7.3

Transition Metal Alkyne Complexes: Transition Metal-catalyzed Cyclotrimerization

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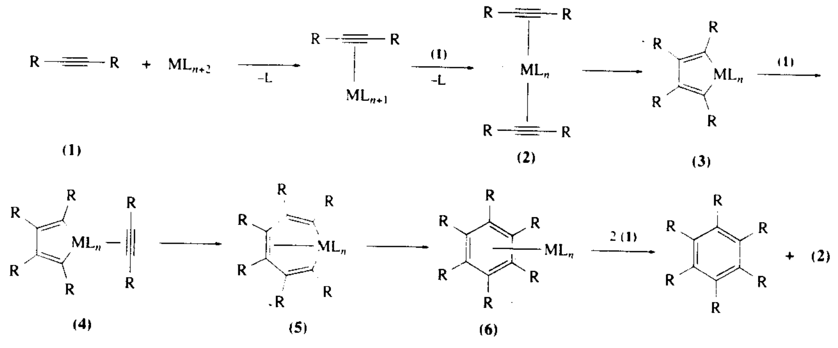
7.3.1 INTRODUCTION

The π-system of alkynes reacts readily with both organic[1] and organometallic reagents. This chapter covers oligomerizations of alkynes mediated by transition metals, focusing on reactions leading to carbo- and heterocycles containing between four and eight atoms. Organization is by product type, starting in Section 7.3.3 with acyclic oligomers and cyclic products featuring rings of four, five, and eight atoms. Subsequent sections discuss planar, aromatic carbo- and heterocycles from alkynes and nitriles or cumulenes, progressing to cyclohexadienes, and finishing with more saturated product types. Literature through the middle of 1993, with an emphasis on the period since 1980, is covered.[2]

7.3.2 MECHANISTIC OVERVIEW

The most common cyclooligomerization product of alkynes in the presence of transition metals is an arene. Ethyne trimerization by a symmetry-allowed [2 + 2 + 2] cycloaddition involving 6π electrons is calculated to be an extremely exothermic process, as indicated by values of $\Delta H^\circ = -594$ kJ mol^{-1},[3] yet entropic considerations preclude practical trimerization. However, it is clear that a metal may act as a template for the formation of arenes, by sequentially binding alkynes and acting as a channel through which electrons flow between ligands. Although debate about the cyclotrimerization mechanism continues,[4–5] this topic will be introduced using what Schore in his excellent review[6a] of metal-mediated alkyne cycloadditions calls the "common mechanism" (Scheme 1).



Scheme 1

A metal complex ML$_{n+2}$ is thought to sequentially bind two alkynes (**1**), giving (**2**). An ensuing redox reaction would lead to (**3**), which might relieve its coordinative unsaturation by coordinating a third alkyne, to give (**4**). In the conversion of (**2**) to (**3**), the alkynes have been reduced with concomitant carbon–carbon bond formation, and the metal has lost two electrons, a change which may explain chemoselectivity in some reactions. The complexed alkyne in (**4**) may insert, affording metallacycloheptatriene (**5**), followed by reductive elimination to arene complex (**6**). Decomplexation by two alkynes would produce arene and (**2**), completing a catalytic cycle.

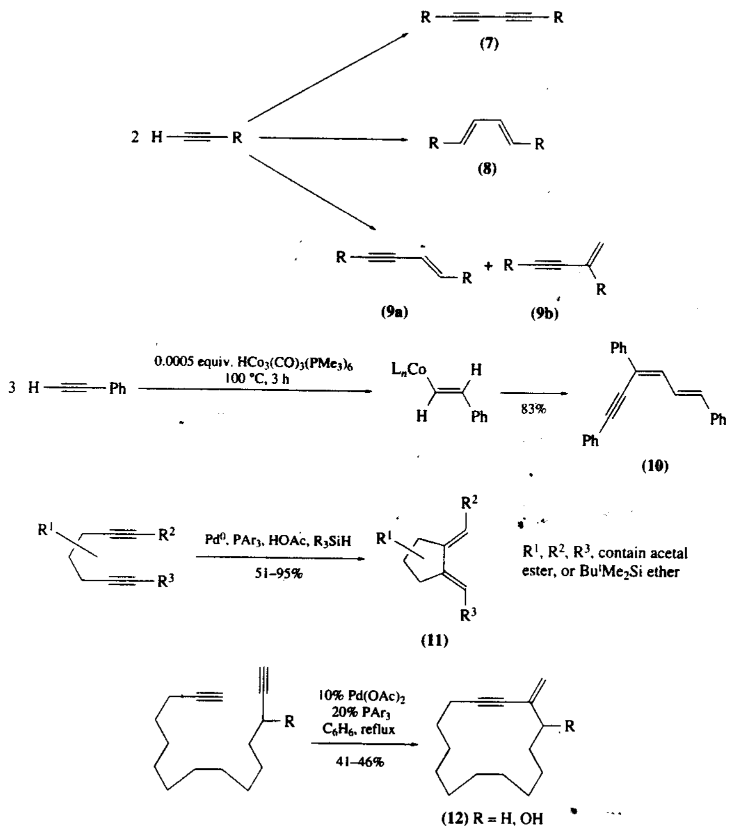
With the exception of (**4**),[7] species (**1**)–(**6**) have all been isolated for a wide variety of metal fragments and alkynes, yet for a *single* combination of fragment and alkyne they have not *all* been isolated, or even detected by kinetic or spectrometric means. Alternative mechanisms are discussed elsewhere,[3–5] but mention will be made here that a coordinatively saturated version of (**3**) [ML$_n$ = CoCp(PR$_3$)] reacted with dimethyl butynedioate *without* prior loss of PR$_3$, suggesting a Diels–Alder-like cycloaddition between the cobaltacyclopentadiene and the third alkyne.[8]

From unsymmetrical cycloaddition partners, regioselective metallacycle formation, to be discussed below, leads to controlled synthesis of highly substituted, unsymmetrical arenes. Unsaturated functions other than alkynes may participate in Scheme 1, filling the palette of products described in following sections.

7.3.3 OLIGOMERIZATION PRODUCTS CONTAINING OTHER THAN SIX ATOMS IN THE NEWLY FORMED RING

7.3.3.1 Linear Oligomers: 1,3-Enynes and Related Diynes and Dienes

Oligomerization of alkynes in the presence of metals can produce a variety of nonarene rings, containing four, five, seven, or eight atoms, as well as linear structures. Linear oligomerization, a facile process for alkenes,[9–10] is rare for alkynes, as indicated by the paucity of examples in earlier reviews.[2,5] Scheme 2 illustrates known linear alkyne dimerization products obtained through oxidation (**7**),[11] reduction (**8**),[12] and metal hydride addition/elimination (**9**).[13] A hydridic tricobalt cluster recently was found to selectively produce trimer (**10**).[14] Elegant conversions of α,ω-diynes to 1,3-dienes or 1,3-enynes are shown by structures (**11**) and (**12**).[15–16] Another route from alkynes to 1,3-dienes will be discussed below, in connection with metallacyclopentadienes. In the absence of preformed metal hydrides[14] or alkyne metathesis catalysts,[17] however, linear oligomerization occurs as a significant side reaction only with terminal alkynes, a process thought to be initiated by metal hydrides which could be formed by addition of the terminal C–H bond to the metal.[5]

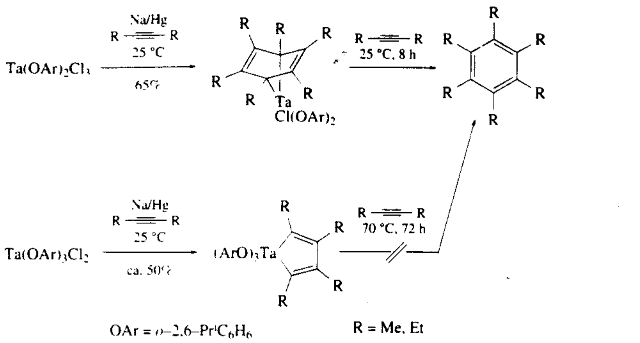


Scheme 2

7.3.3.2 Metallacyclopentadienes Leading to Five-membered Rings

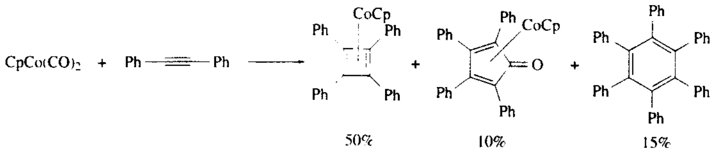
Cyclic products derived from only two alkynes include metallacyclopentadienes, cyclobutadiene complexes, cyclopentadienone complexes, and quinone derivatives, the latter two species arising from incorporation of one and two moles of carbon monoxide, respectively. (Quinones will be considered in Section 7.3.5.) These lower cyclooligomers may predominate over trimers and higher homologues if further alkyne incorporation is disfavored, usually by steric hindrance at the metal, as seen in comparing Equations (1) and (2)[18] or by large alkyne subtituents (Equations (3) and (4)).[19–20]

Metallacyclopentadienes[21] are usually not isolated as side products from alkyne trimerizations and related reactions. Their isolation requires either modifying the reaction conditions (for example, in the case of CpCo, in the presence of phosphine ligands which compete with alkyne[22]) or, more conveniently, by using early transition metal reagents.[23] With appropriate care, stepwise construction of metallacyclopentadienes from two different alkynes is possible (Equation (5)).[23c] In general, unsymmetrical alkynes appear to be incorporated with regioselectivity based on emergence of the larger[22] or more electron-withdrawing[24] substituents α to the metal. However, isomerization of initially

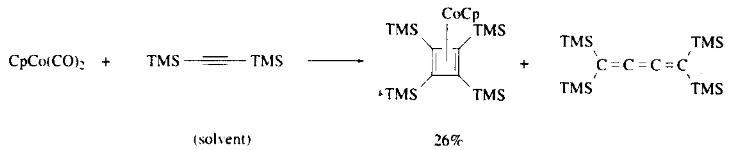


(1)

(2)

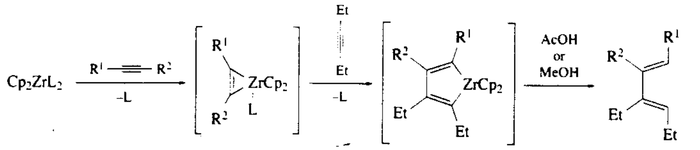


(3)



(4)

isolated (kinetic) products to thermodynamic regioisomers has been observed.[4b] In the case of Equation (5), precoordination of the SMe function to zirconium was suggested to explain the appearance of SMe α to the metal. Tethering of two alkynes enforces regioselectivity. Zirconium- and cobalt-based reagents, those most frequently encountered, are complementary, in that the former tolerate alkyl halides, whereas the latter tolerate C=O functionality. Metallacyclopentadienes may be intercepted by a number of reagents (Table 1). Most notably, Cp_2Zr metallacycles, apparently incompetent in trimerization reactions, are exceedingly versatile in the production of heterocycles[23a,b,25] and 1,3-dienes[23b,c] of defined substitution and geometry. Redox coupling of two alkynes, followed by cleavage of metal–carbon bonds compares favorably with other methods for the regio- and stereoselective synthesis of 1,3-dienes.[26a]

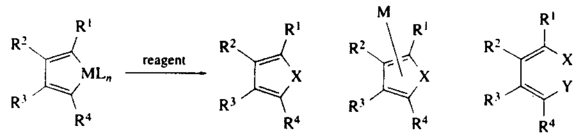


(5)

R^1 = TMS, $R^2 = C_6H_{13}$, 52%
R^1 = SMe, $R^2 = (CH_2)_2OSiR_3$, 63%

Cyclopentadienone complexes may be obtained not only by carbonylation of isolated metallacyclopentadienes (Table 1), but directly from intermolecular reaction of two alkynes and metal carbonyls (Scheme 3); quinone derivatives may also be formed in these reactions. Synthetically useful yields of the former are obtained from two alkynes bearing large[34–5] or polar, electron-withdrawing substituents,[36–40] using iron carbonyls and heat,[35–9,40b] or $CpCo(CO)_2$ and light at low temperatures.[34,40a] Intramolecular cyclizations of α,ω-diynes are relatively efficient,[34,41–2] producing both $Fe(CO)_3$ and CpCo complexes of even terminal alkynes. Cyclization to (**16a,b**) showed modest asymmetric induction; moreover, in (**16c**) the presence of the metal fragment directed nucleophilic attack on the carbonyl function from the face *exo* to the metal fragment.[42] Liberation of the cyclopentadienone ligand from its complexes is successful in some cases, usually from compounds bearing large or electron-withdrawing substituents, but in other cases the metal is difficult to remove[42] or the cyclopentadienone suffers further reactions.[41] Demetallation of the $Fe(CO)_3$ complexes is accomplished with trimethylamine-*N*-oxide, whereas CpCo-complexes require removal of electrons either electrochemically[40c] or using metal salts.[34a] Elaborations of the cyclopentadienone ligand, either in a free or complexed state, leading to novel cyclopentanoids, is a topic of continued interest.[3,41–2] Hindered aryl isonitriles react with α,ω-diynes in the presence of nickel catalysts, giving free ligands (**17**) and (**18**).[43] Similar reactions using nickel or cobalt reagents lead to free cyclopentadienone imines or their CpCo complexes.[44] Reaction of alkynes and TMS-CN, acting as a source of TMS-NC, leads to a N–TMS analogue of (**17**) under nickel catalysis,[45] but to 2-cyano-5-aminopyrroles with other catalysts.[46]

Table 1 Selected transformations of metallacyclopentadienes.



