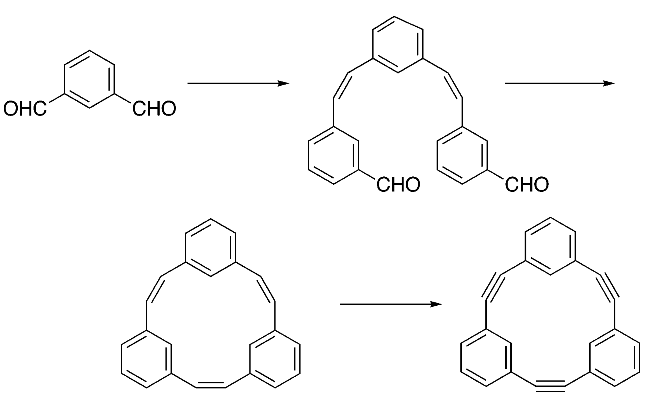
Scheme 53



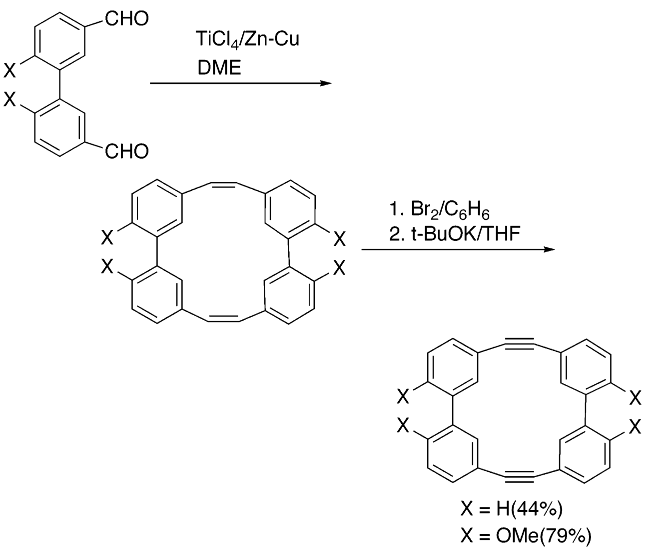
Scheme 54



Scheme 55

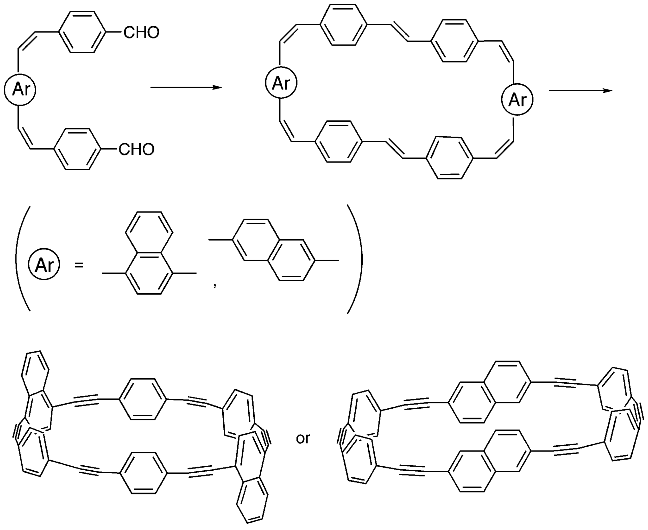


Scheme 56



molecules.[111] C_{60} was much more soluble in $CHCl_3$ in the presence of [6]CPPA, indicative of formation of an inclusion complex.[112] Actually, the complex with bis(ethoxycarbonyl)methanofullerene could be isolated. The cyclophanes with 1,4- and 2,6-naphthalene units were also synthesized (Scheme 57).[113] Through combination of C_{60}, [*n*]CPPA, and their 1,4-naphthalene derivatives, formation of a double-inclusion complex with onion-type structure was suggested.[114]

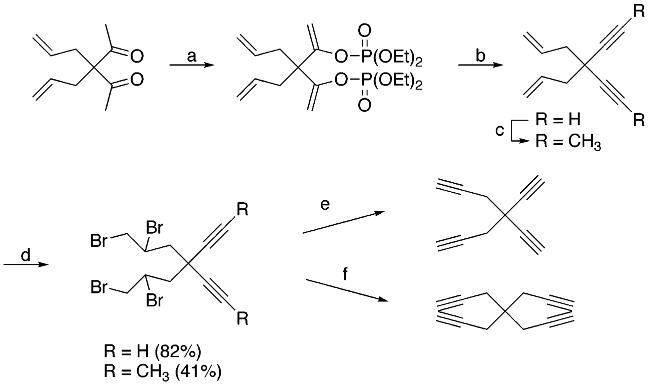
Scheme 57



3.4. From Heteroatom-Substituted Alkenes and Their Equivalents

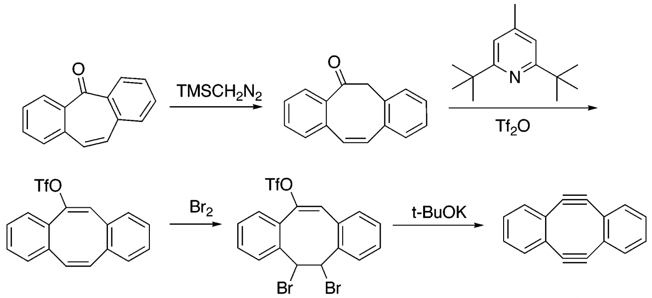
Elimination of alkenyl phosphate was employed for the synthesis of tetraalkynylmethanes. Bunz et al. made use of two elimination reactions for the synthesis of tetraalkynylmethanes: the alkenyl phosphates furnished the ethynyl groups and the dibromopropane moieties the propargyl groups (Scheme 58).[115] Tetraethynylmethane was synthesized again by recourse to two kinds of eliminations: the dehydrobromination of bromoethene was followed by elimination of β-sulfonyl hydrazone, which is an equivalent of alkenyl sulfone (Scheme 59).[116] Wudl et al. reported a new route to dibenzocyclooctadiene−diyne **33** by use of simultaneous eliminations of alkenyl triflate and 1,2-dibromoalkane (Scheme 60).[117] They used this compound for the synthesis of cyclophane **60** (Scheme 61).[118]

Scheme 58[a]



[a] Reaction conditions: (a) 2.1 equiv of LDA, −78 to 20 °C, 1 h, then 2.2 equiv of $ClP(O)(OEt)_2$, 3 h. (b) 4.3 equiv of LDA, −78 to 20 °C, 2 h, then 5 N HCl. (c) 2 equiv of ^{n}BuLi, then CH_3I. (d) 2 equiv of Br_2, CH_2Cl_2, −78 °C. (e) R = H, 11 equiv of $NaNH_2$ in liquid NH_3, then 5 N HCl (67%). (f) R = CH_2, 45 equiv of KNH_2 in liquid NH_3, 8 h, then 5 N HCl (18%).

