Saturated and unsaturated hydrocarbons

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Reviewing the literature published between May 1996 and December 1996
Continuing the coverage in *Contemporary Organic Synthesis*, 1997, **4**, 40

1 Introduction

In this review particular emphasis has been placed on reductive techniques in the synthesis of saturated hydrocarbons, and in the selective synthesis and connection of the multiple bonds in unsaturated hydrocarbons. Wherever possible novel or improved methods have been emphasised as opposed to an exhaustive list of all the synthetic procedures published in the area.

2 Saturated hydrocarbons

2.1 Dehalogenation

Tributyltin hydride mediated methods continue to dominate the area of organic dehalogenation, but silanes have also been used for similar reactions. The previously reported 9,10-dihydro-9,10-disilaanthracenes **1a–c**[1] and the novel 9,10-dihydro-9-sila-10-heteroanthracenes **1d–g** have been compared with the acyclic variants **2** and **3** in their ability to dehalogenate organic halides (**Fig. 1**).[2] 9,10-Dihydro-9,10-dimethyl-9,10-disilaanthracene **1a** was found to be the most reliable reagent for debromination, but all of the silanes were found to be poor reducers of chlorides and iodides.

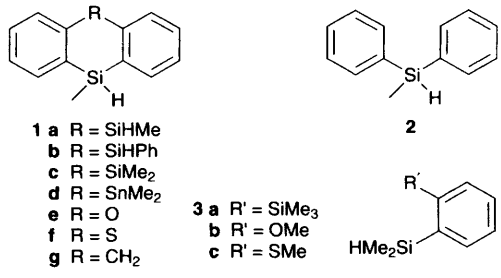
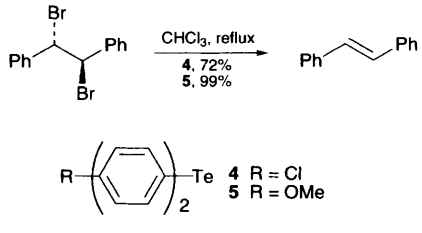


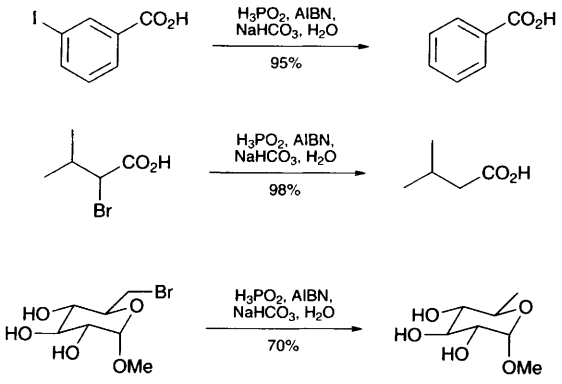
Fig. 1

During the study of redox cycles of organoselenides and organotellurides it was found that the tellurides **4** and **5** efficiently debrominated *erythro*-1,2-dibromo-1,2-diphenylethane in high yields and with high *E* selectivity. *erythro*-1,2-Dichloro-1,2-diphenylethane was inert towards both reagents under identical conditions as was *trans*-dibromocyclohexane (**Scheme 1**).[3]



Scheme 1

In the early 1990s hypophosphorous acid was reported to be a viable substitute for tributyltin hydride in radical reactions.[4] More recently the same reagent has been used with azoisobutyronitrile (AIBN) initiator and buffered with aqueous sodium carbonate to dehalogenate water soluble aromatic



Scheme 2

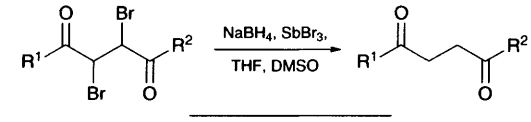
and aliphatic iodides and bromides in good yields (**Scheme 2**).[5]

A mixture of sodium borohydride and antimony tribromide was found to be a potent reducer of α-bromo ketones (**Scheme 3**).[6] A threefold excess of both borohydride and tribromide is crucial for high yielding reductions. The reductive couple is chemoselective, leaving α-chloro ketones and aromatic bromides untouched.

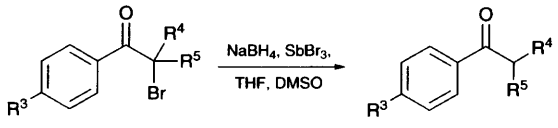
Treatment of *vic*-dibromides with samarium metal in methanol, in general, gives alkene products (*vide infra* Scheme 38).[7] However, when flanked by carboxylic acid derivatives, *vic*-dibromides are reduced, *via* alkene intermediates, to give fully saturated products (**Scheme 4**).

2.2 Deoxygenation

As in dehalogenation, deoxygenation reactions are usually performed by the treatment of substrates, usually activated thioesters, with tin hydride reagents. The 9,10-dihydro-9,10-dimethyl-9,10-disilaanthracene **1a** (**Fig. 1**) has been used as a replacement for tributyltin hydride giving deoxygenated products in good yields.[1]

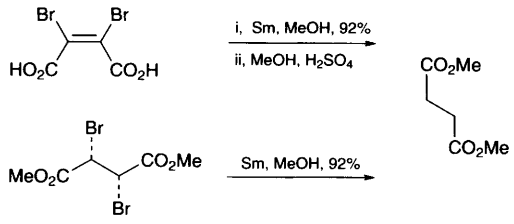


R^1	R^2	Yield (%)
Ph	Ph	91
C_5H_{11}	Me	72
Ph	Me	84
Ph	OEt	51



R^3	R^4	R^5	Yield (%)
H	H	H	88
H	Me	Me	90
Br	H	H	90
MeO	H	H	93

Scheme 3

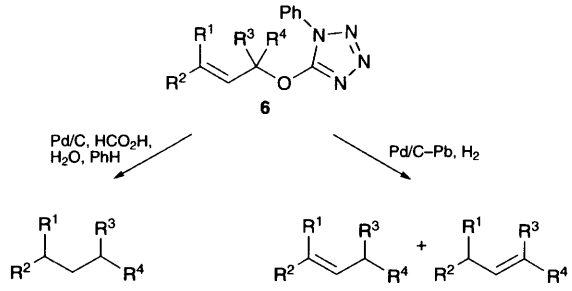


Scheme 4

Transfer hydrogenation of allylic alkoxyphenyltetrazoles **6** over palladium on charcoal has been shown to give alkane products in good yields (**Scheme 5**).[8] Methodical study proved that the carbon–oxygen bond was reduced initially followed by alkene hydrogenation as the final step. Interestingly, the use of either lead poisoned palladium on charcoal or homogeneous palladium catalysts enabled the reaction to be successfully halted at the alkene stage.[8]

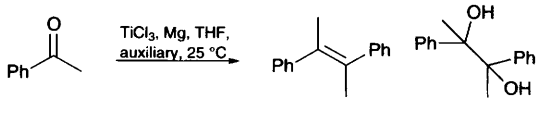
Low valent titanium has been used extensively in deoxygenation reactions such as the McMurry reaction, and many variants of the method have been developed.[9a] The McMurry reaction is usually used for the intermolecular and intramolecular dimerisation of ketones, but can give pinacol side products. It was found that these pinacol products could be formed almost exclusively if either a 1,2- or 1,3-diol or a π-donor such as pyridine was added to the reaction (**Scheme 6**).[9b]

The known lithium triethylborohydride (LTBH) induced rearrangement of β-hydroxy toluene-*p*-sulfonates (tosylates)[10] has been used to good effect in the stereoselective deoxygenation of *myo*-



R^1 = H, Me
R^2 = H, Me, Ph, *p*-NO_2-C_5H_4
R^3 = H, D
R^4 = H, D, Me

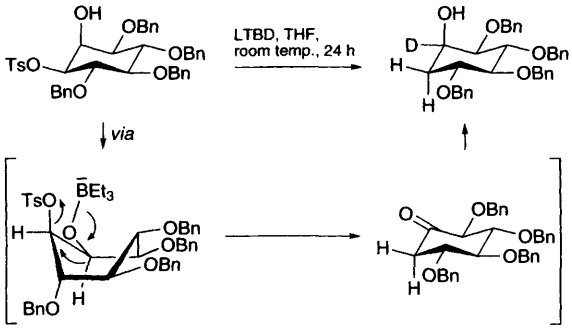
Scheme 5



Additive	Conversion (%)	Alkene (%)	Diol (%) (*dl*/*meso*)
None	84	50	10
Pyridine (10 equiv.)	98	trace	76 (2.03)
Catechol (2 equiv.)	62	0	97 (4.27)

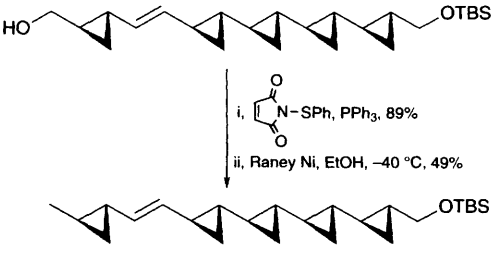
Scheme 6

inositol derivatives.[11] The use of deuterated LTBH (LTBD) showed the key mechanistic feature of the reaction, the 1,2-hydride shift to give a ketone intermediate which was further reduced to give the hydroxy product (**Scheme 7**).



Scheme 7

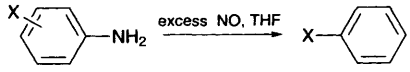
Common methods for the deoxygenation of hydroxy groups are either the Barton–McCombie reaction or the conversion of the hydroxy group to a sulfone, *via* the sulfide, and subsequent low valent metal desulfurisation. In their synthesis of the antifungal agent FR-900848 Barrett *et al.* found that both of these protocols destroyed the sensitive vinyltetrakis(cyclopropane) framework.[12] Eventually the hydroxy group was converted to the phenyl sulfide which was then selectively reduced with Raney nickel in the presence of a double bond to give a deoxygenated product (**Scheme 8**).



Scheme 8

2.3 Deamination

Although benzenes are far from saturated compounds the following reaction is most easily described in this section. The nitrogen–carbon single bond in anilines can be reduced to a carbon–hydrogen bond using excess nitric oxide.[13] The reaction is tolerant of the most common electron withdrawing and donating groups (**Scheme 9**).



X	H	NO_2			Cl			OMe			SMe		
		o-	*m-*	*p-*	*o-*	*m-*	*p-*	*o-*	*m-*	*p-*	*o-*	*m-*	*p-*
Yield (%)	85	85	79	85	92	86	88	55	—	64	75	16	84

Scheme 9

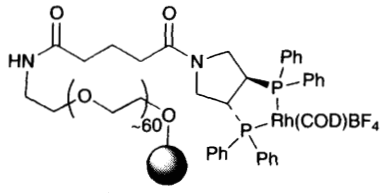
2.4 Hydrogenation

Hydrogenation of carbon–carbon multiple bonds is a very large and expanding field of study. With the advent of homogeneous transition metal catalysis much effort has been expended developing new ligands to give improved or novel catalyst reactivities and physical properties.

Much industrial interest lies in water soluble hydrogenation catalysts to minimise or negate the use of organic solvents which require costly recovery or destruction. One such catalyst, chlorotris(1,3,5-triaza-7-phosphaadamantane)rhodium(I), was recently reported to effectively hydrogenate water soluble alkenes.[14] In the same area, supercritical carbon dioxide has been used as an environmentally benign solvent in hydrogenations and a host of other reactions.[15] Novel ionic liquids have also been used as the solvent during hydrogenation using Wilkinson's catalyst.[16] The reactions are performed in a biphasic mixture of ionic liquid and organic solvent and the products simply isolated by decanting the non-polar organic phase and evaporating. Tests have shown that 98% of the rhodium catalyst remains in the ionic phase.

Over the last fifteen or so years immobilisation of the ligands and therefore of the catalyst has been the goal of many groups.[17] Many of the immobilised catalysts have suffered from reduced activity with respect to their homogeneous counterparts and some systems were also prone to catalyst leaching.[17c] One recent report described the immobilisation of a rhodium complex on a Tentagel polymer support.[18] Importantly, Tentagel resin has a cross linked polystyrene base with long chain polyethers appended. The ligand, when attached to the end of the chain, has almost the same degree of mobility as it would have in the liquid phase. The immobilised catalyst **7** was found to be as active, and induce the same high degree of asymmetry, as the homogeneous catalyst **8** (**Scheme 10**).