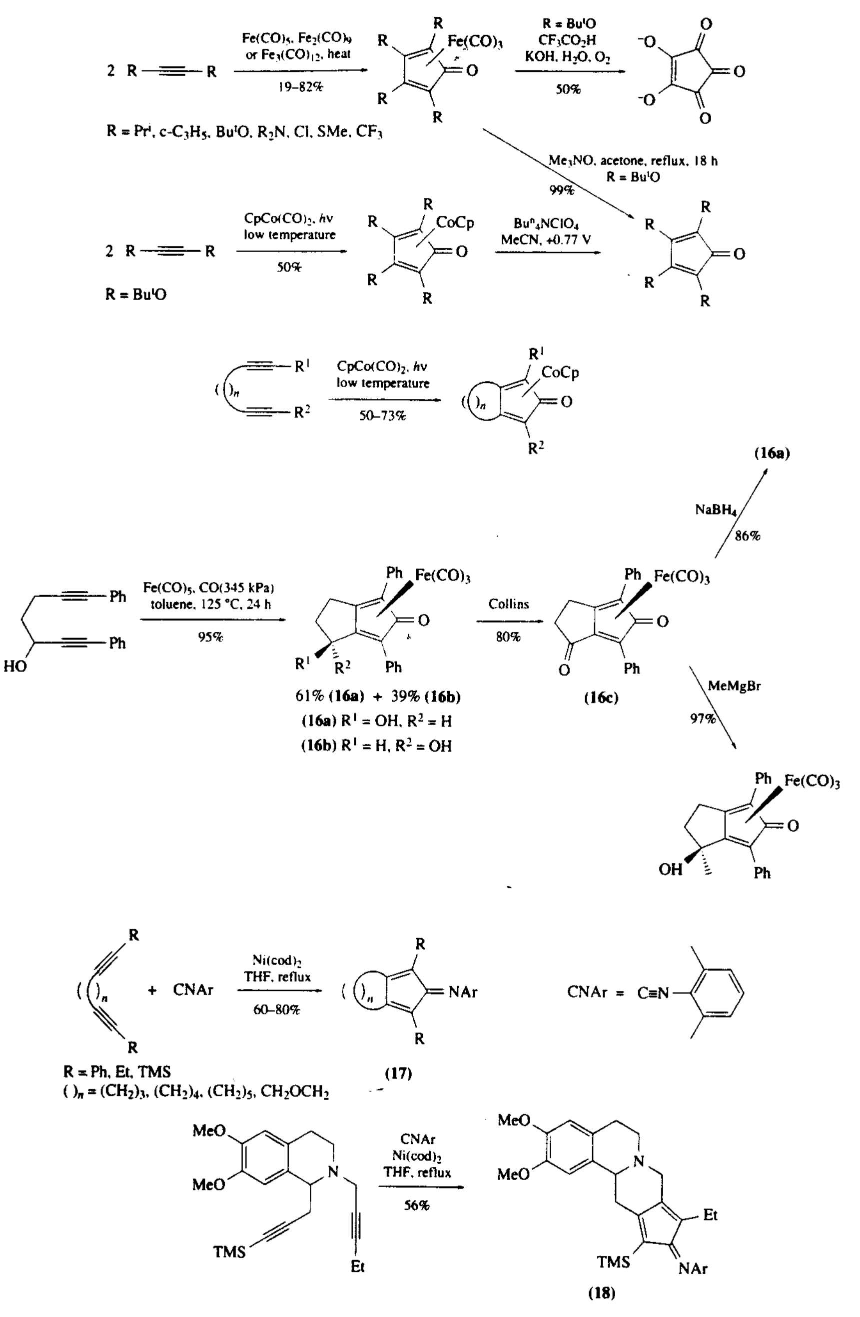
(**13**) (**14**) (**15**)

ML_n	*R¹–R⁴*	*Reagent*	*Product*	*Reference*
$CoCp(PR_3)$	alkyl, aryl	PhNO	(**13**), X = PhN (35%)	27
$CoCp(PR_3)$	Ph, CO_2Me	S	(**13**), X = S (76%)	27
Cp_2Zr	alkyl	$PhSbBr_2$	(**13**), X = PhSb (≥85%)	25
		$PhBiBr_2$	(**13**), X = PhBi (95%)	
		$BiBr_3$,	(**13**), X = BiBr (44%)	
		$RPCl_2$ or $RAsCl_2$	(**13**), X = RP (85%)	
			(**13**), X = RAs (76%)	23f
$Rh(PPh_3)_2Cl$	Ph, alkyl, acyl	O_2 or H_2O_2 S_8, Se	(**13**), X = O, S, Se (13–82%)	28
$CoCp(PPh_3)$	Ph	N_2CHCO_2Et	(**14**), X = $CHCO_2Et$, M = CpCo (39–77%)	29
$CoCp(PR_3)$	alkyl, aryl	CO	(**14**), X = CO, M = CpCo	30
$CoCp(PPh_3)$	Ph	BH_2Cl	(**14**), X = BH, M = CpCo	31
$CoCp(PR_3)$	Ph	pyrrole	(**15**), X = H, Y = pyrrolyl	32
$Co(py)_n$[a]	Ph	H_2	(**15**), X = Y = H (100%)	33
Cp_2Zr	alkyl, aryl, R_3SiO–alkyl	HOAc or MeOH	(**15**), X = Y = H (45–81%)	23b, 23c
	TMS, MeS	I_2	(**15**), X = Y = I (53–86%)	23b

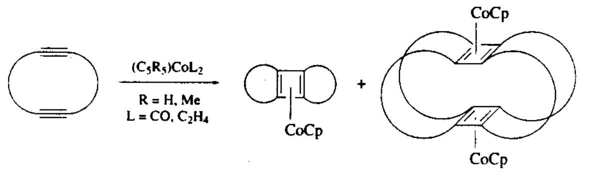
[a] Metallacycle not isolated.

7.3.3.3 Cyclobutadienes and their Complexes

Metal–cyclobutadiene complexes are accessible from alkyne dimerization in the presence of a variety of metals.[47] Their formation as side products in arene synthesis may deplete catalyst; in cyclohexadiene synthesis, they may be significant by-products (see Section 7.3.7). Liberation of the unstable, antiaromatic ligand by oxidation and its trapping (e.g., in Diels, Alder reactions) has proven to be practical in the case of $Fe(CO)_3$ complexes, but not others. Unfortunately, the requisite $Fe(CO)_3$ complexes are not major products from the reaction of alkynes and iron carbonyls. The complexes are accessible from alkynes by a three-step procedure, using $AlCl_3$, followed by $Fe_2(CO)_9$.[48] Winter's review discusses the relationship between cyclobutadiene complexes and other intermediates and products of alkyne cyclooligomerization.[5] In a classic study, trimerization of CD_3CCMe with several metal systems did not give products with three contiguous CD_3 substituents, ruling out product formation through an intermediate with the symmetry of a metal–cyclobutadiene complex.[49] Recently, however, arenes and pyridines were produced in 7–50% yields from reaction of alkynes and nitriles at 200 °C with unusual tricyclic CpCo-cyclobutadiene complexes,[50a] not a generalizable result, but the first use of CpCo–cyclobutadiene complexes in [2 + 2 + 2] cycloadditions. The chemistry of cyclic diynes and $CpCoL_2$ derivatives (Equation (6)) has been explored.[50b] Data from thermolysis of CpCo–cyclobutadiene complexes do not permit distinction between possible formation of a $CpCo(alkyne)_2$ species or a cobaltacyclopentadiene which is not planar, but configurationally stable.[51]



Scheme 3



(6)

7.3.3.4 Cyclooctatetraenes

Synthetically useful yields of cyclooctatetraenes are obtained using certain nickel catalysts. Yields vary greatly, a particular matching of substrate and ligands on nickel being required for each case, particularly to avoid competitive cyclotrimerization. As noted by Jolly,[52] tetramerization appears to be favored by use of poorly ligated Ni^0 species, particularly nickel atoms, or, more recently, by Ni^0–diimine complexes.[53] Derivatives of prop-2-yn-1-ol exhibit a pronounced tendency toward tetramerization.[53–4] Unusual solvent or concentration effects have been noted:[54a] with a given nickel catalyst, prop-2-yn-1-ol itself is converted to tetramer in the absence of solvent, or using butanol, but dilution with THF and addition of PPh$_3$ is reported to lead mainly to trimer. Positional selectivity with prop-2-yn-ol derivatives is possible,[53] but there is no rationale for the observed selectivity. Many of the nickel systems summarized by Jolly lead to trimerization; cocyclizations of α,ω-diynes and a third alkyne give arenes[55] in a reaction whose success is influenced by the nature and position of oxygenated substituents. Although the precise mechanism of cyclotetramerization is still in debate,[56] a growing body of evidence suggests that binuclear nickel complexes are responsible.[53a,57–8]

7.3.4 ARENES FROM CYCLOADDITION OF THREE ALKYNES

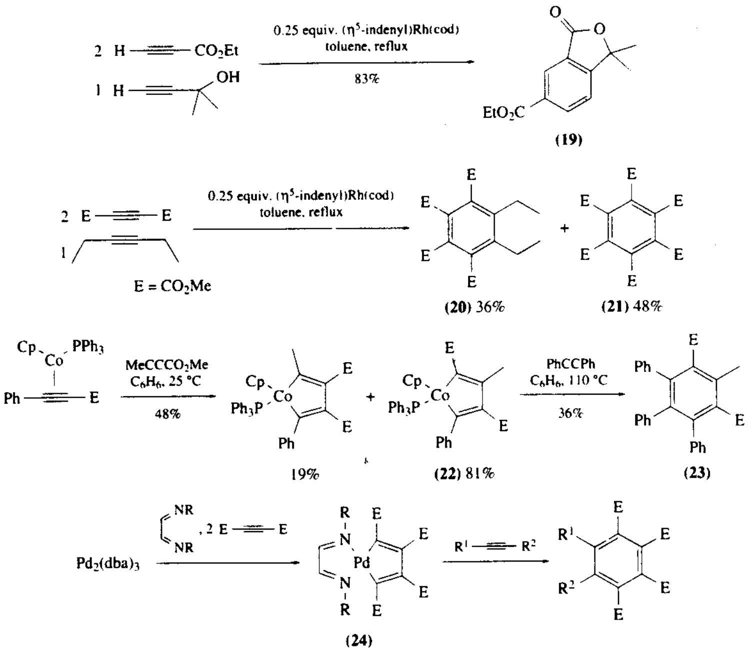
7.3.4.1 From Three Monoalkynes

Arene formation[26b,59] will be introduced by discussing intermolecular alkyne homotrimerization. Attempts to cotrimerize monoalkynes A and B tend to produce mixtures of arenes derived from 3A, 2A + B, A + 2B, and 3B, a problem solved to a great degree by tethering of at least two alkynes and using a third bulky alkyne which does not undergo self-condensation. Using this partially intramolecular variant, or a completely intramolecular one, polycyclic products are formed in a single step.