Scheme 60



33

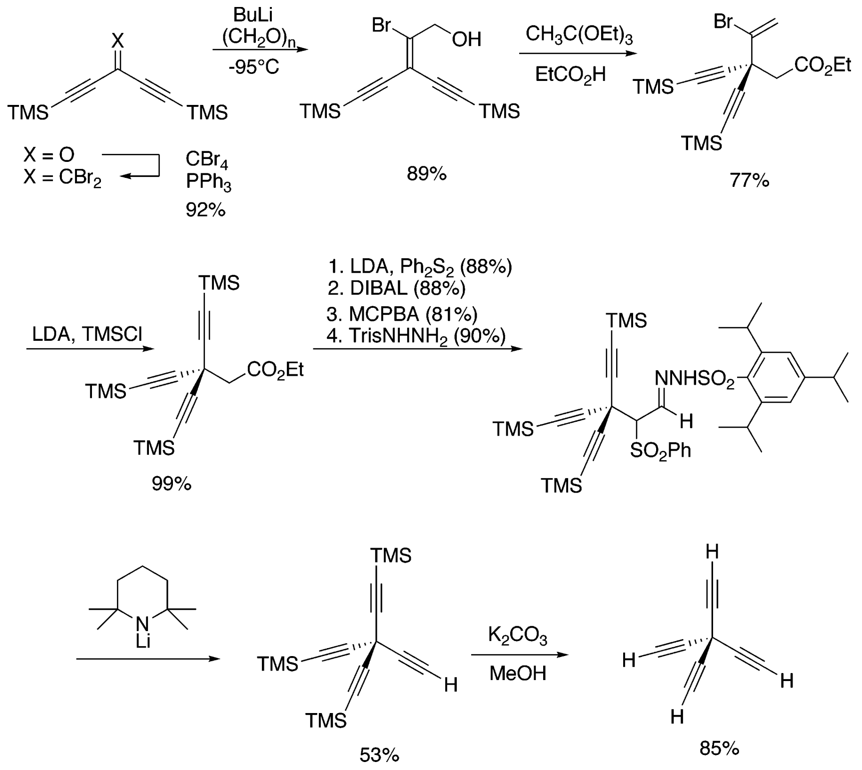
Through recourse to the intramolecular elimination of 3-lithiothiophene derivatives as described in section 2.4, thienyl acetylenes were prepared in one pot from tetrabromothienothiophene (Scheme 62).[119]

A variety of aromatic polyynes were obtained by taking advantage of the extrusion of phosphine oxide from oxo−ylides (Scheme 63).[120] This reaction was also employed to prepare cyanoacetylene **61**, an intermediate in the synthesis of pyrrole fungicide **62** (Scheme 64).[121]

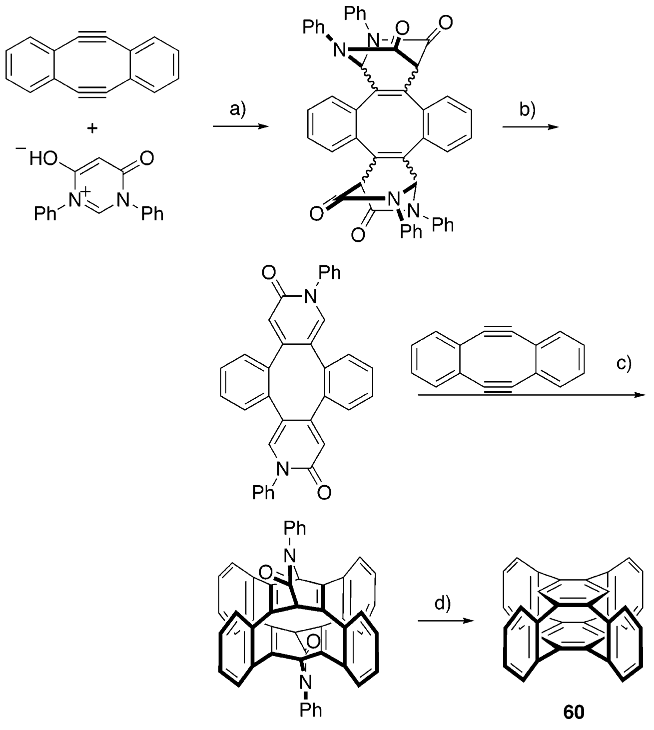
3.5. Double Elimination Reactions

According to the one-pot double elimination of β-substituted sulfones which are derived from α-sulfonyl carbanions

Scheme 59

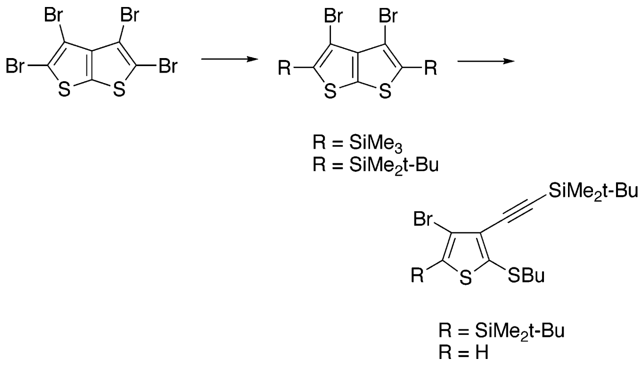


Scheme 61[a]

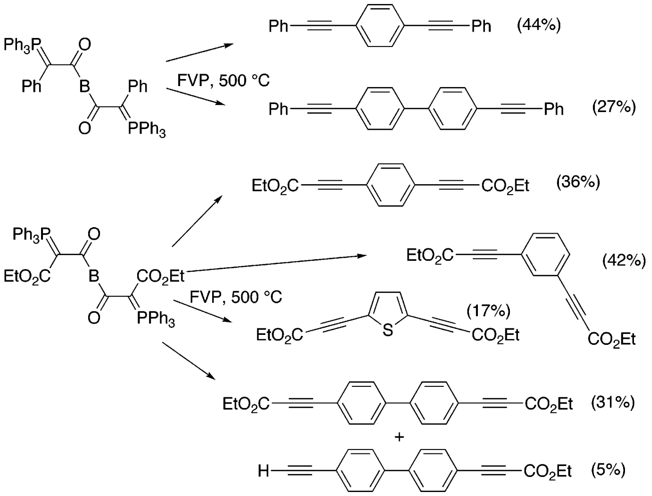


[a] Reaction conditions: (a) *o*-dichlorobenzene (ODCB), 110 °C, 1 day. (b) Neat, 250 °C, 1 h. (c) ODCB, 150 °C, 3 days. (d) Neat, 350 °C, 4 h.