The use of 2,2′-bis(diphenylphosphino)-5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl (H_8-BINAP) as a ligand in the complex $Ru(OAc)_2(H_8$-BINAP) gave much higher enantioselectivities and faster reactions than $Ru(OAc)_2$-



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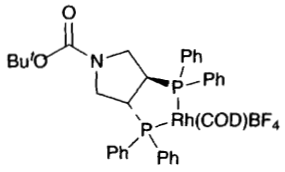
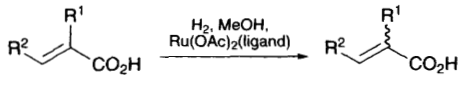
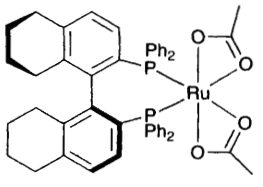


8

Scheme 10

(BINAP) during the hydrogenation of α,β- and β,γ-unsaturated carboxylic acids (**Scheme 11**).[19]



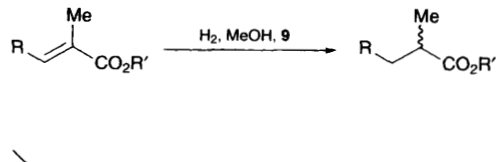


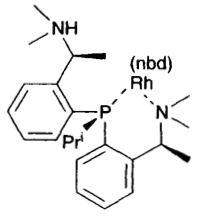
(*S*)-(H$_8$-BINAP)Ru(OAc)$_2$

Ligand	R^1	R^2	Yield (%)	ee (%)
(*S*) H$_8$-BINAP	Me	Et	89	96 (*S*)
(*R*)-BINAP	Me	Et	69	84 (*R*)
(*S*) H$_8$-BINAP	Et	Pr^n	80	95 (*S*)
(*R*)-BINAP	Et	Pr^n	95	88 (*R*)
(*S*) H$_8$-BINAP	Me	Ph	87	89 (*S*)
(*R*)-BINAP	Me	Ph	29	30 (*R*)

Scheme 11

Another catalyst for the hydrogenation of α,β-unsaturated acids is the complex **9** (**Scheme 12**).[20] Here it is thought that the amine incorporated into the ligand becomes protonated by the acid substrate, and the resultant ammonium cation acts as a binding site for the carboxylate anion. Strong evidence for this hypothesis comes from the very slow reactions, low yields and low ees obtained during the reduction of ester derivatives (R′ = Me) (**Scheme 12**).



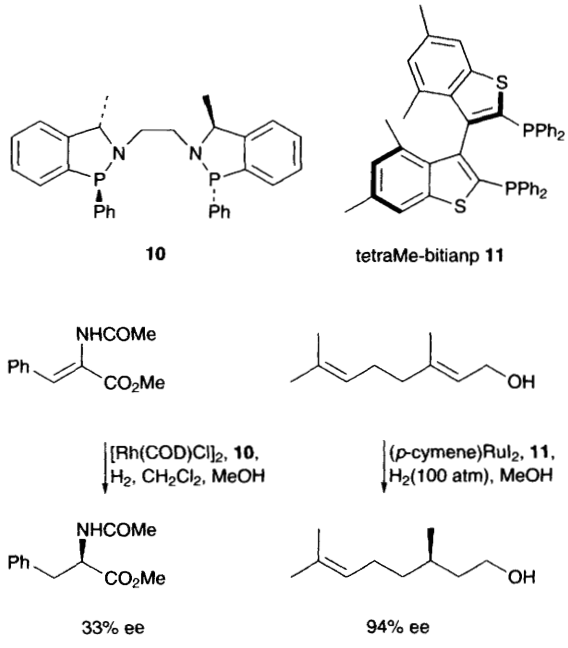


R	R′	Yield (%)	ee (%)
Ph	H	100	84 (*R*)
Ph	Me	<6	—
Me	H	75	75 (*S*)

9 nbd = norbornadiene

Scheme 12

The novel C_2-symmetric bis(benzazaphosphole) ligand **10**, when used in conjunction with rhodium(I) salts, gave hydrogenated amino ester products in moderate ees (**Scheme 13**).[21] The ruthenium(II) complex of axially asymmetric 2,2′-bis(diphenylphosphino)-4,4′,6,6′-tetramethyl-3,3′-bibenzo[*b*]thiophene (tetraMe-bitianp) **11** catalysed the hydrogenation of allylic alcohols such as geraniol giving products with high ees (**Scheme 13**).[22]

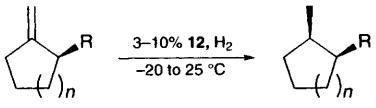


10 tetraMe-bitianp **11**

Scheme 13

Many other catalytic systems have been developed for the hydrogenation of double bonds. Molander *et al.* have shown that the lanthanide complexes of

type **12** are particularly effective catalysts for the diastereoselective hydrogenation of *exo*-methylene compounds with existing stereochemistry (**Scheme 14**).[23] The same catalysts also give highly selective hydrosilylations where the silicon atom is transferred to the terminal carbon.[23]

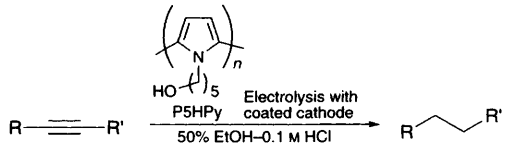


n	R	Yield (%)	*cis:trans*
1	Bu^t	84	100:0
1	$CH_2C_6H_4Cl_2$	32	100:0
2	Me	77	93:7
2	Ph	96	100:0
2	$(CH_2)_3NMe_2$	76	91:9

$Cp^*_2LnCH(SiMe_3)_2$ Ln = Sm, **12**
Ln = Yb

Scheme 14

Heterogeneous catalysis using metals and alloys such as colloidal palladium and gold[24] and polymer immobilised ultrafine palladium particles doped with neodymium ions[25] are just two examples of the large amount of research directed towards the use of colloidal metals in hydrogenations and other common reactions.[26] Acetylenes are quantitatively converted to ethanes by electrochemical reduction in 50% ethanolic aqueous HCl solutions using a platinum anode and a cathode coated in poly[(*N*-hydroxypentyl)pyrrole] (P5HPy) doped with platinum microparticles (**Scheme 15**).[27] Using this method glassy carbon plates (GC) and carbon fibres (CFi) were used as the cathode base materials. High yields were seen for all reactions and quantitative yields (by GC analysis) were seen for the highest loadings of substrate.

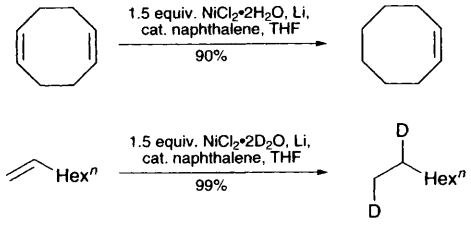


R	R'	Cathode	Substrate:Pd	Yield (%)
Ph	Ph	P5HPy(Pd)CFi	100:1	100
Ph	Ph	P5HPy(Pd)GC	50:1	93
CO_2Me	CO_2Me	P5HPy(Pd)CFi	100:1	100
CO_2Me	CO_2Me	P5HPy(Pd)GC	50:1	94
Ph	H	P5HPy(Pd)CFi	100:1	98
Ph	H	P5HPy(Pd)GC	10:1	96

CFi = Carbon fibre GC = Glassy carbon plate

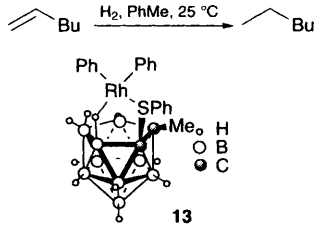
Scheme 15

Lanthanide impregnated catalysts Ln–Ni/SiO_2, Ln–Ru/C, Ln–Cu/SiO_2, Ln–Ag/ZrO_2 (where Ln = Eu or Yb) have been used to effect catalytic transfer hydrogenation of simple alkenes in the gas phase using ammonia as the hydrogen transfer agent and giving nitrogen gas as the by-product.[28] Another indirect way of incorporating hydrogen into alkene reductions without the use of potentially hazardous hydrogen gas has been to use nickel(II) chloride dihydrate, a catalytic amount of naphthalene and an excess of lithium powder in THF.[29] Monohydrogenation of simple non-conjugated dienes can also be achieved with this system using the correct stoichiometry of the nickel salt. If nickel chloride hydrated with deuterium oxide is used effective deuteration of products is seen (**Scheme 16**).



Scheme 16

Comparison of the turnover numbers (TON) has shown that the novel rhodacarborane **13** is eight times more active than Wilkinson's catalyst in the hydrogenation of terminal alkenes (**Scheme 17**).[30] The catalyst has been shown to have good stability under high hydrogen pressures and can be recovered quantitatively from the reaction mixture. However, **13** catalyses the reduction of non-terminal alkenes much more slowly and all reactions are severely retarded by the presence of free phosphine ligands.

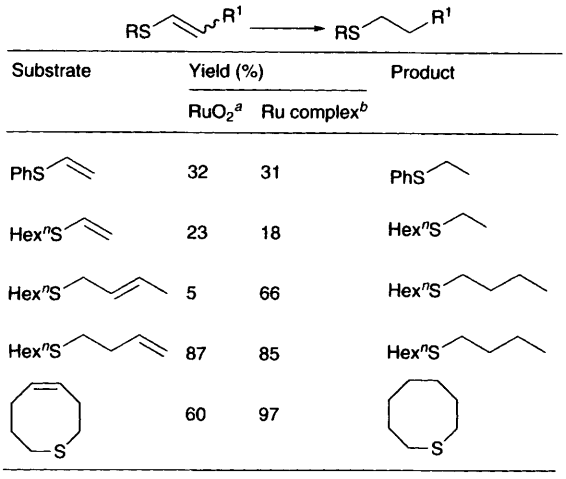


Catalyst	TON
13	715
$RhCl(PPh_3)_3$	90

Scheme 17

Sulfides are known to be potent poisons of many transition metal hydrogenation catalysts. The ruthenium complexes $[Ru_3O(OAc)_6(H_2O)_3]^+AcO^-$ and freshly hydrogenated RuO_2 are effective homogeneous and heterogeneous catalysts respectively for the hydrogenation of alkenes containing sulfide groups (**Scheme 18**).[31] Moderate yields are

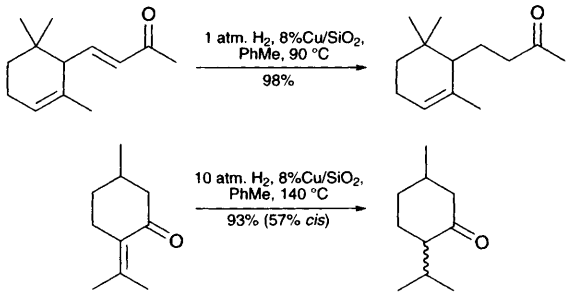
obtained but both reagents gave poor results with phenyl vinyl sulfides.



Substrate	Yield (%)		Product
	RuO_2[a]	Ru complex[b]	
PhS	32	31	PhS
Hex^nS	23	18	Hex^nS
Hex^nS	5	66	Hex^nS
Hex^nS	87	85	Hex^nS
S	60	97	S

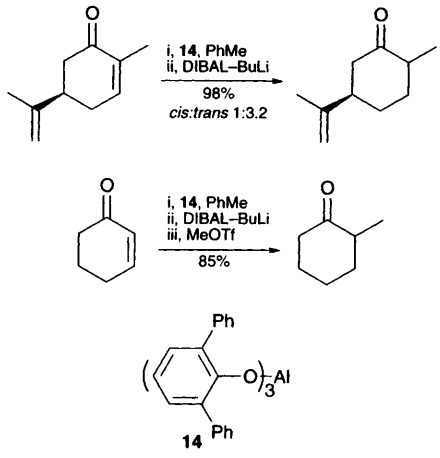
Scheme 18 [a] Heterogeneous RuO_2 yield. [b] Homogeneous yield using $[Ru_3O(OAc)_6(H_2O)_3]^+AcO^-$

Palladium on charcoal in the presence of ephedrine induces low levels (approximately 30% ee) of chiral induction during the reduction of α,β-unsaturated esters.[32] Non-chiral reduction of α,β-unsaturated ketones under one atmosphere of hydrogen at 90° C and over copper impregnated silica gel gives high yields of hydrogenated products (**Scheme 19**).[33] Excellent chemoselectivity is observed as isolated alkenes are inert to the reaction conditions and hindered conjugated alkenes require elevated temperatures and hydrogen pressures to force reduction. Propanol has also been used as a hydrogen transfer agent in place of potentially hazardous hydrogen gas.



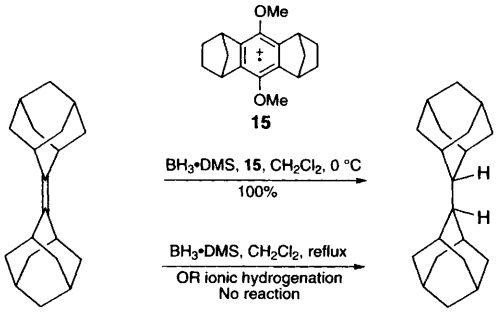
Scheme 19

Similarly, α,β-unsaturated ketones and aldehydes are reduced with very high 1,4-selectivity with a diisobutylaluminiumhydride–butyllithium mixture at −78 °C in the presence of aluminium tris(2,6-diphenylphenoxide) **14** (**Scheme 20**).[34] Interestingly in one case the intermediate enolate was trapped with methyl trifluoromethanesulfonate (triflate) to give the reduced and methylated product (**Scheme 20**).