Many metal systems catalyze arene production; some systems[4,18] have provided mechanistic insight, but the emphasis here will be on the usefulness of nickel, palladium, cobalt, rhodium, and niobium catalysts, which conveniently provide arenes in good yields.[6]

Perhaps the most convenient trimerization of symmetrical internal alkynes to hexasubstituted arenes uses an unknown catalyst derived from a mixture from TMS-Cl and Pd/C; other methods are reviewed in the paper by Jhingan and Maier.[60a] Yields are quantitative, but functional group tolerance remains unexplored. Derivatives of 2-butyne-1,4-diol and the corresponding diamine, however, are cyclotrimerized using Ni^0 catalysts.[60b] Terminal alkynes can give rise to 1,2,4- and 1,3,5-trisubstituted benzenes. The effect of catalyst and alkyne on regioselectivity has been discussed.[6] The TMS-Cl/Pd/C system is relatively unselective with Bu^{t}CCH, producing 1,2,4- and 1,3,5-tris-Bu^t-benzenes in a ratio of 4 to 3, but remarkably Pr^{n}CCMe afforded exclusively the 1,2,4-(Pr^n)$_3$-substitution pattern in a yield of 90%. The relationship of this system to previously characterized alkyne oligomerizations on PdCl$_2$ complexes (which follow a distinctly different mechanism than in Scheme 1, starting with addition of a Pd–Cl bond to an alkyne)[61] is not clear. The dinuclear complex Co$_2$(CO)$_8$ trimerizes both unsymmetrical and internal and terminal alkynes with high 1,2,4-selectivity, apparently following a binuclear mechanism at variance with Scheme 1.[62] CpCo(CO)$_2$ survives supercritical water at 374 °C to trimerize 1-hexyne and phenylethyne with 1,2,4-selectivity.[63] Especially with terminal alkynes featuring electron-withdrawing groups, nickel catalysts bearing CO and phosphine ligands exhibit high 1,2,4-selectivity. Phenylethyne can be converted to 1,2,4-triphenylbenzene in a yield of 90% using (CO)$_2$Ni[P(OPr^i)$_3$]$_2$.[64a] By contrast, [(η^3-allyl)NiCl]$_2$ and (Bu$_3$P)$_2$NiBr$_2$ produce mainly 1,3,5-trialkylbenzenes.[64b] Ziegler–Natta-type catalysts also give mostly 1,3,5-products, and tolerate chloroalkane functions;[6] a reduced niobium catalyst gives mainly 1,3,5-triphenylbenzene from phenylethyne, but is unselective with other terminal alkynes.[65]

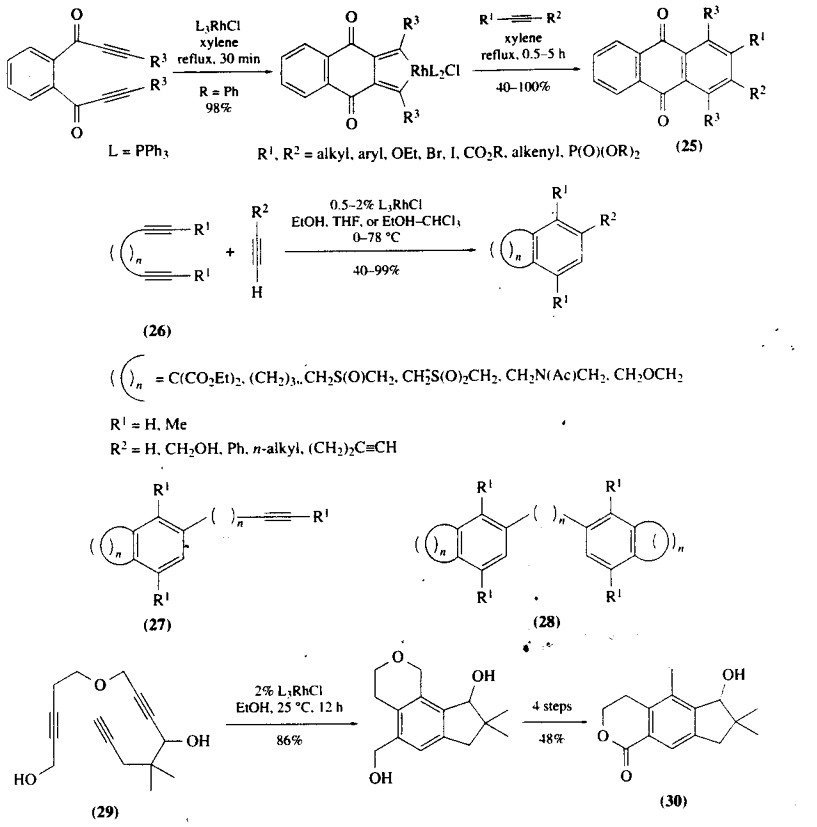
Selective cotrimerization between alkynes of different steric or electronic character is possible in some cases, as in the synthesis of (**19**) (Scheme 4), but a more typical result is the mixture of cotrimer (**20**) and homotrimer (**21**).[66] Other approaches rely on arresting cotrimerization at intermediate stages using appropriate reaction conditions, (**22–24**).[27,67] Homotrimerization often interferes, a result ascribed[6a] to the catalytic activity of the metal fragments released after benzene formation.



Scheme 4

7.3.4.2 Partially and Totally Intramolecular Reactions Leading to Benzocyclobutenes and other Polycycles

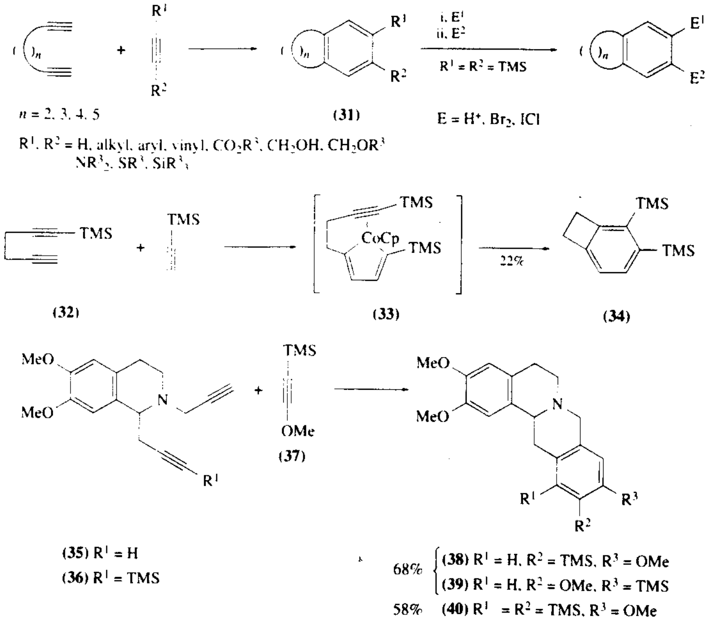
Partially intermolecular cyclizations of diynes with monoalkynes were first developed synthetically by Müller, who built rhodacyclopentadienes from Wilkinson's catalyst and α,ω-diphenyl- and dialkyl diynes in nonpolar solvents and added a wide variety of monoalkynes, producing the anthraquinone skeleton (**25**) (Scheme 5).[28] Other transformations of rhodacyclopentadienes are listed in Table 1. The requirement of a stoichiometric quantity of rhodium makes this methodology ever more costly, but recently Grigg and co-workers have found that the use of polar solvents permits trimerizations to be catalytic in rhodium.[68] These reactions work for 1,6-diynes (**26**) only, and succeed because monoalkynes are not trimerized under the reaction conditions, an unusual characteristic of the system. The monoyne must be terminal and unhindered, otherwise diyne dimer (**27**) and trimer (**28**) are isolated. An advantage of the method is that even ethyne itself is readily incorporated. Thioether or secondary amine functionality in the diyne leads to low yields, presumably because of interfering coordination to the metal. In contrast, CpCoL$_2$ (*vide infra*) as well as Ni^0 systems tolerate amine[60b,69] and oxygen[55] functionality. For ClRh(PPh$_3$)$_3$, the requirement of a polar solvent suggested that ionization of the Rh–Cl bond is responsible for the enhanced reactivity. A RhCl$_3$–R$_4$NCl system trimerizes alkynes and diynes under phase-transfer conditions.[70] Triyne (**29**) underwent completely intramolecular cyclization as a key step in total synthesis of calomelanolactone (**30**) and related Pterosin Z, in which one of the tethers necessary for the cyclotrimerization is later broken.[71]



Scheme 5

The most extensively developed system for partially or completely intramolecular trimerizations is based on CpCoL$_2$, developed by Vollhardt and co-workers, as described in an extensive overview,[3] a review with emphasis on heterocycles,[72] and one covering theoretically interesting arenes.[73] After observing the production of strained benzocyclobutenes from homotrimerization of 1,5-hexadiyne,[74] Vollhardt found that cotrimerization of diynes with monoalkynes using CpCo(CO)$_2$ as catalyst gave (**31**), a reaction that works best for $n = 3$ and 4, poorly for $n = 5$ (Scheme 6). Its success for $n = 2$ makes the reaction a versatile synthesis of benzocyclobutenes, strained systems capable of undergoing further cycloaddition reactions, *vide infra*. Yields with most terminal and internal monoalkynes are moderate, the presence of one or two trimethylsilyl groups affording higher yields because of reduced propensity for the monoalkyne to self-condense.[75] Bis(trimethylsilyl)ethyne (btmse) is resistant to dimer- or trimerization (Equation (4)), but readily cotrimerizes with diynes. In general, highest yields are obtained by adding a solution of diyne and CpCo(CO)$_2$ in btmse slowly to refluxing btmse (b.p. 133 °C), using a slide projector lamp to encourage loss of CO.[76] The TMS groups which emerge on the newly formed arene ring in (**31**) are amenable to further manipulations. Relief of strain between adjacent TMS substituents allows sequential *ipso*-directed electrophilic substitution or isomerization. Trimethylsilyl-substituted arenes are available from reduction/silylation or metallation/silylation of arenes, but such congested examples are not available by these routes. Bis(trimethylstannyl)ethyne leads to arenes bearing even more reactive Me$_3$Sn groups, a useful tactic in cases where electrophilic aromatic substitution of TMS groups is slow.[77-9] Trialkylsilyl substituents on unsymmetrical diynes and monoynes allow regioselective cotrimerizations. For example, (**32**) and trimethylsilylethyne combine to give (**34**) as a single isomer, a result ascribed to the sterically[22] and electronically[23] preferred appearance of the

TMS group α to cobalt in **(33)**. Similarly, **(35)** and **(37)**[80] combine to give equal amounts of protoberberines **(38)** and **(39)**, whereas only isomer **(40)** is formed from **(36)**.

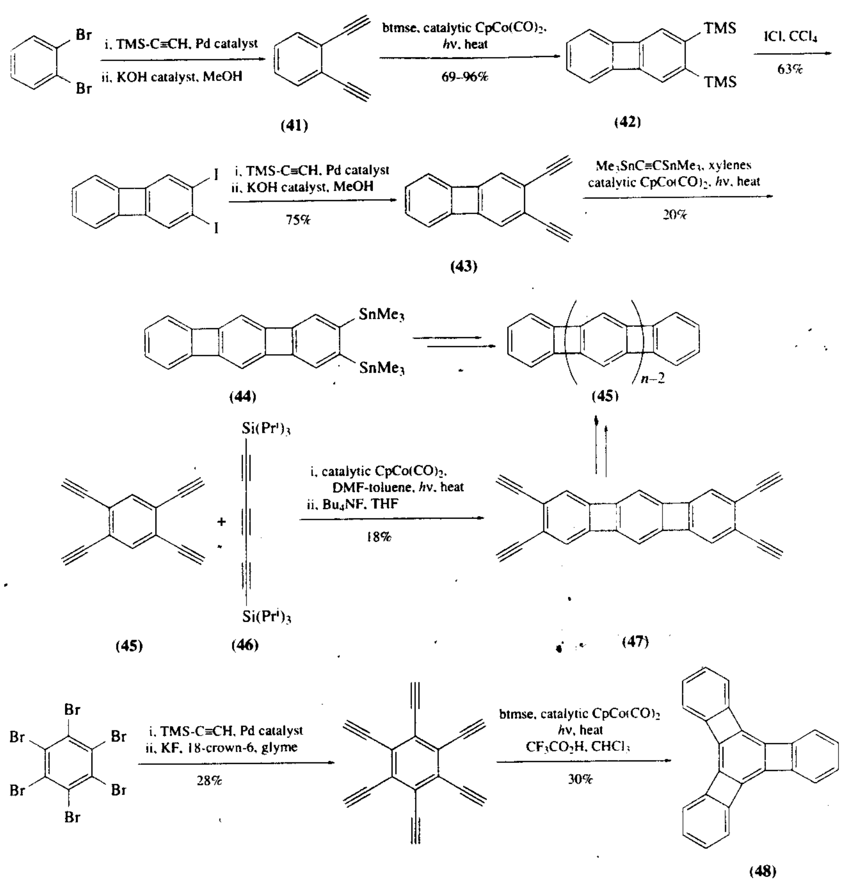


Scheme 6

The juxtaposition of benzene and cyclobutadiene π-systems in benzocyclobutadiene derivatives has allowed chemists to study the concepts of aromaticity and antiaromaticity. Catalysis by CpCo(CO)$_2$ has been crucial to development of iterative routes to extended benzocyclobutadienes.[73] 1,2-Diethynylbenzene **(41)** combines with btmse to give **(42)**, a bis(trimethylsilyl)[2]phenylene, which can be iododesilylated, ethynylated, and protiodesilylated to give a new 1,2-diethynylarene **(43)**, for a repetition of the cycle (Scheme 7). However, the unusual reactivity of the π-system in the bis(trimethylsilyl) analogue of [3]phenylene **(44)** caused halogens to react not by substitution, but by addition and ring-cleavage reactions.[77,81] The heightened reactivity of C–Sn bonds in **(44)** directed *ipso* electrophilic substitution to predominate over other reactions, enabling the synthesis of **(45)**. Triyne derivative **(46)** is sufficiently hindered at the outer triple bonds so as to cotrimerize regioselectively, allowing rapid, bidirectional elaboration to **(47)**.[78] Angular derivatives of **(45)** up to $N = 5$ have been made.[82] Hexabromobenzene serves as starting point for **(48)**, whose central six-membered ring resembles the hypothetical 1,3,5-cyclohexatriene in its reactivity[83] and metrical parameters.[84]