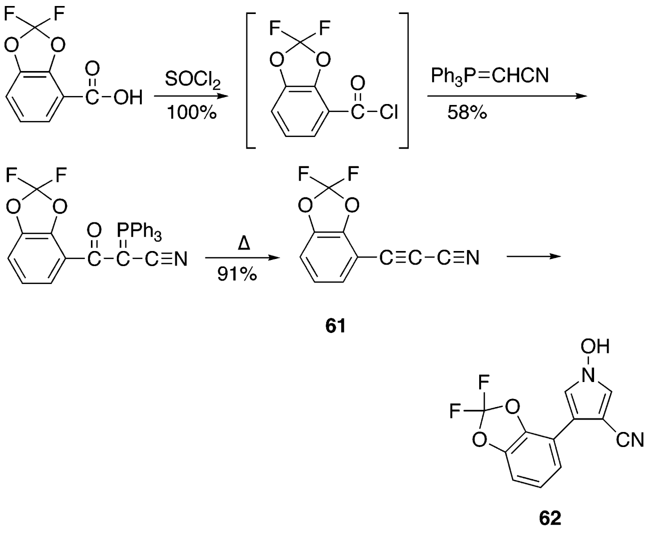
Scheme 62



Scheme 63

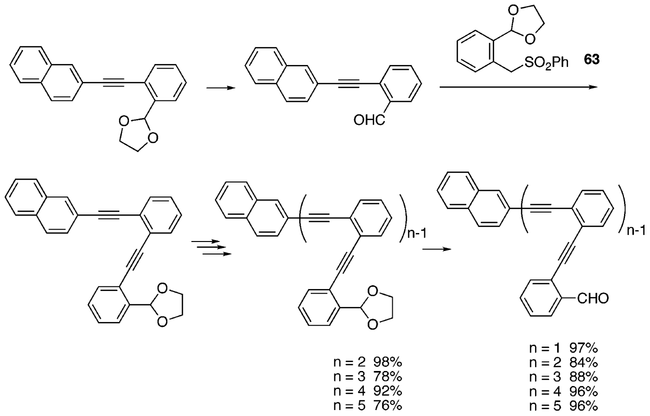


Scheme 64



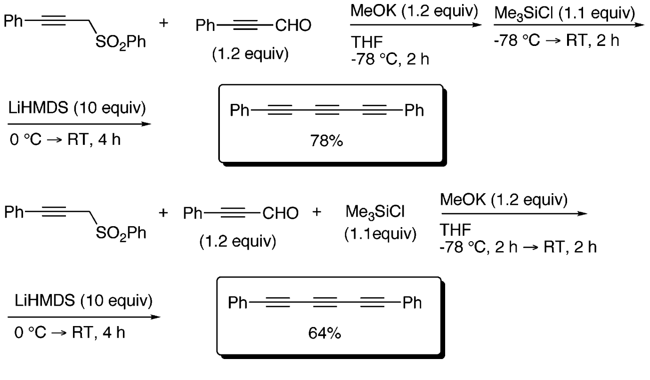
and aldehydes (see section 2.5), Otera and co-workers developed diverse ways to access aromatic acetylenes.[122] *o*-Phenyleneethynylene oligomers were obtained by use of acetal sulfone **63** as a key building block (Scheme 65).[123]

Scheme 65



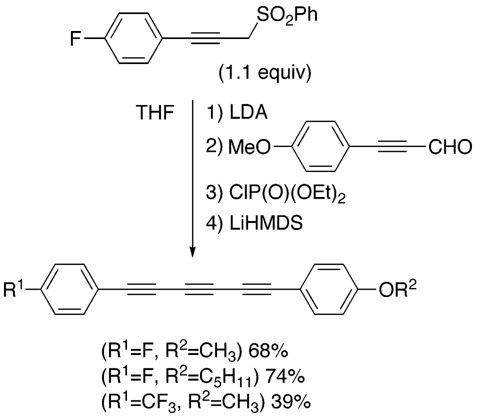
1,6-Diphenyl-1,3,5-hexatriyne was prepared from phenylpropargyl sulfone and phenylpropynal as shown in Scheme 66.[123b] In this procedure, MeOK, TMSCl, and LiHMDS were

Scheme 66



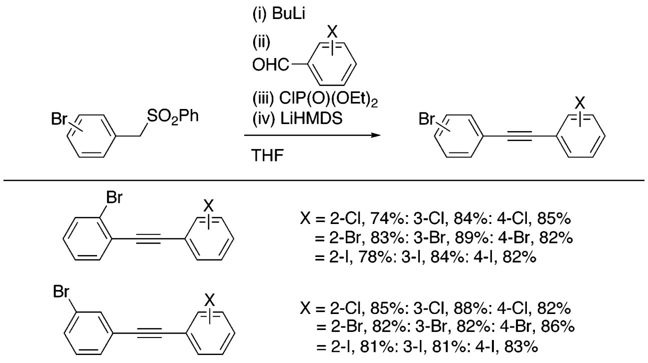
added successively, but a simpler method was found later in which MeOK and LiHMDS were added in this order to the mixture of the sulfone, aldehyde, and TMSCl. Other triynes and bis(diyne)s were also accessible (Schemes 67 and 68).[124] These materials exhibited high degrees of birefringence.

Scheme 67



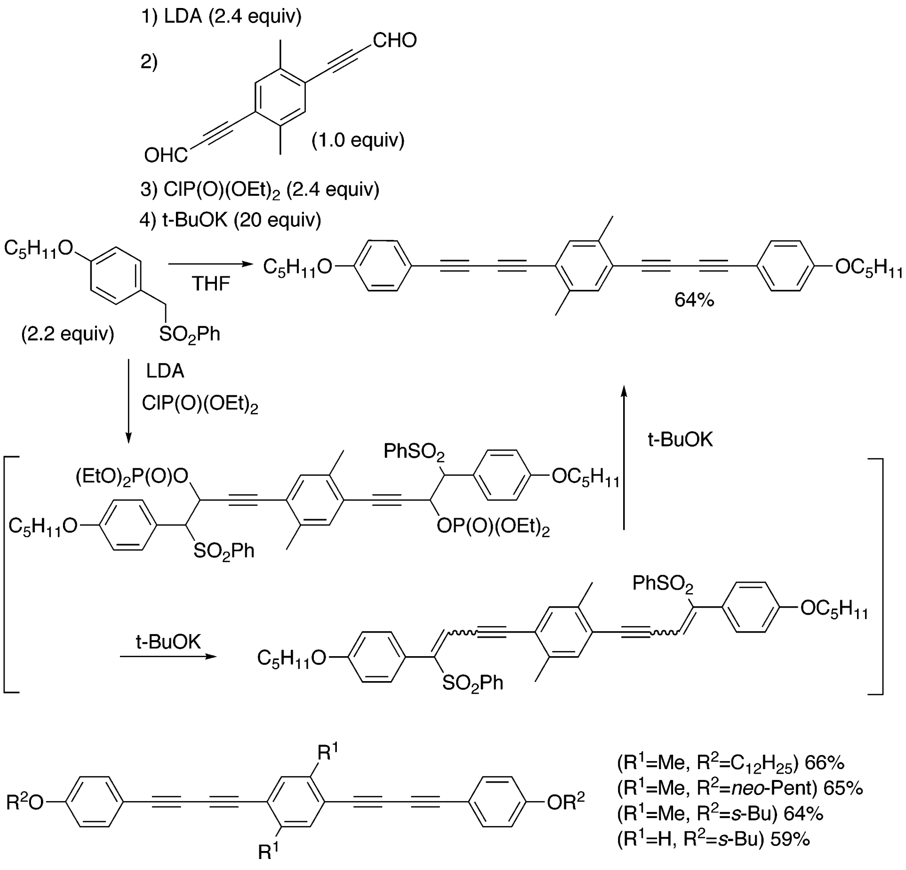
The present double-elimination protocol tolerates various functional groups, thus providing functionalized aromatic acetylenes. In particular, halogens survive the reaction to give halogen-substituted arylacetylenes. Thus, halogen-substituted benzyl sulfones and benzaldehydes were coupled to provide all combinations of chloro-, bromo-, and iodo-substituted diphenyl acetylenes (Scheme 69).[125]