Scheme 20

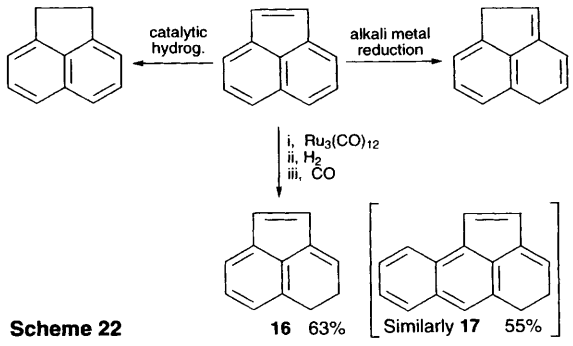
A series of hindered alkenes which were difficult to hydrogenate by standard means have been successfully reduced employing the one electron donor radical cation 'orange CRET $^{\cdot+}$' **15** and borane–dimethyl sulfide complex (**Scheme 21**).[35]



Scheme 21

The reduction of various aromatic hydrocarbons has recently been reviewed;[36] however, the previously unknown hydrocarbons 4,5-dihydroacenaphthylene **16** and 4,5-dihydroaceanthracene **17** have been synthesised by the reduction of the parent hydrocarbons with hydrogen in the presence of trirutheniumdodecacarbonyl (**Scheme 22**).[37] All other methods of hydrogenation reduce at least one of the more reactive *peri* carbon–carbon double bonded atoms, whereas reduction using the

ruthenium cluster complex gives the aforementioned hydrocarbons **16** and **17**.



Scheme 22

2.5 Cyclopropanation

Many new catalysts for the asymmetric cyclopropanation of alkenes have been reported in recent years. The copper[38] and rhodium[39] catalysts **18** and **19** are the most notable and have both been used to form carbenoids from diazo compounds which add to alkenes to give cyclopropanes of high ee (**Fig. 2**). The tartrate derived ligand **20** developed by Knight *et al.* for the copper(I) triflate catalysed reaction also gives good *cis*:*trans* ratios in the cyclopropane products and variable (17–80%) ee (**Fig. 2**).[40] The proline carboxylate catalyst **21** has been used similarly to cyclopropanate vinyldiazomethanes in pentane with very high diastereoselectivities (>40:1 *E*:*Z*) and enantioselectivities (90–92%) (**Fig. 2**).[41]

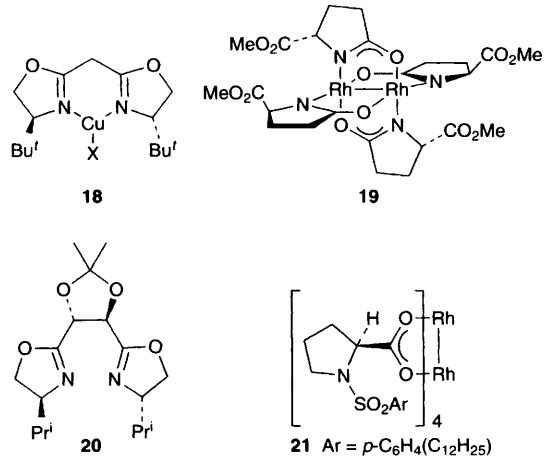
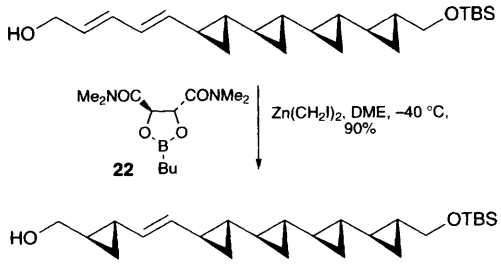


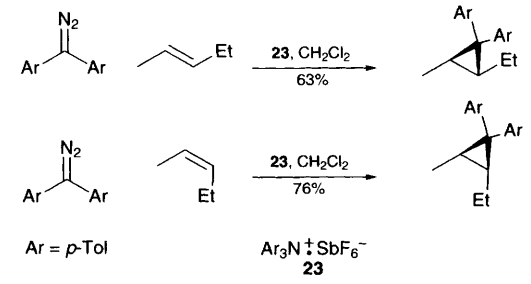
Fig. 2

Another well established cyclopropanation protocol is the modified Simmons–Smith reaction formulated by Charette.[42] Both Charette[43] and Barrett[12,44] have now used this procedure chemo- and enantio-selectively to cyclopropanate allylic alcohols in polyene precursors using the dioxaborolane catalyst **22** (**Scheme 23**).



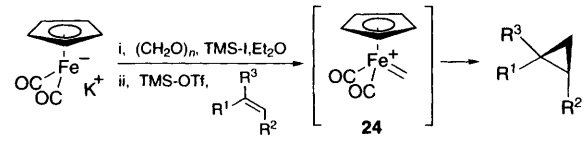
Scheme 23

New achiral catalysts have also been to achieve cyclopropanation. $RhCl(\eta_2\text{-}C_2H_4)_2$, when immobilised on $SiCl_4$ pretreated silica gel, catalyses the cyclopropanation of ethene with diphenyldiazomethane in a yield which is comparable to that obtained with the free rhodium complex.[45] Non-metal stereospecific catalytic cyclopropanations have also been realised using the highly reactive radical cation **23** and diphenyldiazomethane in good yields (**Scheme 24**).[46]



Scheme 24

The stoichiometric reagent **24** cyclopropanates aryl and alkyl substituted alkenes in reasonable yields (**Scheme 25**).[47]

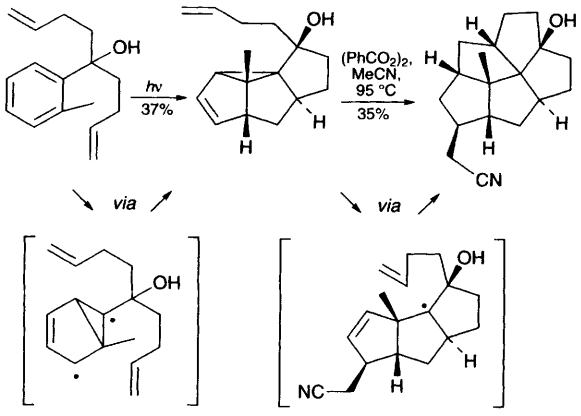


R^1	R^2	R^3	Yield (%)
Ph	H	Ph	100
Ph	H	H	90
p-tol	H	H	80
Ph	H	Me	85
-$(CH_2)_4$-		H	52

Scheme 25

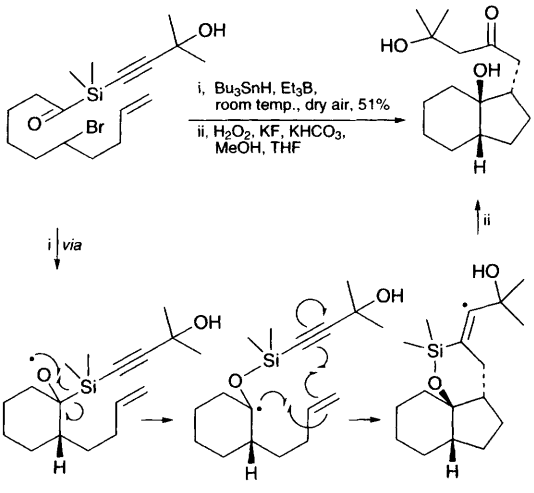
2.6 Miscellaneous

The fenestranes are a group of hydrocarbons that, until recently, have been paid scant synthetic interest. Wender *et al.* have synthesised the thermodynamically least stable member of the family, the *cis, cis, cis, trans*-[5,5,5,5]fenestrane skeleton using a photolytic cycloaddition and subsequent radical induced ring closure (**Scheme 26**).[48]



Scheme 26

Radical methods continue to be popular in constructing complex carbocyclic products. Tsai *et al.* have used a Brook type rearrangement to generate carbon centred radicals from oxygen centred radicals. The carbon radicals formed were trapped intramolecularly giving cyclic products (**Scheme 27**).[49]



Scheme 27

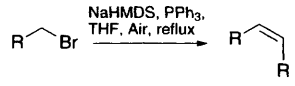
3 Alkenic hydrocarbons

3.1 Carbonyl olefinations

The Wittig[50] and Horner–Wadsworth–Emmons[51] reactions are generally the first methods that organic chemists now consider for the olefination of carbonyl compounds. In 1982 it was reported that phosphonium salts and amide bases could be premixed in the solid state, stored for months and then used as 'instant ylides' for the Wittig reaction.[52a] While the concept worked well, in practice it was limited due to certain heteroatom-containing side chains reacting with the amide base. A recent report overcame this hurdle using potassium hydride in place of the relatively nucleophilic potassium amide.[52b] Chloromethyl-, fluoromethyl- and [(methylthio)methyl]-triphenylphosphonium chloride-containing instant ylides have been made and stored at 0 °C for 12 months with virtually no loss of activity. Storage at 25 °C for 12 months leads to roughly a 25% loss of activity compared to that of instant ylide stored at 0 °C.

Wittig reaction of the novel ylide, [(diethoxyphosphinyl)methylidene]triphenylphosphorane, with aldehydes selectively gives *E*-α,β-unsaturated phosphonates.[53] An extensive review of the synthesis and reactivity of many phosphorus ylides that contain heteroatoms connected to the ylide carbon atom has recently been published.[54]

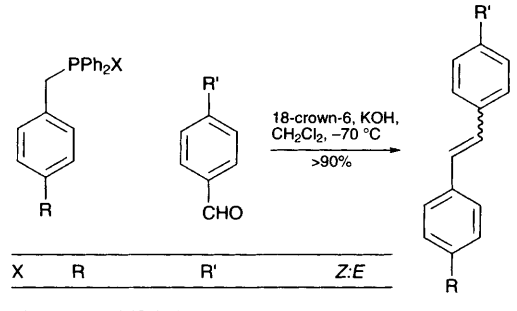
Symmetrical *Z*-alkenes are easily accessed in high yields by reaction of a monomeric alkyl bromide with triphenylphosphine in air (**Scheme 28**).[55] The reactions proceed by the air oxidation of ylide into an aldehyde which then couples to the remaining ylide.



R	Yield (%)	*Z*:*E*
$(CH_2)_4Me$	96	96:4
$(CH_2)_9CO_2Me$	98	100:0
$(CH_2)_5OTHP$	75	95:5
$(CH_2)_7OCONHPh$	45	95:5
$(CH_2)_7OH$	85	95:5
$(CH_2)_6CO_2H$	91	96:4

Scheme 28

By the simple expedient of choosing either benzyltriphenyl- or benzyldiphenylchlorophosphonium halides to react with benzaldehydes in a solid–liquid biphasic system, *Z* or *E* stilbenes can be made selectively in very high yields (**Scheme 29**).[56]

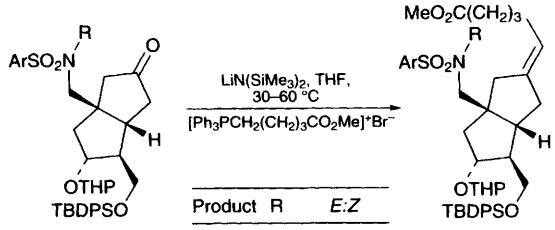


X	R	R'	*Z*:*E*
Ph	*p*-MeO(C_6H_4)	H	85:15
Ph	H	*p*-MeO(C_6H_4)	85:15
Ph	*p*-MeO(C_6H_4)	*p*-MeO(C_6H_4)	>98:2
Ph	*p*-CN(C_6H_4)	*p*-CN(C_6H_4)	>98:2
Cl	H	*p*-MeO(C_6H_4)	1:99
Cl	H	*p*-CF_3(C_6H_4)	4:96
Cl	*p*-CF_3(C_6H_4)	*p*-CF_3(C_6H_4)	1:99

Scheme 29

The stereoselectivity of the Wittig reaction can be influenced by steric and electronic factors.[50] Interaction of ionic neighbouring groups can also affect

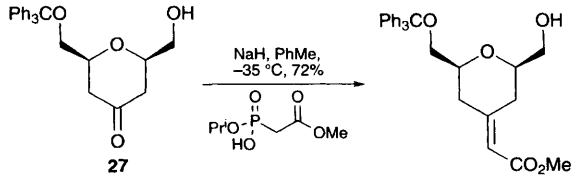
the stereochemical outcome as seen with the directing effect of benzenesulfonamides.[57] The secondary amide (R = H) is deprotonated under the reaction conditions (R = Li) and directs the Wittig reaction to give the *Z*-isomer **25** as the sole product (**Scheme 30**). The tertiary sulfonamide (R = Me) cannot be deprotonated and gives a 1:1 mixture of *Z* and *E* isomers **26**.



