MAGNESIUM

ANNUAL SURVEY COVERING THE YEAR 1978[+]

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[+] Magnesium; Annual Survey covering the year 1977 see J.Organometal. Chem., 176 (1979) 1 - 135.

I. INTRODUCTION

In 1978 there appeared the famous book by Kochi on "Organometallic Mechanisms and Catalysis" which is of extreme value to all chemists engaged in organometallic chemistry [1].

Review articles published during 1978 which are concerned largely with organomagnesium chemistry include:

A review by Meyers of asymmetric carbon-carbon bond formation from chiral oxazolines [2].

A review by Normant on stoichiometric versus catalytic use of copper(I) salts in the synthetic use of main group organometallics [3].

A review by Stirling on nucleophilic eliminative ring fission including a novel nomenclature and classification of organomagnesium ring-chain rearrangements [4].

Other reviews which have a smaller content of organomagnesium chemistry, but which may prove useful for leading references are concerned with:

The synthesis of organophosphorus compounds directly from the element [5].

Propargylic metalation [6].

Oxidative coupling of aromatic systems under the influence of transition metal compounds [7].

Cryptates: the chemistry of macropolycyclic inclusion complexes [8].

Some aspects of organometallic chemistry of nontransition metals [9].

An undergraduate Grignard reaction experiment for polymerization of ethene and propene has been described using a PhMgCl-$TiCl_4$ catalyst [10]. This avoids the hazards involved with the usual Ziegler catalysts and illustrates the generality of organometallic catalysts.

The following doctoral theses with heavy content in organomagnesium chemistry appeared in 1978:

R. M. Bension (Pennsylvania State University), "The addition of Grignard and other organometallic reagents to alkenols" [11].

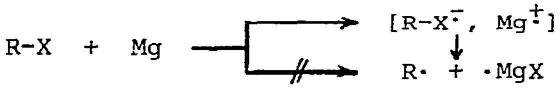
J. S. Bowers, Jr. (Georgia Institute of Technology), "Mechanistic studies concerning the nature of alkyl transfer in main group organometallic compound additions to ketones" [12].

F. A. Hartog (Vrije Universiteit, Amsterdam), "The Barbier Reaction, a mechanistic study" [13].

II. PREPARATION OF ORGANOMAGNESIUM COMPOUNDS

A. Reaction of magnesium metal with organic halogen compounds

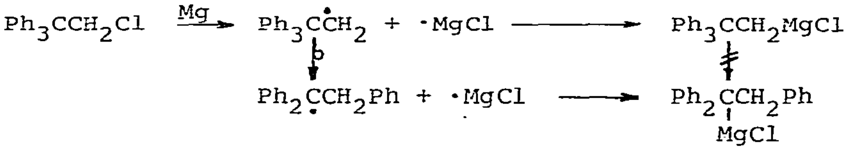
The formation of the Grignard reagent from alkyl halide and magnesium is of continued mechanistic interest. In a study of Grignard reagent formation it was found that there is no carbon kinetic isotope effect in the formation of methylmagnesium iodide from methyl iodide in diethyl ether. Calculations indicate that an observable $^{12}C/^{13}C$ isotope effect should accompany this reaction if it proceeds by an inner-sphere electron-transfer mechanism in which breakage of the carbon-halogen bond must be involved in the rate-determining step. Accordingly, it is proposed that the alternative mechanism must be followed, with the rate-determining step involving formation of a tight radical-ion pair by outer-sphere electron transfer from the magnesium to the organic halide. Subsequently the tight radical-ion pair might collapse to the loose radical pair [14].



In another study it has been demonstrated that, contrary to an earlier report, during the formation reaction of methylmagnesium iodide in allyl phenyl ether almost no methane is formed, but mainly ethane and 1-butene. Approximately 20 % of the initially present iodomethane gave rise to C_2H_6 and C_4H_8 in the ratio 2 : 1. The mechanism of formation of the side products can easily be derived from CIDNP. Thus 1-butene is formed mainly by addition of methyl radicals to the terminal CH_2 group of allyl phenyl ether, followed by ß-scission and extrusion of a phenoxy radical and not by combination of a methyl and an allyl radical [15].

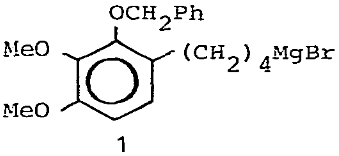
$$PhOCH_2CH{=}CH_2 \xrightarrow{\cdot CH_3} PhOCH_2\dot{C}HCH_2CH_3 \longrightarrow PhO\cdot + CH_2{=}CHCH_2CH_3$$

Evidence for radical formation during the preparation of Grignard reagents was also obtained in the reaction of 2-chloro-1,1,1-triphenylethane and other ß-phenylalkyl halides with magnesium. Although the organomagnesium product itself does not rearrange, an appreciable amount of 1,2-phenyl migration was observed, especially in diethyl ether as the solvent. In THF, on the other hand, the quantity of rearranged organomagnesium compound is negligible. The quantity of rearranged hydrocarbon by-products, however, was appreciable in all of the ethereal solvents investigated [16].

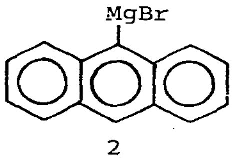


$$\begin{tikzcd}Ph_3CCH_2Cl \arrow[r, "Mg"] & Ph_3C\dot{C}H_2 + \cdot MgCl \arrow[r] \arrow[d] & Ph_3CCH_2MgCl \arrow[d, "/" marking] \\ & Ph_2\dot{C}CH_2Ph + \cdot MgCl \arrow[r] & Ph_2C(MgCl)CH_2Ph\end{tikzcd}$$

Activated magnesium (Rieke) was required for the production of the 4-arylbutylmagnesium bromide 1 [17], and the Grignard reagent 2 has been prepared from 9-bromoanthracene by entrainment with ethylene bromide [18].



1



2

Alkyl- or phenylmagnesium halides were prepared at 80 - 140° C in toluene in the presence of 0.4 - 3.0 mol% $RSi(OEt)_3$ (R=Ph, halophenyl, haloalkyl) as catalyst [19]. Magnesium powder was used to prepare dialkylmagnesium compounds in acyclic liquid hydrocarbons starting from n-alkyl halides, e.g. butyl chloride and octyl chloride.

The addition of sec- or tert-butyllithium yields stable solutions of the corresponding diorganomagnesium ate-complexes [20].

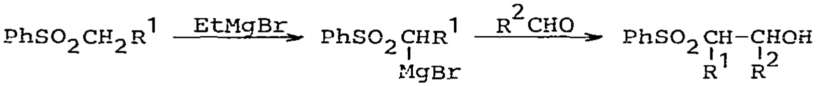
B. Other reactions which form organomagnesium compounds

Introduction of magnesium by deprotonation (metalation) is commonplace for terminal alkynes and cyclopentadienes. This reaction was even used for purification of C_{4-7} hydrocarbons containing acetylene and cyclopentadiene [21].

The metalation kinetics of acetylenes, $R^1C{\equiv}CH$ (R^1 = Bu, Me_3C, Ph) with substituted magnesium diphenyls, $(R^2C_6H_4)_2Mg$ (R^2 = H, m- or p-Me or -Cl) was studied in THF, Et_2O, and Bu_2O. The substituent and solvent effects are interpreted in terms of a four-center reagent-like transition state [22].

The pentamethylcyclopentadienide Grignard reagent, Me_5C_5MgCl, was prepared by metalating pentamethylcyclopentadiene with isopropylmagnesium chloride in refluxing toluene [23].

Alkyl aryl sulfones are also converted to organomagnesium derivatives by deprotonation [24, 25, 26].



$$PhSO_2CH_2R^1 \xrightarrow{EtMgBr} PhSO_2\underset{MgBr}{CHR^1} \xrightarrow{R^2CHO} PhSO_2\underset{R^1}{CH}-\underset{R^2}{CHOH}$$

Magnesium-mercury exchange has been used as the first step for synthesis of the complex compound 3 whose structure is given and which is prepared by the direct reaction of $Hg(SiMe_2Ph)_2$ with magnesium metal in DME solvent. Most interestingly the reaction gives rise to cleavage of a methyl group from DME [27].

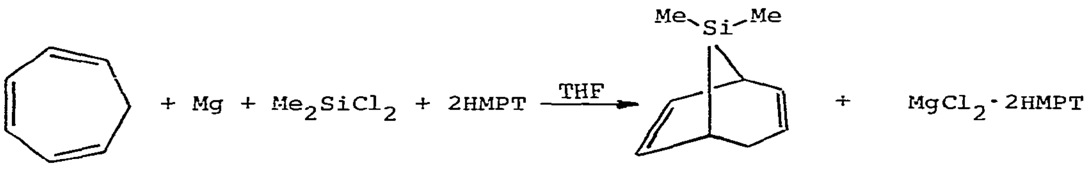
$$Hg(SiMe_2Ph)_2 \xrightarrow[DME]{Mg} Mg(SiMe_2Ph)_2 \longrightarrow \longrightarrow$$

$$[Mg_4(OCH_2CH_2OMe)_6(DME)_2][Hg(SiMe_2Ph)_3]_2$$

3

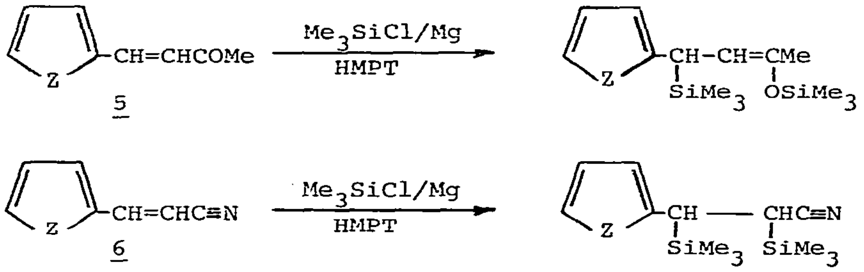
The reaction of propyne and propadiene (allene) on evaporated magnesium films has been studied at 373 and 423 K. Self-hydrogenation was observed in each case with the formation of propene. The organometallic species which remained adsorbed on the magnesium were desorbed by D_2O and characterized as the deuterated hydrocarbons. Monodeuterated (at 423 K perdeuterated) propyne and monodeuterated propene were obtained consistent with a mechanism involving dehydrogenation of the starting material with the formation of magnesium hydride and a two-step hydrogenation via half-hydrogenated intermediates [28].

The bicyclic sila analog of tropadiene 4 has been synthesized in 12 % yield by treating cycloheptatriene with magnesium in the presence of Me_2SiCl_2 and two moles of HMPT [29].



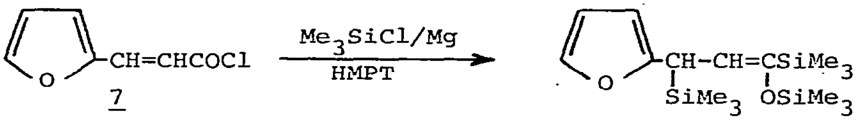
4

The silylation of the α,β-unsaturated ketones 5 using the $Me_3SiCl/Mg/HMPT$ system also occurs in the 1,4 position accompanied by reductive dimerization. The corresponding nitriles 6, on the other hand, yield 1,2 products [30].

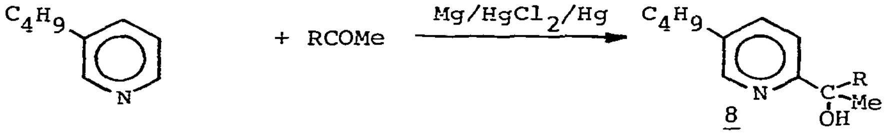


Z = O, S

Starting with the chloride 7 a third trimethylsilyl group is introduced by substitution of the chlorine atom [30].

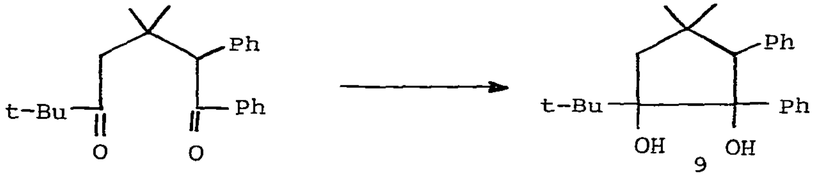


On heating 3-butylpyridine with alkyl methyl ketones in the presence of amalgamated magnesium 5-butyl-2-(1-hydroxyethyl)pyridines 8 were obtained in 60 % yield. Acetone (R = Me), however, reacted less selectively yielding up to 25 % of the 2,3-disubstituted compound. Side reaction in each case is the formation of the corresponding pinacol [31].



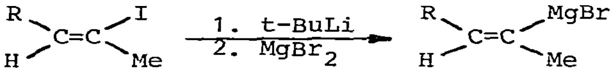
8

Pinacol-d_{12} hexahydrate was prepared from $(CD_3)_2CO$, magnesium, and mercury(II) chloride [32]. An intramolecular pinacol synthesis was used to prepare the 1,2-cyclopentandiol 9 [33].



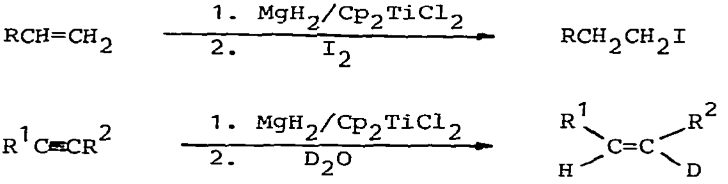
9

A vinyl Grignard reagent 10 was synthesized via the corresponding lithium derivative adding magnesium bromide prepared from 1,2-dibromoethane and magnesium metal [34].

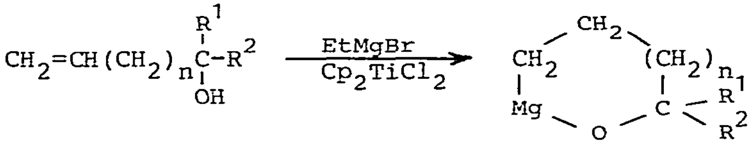


10

Intermediate organomagnesium compounds are also formed during the hydrometallation of alkenes and alkynes with magnesium hydride in the presence of bis-(cyclopentadienyl)titaniumdichloride (Cp_2TiCl_2) as determined by quenching the reaction mixture with iodine or D_2O [35].



The same catalyst was used for the hydromagnesiation of alkenols with ethylmagnesium bromide as source of the magnesium hydride whereby cyclic alkylmagnesium alkoxides are formed. The ethylene evolved serves as an indicator of reaction [36].



n = 0; 1

With the new reagents MgH_2/CuI or $MgH_2/CuOBu\text{-}t$ alkynes may be converted to cis-alkenes. No trans-alkenes or alkanes were detected. The advantages of this method over catalytic hydrogenation lie in the purity of the product formed and in the high stereospecificity of the reaction [37].

Other magnesium hydride derivatives prepared and studied especially in their reaction with carbonyl compounds were 2,6-di-isopropylphenoxymagnesium hydride [38], hydridomagnesium alkoxides, HMgOR [39], dialkylaminomagnesium hydrides, $HMgNR_2$ [40, 41] as well as ate-complexes of the type, $LiMgH_3$, $LiMgH_{3-n}R_n$, $LiMg_2H_5$, $LiMg_2H_{5-n}R_n$ [42], and $HMgAlH_3R$, $HMgBH_3R$ [43].

For organomagnesium compounds formed by the addition of Grignard reagents to carbon-carbon unsaturation see section V. B.

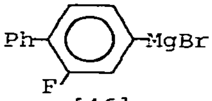
C. Some organomagnesium compounds prepared or studied

In this section, a variety of functionally-substituted organomagnesium reagents or other reagents of less typical structure will be surveyed.

1. Halogen-substituted compounds

The following fluorinated Grignard reagents have been prepared from the corresponding bromides and magnesium metal:

[44, 45]



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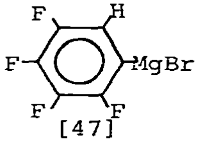

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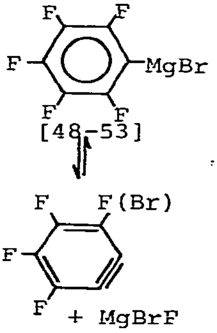
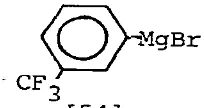
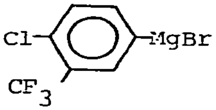


[48-53]



[54]



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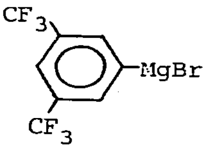
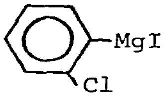


[56]

The elimination of magnesium halide from pentafluorophenylmagnesium bromide in boiling cyclohexane was shown to be reversible yielding 17 % of a bromotrifluorobenzyne adduct with 1-methoxynaphthalene [48].

Selective formation of the following chloro- and bromoaryl mono-Grignard reagents has been reported:



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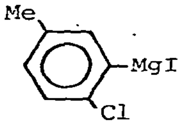
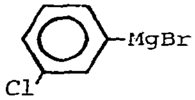


[58]



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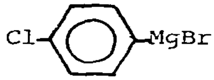
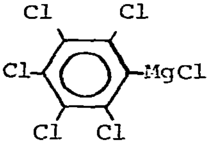


[60-66]



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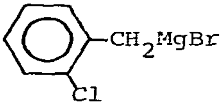

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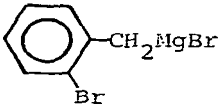

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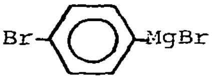
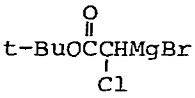


[69]

Even some aliphatic chlorine- and brominesubstituted organomagnesium compounds have been prepared:



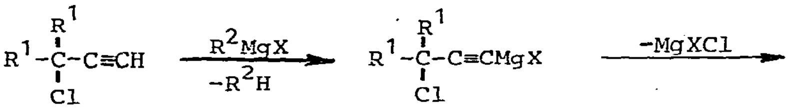
$$t\text{-BuO}\overset{O}{\overset{\|}{C}}\underset{\underset{Cl}{|}}{C}HMgBr$$

[70]

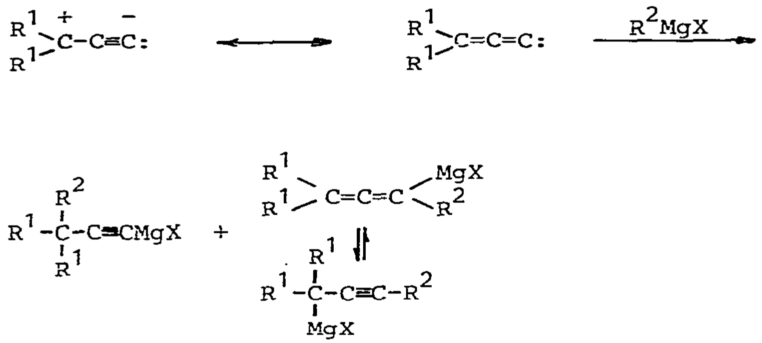
$Br(CH_2)_3C\equiv CMgBr$

[71, 72]

The corresponding reagents from terminal propargylic chlorides, however, eliminate magnesium halide to form an allene carbene-zwitterion intermediate. Reaction of this intermediate with a second molecule of alkyl Grignard reagent generates a mixture of propargyl and allenyl Grignard reagents. No evidence was found for the occurrence of carbonium ion, free radical, or S_N2' reaction pathways [73].



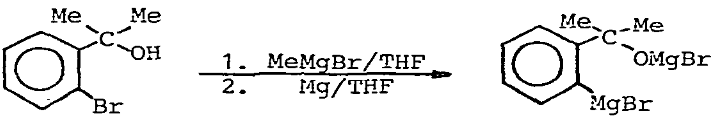
$$R^1-\underset{\underset{Cl}{|}}{\overset{\overset{R^1}{|}}{C}}-C\equiv CH \xrightarrow[-R^2H]{R^2MgX} R^1-\underset{\underset{Cl}{|}}{\overset{\overset{R^1}{|}}{C}}-C\equiv CMgX \xrightarrow{-MgXCl}$$



2. Hydroxy-, alkoxy-, and acetal-substituted compounds

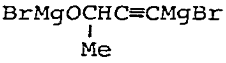
"Nonprotected" hydroxy Grignard reagents were prepared by first converting the OH group to an alkoxide [74, 75, 76]:

$$HO(CH_2)_nCl \xrightarrow[\text{2. Mg/THF}]{\text{1. RMgCl/THF}} ClMgO(CH_2)_nMgCl$$



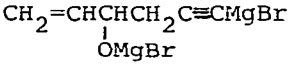
Several organomagnesium compounds were prepared from hydroxy-substituted acetylene and an excess of ethylmagnesium bromide; e.g.

$BrMgOCH_2C{\equiv}CMgBr$ [77]



$BrMgO\underset{Me}{C}HC{\equiv}CMgBr$

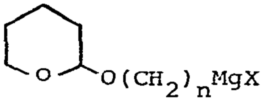
[78]



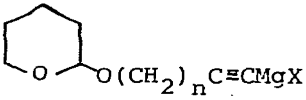
$CH_2{=}CH\underset{OMgBr}{C}HCH_2C{\equiv}CMgBr$

[79]

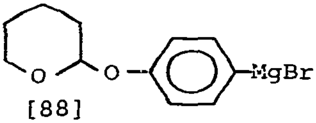
Ether or acetal groups have been used to protect a hydroxyl function, and then removed after formation and reaction of the Grignard reagents. Examples include the following:



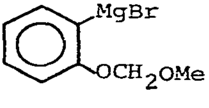
n = 5 - 11 [80-85]



n = 1,2 [86, 87]

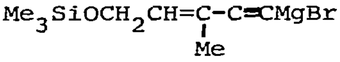


[88]



[89]

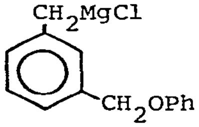
$Me_3SiO(CH_2)_5MgCl$ [90]



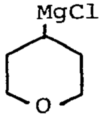
$Me_3SiOCH_2CH{=}\underset{Me}{C}{-}C{\equiv}CMgBr$

[91]

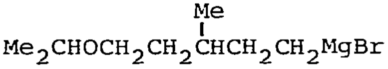
Stable ether or thio ether functions have been introduced by the following organomagnesium compounds whereby the first two were obtained in much better yields by entrainment with bromoethane [92] or 1,2-dibromoethane [93]:



[92]



[93]



$Me_2CHOCH_2CH_2CH(Me)CH_2CH_2MgBr$

[94]

$PhCH_2CH_2OCH_2C{\equiv}CMgBr$

[95]

$X(CH_2)_nMgCl$

X = OMe, SMe

n = 3,4 [96,97]

$PhS(CH_2)_3MgBr$

[98,99]

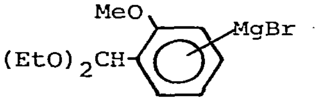
Organomagnesium derivatives of epoxy sulfones on the other hand undergo an intramolecular nucleophilic attack at the terminal C-O bond with the formation of cycloalkanol derivatives in excellent yields [25].

n = 1,2

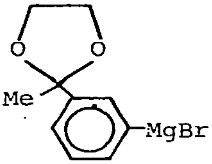
Aldehyde and ketone functions within Grignard reagents of course always have to be protected, as the rule by formation of acetals or ketals, respectively. Examples include the following:

$(EtO)_2CHC{\equiv}CMgBr$

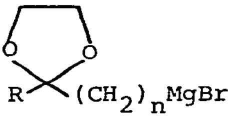
[100, 101]



[102]

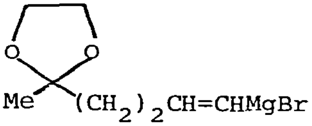


[103]

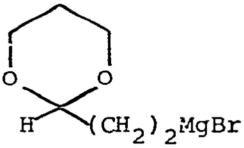


R = H; n = 2 [104]

R = Me; n = 2,6 [99,105]



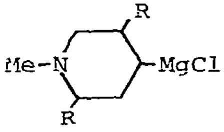
[106]



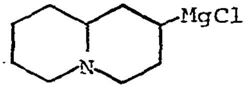
[107]

3. Amino-substituted compounds

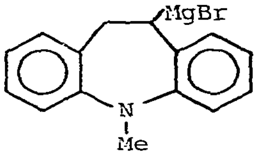
The use of γ-dimethylaminopropylmagnesium chloride has now become quite commonplace, and references will not be given. The following heterocyclic Grignard reagents also bearing the nitrogen in the γ position have been prepared:



R = H, Me [108-111]

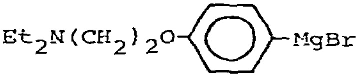


[112]

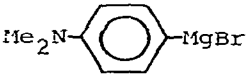


[113,114]

Examples of amino- and phosphino-substituted phenylmagnesium bromides include the following:



[115]

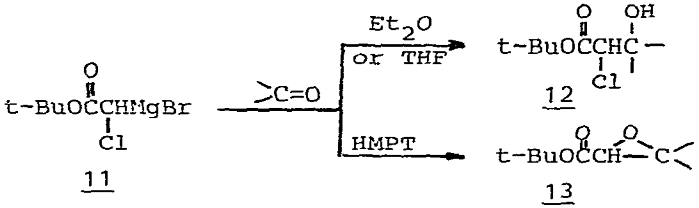


[116]

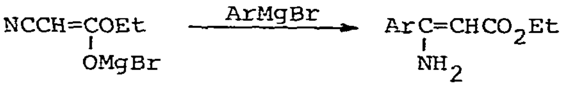
[117]

4. Carboxy- and carbonyl-substituted compounds; enolates

The organomagnesium compound 11 adds to cyclohexanone derivatives whereby different products are formed depending on the solvent. While α-chloro-β-hydroxy esters 12 were obtained in Et_2O or THF as the solvent, the corresponding epoxides 13 were formed in the presence of HMPT [70]:

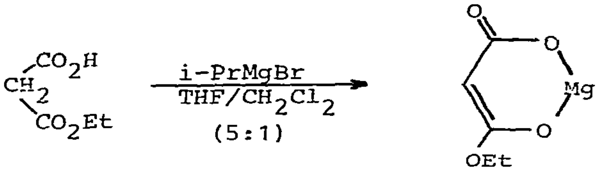


β-Aminocinnamates 15 have been prepared in moderate yields by the addition of an appropriate aryl Grignard reagent to the enolate 14 formed from phenylmagnesium bromide and ethyl cyanoacetate [118].

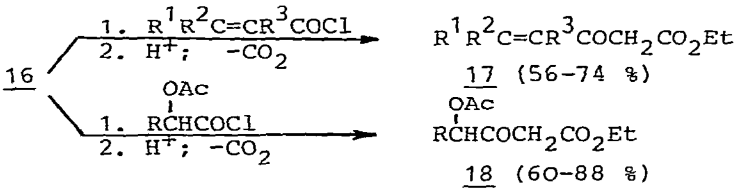


$$\underset{\textstyle 14}{NCCH{=}C(OMgBr)OEt} \xrightarrow{ArMgBr} \underset{\textstyle 15}{ArC(NH_2){=}CHCO_2Et}$$

The magnesium enolate 16 prepared by reaction of ethyl hydrogen malonate with isopropylmagnesium bromide provides a useful route to γ,δ-unsaturated ß-ketoesters 17 and γ-acetoxy ß-ketoesters 18 [119,120,121].



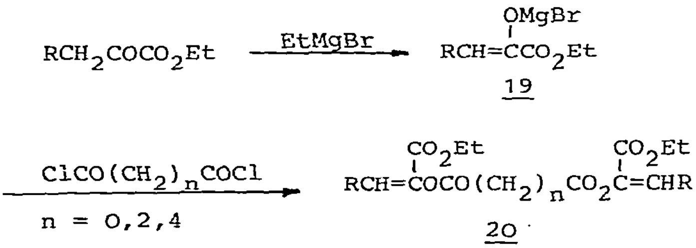
16



$16 \xrightarrow[\text{2. } H^+;\ -CO_2]{\text{1. } R^1R^2C{=}CR^3COCl} R^1R^2C{=}CR^3COCH_2CO_2Et$ 17 (56-74 %)

$16 \xrightarrow[\text{2. } H^+;\ -CO_2]{\text{1. } RCH(OAc)COCl} RCH(OAc)COCH_2CO_2Et$ 18 (60-88 %)

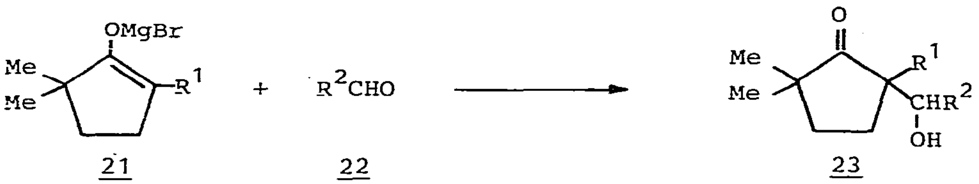
Bis(ß-alkyl-α-carbalkoxyvinyl)esters of dicarboxylic acids 20 were prepared via the enolates 19 from α-ketoesters [122].



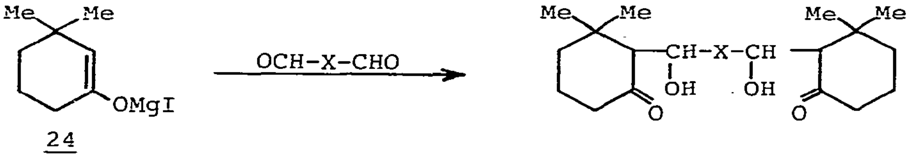
$RCH_2COCO_2Et \xrightarrow{EtMgBr} RCH{=}C(OMgBr)CO_2Et$ 19

$\xrightarrow[n\,=\,0,2,4]{ClCO(CH_2)_nCOCl} RCH{=}C(CO_2Et)OCO(CH_2)_nCO_2C(CO_2Et){=}CHR$ 20

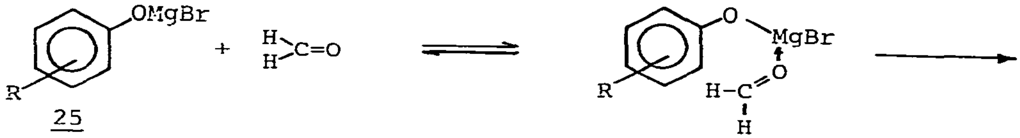
The reaction between the enolates 21 and the aldehydes 22 gives diastereomeric ketols 23 formed under kinetic control in proportions strongly dependent on the size of the alkyl substituents R^1 and R^2. Thus with 21 (R^1 = Me) and different aldehydes 22 (R^2 = Me, Et, i-Pr, t-Bu) the amount of the threo ketol 23 in the erythro/threo mixture increased from 93.5 % for R^2 = Me to more than 99 % for R^2 = t-Bu. On the other hand with different enolates 21 (R^1 = Me, Et, i-Pr, t-Bu) keeping the aldehyde 22 (R^2 = Me) unchanged the amount of the threo product 23 was going down from 93.5 % for R^1 = Me to 29 % for R^1 = t-Bu. The observed stereoselectivity is accounted for by a transition state with a cationic bridge [123].

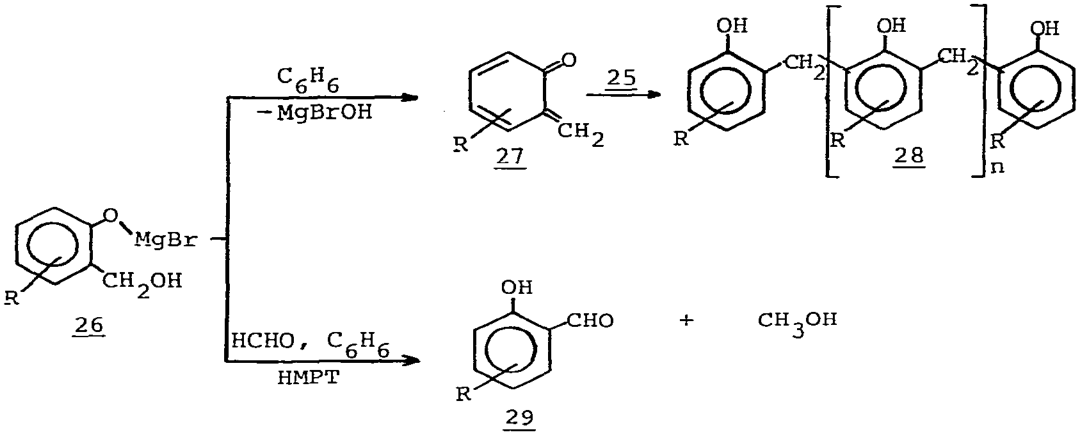


The same reaction was used to prepare cyclohexanone derivatives of carotenes by condensation of the enolate 24 obtained from 3-methyl-2-cyclohexene-1-one and MeMgI with appropriate dialdehydes [124].

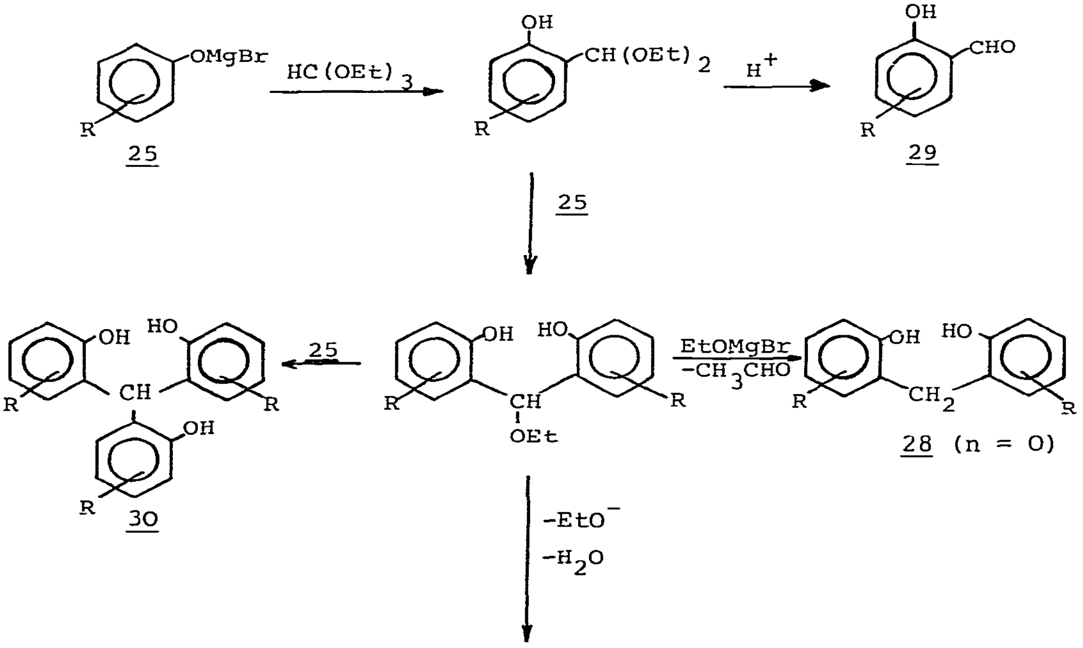


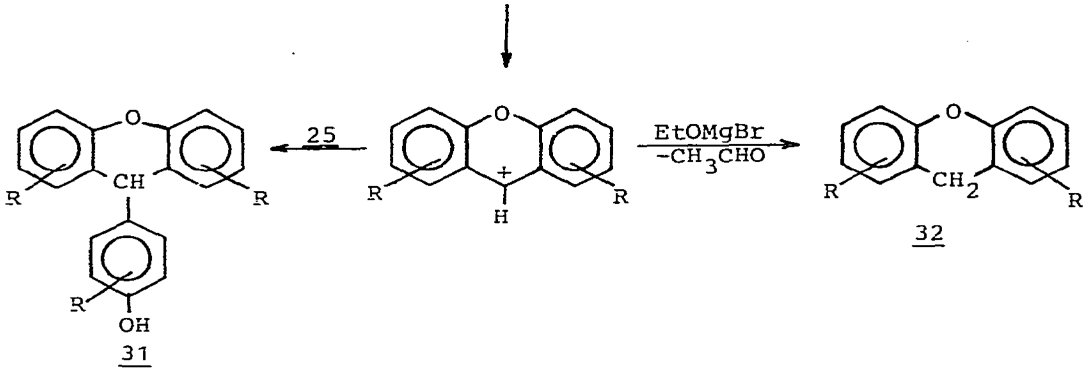
An interesting influence of the solvent on the reaction of magnesium phenoxides 25 with paraformaldehyde in refluxing benzene was reported. In the absence of HMPT 2,2'-dihydroxydiphenylmethanes and higher oligomers 28 (n = 0-6) were obtained, while in the presence of stoicheiometric amounts of HMPT 2-hydroxybenzaldehydes 29 were produced in high yields. The formation of 29 has been shown to occur via an oxidation-reduction process, promoted by HMPT, between the 2-hydroxybenzyl alcohol intermediate 26 and formaldehyde. The postulated ortho-quinone methide intermediate 27 involved in the formation of 28 could be trapped as Diels-alder adduct with ethyl vinyl ether [125, 126, 127].





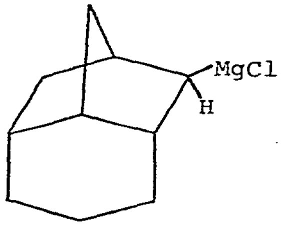
The formation of 2-hydroxybenzaldehydes 29 was also observed in the reaction of substituted phenoxymagnesium bromides 25 with ethyl orthoformate in benzene, although in less than 10 % yield. Depending upon the nature and the position of the substituents R on the phenolic ring mainly 2,2'-dihydroxy-diarylmethanes 28 (n=0), 2,2'2"-trihydroxytriarylmethanes 30, xanthenes 32 and/or 9-arylxanthenes 31 were obtained [128].



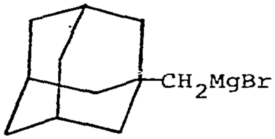


5. Unsaturated and polycyclic compounds

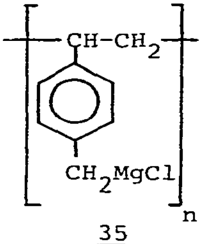
The Grignard reagent 33 from 2-chloro-4-homobrendane was characterized by carboxylation and yielded 46 % pure 4-homobrendane-exo-2-carboxylic acid [129]. The alcohol obtained from 34 and acetone was used as starting material for the synthesis of other adamantane derivatives [130]. Chloromethylated polystyrene was converted to the poly-Grignard reagent 35 [131]. New monomers were prepared from the Grignard reagent of p-bromostyrene [132, 133].



33



34

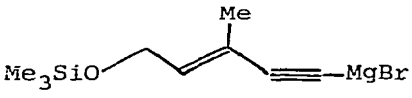


35

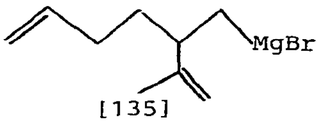
Examples of unsaturated organomagnesium compounds include the following:

$CH_2=CHC\equiv CMgBr$

[134]



[91]

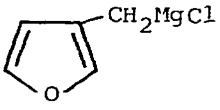


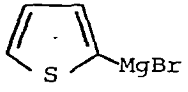
[135]

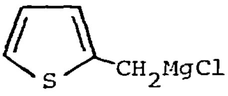
"Allylic isomerism" of allylic, propargyl, or allenic Grignard reagents is covered in section III. C.

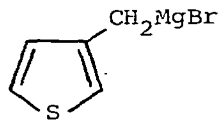
6. Heteroaromatic compounds

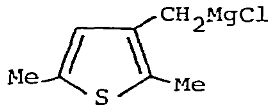
A variety of heteroaromatic Grignard reagents have been prepared conventionally and used synthetically. Examples include the following:

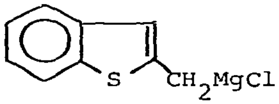

[136]

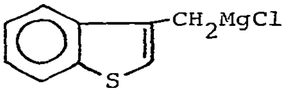

[137, 138, 139]


[140, 141]


[142,143,144]


[145,146]


[147-151]


[151,152,153]

7. Di-magnesium derivatives and other metal-substituted or metallomagnesium compounds

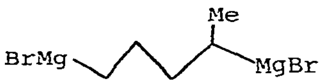
The following di-Grignard reagents have been prepared in the usual manner by reaction between the dibromide and magnesium metal:

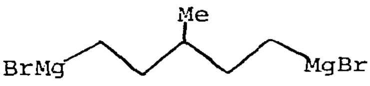
$BrMg(CH_2)_nMgBr$

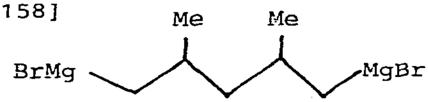
n = 4 [154-158]

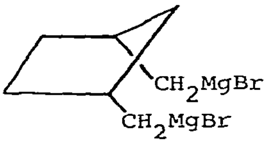
n = 5,6 [157,158]

n = 8,10 [158]


[159]


[160]


[161]

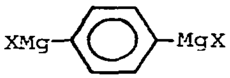

[161]

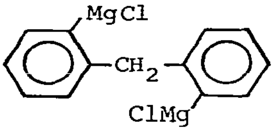
Di-magnesium derivatives prepared from the corresponding alkyne and a Grignard reagent include:

$BrMgC\equiv CMgBr$ [162,163]

$BrMgC\equiv C(CH_2)_nC\equiv CMgBr$ n = 2,4 [164]

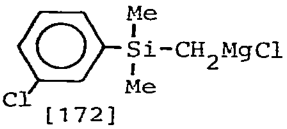
The following aromatic di-Grignard reagents have been prepared conventionally, although a Barbier version of the Grignard coupling of p-dichlorobenzene with $Me_2Si(OPr)_2$ in the presence of CuCl obviously gives much better yields [165].

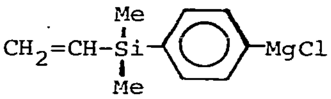

X = Cl [165]
X = Br [158,166-168]

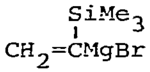

[169]

Examples of metal-substituted Grignard reagents formed by reaction between the halide and magnesium metal include:

Me_3SiCH_2MgCl
[170,171]


[172]


[63,173]


$CH_2{=}\overset{SiMe_3}{C}MgBr$
[174]

$Me_3SiC{\equiv}C(CH_2)_3MgBr$
[72]

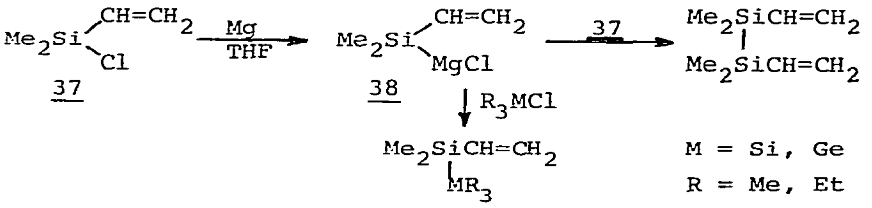
$Me_3Sn(CH_2)_5MgBr$
[175]

Bis(trimethylsilylmethyl)magnesium has also been prepared and used synthetically [176, 177, 178].

The lead-Grignard reagent 36 has been prepared from phenylmagnesium bromide and lead dichloride and used to synthesize 3-chloro-3-trimethylsilylallyllead [179].

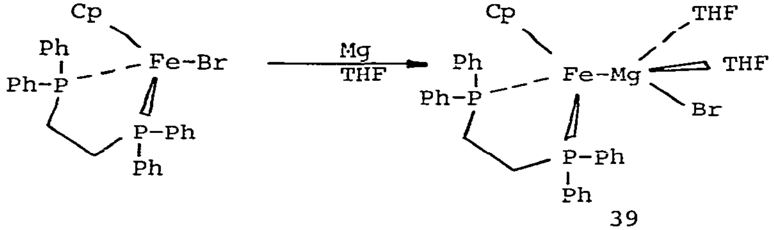
$$\underset{\underline{36}}{Ph_3PbMgBr} + ClCH_2CH{=}C(Cl)SiMe_3 \longrightarrow Ph_3PbCH_2CH{=}C(Cl)SiMe_3$$

A silyl-Grignard reagent 38 formed via 37 is probably involved in the Barbier reaction of vinyl bromide with Me_2SiCl_2/Mg/THF [180]:

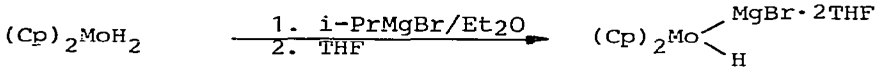


Previous mention has been made of the synthesis of a similar (triorgano)silylmagnesium derivative by metal exchange [27] (section II.B).