Scheme 69

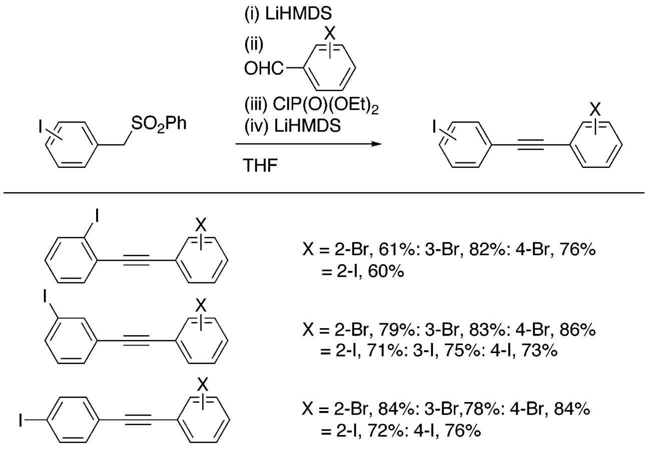


Employment of LiHMDS for the initial aldol reaction enabled the use of iodobenzyl sulfones (Scheme 70). On the basis of this technology, higher homologues of unsymmetrical arylene ethynylenes were synthesized (Scheme 71).[126] Dihalotolanes thus obtained worked as useful building blocks for tailor-made phenylene ethynylenes through transition-metal-catalyzed coupling reactions (Schemes 72 and 73).[125] 2,2′-Dibromodiaryl acetylenes were transformed into the corresponding diformyl derivatives, which reacted with bisphosphonium ylide to give magazine-rack molecules

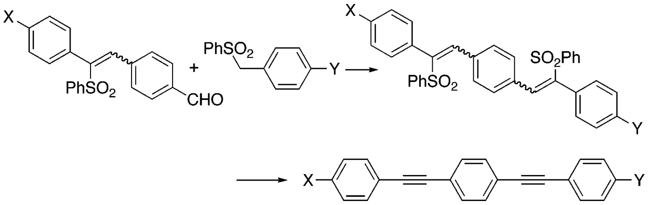
Scheme 68



Scheme 70



Scheme 71



64 (Scheme 74).[127] Treatment of this compound with $Co_2(CO)_8$ furnished **64**·$Co_2(CO)_6$ complex.[128] Functional group toleration led to the synthesis of arylene ethynylenes containing heteroaromatic rings.[129] A variety of molecular wires with thiophene, pyridine, and ferrocene subunits **65**−**76** (Chart 1) were synthesized.

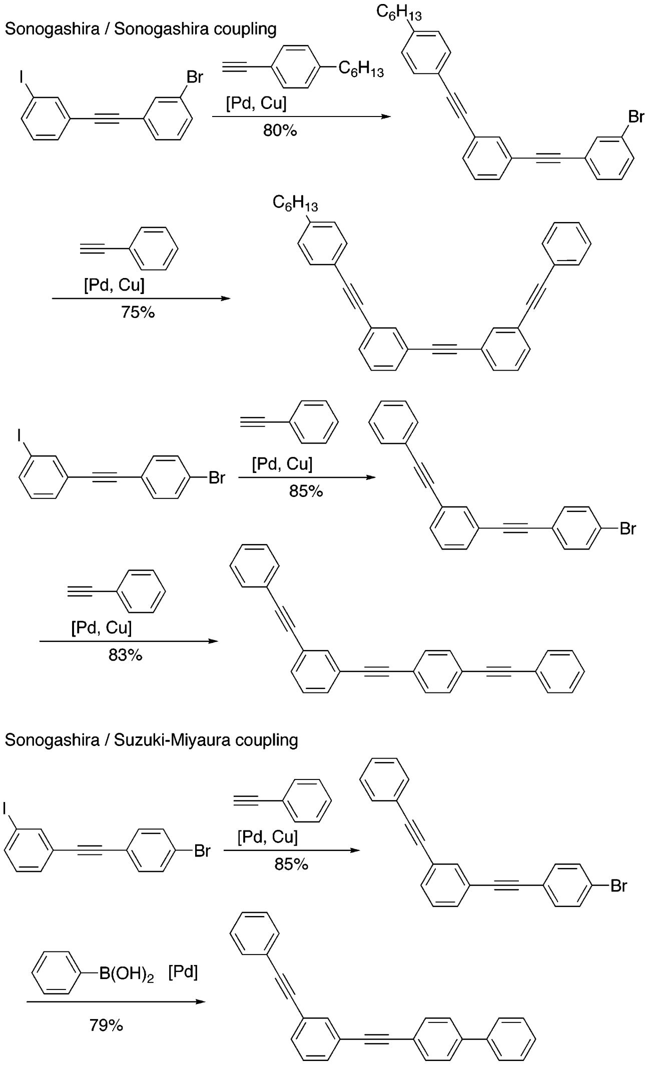
A convenient and high-yielding synthesis of octadiene−diyne **33** was realized by subjection of 2-formylbenzyl sulfone to the double-elimination reaction (Scheme 75).[130] Reaction of **33** with $Co_2(CO)_8$ afforded **33**·$Co_2(CO)_6$ complex.[131] Diels−Alder reaction of **33** with cyclopenta[*a*]-acenaphthylenone smoothly occurred to give adduct **77** (Scheme 76).[132] Gleiter et al. used **33** for the synthesis of beltene **78** (Scheme 77).[133]

In cases where phenyl sulfones react sluggishly in the double-elimination reaction, the corresponding sulfoximines can be employed. For instance, binaphthyl derivative **79** was obtained by this technology (Scheme 78).[134] This compound gave enantiopure double-helical aromatic acetylenes upon complexation with silver and copper (Scheme 79).[135] The sufoximine version was also successfully applied to the synthesis of chiral acetylenic cyclophanes (Scheme 80).[136]

3.6. From Fused Cyclic Compounds

Tobe et al. extended their cycloreversion protocol (see section 2.6) to the synthesis of cyclic aromatic acetylenes. Thus, dibenzoannulenes **80** were prepared (Scheme 81).[137] The [12]annulene, **80a**, was unstable and, hence, detected by mass spectroscopy and UV−vis as well as FTIR spectra in an argon matrix. The existence of **80a** was confirmed by trapping with furan (Scheme 82).[137a] On the other hand, [14]annulene **80b** was stable enough to be characterized by ^{1}H NMR spectroscopy.[137b] By recourse to the same technology, [12,12]paracylophanedodecaynes **81** were generated in a matrix at low temperature (Scheme 83).[138]