Product	R	*E*:*Z*
25	H (Li)	0:100
26	Me	50:50

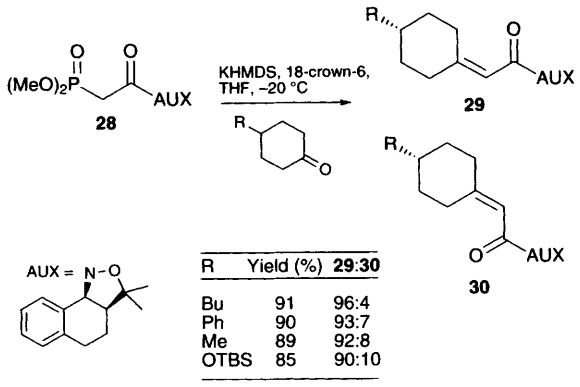
Scheme 30

The stereoselectivity of the Wadsworth–Horner–Emmons reaction is sensitive to the steric bulk of neighbouring groups.[58] The monotritylated *meso*-dihydroxy ketone **27** was olefinated to give products in a 9:1 ratio, where the major isomer contained the methoxycarbonyl group *syn* to the sterically least demanding hydroxy group (**Scheme 31**).[59]



Scheme 31

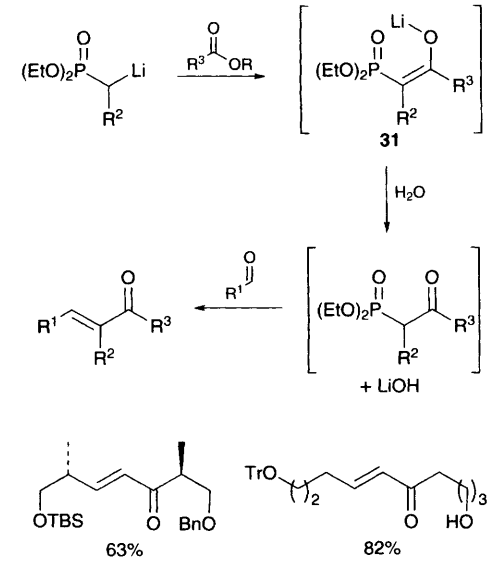
A similar reaction would not have been possible if the steric blocking group was too distant from the ketone to bias the alkene geometry. Such is the case in *meso*-4-substituted cyclohexanones, and here the asymmetric Wadsworth–Horner–Emmons reagent **28** has been used to good effect (**Scheme 32**).[60] Very high diastereomeric ratios of products are obtained when **28** is used in conjunction with potassium hexamethyldisilazide (KHMDS) and 18-crown-6. The auxiliary can be removed in a number of ways to give a range of useful products. Lithium borohydride or lithium aluminium hydride give allylic alcohols, Grignards give ketones and diisobutylaluminium hydride gives aldehydes all in good yield.[60]



R	Yield (%)	**29**:**30**
Bu	91	96:4
Ph	90	93:7
Me	89	92:8
OTBS	85	90:10

Scheme 32

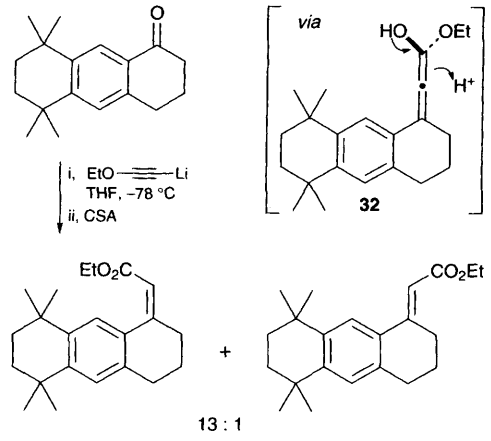
The ketophosphonates used in the Wadsworth–Horner–Emmons reaction with aldehydes are commonly made by the reaction of α-lithiated phosphonates with esters. A one-pot, three component approach to make the phosphonates and react them with aldehydes *in situ* has recently been reported.[61] Simple treatment of the α-lithiated phosphonate with an ester or lactone gives the oxyanion intermediates **31** which when reacted with equimolar amounts of water and aldehyde liberate lithium hydroxide which then promotes the olefination reaction. Two synthetically useful alkenes made by this method are shown in **Scheme 33**. The use of the diphenylphosphoryl group in synthesis has recently been reviewed, and the article carries a section detailing the related olefination reaction, the Horner–Wittig reaction.[62]



Scheme 33

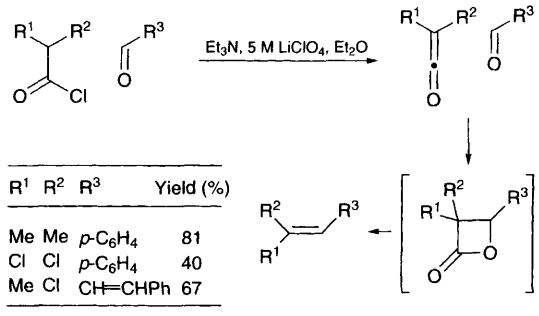
Addition of lithium ethoxyacetylide to bicyclic and tricyclic ketones gives a maximium 13:1 diastereomeric mixture of alkenes where the major isomer contains the methoxycarbonyl group *syn* to the bicyclic junction (**Scheme 34**).[63] The stereoselectivity is proposed to arise from the diastereoselective

protonation of the allene intermediate **32** from the least hindered right hand face.



Scheme 34

One-pot cycloaddition of aromatic or allylic aldehydes with ketenes in 5 M lithium perchlorate gives 2-oxetanones which then cyclodecarboxylate (**Scheme 35**).[64] This process gives an overall olefination of the aldehyde.

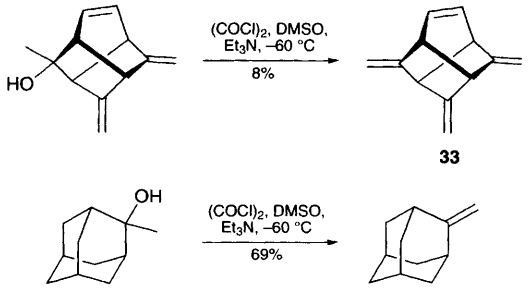


R^1	R^2	R^3	Yield (%)
Me	Me	*p*-C_6H_4	81
Cl	Cl	*p*-C_6H_4	40
Me	Cl	CH=CHPh	67

Scheme 35

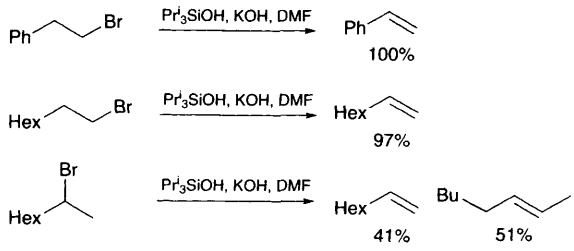
3.2 Elimination reactions

During attempts to form the thermally labile and highly strained alkene **33** it was found that tertiary alcohols with β-hydrogens when treated under standard Swern oxidation conditions gave alkenes (**Scheme 36**).[65] Highly strained alkenes are only produced in low yields, but other less strained alkenes were formed in good yields.



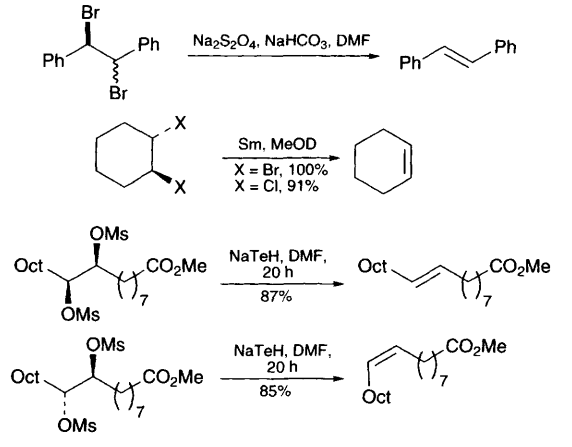
Scheme 36

Triisopropylsilanol is an effective solid–liquid phase transfer catalyst for the dehydrodehalogenation of primary alkyl bromides with potassium hydroxide in DMF (**Scheme 37**).[66] The elimination of secondary halides is not regiospecific and gives a mixture of 1- and 2-alkenes.



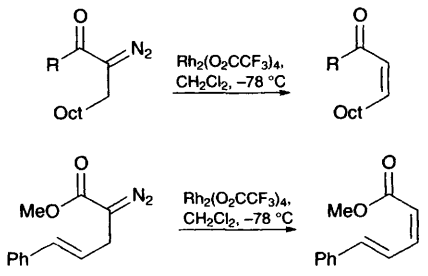
Scheme 37

Aromatic vicinal dibromoethanes are effectively dehalogenated to *E*-alkenes with two equivalents of sodium dithionite in DMF at room temperature (**Scheme 38**).[67] The eliminations are not stereospecific as *meso* and *dl* substrates both give the same *E*-products. Samarium in methanol effects the same reaction, but the method works most effectively for alkyl substituted dibromides (**Scheme 38**).[7] For acyclic substrates the reaction is non-stereospecific and care must also be taken when the dibromide is flanked by ester or acid groups as over-reduction of the alkene to alkane can occur (*vide supra*, **Scheme 4**). Unlike the two reductions above the elimination of *meso* and *dl* vicinal methanesulfonates (mesylates) with sodium hydrogen telluride is stereospecific (**Scheme 38**).[68,69]



Scheme 38

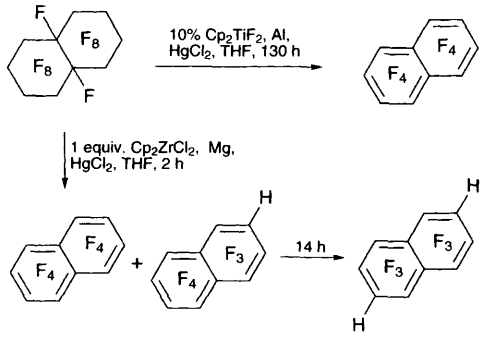
Modification of the Clemmensen reduction of aryl ketones using formic acid gives good alkene to alkane ratios. These milder conditions also leave aliphatic ketones untouched.[70] Decomposition of diazoketones in the presence of rhodium acetate can give β-elimination if there is no 1,5-insertion competitive pathway.[71] However, if the more reactive dirhodium tetrakis(trifluoroacetate) catalyst is used at low temperature, high yields of *Z*-α,β-unsaturated compounds are formed, even if insertion processes are available (**Scheme 39**).[72]



R	Yield (%)
MeO	80
EtO	85
Bu^tO	91
Me	92

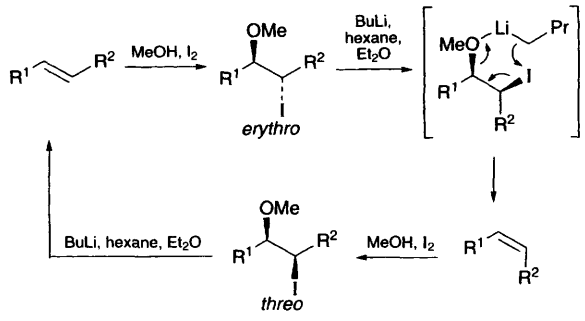
Scheme 39

In recent years advances have been made into the catalytic defluorination of fluorocarbons.[73] Titanocene difluoride catalysed defluorination of perfluoronaphthalene with aluminium and mercuric chloride at ambient temperature gives octafluoronaphthalene in approximately 50% yield (**Scheme 40**).[74] The same reaction when performed with stoichiometric zirconocene dichloride, magnesium and mercuric chloride gave octafluoro- and heptafluoro-naphthalene in 55% and 35% yield respectively. When the reaction was allowed to proceed further hexafluoronaphthalene was the principal product.



Scheme 40

An important synthetic reaction is the inversion of alkene geometry. Most commonly an undesired diastereomer is equilibrated radically or photochemically to a mixture of alkenes and the desired isomer separated. However stereoselective methoxyiodination of *E* and *Z* alkenes gives *erythro*- and *threo*-methoxyiodoalkanes respectively (**Scheme 41**).[75] Treatment of these methoxyiodoalkanes with butyllithium gives a *syn* elimination process with overall alkene inversion in good yield and with nearly complete stereoselectivity. Trisubstituted alkenes have also been inverted with reasonable to excellent selectivities.



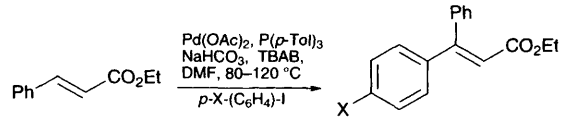
R^1 (R^2)	R^2 (R^1)	*erythro*:*threo*	Yield (%)	*E*:*Z*
Oct	Et	99:1	70	3:97
$(CH_2)_8OMe$	Oct	88:12	66	87:13
$-(CH_2)_6-$		1:99	94	95:5

Scheme 41

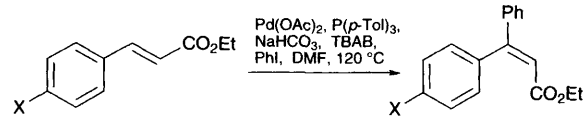
3.3 Alkene sp^2–sp^2 coupling reactions

3.3.1 Heck reaction

The Heck reaction remains an extremely important reaction for the synthesis of arylated alkenes and many other aromatic and vinylic compounds. An example of the stereoselectivity that can be achieved with the Heck and not *via* Wittig type olefinations is in the synthesis of β,β-diarylpropenoates.[76] Wadsworth–Emmons type olefinations of diaryl ketones generally give 1 : 1 mixtures of *E* and *Z* isomers.[77] On the other hand arylation of (*E*)-ethyl 2-arylpropenoates, readily made by Heck arylation of ethyl acrylate, gives good to excellent yields of 2,2-diarylpropenoates with high *E* : *Z* selectivity (**Scheme 42**).[76] Both the *E* and *Z* isomers can easily be accessed simply by altering the order of arylation of ethyl acrylate.