The crystalline "inorgano-Grignard reagents" 39 [181] and 40 [182] have been studied.



39



40

The former with a covalent iron-magnesium bond was prepared in 40 - 60 % yield by treating magnesium metal with the corresponding bromide in THF. It readily reacts with organic bromides by a single electron transfer process as shown by the formation of cyclic products from 5-hexenyl bromide [181]. The latter which contains a Mo-Mg covalent bond is formed via a dimeric compound in Et_2O. This time no evidence for a radical path in the reaction of 40 with 5-hexenyl bromide has been found. Its reaction with water (Cp_2MoH_2), carbon dioxide (Cp_2MoCO), benzyl chloride (Cp_2Mo benzyl$_2$), allyl bromide ($[Cp_2Mo-\pi$-allyl$]^+$), methyl iodide (Cp_2MoHI), and acetyl chloride ($Cp_2MoHCOMe$ + $Cp_2Mo(COMe)_2$) has also been reported [182].

III. SPECTRA, PROPERTIES, AND STRUCTURES OF ORGANO-MAGNESIUM COMPOUNDS

A. Spectroscopic Studies

^1H and ^{13}C NMR spectra of dibenzylmagnesium in THF and C_6D_6 have been reported and compared with those of other benzyl metal compounds. Chemical shift considerations indicate that the carbon-metal bonds of the benzyl carbanions in THF increase in ionic character as the counterion varies in the order Mg<Ca<Sr<Li<Ba<K [183].

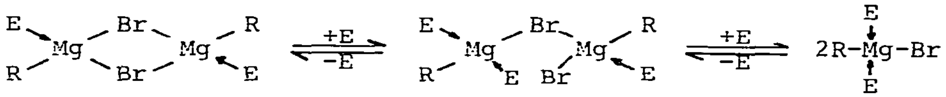
The ^{19}F chemical shifts of magnesium meta- and para-fluorophenylcyclopentadienide in THF occupy an intermediate position between alkali cyclopentadienides and covalent iron or palladium derivatives and are close to the values of the lithium derivative. Therefore, it is reasonable to assume that m- and $p-FC_6H_4C_5H_4MgBr$

exists in THF predominantly in the form of tight ion pairs [44].

The ^{1}H NMR chemical shift of the protons α to magnesium in EtMgBr and Et$_2$Mg in various donor solvents provide a measure of the basicity of the solvents. The following tentative order of basicity of the solvents has been found: DME $>$ THF $>$ Et$_2$O $>$ n-Bu$_2$O $>$ EtMeCHCH$_2$OEt $>$ Et$_3$N $>$ i-Pr$_2$O $>$ anisol [184].

B. Other physical measurements, MO calculations

The association numbers of RMgBr (R = Me,Et,i-Bu) with one equivalent of an electron donor E(E = Et$_3$N, Et$_2$O or THF) were determined by measuring the rate of quasi-isothermal distillation of mixtures of benzene with E to a solution of the organomagnesium compound in the same solvent mixture. The complexes formed were partly dimeric further addition of E causing a decrease in the degree of association. Contrary to earlier results the order of basicity was found to be THF $>$ Et$_2$O $>$ Et$_3$N [185].



41 42 43

Equilibrium constants were calculated, assuming that the conversion from dimer to monomer proceeds via two equilibria: a dimer 41 containing two molecules of E gives a dimer 42 containing three molecules of E which gives a monomer 43 with two ligands. 42 probably exists in appreciable amounts only if most of the ligands are relatively small (R = Me, Et; E = THF).

The Et$_2$Mg/Et$_2$O complex in benzene, studied in the same way, was found to be partly tetrameric at low Et$_2$O/Et$_2$Mg ratios. At higher Et$_2$O concentrations dimeric and monomeric species are present the most probable equilibria involving a tetramer with two molecules of E in equilibrium with a dimer · 2E which is in equilibrium with Et$_2$Mg · 2Et$_2$O [185].

Electrochemical measurements at a hydrogen electrode showed an increase in basicity of aliphatic and aromatic Grignard reagents (MeMgCl, EtMgCl, PhMgCl) in THF solutions when one or two moles of HMPT per mole of Grignard reagent were added. The increase in the basicity is associated with a decrease of the oxidizing properties, and probably results from the formation of a complex between one mole of Grignard reagent and two moles of HMPT [186].

Dimesitylmagnesium prepared from mesitylmagnesium bromide and dioxan in THF was shown cryoscopically to be a monomer $Mg(C_6H_2Me_3$-2,4,6)$(THF)_2$ in benzene [187].

Single crystal X-ray analysis has been used to determine the structure of $Ph_2Mg \cdot$ TMEDA prepared from diphenylmagnesium and TMEDA. In the molecule the phenyl groups and the N atoms of the bidentate ligand form a tetrahedron around the magnesium atom. The phenyl groups are slightly distorted hexagons as in similar phenyl compounds of lithium and aluminum [188].

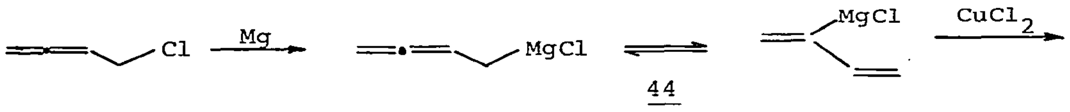
The first ate-complex with phenyl bridges, $[Li(TMEDA)]_2[Mg_2Ph_6]$, has been obtained from equimolar amounts of phenyllithium, diphenylmagnesium, and TMEDA and its crystal structure has been determined by X-ray analysis. The central part of the compound consists of the dimeric triphenylmagnesate $[Ph_2MgPh_2MgPh_2]^{2-}$, which is isoelectronic and isostructural to $(Ph_3Al)_2$. Both Li(TMEDA) moieties are linked to this unit with each Li atom between two terminal phenyl groups [189].

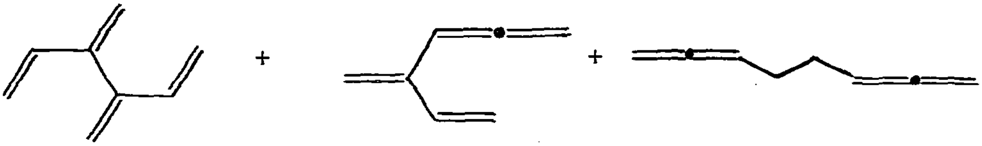
Single crystal X-ray analysis also has been used to determine the structure of the complex compound 3 already mentioned in section II. B. The cation consists of four six-coordinated magnesium atoms tightly bound by two types of $MeOCH_2CH_2O^-$ bridging units in a distorted octahedral symmetry about the magnesium atoms [27].

Ab initio valence-only molecular orbital calculations have been reported for Me_2Mg and MeMgCl at experimental (electron diffraction) geometries. As expected the bonding was found to be nearly all of σ type. Orbital energies and population analysis have been contrasted with expectations based on electronegativities and Pearson's hard-soft principle; the latter seems slightly more helpful [190].

C. Isomerism in structure and reactions of allylic and related organomagnesium compounds

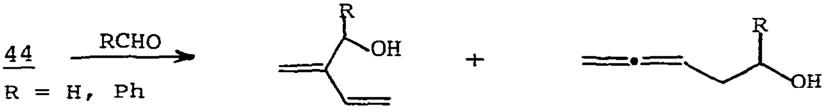
Oxidative coupling of the Grignard reagent 44 from 4-chloro-1,2-butadiene with copper(II) chloride yields mainly 45 [191]:





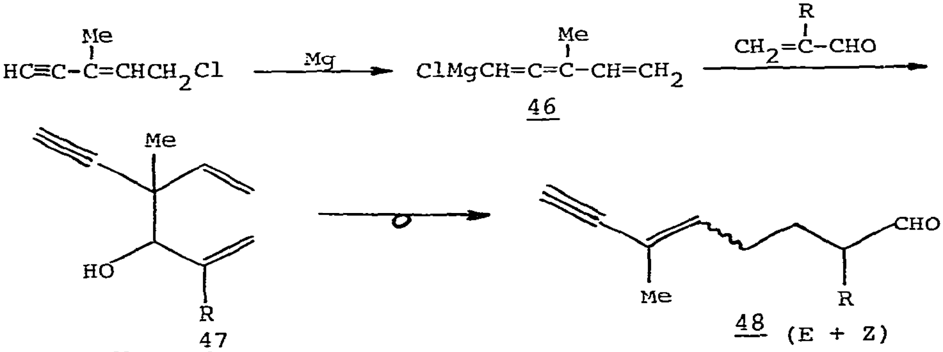
45 (83 %) (9 %) (8 %)

The same reagent 44 has been prepared from 2-chloro-1,3-butadiene and magnesium metal in THF promoted by methyl iodide in the presence of $ZnCl_2$ as catalyst. Treatment with aldehydes gives a mixture of the corresponding 1,3-dienol and allenic alcohol [192]:



R = H, Ph

The "vinylallenic" Grignard reagent 46 reacts with acrolein or methacrolein leading to acetylenic alcohols 47, oxy-Cope rearrangement of which to the corresponding aldehydes 48 – after alkylation of the terminal acetylenic carbon atom – provided a useful synthetic sequence [193,194]:

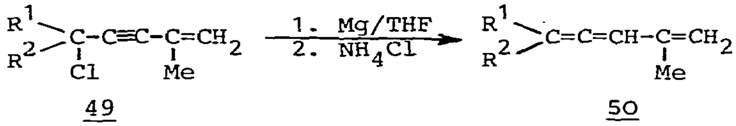


$$HC\equiv C-\overset{\mathrm{Me}}{\overset{|}{C}}=CHCH_2Cl \xrightarrow{Mg} \underset{\mathbf{46}}{ClMgCH=C=\overset{\mathrm{Me}}{\overset{|}{C}}-CH=CH_2} \xrightarrow{CH_2=\overset{\mathrm{R}}{\overset{|}{C}}-CHO}$$

R = H, Me 47

48 (E + Z)

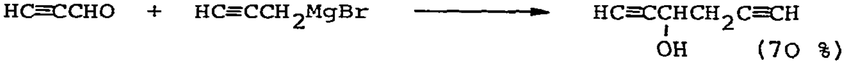
Hydrolysis of the Grignard reagents from the vinylacetylenic chlorides 49, on the other hand, gave vinylallenic hydrocarbons 50 in 59 – 74 % yield [195]:



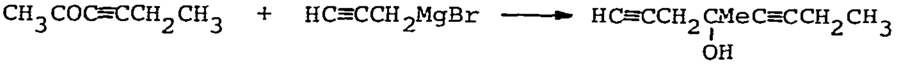
$$\underset{\mathbf{49}}{\begin{matrix}R^1\\R^2\end{matrix}\!>\!\underset{\mathrm{Cl}}{\underset{|}{C}}-C\equiv C-\underset{\mathrm{Me}}{\underset{|}{C}}=CH_2} \xrightarrow[2.\ NH_4Cl]{1.\ Mg/THF} \underset{\mathbf{50}}{\begin{matrix}R^1\\R^2\end{matrix}\!>\!C=C=CH-\underset{\mathrm{Me}}{\underset{|}{C}}=CH_2}$$

R^1 = H, Me; R^2 = Me, Et, Pr, Bu; R^1R^2 = $(CH_2)_5$

Three different products have been reported starting from propargylmagnesium bromide. The following reactions lead to normal products [196,197]:

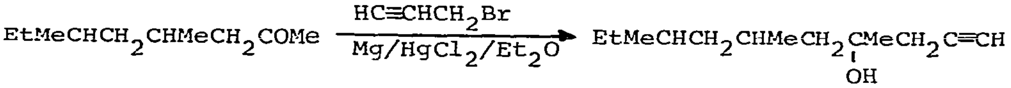


$$\mathrm{HC{\equiv}CCHO + HC{\equiv}CCH_2MgBr \longrightarrow HC{\equiv}C\underset{\underset{OH}{|}}{C}HCH_2C{\equiv}CH} \quad (70\ \%)$$



$$\mathrm{CH_3COC{\equiv}CCH_2CH_3 + HC{\equiv}CCH_2MgBr \longrightarrow HC{\equiv}CCH_2\underset{\underset{OH}{|}}{C}MeC{\equiv}CCH_2CH_3}$$

The same is true for a Barbier reaction with propargyl bromide [198]:



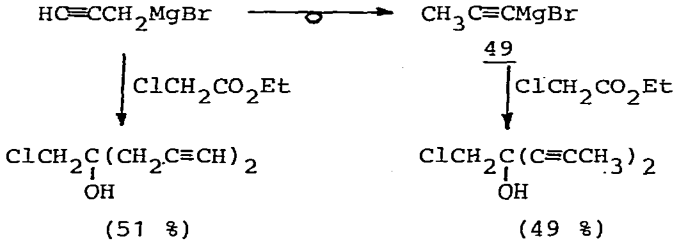
$$\mathrm{EtMeCHCH_2CHMeCH_2COMe \xrightarrow[Mg/HgCl_2/Et_2O]{HC{\equiv}CHCH_2Br} EtMeCHCH_2CHMeCH_2\underset{\underset{OH}{|}}{C}MeCH_2C{\equiv}CH}$$

With chlorosilanes, however, a mixture of acetylenic and allenic products has been obtained [199]:

$$\mathrm{HC{\equiv}CCH_2MgBr \xrightarrow{R_3SiCl} R_3SiCH_2C{\equiv}CH + R_3SiCH{=}C{=}CH_2}$$

R = H, Me, Et, $PhCH_2$, p-tolyl, vinyl

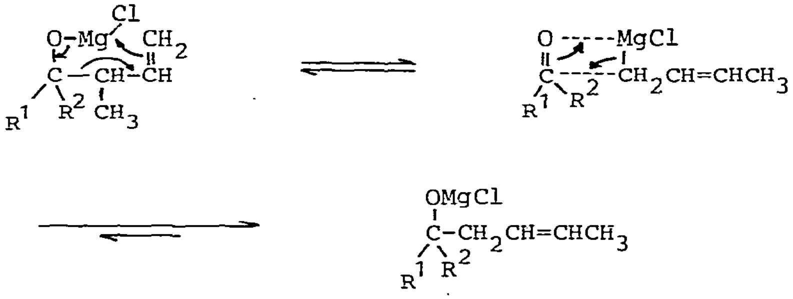
Evidence for a 1,3 proton shift has been found in the reaction of propargylmagnesium bromide with ethyl chloroacetate yielding in the reaction mixture 49 % product of the rearranged propynyl Grignard reagent 49 [200]:



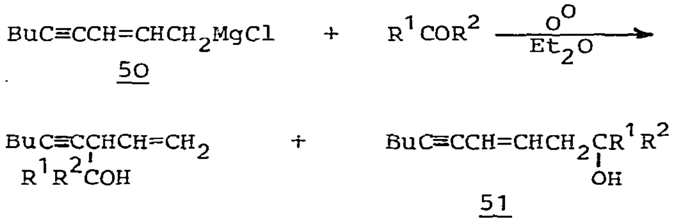
With ß-amino ketones up to 15 % of the corresponding isomeric alcohols could be detected [201].

D. Reversibility in reactions of allylic organomagnesium compounds

The reversibility of addition of allylic-type Grignard reagents to a variety of hindered ketones has been studied. At -78°C in THF with crotylmagnesium chloride only the pure kinetic product, the α-methallyl adducts were formed. Only di-*tert*-butyl ketone failed to give exclusively α-methallyl adduct under the aforementioned conditions. After 30 minutes crotyldi-tert-butylcarbinol was obtained as the sole product, which could not have arisen from an initially formed α-methallyl product. One must conclude that when steric hindrance in the carbonyl substrate is extremely severe, the crotyl Grignard can react directly via a four-center pathway. It follows, therefore, that crotyl products can be formed both from a reversal process involving the α-methallyl adduct and directly from the ketone and the crotyl Grignard via a four-center transition state. The ketones which form occasionally when the alkoxides of the α-methallylcarbinols undergo reversal result from the formation of the ketone enolates. When there are no enolizable hydrogens on the ketones no ketones are found in the final product [202].



Similar results have been obtained with the Grignard reagent 50 which at 0° C with diisopropyl ketone ($R^1 = R^2$ = i-Pr) yields 51 as the sole product while with $R^1 = R^2$ = Me or R^1 = i-Pr; R^2 = Me the portion of this adduct was only 5 or 20 % respectively. The reactivity of 50 towards aldehydes and ketones was compared with that of $CH_2{=}CHCH{=}CH\text{-}CH_2MgCl$ and the reversibility of these reactions was found to be more difficult with 50 [203].



$$\mathrm{BuC{\equiv}CCH{=}CHCH_2MgCl} + \mathrm{R^1COR^2} \xrightarrow[\mathrm{Et_2O}]{0^{\circ}} \mathrm{BuC{\equiv}C\underset{R^1R^2COH}{C}HCH{=}CH_2} + \mathrm{BuC{\equiv}CCH{=}CHCH_2\underset{OH}{C}R^1R^2}$$

50

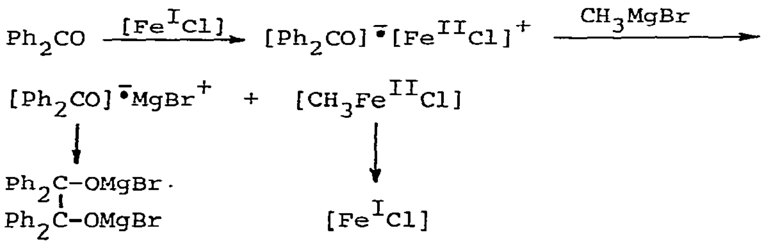
51

IV. REACTIONS OF ORGANOMAGNESIUM COMPOUNDS WITH CARBONYL FUNCTIONS

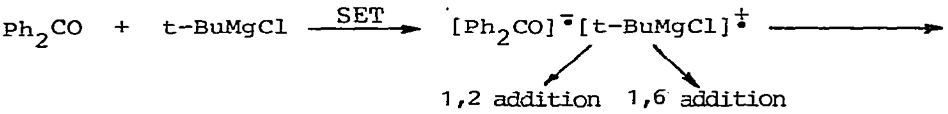
A. Mechanism of the Grignard addition

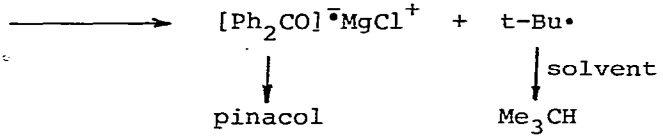
The reactions of benzophenone, fluorenone, and acetone with tert-butylmagnesium chloride and methylmagnesium bromide have been studied under a variety of conditions [204]. The nature of the alkyl group of the Grignard reagent is probably the most important single factor involved in determining the extent of single electron transfer (SET) to be observed in the reaction with a given ketone. The methyl Grignard reactions with aromatic ketones were dramatically affected by transition metal impurities in the magnesium used to prepare the reagent; however the corresponding tert-butyl Grignard reactions were unaffected by transition metal content. The reduction potential of the ketone and the nature of the solvent in which the reaction is carried out are also important factors. It is apparent that reaction of t-BuMgCl with benzophenone and fluorenone proceeds via a SET pathway while the reaction of t-BuMgCl with acetone appears to follow a polar pathway. When SET occurred, it was enhanced by an increase in solvent polarity.

An iron(I) intermediate is proposed to be the active species leading to iron catalyzed pinacol formation in methyl Grignard reactions with aromatic ketones [204]:



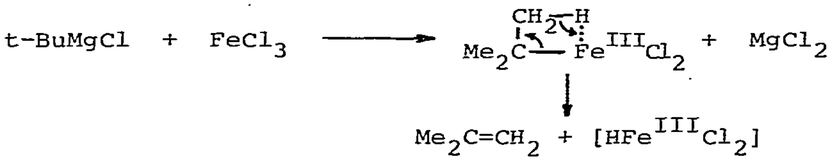
The reaction of t-BuMgCl with benzophenone and fluorenone apparently occur via a SET pathway involving a radical anion - radical cation pair which can collapse to give addition products or diffuse to give pinacol and isobutane. The presence of p-dinitrobenzene was shown to inhibit pinacol formation, but to have no effect on the ratio of 1,2 : 1,6-alkylation [204]:





$$\longrightarrow [Ph_2CO]^{\bar{\bullet}}MgCl^+ + t\text{-}Bu\bullet$$
$$[Ph_2CO]^{\bar{\bullet}}MgCl^+ \longrightarrow \text{pinacol} \qquad t\text{-}Bu\bullet \xrightarrow{\text{solvent}} Me_3CH$$

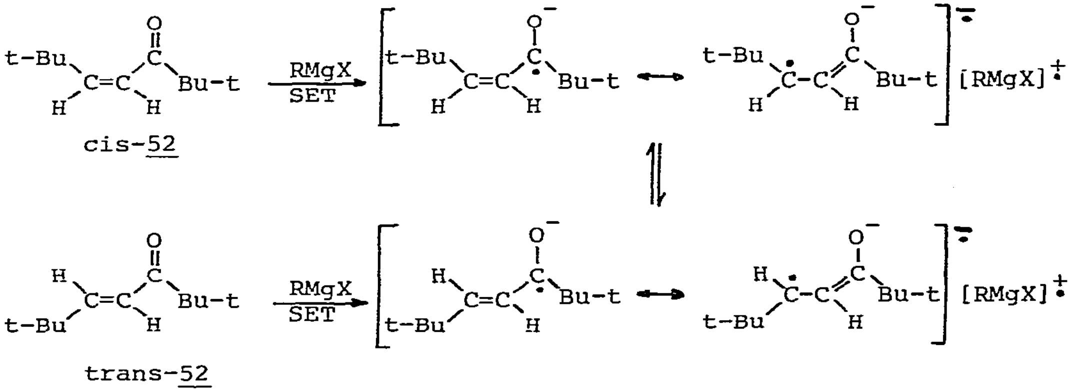
The addition of $FeCl_3$ to the reaction of t-BuMgCl with acetone leads to high yield of reduction product. An iron hydride intermediate was proposed which is capable of reducing acetone more quickly than Grignard addition to acetone but which does not react with benzophenone or fluorenone in the presence of the Grignard reagent [204]:



$$t\text{-}BuMgCl + FeCl_3 \longrightarrow Me_2C(CH_2\text{-}H)\text{-}Fe^{III}Cl_2 + MgCl_2$$
$$\longrightarrow Me_2C{=}CH_2 + [HFe^{III}Cl_2]$$

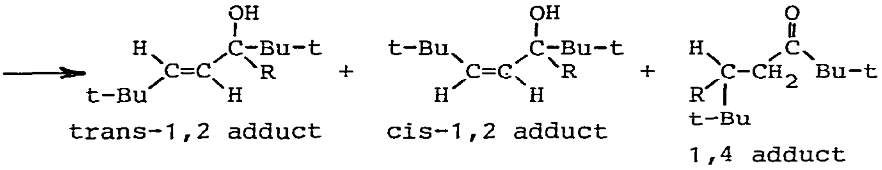
Methyl Grignard reactions with acetone, on the other hand, were found to be unaffected by changes in reaction conditions [204].

In another study 2,2,6,6-tetramethyl-hept-4-en-3-one 52 has been used as a probe to gain insight into the nature of Grignard reactions with ketones [205]. It seems apparent that tert-butylmagnesium chloride reacts with the cis and trans enone 52 at least predominantly via a SET pathway. Almost complete isomerization of both excess starting material and product are observed in reactions with the cis enone. Equally convincing is the observation of small amounts of cis enone produced in the reaction of t-BuMgCl with excess trans enone. This indicates that an equilibrium amount of cis ketyl was produced in the reaction [205].



cis-52

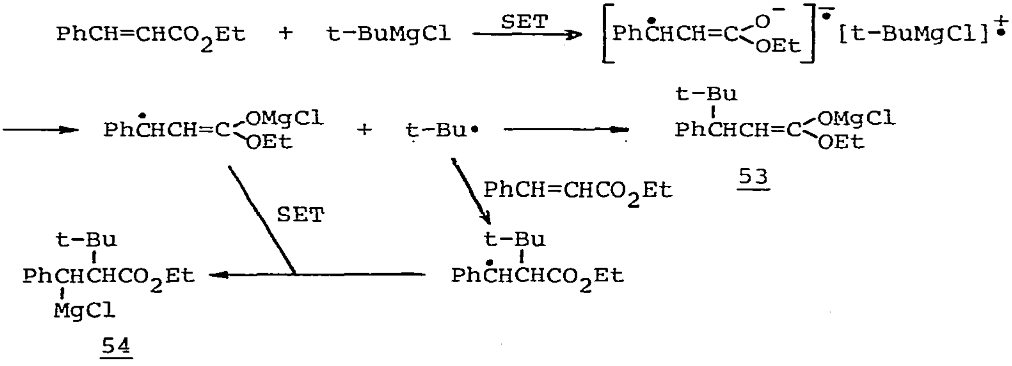
trans-52



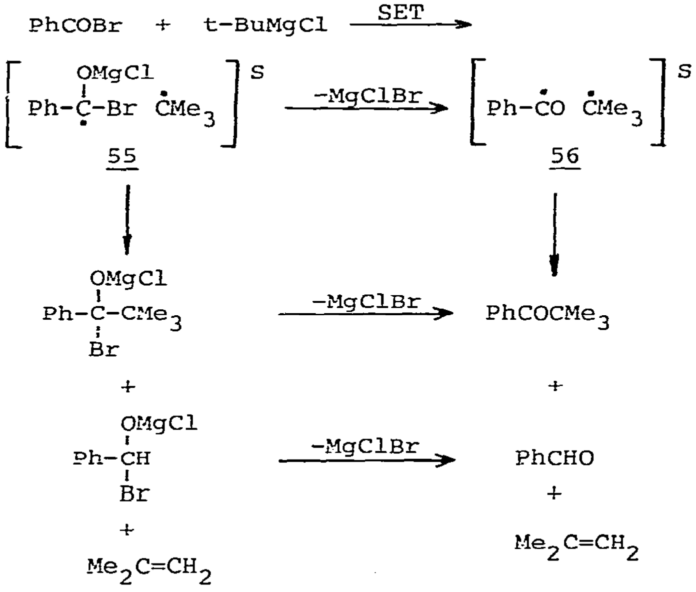
The reactions of allyl Grignard reagents with these enones are very rapid and give indications of only a polar mechanism. Cis enone reacts with allyl magnesium bromide to give only cis-1,2 addition and trans enone reacts to give only trans-1,2 addition. The reaction is not affected by the addition of $FeCl_3$ [205].

Methyl Grignard reactions with these enones are more complicated; however, trends indicate that these reagents are reacting via a polar pathway complicated by a side reaction involving transition metal impurities in the magnesium that leads to SET isomerization of the enone. The addition of p-dinitrobenzene to reactions of MeMgBr with cis-52 retards isomerization of the enone [205].

Free tert-butyl radicals are involved in the reaction of ethyl cinnamate with tert-butylmagnesium chloride yielding a mixture of the normal 1,4-addition product 53 and the abnormal addition product 54. The production of tert-butyl radicals is initiated by SET from the Grignard reagent to the ester in analogy with the above mentioned SET mechanism in the reaction of t-BuMgCl with benzophenone [206]:



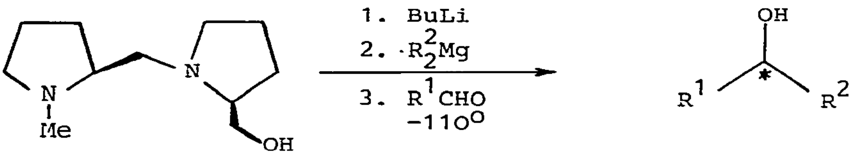
CIDNP signals were found in the products from the reaction of tert-butylmagnesium chloride and benzoyl bromide in 1,2-dimethoxyethane. The reaction involves electron transfer from the organomagnesium compound to the acid bromide. As a result the primary radical pair 55 in the singlet electronic state is formed. Subsequent rapid elimination of magnesium halide will lead to a secondary radical pair 56 with retention of the spin multiplicity. The recombination and disproportionation reactions of the radicals give *tert*-butyl phenyl ketone, *iso*butylene, and benzaldehyde, the latter being used up rapidly in a secondary reaction with t-BuMgCl yielding *tert*-butylphenylcarbinol [207]:



B. Stereochemistry of addition to aldehydes and ketones

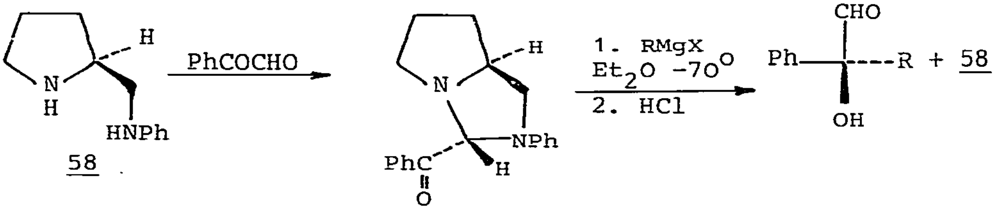
1. Stereochemistry with aldehydes and acyclic ketones

Optically active alcohols, R^1R^2CHOH, possessing the R-configuration have been produced in up to 92 % optical yields by treating aromatic or aliphatic aldehydes, R^1CHO, with dialkylmagnesiums, R^2_2Mg, by using the lithium salt of 57 as a chiral ligand. The effects of both solvent and temperature were studied in the corresponding reaction of dibutylmagnesium with benzaldehyde. Greater optical purity was exhibited at lower temperature and toluene was found to be better than ether type solvents, probably because this solvent favours the formation of an ate-complex between the lithium alcoholate and dialkylmagnesium and facilitates the approach of an aldehyde to this complex. Dialkylmagnesiums were found to be much more effective than Grignard reagents [208].

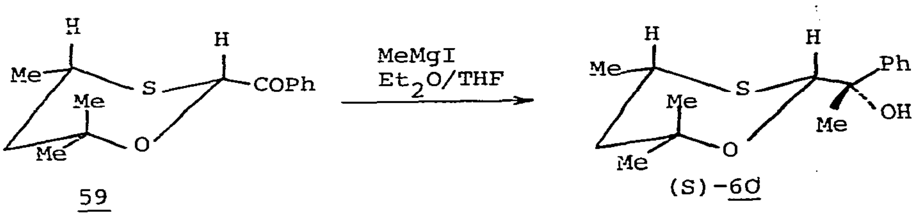


57

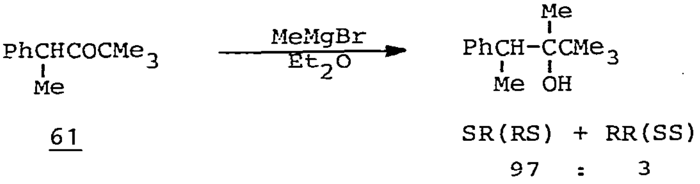
An asymmetric synthesis of α-hydroxy aldehydes was achieved in high optical yields starting from a keto aminal, prepared from phenylglyoxal and (S)-2-(anilinomethyl)pyrrolidine (58). By treating the keto aminal with Grignard reagents and the hydrolysis of resulting hydroxy aminals, α-hydroxy aldehydes were obtained in 94 - 95 % optical yields. This new asymmetric synthesis offers some important advantages over the known procedures, that is, the chiral auxiliary reagent is very easily prepared from commercially available (S)-proline, it may be recovered unchanged after use, and the reaction procedure is very simple [209].



A virtually completely asymmetric synthesis was achieved by adding the ketone 59 in ether/THF to an excess of methylmagnesium iodide in ether, which afforded diastereomer 60 with S configuration at the exocyclic carbon in 95 % yield. No R diastereomer could be detected by either ^1H NMR or ^{13}C NMR spectroscopy. The magnesium of the Grignard reagent (hard acid) complexes simultaneously with the ketone oxygen and the ring oxygen (hard base) in preference to the ring sulfur (soft base) [210].



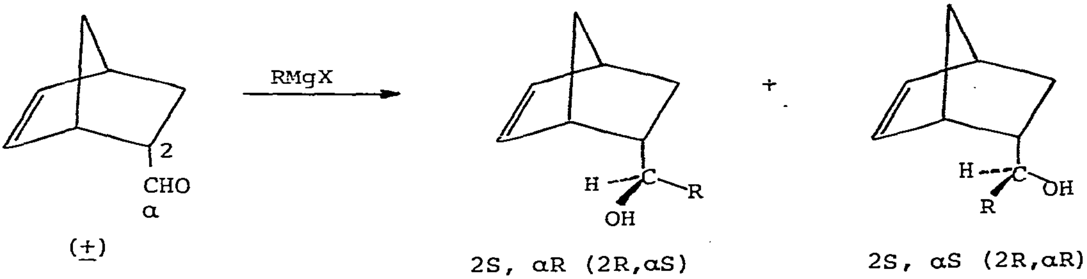
High stereoselectivity was also observed in the reaction of the ketone 61 with MeMgBr in ether at 0° C [211]:



$$\underset{\underset{\textstyle 61}{\text{Me}}}{\text{PhCHCOCMe}_3} \xrightarrow[\text{Et}_2\text{O}]{\text{MeMgBr}} \text{PhCH(Me)-C(Me)(OH)CMe}_3$$

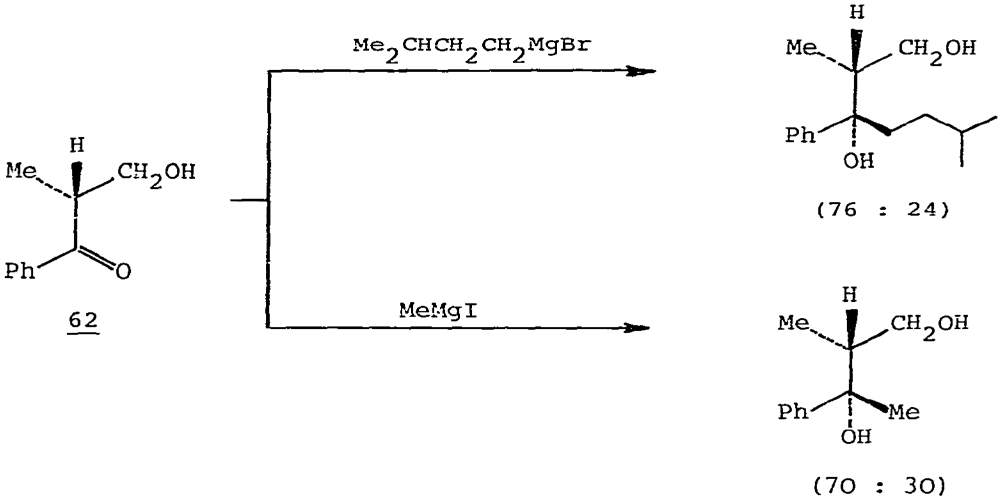
SR(RS) + RR(SS)
97 : 3

In the reaction of racemic endo-5-norbornene-2-carboxaldehyde with methyl, ethyl, and isopropyl Grignard reagents endo-α-alkyl-5-norbornene-2-methanols with 2S, αR or 2R, αS configuration were always formed in excess over the corresponding diastereomeric endo-alcohols with 2S, αS or 2R, αR configuration. Stereoselectivity increased with the bulk of the alkyl group from 52 : 48 for R = Me to 67 : 33 for R = i-Pr [212].



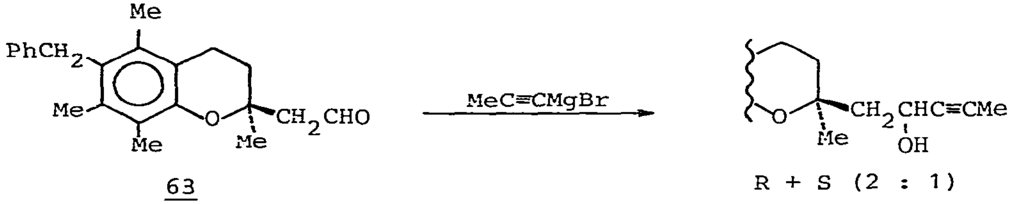
2S, αR (2R,αS) : 2S, αS (2R,αR)
52-67 : 48-33

The bulk of the alkyl group also determined the excess of the erythro derivative over the threo product in the reaction of the ketone 62 with Grignard reagents [213]:



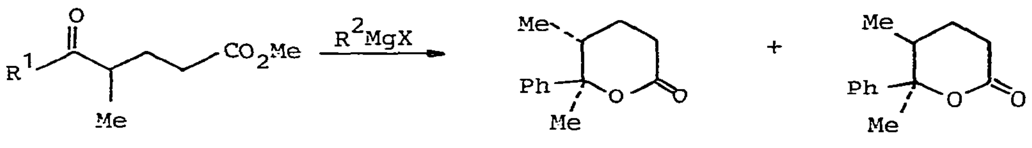
62

Treatment of the (S)-chromanylacetaldehyde 63 with propynylmagnesium bromide gave a 2 : 1 mixture of two diastereomeric acetylenic carbinols [214]:



63

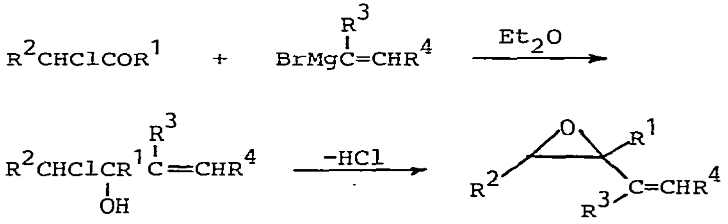
The reaction of the δ-keto esters 64a and 64b with PhMgX and MeMgX, respectively, yield mixtures of cis and trans products the ratio depending on the solvent and on the reactants. Starting with 64a the cis/trans ratio rises from 0.30 to 0.48 on going from benzene over diethyl ether (with X = I) to THF (with X = Cl) while with 64b the ratio goes down from 1.23 to 0.70 [215].



64 cis trans

a: R^1 = Me; R^2 = Ph
b: R^1 = Ph; R^2 = Me

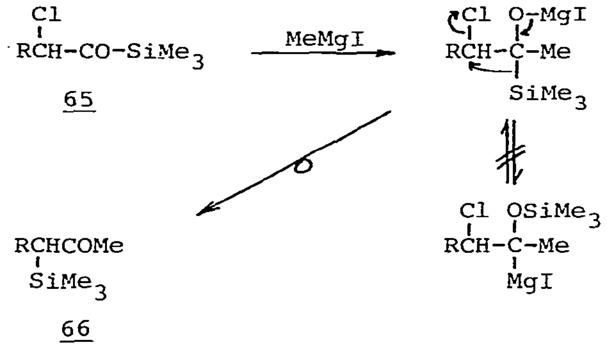
The addition of vinylic Grignard reagents to chiral α-chlorocarbonyl compounds leads to a mixture of diastereoisomeric α,β-ethylenic chlorohydrins, the proportions of which depend on the steric requirements of the nucleophilic reagent. Identification and determination of the configuration of the chlorohydrins were based on NMR studies of the oxirane mixtures formed by alkaline dehydrochlorination. The stereoselectivity of the reaction could not be explained solely on the basis of Felkin's model [216].



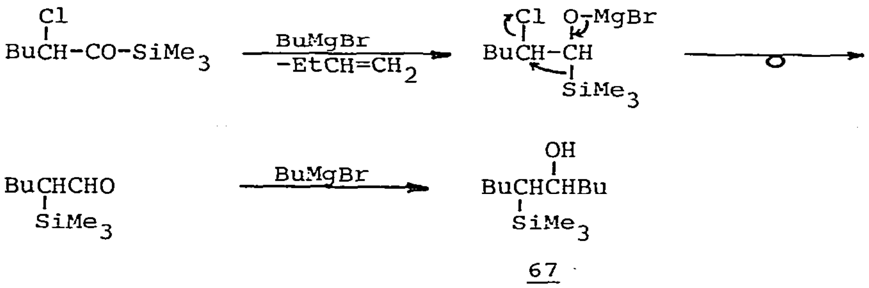
$$R^2CHClCOR^1 + BrMg\overset{R^3}{\overset{|}{C}}{=}CHR^4 \xrightarrow{Et_2O}$$

$$R^2CHCl\underset{OH}{\underset{|}{C}}R^1\overset{R^3}{\overset{|}{C}}{=}CHR^4 \xrightarrow{-HCl}$$

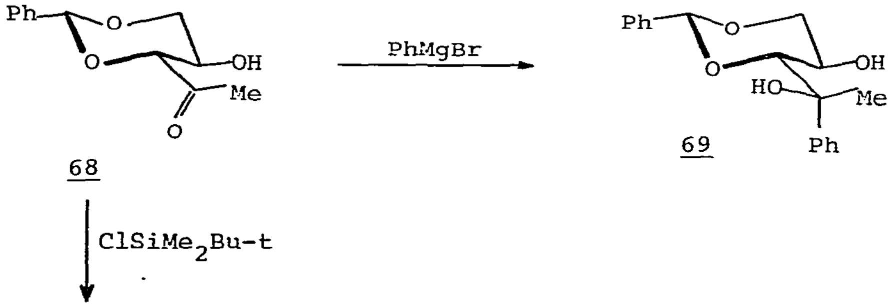
A new rearrangement reaction has been observed upon treatment of α-chloroacylsilanes <u>65</u> with Grignard reagents. Thus β-ketoalkyltrimethylsilanes <u>66</u> were obtained in excellent yields when <u>65</u> was treated with an equimolar amount of methylmagnesium iodide at -78° in ether/THF. The expected Brook rearrangement on the other hand could not be detected [217]:

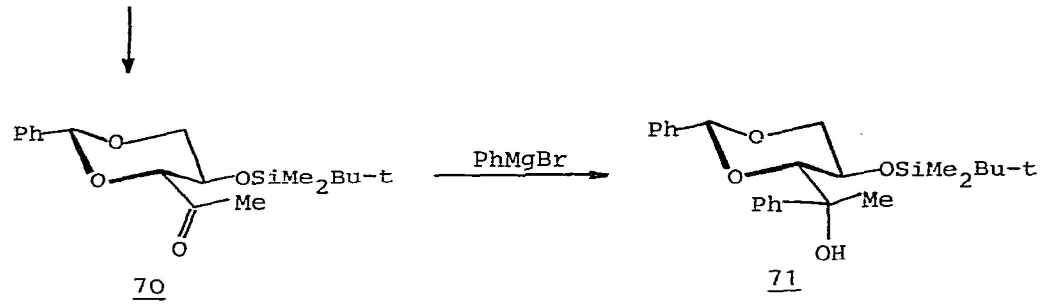


With Grignard reagents possessing ß-hydrogen, however, ß-hydroxyalkyltrimethylsilanes 67 resulted instead. The selective formation of the erythro isomer (96 : 4) according to Cram's rule was demonstrated in the following example [217]:

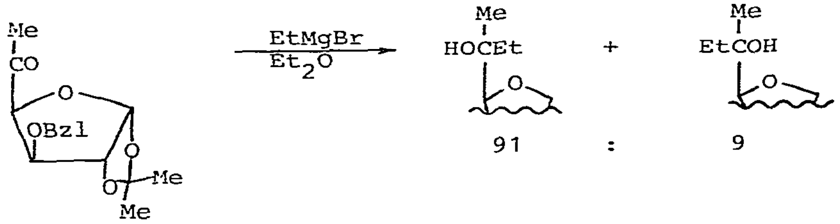


Grignard addition of phenylmagnesium bromide to 3,5-O-benzylidene-1-deoxy-D-erythro-2-pentulose (68) afforded C-phenyl branched-chain pentitols having exclusively either D-arabino (69) or D-ribo (71) stereochemistry according to the mode of substitution of 68. Thus after silylation of 68 to give 70 the mode of addition is completely reversed [218]:

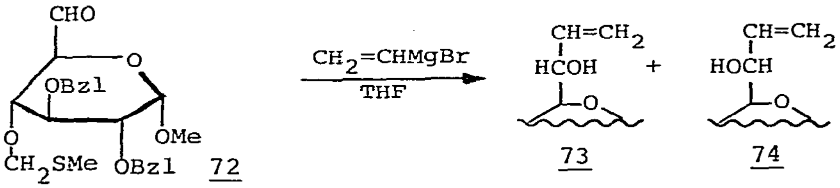




Several other sugar derivatives have been prepared by Grignard syntheses with more or less stereoselectivity. In the following reaction a 91 : 9 mixture has been obtained [219]:

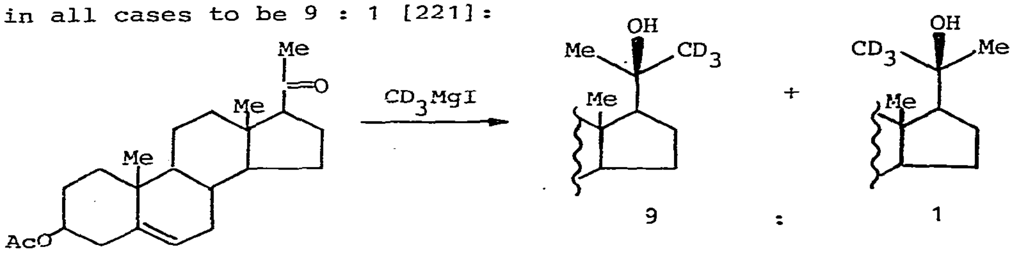


Vinylmagnesium bromide with the aldehyde 72 afforded a mixture of the epimeric products 73 (67.4 %) and 74 (12.2 %) [220]:



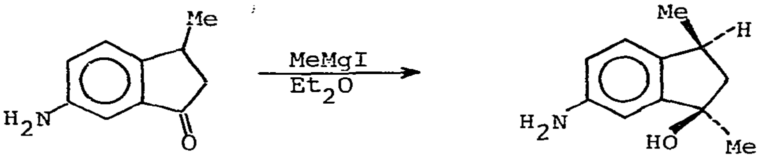
New epimeric hexynoses and octynoses have been prepared by treating the corresponding sugar aldehydes with $(EtO)_2CHC{\equiv}CMgBr$ [100, 101].