The observation that benzocyclobutenes open to *o*-xylylenes which act as 4π components with alkenes and other dienophiles prompted a total synthesis of estrone, using CpCo-catalyzed [2 + 2 + 2] cycloaddition of **(49)** and btmse to **(50)**, followed by reaction at higher temperatures to **(51)** (Scheme 8). Control experiments showed that the metal was not involved in the conversion of **(50)** to **(51)**. Selective protiodesilylation and oxidative functionalization furnished racemic estrone **(52)**.[85] An oxime function acted as dienophile in a similar reaction.[85] Totally intramolecular cyclotrimerization to a benzocyclobutene, followed by Diels–Alder cycloaddition with a pendant alkene led to an unusual B-ring aromatic steroid in a single operation from an acyclic precursor.[86] The basic skeleton of tetracyclic diterpenes phyllocladane and kaurane was assembled using a combination of palladium-catalyzed [3 + 2], cobalt-catalyzed [2 + 2 + 2], and thermal [4 + 2] cycloadditions. The diastereoselectivity of the latter process being strongly influenced by the use of acetal **(53)** or the corresponding ketone, which led to the deprotected analogue of **(54)** with only 58:42 selectivity.[87]

Early transition metal catalysts have been much less studied from a synthetic standpoint, an exception being CpNbCl$_3$/Mg, which allows efficient cocyclization of α,ω-diynes containing carbamate or ester functions with terminal alkynes, notably TMS-C≡CH.[65]

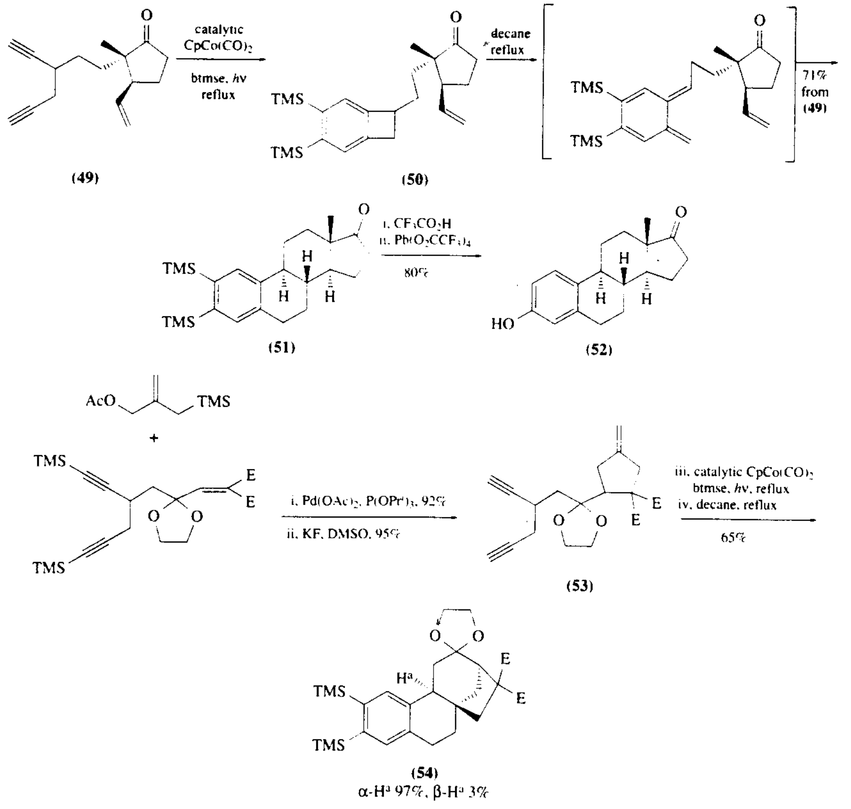


Scheme 7

Although arenes were long known to be formed from alkynes and palladium(II) complexes,[61] use of this chemistry in organic synthesis has been scarce until recently.[88–90] Putative intermediates of type **(57)** have been generated either by addition of Pd–H to the alkyne function of **(55)**, or by oxidative addition of Pd^0 to the C–Br bond in **(56)** Scheme 9. The addition of Pd–H to **(55)** is reminiscent of the addition of Pd–Cl to alkynes, the initial step in alkyne trimerization by PdCl$_2$.[61] Ring closure of **(58)** to **(59)** might occur by an intramolecular Heck reaction or by an electrocyclic pathway, followed by β-hydride elimination.[88] Cyclohexadienes (which may be aromatized to arenes[91]) have been formed in related reactions (see Section 7.3.7). Multiple insertions of alkynes into Pd–C bonds can lead to benzannulation of heterocycles, exemplified by conversion of **(60)** to **(61)**.[92]

7.3.5 QUINONES AND HYDROQUINONES

Quinones and their metal complexes were first isolated among the many products of the reaction of metal carbonyls and alkynes. Industrial development of metal-catalyzed reactions of ethyne, CO, and water using high pressures and temperatures has produced hydroquinone in up to 70% yield.[93] A putative intermediate in this chemistry is maleoyl complex **(62)**. However, a general laboratory-scale synthesis of complicated quinone derivatives from alkynes was not possible until Liebeskind and co-

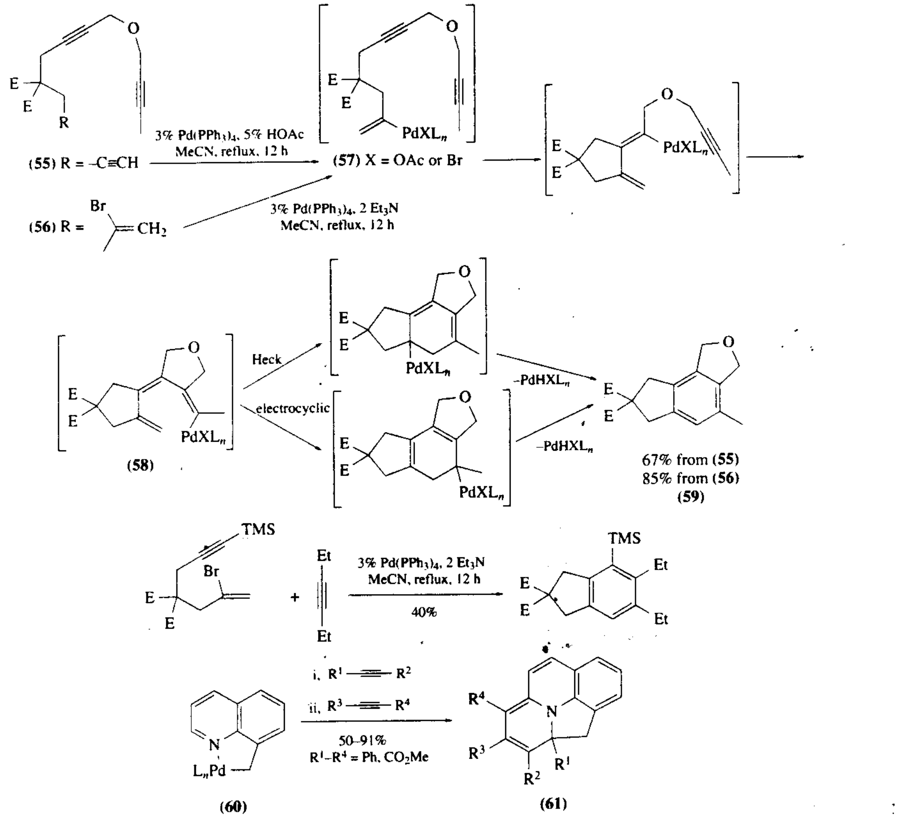


Scheme 8

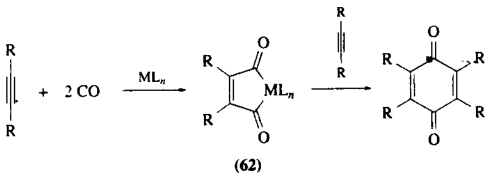
workers found a controllable, alternative route to structures of type (**62**) and phthaloyl analogues (Equation (7)).[94]

Benzocyclobutenedione (**63**) and ClCo(PPh$_3$)$_3$ combine to give air- and moisture stable (**64**), which is unreactive with alkynes until treatment with silver(I) salts (Scheme 10). A less expensive activation of (**64**) occurred after equatorial chelation by dimethylglyoxime and labile, axial ligation by pyridine in (**65**). Subsequent reaction with terminal, internal, and heteroatom-functionalized alkynes produced naphthoquinones (**66**). The influence of R on regiochemistry of unsymmetrical alkyne incorporation was not studied in this system, but tethering of an alkyne to (**63**) (R = OH) gave (**67**), allowing a completely regioselective cyclization to (**68**), an intermediate in the synthesis of nanaomycin A (**69**).

Extension of this chemistry to unsymmetrical cyclobutenediones and alkynes (Scheme 11) did not require tethering, but studies to improve regioselectivity[95–6] (3:1 to 20:1) revealed the beneficial effect of Lewis acids, presumed to aid in chloride ionization or to polarize alkynes bearing carbonyl-containing substituents. The observed preferences for alkyne incorporation into (**71**) were rationalized by invoking both the inductive effect of MeO on the nearby C=O carbon and the resonance effect of MeO on the more distant C=O carbon (Scheme 11). Although phenyl- and diphenylcyclobutenediones are available from phenyl- and diphenylethyne, CO, and Ni(bipy)(CO)$_2$,[97] cyclobutenediones are more generally synthesized from the inexpensive squaric acid. In the course of extensive studies on derivatization of squaric acid,[98] thermal rearrangement of vinylcyclobutenols (**73**), followed by oxidation, emerged as a superior route to quinones and hydroquinones, in part because addition of (**72**) to (**70**) occurs with far higher regioselectivity than reaction of the corresponding alkyne with (**71**). Cyclobutenones (**74**) react with alkynes under Ni(cod)$_2$ catalysis to give phenols (Scheme 12); regioselectivity is poor for unsymmetrical alkynes, but a wide variety of substituents are tolerated.[99]



Scheme 9

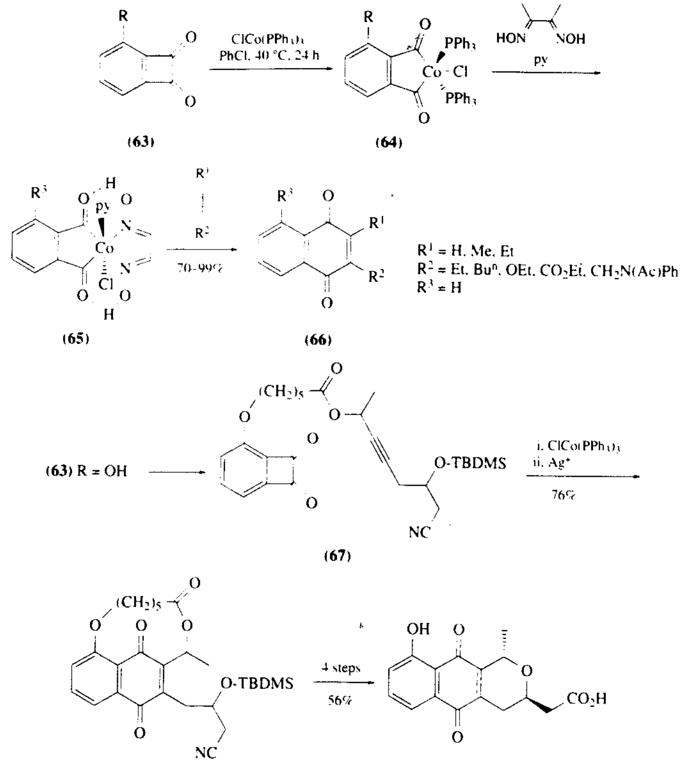


(7)