X	MeO	AcNH	Me	Br	MeCO	CF_3
Yield (%)	73	80	67	32	33	19
E:*Z*	83:17	86:14	100:0	70:30	75:25	100:0

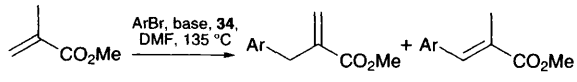


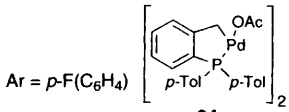
X	MeO	AcNH	Me	Br	MeCO	CF_3
Yield (%)	47	63	47	68	100	75
Z:*E*	98:2	80:20	92:8	96:4	60:40	75:25

Scheme 42

The final stage of the Heck reaction is the β-elimination of a palladium hydride species to

reform a carbon–carbon double bond. If more than one β-proton is present there exists the chance of obtaining regioisomeric alkene products. During studies of the arylation of methyl methacrylate the choice of tributylamine as base was found to be crucial for maximising the ratio of terminal : internal alkenes (**Scheme 43**).[78] Kinetic studies showed that the highly active palladacycle catalyst **34** gives the highest turnover numbers yet measured for the Heck reaction.[78] Palladium catalysed alkene isomerisation prior to Heck arylation is also a common, troublesome side reaction. In the arylation, and one case of vinylation, of 3,4-dihydropyrroles this isomerisation was completely eliminated using silver carbonate and tri-*o*-tolylphosphine additives.[79]





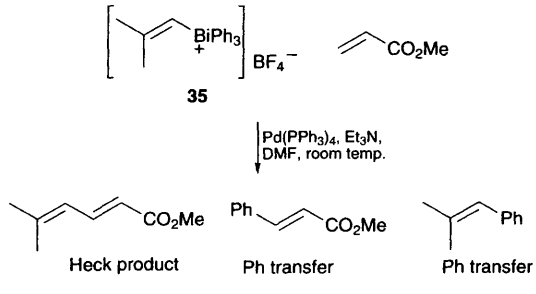
34

Base	Terminal:internal	Yield (%)
NaOAc	1.1:1	27
Bu_3N	9.3:1	60

Scheme 43

Substrates have been immobilised on solid phase for both intermolecular and macrocyclic versions of the Heck reaction.[80] A recent report showed the applicability of the method to the synthesis of indoles on solid support.[81] Molten hexadecyltributylammonium bromide has been used as a solvent for simple Heck reactions of aryl bromides with butyl acrylates at 100 °C.[82] These stable solvents allow products to be simply separated from the catalyst and solvent by distillation.

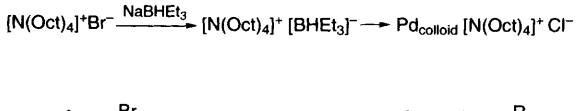
It is known that arylbismuth compounds undergo Heck reactions.[83a] The newly synthesised vinylbismuthonium salt **35** has now also been shown to react with ethyl acrylate in a Heck manner (**Scheme 44**).[83b] From the mixture of products obtained it is obvious that the bismuth centre is capable of transferring either its aryl or vinyl ligands. Similarly, hypervalent aryliodonium salts have been used to arylate allylic alcohols in very high yields using palladium(II) acetate and sodium hydrogen carbonate under semi-aqueous conditions.[84]

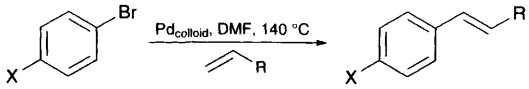


Scheme 44

A systematic study of the use of tetraalkylammonium salt additives in the Heck reaction revealed that tetraalkylammonium hydrogen sulfates are just as effective as the more commonly used tetraalkylammonium halides.[85] In fact the correct choice of palladium catalyst allows efficient reaction in either strictly anhydrous, semi-aqueous or fully-aqueous solvents.[85]

There is an increasing interest in the use of transition metal clusters or colloids as catalysts in organic chemistry. Two reports have shown that tetrabutylammonium stabilised palladium clusters[86,87] palladium–nickel bimetallic clusters[87] and poly(vinylpyrrolidinone) stabilised palladium clusters[87] are all good catalysts for the Heck reaction (**Scheme 45**).

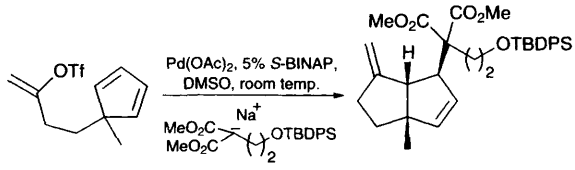




X	R	Yield (%)
CHO	CO_2Bu	90
F	Ph	55
H	Ph	13
MeCO	CN	93
MeO	Ph	9

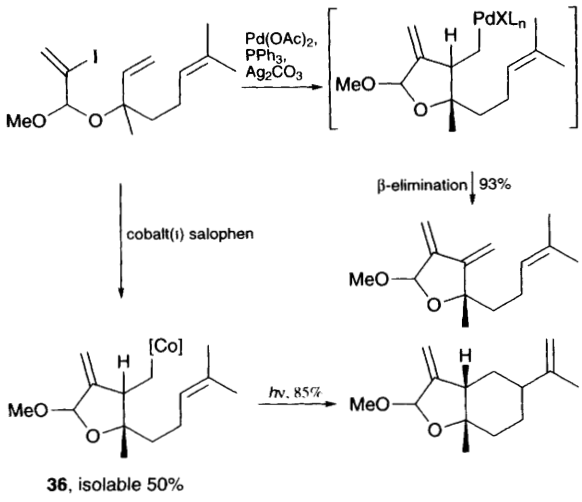
Scheme 45

An extensive study of the Heck reaction under a carbon monoxide atmosphere and in alcoholic co-solvents showed that it can be used to access a large number of cyclic ketone and ester products.[88] An asymmetric Heck reaction has been used for the total synthesis of (−)-$\Delta^{9(12)}$-capnellene.[89] Instead of the final process being dehydropalladation, the intermediate allylpalladium species was trapped with a malonate nucleophile (**Scheme 46**).[89]



Scheme 46

A comparative study of the Heck reaction and the cyclisation of organocobalt complexes recently showed the complementary nature of the two mechanistically dissimilar but topologically similar reactions. As previously mentioned, in general, the final step of the Heck reaction is dehydropalladation, reforming an alkene. When organocobalt precursors are used in place of aryl or vinyl bromides the product is a topologically similar cobalt complex **36** (**Scheme 47**).[90] These products are isolable and can be either converted into



Scheme 47

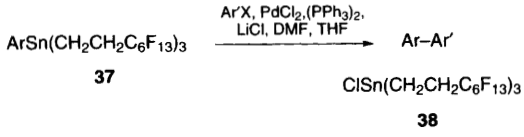
alkenes or more importantly, can be irradiated to form radicals that may be used in further carbon–carbon bond formation reactions.

3.3.2 Stille reaction

The Stille coupling reaction, like the Heck, occupies a prominent position at the head of the set of reactions available for the coupling of sp^2 carbon centres. Factors limiting its growth into large scale and industrial use have been the toxicity of the tin residues and the expense of their disposal. Importantly purification of products can also be problematic. In an effort to solve these problems fluorinated trialkylstannylarenes **37** have been used (**Scheme 48**).[91] Standard Stille reaction of **37** with a range of aromatic halides and pseudohalides gave excellent yields of coupled products. The tin residues were readily separated from the products by three-phase extraction between water, dichloromethane and FC-72 (a commercially available mixture of C_6F_{14} isomers). 80–90% of the trialkyltin chloride **38** is isolated from the fluorocarbon phase, and the remaining **38** is isolated by extracting the dichloromethane phase once with FC-72. The reagent **38** thus obtained is suitable for reuse and recycling. The same strategy has also been used to render tributyltin hydride and chloride more easily extractable and recyclable.[92]

Another potential problem associated with the Stille reaction is the formation of cine substituted products.[93] The cine product is the isomer where the aryl residue is attached to the sp^2 carbon atom that was not originally attached to the tin atom. A recent experiment with a 1:1 mixture of vinylstannanes **39** has shown that the product arises by a 1,2-hydride shift (**Scheme 49**).[94]

The novel 3- and 4-tributylstannylfuranones **40** and **41** have both been successfully arylated with iodoarenes using dichlorobis(triphenylphosphine)palladium(II) as a catalyst (**Scheme 50**).[95] Other heterocycles such as 4-(tributylstannyl)imidazoles[96] and 2-(tributylstannyl)pyridines[97] have been vinylated and arylated respectively.



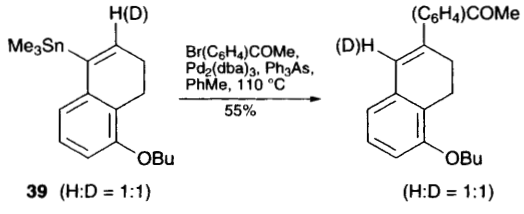
Ar'X	Yield (%) Ar = Ph	Ar = (C_6H_4)OMe	Ar = furyl
PhI	90	97	45
p-MeCO(C_6H_4)Br	90	87	72
p-$NO_2(C_6H_4)$Br	94	98	93
p-$NO_2(C_6H_4)$OTf	82	96	83
$PhCH_2$Br	77	98	32

Scheme 48

α- and β-substituted vinyl trifluoromethyl sulfones have been constructed under standard Stille conditions by coupling a number of vinyl and aryl stannanes with both *E* and *Z* β-iodovinyl trifluoromethyl sulfones.[98] Macrocyclic Stille couplings have continued to be used for the efficient synthesis of macrocyclic polyene natural products (**Scheme 51**).[99]

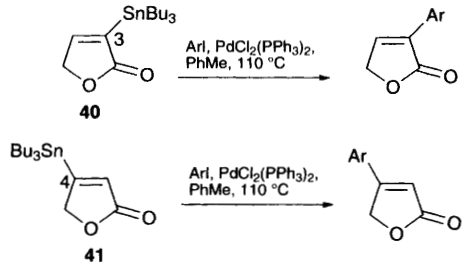
3.3.3 Suzuki reaction

Like the Stille and Heck reactions, the Suzuki reaction enjoys widespread use for the construction of biaryls and styrenes and it has been successfully carried out on solid support.[80,100] Immobilised iodoarenes have been coupled to both vinyl-, aryl-, prop-2-ynyl- and alkyl-boronic acids, esters and



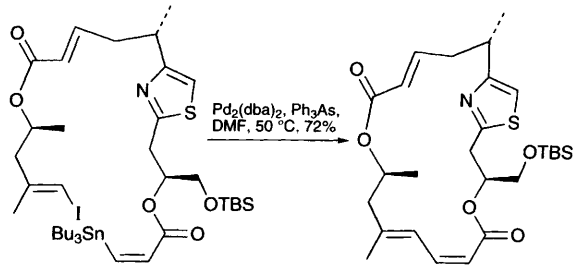
39 (H:D = 1:1) (H:D = 1:1)

Scheme 49



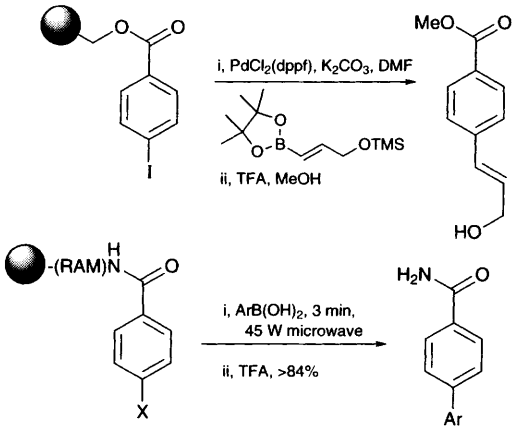
3-Ar	4-Ar	Yield (%)
Ph		45
o-$MeO_2C(C_6H_4)$		85
m-$CF_3(C_6H_4)$		23
o-Tol		36
m-$CF_3(C_6H_4)$		76
	Ph	65
	o-$MeO_2C(C_6H_4)$	72
	o-Tol	61