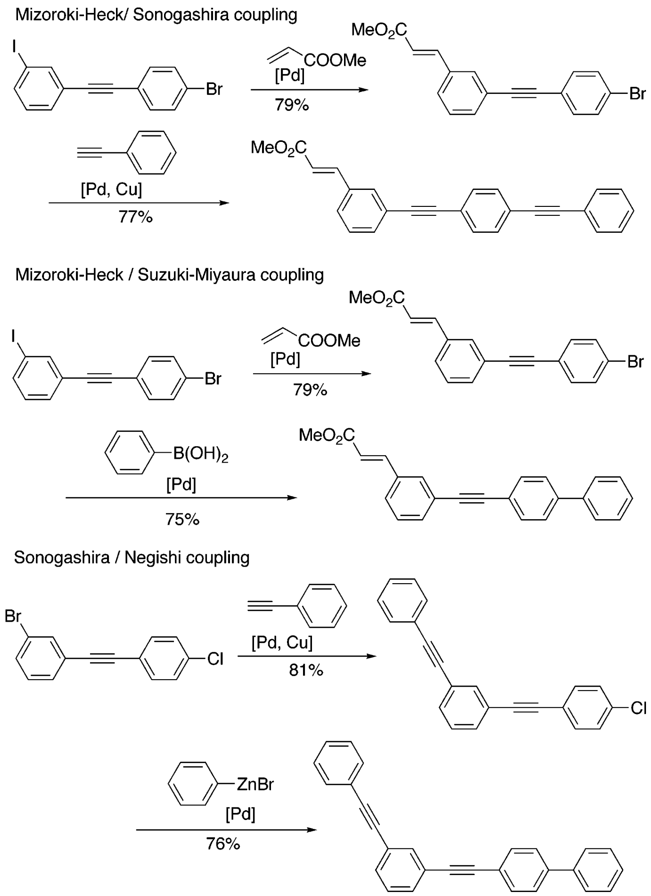
Scheme 72



Decarbonylation of cyclopropenones, which has been briefly discussed in section 2.6, was utilized for the synthesis of aromatic acetylenes. Thus, photolysis of 2-alkoxy-3-arylcyclopentenones, prepared from cyclopropenium ions, provided acetylenic ethers (Scheme 84).[139] West made use of this method for obtaining an acetylene with anthrylphenol moieties **82** (Scheme 85).[67,140] Oxidation of **82** with PbO_2 afforded quinone **83**. Acenaphthyne **84** was also synthesized through this technology (Scheme 86).[141] This highly strained acetylene underwent various derivatizations. Reaction with oxygen in a matrix gave acenaphthoquinone **85**, and warming to room temperature afforded-decacylene (**86**). Trace amounts of water trapped **84** to give acenaphthenone **87**, while reaction with methanol afforded ester **88**.

Gleiter et al. made use of the selenodiazole protocol (see section 2.6) to generate carbon−carbon triple bonds in

Scheme 73



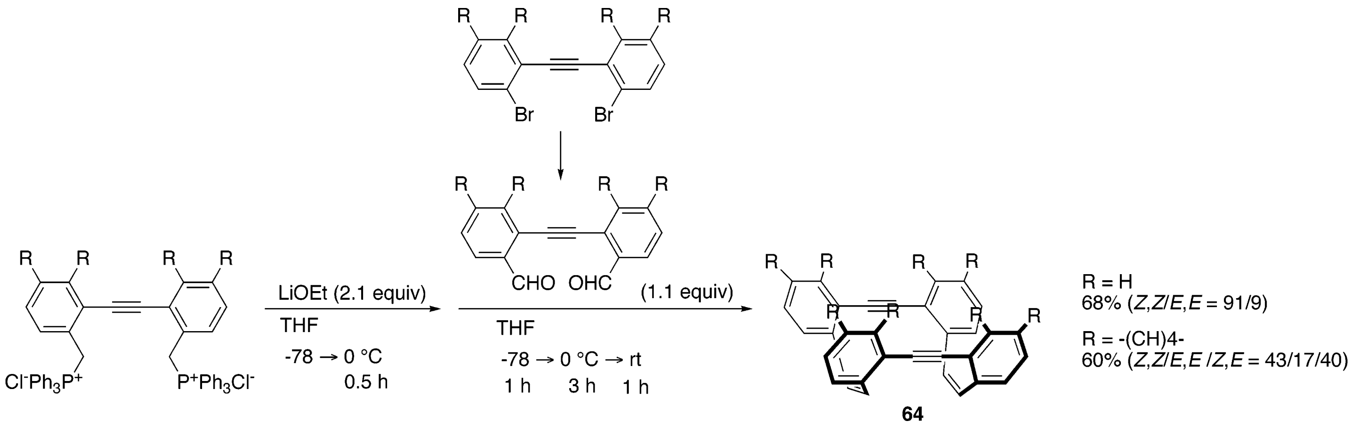
the synthesis of superphanes and beltenes. Diacetylene **89** was prepared from 5-cyclodecynol (Scheme 87).[142] Subjection of the C-11 higher homologue gave a mixture of **90** and **91** (Scheme 88). A variety of superphanes were obtained from **89** as shown in Scheme 89, whereas reaction of the mixture of **90** and **91** gave superphane **92** together with **93** and **94** (Scheme 90). Analogously, cyclopentadienone superphanes **95** and **96** were synthesized as shown in Scheme 91.[143] An extension of this technology enabled to the creation of belt-like macrocycles (beltenes).[144] The diyne precursor **97** was prepared via the selenodiazole protocol, and treatment of this compound with [RCpCo(COD)] afforded beltenes **98** and **99** (Scheme 92).

4. Conclusion

Elimination pathways are as useful as the coupling of terminal alkynes for the synthesis of aromatic acetylenes. In general, the former reactions are promoted by a base while the latter are promoted by transition-metal catalysts. The advantages of the elimination protocols are as follows: (1) the reactions can usually be carried out on a large scale, (2) the products are free from transition-metal catalyst residues, (3) the carbon−carbon bond formation between sp^2 or sp^3 carbons followed by generation of sp carbons facilitates formation of cyclic compounds, and (4) no manipulation of sometimes unstable terminal acetylenes is needed. On the other hand, the disadvantages lie in (1) the necessity for a somewhat large amount of base and thus (2) no tolerance for base-sensitive functional groups. Moreover, elimination reactions are essentially not atom economical.

As is apparent from the examples in section 3, only a limited number of the elimination reactions among the many possibilities given in section 2 can be actually employed for the synthesis of complex aromatic acetylenes due to the lack of general applicability under diverse conditions. Hence, further invention of elimination reactions that are really practical is highly desirable.