7.3.6 HETEROARENES

7.3.6.1 Pyridines, Triazenes, and Pyrazines

Of the numerous approaches to the pyridine nucleus,[100] transition metal catalyzed cotrimerization of two alkynes and one nitrile is a method of commerical[93] and synthetic importance. Most catalysts competent in alkyne cyclotrimerization are capable of producing pyridines, and the mechanistic considerations advanced above apply here. However, successful pyridine synthesis demands selectivity for combination of alkyne and nitrile in a ratio of 2:1, over the other three possibilities of 3:0, 1:2, and

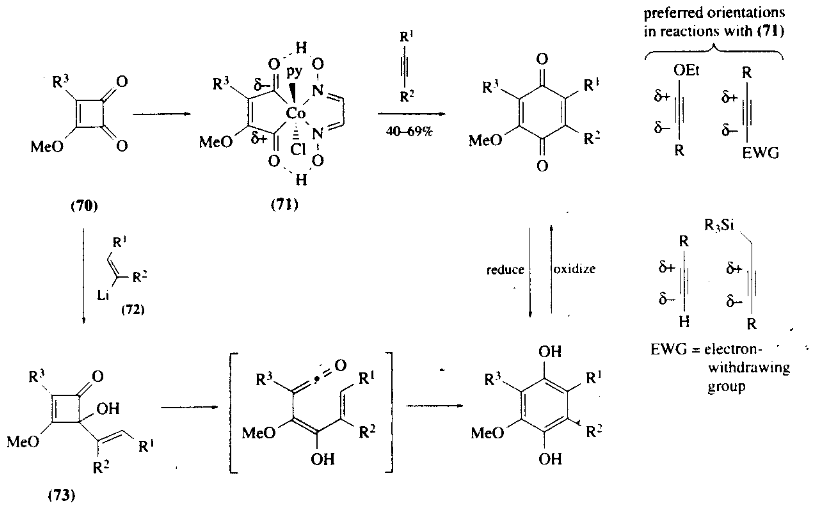


Scheme 10

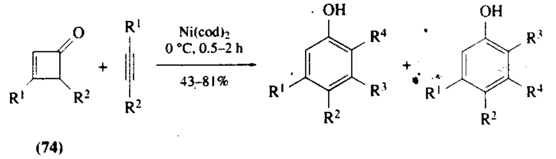
0:3. Furthermore, unsymmetrical alkynes could give rise to regioisomeric heterocycles. Fortunately, compared to alkynes, nitriles show a reduced propensity to trimerize in the presence of metals, although 1,2,4-triazene formation is possible in some cases (Equation (8)).[101] Thus, pyridine synthesis on late transition metals is generally accepted to begin by redox coupling of two alkynes[23a,23e,102] (illustrated in Scheme 13 for two terminal alkynes), raising the oxidation number of the metal center by two, and favoring subsequent complexation to a nitrile rather than an alkyne (**77, 78**). Nitrile insertion with bonding of nitrogen to the metal, followed by reductive elimination of pyridine and coordination of two alkynes to the metal would complete a catalytic cycle. The rate of pyridine formation is independent of nitrile concentration; the amount of alkyne homotrimerization may be kept low by using an excess of nitrile, when practical.

The reduction of this scheme to practice began with Wakatsuki, Yamazaki and co-workers[102] but was refined substantially by Bönnemann and co-workers.[103] Using ethyne and excesses of nitrile, 2-substituted pyridines (**79**) are available using CpCo(cod) or other more exotic sources of cobalt(I) (Scheme 14). Reaction of HCN and ethyne produces pyridine itself. Pyridine-2-carbonitrile reacts with ethyne to afford the chelating ligand bipy in 95% yield. Bipyridines bearing chiral substituents in the 2-position, of potential interest in chiral catalyst design, have been made from chiral nitriles.[104] 2-Thiomethyl- and 2-dialkylaminopyridines are also accessible, albeit in lower yield; nitriles with electron-withdrawing groups do not react.

Symmetrical internal alkynes give pentasubstituted pyridines in high yields. However, from terminal alkynes, 2,4,6- and 2,3,6- trisubstituted products usually are formed in comparable amounts. The reaction of substituted cobaltacyclopentadienes with a nitrile is regiospecific, retaining the substitution pattern of the metallacycle.[102] Thus, in contrast to results from alkyne trimerization, it appears that

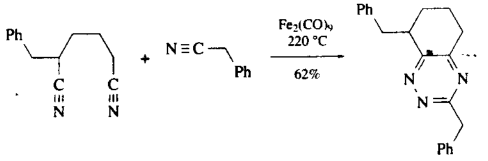


Scheme 11



R¹ = Bu, Ph, SnBu₃
R² = H, Me
R³ = Et, Me
R⁴ = Prⁱ, TMS, (CH₂)₂Cl, (CH₂)₂O-TBDMS, CH₂CH=CH₂

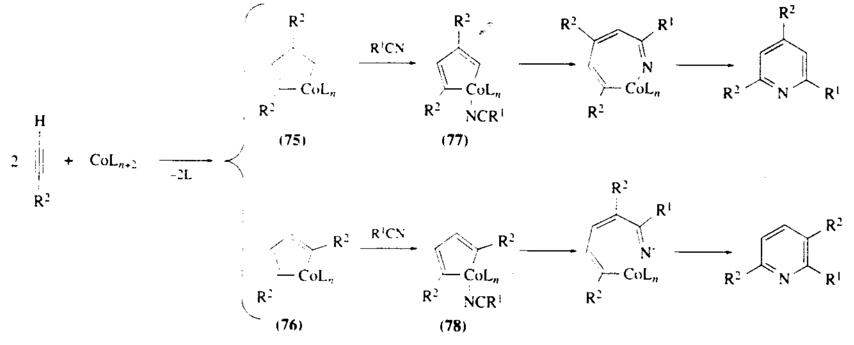
Scheme 12



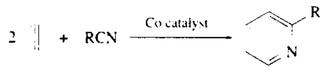
(8)

not tolerated: $NCCH_2CO_2Et$, $NCCH_2OCH_2Ph$, $NC(CH_2)_nCN$ (n = 1,2,3)

formation of a 2,4-disubstituted metallacycle (**75**) and its further reaction with nitrile is competitive with formation and reaction of a 2,5-disubstituted metallacycle (**76**). Bönnemann's group has examined a series of catalysts by physicochemical methods, including ^{59}Co NMR, to understand the relationships between catalysts, properties and performance. The lower the electron density on the catalyst, the higher the catalyic activity, and the lower the ratio of 2,4,6- to 2,3,6-trisubstituted product. The larger the ligands on the metal, the higher the amount of 2,4,6- trisubstituted pyridine, but at the cost of severely attenuated activity. Steric repulsions between alkyne substituents and large ligands on the metal may explain favored formation of a 2,4-disubstituted metallacyclopentadiene. Mono- or 1,2-bis(trimethylsilyl)cyclopentadienyl and η^6-borinato ligands gave the best pyridine/benzene chemo- and regioselectivity with reasonable activity.[103,105] The analogous rhodium systems have shown similar or reduced selectivities and yields,[106a] with the exception of the bulky, electron-rich complex $(C_5H_4NMe_2)Rh(C_2H_4)_2$,[106c] which gives ≥90% 2,4,6-isomer. The $ClRh(PPh_3)_3$/EtOH catalyst system

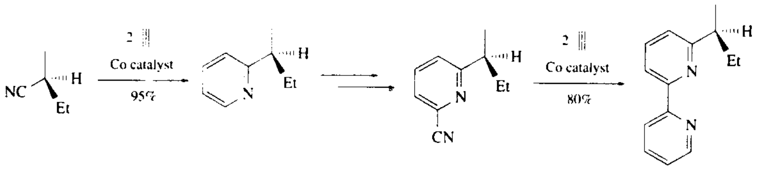


Scheme 13



R = H, alkyl, cyclopropyl, CH=CH$_2$, thien-2-yl
Ph, hydroxyaryl, chloroaryl, aminoaryl

(79)



Scheme 14

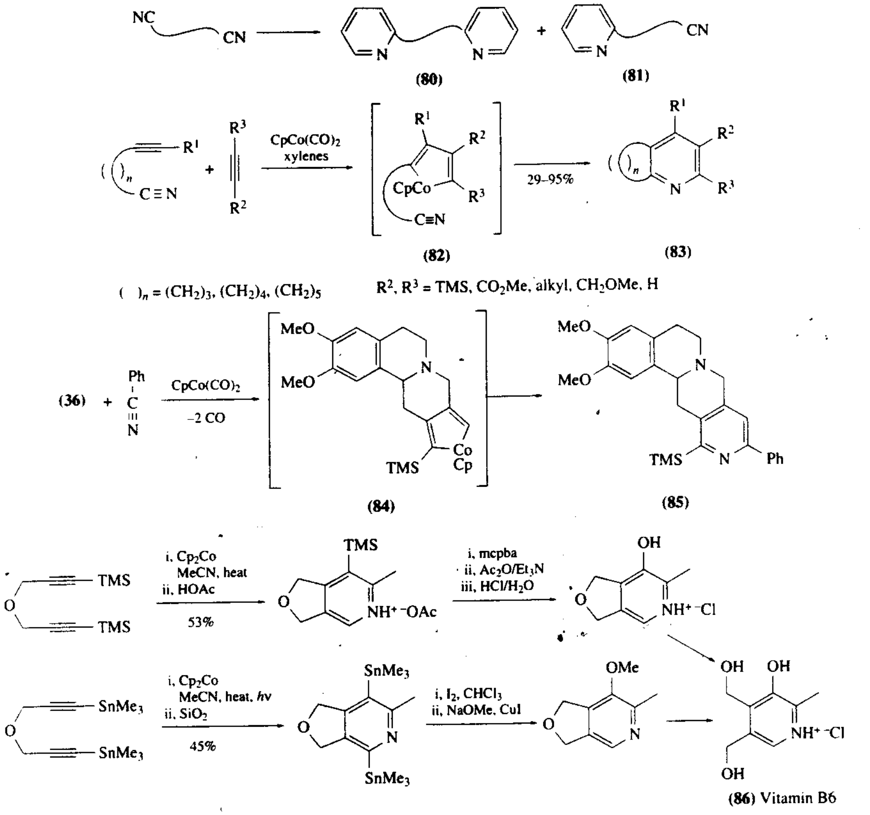
shows no tendency toward pyridine formation, preferring to react with the C=C double bond of acrylonitrile.[107] Cobalt atoms are active catalysts at room temperature, and show some interesting selectivity in partially intramolecular reactions.[108b]

As is the case in alkyne trimerizations, tethering of two partners can improve selectivity, as well as providing an entry into bicyclic derivatives. With the cobalt systems α,ω-dinitriles do not react intramolecularly (Scheme 15), but give either α,ω-di-2-pyridylalkanes (**80**) or 2-(ω-cyanoalkyl)pyridines (**81**).[103b] However, α,ω-cyanoalkynes and sterically or electronically biased monoalkynes produce (**83**) with regioselectivities explainable by putative intermediate (**82**).[109] This reaction is envisaged to be the basis of a lysergic acid synthesis.[73] α,ω-Diynes also react to give bicyclic pyridines in good yields, unless the nitrile RCN bears a strongly electron-withdrawing group R = C_6F_5 or CO_2Et.[110] The highly regioselective formation of (**85**) may arise from preferential nitrile insertion into the least hindered Co–C bond of (**84**).[80] Two approaches to vitamin B6 (**86**) had as their key step cyclization of a bis(propynyl) ether and acetonitrile, the ether linkage being broken after pyridine formation.[79,111] Activation of the pyridine nucleus to substitution was achieved through the use of Me_3Sn groups or with a combination of TMS and *N*-oxide functions.

Pyrazines are produced from four molecules of nitrile, using reduced titanium reagents.[112] Trimethylsilyl cyanide reacts with two alkynes as its isomeric isocyanide, to give pyrroles[46] or cyclopentadieneone imines,[44-5] rather than pyridine derivatives.