Scheme 50



Scheme 51

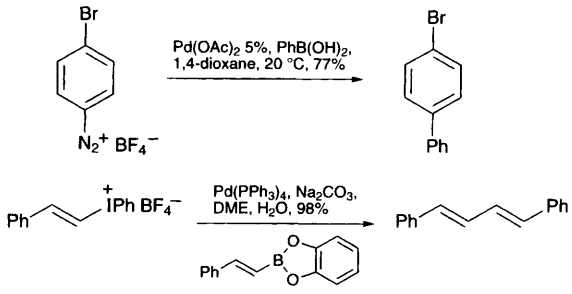
boranes, but both solid supported aryl chlorides and bromides were inert under similar reaction conditions (**Scheme 52**).[100] In the same study solid supported arylboronic esters were successfully coupled with aryl bromides and iodides.[100] A separate research group have also performed Suzuki reactions with immobilised aryl iodides and bromides and have achieved extremely rapid reactions using 45 W microwave irradiation (**Scheme 52**).[101]



X = I, Br
Ar = Ph, *o*- and *p*-MeO(C_6H_4), *o*- and *p*-NO_2(C_6H_4), 2-naphthyl
RAM = Rink amide

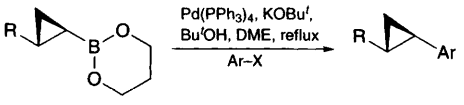
Scheme 52

Colloidal palladium and palladium–nickel clusters are active catalysts for the Heck reaction (**Scheme 45**) and are also excellent catalysts for the Suzuki coupling of boronic acids to haloarenes giving biaryls in near quantitative yields.[87] Diazonium salts have been used as reactive coupling partners in the Stille and Heck reactions and now, for the first time, they have been used in a palladium acetate catalysed Suzuki reaction forming a variety of biaryls at room temperature (**Scheme 53**).[102] The solvent was found to be of the utmost importance with 1,4-dioxane being the solvent of choice. Similarly iodonium salts have been successfully coupled to arylboronic acids with palladium catalysis and under aqueous conditions in near quantitative yields.[103]



Scheme 53

Cyclopropylboronic esters have been coupled to aryl halides with complete retention of cyclopropane geometry for the first time (**Scheme 54**).[104] Under standard Suzuki conditions alkylboronic esters couple only very poorly; however, the hybridisation state of the carbon atoms in the strained cyclopropane ring is of a more sp^2 nature than sp^3 therefore promoting reaction.[104c]



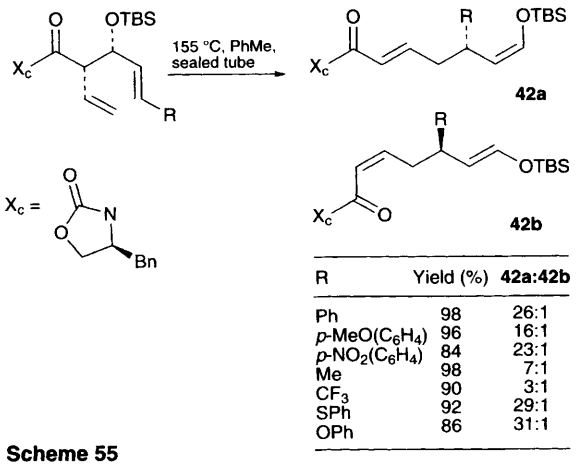
R	Ar–X	Yield (%)
Hex	*p*-MeO(C_6H_4)Br	80
Hex	*p*-Me(C_6H_4)Br	69
Ph	PhI	52

Scheme 54

3.4 Rearrangements

3.4.1 Cope rearrangement

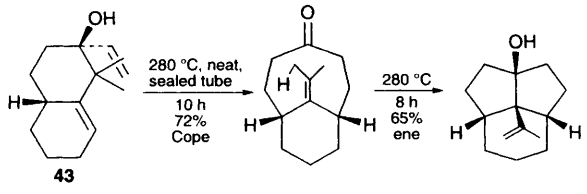
The Cope rearrangement and its variants are important methods for the construction of stereochemically defined alkenes and secondary sp^3 carbon centres. Two separate studies of the siloxy-Cope [3,3] rearrangement of 1,5-dienes made by chiral aldol reactions using the auxiliaries of either Evans or Oppolzer have been reported (**Scheme 55**).[105,106] Analogous oxy-anionic Cope rearrangements in both reports gave low yields due to retroaldol reactions. Cope rearrangement at 220 °C of similar substrates lacking the siloxy substituents also gives high yields of products with excellent stereochemical transmission.[107]



R	Yield (%)	42a:42b
Ph	98	26:1
p-MeO(C_6H_4)	96	16:1
p-NO_2(C_6H_4)	84	23:1
Me	98	7:1
CF_3	90	3:1
SPh	92	29:1
OPh	86	31:1

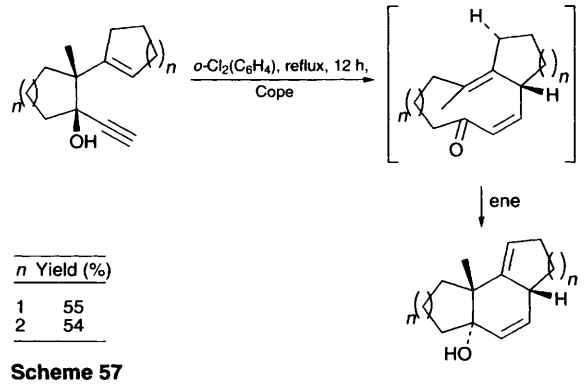
Scheme 55

The oxy-anionic Cope reaction has been previously explored in relation to the synthesis of the taxane skeleton.[108] A new entry to the bicyclo[5.3.1]undecane ring system has been realised by Cope reaction of the readily available decalin 1,5-diene **43** (**Scheme 56**).[109] Caution had to be exercised as extended reaction times promoted a further undesired ene reaction to give a tricyclic hydrocarbon.



Scheme 56

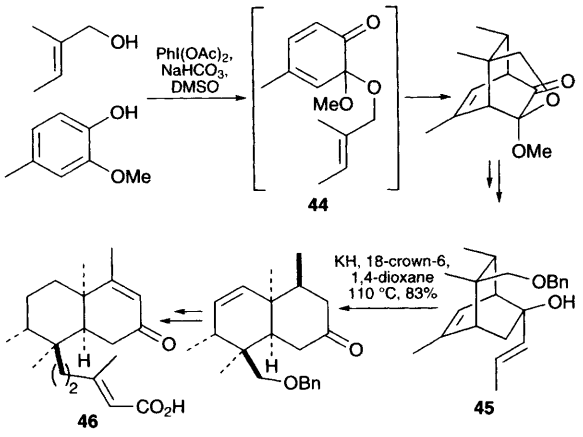
Similarly, tandem Cope–ene rearrangements of 1,5-enynes have allowed access to linearly fused tricyclic compounds (**Scheme 57**).[110]



n	Yield (%)
1	55
2	54

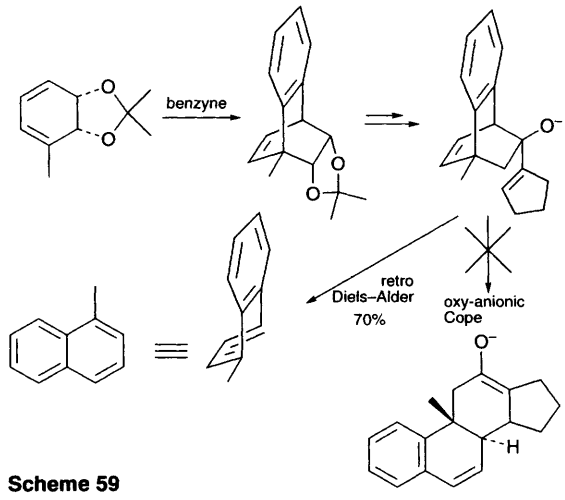
Scheme 57

Oxy-anionic Cope rearrangements of 2-vinylbicyclo[2.2.2]oct-5-en-2-ols gives rise to *cis*-fused decalins with an extremely high degree of stereocontrol.[111] Racemic clerodane diterpenic acid **46** was made using this strategy employing an intramolecular Diels–Alder reaction of a masked *ortho*-quinone **44** to construct the initial [2.2.2] bicyclic ring system **45** (**Scheme 58**).[111a]



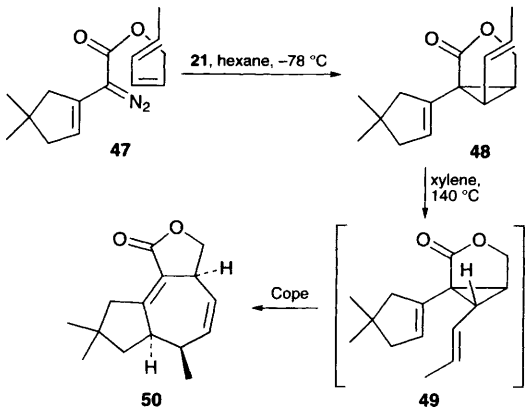
Scheme 58

Enantiopure *cis*-decalins have been constructed using similar methodology, but employing a microbially derived homochiral Diels–Alder diene.[111c] However when trying to synthesise benzo-fused decalins a similar oxy-anionic Cope rearrangement did not occur, only retro-Diels–Alder reaction (**Scheme 59**).[112]

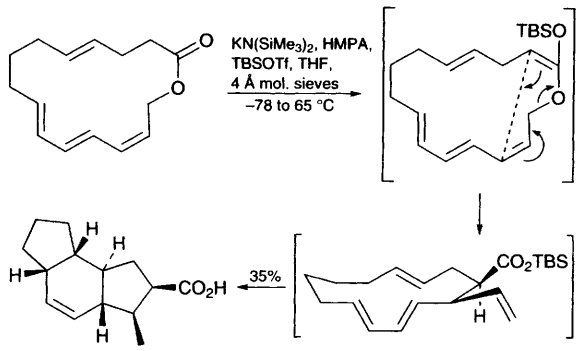


Scheme 59

Tandem cyclopropanation–Cope rearrangement is a popular method for the construction of seven-membered carbocycles and the racemic reaction has been extensively studied.[113] The intermolecular asymmetric reaction has been developed[114] and most recently the intramolecular reaction has been rendered asymmetric (**Scheme 60**).[115] Asymmetric induction was introduced during the cyclopropanation reaction of the diazonium triene **47** using the rhodium prolinate catalyst **21** (**Fig. 2**). Cyclopropanation of the (*E,E*)-1,3-diene occurred in low ee at −78 °C, whereas the *Z,E*-1,3-diene **47** was cyclopropanated in 93% ee at the same temperature. The resultant *trans*-dienylcyclopropane **48** is incapable of undergoing a Cope rearrangement, but at elevated temperatures it isomerises to the *cis*-dienylcyclopropane **49** which then undergoes facile rearrangement to give the desired carbocycle **50**.[115]



Scheme 60



Scheme 62

The same authors have published similar racemic reactions using furans which give 8-oxabicyclo-[3.2.1]octane systems.[116]

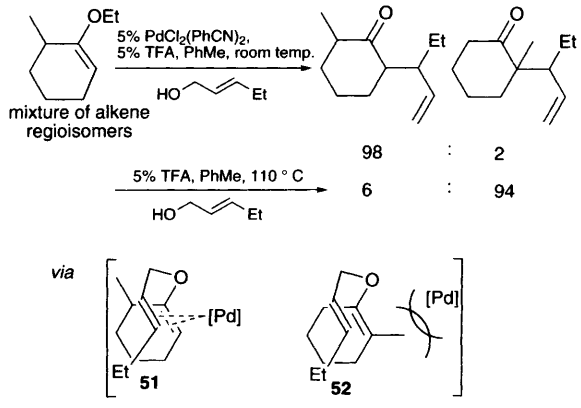
3.4.2 Claisen rearrangement

The Claisen rearrangement and its many variants have recently been reviewed.[117] The rearrangement of 2-(3,3-dimethylallyloxy)indole has been used to efficiently place the 'reverse prenyl' group at the C-3 position of indoles.[118] Palladium(II) catalysed reaction of unsymmetrical cyclohexanone derived enol ethers with allylic alcohols and subsequent Claisen reaction gives 1,3-disubstituted ketones in preference to the tertiary ketones normally seen in the absence of palladium catalysis (**Scheme 61**).[119] The selectivity is argued to arise from the faster reaction of the least substituted enol ether **51**, over the most substituted enol ether **52**.