Stereoselectivity of Grignard addition to 20-keto steroids has been studied by treating pregnenolon acetate with CD_3MgI or $^{13}CH_3MgI$. The ratio of 20S- to 20R-labelled methylpregnenediols was observed in all cases to be 9 : 1 [221]:

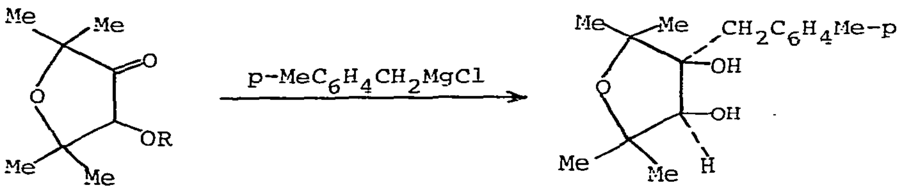


2. Stereochemistry with cyclic ketones

The addition of MeMgI to 6-amino-3-methylindan-1-one gave trans-6-amino-1,3-dimethylindan-1-ol in 33 % yield [222]:



The α-ketol 75a with p-methylbenzylmagnesium chloride afforded the cis-diol 76 in nearly quantitative yield, while the trans-diol together with 76 was obtained starting from the corresponding esters 75b [223]:

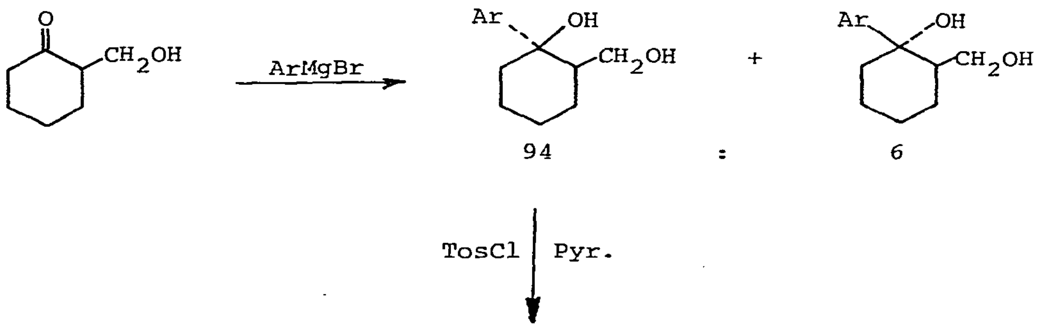


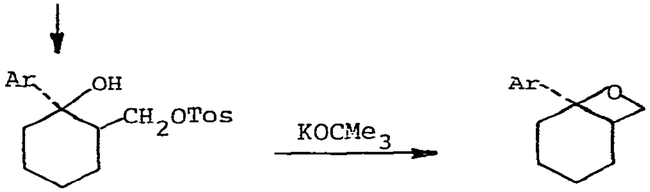
75   76

a: R = H

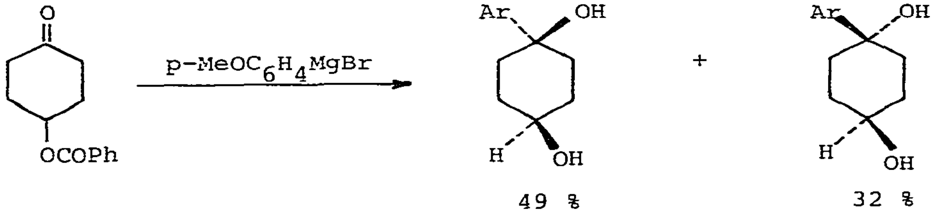
b: R = p-MeOC$_6$H$_4$CO, PhCO, p-ClC$_6$H$_4$CO, EtCO

The formation of cis-diols was also favoured in the reaction of 2-hydroxymethylcyclohexanone with aryl Grignard reagents, the products being used for the synthesis of oxetanes [224]:

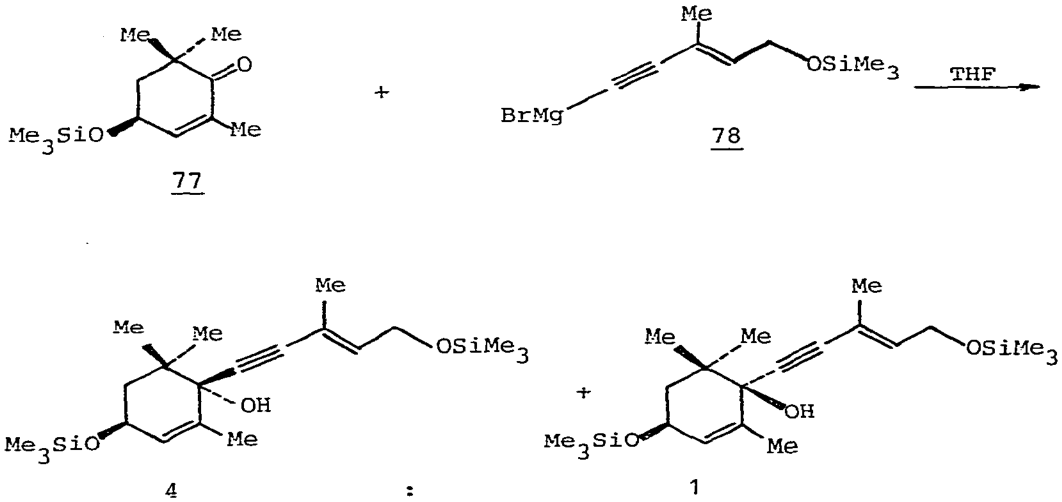




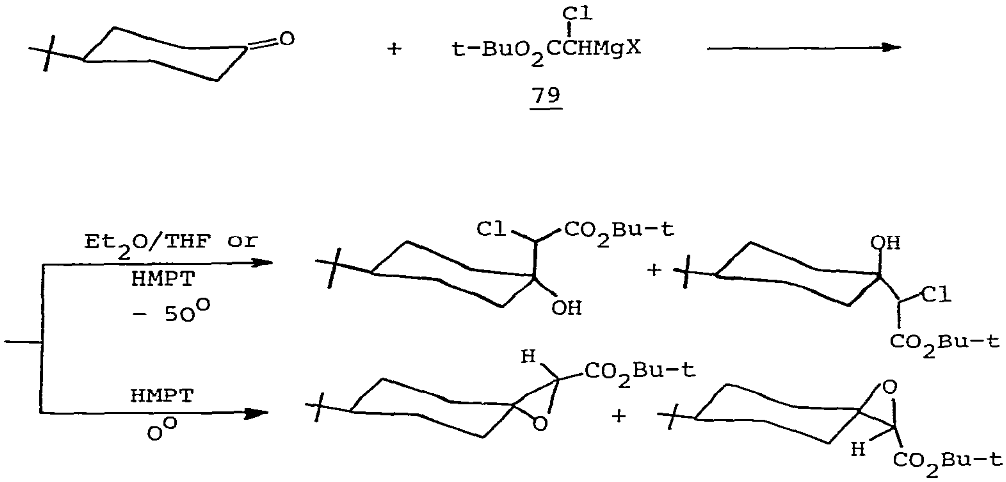
The reaction of 4-hydroxycyclohexanone with p-methoxyphenylmagnesium bromide afforded poor yields only. Satisfactory yields (81 %) were obtained, however, when 4-benzoyloxycyclohexanone was used as starting material, the benzoyl group being removed during the reaction. In each case the cis-diol was the major product [225]:



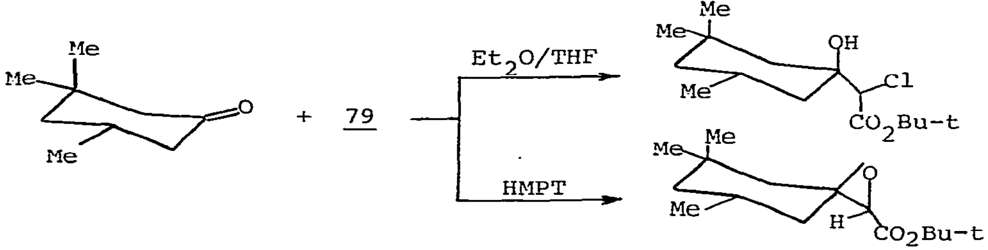
A 4 : 1 mixture favouring the oxygens trans to each other was obtained in the reaction of the Grignard reagent 78 with the cyclohexenone 77 [91]:



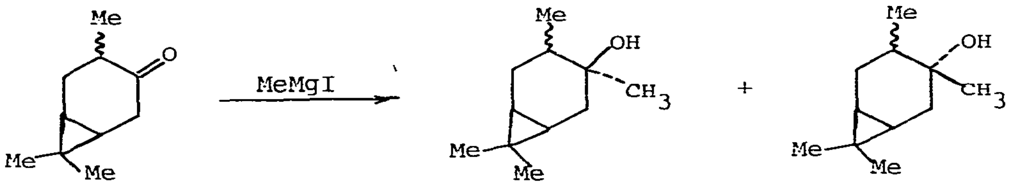
40 - 45 % Axial attack of the Grignard reagent <u>79</u> on 4-*tert*-butylcyclohexanone has been observed in Et_2O/THF or HMPT at −50° C, while in HMPT at 0° C a 1 : 1 mixture of the corresponding epoxides was formed [70]:



The reaction with 3,3,5-trimethylcyclohexanone, on the other hand, occurs with less than 2 % axial attach [70]:



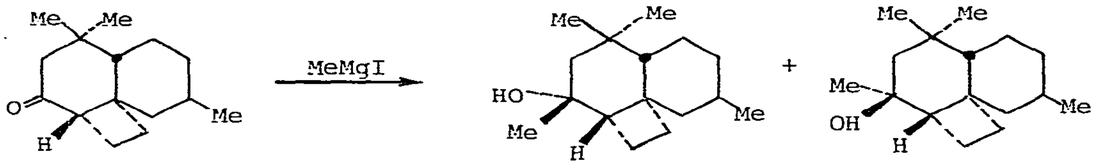
The addition of MeMgI to cis- and trans-4-caranones is stereoselective with the predominant formation of methylcaranols having the OH group cis to the cyclopropane ring [226]:



cis 15 : 1

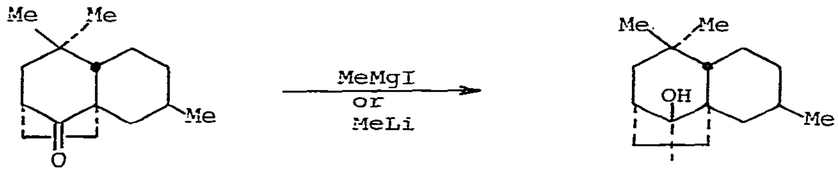
trans 3 : 1

Similar results were obtained with the tricyclic ketone 80, however by using MeLi instead of MeMgI the ratio of products is just reversed [227]:



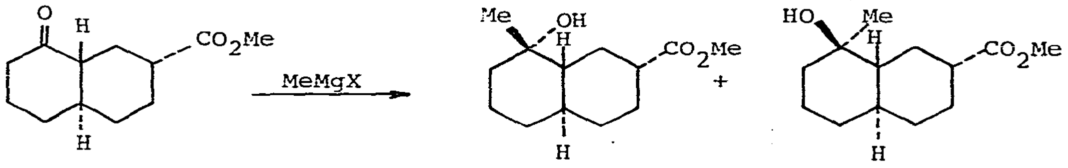
80 4 : 1

Starting with the isomeric ketone 81, on the other hand, a single product is formed with MeMgI as well as with MeLi [227]:



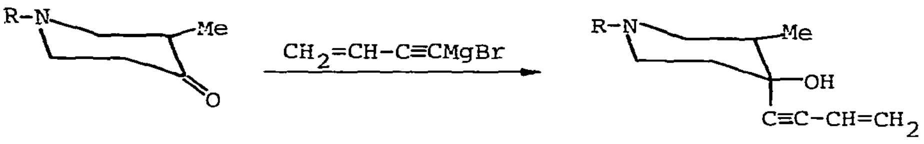
81

The stereochemistry of the Grignard reactions of the (methoxycarbonyl)decalone 82 with MeMgI in C_6H_6 and MeMgCl in THF to give mixtures of 83 and 84 was studied and compared with the results obtained with the corresponding open-chain δ-keto esters like 64 [215]. The ratios 83/84 rising from 7.3 in benzene to 13.5 in THF suggest that conformational mobility is important in determining the variations of stereospecificity with varying reaction conditions. In conformationally mobile δ-keto esters the ester group anchimerically assists the Grignard reactions of the keto group when the reaction conditions favour a folded transition state [228].



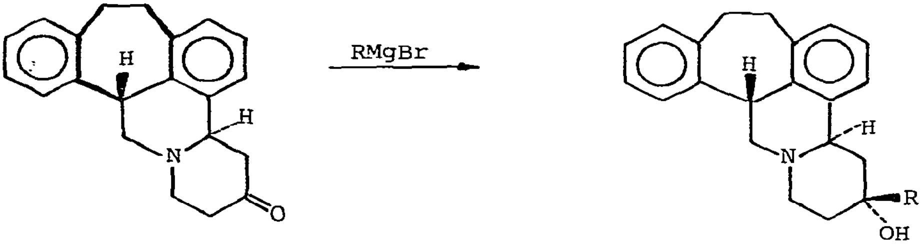
82 83 84

Stereoselectively was also reported for the reaction of Grignard reagents with cyclic 4-aminoketones [134]:



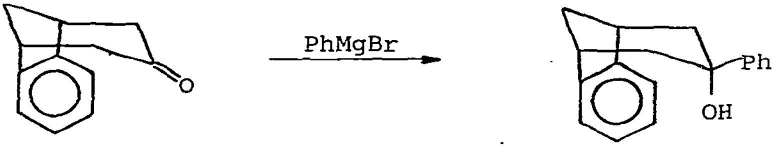
. R = Me, Et, CH_2=CH-CH_2, $PhCH_2$.

The same reaction was used to synthesize butaclamol 85 (R = t-Bu) and numerous butaclamol analogs [229, 230, 231]:



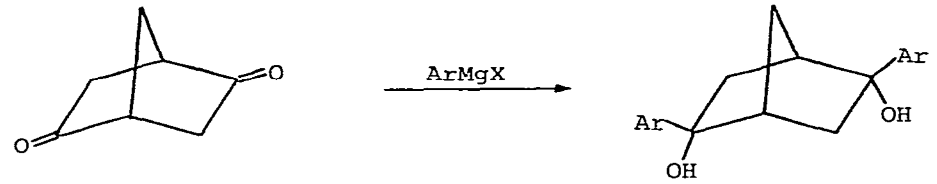
85

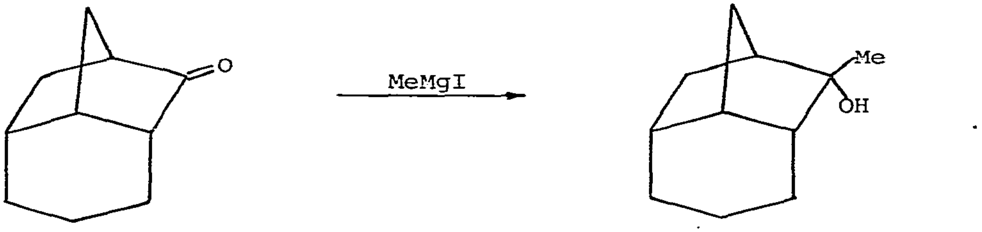
The carbinol 86 has been prepared in 57 % yield [232]:



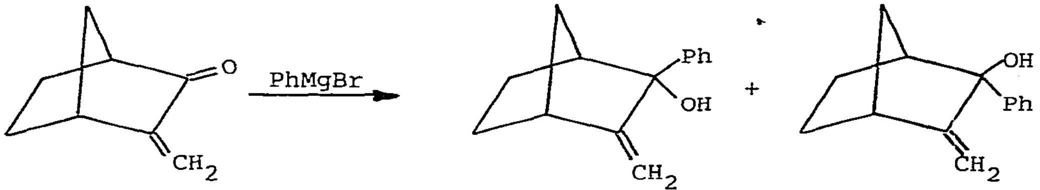
86

Exclusive exo-attack has also been observed in the reaction of aryl Grignard reagents with bicyclo[2.2.1]heptane-2,5-dione [233]and "most probably" in the reaction of MeMgI with 4-homobrendan-2-one [129]:



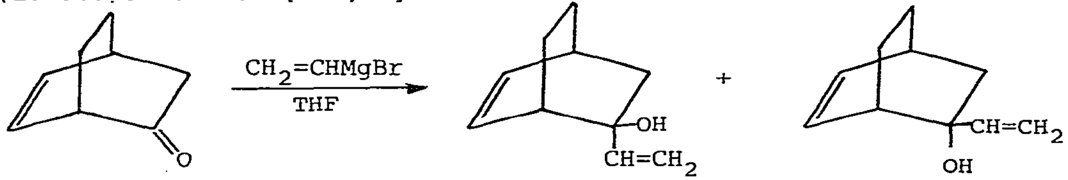


The Grignard reaction of 3-methylen-2-norbornanone with PhMgBr gives a 55 : 33-mixture of exo- and endophenyl adduct the rest (13 %) being the corresponding 1,4-addition product [234]:

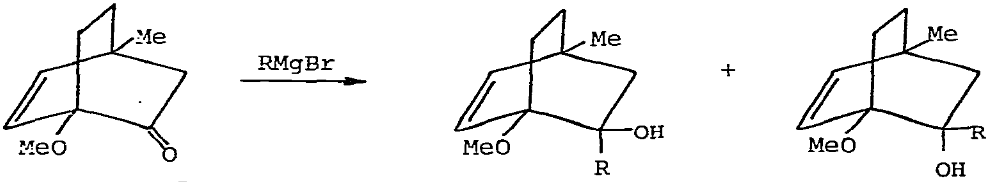


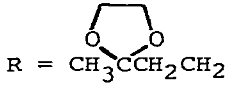
55 : 32

More endo- than exo-attack has been reported for bicyclo [2.2.2.]octenones [235,99]:

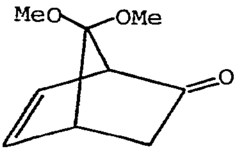


2 : 1

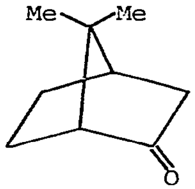


R = $CH_3CCH_2CH_2$ 	68 %	27 %
R = $PhSCH_2CH_2CH_2$	74 %	21 %

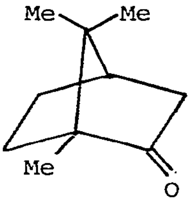
With the following bicyclo[2.2.1]heptanone derivatives exclusive endo-attack takes place:



[236]

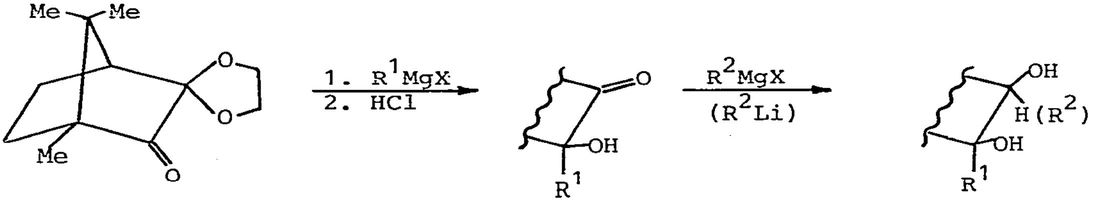


[237]



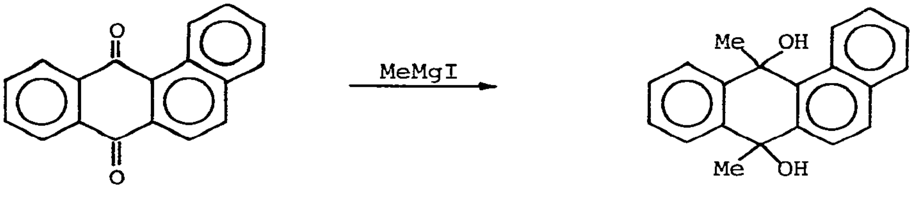
[60]

Addition to the second carbonyl group only works with MeMgI or alkyllithium compounds. Ethyl- or higher alkylmagnesium halides yield the product of hydride attack [238, 239]:



R^1 = Me, Et; R^2 = Et, Pr, Bu

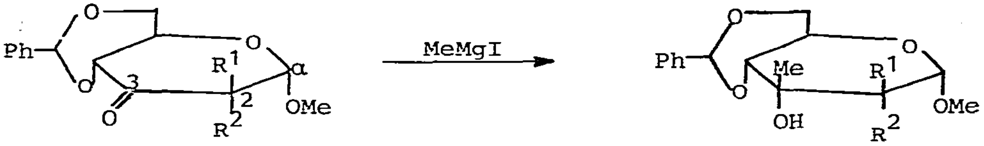
Contrary to an earlier report treatment of 7,12-benz[a]anthraquinone with MeMgI yields 20 - 25 % trans-diol, the main product being the cis-isomer. The reaction - also with methyllithium - is difficult to reproduce. In all cases varying amounts of unreacted quinone are present regardless of the excess organometallic reagent used or the time of reaction [240].



cis + trans (3-4 : 1)

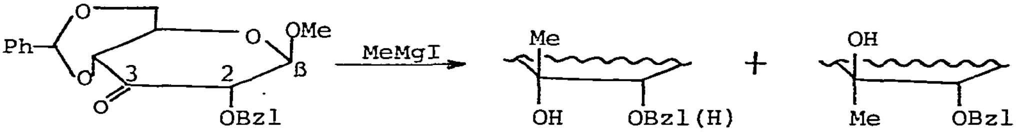
The stereoselectivities in the Grignard reactions of some uloses also have been examined. While both 2-epimers <u>87a</u> and <u>87b</u> with CH_3MgI yield one product only, the corresponding ß-anomer <u>88</u>

gives a 52 : 8-mixture of 3-epimeric compounds [241]:



87

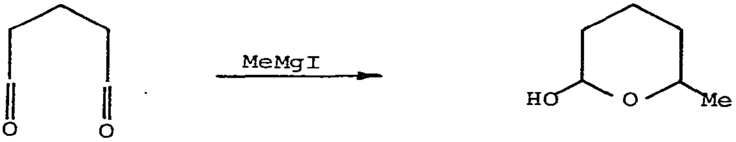
a: $R^1 = H$; $R^2 = OMe$
b: $R^1 = OMe$; $R^2 = H$



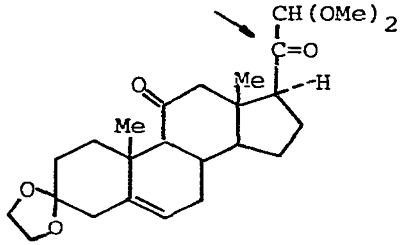
88 52 : 8

C. Selective additions to aldehydes and ketones

With anthraquinone [242, 243] and acenaphthenequinone [244], addition of one or two moles of Grignard reagent can be selected. Glutaraldehyde has been treated with MeMgI to yield 2-hydroxy-6-methyltetrahydropyran as a mixture of two isomers (ratio 3 : 2) [245]:

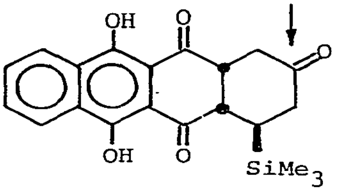


Selective reaction at one carbonyl group (as indicated) is illustrated by the following examples:



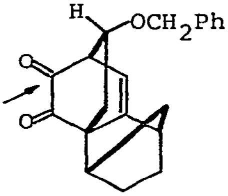
+ MeMgBr

[246]



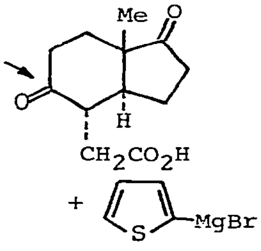
+ HC≡CMgBr

[247]

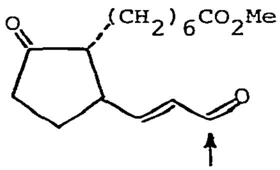


+ Me_3SiCH_2MgCl

[171]

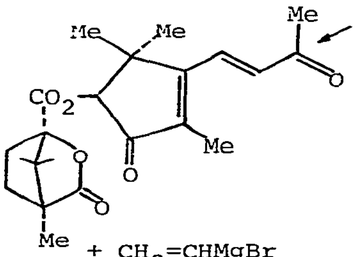


[138]



+ n-$C_5H_{11}MgBr$

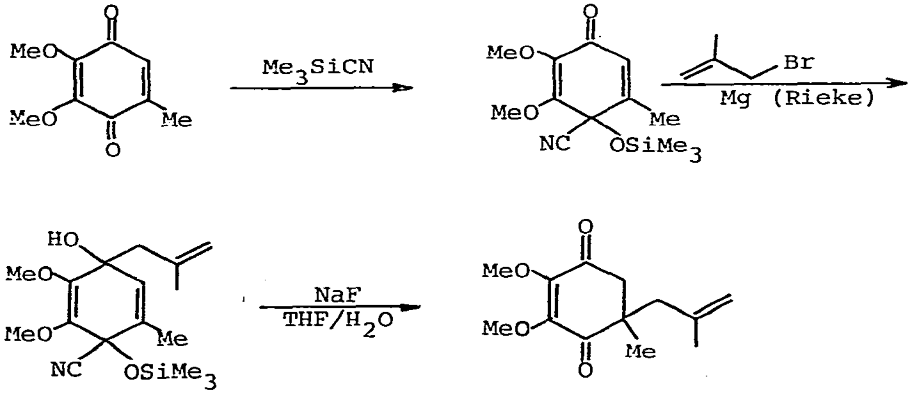
[248]



+ CH_2=CHMgBr

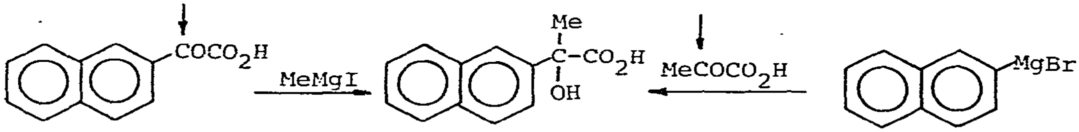
[249]

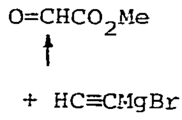
One of the carbonyl groups may be protected with trimethylsilyl cyanide as described for the Barbier synthesis of the relatively unstable allylquinol derivative 89 [250]:



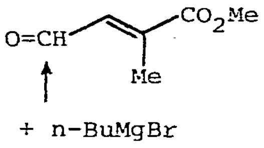
89

Preferential reaction at an aldehyde or ketone group in the presence of an acid or ester function is standard as shown in the following examples [251]:

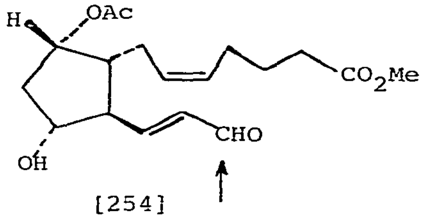




[252]



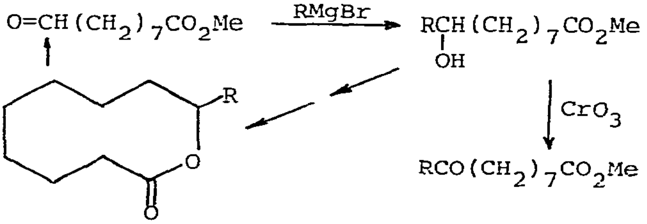
[253]



[254]

Additional examples are found in other prostanoid or natural product syntheses [248,249,255,256].

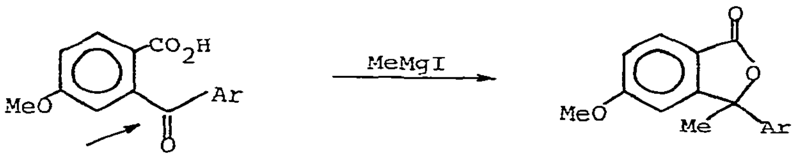
Starting from methyl 8-formyloctanoate a 9-keto ester [257] and two 10-membered lactones [258]have been prepared:

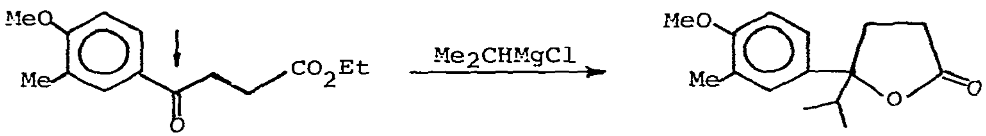


R = Me, C_6H_{13}

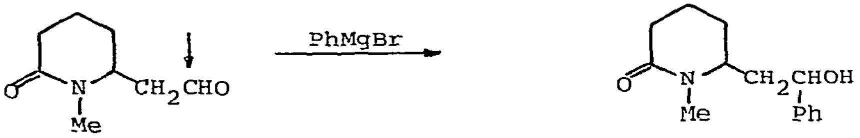
R = CH_2=CH-CH_2-CH_2

The reaction of γ- and δ-keto acids or esters with Grignard reagents instantaneously leads to the corresponding 5- and 6-membered lactones as already mentioned [138, 215]. Additional examples are the following [259, 260]:

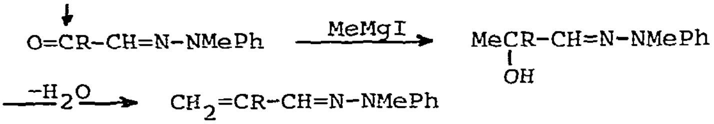




An aldehyde group is also preferentially attacked in the presence of an amide or lactam function as shown in the following example [261]:

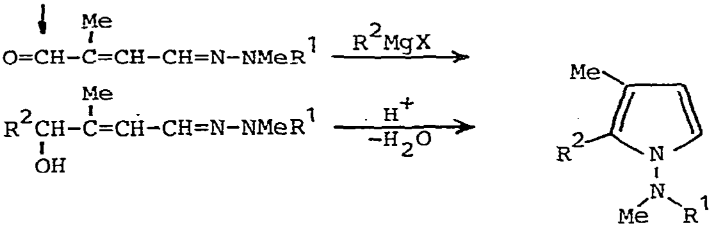


Addition to a carbonyl group in the presence of carbon-nitrogen unsaturation is reported for several monohydrazones of dicarbonyl compounds as hydrazonoaldehydes and hydrazonoketones. The adducts of Grignard reagents with α,ß-unsaturated 4-hydrazonoaldehydes cyclized to N-amino pyrroles [262]:



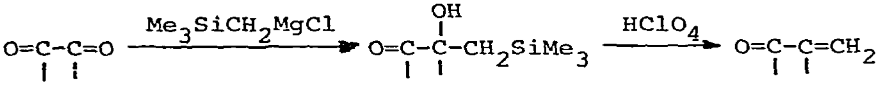
$$\overset{\downarrow}{O}{=}CR{-}CH{=}N{-}NMePh \xrightarrow{MeMgI} Me\underset{OH}{C}R{-}CH{=}N{-}NMePh \xrightarrow{-H_2O} CH_2{=}CR{-}CH{=}N{-}NMePh$$

R = H, Me



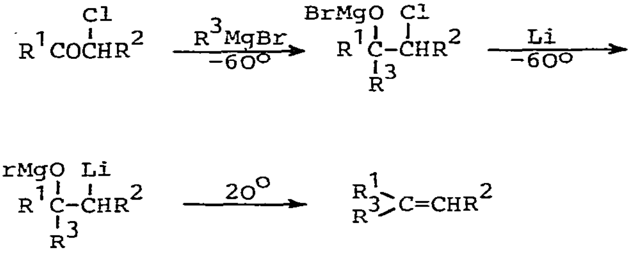
D. Other additions to aldehydes and ketones

Treatment of an α-diketone with trimethylsilylmethylmagnesium chloride in THF gave 64 % of an alcohol which yielded 83 % of the corresponding α,ß-unsaturated ketone on warming with perchloric acid in THF [171]:



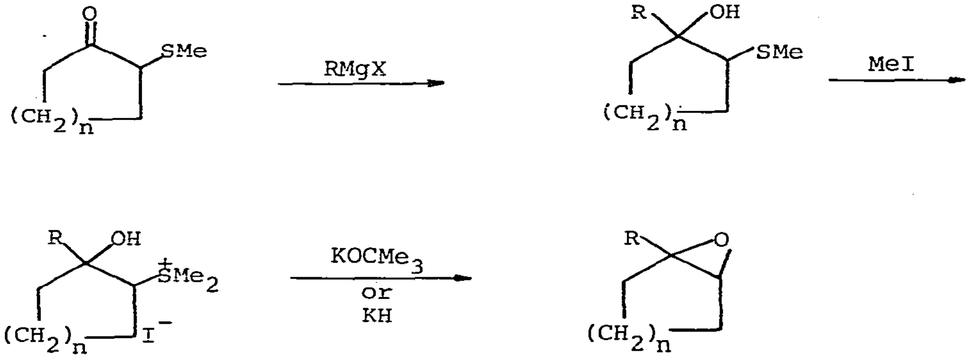
$$O{=}C{-}C{=}O \xrightarrow{Me_3SiCH_2MgCl} O{=}C{-}\overset{OH}{C}{-}CH_2SiMe_3 \xrightarrow{HClO_4} O{=}C{-}C{=}CH_2$$

A new synthesis of alkenes with double bonds in predetermined positions involves the low-temperature addition of a Grignard reagent to an α-chloroketone followed by lithiation and room-temperature elimination of "LiMgOBr" to give the product in 33 - 99 % yield [263]:



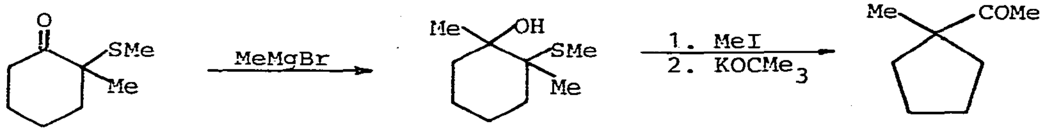
$$\mathrm{R^1CO\overset{Cl}{C}HR^2} \xrightarrow[-60^\circ]{\mathrm{R^3MgBr}} \mathrm{R^1\underset{R^3}{\overset{BrMgO}{C}}-\overset{Cl}{C}HR^2} \xrightarrow[-60^\circ]{\mathrm{Li}} \mathrm{R^1\underset{R^3}{\overset{BrMgO}{C}}-\overset{Li}{C}HR^2} \xrightarrow{20^\circ} \mathrm{R^1R^3C{=}CHR^2}$$

The reaction of α-chlorocarbonyl compounds with Grignard reagents has been mentioned earlier in connection with the formation of oxiranes by alkaline dehydrochlorination of the chlorohydrin intermediates [216]. A general synthesis of oxiranes has been reported involving cyclization of β-hydroxy-dimethylsulphonium salts prepared by the Grignard reaction of the corresponding α-sulfenylated ketones [264]:

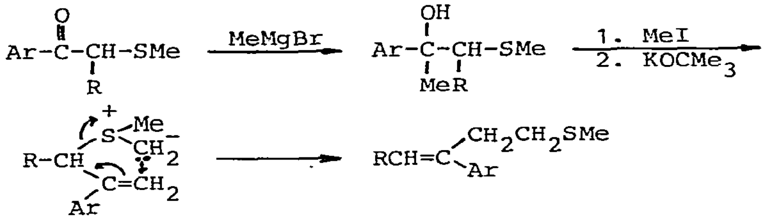


n = 1,2; R = Me, Et

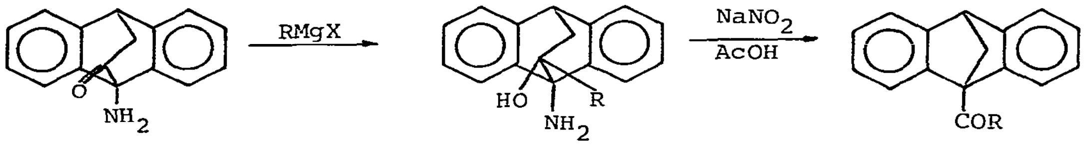
In contrast, the corresponding methyl-substituted cyclohexanone afforded 1-acetyl-1-methyl-cyclopentane by ring contraction [264]:



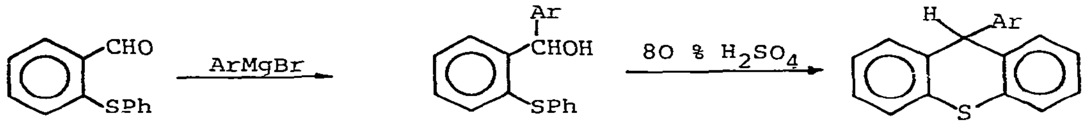
The following side reaction probably via an S-ylide intermediate was observed starting with open-chain ß-hydroxy sulfides [265]:



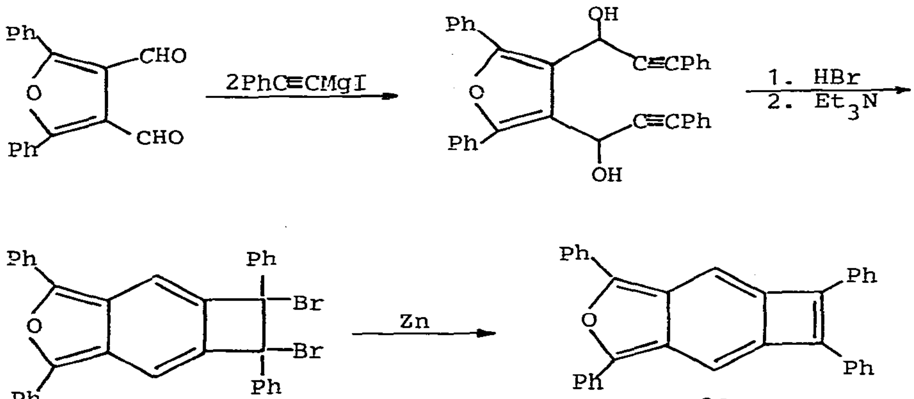
A ring contraction is also involved in the following synthesis of 9,10-dihydro-9,10-methano-anthracenes. With R = Me, Et, and i-Pr yields amount to 75 - 80 % but only a trace of product is obtained with R = Ph [266]:



9-Arylthioxanthenes have been prepared starting from o-phenylthiobenzaldehyde and mesityl or durylmagnesium bromide [267]:

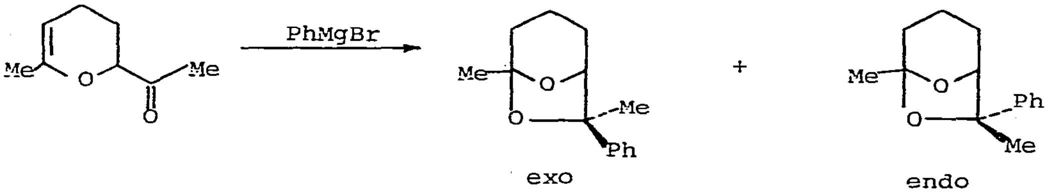


Another cyclization reaction was used to prepare the new stable antiaromatic compound 90 [268]:

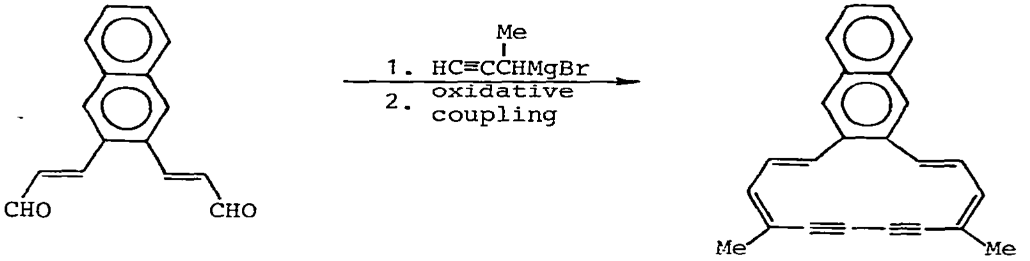


90

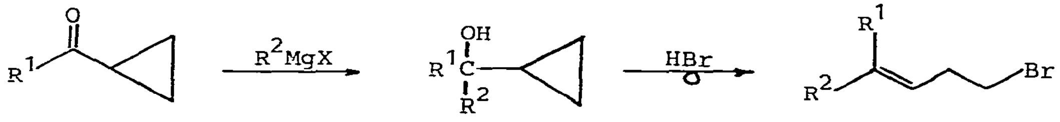
The reaction of the dimer of methyl vinyl ketone with phenylmagnesium bromide afforded a 3 : 1 (exo : endo) mixture of interesting bicyclic ketals [269]:

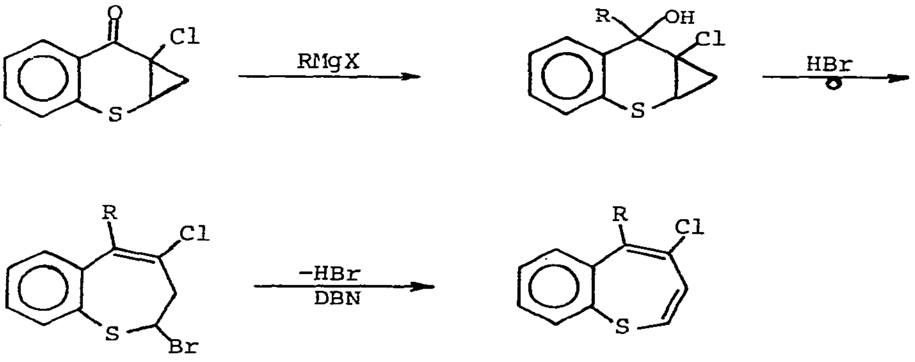


Grignard addition reactions play an important role in routes to macrocyclic annulenes [162, 270]: e. g.