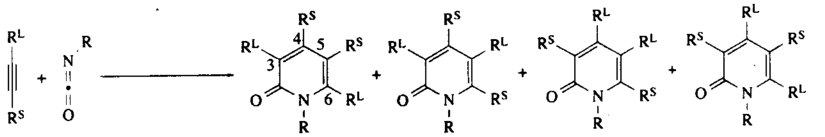
7.3.6.2 Pyridones and Iminodihydropyridines

Both Co^{I} and Ni^{0} species catalyze the transformation of two alkynes and an isocyanate to the pyridone nucleus, but assembly of the components occurs in a different order. The cobalt systems appear to follow Scheme 1, redox coupling of two alkynes being followed by insertion of isocyanate into a Co–C bond of a cobaltacyclopentadiene.[113] Thus, cocyclization of propyne and phenylisocyanate



Scheme 15

catalyzed by CpCo(ethene)$_2$ gives exclusively 3,6-dimethyl-1-phenylpyridone (Scheme 16),[114] presumably by way of the favored 2,5-dimethylcobaltacyclopentadiene. Homotrimerization of propyne occurs extensively in this system. Two other examples of cobalt catalysts appear in Scheme 16.[115-16]



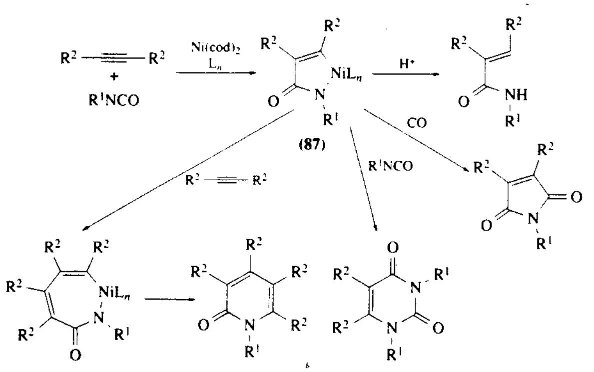
	Catalyst	*Total yield*				
R^L = Ph, R^S = Et R = $(CH_2)_2Ph$	$CpCo(CO)_2$	76%	62%	0	17%	21%
	$Ni(cod)_2$	46%	0	0	0	100%
R^L = Ph, R^S = CO_2Me, R = Me	Cp_2Co	32%	63%	0	0	37%
R^L = Me, R^S = H, R = Ph	$CpCo(C_2H_4)_2$	30%	100%	0	0	0

Scheme 16

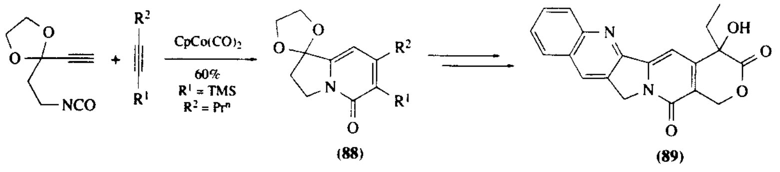
Although Ni^0 catalysts give low yields of pyridones from terminal alkynes, with internal, unsymmetrical examples they display regioselectivity complementary to that from the cobalt catalysts, as illustrated nicely at the top of Scheme 16.[117] As demonstrated by Hoberg and co-workers, in the nickel systems, cyclization begins with redox coupling between alkyne and isocyanate (Scheme 17); with appropriate care, the nickelacycle (**87**) may be trapped with CO or acid to afford imides or unsaturated amides, respectively.[112a,112c] Reaction of (**87**) with an alkyne, followed by reductive elimination, leads to pyridones in which the larger substituents emerge in positions 4 and 6. Insertion of a second molecule of isocyanate into (**87**) can also occur, albeit in lower yields.

Earl and Vollhardt cocyclized α,ω-isocyanatoalkynes and alkynes in two formal total syntheses of camptothecin (**89**), exploiting the regiospecific electrophilic substitutions of silylated pyridones such as (**88**), R^1 = TMS[117](Scheme 18).

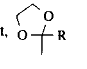
Carbodiimides and two alkynes give 2-imino-1,2-dihydropyridines.[114,115,118]



Scheme 17



Alkyne substituents tolerated: TMS, alkyl, $CH_2OSiBu^tPh_2$, CO_2Et,

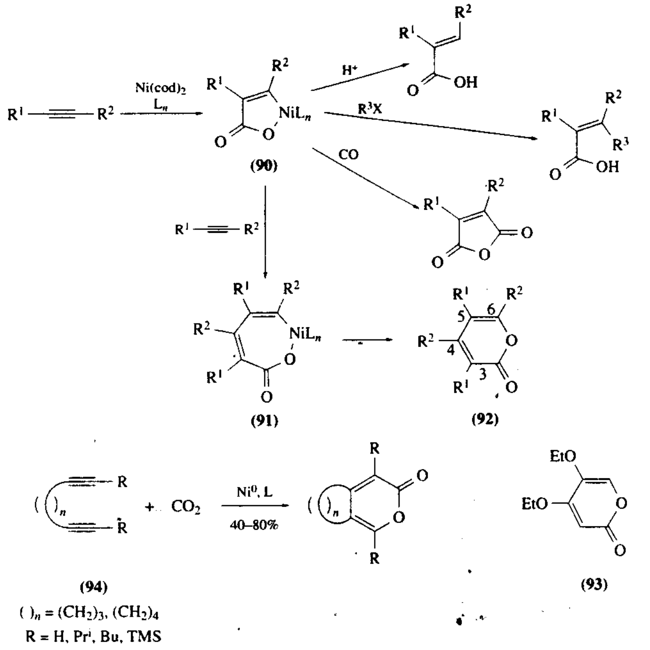


Scheme 18

7.3.6.3 Pyranones and Pyrans

Nickel catalysts effectively cocyclize internal alkynes with carbon dioxide to pyranones.[119] In stoichiometric conversions the initial intermediate, nickelafuranone (**90**), may be intercepted by CO, acid, or alkyl or aryl halides to afford anhydrides or unsaturated carboxylic acids.[120] From (**90**), insertion of another alkyne into the Ni–C bond gives (**91**), a crystal structure for which was presented. Reductive elimination gives product (**92**)[121] (Scheme 19). Larger substituents are placed in the 4 and 6 positions. Excellent yields are obtained, especially after optimization of conditions.[122] The reaction does not give good yields for arylalkynes, but ethoxyethyne gives (**93**) in 56% yield.[123] Diynes with three to five atoms between alkyne functions give modest to excellent yields of bicyclic pyrones,[124] although terminal[125] and trimethylsilyl-substituted diynes[126] required fine tuning of the catalyst.[127] Monosubstituted diynes (**94**) reacted with a regioselectivity indicative of initial redox coupling between the less-substituted terminal alkyne and CO_2. Diynes with two[128] or eight[129] atoms in between the alkyne unit produced alternating copolymers containing pyranone units.

Pyran derivatives are produced from two alkynes and an aldehyde in the coordination sphere of nickel[130] or CpCo, the latter affording pyran complexes, to be discussed in Section 7.3.7.3, from which



(**94**)

$( )_n = (CH_2)_3, (CH_2)_4$

R = H, Pr^i, Bu, TMS

Scheme 19

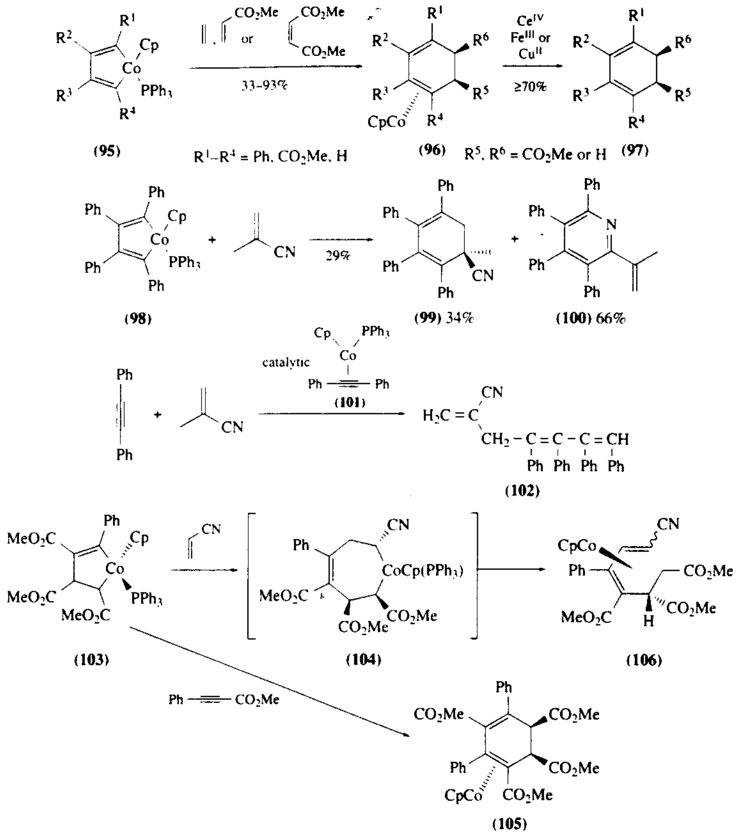
the pyran ligand may be freed by oxidation. The product distribution from the catalytic nickel system is strongly dependent on the substrate structure.

7.3.7 CYCLOHEXADIENES AND COMPLEXES FROM TWO ALKYNES AND AN ALKENE

7.3.7.1 Completely Intermolecular Reactions, Stoichiometric and Catalytic

As seen in Sections 7.3.3–7.3.6, alkynes and other π-systems containing *sp*-hybridized carbons undergo [2 + 2 + 2] cycloadditions to generate planar structures. Analogous cyclization of two alkynes and an alkene in the presence of metal complexes can lead to a cyclohexadiene in a catalytic process, or to a metal–cyclohexadiene complex in a stoichiometric variant. This section examines the known metal systems of synthetic utility and discusses the regio-, chemo- and stereochemical issues involved.

Early work from Wakatsuki, Yamazaki, and co-workers explored the stepwise oligomerization of monoalkynes and monoalkenes via metallacycles. Cobaltacyclopentadienes (**95**) react with ethene itself or with electron-poor alkenes to give CpCo–cyclohexadiene complexes (**96**), from which the cyclohexadiene (**97**) may be liberated by oxidation.[27,131–2] Alkenes are incorporated sterospecifically. Reaction of (**98**) with 2-methylpropenenitrile gave both cyclohexadiene (**99**) and pyridine (**100**).[133a] In contrast, combination of a mixture of diphenylethyne and 2-methylpropenenitrile with a catalytic amount of alkyne complex (**101**) gave only acyclic products (**102**), indicating that formation of (**98**) and subsequent reaction with alkene did not compete with reaction of (**98**) and alkene, followed by β-hydride elimination.[132] In comparison, cobaltacyclopentene (**103**), once formed, reacts with alkyne to give CpCo–cyclohexadiene complex (**105**), but with alkene gives linear product (**106**).[133b] The foregoing results indicate that at least in the CpCo system, electron-poor alkenes compete with alkynes sufficiently well as to preclude cyclohexadiene formation from cobaltacyclopentenes, and that cyclohexene production (from two alkenes and one alkyne) is thwarted because β-hydride elimination from putative intermediate (**104**) predominates over reductive elimination and ring closure. Thus, in the CpCo system, successful cyclohexadiene formation from untethered cocyclization partners generally[27] requires prior formation of a cobaltacyclopentadiene, followed by reaction with alkene (Scheme 20).