Scheme 74



Scheme 75

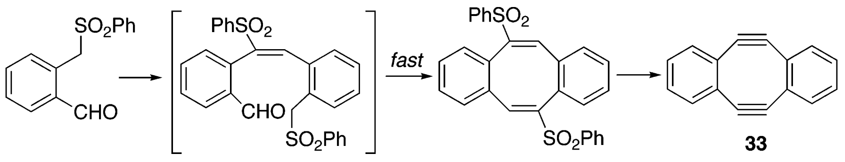
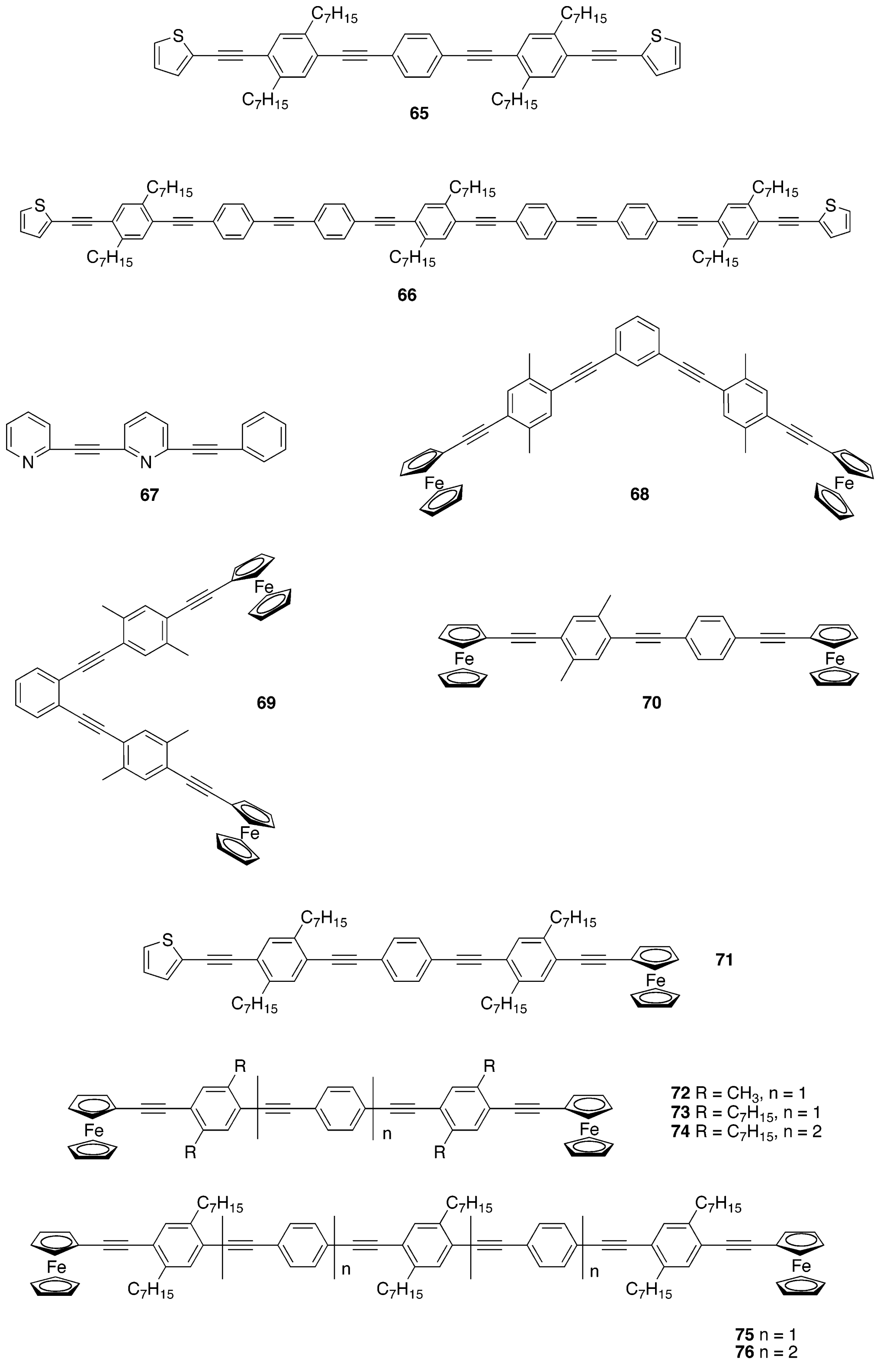
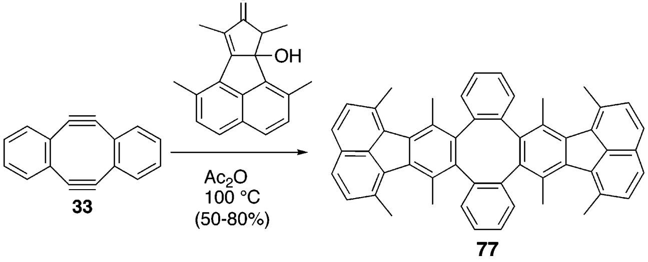