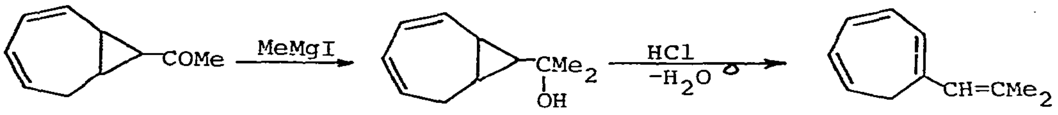


Ring-opening reactions are involved in the Grignard syntheses of homoallyl bromides [271], 1-benzothiepin [272], and tropilidene [273] derivatives:

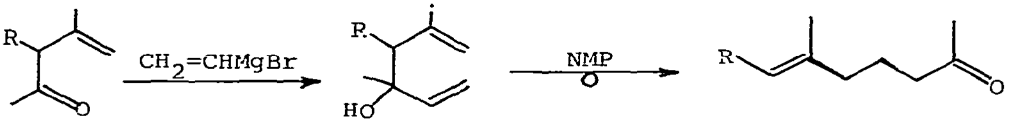




DBN = 1,5-diazabicyclo[4.3.0]non-5-ene

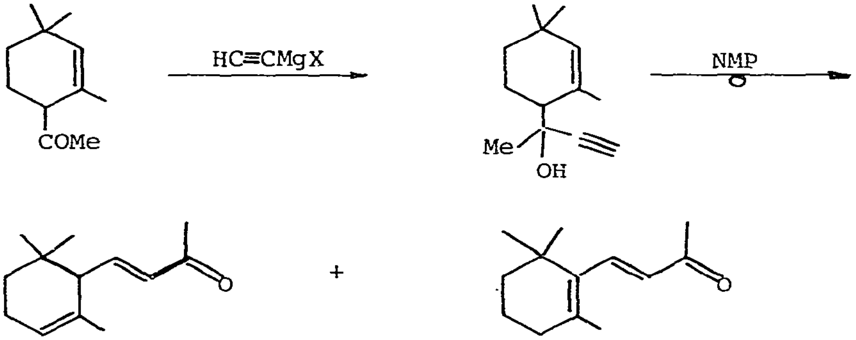


Vinyl Grignard addition has been used for the synthesis of unsaturated ketones via solvent-assisted oxy-Cope rearrangement [274, 275, 276]:



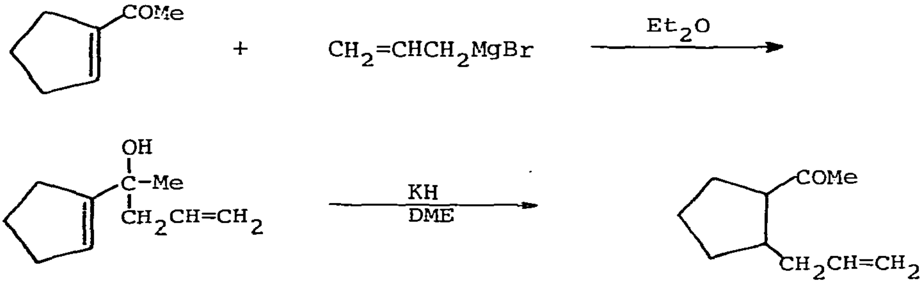
NMP = N-methyl-2-pyrrolidone

The corresponding acetylenic oxy-Cope rearrangement has been investigated as a novel synthetic method for the preparation of ionone and its analogues [277, 278]:

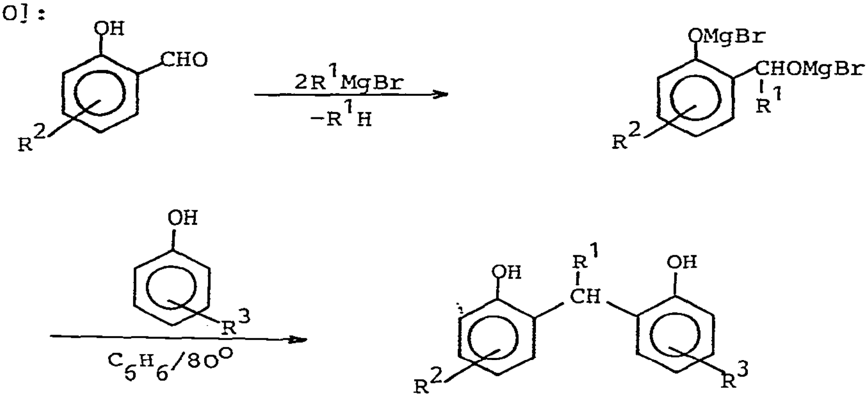


α- β-ionone (2 : 3)

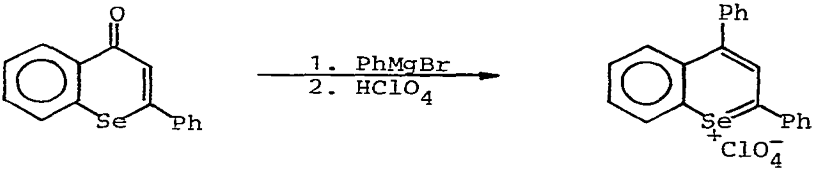
An example of a base-catalyzed oxy-Cope rearrangement is the following [279]:



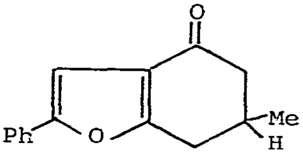
A new simple one-pot method for the synthesis of both symmetrical ($R^2 = R^3$) and unsymmetrical ($R^2 \neq R^3$) 1,1-bis [2-hydroxyaryl]alkanes starting from 2-hydroxybenzaldehydes has been reported [280]:

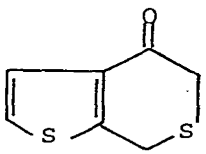


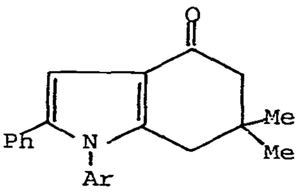
A selenopyrylium salt has been synthesized from selenoflavone and phenylmagnesium bromide [281]:



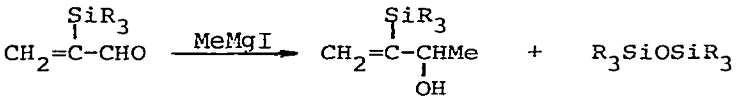
An excellent correlation between the carbonyl ^{13}C chemical shift and the chemical reactivity towards Grignard reagents has been observed for the following tetrahydrobenzofuran and dithiaindan ketones, whereas this correlation is absent for the corresponding 4-keto tetrahydroindole derivatives. The latter on treatment with either ethylmagnesium iodide or vinylmagnesium bromide in THF failed to react even under forcing conditions although ^{13}C NMR spectra on these ketones indicated very clearly the magnetic similarity of the carbonyl carbon with that of the former or aryl conjugated ketones [282].





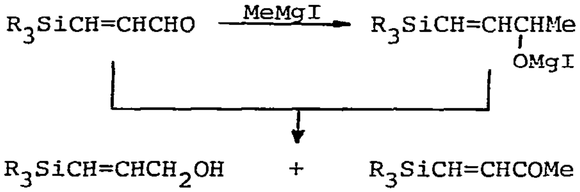


Interesting side reactions have been observed upon treatment of α- and β-(trialkylsilyl)acroleins with methylmagnesium iodide. The α-isomers to a considerable extent undergo cleavage of the Si-C bond giving up to 27 % hexaalkyldisiloxane [283]:



$$CH_2{=}\overset{SiR_3}{C}\text{-}CHO \xrightarrow{MeMgI} CH_2{=}\overset{SiR_3}{C}\text{-}\underset{OH}{C}HMe \quad + \quad R_3SiOSiR_3$$

In the case of the β isomers, on the other hand, part of the primarily formed alcoholate is oxidized by another molecule of the starting aldehyde to the ketone with the concomitant formation of the reduction product of the aldehyde, the γ-(trialkylsilyl)allyl alcohol. These oxidation-reduction side reactions, however, do not exceed 6 % [283]:

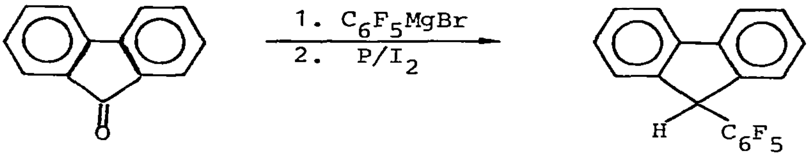


$$R_3SiCH{=}CHCHO \xrightarrow{MeMgI} R_3SiCH{=}CH\underset{OMgI}{C}HMe$$

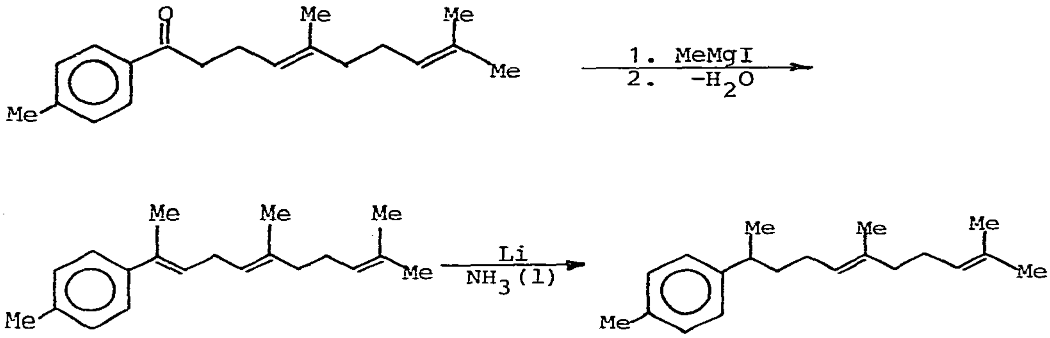
$$\downarrow$$

$$R_3SiCH{=}CHCH_2OH \quad + \quad R_3SiCH{=}CHCOMe$$

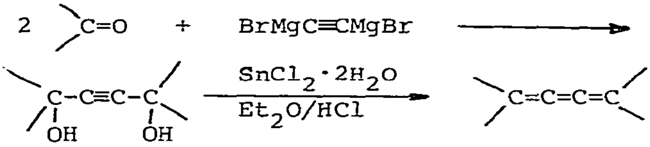
Several methods have been used to prepare hydrocarbons via the addition of Grignard reagents to carbonyl functions followed by reduction of the primarily formed alcohol. An example is the following synthesis of a fluorene from fluorenone [49]:



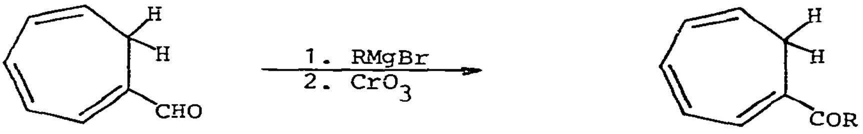
Red phosphorus in 57 % HI [46], PBr_3 followed by $NaBH_4$ [284], $LiAlH_4$ [285], Zn/HCl [286], catalytic hydrogenation [287, 288], and Birch conditions [289, 290] have also been successfully used. In the following example water was eliminated first and the product treated with lithium in liquid ammonia, whereby the double bond conjugated with the aromatic ring was reduced selectively [291]:



In a cumulene synthesis H_2O_2 was eliminated from the corresponding diol by treating with stannous chloride dihydrate in ether, which had been saturated with HCl gas [162]:

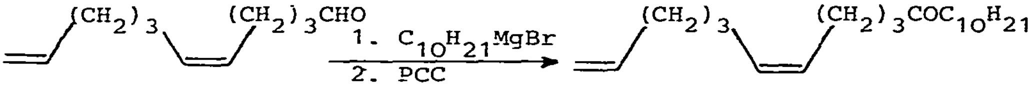


Numerous examples have been reported for the synthesis of ketones via addition of Grignard reagents to aldehydes followed by oxidation of the primarily formed alcohol. Mostly Jones oxidation [196, 286, 292-296] has been used as in the synthesis of 1-acetyl- and 1-benzoylcycloheptatriene [296]:



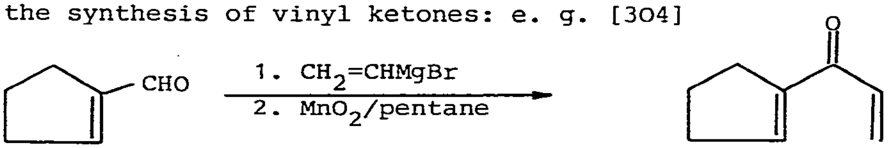
R = CH_3, Ph

The pheromone 91 [297] and several other ketones [289, 298, 299, 300] have been prepared by oxidation of the corresponding alcohols with pyridinium chlorochromate (PCC):

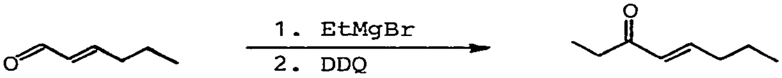


91

Manganese dioxide oxidation [301-304] has been used especially for the synthesis of vinyl ketones: e. g. [304]



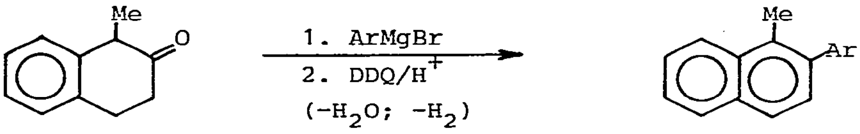
Other oxidation reagents include 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) [305], $Cu(OAc)_2$ [306], and periodate cleavage of glycols [307]:



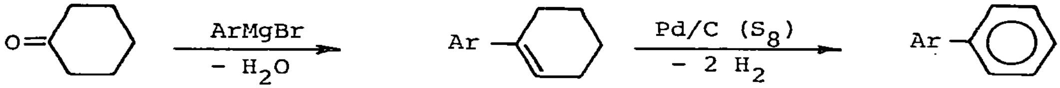
$$\mathrm{PhCOCHO} \xrightarrow[\text{2. Cu(OAc)}_2]{\text{1. } C_6D_5MgBr} \mathrm{PhCOCOC_6D_5}$$

$$\mathrm{R{-}CO{-}CH_2OH} \xrightarrow[\text{2. periodate}]{\text{1. } {}^{14}CH_3MgI} \mathrm{R{-}CO\overset{14}{-}CH_3}$$

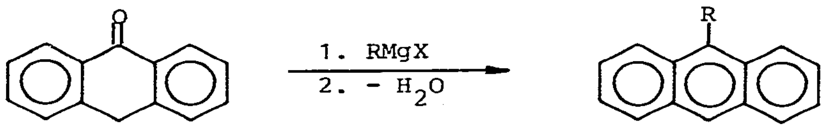
DDQ has also been used for the dehydrogenation of dihydronaphthalene derivatives prepared by a Grignard reaction [308]:



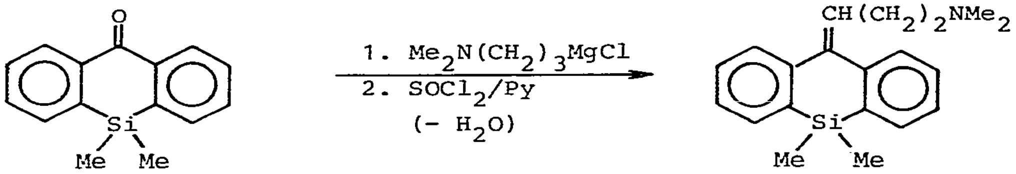
Aromatization of 1-arylcyclohexenes on the other hand, has been achieved with palladium on carbon at 280° [309], in the presence of sulfur already at 235 - 240° [310]:



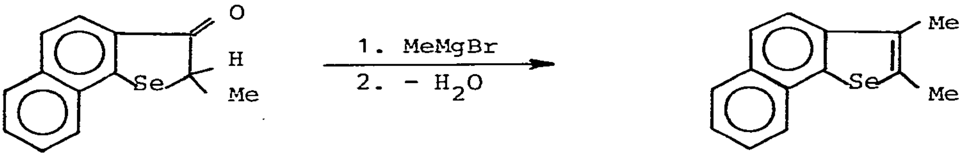
Dehydration only is necessary for the synthesis of anthracene derivatives from anthraquinone; phosphorus pentoxide [132], thionylchloride/pyridine [311], or p-toluenesulfonic acid [259] have been used as dehydrating agents:



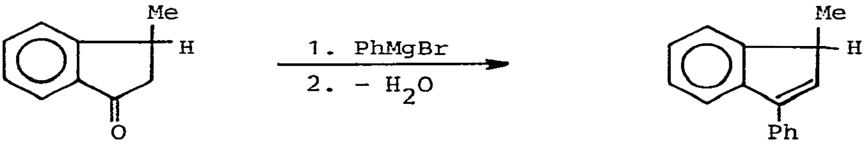
Under the same conditions an exocyclic double bond has been introduced into the following silaanthracene framework [169]:



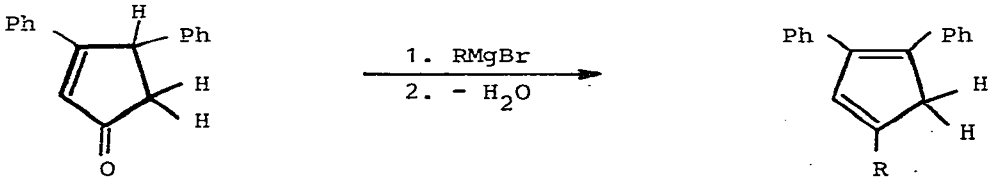
A selenophene derivative has also been prepared by a Grignard reaction [312]:



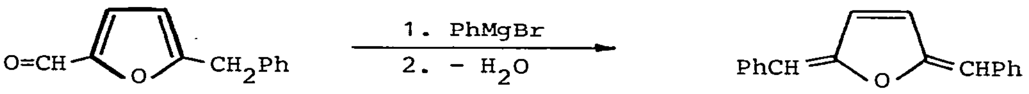
Similarly 1-phenyl-3-methylindene has been obtained from 3-methyl-1-indanone [313]:



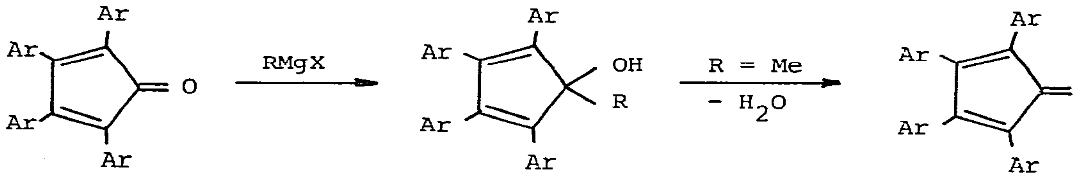
1,4 Elimination of water instead of 1,2 elimination takes place following the addition of Grignard reagents to 3,4-diphenylcyclopent-2-enone [314]:



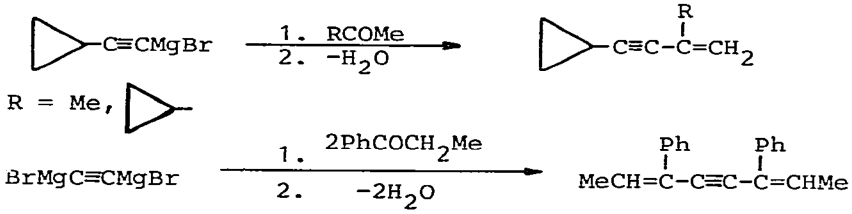
1,6 Elimination of water is even observed in the reaction of 5-benzylfurfural with phenylmagnesium bromide yielding 30 % 2,5-dibenzylidene-2,5-dihydrofuran [315]:



Starting with tetracyclone (Ar = Ph) or other tetraarylcyclopentadienones pentaarylcyclopentadienols (R = Ar) [316] or fulvenes (R = Me) [317] have been prepared:



Starting with acetylenic Grignard reagents the following vinyl- [318] and divinylacetylenes [163] have been synthesized:



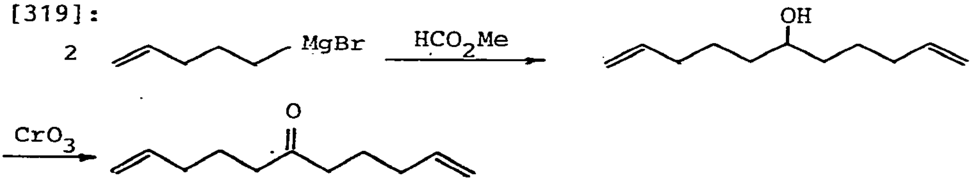
$$BrMgC\equiv CMgBr \xrightarrow[2.\ -2H_2O]{1.\ 2PhCOCH_2Me} MeCH{=}\overset{Ph}{C}{-}C\equiv C{-}\overset{Ph}{C}{=}CHMe$$

E. Reactions with carboxylic acids and derivatives

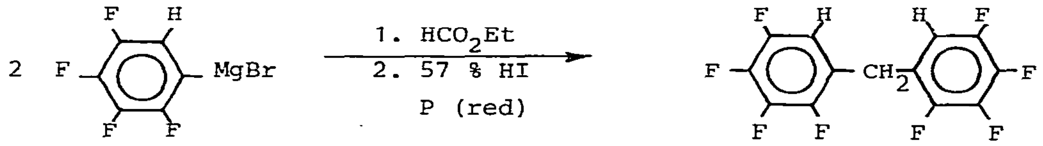
1. Open-chain derivatives

The reaction of tert-butylmagnesium chloride with ethyl cinnamate [206] and benzoyl bromide [207] via SET has been noted previously (section IV. A).

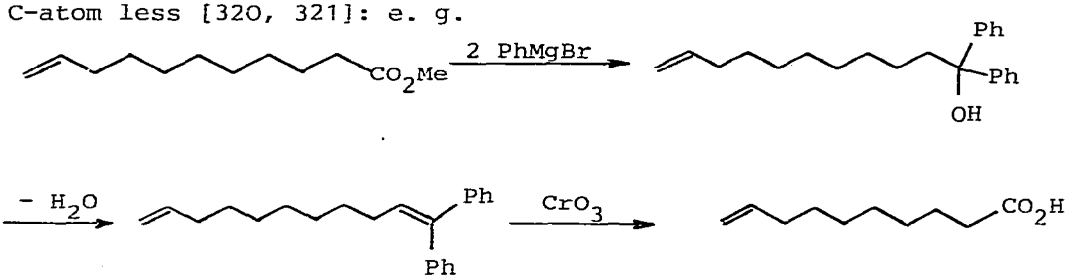
Normally an ester with excess Grignard reagent gives an alcohol which - in the case of starting with methyl formate - can be oxidized to the corresponding ketone as shown in the following example [319]:



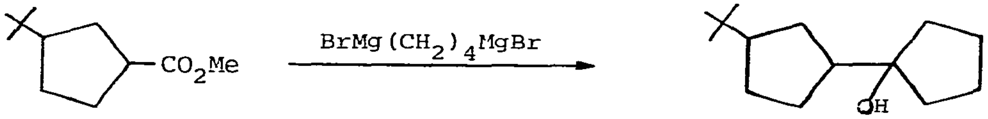
The carbinol prepared from ethyl formate and tetrafluorophenylmagnesium bromide has been reduced to octafluorodiphenylmethane [47]:



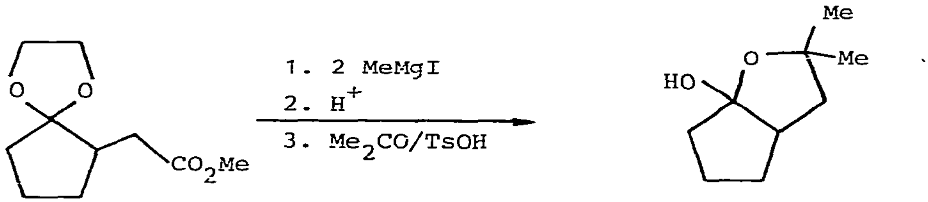
The Barbier-Wieland degradation starting with an ester and phenylmagnesium bromide has been used to prepare the acid with one C-atom less [320, 321]: e. g.



The Grignard reagent prepared from 1,4-dibromobutane upon treatment with a cyclopentanecarboxylate yielded a 1-cyclopentylcyclopentanol derivative [156]:

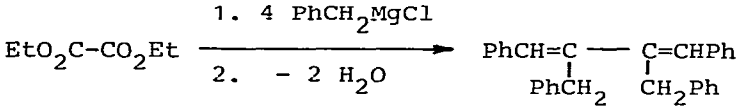


The bicyclic hemiketal 92 was obtained by the following sequence of reactions [322]:



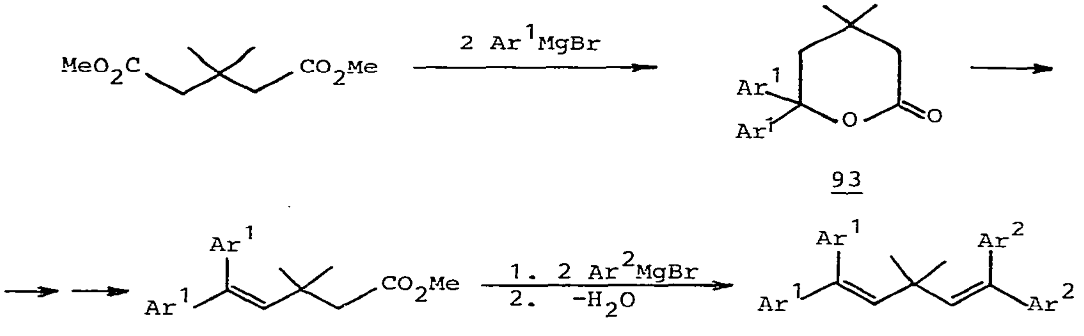
92

Diethyloxalate reacts with four moles of benzylmagnesium chloride to yield a 1,3-butadiene derivative after dehydration of the corresponding diol [323]:



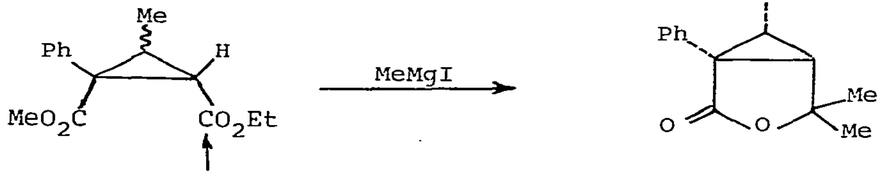
$$EtO_2C\text{-}CO_2Et \xrightarrow[2.\ -2\ H_2O]{1.\ 4\ PhCH_2MgCl} \underset{PhCH_2}{PhCH{=}C}\text{—}\underset{CH_2Ph}{C{=}CHPh}$$

Methyl 3,3-dimethylglutarate and aryl Grignard reagents, on th other hand, did not lead to a 1,5-diol; rather the δ-lactone 93 resulted which could be converted into unsymmetrically substituted 1,4-dienes [324, 325]:



93

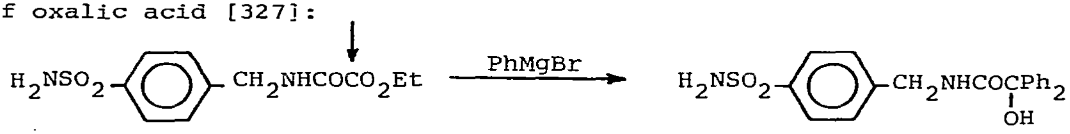
The di-ester 94 was selectively attacked by methylmagnesium iodide to give the bicyclic lactone 95 [326]:



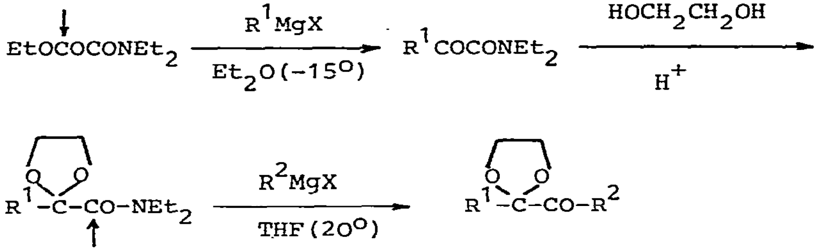
94

95

Grignard reagents furthermore add selectively to ester groups in the presence of acid amide groups as shown by the following derivative of oxalic acid [327]:



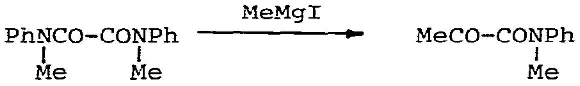
This selectivity was also used for the synthesis of monoacetals of α-diketones [328]:



Dropwise addition of CD_3MgI to diethyl oxalate in Et_2O at -78° gave 46 % ethyl pyruvate-d_3 [329]:

$$EtO_2\overset{\downarrow}{C}-CO_2Et \xrightarrow[Et_2O(-78^{\circ})]{CD_3MgI} CD_3CO-CO_2Et$$

The corresponding reaction with N,N'-dimethyloxanilide, on the other hand, yielded only a 1:1 mixture of N-methylpyruvanilide and unreacted starting material [330]:



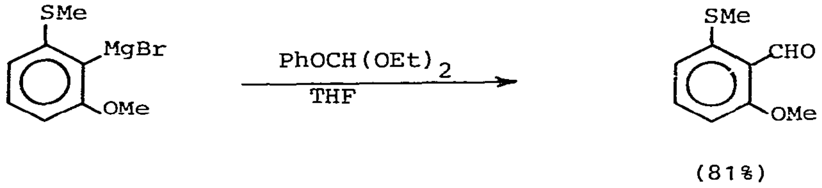
$$\underset{\mathrm{Me}}{\mathrm{Ph\underset{|}{N}}}CO-CO\underset{\mathrm{Me}}{\mathrm{\underset{|}{N}Ph}} \xrightarrow{MeMgI} MeCO-CO\underset{\mathrm{Me}}{\mathrm{\underset{|}{N}Ph}}$$

Facile formylation (R^1=H) or acylation (R^1=Et,Ph) of Grignard reagents, however, take place with the 2-aminopyridine derivative 96. The ready formation of a six-membered chelate 97 prohibits release of the aldehyde or ketone under the reaction conditions protecting them from further reaction with the Grignard reagent [331, 332]:

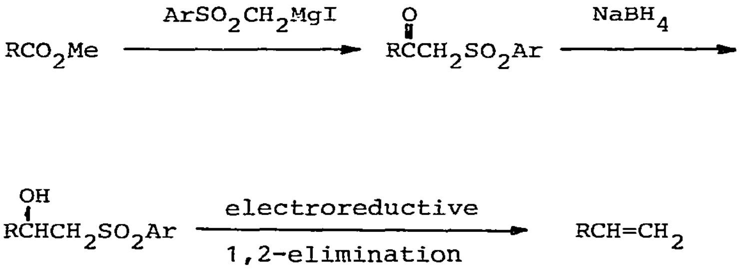
96

97

N,N-Dimethylformamide [133], ethyl orthoformate [333] and diethyl phenyl orthoformate [102, 334] have also been used as formylating agents: e.g. [334].



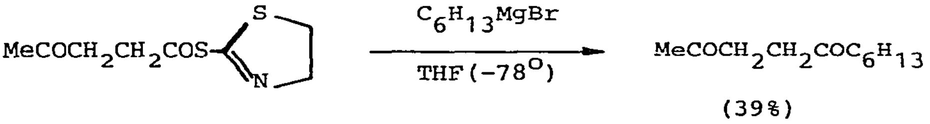
A facile transformation of ester groups to vinyl groups via ß-ketosulfones prepared by a Grignard reaction has been reported [26]:



$$RCO_2Me \xrightarrow{ArSO_2CH_2MgI} R\overset{O}{\overset{\|}{C}}CH_2SO_2Ar \xrightarrow{NaBH_4}$$

$$R\overset{OH}{\overset{|}{C}}HCH_2SO_2Ar \xrightarrow[\text{1,2-elimination}]{\text{electroreductive}} RCH{=}CH_2$$

2-Mercaptopyridine [34] and -thiazoline esters [335] have also been used for ketone syntheses. Unusual selectivity, with the ester function more reactive than a ketone, was found in the following example [335]:



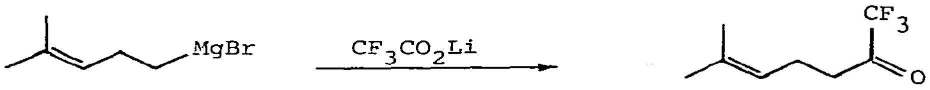
A general method for the preparation of α-fluoro-ß-chloroethyl ketones has been described [336]:

$$R^1\text{-CHCl-CHF-CO}_2R \xrightarrow[Et_2O(-45^\circ)]{R^2MgX} R^1\text{-CHCl-CHF-CO-}R^2$$

The corresponding acids have been used as starting material for the synthesis of allyl ketones [276], trifluoromethyl ketones [337], and fluorinated α-diketones [338]: e.g.

$$C_3F_7CO_2H \xrightarrow[Et_2O(10^\circ)]{PhCH_2MgCl} C_3F_7COCH_2Ph \xrightarrow{SeO_2} C_3F_7COCOPh$$

Lithium salts of carboxylic acids in this case do not work as well [338] although usually they are reported to give higher yields compared with other methods [339]: e.g.

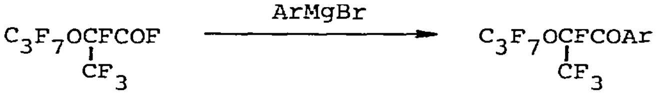


(80%)

Aryloxymethyl vinyl ketones have been prepared similarly [340]:

$$ArOCH_2CO_2Li \xrightarrow{CH_2=CHMgBr} CH_2=CHCOCH_2OAr$$

Fluoro-ketones also have been synthesized by the reaction of Grignard reagents with perfluoroacid fluorides [341]: e.g.

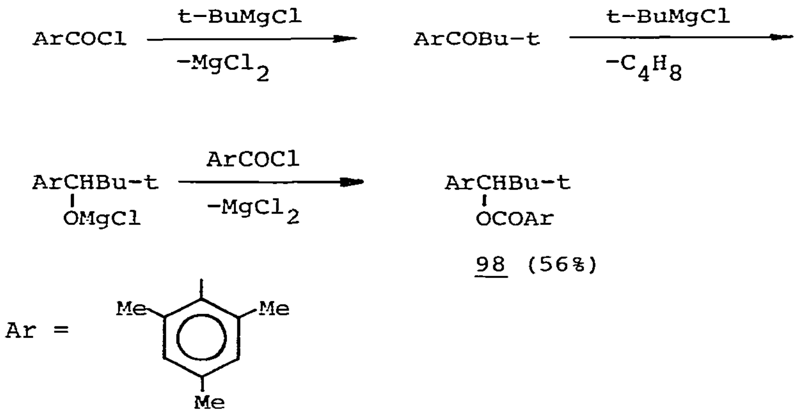


$$C_3F_7O\underset{CF_3}{\underset{|}{C}}FCOF \xrightarrow{ArMgBr} C_3F_7O\underset{CF_3}{\underset{|}{C}}FCOAr$$

For the preparation of highly branched ketones from hindered acid chlorides and Grignard reagents the presence of copper(I) salts has proven advantageously [342]: e.g.

$$t\text{-BuEt}_2CCOCl \xrightarrow[CuCl]{t\text{-BuMgCl}} \underset{(83\%)}{t\text{-BuEt}_2CCOBu\text{-}t}$$

When 2,4,6-trimethylbenzoyl chloride was treated with an excess of t-BuMgCl reductive 1,2-addition occurred giving the ester 98 as the sole product [343]:

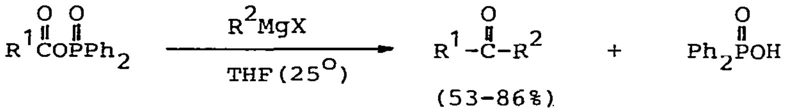


$$\mathrm{ArCOCl} \xrightarrow[-\mathrm{MgCl_2}]{t\text{-BuMgCl}} \mathrm{ArCOBu\text{-}t} \xrightarrow[-\mathrm{C_4H_8}]{t\text{-BuMgCl}} \underset{\mathrm{OMgCl}}{\mathrm{ArCHBu\text{-}t}} \xrightarrow[-\mathrm{MgCl_2}]{\mathrm{ArCOCl}} \underset{\mathrm{OCOAr}}{\mathrm{ArCHBu\text{-}t}}$$

98 (56%)

As mentioned earlier CIDNP signals had been detected during the corresponding reaction of t-BuMgCl with benzoyl bromide [207] (section IV.A).

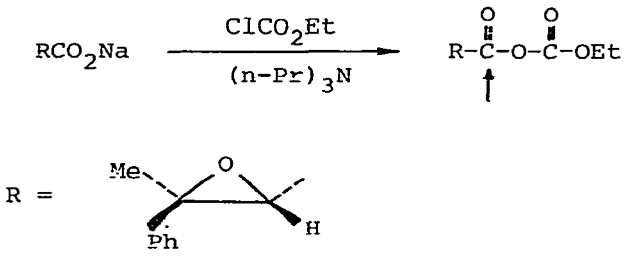
Carboxylic-diphenylphosphinic anhydrides are useful reagents for carbon-acylation, as they react smoothly with Grignard reagents to give ketones in satisfactory yields. Alcohols were not observed unless excess Grignard reagent was used. With vinylmagnesium bromide, however, only unidentified nonketonic material has been observed [344]:



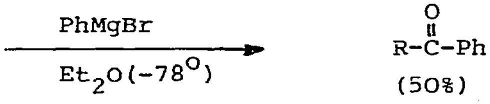
$$R^1\overset{O}{\overset{\|}{C}}O\overset{O}{\overset{\|}{P}}Ph_2 \xrightarrow[\mathrm{THF}(25^\circ)]{R^2MgX} R^1\text{-}\overset{O}{\overset{\|}{C}}\text{-}R^2 + Ph_2\overset{O}{\overset{\|}{P}}OH$$

(53-86%)

A new reaction sequence has been developed to produce acid- and base-sensitive epoxy ketones using a mixed carbonate functional group to activate the carbonyl group [345]:



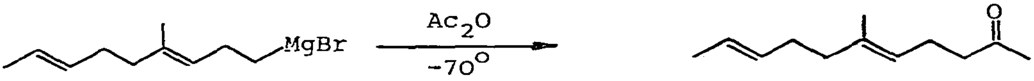
$$RCO_2Na \xrightarrow[(n\text{-}Pr)_3N]{ClCO_2Et} R\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}\overset{O}{\overset{\|}{C}}\text{-}OEt$$



$$\xrightarrow[Et_2O(-78^{\circ})]{PhMgBr} R-\overset{O}{\overset{\|}{C}}-Ph$$

(50%)

"Reversed"Grignard reaction with acetic anhydride in Et_2O afforded the ketone 99 [271]:



99 (72%)

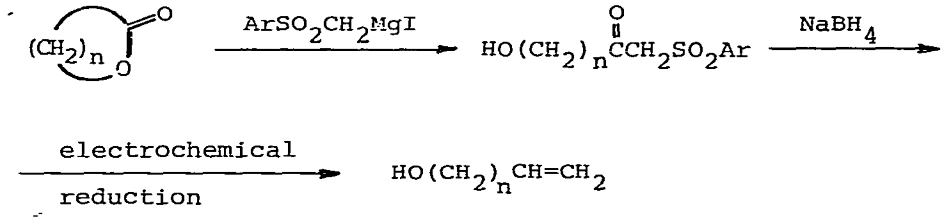
Only a single out of numerous examples will be noted for the reaction of a Grignard reagent with carbon dioxide. In the following synthesis of 4-phenylbutanoic acid [2-^{13}C] there are two carboxylation steps involved [48]:

$$PhCH_2CH_2MgBr \xrightarrow{^{13}CO_2} PhCH_2CH_2{}^{13}CO_2H \xrightarrow[\substack{3.\ Mg\\ 4.\ CO_2}]{\substack{1.\ LiAlH_4\\ 2.\ HBr}} PhCH_2CH_2{}^{13}CH_2CO_2H$$

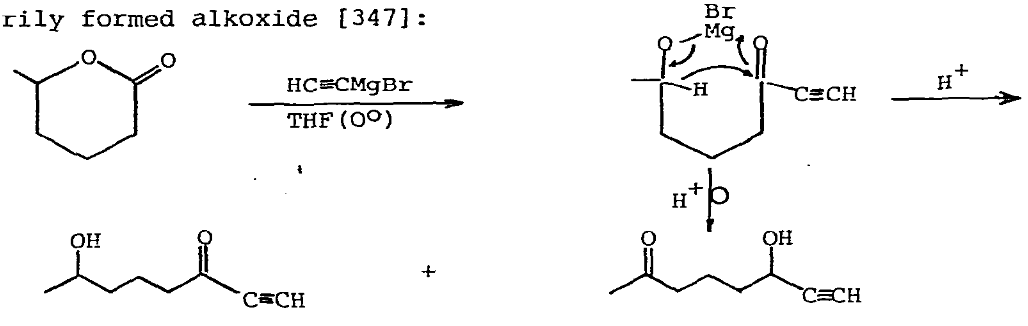
The kinetic isotope effect for carboxylation of a Grignard reagent at -78° has been determined to be $^{12}k/^{13}k = 1.059$ [346].