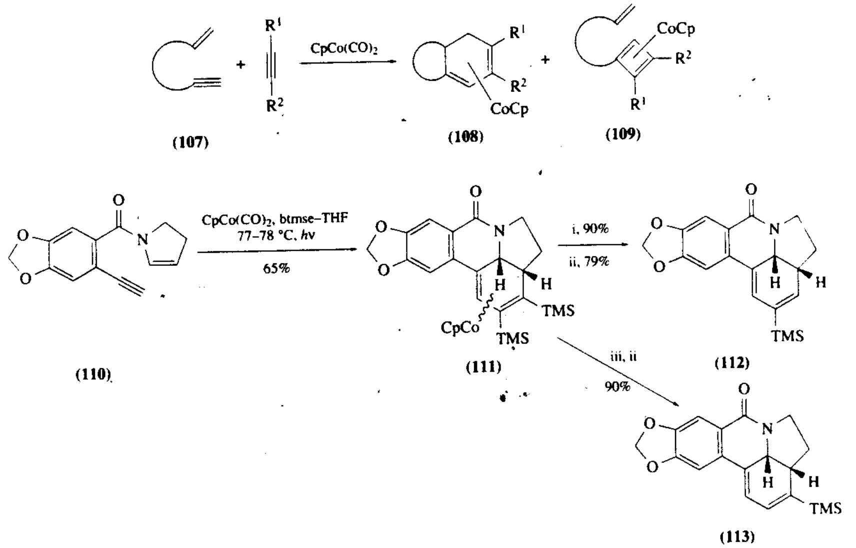
Scheme 20

Efficient catalytic cocyclization of two alkynes and an alkene without recourse to a tether between two components remains a difficult problem, without a general solution. Phenylethyne and *N*-methylmaleimide combine under Ni^0 catalysis, with an unusual 1,3-selectivity that would be consistent with initial alkyne–alkene coupling.[134] Electron-poor palladacyclopentadienes catalyze the efficient reaction of two molecules of dimethyl butynedioate with cyclic alkenes.[135] The generalization of this chemistry to more electron-rich alkynes has not been reported, but related partially intramolecular reactions have been reported by Trost and co-workers,[15] see Section 7.3.7.2. Titanacyclopentadiene complexes catalyze the reaction of alkynes and alkenes to give mixtures of isomeric cyclohexadienes via putative isomeric titanacyclohexadiene complexes.[136]

7.3.7.2 Partially or Totally Intramolecular Reactions, Stoichiometric and Catalytic

Controlled cyclization of two alkyne functions and an alkene unit is eased if at least two of the three components are tethered. Stoichiometric conversions will be discussed first, followed by catalytic methods. Although the requirement of stoichiometric amounts of metal might be seen as a nuisance, the metal may activate the cyclohexadiene ligand toward novel functionalizations, and may serve as a protecting group as well, *vide infra*. Cycloaddition of α,ω-enynes (**107**) with alkynes in the coordination sphere of CpCo at best give moderate yields of ring-fused cyclohexadiene complexes (**108**), even with

the oligomerization-resistant btmse[137] (Scheme 21). Competitive formation of isomeric CpCo-cyclobutadiene complexes (**109**), particularly pronounced with silyl-substituted alkynes, accounted for much of the reduced yields in these conversions. More successful was the cocyclization of enamide-alkyne (**110**) with btmse.[138] The ratio of (**111**) to the isomeric CpCo–cyclobutadiene complex could be increased to 20:1 by optimization of reaction conditions. Oxidative demetallation, followed by protiodesilylation, gave (**112**). Regioisomeric diene (**113**), eventually carried on in a formal synthesis of γ-lycorane, was available by unusually mild and regioselective fluoride-mediated protiodesilylation of (**111**). The regioselectivity of this reaction was explained by invoking the increased electron density at terminal carbons of the complexed diene as a result of Co–diene backbonding, indicating a unique role for the CpCo fragment.

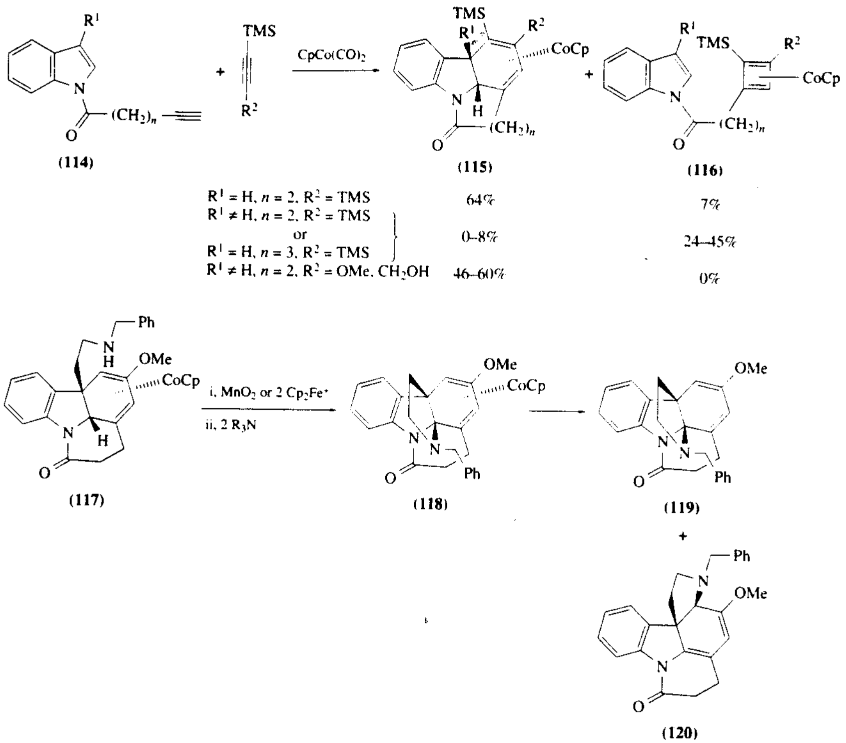


i, $Fe(NO_3)_3 \cdot 9H_2O$, THF–H_2O, 0 °C, 5 min; ii, CF_3CO_2H, deoxygenated $CDCl_3$, 25 °C, 4 d; iii, $Bu^n{}_4NF$, THF, 25 °C, 2–4 h.

Scheme 21

Not only may an enamide double bond be annulated by two alkynes and CpCo, but double bonds of π-excessive heterocycles indole,[139] pyrrole,[140] imidazole,[141] and uracil[142] participate as well (Scheme 22). In the indole series (**114**), reaction with btmse provides a single diasteromer of (**115**), but yields are low if access to the indole 2,3-bond is impeded by 3-substitution. The curious propensity for btmse to form cyclobutadiene complexes (**116**) is highlighted by successful cocyclizations of (**114**) ($R^1 \neq H$) with *mono*trimethylsilylated alkynes, which in this and interactions of other heterocycles are generally incorporated so as to place the larger or more electron-withdrawing substituent (e.g., TMS) at the terminus of the diene function. Higher regioselectivities in these cocyclizations are seen when the more labile mediator $CpCo(C_2H_4)_2$, rather than $CpCo(CO)_2$, is used.[139–40] The presence of the CpCo fragment activated the diene unit in (**117**) and related complexes toward oxidative cyclization; propellane (**118**) could be induced to produce either (**119**) or (**120**) as major product upon oxidative demetallation,[143] both oxidations further illustrating a unique role of the metal. Imidazoles reacted at the C=C, not the C=N bond.[141] Uracil-based nucleosides reacted with high diastereoselectivity in some cases (**121**) (Scheme 23). The origins of diastereoselectivity in these reactions are not altogether clear, but inasmuch as cycloadditions involving the π-excessive heterocycles as 2π components are rather rare,[144] the CpCo-mediated annulation (which may well proceed by insertion of the heterocyclic double bond at some stage of the process) provides an unusual functionalization of heterocycles.

Fully intramolecular reactions of substrates containing two alkynes and an alkene function have been used in approaches to several natural products. In all cases examined, the alkene function is incorporated

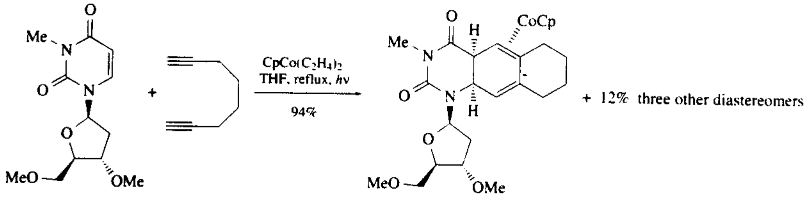


(114) (115) (116)

	(115)	(116)
R¹ = H, *n* = 2, R² = TMS	64%	7%
R¹ ≠ H, *n* = 2, R² = TMS or R¹ = H, *n* = 3, R² = TMS	0–8%	24–45%
R¹ ≠ H, *n* = 2, R² = OMe, CH₂OH	46–60%	0%

(117) (118) (119) + (120)

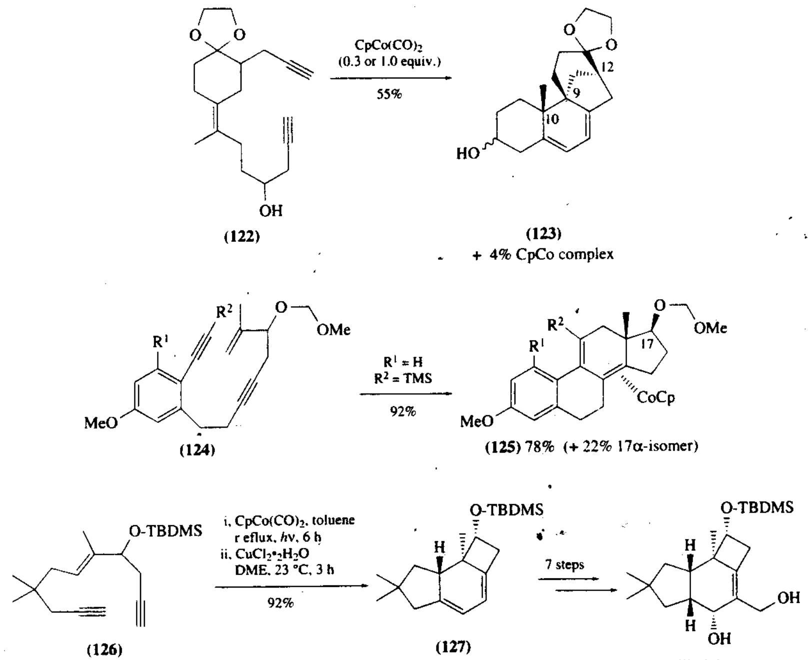
Scheme 22



(121) 88%

Scheme 23

stereospecifically, and in some instances existing stereogenic centers in the cyclization substrate cause the alkene and/or the CpCo fragment to be incorporated with high diastereoselectivity, although the origins of this selectivity are not completely understood.[3,145] For example, the stemodane derivative (**123**)[146] was produced with complete specificity at stereocenters C-9, C-10, and C-12 (Scheme 24). Although less-hindered but topologically similar substrates formed stable CpCo–cyclohexadiene complexes in stoichiometric reactions,[147] the formation of (**123**) could be performed with as little as 0.3 equiv. of metal without a change in yield or product distribution. All-intramolecular cyclizations proceed even in the face of extreme steric hindrance not only at the alkene, as in (**122**), but at the alkyne function(s), as in the conversion of (**124**) to steroidal dienes (**125**), which also succeeds (albeit in low yield) when R¹ and R² are trimethylsilyl groups.[148] Moreover, rather strained ring systems may be formed, as shown by cyclization of (**126**) to (**127**), a precursor to illudol.[149] Metal-mediated double-bond isomerizations of systems similar to (**127**) have been observed,[150] and the CpCo fragment in certain cyclohexadiene complexes migrates from one face of the diene to the other in an intramolecular reaction (Equation (9)),[151] but these are not general processes. Cyclization of (**128**), followed by demetallation, aromatization, and cleavage of the tether gives tricycle (**129**)[152] (Scheme 25).