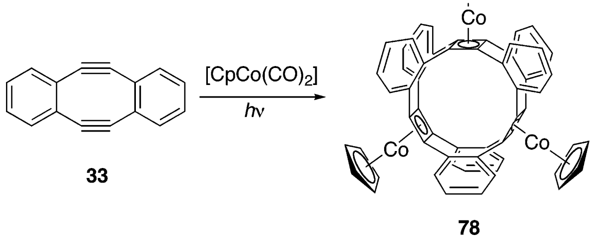
Chart 1



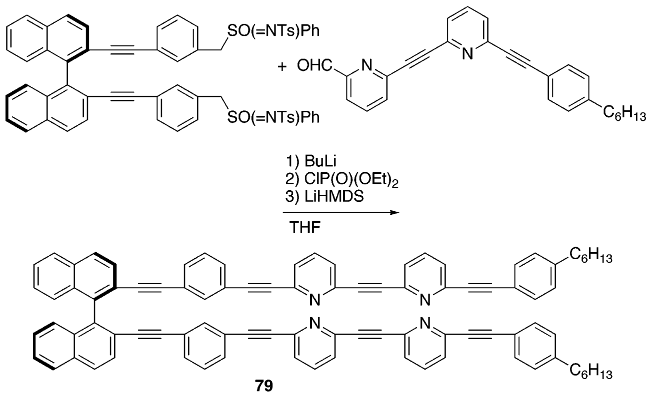
Scheme 76



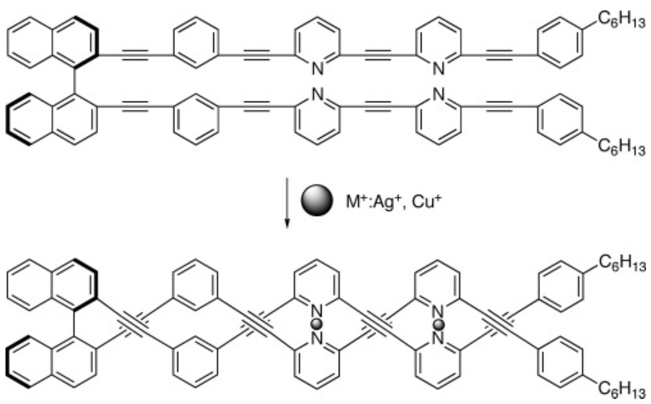
Scheme 77



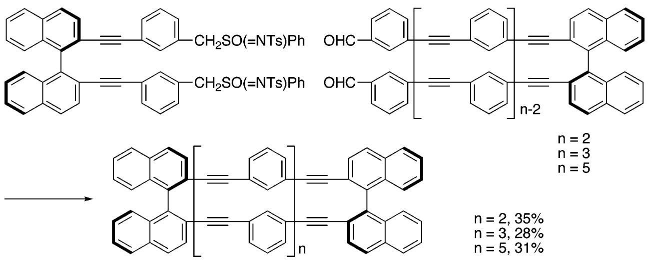
Scheme 78



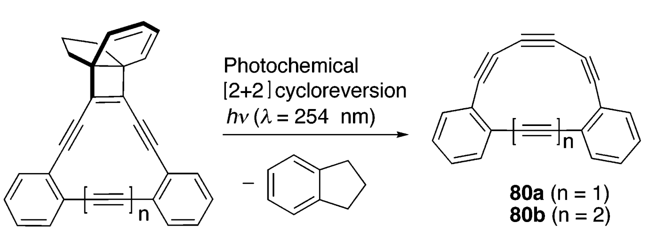
Scheme 79



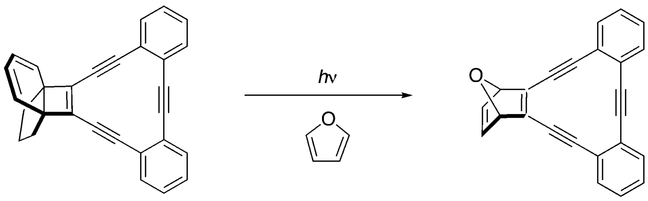
Scheme 80



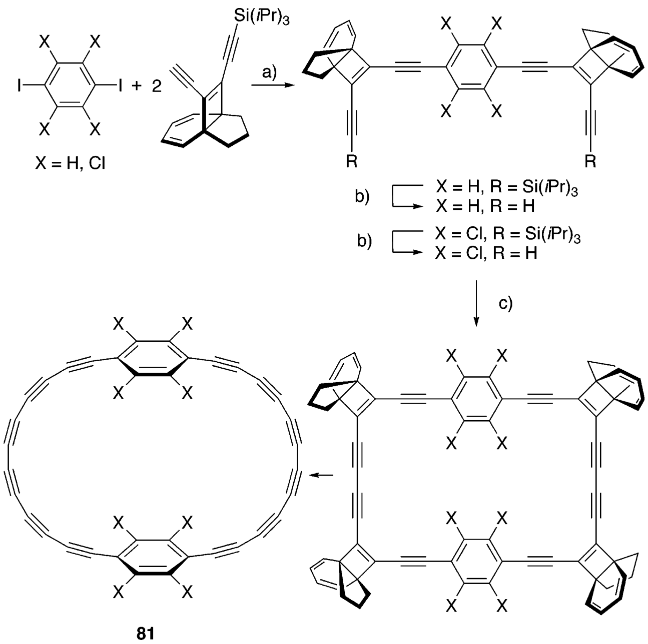
Scheme 81



Scheme 82

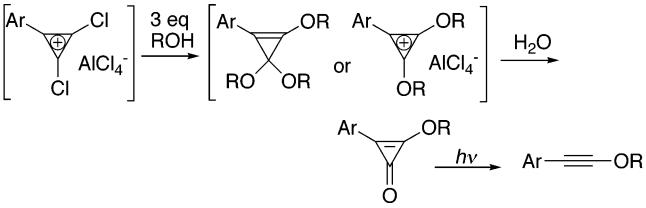


Scheme 83[a]

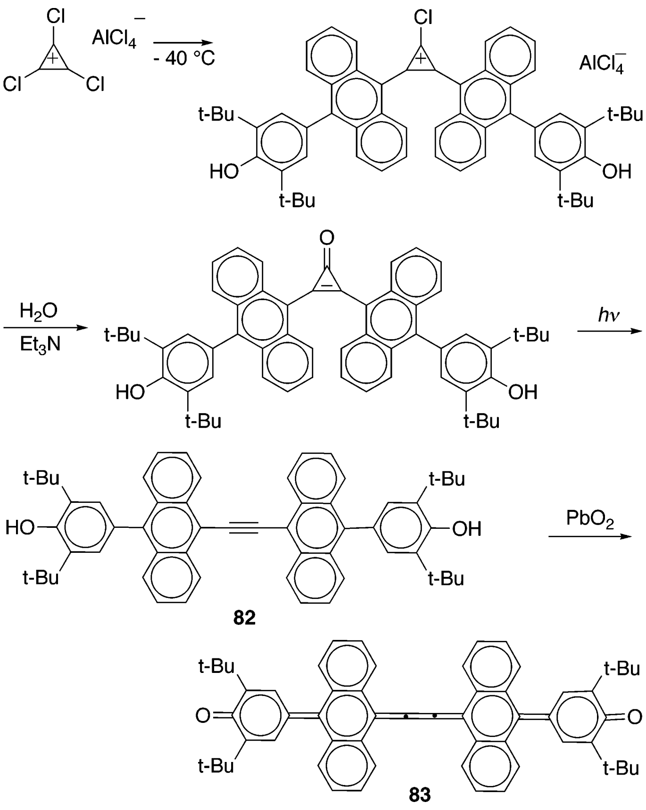


[a] Reaction conditions: (a) For X = H, [Pd(PPh$_3$)$_4$], CuI, (^{i}Pr)$_2$NH, THF, RT, 93%. For X = Cl, [Pd$_2$(dba)$_3$]·CHCl$_3$, CuI, PPh$_3$, Et$_3$N, 90 °C, 65%. (b) Bu$_4$NF, AcOH, THF, RT. (c) Cu(OAc)$_2$, pyridine, RT, 79% for X = H, 75% for X = Cl. dba = *trans*,*trans*-dibenzylideneacetone.