2. Lactones, lactams, and cyclic anhydrides

Reactions of lactones with Grignard reagents often correspond to those of open-chain esters as shown in the following synthesis of ω-hydroxyolefins according to a procedure already noted in section IV.E.1 [26]:



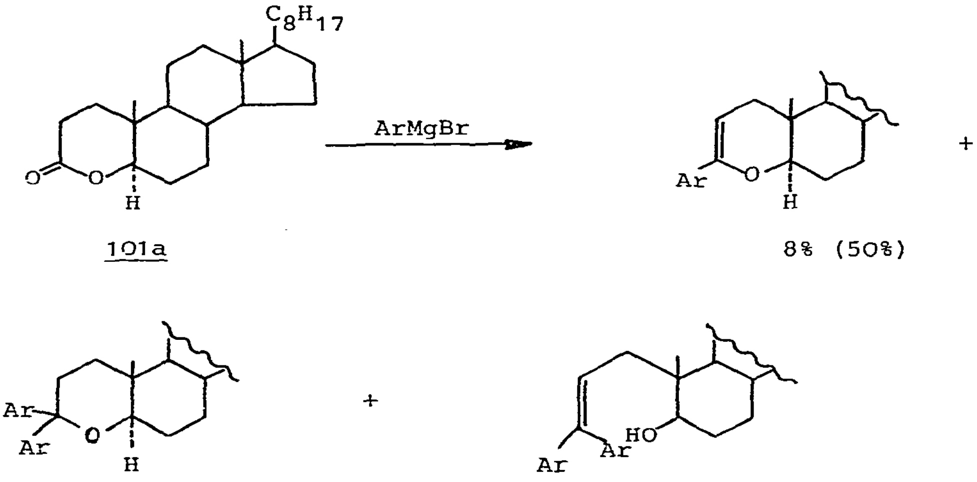
Condensation of acetylenemagnesium bromide with 5-caprolactone gave the expected hydroxy ketone 100 and an unexpected hydroxy ketone 101 in a ratio of ca. 2:1. This unusual redox reaction can be explained via a six-membered intramolecular hydride transfer within the primarily formed alkoxide [347]:



100

101

The steroidal δ-lactone 101a reacts with p-methoxyphenylmagnesium bromide giving three different products, while with Ar=Ph only the first dihydropyran derivative is formed in 50% yield [348]:



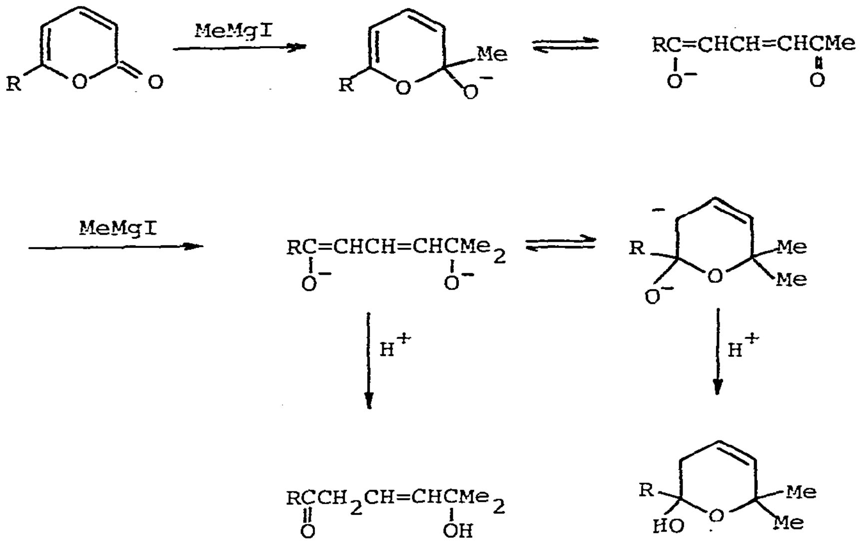
101a

8% (50%)

35%

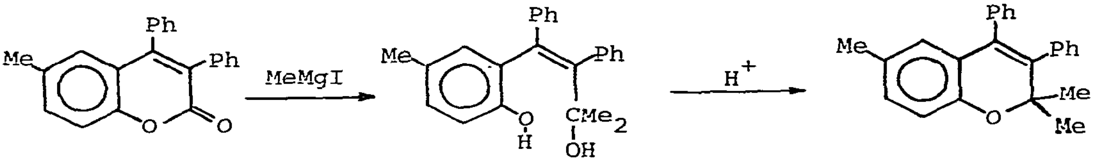
16%

In the Grignard reaction of MeMgI with 2-pyrones the formation of ketols and dihydropyranols involves, before hydrolysis, an equilibrium between the open and cyclic ionic intermediates [349]:

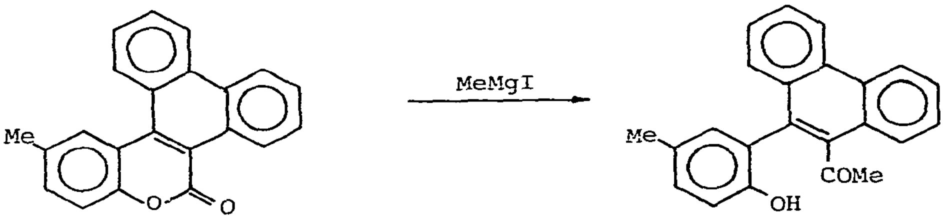


R = Me, Ph

The 3,4-diphenylcoumarin 102 reacts with excess MeMgI to give the carbinol 103 which readily cyclizes to the corresponding chromene 104. The coumarin derivative 105, on the other hand, yields 60% of the ketone 106 [350]:

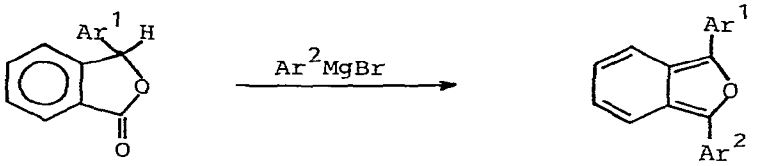


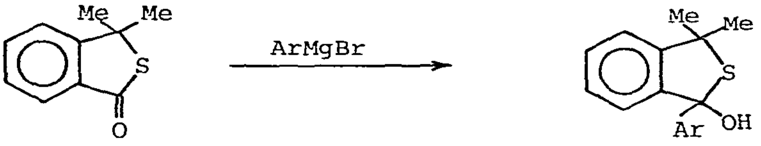
102 103 (65%) 104



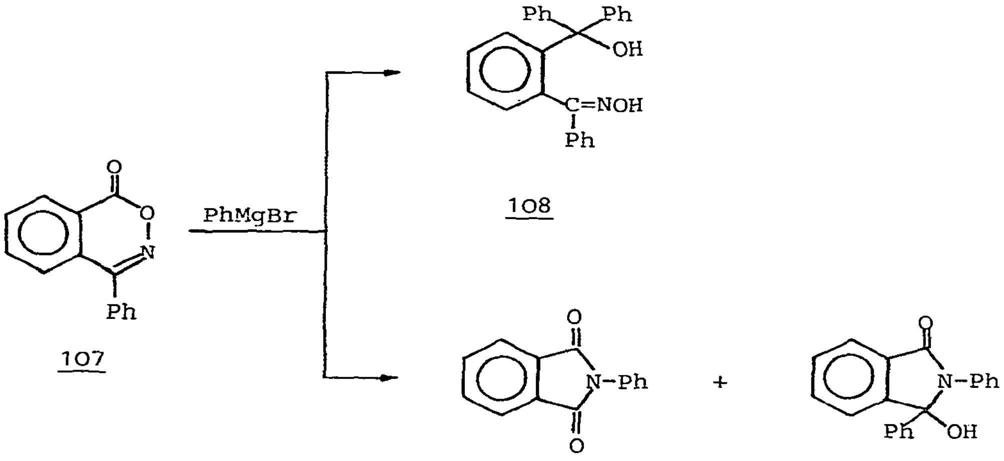
105 106

Diarylisobenzofurans have been prepared from 3-arylphthalides [351], while 3,3-dimethyl-2-thiophthalid with arylmagnesium bromides yields 1-aryl-1-hydroxy-3,3-dimethyl-thiophthalans [352]:

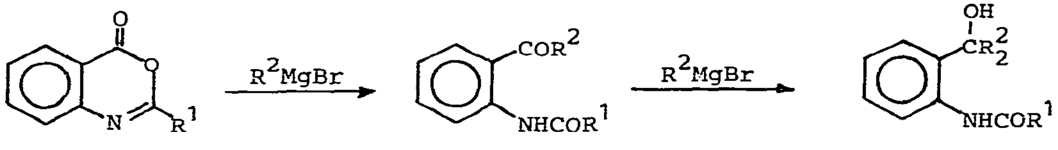




Different products depending on the conditions have been obtained from 4-phenyl-2,3-benzoxazin-1-one 107 and phenylmagnesium bromide. Addition of 107 to a fourfold amount of the Grignard reagent afforded the normal product 108, while the reversed addition of PhMgBr to 107 in boiling benzene yielded N-phenylphthalimide formed by a rearrangement of the Beckmann type and its reaction product with PhMgBr [353]:

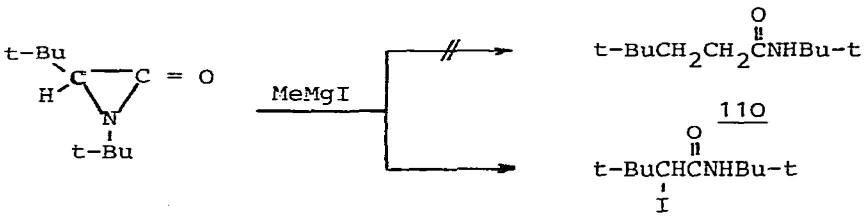


3,1-Benzoxazin-4-ones 109, on the other hand, have been reported to yield ketones [354] or the corresponding carbinols [355]:



109

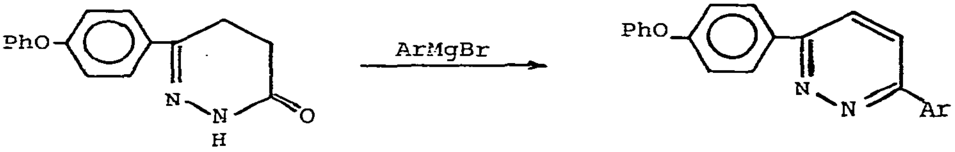
The reaction of α-lactams with alkylmagnesium halides has been reinvestigated. Contrary to the literature no 110 could be detected under the reaction products of 1,3-di-*tert*.-butylaziridone with MeMgI. Instead, the principal set of products consists of the α-iodo amide 111 along with varying amounts of substances derived from this halo amide [356]:



110

111

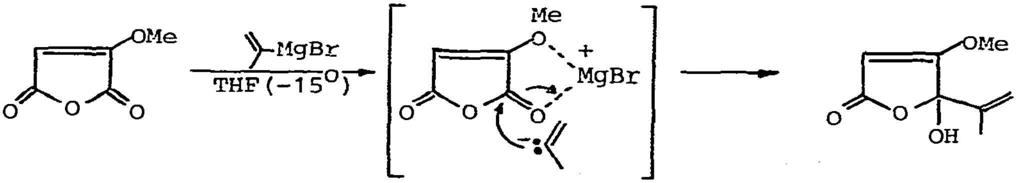
Reaction of the pyridazinone 112 with phenyl- and p-anisylmagnesium bromide gave the corresponding 3,6-diarylpyridazines 113 [357]:



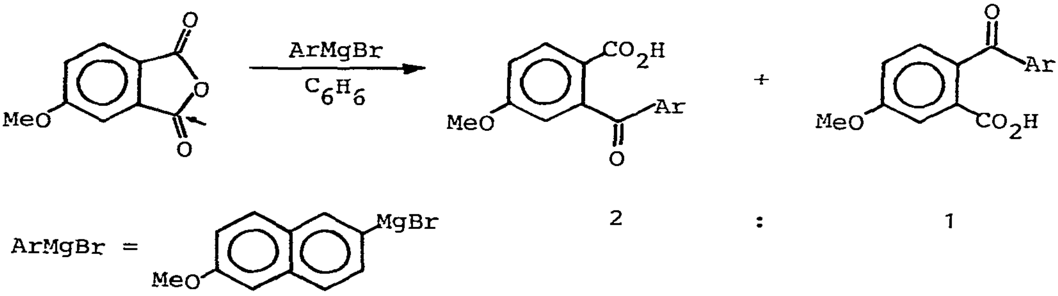
112

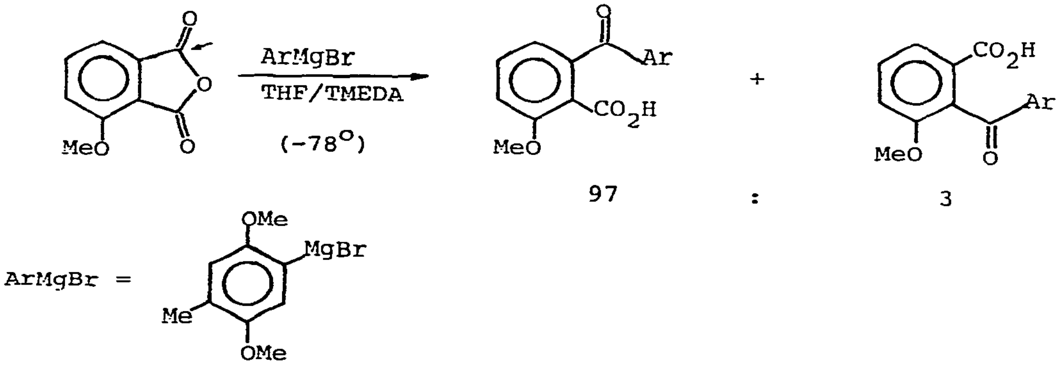
113

Treatment of methoxymaleic anhydride with 2-propenylmagnesium bromide selectively afforded penicillic acid in 52% yield [358]:

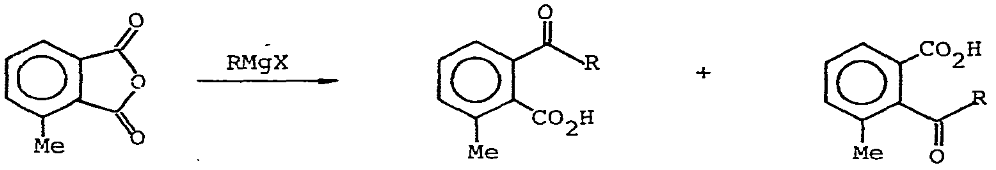


In the following reactions of methoxyphthalic anhydrides attack of the Grignard reagent at the carbonyl group in meta position to the methoxy group is favoured [259, 359]:



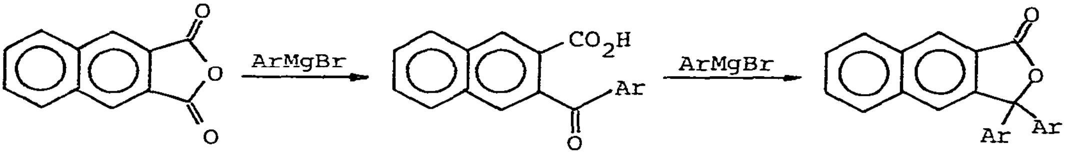


The effect of bulkiness on the regioselectivity of Grignard additions to 3-methylphthalic anhydride has been investigated [360]:

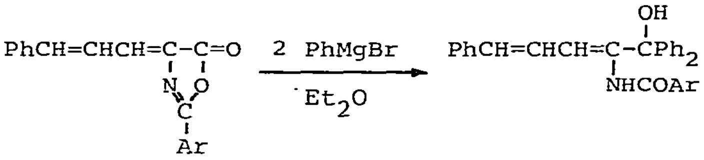


R = Ph	43%	14%
R = 2,4-$Me_2C_6H_3$	39%	4%
R = 2,4,6-$Me_3C_6H_2$	66%	1%

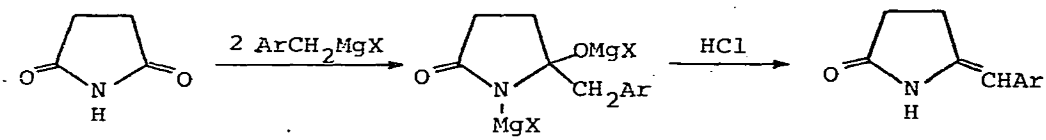
With excess Grignard reagent lactones are formed [361, 362]: e.g.



Similarly oxazolin-5-ones have been cleaved with phenylmagnesium bromide [363]:

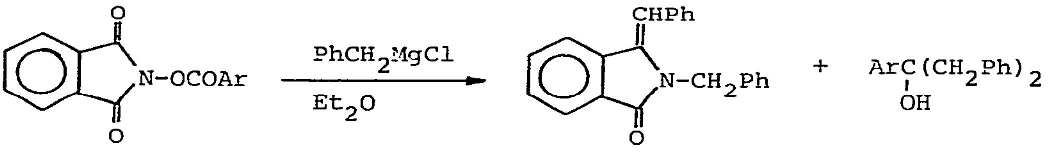


2-Benzal-5-pyrrolidones have been synthesized by treating succinimide with benzyl Grignard reagents, followed by decomposition of the reaction product with dilute hydrochloric acid. The reaction was carried out in Et_2O, THF, benzene, or toluene the latter giving 10% higher yields [364]:



(20–56%)

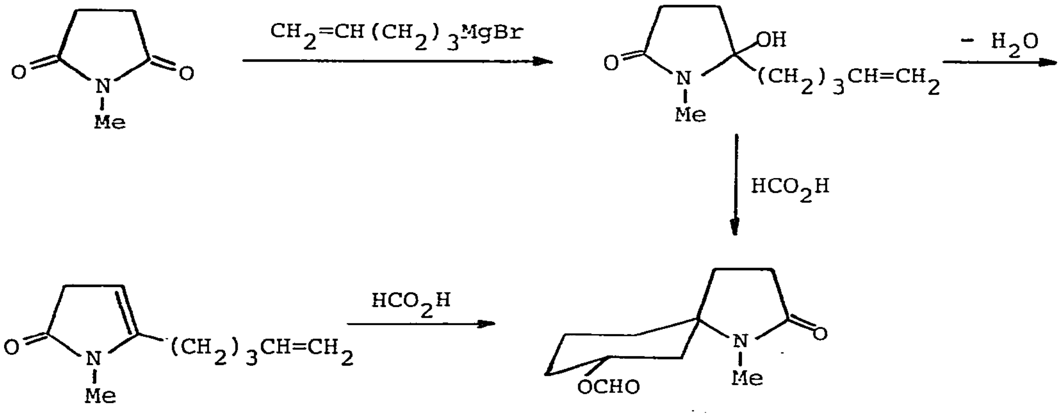
The N-(aroyloxy)phthalimides 114 react similarly [365]:



114

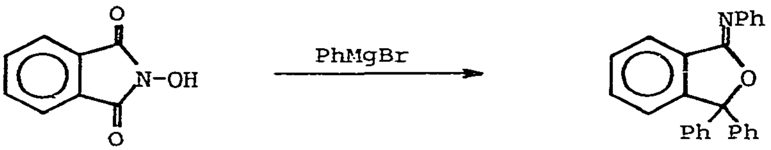
(50-65%) (27-40%)

N-Methylsuccinimide, N-Methylglutarimide, and glutarimide itself has also been treated with Grignard reagents [366, 367]. In this case dehydratization of the primarily formed hydroxylactam leads to an enamide with an endocyclic double bond. Cyclisation in HCO_2H afforded the spirocyclic formate ester 115 [366]:

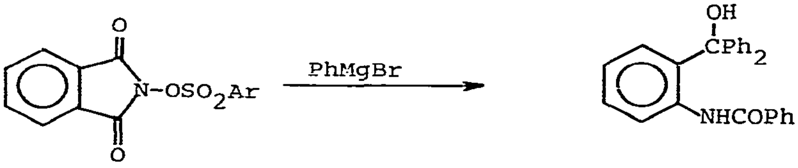


115

N-Hydroxyphthalimide reacts with PhMgBr to give 116 via ring opening followed by Beckmann rearrangement, while N-(arylsulfonyloxy)phthalimides gave mixtures of 117 and arenesulfonic acids via ring opening followed by Lossen rearrangement [355]:



116

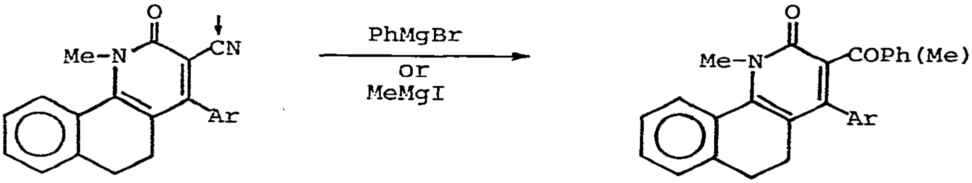


117

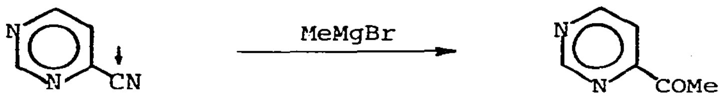
V. ADDITION OF ORGANOMAGNESIUM COMPOUNDS TO OTHER UNSATURATED FUNCTIONS

A. Reaction with carbon-nitrogen unsaturation

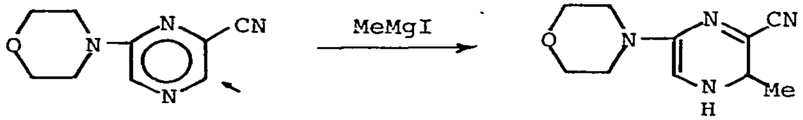
Selective addition to the cyano group in the presence of another potentially reactive functional group produced the expected ketone from the following substrate whose carbonyl group is attacked in the absence of the cyano group [368]:



Similarly acylpyrimidines can be prepared from 118 [369], while the nitrile function in the pyrazine derivative 119 was not affected [370]:

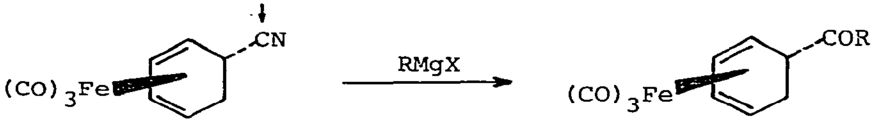


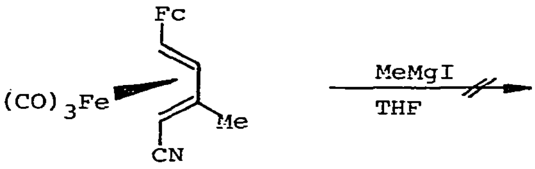
118



119

(5-Cyanocyclohexa-1,3-diene)tricarbonyliron reacts with Grignard reagents to yield a series of 5-acyl derivatives [371], while the nitrile group in the similar complex 120 was shown to be inert [372]:

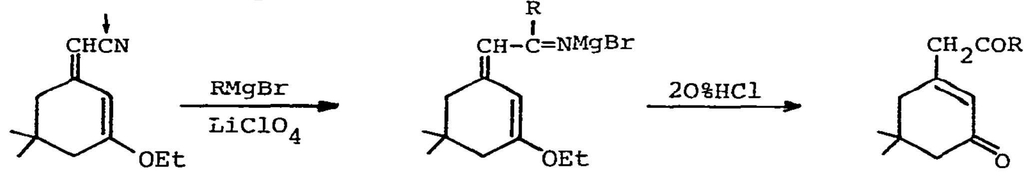




120

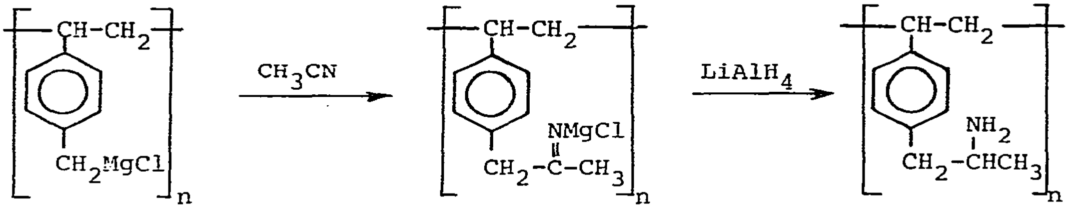
Fc = $C_5H_5FeC_5H_4$ (ferrocenyl group)

Condensation of the nitrile 121 with a complex of lithium perchlorate and various Grignard reagents (R = alkyl or aryl) in ether results in the formation of iminates, which are hydrolyzed to δ-diketones in good yields [373]:



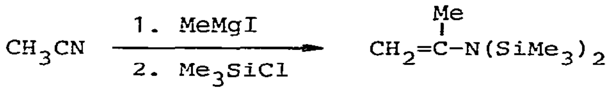
121

The ketimine intermediate 122 of the poly-Grignard reagent 35 and acetonitrile has been reduced with $LiAlH_4$ to the corresponding 2-aminopropyl derivative 123 [131]:



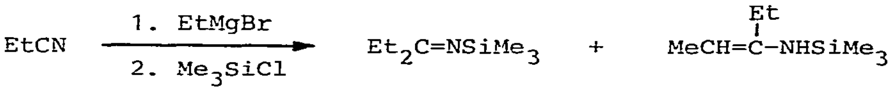
35 122 123

The reaction of acetonitrile with MeMgI in benzene followed by treatment of the reaction mixture with trimethylchlorosilane gave the disilazane 124 in 19% yield. With nitriles of higher aliphatic acids and EtMgBr only monosilylated products were obtained, the N-trimethylsilylated ketimines 125 almost completely isomerize to the corresponding enamines 126. The latter treated with EtMgBr and Me_3SiCl is silylated at the ß-carbon [374]:



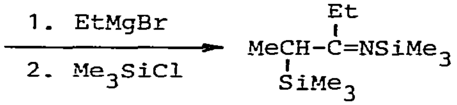
$$\mathrm{CH_3CN} \xrightarrow[\text{2. Me}_3\text{SiCl}]{\text{1. MeMgI}} \mathrm{CH_2{=}\overset{\displaystyle Me}{\overset{|}{C}}{-}N(SiMe_3)_2}$$

124



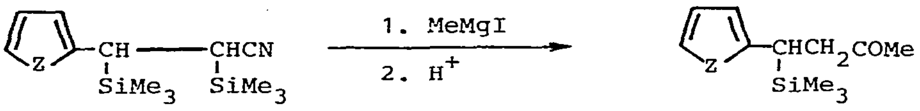
$$\mathrm{EtCN} \xrightarrow[\text{2. Me}_3\text{SiCl}]{\text{1. EtMgBr}} \mathrm{Et_2C{=}NSiMe_3} + \mathrm{MeCH{=}\overset{\displaystyle Et}{\overset{|}{C}}{-}NHSiMe_3}$$

125 126



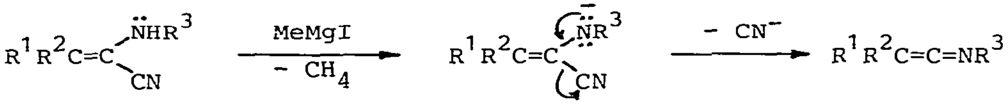
$$\xrightarrow[\text{2. Me}_3\text{SiCl}]{\text{1. EtMgBr}} \mathrm{\underset{\displaystyle SiMe_3}{\underset{|}{MeCH}}{-}\overset{\displaystyle Et}{\overset{|}{C}}{=}NSiMe_3}$$

A trimethylsilyl group is lost during work up in the following reaction of disilylated nitriles with MeMgI [30]:

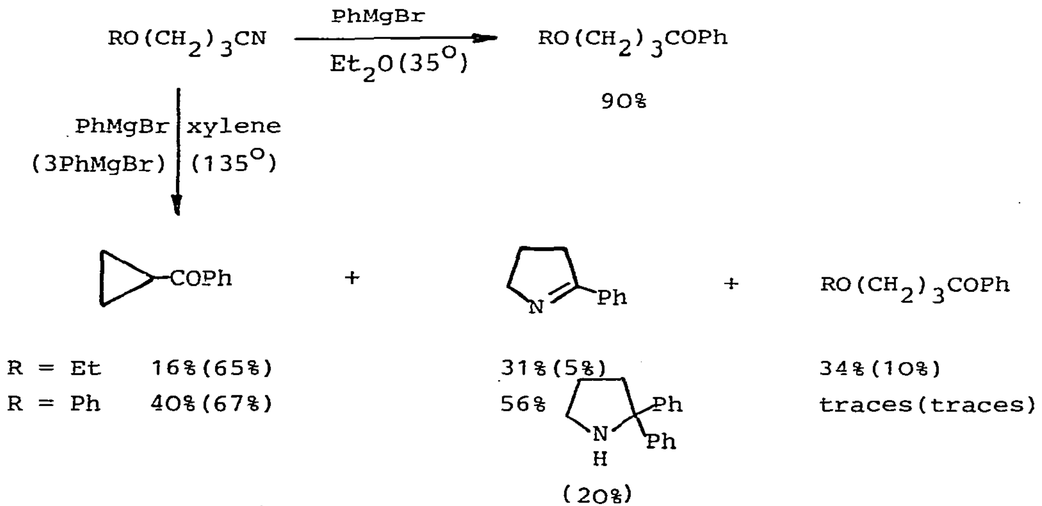


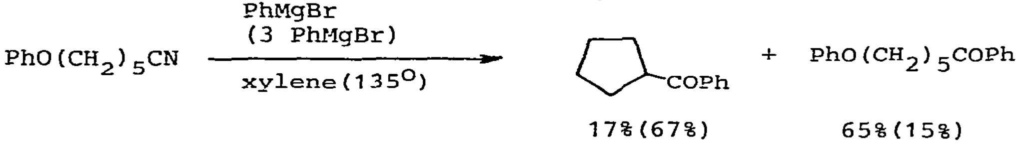
Z = O, S

No ketone is formed starting with α-cyano enamines; the Grignard reagent acting as a base cleaves off HCN with the formation of trialkylketenimines [375]:

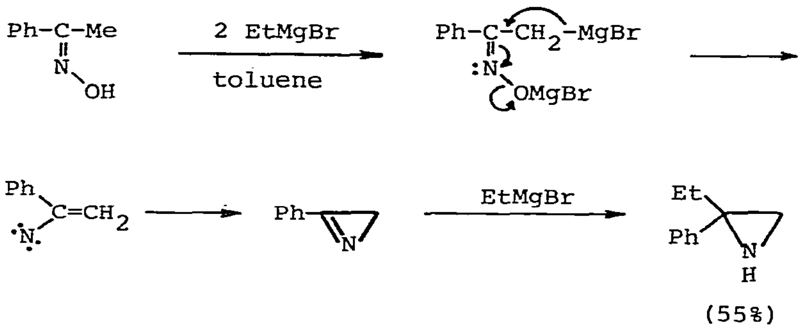


Part of the Grignard reagent is also used up as a base in the reaction of ω-alkoxynitriles with phenylmagnesium bromide in refluxing xylene which besides the normal product yields cyclopropyl and cyclopentyl phenyl ketone respectively. The formation of these products was favoured by the use of excess PhMgBr [376]:

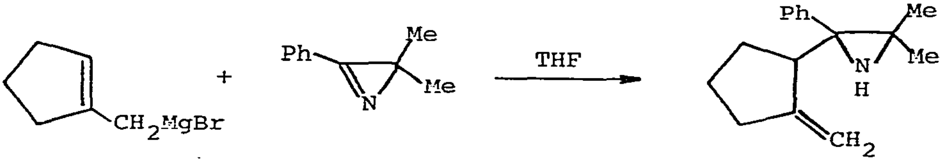




The mechanism of the Hoch-Campbell reaction for the synthesis of secondary aziridines from oximes has been studies. It involves addition of a Grignard reagent to an azirine formed via a vinylic nitrene intermediate [377]:

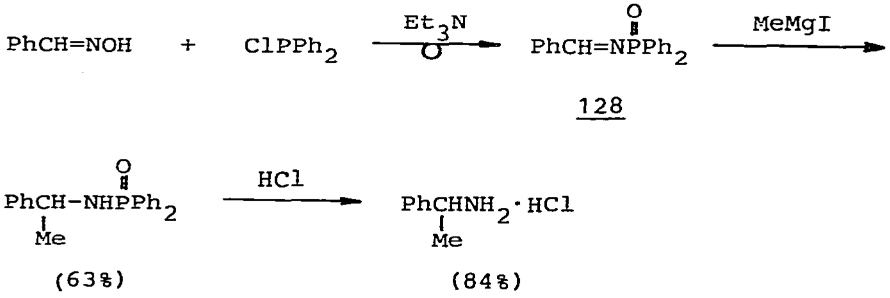


The following addition to 2-phenyl-3,3-dimethylazirine afforded the rearranged product 127. The yield was 19% with 1 mole but 95% with 4 moles of RMgBr [378]:



127

N-Diphenylphosphinyl imines 128 accessible from oximes and chlorodiphenylphosphine can be used as starting material for the preparation of primary amines [379]: e.g.



$$PhCH{=}NOH + ClPPh_2 \xrightarrow[O]{Et_3N} PhCH{=}N\overset{O}{\overset{\|}{P}}Ph_2 \xrightarrow{MeMgI}$$

128

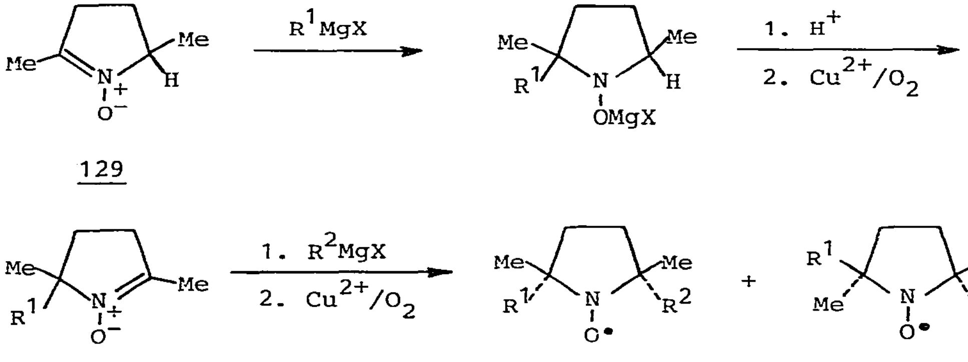
$$\underset{\underset{Me}{|}}{PhCH}{-}NH\overset{O}{\overset{\|}{P}}Ph_2 \xrightarrow{HCl} \underset{\underset{Me}{|}}{PhCH}NH_2\cdot HCl$$

(63%) (84%)

Amides of arylacetic acids have been prepared from isocyanates and the corresponding benzyl Grignard reagents [380]:

$$RN{=}C{=}O \xrightarrow[2.\ H^+]{1.\ ArCH_2MgCl} RNHCOCH_2Ar$$

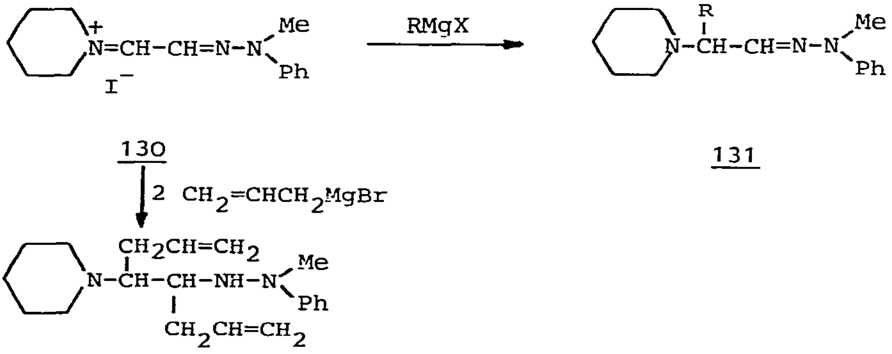
Starting with nitrone 129 two successive Grignard addition-air oxidation sequences yielded a 1:3 cis/trans mixture of a nitroxide with side chains attached at positions 2 and 5 of the pyrrolidine ring [381, 382]:



129

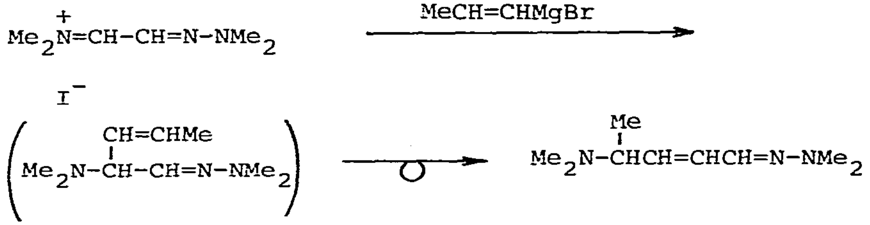
25 : 75

α-Aminohydrazones 131 were obtained by reaction of Grignard compounds with hydrazonoethylidenammonium salts 130. Allylmagnesium bromide adds to both the C=N double bonds, while with propenylmagnesium bromide rearrangement of the reaction product has been observed [262]:



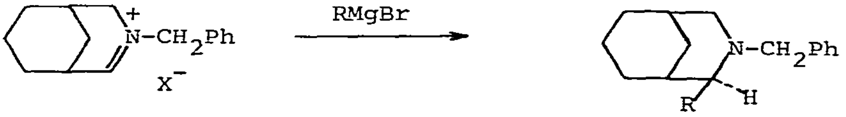
130

131



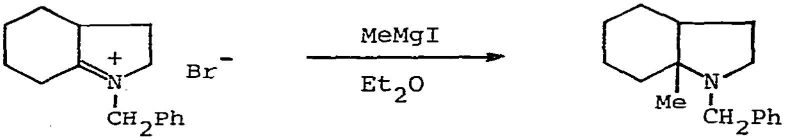
$$\mathrm{Me_2\overset{+}{N}{=}CH{-}CH{=}N{-}NMe_2}\quad \mathrm{I^-} \xrightarrow{\mathrm{MeCH{=}CHMgBr}} \left(\mathrm{Me_2N{-}\overset{\overset{\displaystyle CH{=}CHMe}{|}}{C}H{-}CH{=}N{-}NMe_2}\right) \xrightarrow[\bigcirc]{} \mathrm{Me_2N{-}\overset{\overset{\displaystyle Me}{|}}{C}HCH{=}CHCH{=}N{-}NMe_2}$$

Stereoselective addition of Grignard reagents to the aldimmonium ion 132 afforded 2-exo-alkyl-3-benzyl-3-azabicyclo[3.3.1]-nonanes in 20-40% yield [383]:



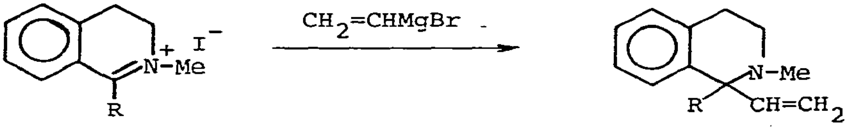
132 R = Me, Et, i-Pr

The angularly methylated perhydroindole 133 was obtained as a cis/trans mixture in 66% yield [384]:



133

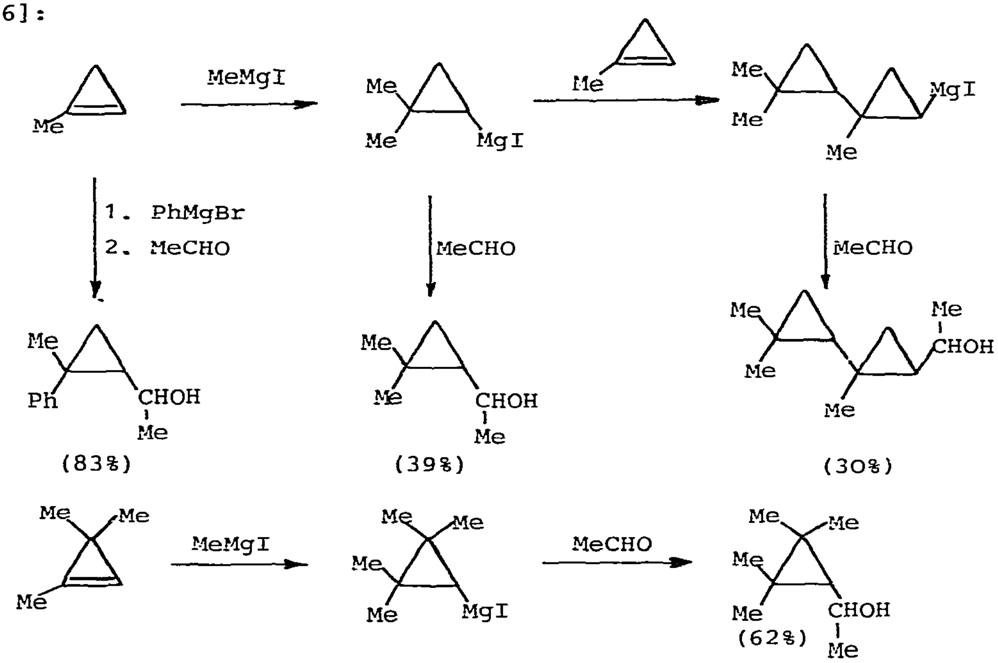
Similarly 3-methyl-1-vinyl-1,2,3,4-tetrahydroisochinoline derivatives have been prepared [385]: e.g.



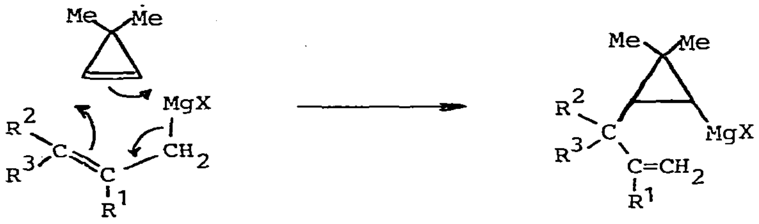
R = H, Me, Ph

B. Reaction with carbon-carbon unsaturation

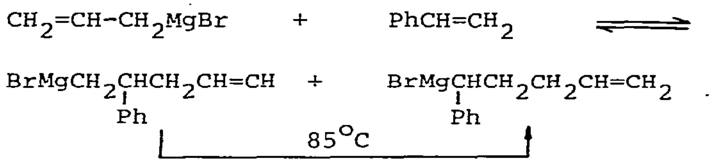
Addition of methylmagnesium iodide to 1-methylcyclopropene produced a mixture of monomeric and dimeric products on reaction with acetaldehyde, while a single carbinol was formed with phenylmagnesium bromide or starting with 1,3,3-trimethylcyclopropene [386]:



Stereoselective cis addition of 2-alkenylmagnesium halides to 3,3-dimethylcyclopropene also occurs readily. A six-membered transition state is assumed because Grignard reagents with a C=C bond in the 1-,3- or 4-position react less uniformly [387]:



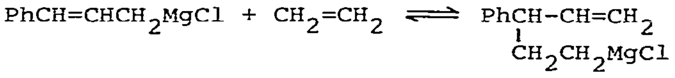
Reversibility has been detected for the addition of 2-alkenylmagnesium halides to styrene giving a mixture of metal-to-C_{prim} and metal-to-C_{sec} adducts. At 85°C an isomerization of the Mg-C_{prim} into the Mg-C_{sec} adducts is observed. The isomerization occurs via cleavage into 2-alkenylmagnesium and styrene followed by addition in the opposite direction. Styrene can be removed from the equilibrium. Similarly the adduct 134 formed from cinnamylmagnesium chloride and ethylene loses ethylene on heating to 85°C [388]:



$$\mathrm{CH_2{=}CH{-}CH_2MgBr + PhCH{=}CH_2 \rightleftharpoons}$$

$$\mathrm{BrMgCH_2\underset{Ph}{C}HCH_2CH{=}CH + BrMg\underset{Ph}{C}HCH_2CH_2CH{=}CH_2}$$

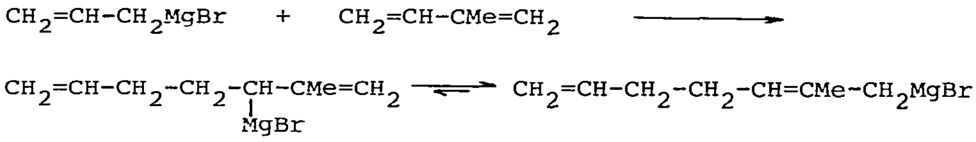
$$\xrightarrow{85^{\circ}C}$$



$$\mathrm{PhCH{=}CHCH_2MgCl + CH_2{=}CH_2 \rightleftharpoons Ph\underset{CH_2CH_2MgCl}{C}H{-}CH{=}CH_2}$$

134

2-Alkenylmagnesium halides finally reacted with more than 90% regioselectivity with butadiene via metal-to-C-2 addition and simultaneous inversion of the 2-alkenyl group followed by a 2,4-metal shift. With isoprene, the metal predominantly adds to the less substituted C-atom [389]: e.g.

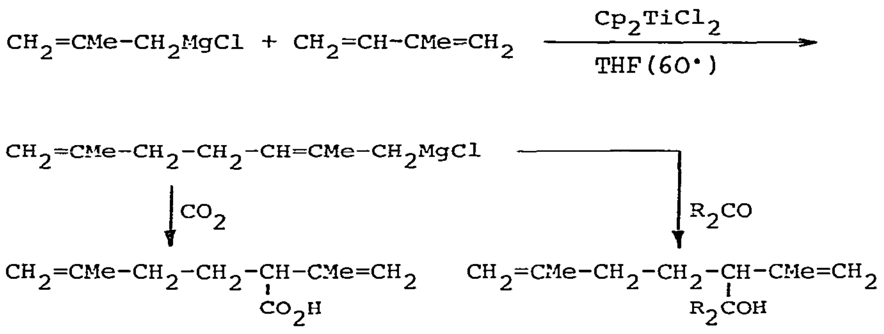


$$\mathrm{CH_2{=}CH{-}CH_2MgBr + CH_2{=}CH{-}CMe{=}CH_2 \longrightarrow}$$

$$\mathrm{CH_2{=}CH{-}CH_2{-}CH_2{-}\underset{MgBr}{C}H{-}CMe{=}CH_2 \rightleftharpoons CH_2{=}CH{-}CH_2{-}CH_2{-}CH{=}CMe{-}CH_2MgBr}$$

In the presence of an excess of 1,3-diene the 1:1-adducts react further to give 1:2-addition products which undergo fast intramolecular cyclization [389](see section VII.A).

The reaction of allylic Grignard reagents with isoprene was also investigated in the presence of a catalytic amount of Cp_2TiCl_2. Contrary to the literature the reaction product showed complete allylic rearrangement in its reaction with carbon dioxide and carbonyl compounds [390]:



$$CH_2{=}CMe{-}CH_2MgCl + CH_2{=}CH{-}CMe{=}CH_2 \xrightarrow[THF(60^\circ)]{Cp_2TiCl_2}$$

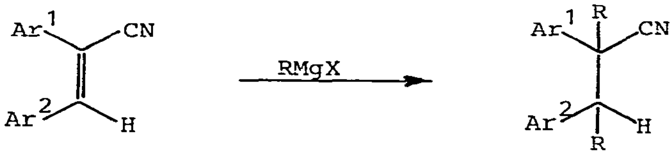
$$CH_2{=}CMe{-}CH_2{-}CH_2{-}CH{=}CMe{-}CH_2MgCl$$

$$\xrightarrow{CO_2} CH_2{=}CMe{-}CH_2{-}CH_2{-}\underset{CO_2H}{CH}{-}CMe{=}CH_2$$

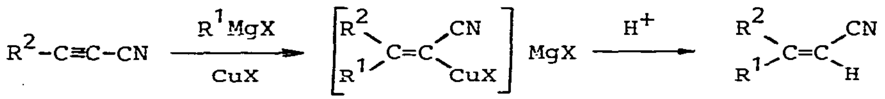
$$\xrightarrow{R_2CO} CH_2{=}CMe{-}CH_2{-}CH_2{-}\underset{R_2COH}{CH}{-}CMe{=}CH_2$$

The kinetics of the addition of 2-alkenylmagnesium compounds to alkenes has been studied and found to be first order with respect to organomagnesium compound and olefin. The reactivity increases as follows: 1-octene $<$styrene $<$norbornene. $\Delta H^{\ddagger}$ lies between 20 and 22 kcal/mol and $\Delta S^{\ddagger}$ between -18 and -24 Clausius. In Et_2O a decrease in the concentration of the organomagnesium compound is accompanied by a decrease in the rate constant. 2-Methylallylmagnesium chloride is more reactive than the corresponding bromide. The rate of reaction increases with decreasing chloride content for mixtures of diorganomagnesium and organomagnesium chloride. The Et_2O complexes are more reactive than those with dioxane or THF [391].