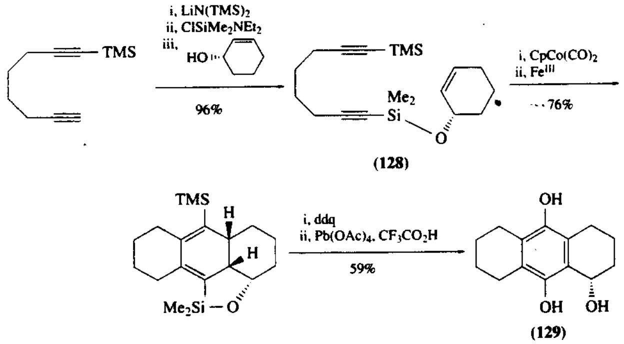


(122) (123) + 4% CpCo complex

(124) (125) 78% (+ 22% 17α-isomer)

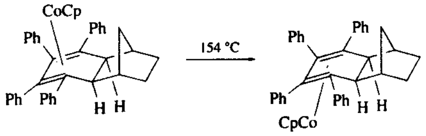
(126) (127) illudol

Scheme 24



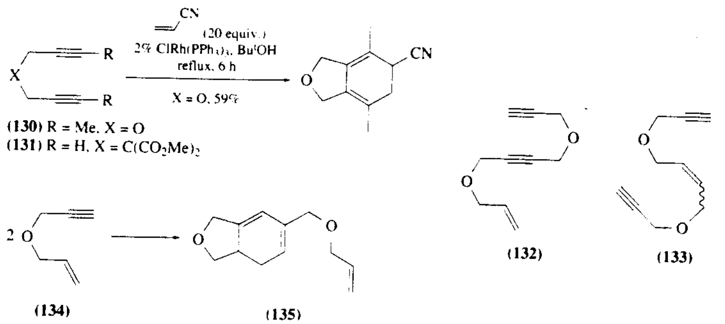
(128) (129)

Scheme 25



(9)

As seen above, formation of especially hindered CpCo–cyclohexadiene complexes may occur with substoichiometric amounts of metal, but this does not appear to be a general result. A catalytic reaction of apparently limited generality is the cocyclization of diyne (**130**) and propenenitrile[106] (Scheme 26). Neither closely related diyne (**131**) (with various alkenes), enediyne (**132**), nor (**133**) formed cyclohexadienes. Two molecules of enyne (**134**) formed (**135**), but (**134**) failed to react with other alkynes. Ethene and substituted 1,7-diynes form mixtures of isomeric hexahydronaphthalenes under titanocyclopentadiene catalysis.[136]



Scheme 26

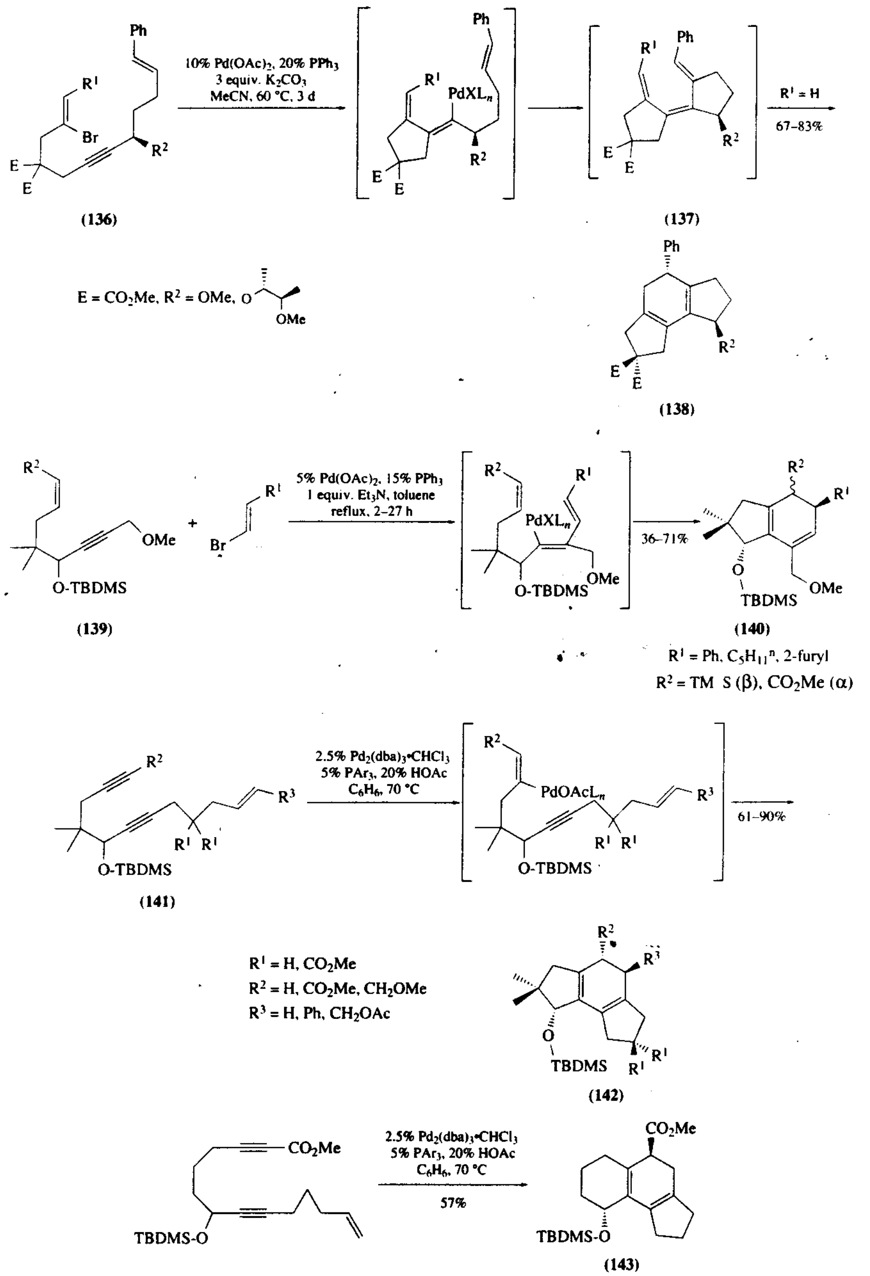
Recent developments in palladium catalysis have provided new routes to cyclohexadienes via 1,3,5-trienes. Although these transformations are mechanistically quite different from the other reactions discussed in this section so far, they do involve cyclization of enynes and diynes (Scheme 27). Thus, substrate (**136**) ($R^1 = H$) smoothly produces (**138**), presumably by oxidative addition, alkyne insertion, alkene insertion, and β-hydride elimination, which would give (**137**), which would suffer electrocyclic ring closure to give product. If R^1 is a butyl group, rearrangement of (**137**) occurs by 1,7-hydrogen shift to give an acyclic triene.[153b] The chemistry tolerates an unprotected tertiary alcohol function,[153a] and produces enantiopure product from enantiopure substrate.[153b] In a partially intramolecular variant, carbopalladation of enyne (**139**) apparently occurs chemoselectively at the triple bond, leading to (**140**).[154] A perhaps more striking example of chemoselectivity is the cyclization of (**141**) to (**142**), initiated by addition of a putative Pd–H at the alkyne function bearing R^2.[155] Both 5–6–5 and 6–6–5 tricyclic systems (**143**) have been formed in this way. Note that application of CpCo-methodology to (**141**) would probably produce an isomer of (**142**). Another route to 1,3,5-trienes and cyclohexadienes involves double Heck reaction on *cis*-1,2-dibromoalkenes.[156] 1,6-Enynes cocyclize with esters of butynedioic acid or undergo intramolecular metathesis, depending on the electronic nature of palladacyclopentadiene catalysts.[157] The ability of other alkynes to participate in the cocyclization has not been reported, but a completely intermolecular variant was mentioned at the end of the last section.

7.3.7.3 Pyrans from Two Alkynes and a Carbonyl Function

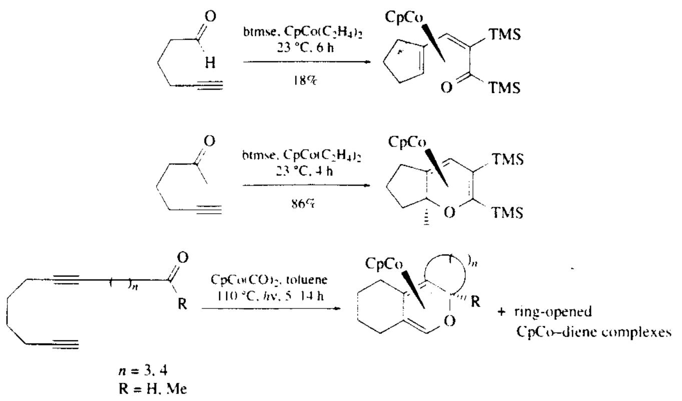
The carbonyl function of aldehydes and ketones may cocyclize with two alkynes in a catalytic reaction with nickel complexes as mentioned in Section 7.3.6.3, or in a stoichiometric fashion with $CpCoL_2$ reagents (Scheme 28).[158] The expected CpCo–pyran complexes are stable to the conditions of their formation,[158b] yet in many cases isomeric CpCo–diene complexes, in which a C–O bond of the pyran ring has been cleaved, are isolated.

7.3.8 CYCLOHEXENES AND CYCLOHEXANES

Direct synthesis of cyclohexene or cyclohexane rings by cyclooligomerization of an alkyne and two alkenes, or of three alkenes, respectively, could be a powerful synthetic tool. However, an illustration of the problems encountered is provided by the reactions of cobaltacyclopentane (**144**)[159] (Scheme 29). As with other metallacyclopentanes, particularly of late transition metals, thermolysis of (**144**) at room temperature gives 1-butene, whose origin is ascribed to β-hydride elimination/reductive elimination, and

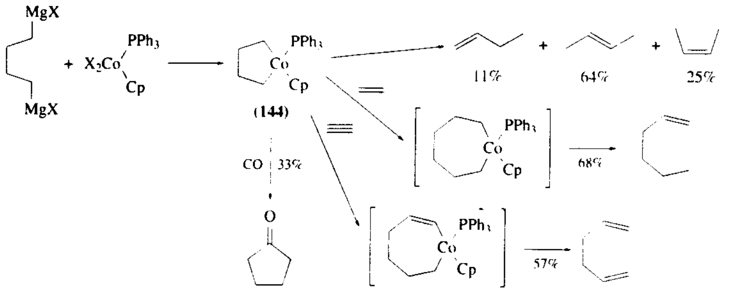


Scheme 27



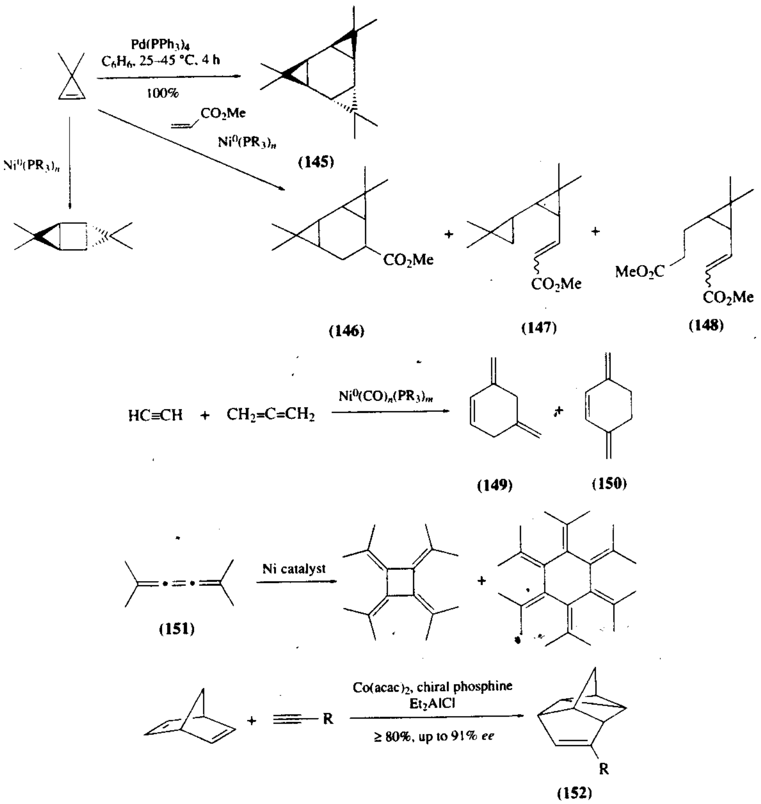
Scheme 28

2-butenes, from metal-catalyzed isomerization of the alkene function. Interaction of (**144**) with CO gives a cyclic ketone, but reaction with ethyne or ethene leads to 1,5-hexadiene or 1-hexene, consistent with decomposition of intermediate cobaltacyloheptene or cobaltacycloheptane by β-hydride elimination/reductive elimination.



Scheme 29

Thus, special alkenes or dienes in which β-hydride elimination from metallacyclic intermediates is blocked seem to be the only reported participants in successful cyclotrimerization. Perhaps the most spectacular example is 3,3-dimethylcyclopropene, which dimerizes in the presence of some Ni^0 catalysts but trimerizes to (**145**) in nearly quantitative yield under $Pd(PPh_3)_4$ catalysis (Scheme 30).[160] Under nickel catalysis, 3,3-dimethylcyclopropene could be induced to enter into cotrimerization with methyl propenoate to produce (**146–148**); variation in phosphine ligands allows one to increase the proportion of any of the three products to at least 65% of the mixture.[161] Two molecules of propadiene combine with one of ethyne using Ni^0 catalysts to form (**149**) and (**150**),[162] selectivity being possible by variation of ligands. 1,2,3-butatriene derivative (**151**) may be induced to trimerize or dimerize under the appropriate conditions.[163] Norbornadiene undergoes [2 + 2 + 2] cyclization with alkenes and alkynes under nickel and cobalt catalysis. Since cyclization with unsymmetrical alkynes produces six new chiral centers in the product, enantioselective versions of the processes have been developed, with the goal of using adduct (**152**) as a starting material for organic synthesis.[164]



Scheme 30

7.3.9 REFERENCES

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