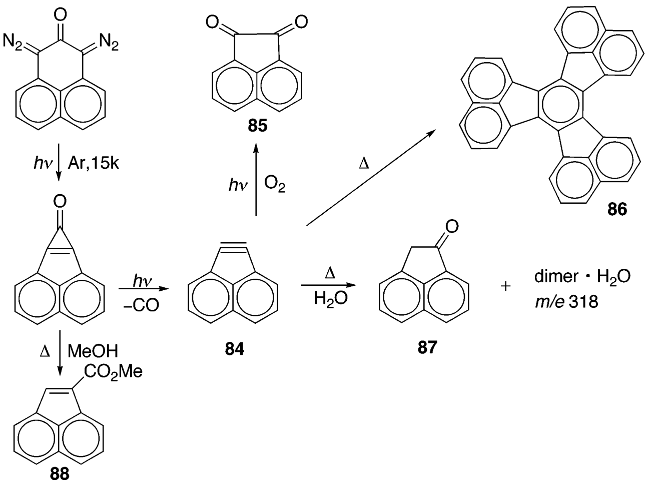
Scheme 84



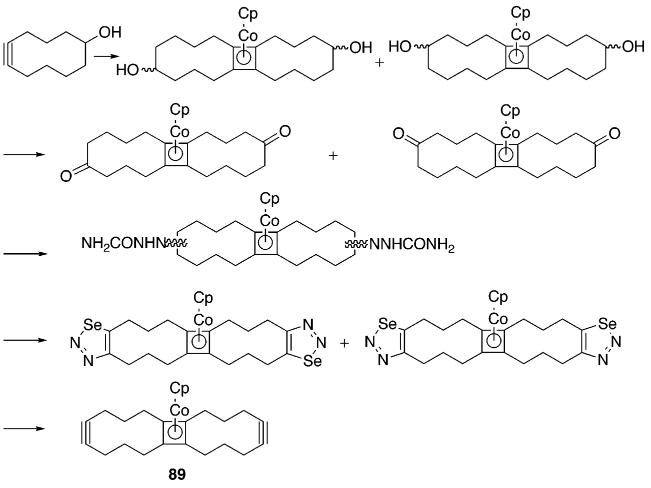
Scheme 85



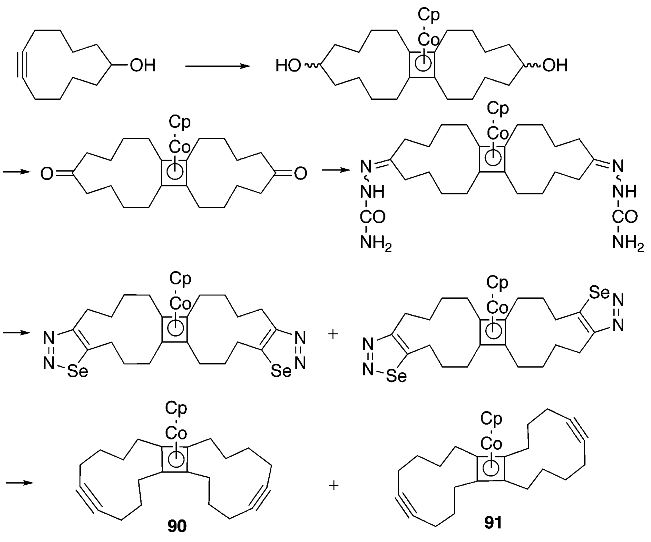
Scheme 86



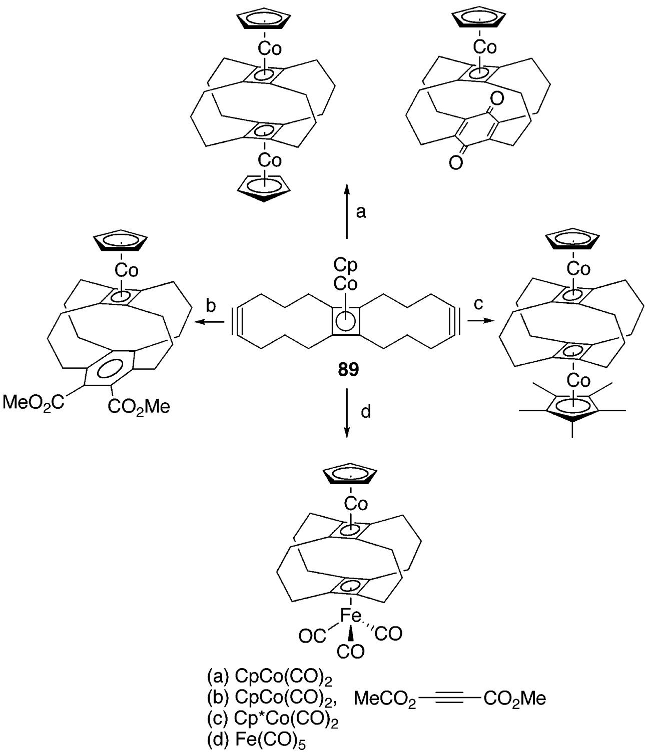
Scheme 87



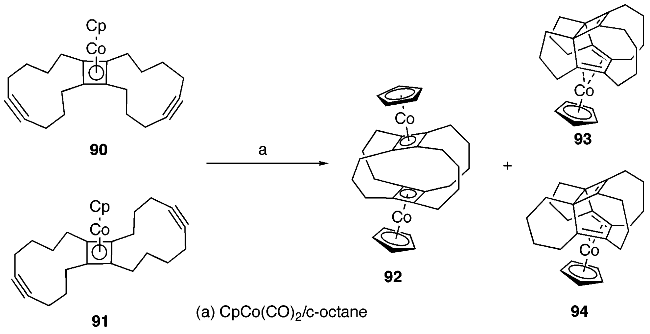
Scheme 88



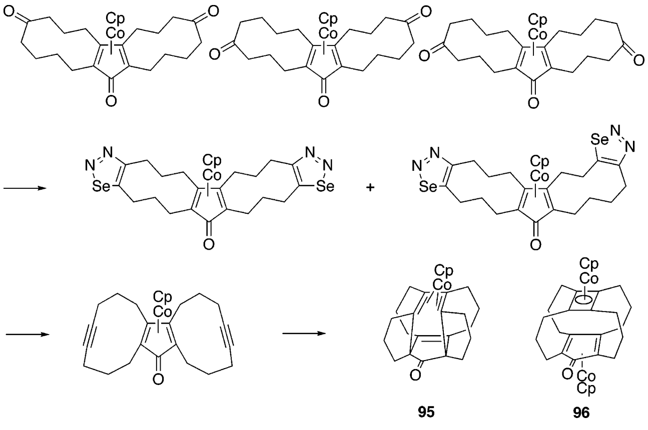
Scheme 89



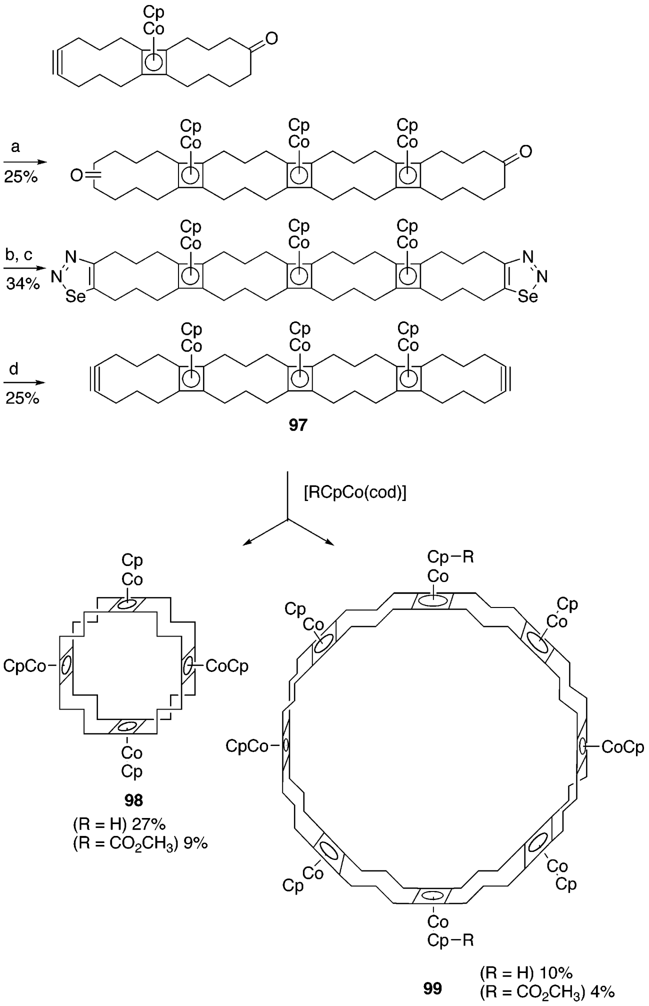
Scheme 90



Scheme 91



Scheme 92[a]



[a] Reaction conditions: (a) [CpCo(cod)], Decalin, 170 °C, 1 day. (b) semicarbazide acetate, EtOH, 90 °C, 4 h. (c) SeO$_2$, HOAc, 40 °C, 6 h. (d) Cu, 190 °C, 30 min.

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