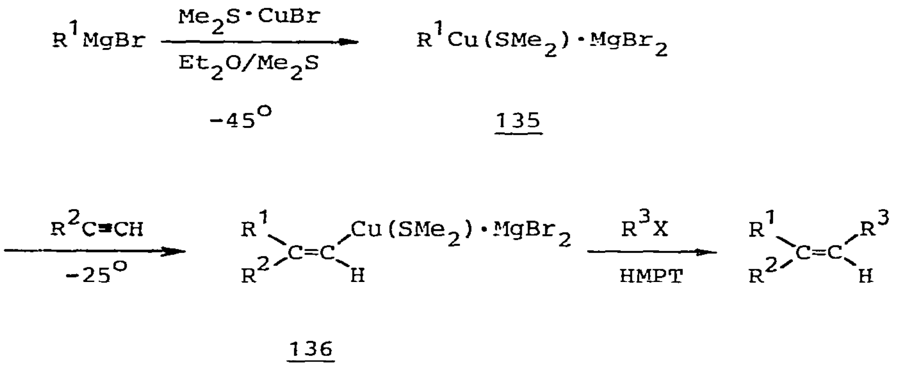
An unusual Grignard reaction of α-arylcinnamonitriles with excess alkylmagnesium halides has been reported yielding predominantly the erythro isomer of α,β-dialkyl-α,β-diarylpropionitriles, i.e. the simultaneous alkylation of α- and β-carbon atoms [392]:



2-Alkynenitriles, on the other hand, readily react with magnesium organocuprates in a stereospecific manner with the formation of α-cyanovinylcuprates with the groups R^2 and CN in cis position, from which pure (E or Z)-2-alkenenitriles can be obtained by protonolysis in excellent yields [393]:



The alkylcopper complex 135, prepared in situ from $Me_2S\cdot CuBr$ complex, dimethyl sulphide, and alkylmagnesium bromide in ether at -45°, reacts smoothly with terminal alkynes to give the intermediate adducts 136. The reactions of 136 with various electrophiles usually in the presence of HMPT produce trisubstituted olefins in a stereospecific manner [394-397]:

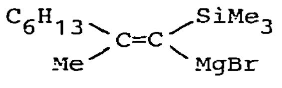


135

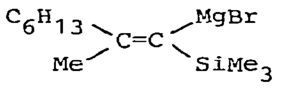
136

Tetrasubstituted alkenes, on the other hand, have been synthesized by the nickel-catalyzed addition of Grignard reagents to terminal silylacetylenes. Thus MeMgBr adds to 1-trimethyl-1-octyne in the presence of 10mol% 1:1-nickel acetylacetonate/Me_3Al in THF to give the vinylorganometallic compound 137, which on standing slowly isomerises to a mixture of 137 and 138. The latter reacted with a variety of electrophiles to yield tetrasubstituted alkenes [398]:

$$C_6H_{13}C{\equiv}CSiMe_3 \;+\; MeMgBr \xrightarrow[Me_3Al]{Ni(acac)_2}$$

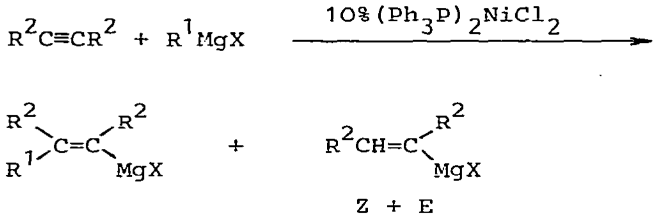


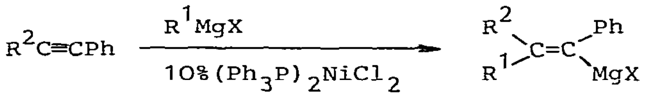
137



138

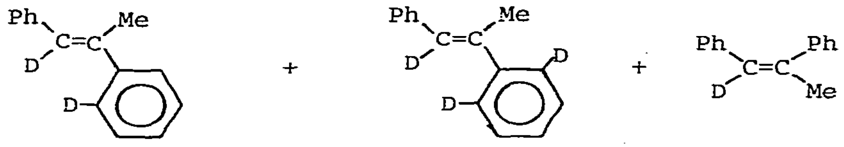
Non reducing Grignard reagents also in the presence of $(Ph_3P)_2NiCl_2$ undergo syn-addition to acetylenic compounds, while with reducing Grignard reagents addition and reduction reactions are observed the latter being not stereospecific. The addition to alkyl phenyl acetylenes occurs regioselectively [399]:





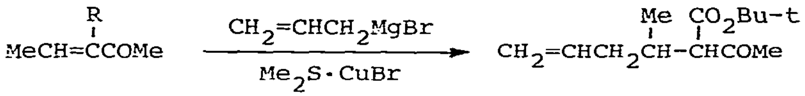
The reaction of diphenylacetylene with MeMgBr in the presence of $(Ph_3P)_3RhBr$ which yields mostly trans-1,2-diphenyl-propene was studied in more detail. When the reaction was terminated with D_2O trans-1,2-diphenylpropene was deuterated at the vinylic position and at the ortho-position of the aromatic ring adjacent to the methyl group, while the cis isomer was deuterated at the vinylic position only. These results offer an explanation of the mechanism of trans-addition in this case via a PhC≡CPh/Rh linear π complex which is converted to a σ complex; ring metalation then becomes a driving force for the formation of the trans compound [400].

$$PhC{\equiv}CPh \xrightarrow[2.\ D_2O]{1.\ MeMgBr/(Ph_3P)_3RhBr}$$



C. Reaction with conjugated carbonyl and carboxy derivatives

While allylmagnesium bromide with the enone 139 (R=H) gave primarily the 1,2-addition product even in the presence of added $Me_2S\cdot CuBr$ catalyst, the Cu-catalyzed addition of $CH_2{=}CHCH_2MgBr$ to the enone 139 with R = CO_2Bu-t produced cleanly the conjugate adduct 140 in 75% yield [401]:

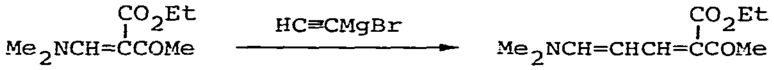


$$\mathrm{MeCH{=}\overset{R}{C}COMe} \xrightarrow[\mathrm{Me_2S\cdot CuBr}]{\mathrm{CH_2{=}CHCH_2MgBr}} \mathrm{CH_2{=}CHCH_2\overset{Me}{C}H{-}\overset{CO_2Bu\text{-}t}{C}HCOMe}$$

139 140

(R = CO_2Bu-t)

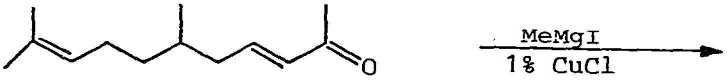
With the corresponding enamine 141 and $HC\equiv CMgBr$ insertion of a C=C bond has been observed in 90% yield [402]:



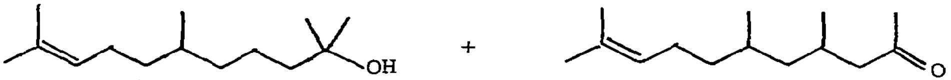
$$\mathrm{Me_2NCH{=}\overset{CO_2Et}{C}COMe} \xrightarrow{\mathrm{HC{\equiv}CMgBr}} \mathrm{Me_2NCH{=}CHCH{=}\overset{CO_2Et}{C}COMe}$$

141

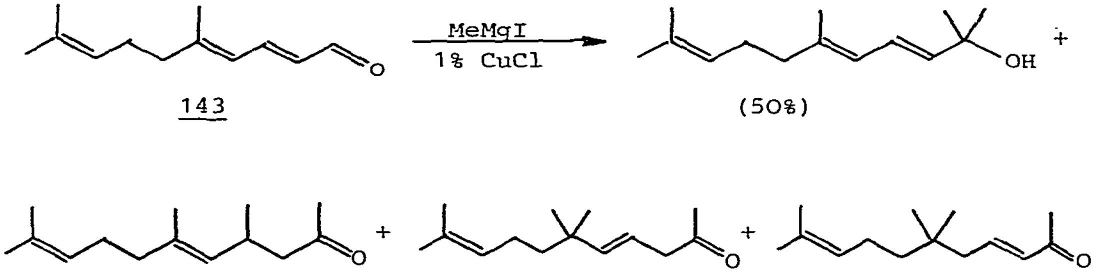
The dihydropseudoionone 142 with MeMgI in the absence of cuprous catalyst yields only 4% of the product of 1,4-addition compared with 67% in the presence of 1%CuCl [403]:



142

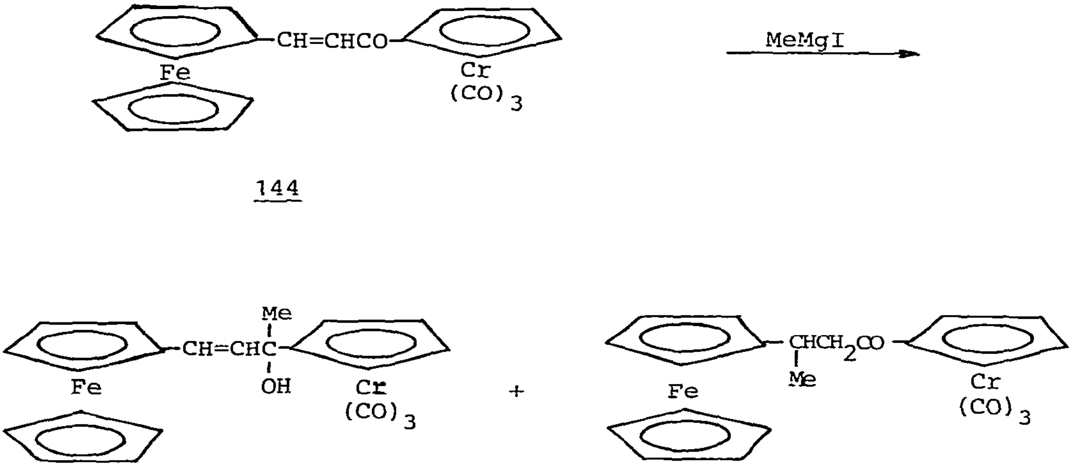

(17%) (67%)

Pseudoionone 143 under the same conditions moreover yields 31% 1,6-addition products [403]:



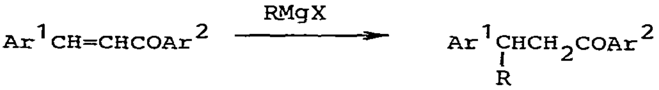
143 (50%) (18%) (29%) (3%)

A mixture of 1,2- and 1,4-addition products was also obtained from the enone 144 and MeMgI [404]:



144 (19%) (77%)

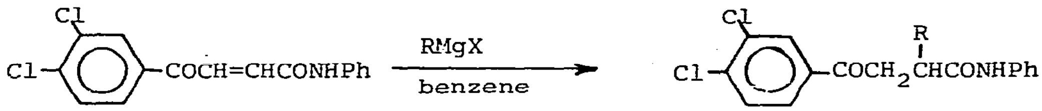
Chalcones 145 with Grignard reagents, on the other hand, yield pure propiophenone derivatives [405, 406]:



$$Ar^1CH{=}CHCOAr^2 \xrightarrow{RMgX} Ar^1\underset{\displaystyle R}{\underset{|}{C}}HCH_2COAr^2$$

145

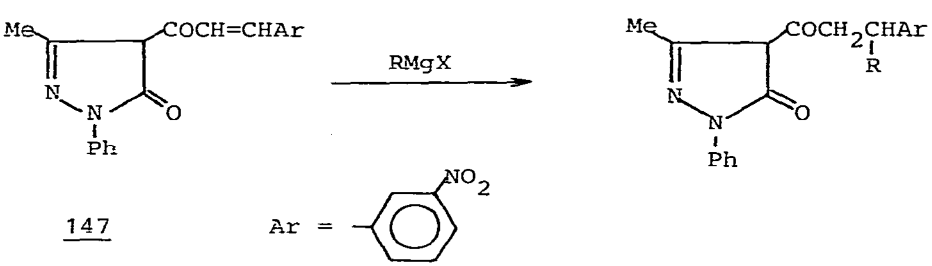
With the β-aroylacrylanilide 146 regiospecific 1,4-addition has been observed [407]:



146

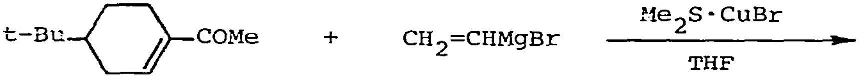
(70%)

Also the cinnamoylpyrazolinone 147 is selectively attacked by EtMgI and PhMgBr [408]:

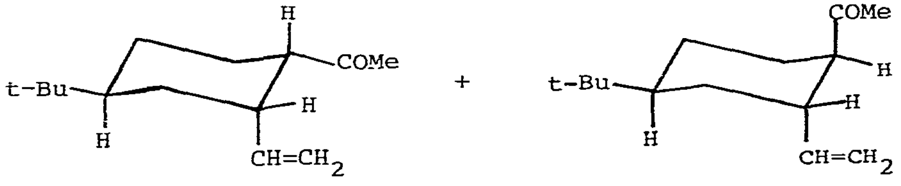


147

By use of a Cu(I) catalyst vinylmagnesium bromide has been found to add to the enone 148 to form mixtures of four stereoisomeric ketones in which the epimers with an axial vinyl group constitute >90% of the ketone product [409]:



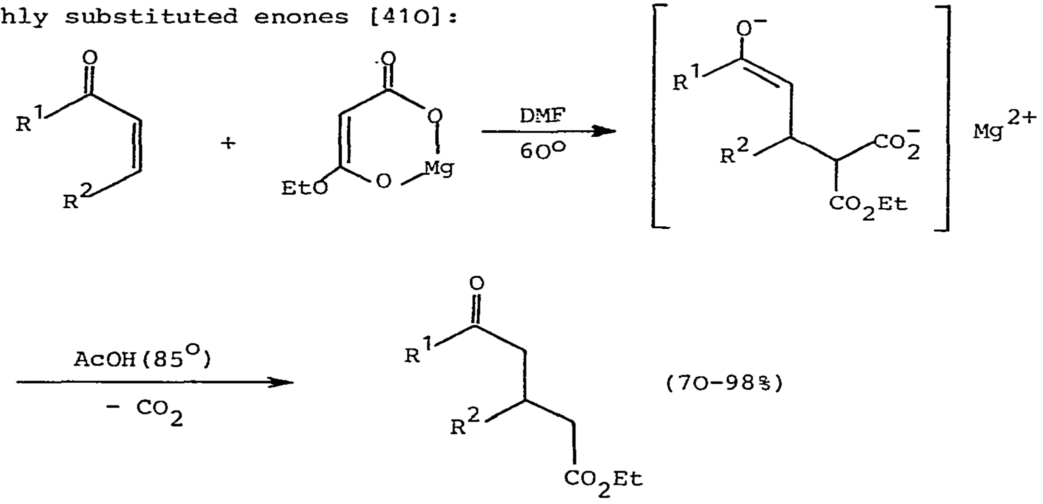
148



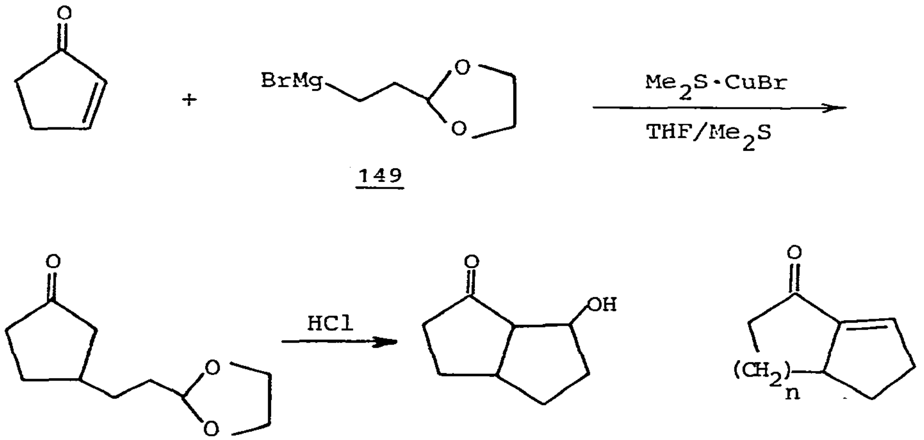
5

3

Open-chain as well as cyclic enones have been converted into 5-oxoalkanoates by conjugate addition of magnesium monoethyl malonate followed by decarboxylation. In no case were 1,2-addition products observed. However, the one-pot reaction has only been successful with substrates containing disubstituted double bonds but not with more highly substituted enones [410]:



Copper-catalyzed conjugate addition of the acetal Grignard reagent 149 to cycloalkenones has been used to prepare bicyclic ketones. With higher cycloalkenones bicyclic enones 151 (n = 2 ; 3) are formed instead of the aldol product 150 [104]: e.g.

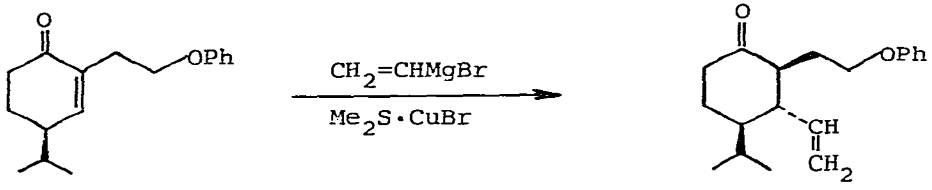


149

150

151

Under the same conditions vinylmagnesium bromide reacts smoothly with the cyclohexenone 152 to give the trans,trans-trisubstituted cyclohexanone 153 in 52% yield [411]:

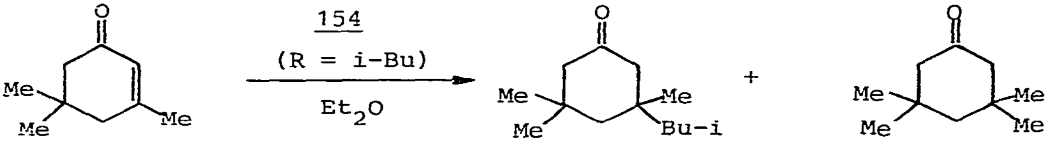


152 153

Polyalkylmagnesiocuprates of type 154 generated in Et_2O or in THF appear to be the most effective 1,4-addition reagents presently known. They lead to regiospecific 1,4-addition reactions involving almost exclusively the ligand R. They do add on sterically hindered enones like isophorone 155 and are able to transfer even the t-butyl group [412, 413]: e.g.

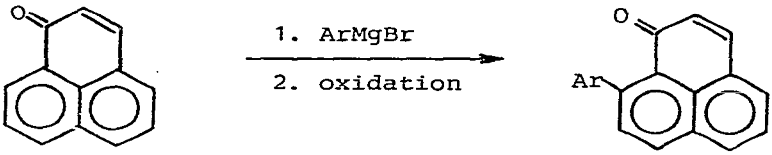
$$4\ RMgBr + 3\ CuI + MeLi \longrightarrow R_4(Me)Cu_3(MgBr)_2 + 2\ MgBrI + LiI$$

154

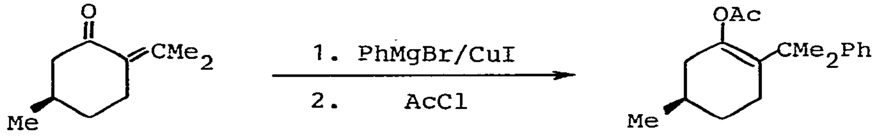


155 (75%) (2 %)

Conjugate addition of aryl Grignard reagents to phenalenone followed by chloranil oxidation afforded 9-arylphenalenones [414]:

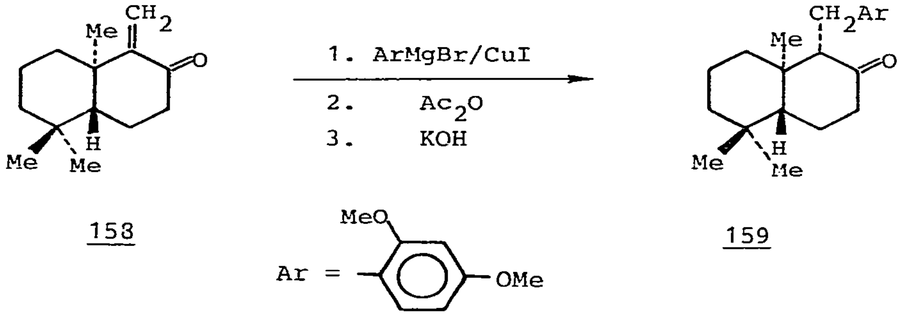


Cuprous iodide catalyzed conjugate addition of phenylmagnesium bromide to (R)-(+)-pulegone 156 followed by trapping the resulting enolate with excess acetyl chloride afforded the optically active enolacetate 157 in 90% yield [415]:



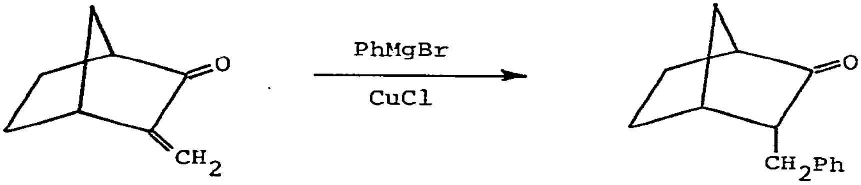
156 157

Similarly the Grignard reagent prepared from 1-bromo-2,5-dimethoxybenzene and Rieke magnesium in DME adds to the exocyclic double bond of the enone 158 producing the ketone 159 via the enol acetate in 70% overall yield [416]:



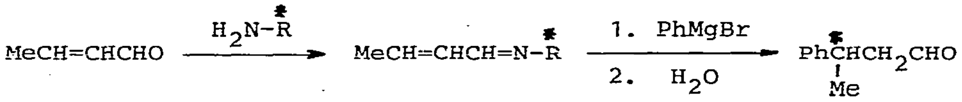
158 159

3-endo-Benzyl-2-norbornanone 160 is the only ketone product in the reaction of PhMgBr with 3-methylene-2-norbornanone. In the absence of CuCl the reaction mixture contains only 13% of 160 compared with 83% in the presence of CuCl the rest being 1,2-addition products respectively [234]:



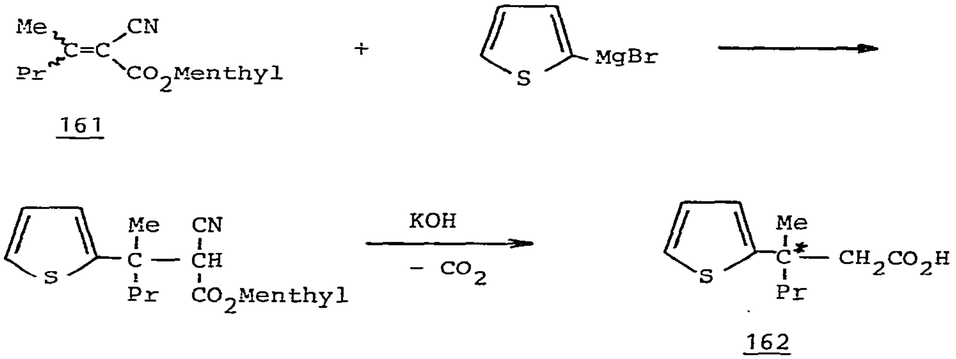
160

Optically active ß-substituted aldehydes have been prepared from the corresponding α,ß-unsaturated aldehydes via Schiff bases with optically active α-amino acid esters, e.g. L-valin <u>tert</u>-butylester (H_2N-R) [417]:



$$\mathrm{MeCH{=}CHCHO} \xrightarrow{\mathrm{H_2N\text{-}\overset{*}{R}}} \mathrm{MeCH{=}CHCH{=}N\text{-}\overset{*}{R}} \xrightarrow[\text{2. } \mathrm{H_2O}]{\text{1. PhMgBr}} \mathrm{Ph\underset{Me}{\overset{*}{C}}HCH_2CHO}$$

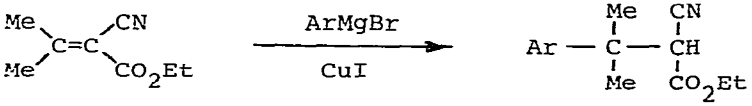
Similarly the menthylester 161 with thienylmagnesium bromide afforded, after hydrolysis and decarboxylation, the optically active 2-thiophenepropionic acid 162 in 63% yield [139]:



161

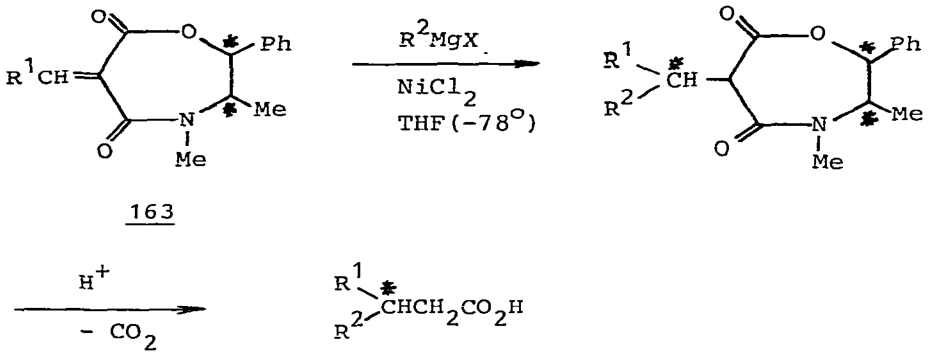
162

Only 38% yield was obtained in the reaction of anisylmagnesium bromide with ethyl 2-cyanocrotonate when CuI was omitted compared with 90% in the presence of CuI [418]:



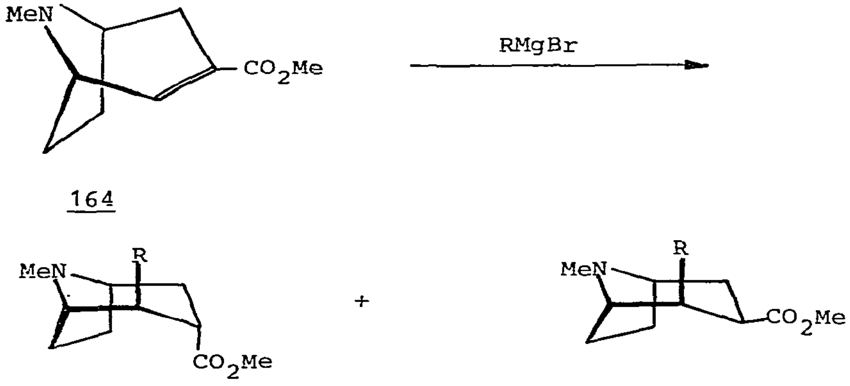
$$\mathrm{Me_2C{=}C(CN)CO_2Et} \xrightarrow[\mathrm{CuI}]{\mathrm{ArMgBr}} \mathrm{Ar-C(Me)_2-CH(CN)CO_2Et}$$

The conjugate addition of Grignard reagents to 163 in the presence of nickel chloride, followed by hydrolysis and decarboxylation, afforded highly optically pure ß-substituted alkanoic acids in good yields [419]:



163

The presence of copper salts was not necessary in order to obtain 1,4-addition of Grignard reagents to the unsaturated ester 164. Further reaction of the primary products with RMgBr was minimized by adopting a reaction temperature of -20 to -25°C and using Et_2O rather than THF as the solvent. Esters 165 and 166 were formed in nearly equal amounts [420, 421]:

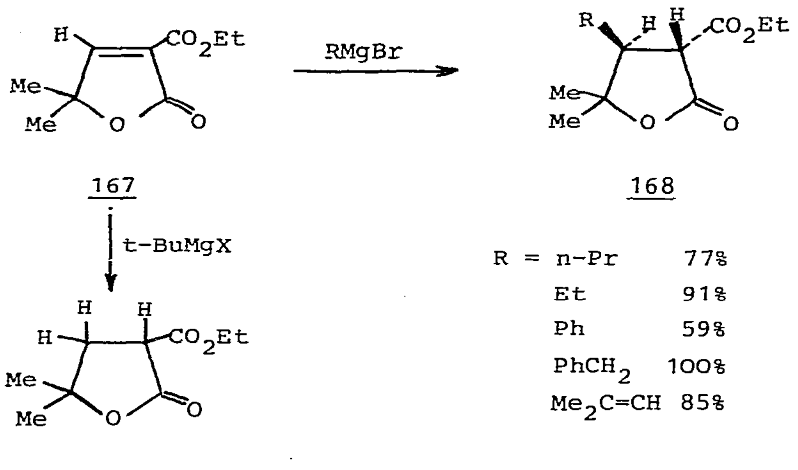


164

165

166

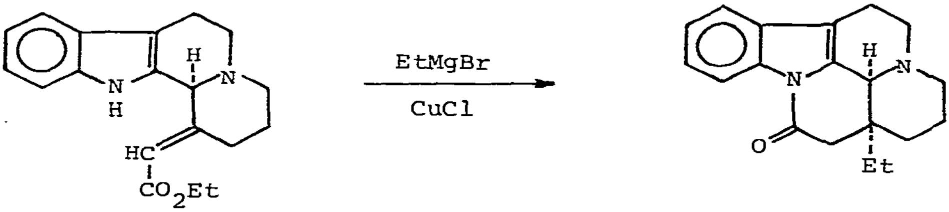
The reaction of the lactone 167 with Grignard reagents resulted in formation of the 1,4-addition products 168 with trans configuration. The reaction with t-BuMgX, however, gave the saturated lactone 169 and not the Michael addition compound [422, 423]:



167 168 169

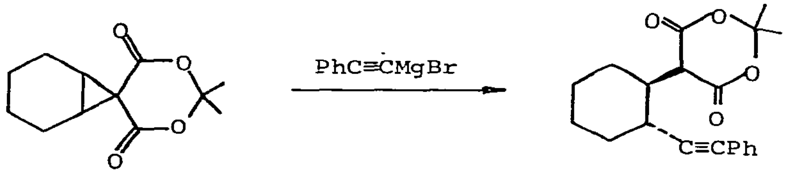
R = n-Pr 77%
Et 91%
Ph 59%
$PhCH_2$ 100%
$Me_2C{=}CH$ 85%

The 1,4-addition of EtMgBr to the conjugated ester 170 allows the stereospecific introduction of the ethyl group cis to the angular C_{21} hydrogen atom. In situ cyclization between the magnesium enolate and the indole nitrogen leads directly to racemic Eburnamonine 171 [424]:



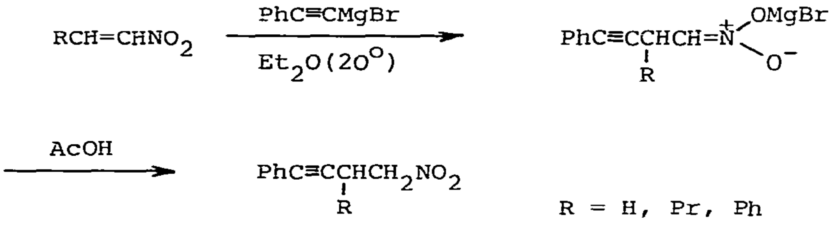
170 171

The homoconjugate addition of phenylethynylmagnesium bromide to the spiroactivated cyclopropane 172 in Et_2O at 0° afforded 173 as the exclusive product. Additions of aryl Grignard reagents failed with diethyl ether as the solvent, CH_2Cl_2, however, was successfully used. Surprisingly, efforts to open spiroactivated cyclopropanes with vinylmagnesium halides have failed so far [425].



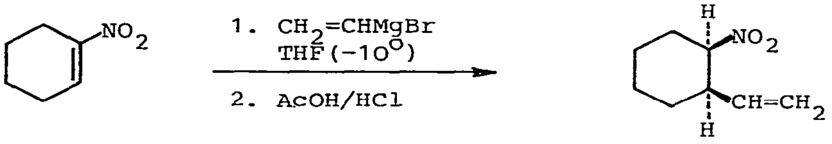
172 173 (82%)

1,4-Addition of Grignard reagents to conjugated nitroalkenes have also been reportet [410, 426, 427]: e.g.


$$RCH{=}CHNO_2 \xrightarrow[Et_2O(20^{o})]{PhC{\equiv}CMgBr} PhC{\equiv}C\underset{R}{C}HCH{=}\overset{+}{N}{<}^{OMgBr}_{O^-} \xrightarrow{AcOH} PhC{\equiv}C\underset{R}{C}HCH_2NO_2$$

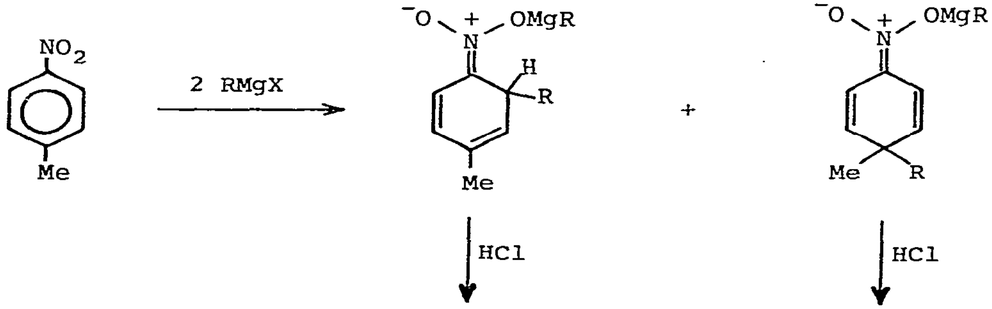
R = H, Pr, Ph

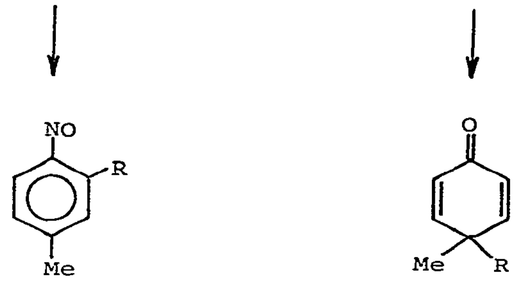
(32-51%)



(80%)

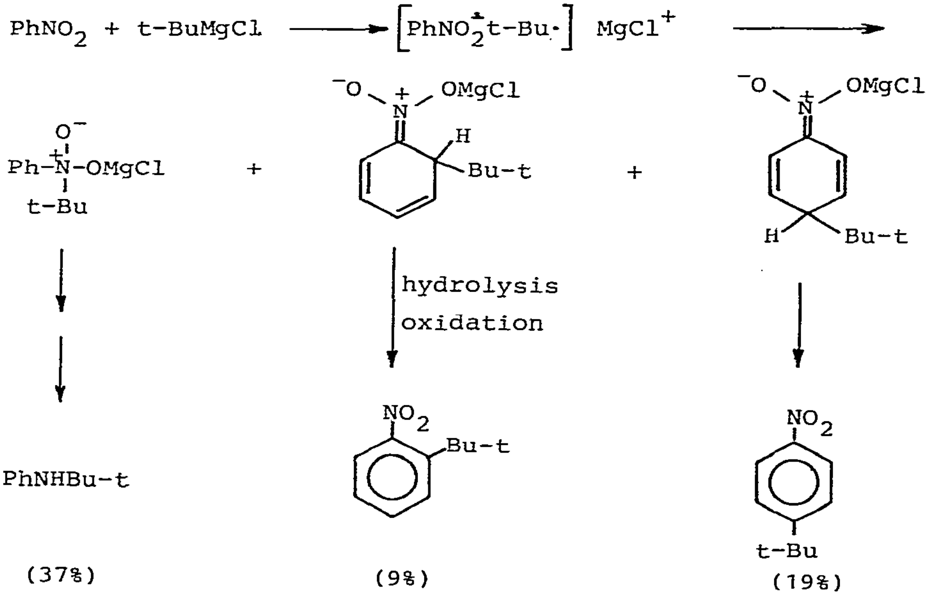
Conjugate addition of Grignard reagents to p-nitrotoluene occurs in the ortho- and para-position to the nitro group. The 1,4- and 1,6-addition products are hydrolyzed to give 2-alkyl-4-methylnitrosobenzenes and 4-alkyl-4-methyl-2,5-cyclohexadienones respectively [428]:





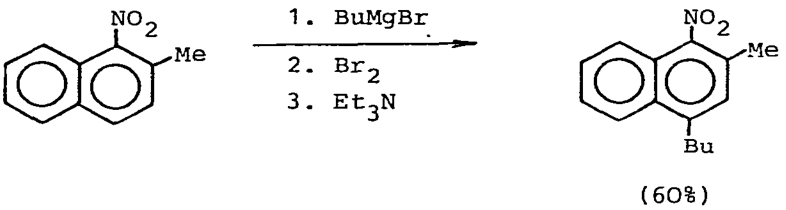
R = Me	53%	15%
R = n-Bu	50%	25%

In the reaction of t-BuMgCl with nitrobenzene in DME first an electron is transferred with the formation of nitrobenzene radical anion. ESR and CIDNP experiments are in accordance with the following mechanism of the reaction [429]:

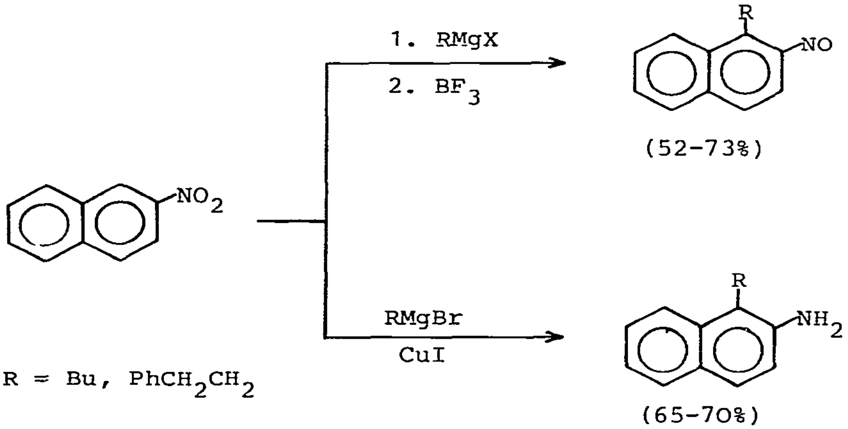


Other products were isobutane (12%), isobutylene (7%), tetramethylbutane (3%), and nitrosobenzene (1%) [429].

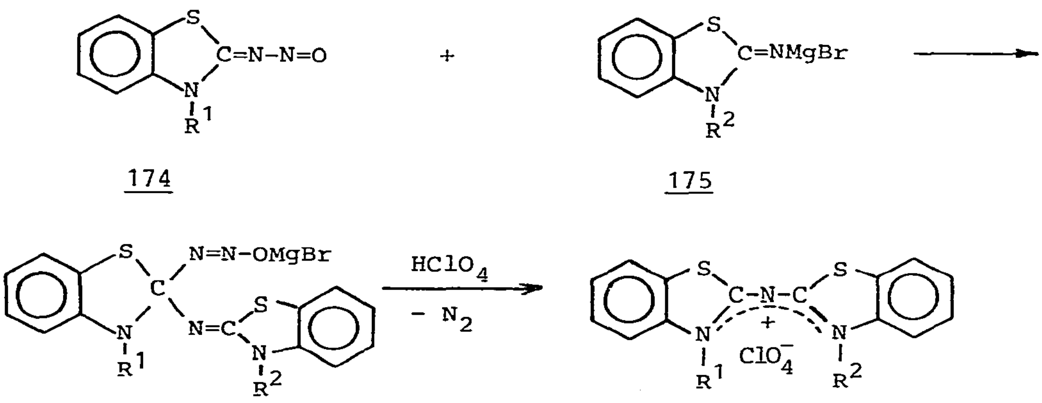
Nitronaphthalenes also have been alkylated by treatment with Grignard reagents [430]: e.g.



Interconversion to nitroso [431]or amino compounds [432]by reductive C-alkylation has also been reported: e.g.



1,4-Addition of the Grignard-type reagents 175 to the nitrosoimino compounds 174 gave azamonomethinecyanines 176 in high yields (71-96%) [433]:

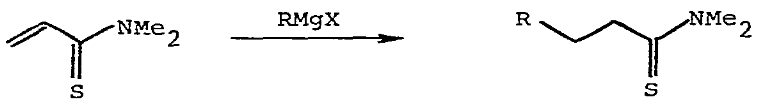


174

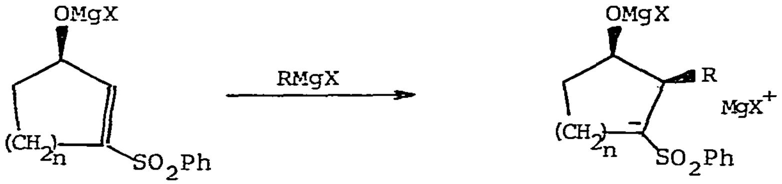
175

176

Conjugate addition of Grignard reagents have also been reported for α,ß-unsaturated thioamides [434] and sulfones [435] as well as for 1-trialkylsilylbutadienes [436]: e.g.



R = Me, Et, Ph, CH_2=CH

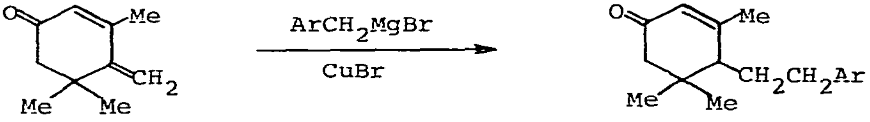


n = 1, 2, 3   cis - adducts

$$R^1_3SiCH{=}CH{-}CH{=}CH_2 \xrightarrow{R^2MgBr} R^1_3SiCH_2CH{=}CHCH_2R^2$$

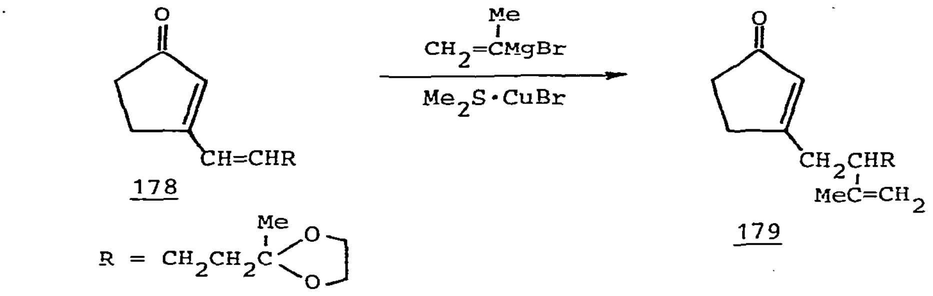
R^1 = Me, Et; R^2 = Et, Pr

In the presence of CuBr, the cyclohexenone 177 underwent 1,6-addition with m- and p-methoxybenzyl Grignard reagents, while in the absence of copper(I) salts also 1,2- and 1,4-addition products were formed [437]:



177

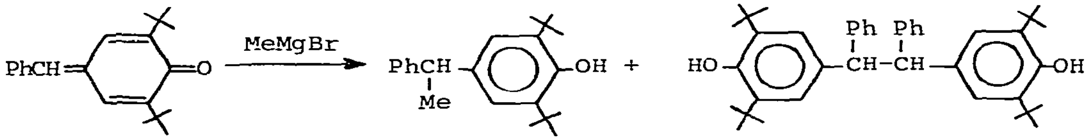
Similarly, copper-catalyzed 1,6-addition of 2-propenylmagnesium bromide to the dienone 178 yielded 66% of the cyclopentenone 179 [106]:



178

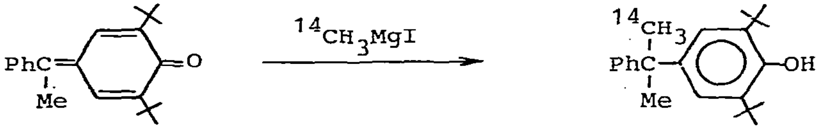
179

During the 1,6-addition of Grignard reagents to methylenequinones yielding phenols, radical anions are probably involved as intermediates [438, 439, 440]: e.g.