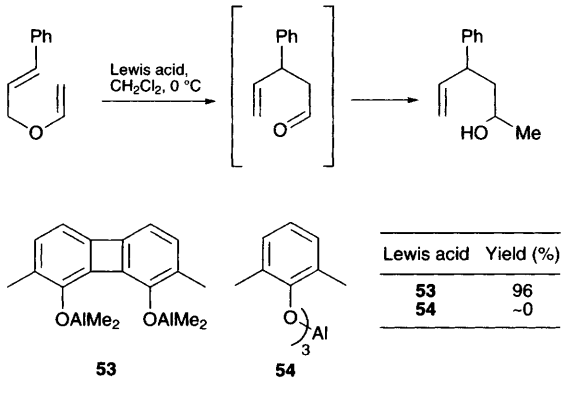
Room temperature *tert*-butyldimethylsilyl triflate (TBS–OTf) promoted formation of ketene silyl acetals and their subsequent Claisen rearrangement was found to be an effective process when dicyclohexylmethylamine was used as base.[120] A more standard silyl ketene acetal Claisen rearrangement was performed where the triene product performed a subsequent transannular Diels–Alder reaction *in situ* (**Scheme 62**).[121]

Lewis acid catalysed rearrangements are generally performed at low temperatures. The previously described Lewis acid tris(2,6-diphenylphenoxy)-aluminium **14** (**Scheme 20**) and the related catalyst tris(4-bromo-2,3-diphenylphenoxy)aluminium have both been used successfully to catalyse the Claisen rearrangement.[122] Similarly the bimetallic Lewis acid **53** has been used for low temperature Claisen rearrangement, with concomitant methyl addition to the aldehyde product (**Scheme 63**).[123] Interestingly the analogous monometallic Lewis acid **54** gave extremely slow reaction under identical conditions.

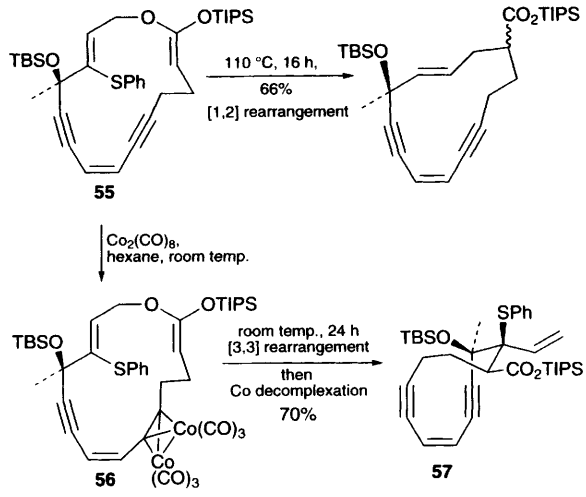
Claisen rearrangements can only take place in a concerted manner if the diene termini can approach to within bonding distance of each other under the reaction conditions. The trienediyne **55** when heated does not undergo Claisen rearrangement as the alkynes hold the molecule in an unreactive conformation. The molecule instead performs a non-concerted [1,2]sigmatropic shift (**Scheme 64**).[124] Complexation of one of the alkynes with dicobalt octacarbonyl narrows the bond angles of the triple bond and therefore the overall molecular conformation is altered. When the complexed substrate **56** is stirred in hexane at room temperature for twenty-four hours the Claisen rearranged product **57** is obtained in 70% yield, after cobalt decomplexation.



Scheme 61



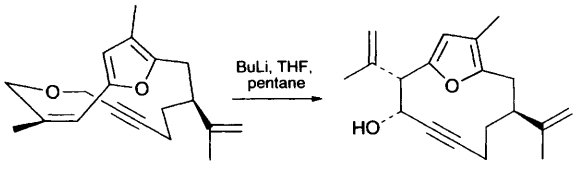
Scheme 63



Scheme 64

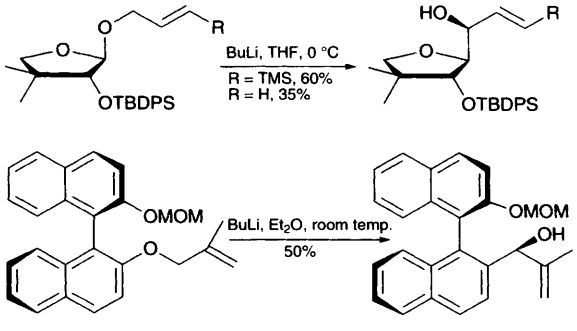
3.4.3 Wittig rearrangement

Marshall *et al.* used a highly diastereoselective [2,3]Wittig rearrangement in their synthesis of racemic kallolide B and have now performed the reaction in the enantiomerically pure (−)-series (**Scheme 65**).[125] The rearrangement is unusually selective and this has been argued to arise from the good collinear alignment of the alkene π system and one of the prop-2-ynyl carbon–hydrogen bonds.



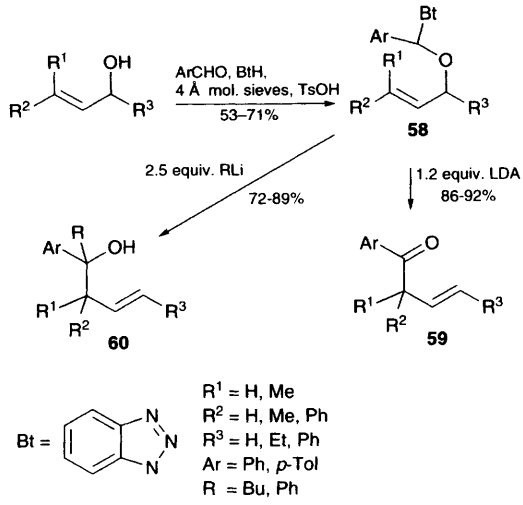
Scheme 65

Sugar substrates have also been used in highly diastereoselective Wittig [1,2]rearrangements (**Scheme 66**).[126] Similarly, complete stereochemical transfer is seen in the Wittig [1,2]reactions of monoallyl protected binaphthols (**Scheme 66**).[127]



Scheme 66

[2,3]Wittig rearrangements have been successfully carried out using the benzotriazole (BtH) methodology pioneered by Katritzky *et al.* (**Scheme 67**).[128] Interestingly the ketones **59** formed by the addition of 1.2 equiv. of LDA to allyl ethers **58** can be isolated or, if a two fold excess of alkyllithium or aryllithium is used as base, the tertiary alcohols **60** are isolated in good yields.



Scheme 67

3.5 Alkene metathesis

The current trend of exploiting alkene metathesis in synthesis has been highlighted as the key macrocyclisation steps in two different approaches to the potent anticancer agent epothilone by the research groups of Nicolaou[129] and Danishefsky.[130] Fürstner *et al.* reported the falsehood of the notion that a macrocyclic ring closing alkene metathesis reaction needs a certain amount of preorganisation. Studies showed that conformationally flexible substrates can be cyclised in high yield.[131] Other researchers have used ring closing alkene metathesis in the synthesis of novel β-lactams,[132] rigidified amino acids and peptides,[133] crown ethers[134] and bridged calix[4]-arenes.[135] The rise of the metathesis as a synthetically useful reaction has been promoted by the availability of the transition metal carbene catalysts such as the Grubbs' catalyst **61** (**Fig. 3**). Grubbs *et al.* have developed the modified catalysts **62a** and **62b** (**Fig. 3**) which have both been used to perform ring opening polymerisation of alkenes in aqueous solution.[136]

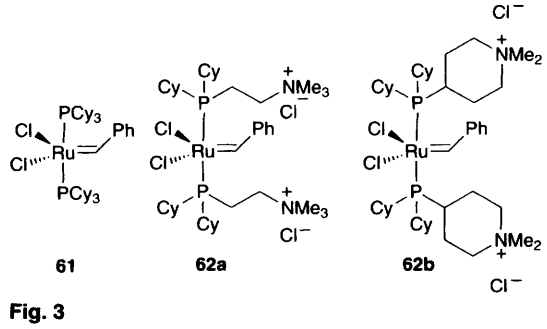
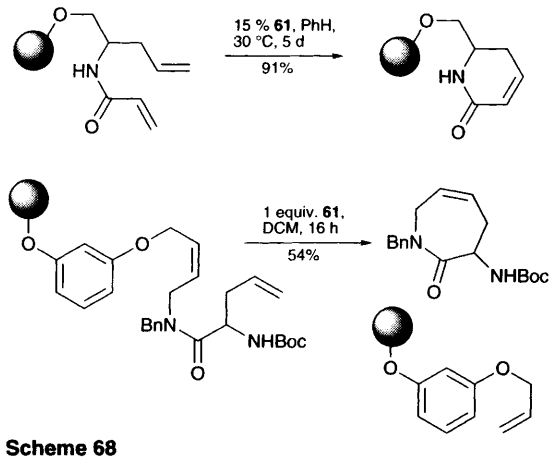


Fig. 3

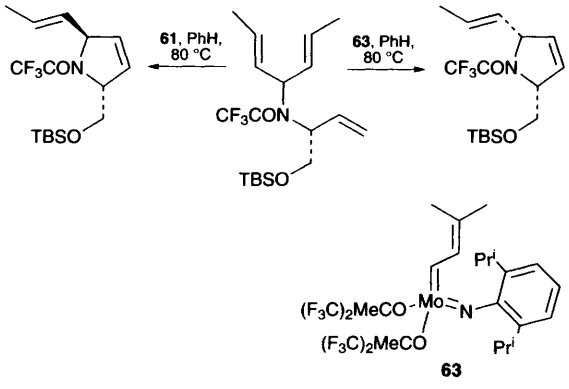
Two solid phase applications of ring closing metathesis have been reported. In the first approach

dienes immobilised on a tentagel resin were cyclised giving nitrogenous heterocycles in very high yields.[137] This method gives the cyclised product immobilised on the solid support (**Scheme 68**). An alternative method uses a diene that is attached to the resin at an alkene terminus which on treatment with catalyst **61** releases cyclised products into solution (Scheme 68).[138] This second method has the disadvantage that stoichiometric amounts of **61** are needed to effect relatively rapid reactions in reasonable yields.



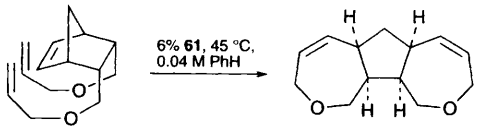
Scheme 68

Synthetically useful and complementary levels of *syn*:*anti* selectivity have been achieved in the synthesis of nitrogen heterocycles using either Schrock's catalyst **63** or Grubbs' catalyst **61** (**Scheme 69**).[139]



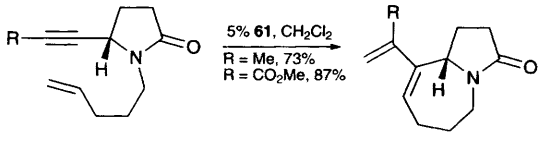
Scheme 69

Recently Grubbs *et al.* published an interesting slant on the metathesis reaction, a tandem ring opening–ring closing metathesis cascade.[140] The example given (**Scheme 70**) uses the ring strain of the norbornene ring to drive the initial ring opening. Other examples have also been reported where central monocyclic rings of different sizes (four- to eight-membered) have been cross-metathesised giving good yields of bicyclic products.



Scheme 70

Metathesis of enynes gives cyclic alkenes with vinyl substituents in good yields (**Scheme 71**).[141] Tungsten based metathesis catalysts have been used to macrocyclise alkenes appended to glucose based centres.[142] The tungsten based catalysts, though less widely used, are considerably cheaper to synthesise than the Grubbs and Schrock catalysts **61** and **63**.

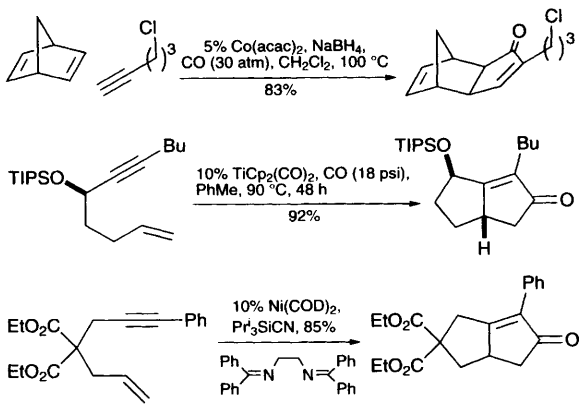


Scheme 71

3.6 Miscellaneous

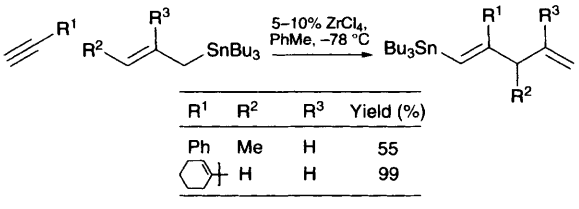
The large number of alkene syntheses in the chemical literature, even over the narrow period of coverage of this article, prevents the publication of an exhaustive list of all reactions. However, a selection of interesting reactions that do not easily fit into the sections above is given here.