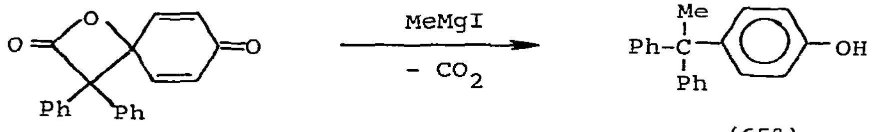


(81%)

(5%)



(23%)

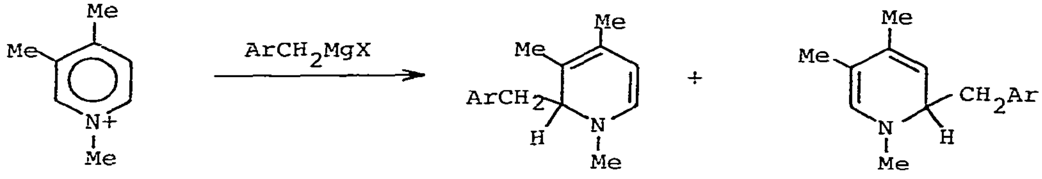


(65%)

D. Addition to heteroaromatic compounds

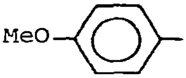
A number of reactions described earlier as additions to cyclic carboxylic acid derivatives (section IV.E.2.), to carbon-nitrogen unsaturation (section V.A.) and as conjugate additions (section V.C.) can equally well be described as additions to heterocyclic rings.

Other additions to nitrogen heterocyclic compounds include:

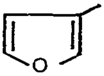


minor component

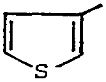
Ar =



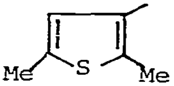
[441, 442]



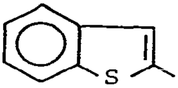
[136]



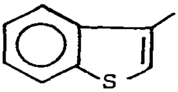
[143,144]



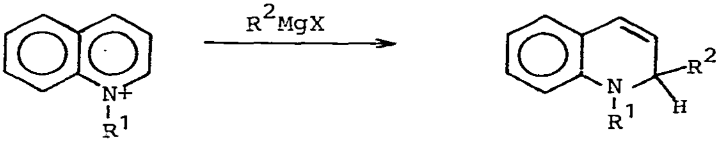
[145, 146]



[147-151]



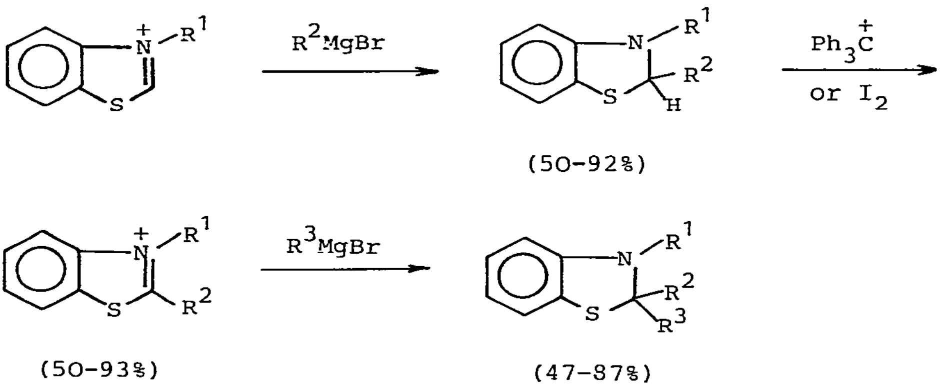
[151, 152, 153]



[443, 444]

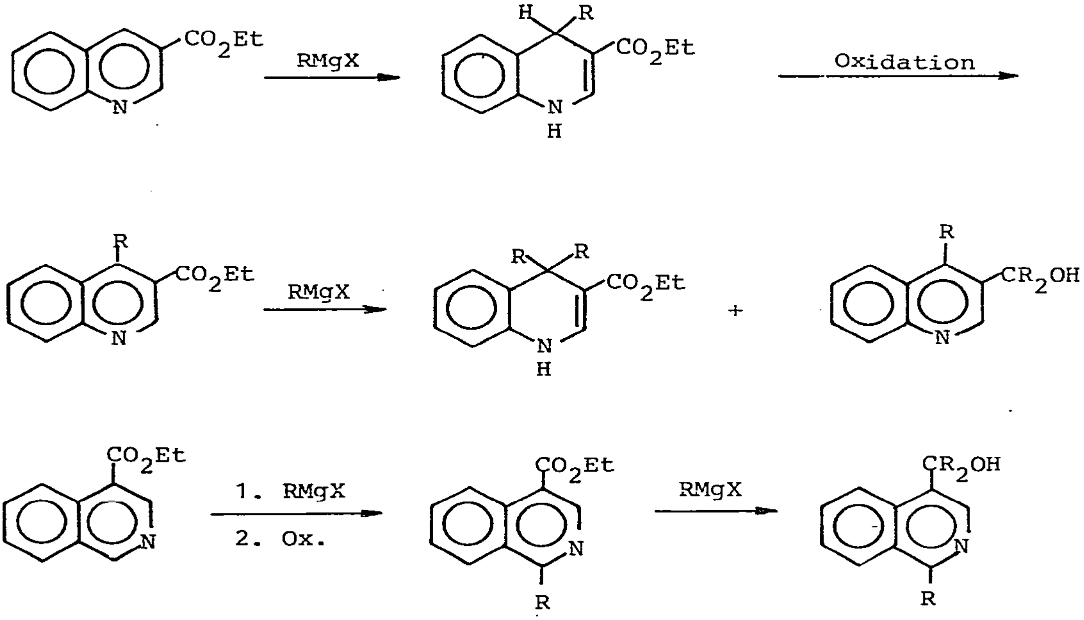
R^1 = Me, Et, Pr, Ph
R^2 = Me, Et, Pr, Bu, i-Bu, Ph, $PhCH_2$, p-methoxyphenyl

Two successive additions of Grignard reagents to benzothiazolium salts were used to prepare 2,2,3-trisubstituted benzothiazoline derivatives [445]:

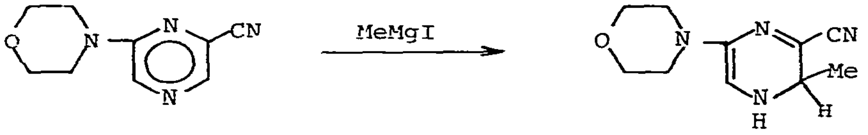


R^1 = Me, Et; R^2 = Me, Ph, $PhCH_2$; R^3 = Ph, $PhCH_2$

The reaction of ethyl 3-quinolinecarboxylate and ethyl 4-isoquinolinecarboxylate with Grignard reagents selectively yields 4- and 1-substituted compounds, respectively. In the successive step the ester group is partly attacked in the first case and exclusively in the second case [446]:

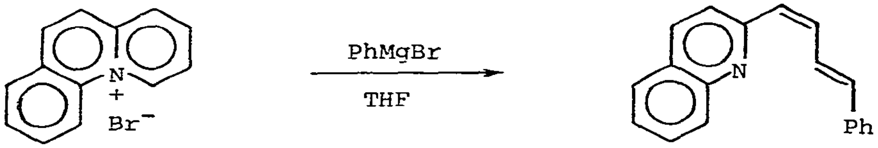


Addition of MeMgI to the pyrazine ring 119 in preference to the cyano group has already been mentioned [370]:

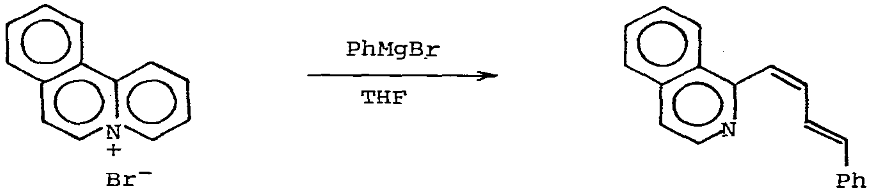


119

The benzo[a]- and benzo[c]quinolizinium bromides 180 and 181 with PhMgBr undergo ring-opening to give phenylbutadienylquinoline and isoquinoline, respectively [447]:

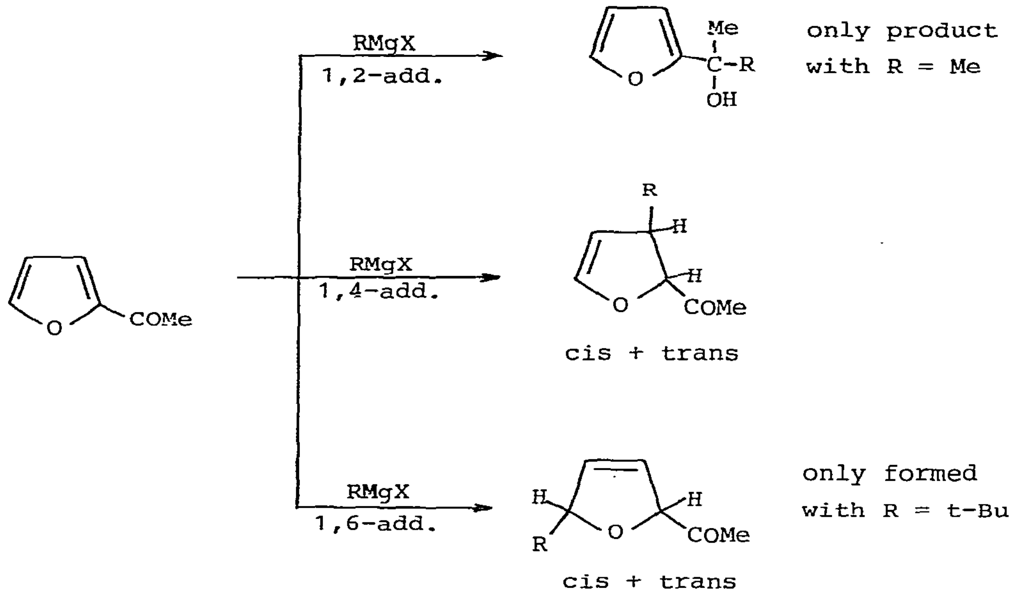


180



181

Furfural and 2-acetylfuran react with Grignard reagents to give 1,2-, 1,4-, and 1,6-addition products [448, 449]: e.g.


only product with R = Me

cis + trans

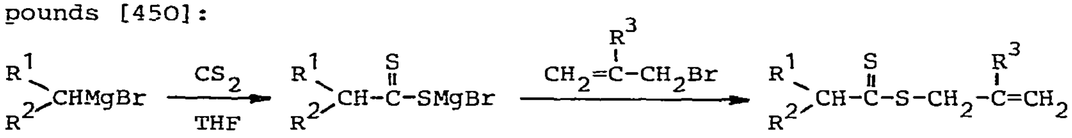
only formed with R = t-Bu

cis + trans

R = Me, i-Pr, t-Bu, PhCH$_2$

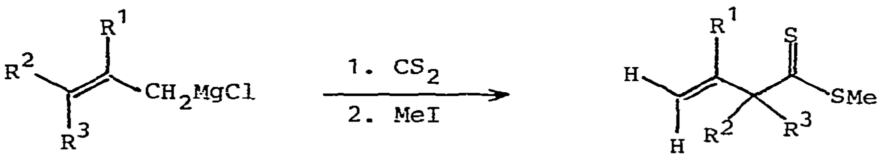
E. Addition to C=S groups

The addition of Grignard reagents to carbon disulfide, followed by reaction of the adduct with allyl bromides, provides a synthesis of 2-alkenyl alkanedithioates, which has been used as starting compounds for the synthesis of new types of sulfur compounds [450]:

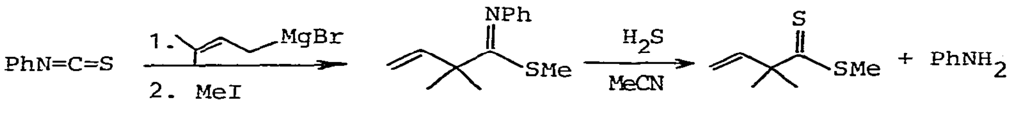


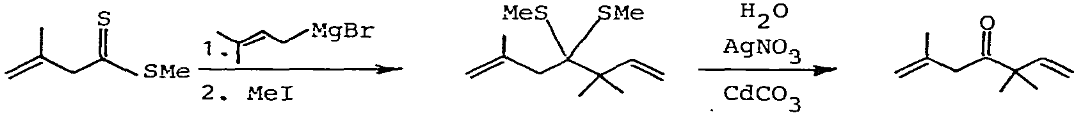
$$\begin{matrix}R^1\\R^2\end{matrix}\!>\!CHMgBr \xrightarrow[THF]{CS_2} \begin{matrix}R^1\\R^2\end{matrix}\!>\!CH-\overset{S}{\overset{\|}{C}}-SMgBr \xrightarrow{CH_2=\overset{R^3}{\overset{|}{C}}-CH_2Br} \begin{matrix}R^1\\R^2\end{matrix}\!>\!CH-\overset{S}{\overset{\|}{C}}-S-CH_2-\overset{R^3}{\overset{|}{C}}=CH_2$$

With the more reactive allylic Grignard reagents the reaction was carried out at -78° (inverse addition) in an ether-tetrahydrofuran mixture. Methylation affords dithioesters bearing an inversed allylic chain as expected [451]:

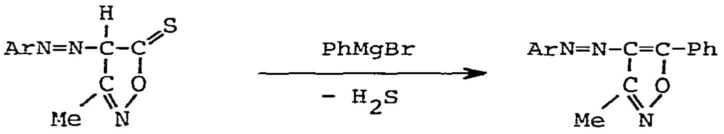


Similarly the carbophilic addition of prenylmagnesium bromide and other allylic Grignard reagents to the thiocarbonyl group of phenylisothiocyanate and dithioesters occurs exclusively with "inversion" of the allylic chain [452, 453]: e.g.



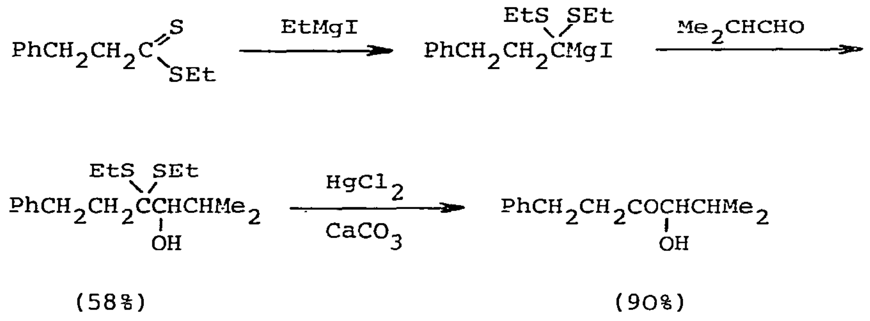


Treatment of 4-arylazo-3-methyl-2-isoxazolin-5-thiones with phenylmagnesium bromide effected 1,2-addition on the thiocarbonyl group followed by hydrogen sulphide elimination to yield the corresponding 4-arylazo-3-methyl-5-phenylisoxazoles [454]:



Ar = Ph, p-MeC_6H_4, p-ClC_6H_4 (55-62%)

Thiophilic addition of EtMgI to dithioesters leads to acyl anion equivalents which react with electrophilic reagents to yield dithioacetals. The latter compounds can be transformed into the corresponding carbonyl compounds on hydrolysis with $HgCl_2/CaCO_3$ buffer [455]: e.g.

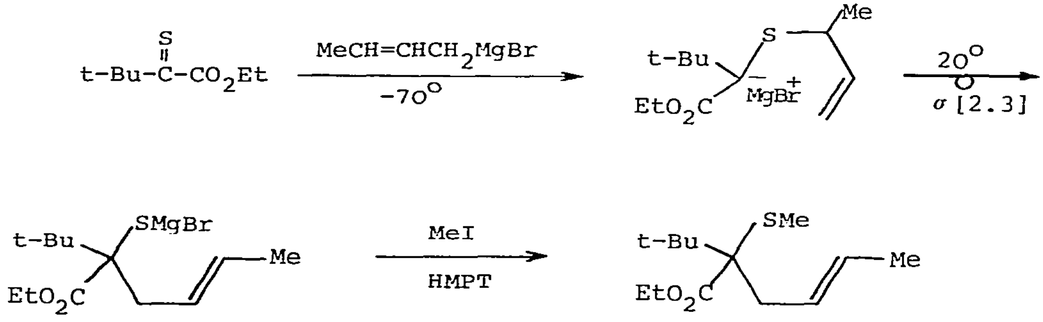


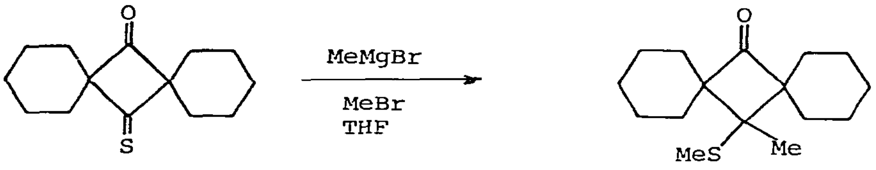
$$PhCH_2CH_2C\begin{matrix}{\scriptstyle =S}\\ {\scriptstyle SEt}\end{matrix} \xrightarrow{EtMgI} PhCH_2CH_2\overset{EtS\ SEt}{C}MgI \xrightarrow{Me_2CHCHO}$$

$$PhCH_2CH_2\overset{EtS\ SEt}{C}\underset{OH}{C}HCHMe_2 \xrightarrow[CaCO_3]{HgCl_2} PhCH_2CH_2CO\underset{OH}{C}HCHMe_2$$

(58%) (90%)

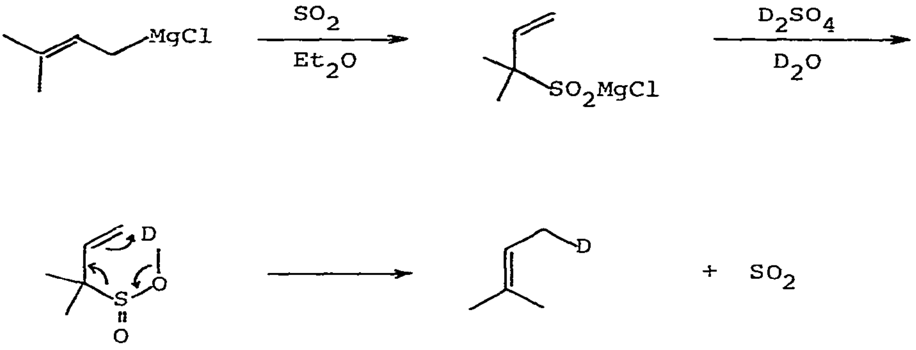
Selective thiophilic additions of Grignard reagents to thioketone functions have also been reported [456, 457]: e.g.





F. Additions to other unsaturated compounds

Treatment of allylic Grignard reagents with liquid sulfur dioxide in ether produced the magnesium salt of the corresponding allylic sulfinic acid which on acid hydrolysis undergoes smooth decomposition to sulfur dioxide and the olefin [458]: e.g.



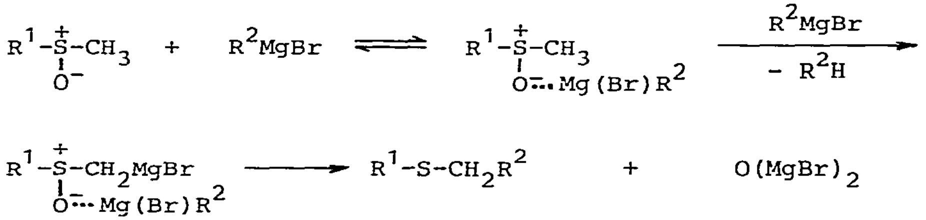
The reaction between sulfonyl fluorides and arylmagnesium bromides yields sulfones, while the corresponding cadmium reagents were found to be unreactive toward these sulfonyl fluorides [459]:

$$Ar^1SO_2F \quad + \quad Ar^2MgBr \longrightarrow Ar^1SO_2Ar^2$$

(44–82%)

With sulfoxides, on the other hand, the possibility of alkyl group exchange between R^1-SO-R and R^2MgBr was demonstrated followed by reduction to the corresponding sulfides. In another reaction an α-hydrogen in R or R^1 is replaced by R^2 [460, 461]:

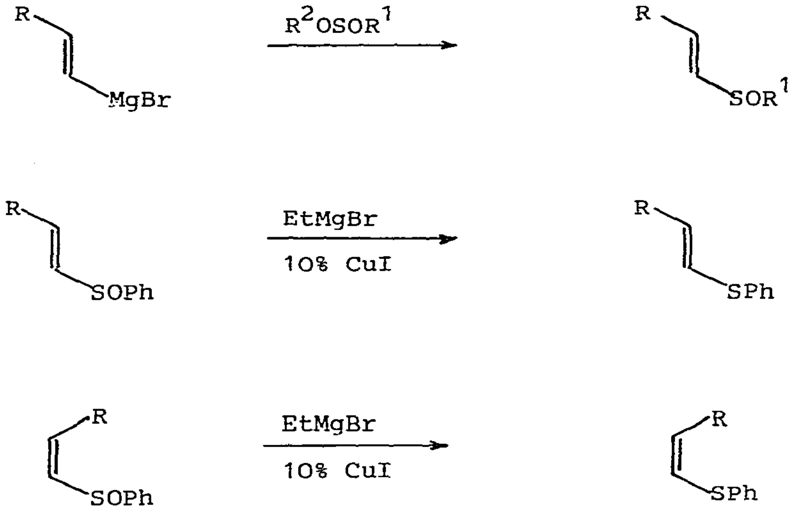
$$R^1\text{-SO-R} \quad + \quad R^2MgBr \longrightarrow R^1\text{-S-R} \quad + \quad R^2\text{-S-R} \quad + \quad R^1\text{-S-}R^2$$



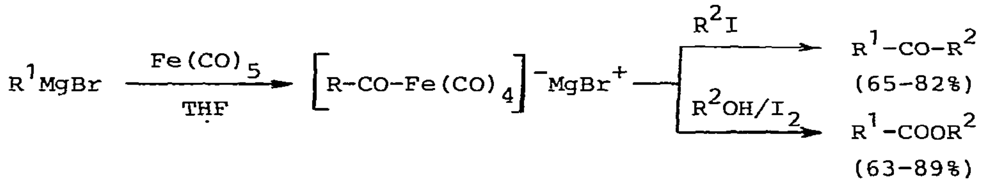
$$R^1\text{-}\underset{O^-}{\overset{+}{S}}\text{-}CH_3 \quad + \quad R^2MgBr \rightleftharpoons R^1\text{-}\underset{O^{-}\cdots Mg(Br)R^2}{\overset{+}{S}}\text{-}CH_3 \xrightarrow[-\ R^2H]{R^2MgBr}$$

$$R^1\text{-}\underset{O^{-}\cdots Mg(Br)R^2}{\overset{+}{S}}\text{-}CH_2MgBr \longrightarrow R^1\text{-S-}CH_2R^2 \quad + \quad O(MgBr)_2$$

(E)-1-Alkenylmagnesium bromides react cleanly and stereospecifically with chiral menthyl sulfinate esters to produce chiral (E)-1-alkenyl sulfoxides; no alkenyl sulfide is formed in this process. 1-Alkenyl aryl sulfoxides, on the other hand, are easily reduced to the corresponding vinylic sulfides upon treatment with ethylmagnesium bromide / 10% cuprous iodide at 0^o for 1h; no double bond isomerization occurs during this sulfoxide deoxygenation [462]:



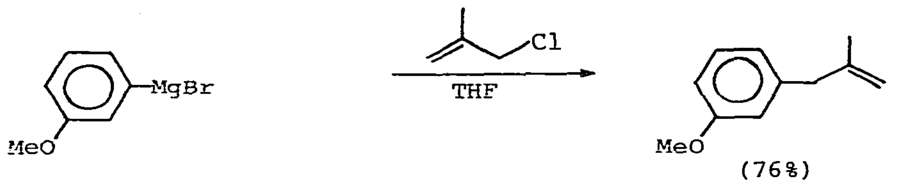
The reaction of Grignard reagents with pentacarbonyliron in THF at room temperature, followed by addition of an alkyl iodide or iodine in an alcohol gave ketones or esters, respectively, in high yield. The reactions proceed via acyltetracarbonylferrate intermediates [463, 464]:



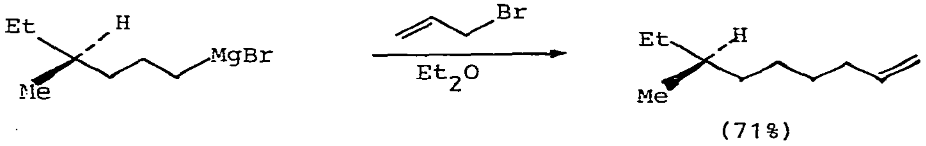
VI. DISPLACEMENT REACTIONS BY ORGANOMAGNESIUM COMPOUNDS

A. Coupling or displacement reactions with organic halides

A halogen that is allylic, benzylic, propargyl, or α to an ether is readily displaced by Grignard reagents. Some examples reported in 1978 are:



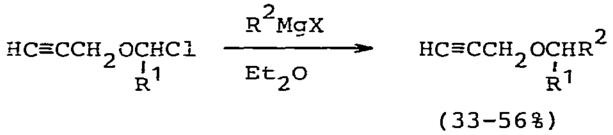
[465]



[466]

$HC\equiv CCH_2MgBr \xrightarrow[THF]{PhCH_2Br} HC\equiv CCH_2CH_2Ph$ [467]

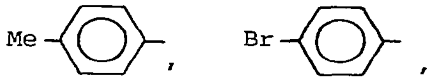
(59%)



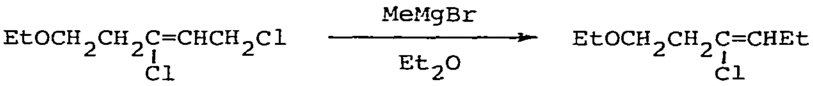
$HC\equiv CCH_2O\underset{R^1}{CHCl} \xrightarrow[Et_2O]{R^2MgX} HC\equiv CCH_2O\underset{R^1}{CHR^2}$ [95]

(33-56%)

R^1 = H, Me

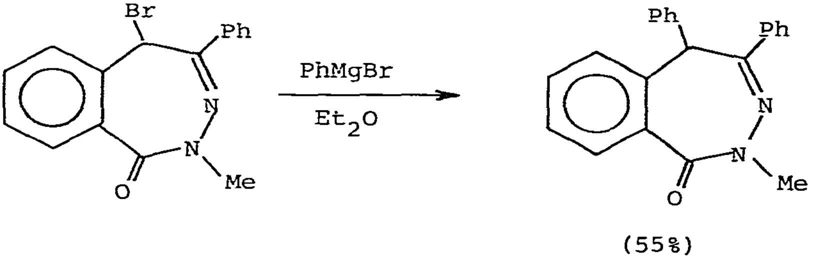
R^2 = $PhCH_2$,  PhC≡C-

These displacement reactions often can be performed selectively: e.g.



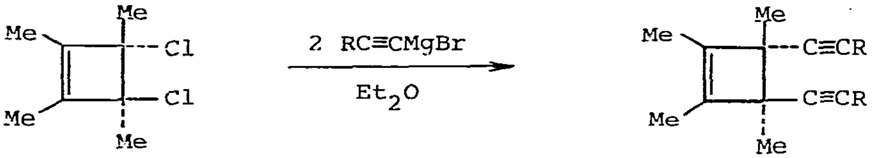
$EtOCH_2CH_2\underset{Cl}{C}{=}CHCH_2Cl \xrightarrow[Et_2O]{MeMgBr} EtOCH_2CH_2\underset{Cl}{C}{=}CHEt$ [468]

(85%) "E + Z"



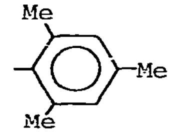
[469]

The following coupling of trans-3,4-dichlorotetramethylcyclobutene with ethynylmagnesium bromides, which does not work in THF as the solvent, yields trans-products only. With R = Ph, however, some cis-isomer is also formed [470]:

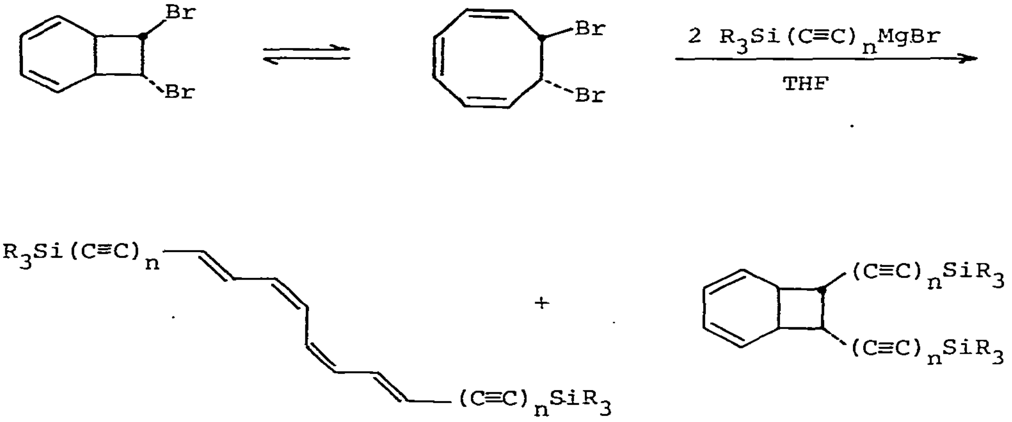


(29-57%)

R = Me, t-Bu, SiMe$_3$,



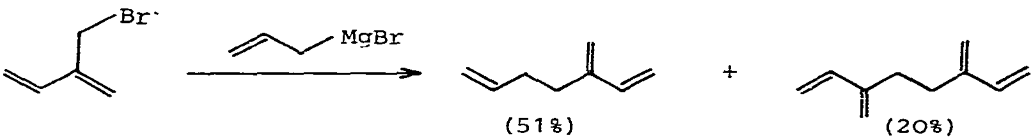
Cyclooctatetraene dibromide, on the other hand, couples with the corresponding Grignard reagents in THF to give, as major products, silyl-stabilized E,Z,Z,E-polyeneynes together with minor proportions of configurational isomers (Z,E,Z,Z and all-E) and compounds in which a bicyclo-octadiene structure is retained [471]:



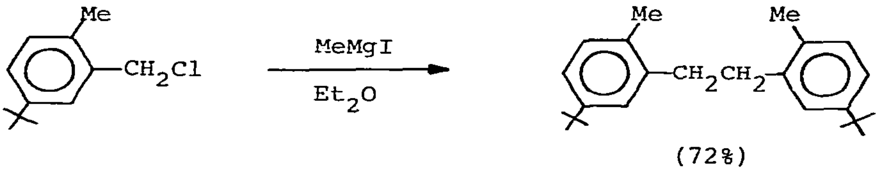
(25-33%)

(4-27%)

A 1,4-polybutadiene, brominated with NBS, was treated with aryl Grignard reagents in order to replace the bromine by the corresponding aryl groups [472]. 20% Homocoupling has been observed during the reaction of 2-bromomethyl-1,3-butadiene with allylmagnesium bromide [473]:



Benzyl chlorides with MeMgI yield bibenzyl derivatives only [474, 475]: e.g.



The homocoupling reaction between phenylmagnesium bromide and benzyl chloride to give biphenyl and bibenzyl is selectively catalyzed by CpL_2FeX. A catalytic cycle is proposed with SET processes between iron complexes, containing in some cases an iron-magnesium bond, and benzyl halide [476]:

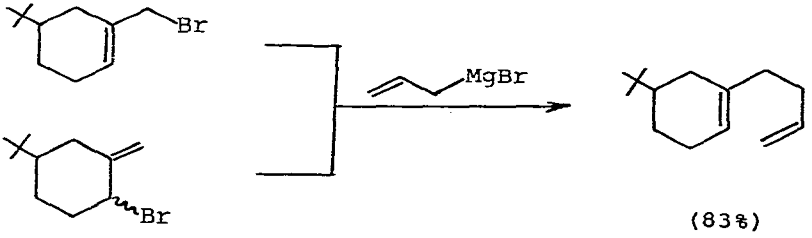
$$PhMgBr + PhCH_2Cl \xrightarrow[Et_2O]{CpL_2FeX}$$

$$\underset{(31-46\%)}{Ph-Ph} + \underset{(30-42\%)}{PhCH_2CH_2Ph} + \underset{(1-12\%)}{PhCH_2Ph}$$

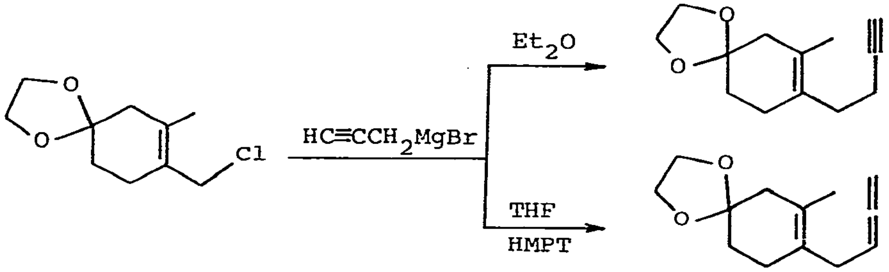
$L = PhPMe_2$; $L_2 = Me_2P(CH_2)_2PMe_2$

$X = Br, Ph$

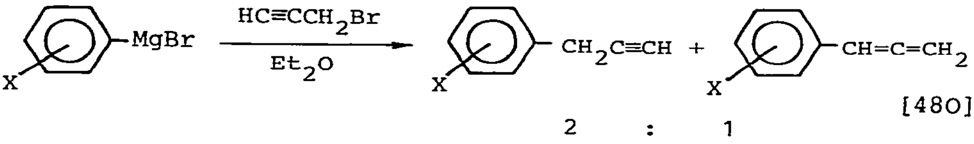
Allylic or propargyl halides may undergo displacement with allylic rearrangement:



[477]



[478,479]



[480]

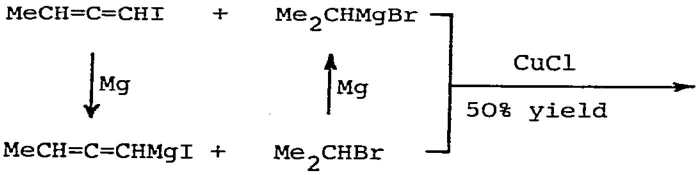
X = 4-MeO, 4-Me, 3-CF_3

Allene formation from Grignard reagents and propargyl chlorides can be catalyzed by iron, cobalt, nickel, and copper salts. Chromium, manganese, rhodium, and silver salts do not catalyze the reaction. A mechanism for allene formation is proposed involving initial formation of a low valence state metal species from reaction of the Grignard reagent with the metal salt, which undergoes oxidative insertion into the carbon-chlorine bond of the propargyl chloride. Displacement of halogen by alkyl from the Grignard reagent forms a bisorganometal species which decomposes to allene [481]: e.g.

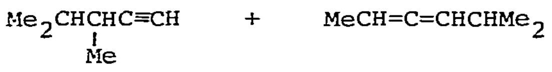
$$\text{n-BuMgBr} \quad + \quad \text{HC}{\equiv}\text{CCH}_2\text{Cl} \xrightarrow{\text{FeCl}_3} \text{n-BuCH=C=CH}_2$$

$$(85\%)$$

The following cuprous chloride catalyzed coupling reactions, however, yield only a small portion of the corresponding allenic compound [482]:



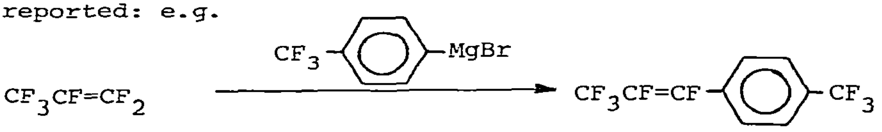
$$\left.\begin{array}{ccc} \text{MeCH=C=CHI} & + & \text{Me}_2\text{CHMgBr} \\ \big\downarrow \text{Mg} & & \big\uparrow \text{Mg} \\ \text{MeCH=C=CHMgI} & + & \text{Me}_2\text{CHBr} \end{array}\right] \xrightarrow[\text{50\% yield}]{\text{CuCl}}$$



$$Me_2CH\underset{Me}{CH}C{\equiv}CH \quad + \quad MeCH{=}C{=}CHCHMe_2$$

(95% or 85%) (5% or 15%)

Several uncatalyzed displacements of a vinyl fluorine have been reported: e.g.

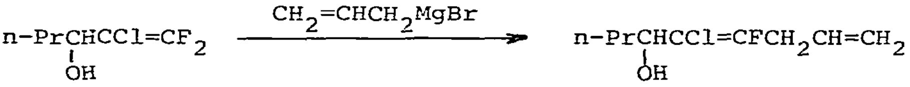


[483]

E/Z = 10

$$CF_3N{=}CF_2 \xrightarrow{PhMgBr} CF_3N{=}CFPh$$ [484]

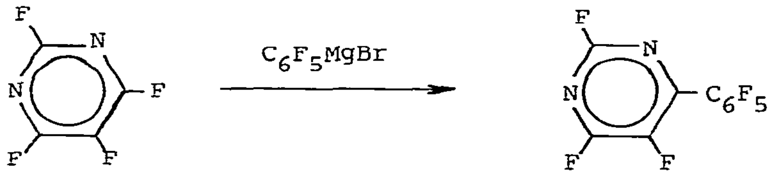
(50%)

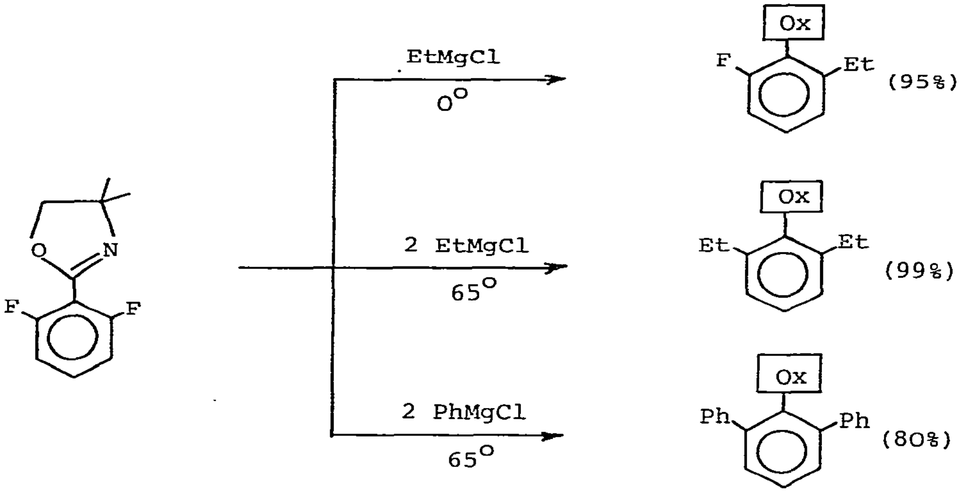


$$n\text{-}Pr\underset{OH}{CH}CCl{=}CF_2 \xrightarrow{CH_2{=}CHCH_2MgBr} n\text{-}Pr\underset{OH}{CH}CCl{=}CFCH_2CH{=}CH_2$$ [485]

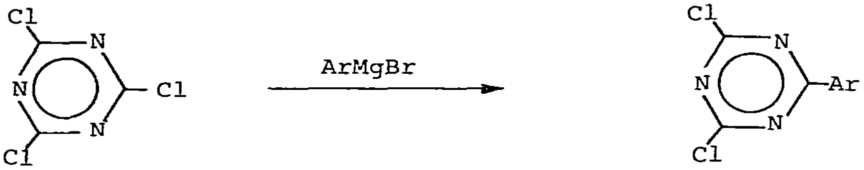
E/Z = 6

Tetrafluoropyrimidine [50]and activated fluorobenzenes [486] also undergo nucleophilic displacement of fluoro substituents by organomagnesium compounds:

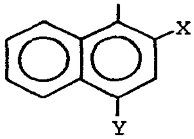




The same is true for a chloro substituent in cyanuric chloride [487]:

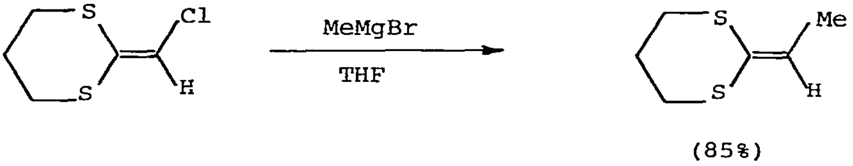


Ar =

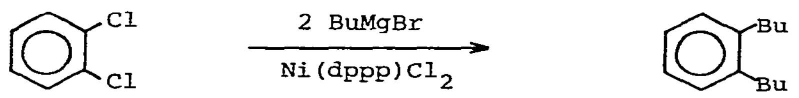


X = Y = H
X = Me; Y = H
X = H; Y = Me

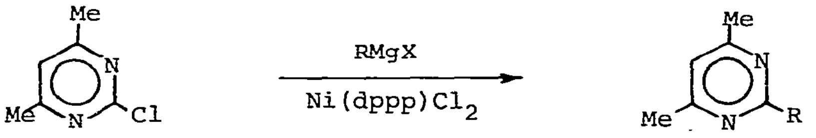
Chlorine displacement is also the net result in the reaction of Grignard reagents with chloroketene dithioacetals which probably proceeds via an addition intermediate [488]:



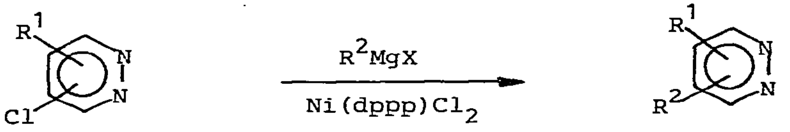
Cross-coupling of Grignard reagents with other aryl, heteroaryl, and alkenyl chlorides can be catalyzed by nickel-phosphine complexes: e.g.



(79-83%) [489]



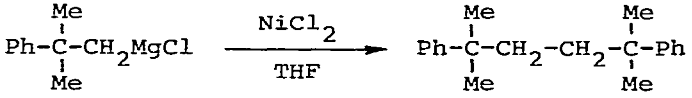
(46-74%) [490]



(20-100%) [491]

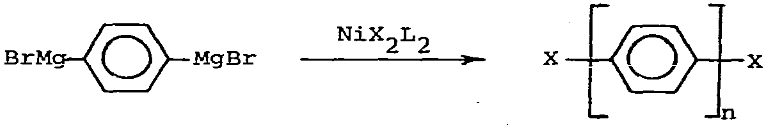
dppp = $Ph_2P(CH_2)_3PPh_2$

Ni(II), Co(II), and Cu(II) salts have also been used as catalysts for Kharasch-type homocoupling reactions. None of the reactions appear to have appreciable radical character [492]: e.g.