The synthesis of cyclopentenones is a vigorous area of research. The Pauson–Khand reaction, a cyclisation of alkene, alkyne and carbon monoxide mediated by stoichiometric amounts cobalt carbonyl complexes, is a popular method for the construction of this ring system.[143] The Pauson–Khand reaction does have its limitations but a recent report has achieved similar reactions using catalytic amounts of cobalt(II) acetoacetate in the presence of sodium borohydride under 30 atmospheres of carbon monoxide (**Scheme 72**).[144] Buchwald *et al.* have used catalytic amounts of $Cp_2Ti(CO)_2$ to similarly cyclise alkene, alkyne and carbon monoxide,[145] and $Ni(COD)_2$ to cyclise alkene, alkyne and cyanides (**Scheme 72**).[146]



Scheme 72

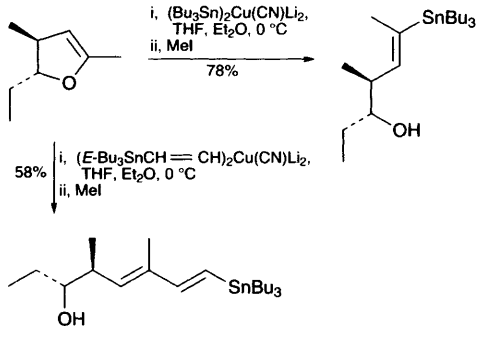
Alkynes are extremely versatile starting materials for the synthesis of alkenes. A popular synthetic strategy is the allylmetallation of activated alkynes to give 1,4-dienes.[147] Similar reactions of unactivated alkynes are limited to the addition of only a few allylmetals.[147] Zirconium tetrachloride catalysed allylstannylation of simple alkyl, alkenyl and aryl alkynes, however, gives 1-stannyl-1,4-dienes in good yields (**Scheme 73**).[148] The stannanes produced are ideal substrates for Stille coupling reactions to synthesise polyenes.



R^1	R^2	R^3	Yield (%)
Ph	Me	H	55
	H	H	99

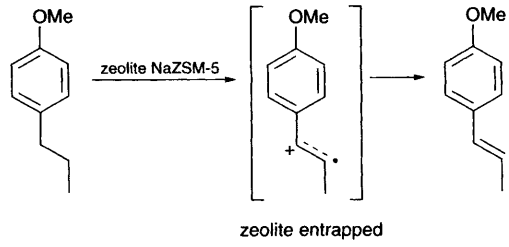
Scheme 73

The metallate rearrangement first used by Kocienski *et al.* in their synthesis of lacrimin A[149] has been adapted to allow the incorporation of tributylstannyl and (2-tributylstannyl)vinyl groups (**Scheme 74**).[150] Once again, the vinylstannanes made by this method are extremely versatile intermediates for the synthesis of polyene products.



Scheme 74

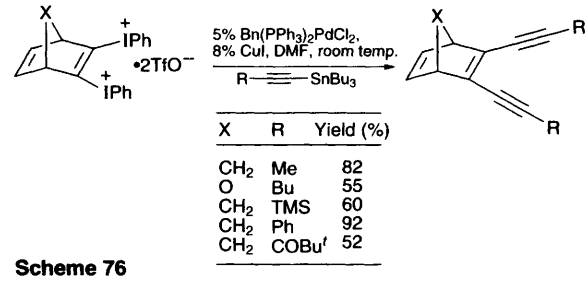
Alkane transfer dehydrogenation is a potentially useful industrial process and academic interest in various transition metal complexes that catalyse the reaction has been intensive over the last 15 years.[151] Recently, rhodium catalysts with,[152] and without,[153] the presence of a hydrogen atmosphere and iridium catalysts,[154,155] with the aid of a hydrogen acceptor, have been the subject of study. Zeolites can also effect dehydrogenation of hydrocarbons.[156] In fact, the radical cation intermediates are long lived and can be detected by EPR spectroscopy (**Scheme 75**).[157]



Scheme 75

4 Alkynic hydrocarbons

The enhanced acidity and ready deprotonation of terminal alkynes means that triple bonds are most easily incorporated into organic molecules in one fragment, rather than by actual triple bond construction. The discovery, synthesis and continued interest in the enediyne natural products has brought about a host of methods for the coupling of alkynes to alkenes, with palladium catalysed reactions dominating the area of $sp–sp^2$ couplings. Catechol ditriflates have been coupled to two terminal alkynes in the presence of palladium(0) catalysts, copper(I) iodide and tetrabutylammonium iodide.[158] Other activated dienyl fragments such as bis[phenyl(trifluoromethanesulfonyl)oxy]iodoalkenes have been used in coupling reactions with alkynylstannanes and alkynylcuprates at room temperature or below (**Scheme 76**).[159] These mild conditions have allowed the synthesis of several sensitive enediynes that were inaccessible *via* other routes. Similarly terminal alkynes[160] and alkynyl boronates[103] have been arylated with diphenyliodonium salts and iodanes under palladium catalysis in aqueous media. Terminal alkynes are readily acylated, without the need for a strong base, using acyl chlorides, amine bases and a catalytic amount of copper(I) iodide.[161]

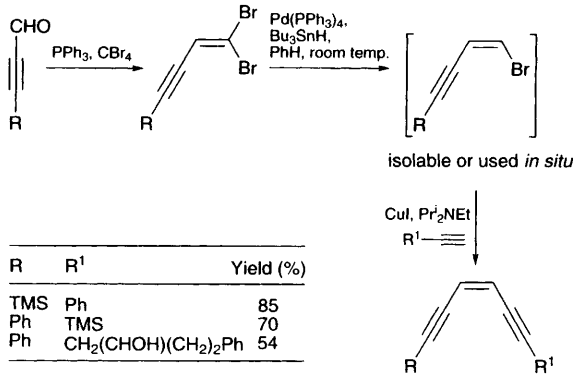


X	R	Yield (%)
CH_2	Me	82
O	Bu	55
CH_2	TMS	60
CH_2	Ph	92
CH_2	$COBu^t$	52

Scheme 76

A regioselective palladium catalysed dehalogenation of alkenyl *gem*-dibromides gives *Z*-vinyl

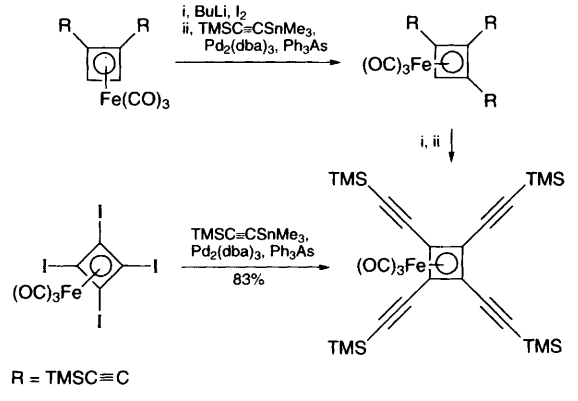
bromides which can be coupled to alkynes *in situ* giving enediynes in good yields (**Scheme 77**).[162] Terminal alkynes regioselectively insert into stable palladacycles at room temperature to form alkynated products, whereas internal alkynes insert non-selectively to give cyclic alkenes.[163]



R	R^1	Yield (%)
TMS	Ph	85
Ph	TMS	70
Ph	$CH_2(CHOH)(CH_2)_2Ph$	54

Scheme 77

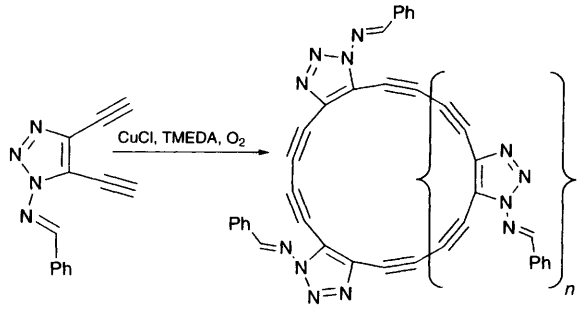
Chemists trying to create novel carbon frameworks are limited by the bond angles that stable carbon rings and chains can form. Stable compounds with 90° angles, ideal for the construction of polyalkyne networks, are not readily available. However, Stille couplings of tricarbonyl iron complexes of tetraiodocyclobutadiene with alkynylstannanes gives the desired product where all four alkynyl substituents are at right angles to each other.[164] Iterative Stille reaction–iodination sequences have given mono-, di- and tri-alkynyl substituted tricarbonyl iron cyclobutadienes (**Scheme 78**).[164]



R = TMSC≡C

Scheme 78

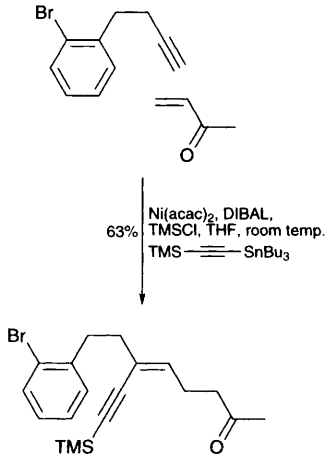
Oligimerisation of 4,5-dialkynyltriazoles promoted by copper(I) chloride and dioxygen gives tri-, tetra- and penta-meric structures; however attempted decomposition of the triazoles to give cycloalkynes was unsuccessful (**Scheme 79**).[165]



Scheme 79

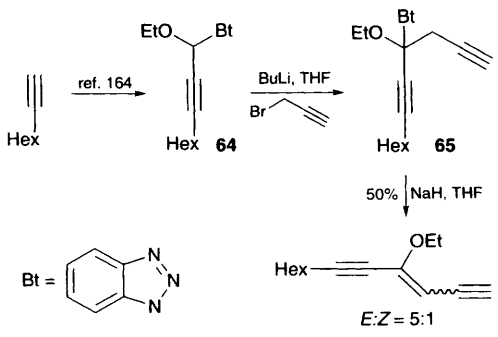
n = 1,2,3

One-pot three-component nickel catalysed couplings of an alkyne, an enone and a tributylstannylalkyne give *Z*-enyne products in moderate yields (**Scheme 80**).[166] The reaction is extremely general, allowing both terminal and internal alkynes, cyclic and aliphatic and aromatic acyclic enones (and enals) to take part in the cascade reaction. Rhodium catalysed dimerisations of terminal alkynes give regiomeric and geometric mixtures of enyne products that vary depending on the nature of the groups attached to the triple bond.[167]



Scheme 80

Previously synthesised prop-2-ynyl substituted benzotriazole **64**[168] is readily coupled with prop-2-ynyl bromide to give the diyne **65**. Base induced benzotriazole elimination of **65** gives an enediyne product, with the *E*-isomer predominating (**Scheme 81**).[169]

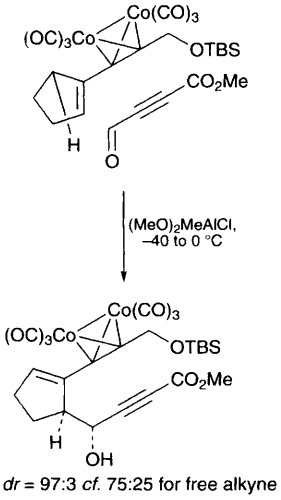


Scheme 81

Good yields of alkynyl substituted cyclohexanes with modest equatorial selectivity have been achieved by the isomerisation of allenes with potassium *N*-methylbutylamide.[170] Conversely, treatment of prop-2-ynylboranes derived from chiral diisopinocampheylboron chloride with aldehydes gives good yields of allenes with very high ees.[171]

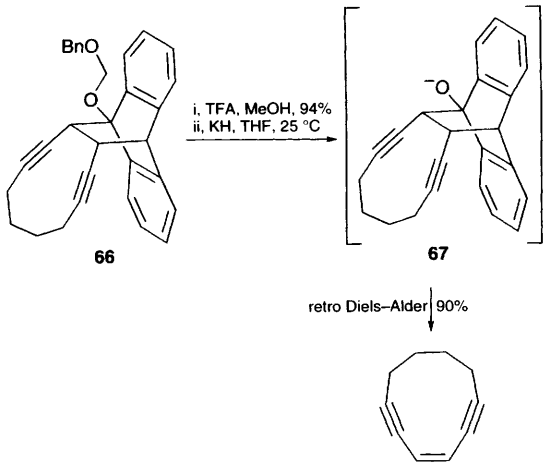
Two alkynes can be 1,5-linked using an intermolecular ene reaction; however this was only mildly selective.[172] 94% *erythro*-selectivity was achieved when the alkyne was complexed to a dicobalthexacarbonyl cluster (**Scheme 82**).[172] The enhanced selectivity is postulated to come about due to the increased steric demands of the cobalt coordinated alkyne in the chairlike transition state. Complexation of an alkyne to a dicobalthexacarbonyl cluster is a common method for alkyne protection; however one of the carbonyl ligands can be exchanged with a triphenylphosphine ligand under ultraviolet irradiation to give new complexes.[173] The chiral glyphos ligand has also been coordinated to one of the cobalt centres to give optically active complexes for use in asymmetric Pauson–Khand reactions.[174]

A novel method for generating sensitive enediynes from stable precursors has been reported by Nicolaou *et al.*[175] Retro-Diels–Alder reactions in general require high temperatures, but the 9-benzyloxymethoxyanthracene Diels–Alder adduct **66**



dr = 97:3 *cf.* 75:25 for free alkyne

Scheme 82



Scheme 83

undergoes facile room temperature retro-Diels–Alder reaction to give enediyne on generation of the oxyanion **67** (**Scheme 83**).

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