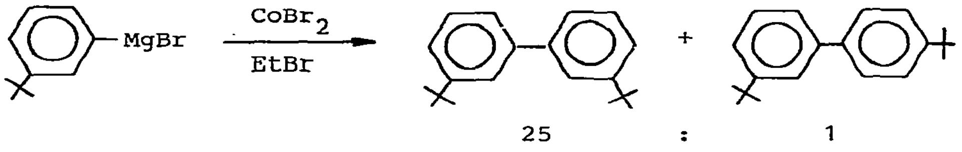


$$\mathrm{Ph-\underset{Me}{\overset{Me}{C}}-CH_2MgCl} \xrightarrow[\text{THF}]{\text{NiCl}_2} \mathrm{Ph-\underset{Me}{\overset{Me}{C}}-CH_2-CH_2-\underset{Me}{\overset{Me}{C}}-Ph}$$

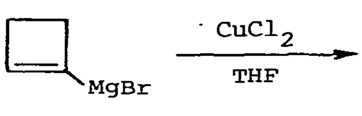
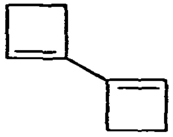
[492]



[168]



[493]



(40%)

[191]

A novel synthesis of biaryls uses diaryliodonium salts as starting material [494]:

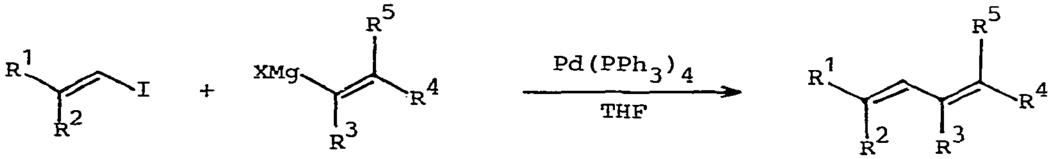
$$\left[\mathrm{Ar{-}\overset{+}{I}{-}Ar}\right]\mathrm{Br^-} \xrightarrow[\mathrm{NiCl_2}]{\mathrm{MeMgI/Et_2O}} \mathrm{Ar{-}Ar}$$

(33-96%)

$$\left[\mathrm{Ar^1{-}\overset{+}{I}{-}Ar^2}\right]\mathrm{Br^-} \longrightarrow \mathrm{Ar^1{-}Ar^2} \quad + \quad \mathrm{Ar^1{-}Ar^1} + \mathrm{Ar^2{-}Ar^2}$$

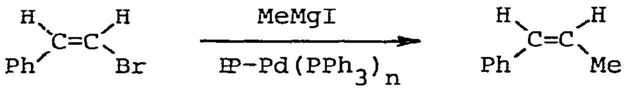
(45-66%) (12-30%)

Vinylic iodine can be replaced stereospecifically by the palladium-catalyzed reaction with Grignard reagents whereby even 1,3-dienes can be prepared under mild conditions by direct coupling of unlike alkenyl groups [495]:



(75-87%)

Similarly works a polymer-bound palladium(0) complex starting with alkenyl bromides [496]:



(98% "Z")

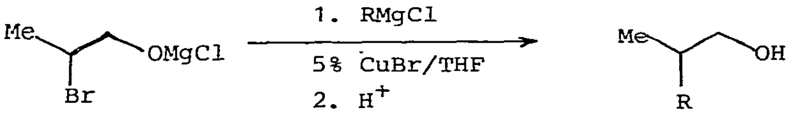
Ⓟ = polymeric ligand

Two vinylic bromines have been displaced simultaneously by cuprous bromide catalyzed coupling with allylmagnesium bromide [497]:

$$\mathrm{RCH{=}CBr_2} \xrightarrow[\mathrm{CuBr}]{\mathrm{2\ CH_2{=}CHCH_2MgBr}} \mathrm{RCH{=}C(CH_2CH{=}CH_2)_2}$$

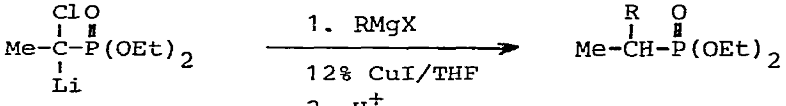
R = H, Ph

Copper(I) salts have also been used as catalysts for halogen substitution in 2-bromoalkanols [498]and 1-chloro-1-lithioalkanephosphonates [499, 500] by organomagnesium compounds:



(60-80%)

R = Ph, $CH_2{=}CH$, $CH_2{=}CHCH_2$, $CH_2{=}CMeCH_2$, $Me_2C{=}CHCH_2$

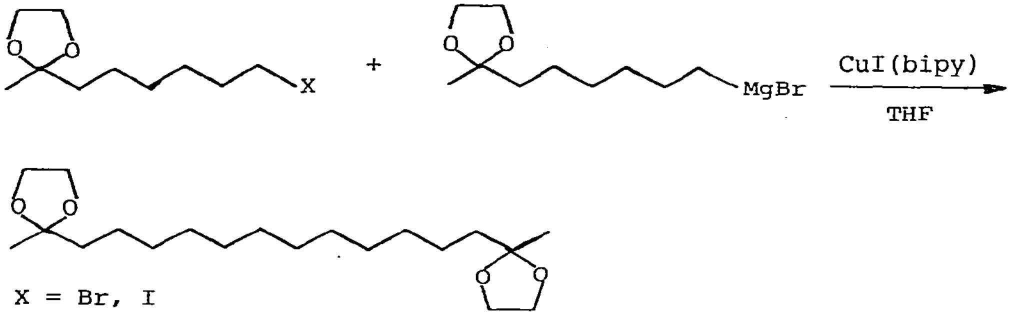


$$\mathrm{Me{-}\underset{Li}{\overset{Cl}{C}}{-}\overset{O}{\overset{\|}{P}}(OEt)_2} \xrightarrow[\substack{\text{12\% CuI/THF} \\ \text{2. H}^+}]{\text{1. RMgX}} \mathrm{Me{-}\overset{R}{C}H{-}\overset{O}{\overset{\|}{P}}(OEt)_2}$$

(45-63%)

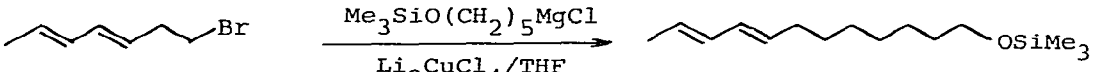
R = Et, i-Pr, n-Bu

In the following coupling reaction with CuI coordinated by 2,2′-bipyridyl as the catalyst the yield increased from 60% to 79% by using the corresponding iodide instead of the bromide [105]:

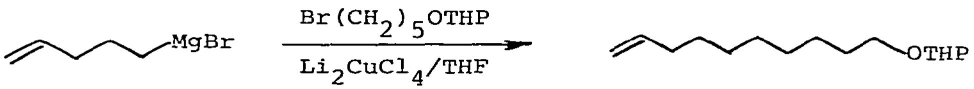


X = Br, I

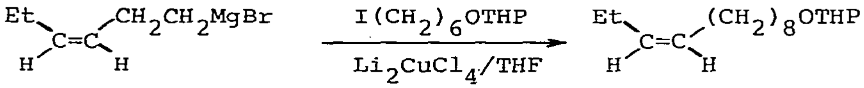
Finally a variety of coupling reactions catalyzed by dilithium tetrachlorocuprate may be noted:



(72%) [90]



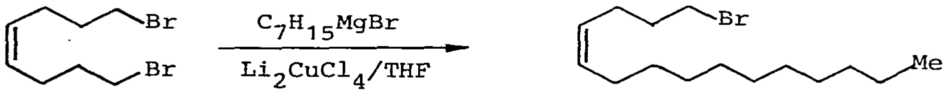
(65%) [501]



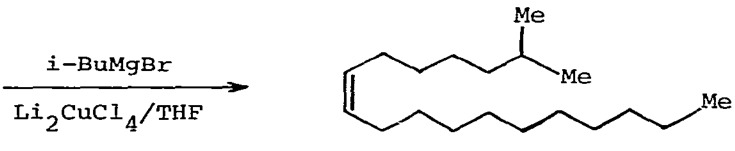
[502]

$$I(CH_2)_{12}I \xrightarrow[Li_2CuCl_4/THF]{THPO(CH_2)_{11}MgBr} THPO(CH_2)_{34}OTHP$$ [85]

(67%)

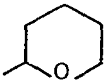


(91%) [503,504]



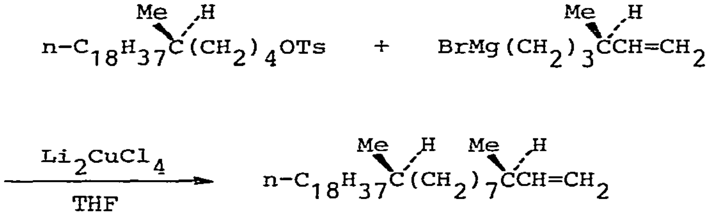
(78%)

THP =



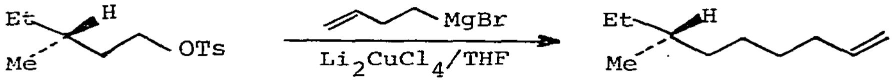
B. Displacement reactions at C-O and C-S bonds

Displacement reactions of sulfonate esters by Grignard reagents are known to proceed similarly to those of halides noted in the previous section: e.g.



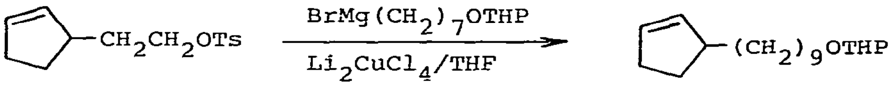
$$n\text{-}C_{18}H_{37}\overset{Me\ \ H}{C}(CH_2)_4OTs + BrMg(CH_2)_3\overset{Me\ \ H}{C}CH{=}CH_2 \xrightarrow[THF]{Li_2CuCl_4} n\text{-}C_{18}H_{37}\overset{Me\ \ H}{C}(CH_2)_7\overset{Me\ \ H}{C}CH{=}CH_2$$

[505]

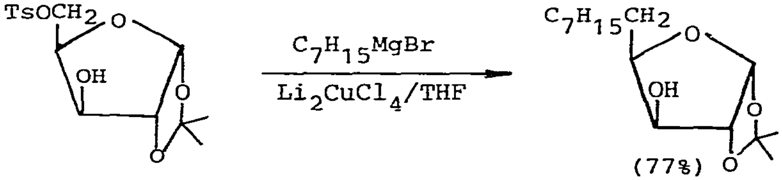


(50%)

[466]



[83]



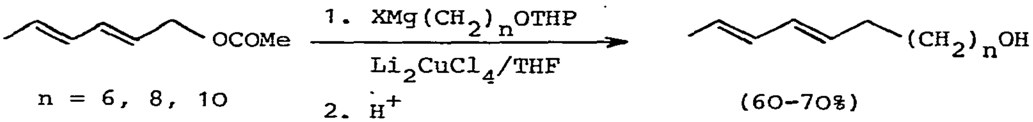
(77%)

[506]

$$TsO(CH_2)_{13}OTs \xrightarrow[\text{2. } H^+]{\text{1. 2 } THPO(CH_2)_{11}MgBr,\ Li_2CuCl_4/THF} HO(CH_2)_{35}OH \quad (35\%)$$

[85]

Displacements of allylic acetates are illustrated in the following reactions starting from sorbyl acetate [81,82,84]:



n = 6, 8, 10

(60-70%)

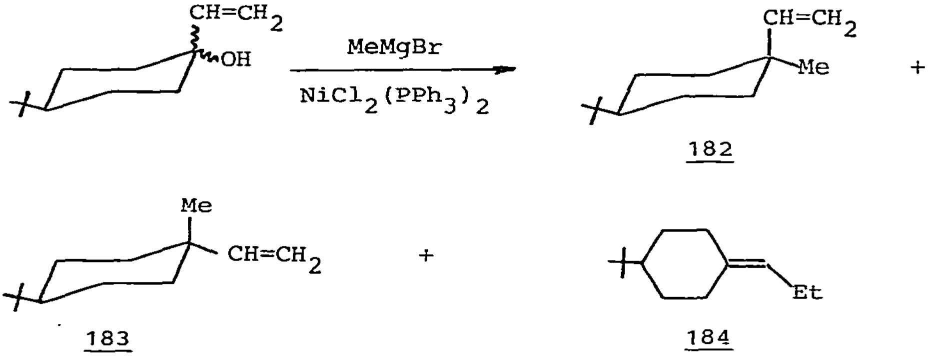
Only alkylation of the E/E isomer is stereospecific, the other isomers give a mixture of stereoisomers [80].

During the following displacement reaction rearrangement occurs with the formation of 1,1-diphenylallene [507]:

$$HC{\equiv}CCH(OCOMe)_2 \xrightarrow{PhMgBr} Ph_2C{=}C{=}CH_2$$

(60%)

In the presence of bis(triphenylphosphine)nickel dichloride even allylic alcohols may couple with Grignard reagents, both cis- and trans-4-tert-butyl-1-vinylcyclohexanol with MeMgBr affording the same mixture of 182, 183, and 184 in a 19:1:5 ratio. This indicates that the methyl group delivery process shows high preference for quaternization over terminal carbon alkylation and, most importantly, is greatly stereoselective [508].

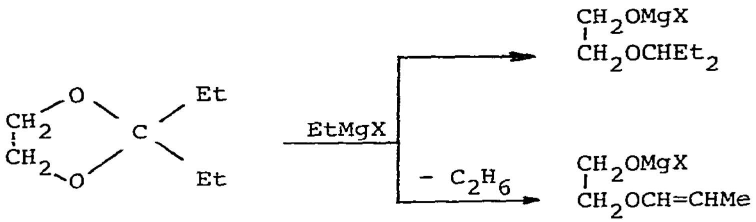


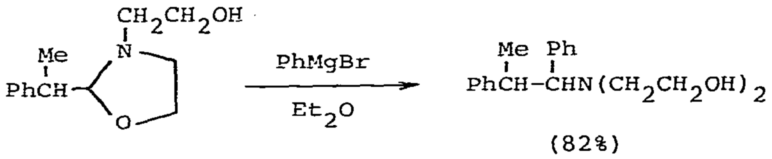
182

183

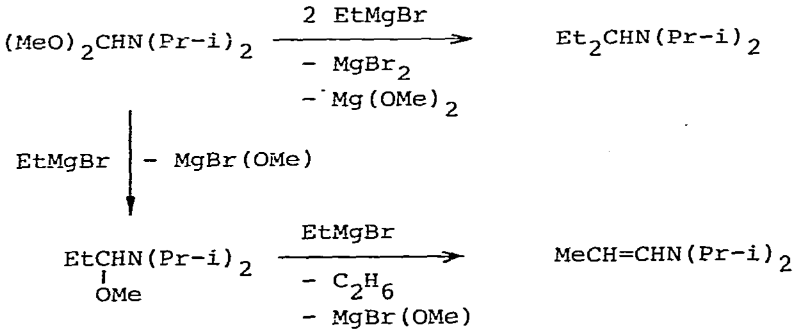
184

Ring-opening occurs upon reaction of Grignard reagents with 1,3-dioxolanes [509,510,511] or oxazolidines [512]. Starting with 2-substituted 1,3-dioxolanes besides ß-hydroxyethyl sec-alkyl ethers, the normal products of the ring-opening/addition reaction, 2-hydroxyethyl enol ethers were formed as products of a ring-opening/elimination reaction. Kinetic studies suggest an E_1 mechanism for this novel reaction [510]: e.g.

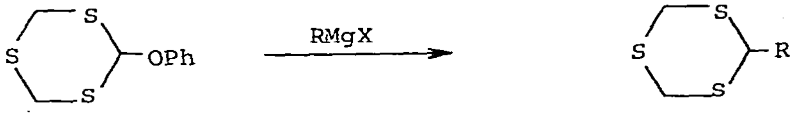




ß-Elimination with the formation of enamines has also been observed as a side reaction during the synthesis of tertiary amines from dialkylformamide acetals and Grignard reagents [513]: e.g.



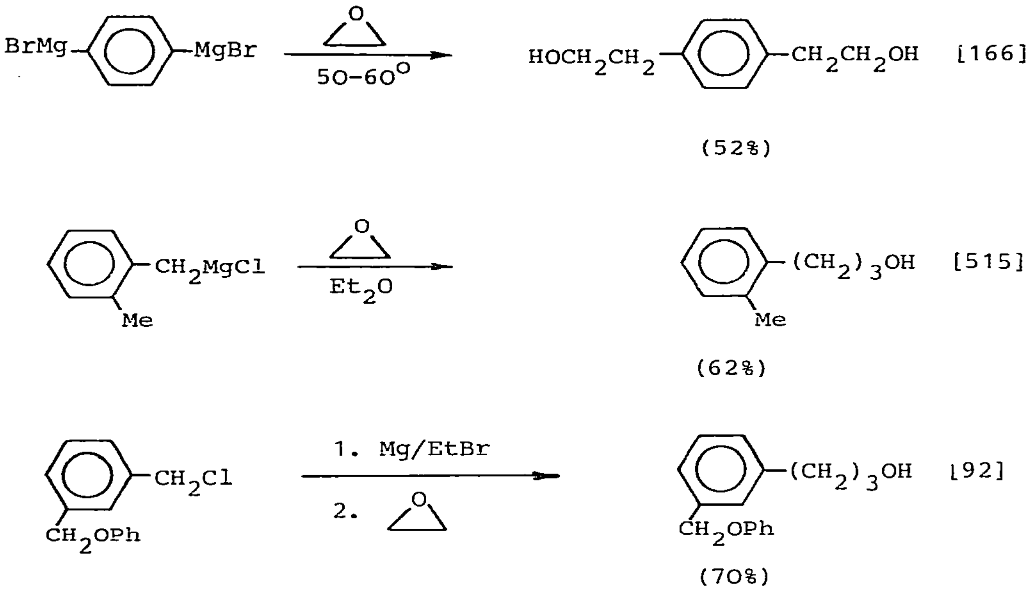
During the reaction of phenoxytrithiane 185 with excess Grignard reagent no ring-opening takes place, the 2-substituted trithianes 186 are rather formed in good yields. The corresponding methoxy derivative, on the other hand, does not react [514]:



185

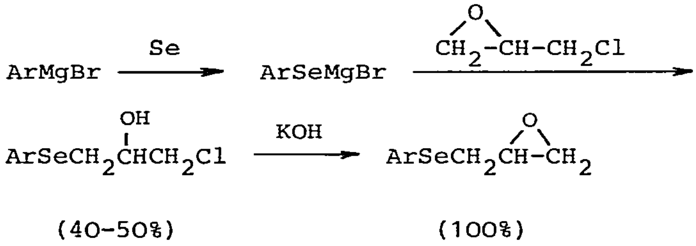
186

Some reported displacement reactions at an epoxide group are:



In the last case without using the entrainment method the yield was only 30% [92].

The reaction of arylselenomagnesium bromide with epichlorohydrin yields chlorohydrins which are easily converted into the corresponding epoxy compounds by the action of potassium hydroxide [516]:

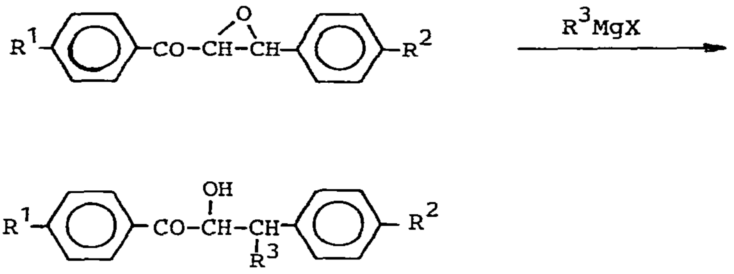


$$\text{ArMgBr} \xrightarrow{\text{Se}} \text{ArSeMgBr} \xrightarrow{\overset{\text{O}}{\text{CH}_2\text{-CH}}\text{-CH}_2\text{Cl}}$$

$$\text{ArSeCH}_2\overset{\text{OH}}{\text{CH}}\text{CH}_2\text{Cl} \xrightarrow{\text{KOH}} \text{ArSeCH}_2\overset{\text{O}}{\text{CH-CH}_2}$$

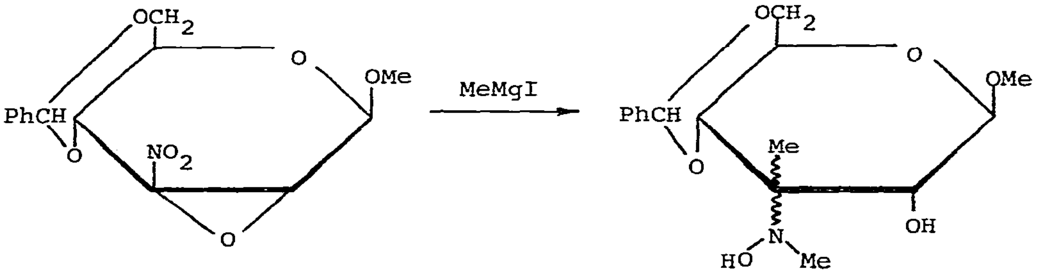
$$(40\text{-}50\%) \qquad\qquad (100\%)$$

Starting with chalcone epoxides several α-hydroxypropiophenones have been prepared [517]:



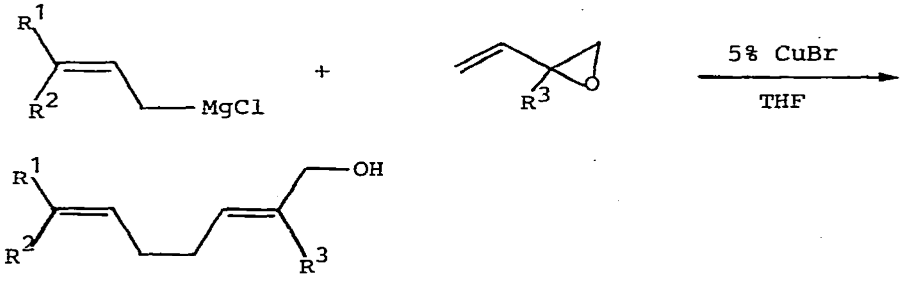
Cleavage of epoxide rings in various steroids by methyl [518–521] and methallyl [522] Grignard reagents has also been reported.

During the reaction of the carbohydrate α-nitroepoxide 187 with MeMgI the nitro group is converted into an N-hydroxy-N-methylamino group [523]:

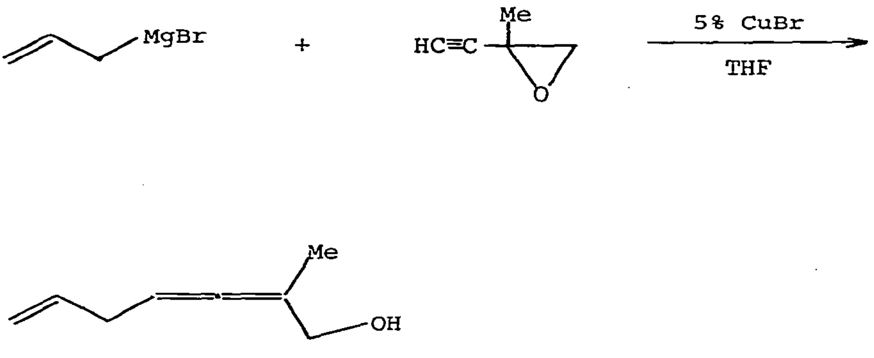


187

Allyl Grignard reagents react with butadiene monoepoxide or other vinyl oxiranes in the presence of CuBr to give 2,6-dienols in excellent yields. Use of ethynyl epoxides gives allenes [75,524]:

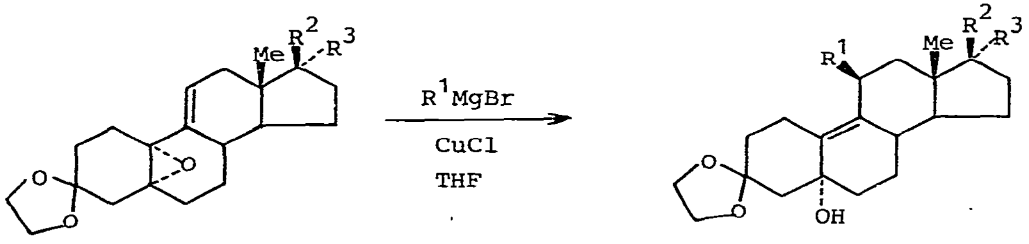


(90–95%)



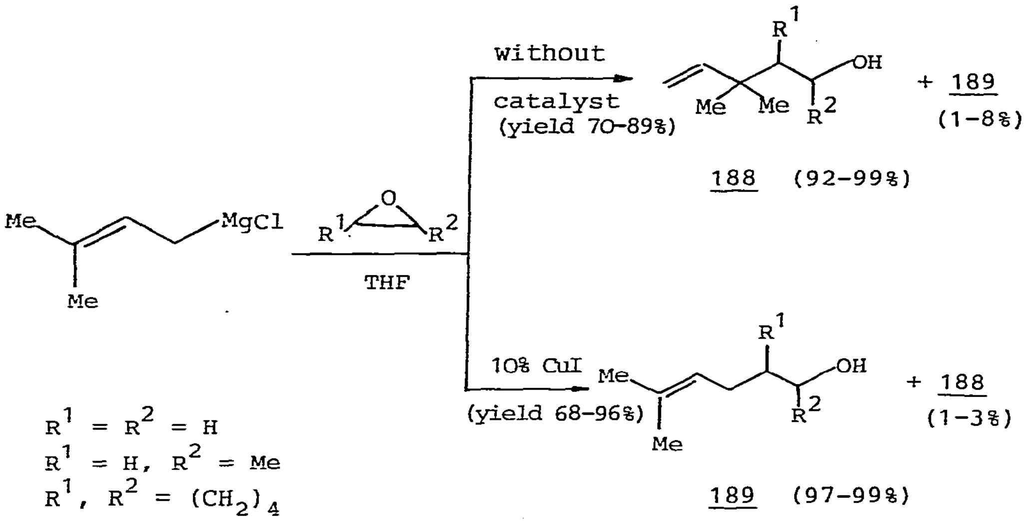
(80%)

Copper(I) catalyzed conjugate attack of phenyl [525] and allyl [526] Grignard reagents on corresponding steroid epoxides has also been observed:



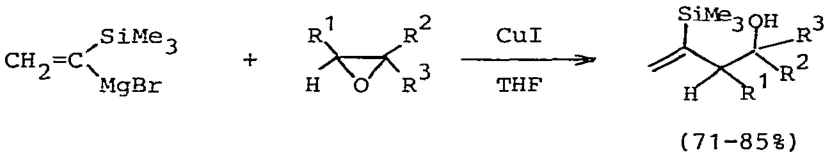
R^1 = Ph, $CH_2{=}CHCH_2$

The reaction of allylic Grignard reagents with oxiranes is highly regioselective: without catalyst the γ-products 188 are formed, where as in the presence of 10% CuI the α-products 189 are obtained [527]:

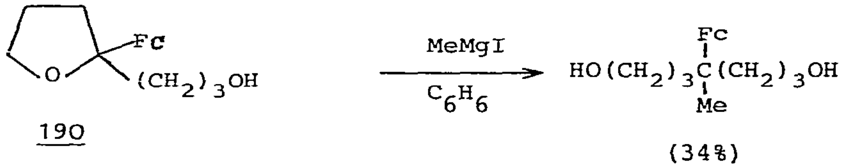


$R^1 = R^2 = H$
$R^1 = H,\ R^2 = Me$
$R^1,\ R^2 = (CH_2)_4$

Cuprous iodide is also a catalyst for the stereospecific synthesis of homoallyl alcohols from vinyl Grignard reagents and epoxides [174,394,395]. When the catalyst was absent the homoallyl alcohols were not obtained at all [174]:

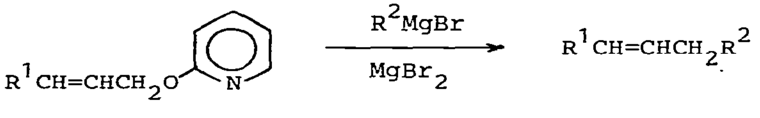


In the ferrocene derivative 190 the THF ring has been cleaved with MeMgI in refluxing benzene [528]:



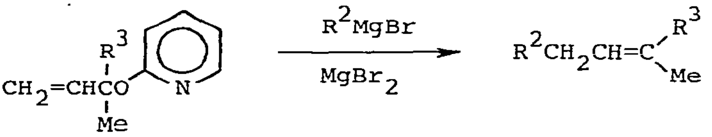
Fc = $C_5H_5FeC_5H_4$ (ferrocenyl group)

Open-chain ethers which are allylic or propargylic may also undergo displacement reactions with Grignard reagents. A regioselective coupling reaction of Grignard reagents with allyl pyridyl ethers in the presence of $MgBr_2$ is reported. Primary ethers 191 give in THF almost exclusively the product 192 of an S_N2 reaction, while secondary or tertiary ethers 193 in benzene or THF yield only the product 194 of an S_N2' substitution [529]:



191

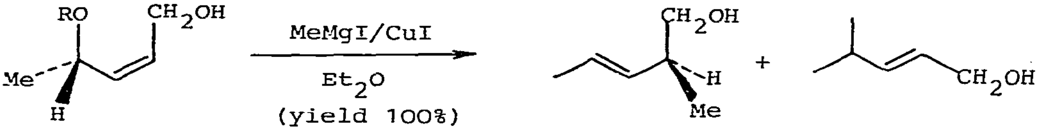
192 (58-95%)



193

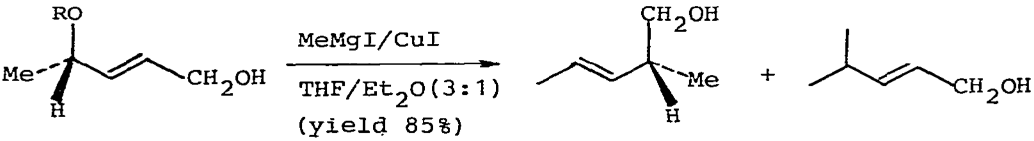
194 (84-87%)

The two cis-trans isomeric allylic ethers 195 and 196 react with 5 equiv. of MeMgI/CuI (9:1) to give (S) and (R)-2-methyl-3-pentenol respectively in an overall trans substitution [530]:



195

4 : 1

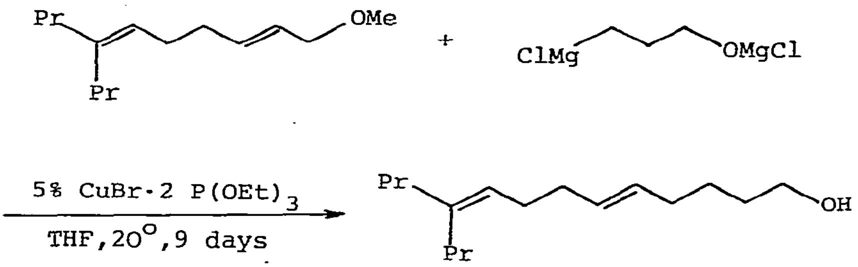


196

1 : 2

R = EtOCHMe

The following hydroxypropylation was performed with a "non protected" hydroxy Grignard reagent [75]:



Cinnamyl methyl ether reacts with EtMgBr containing 10% CuBr with the formation of only 10% of the expected substitution product 198 the main reaction yielding reduction products probably via an organometallic intermediate 197 [531]:

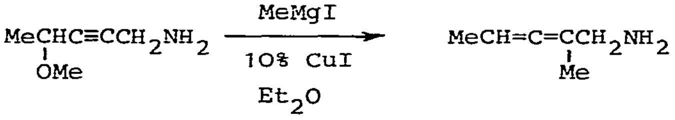
$$\mathrm{PhCH{=}CHCH_2OMe} \xrightarrow[\mathrm{CuBr}]{\mathrm{EtMgBr}} \underset{\underline{197}\ (90\%)}{\mathrm{PhCH{=}CH{-}CH_2\overset{(Cu)}{MgBr}}} + \underset{\underline{198}\ (10\%)}{\mathrm{PhCH{=}CHC_3H_7}}$$

$$\big\downarrow \mathrm{D_2O}$$

$$\mathrm{PhCH{=}CHCH_2D} + \mathrm{PhCHDCH{=}CH_2}$$

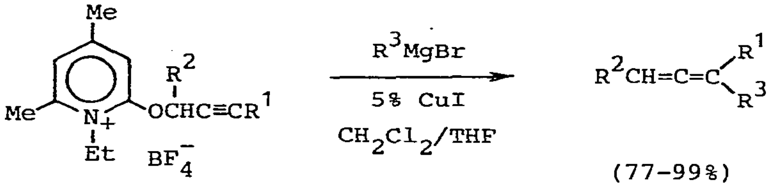
The corresponding cinnamyl acetate, on the other hand, yields only minor amounts of reduction products, this time 198 being the main product [531].

The reaction of Grignard reagents with propargylic ethers in the presence of CuI yields allenes containing no acetylenes [532,533] e.g.



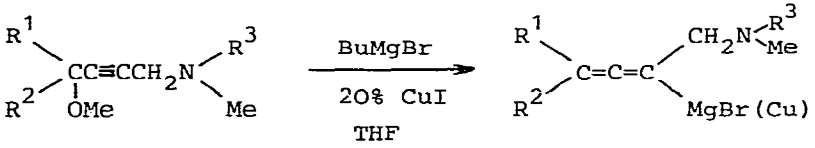
$$\underset{\mathrm{OMe}}{\mathrm{MeCHC{\equiv}CCH_2NH_2}} \xrightarrow[\substack{10\%\ \mathrm{CuI}\\ \mathrm{Et_2O}}]{\mathrm{MeMgI}} \underset{\mathrm{Me}}{\mathrm{MeCH{=}C{=}CCH_2NH_2}}$$

(75%)



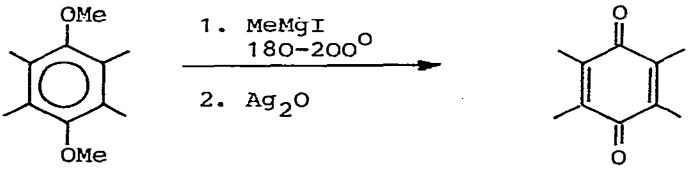
(77-99%)

Treatment of the acetylenic amino ethers with butylmagnesium bromide and 20% CuI in THF or THF/Et_2O (3:1), on the other hand, gives rise to the introduction of hydrogen instead of an alkyl group, probably via the organometallic intermediate 199 which can be hydrolyzed to an allenic amine [532]:

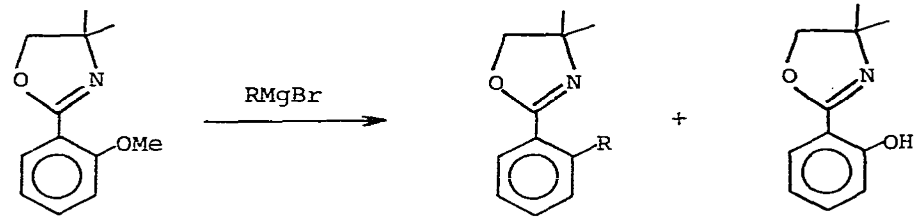


199 (40-70%)

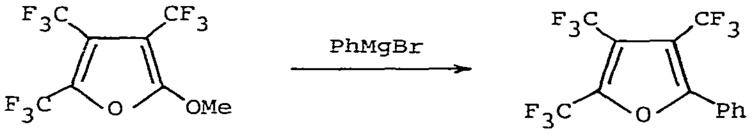
For the cleavage of unactivated aryl methyl ethers with Grignard reagents vigorous conditions are necessary. Thus several cyclophanes with hydrochinon dimethyl ether functions have been demethylated by heating at 180-200° C with MeMgI followed by oxidation to the corresponding chinone [534,535,536]:



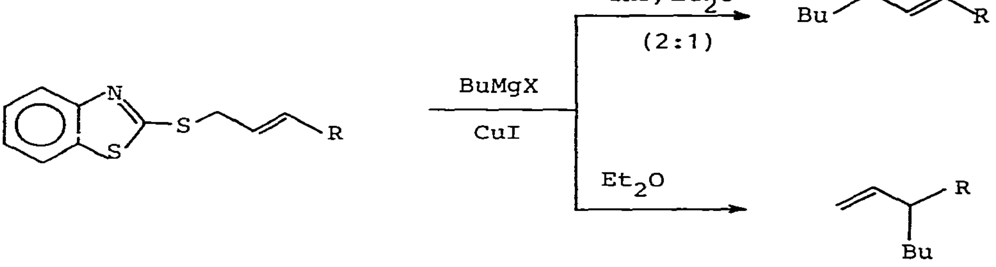
The reaction of o-(methoxy)aryloxazolines with organomagnesium compounds, on the other hand, results in methoxy displacement, methyl-oxygen-cleavage with the formation of the corresponding phenol in this case being only a side reaction. This nucleophilic aromatic substitution which does not work with allyl and benzyl Grignard reagents was shown not to proceed via radical intermediates [537]:

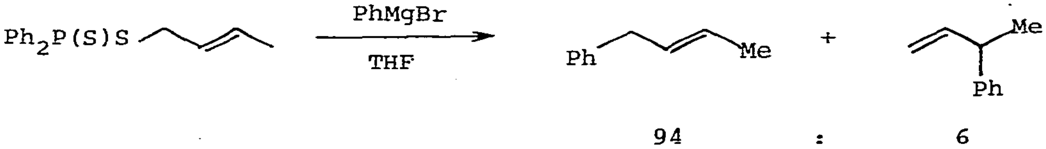


Nucleophilic attack of PhMgBr on the following furan derivative has also been reported [538]:

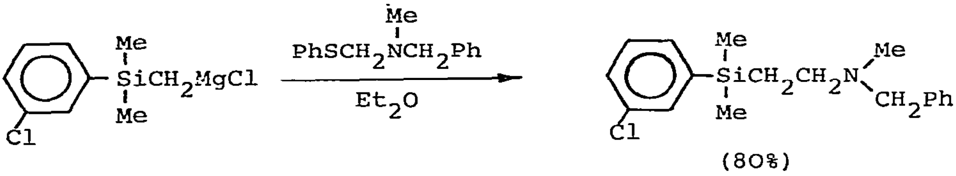


Displacement reactions at allyl-sulfur bonds have been used in the following regioselective synthesis of olefins. Depending on the solvent, olefins with or without allylic rearrangement are formed [539,540]:

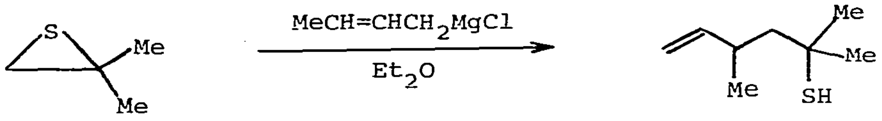




The following aminomethylation reaction also uses C-S bond cleavage by a Grignard reagent [172]:

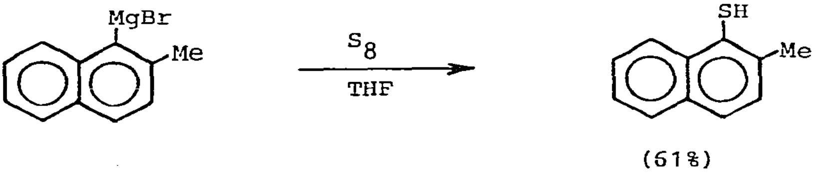


Finally ring opening of a thioepoxide has been reported [541]:

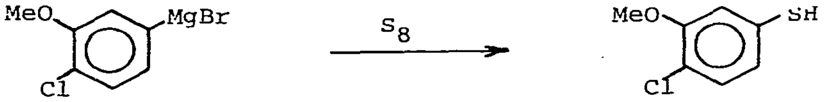


C. Displacement reactions at sulfur

Grignard reagents are known to react with elementary sulfur with the formation of thiols. Two examples reported in 1978 are given:

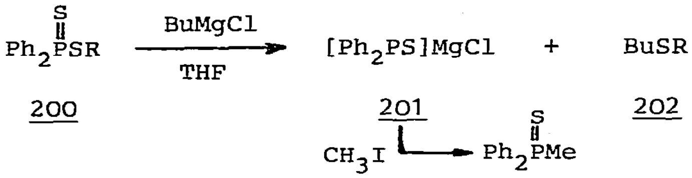


[542]



[543]

In the reaction of diphenylphosphinodithioate esters 200 with butylmagnesium chloride in refluxing THF sulfur was attacked by an $S_N2(S)$ mechanism yielding butyl sulfides 202 and diphenylphosphinothioylide 201, the latter affording methyldiphenylphosphine sulfide upon treatment with methyl iodide [544]:



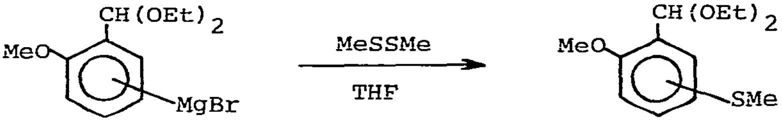
$$\underset{\underline{200}}{Ph_2\overset{S}{\overset{\|}{P}}SR} \xrightarrow[THF]{BuMgCl} \underset{\underline{201}}{[Ph_2PS]MgCl} + \underset{\underline{202}}{BuSR}$$

$$\underline{201} \xrightarrow{CH_3I} Ph_2\overset{S}{\overset{\|}{P}}Me$$

Displacement at the thiocyanate sulfur of 203 combined with dehydrochlorination, provides a convenient method for the introduction of a vinylthio group [545]: e.g.

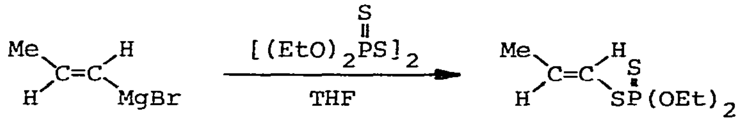
$$\underset{\underline{203}}{\mathrm{ClCH_2CH_2SCN}} \xrightarrow[\mathrm{THF}]{\mathrm{PhMgBr}} \mathrm{PhSCH_2CH_2Cl} \xrightarrow{\mathrm{KOCMe_3}} \underset{(80\%)}{\mathrm{PhSCH{=}CH_2}}$$

Other displacements at divalent sulfur include:



(48-70%)

[102]

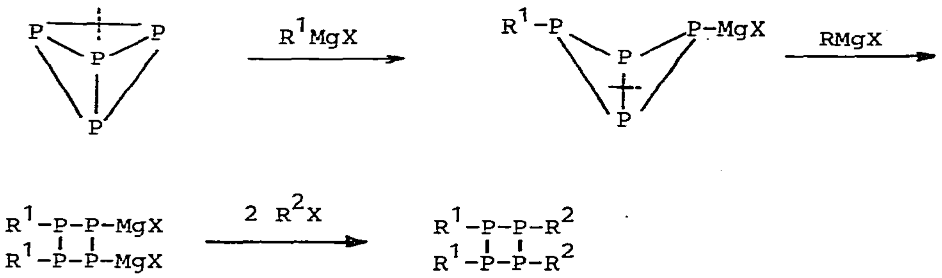


(12%)

[546]

D. Displacement reactions at phosphorus

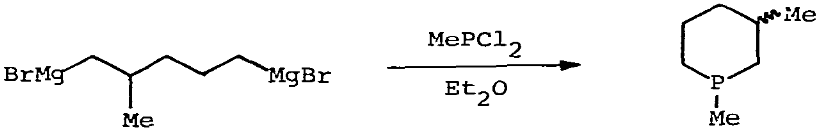
The synthesis of organophosphorus compounds directly from the element and organomagnesium compounds has been reported [5]:



A number of papers including a chapter in "Inorganic Syntheses" [547] report alkylation or arylation of chlorophosphines or -phosphine oxides with Grignard reagents. Some selected examples are:

$$2\ \text{t-BuCH}_2\text{MgCl} \xrightarrow[\text{Et}_2\text{O/C}_6\text{H}_6\ (1:1)\ \ 10\ \text{d reflux}]{\text{t-BuPCl}_2} \text{t-BuP(CH}_2\text{Bu-t)}_2$$

(46%) [548]



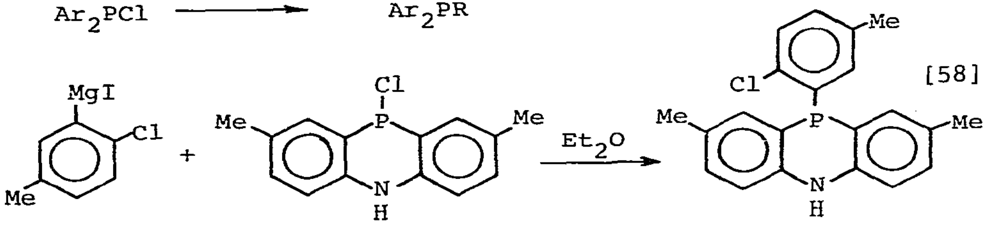
[160]

(21%;cis:trans=3:2)

$$2\ \text{ArMgX} \xrightarrow{\text{Cl}_2\text{PNEt}_2} \text{Ar}_2\text{PNEt}_2 \xrightarrow{\text{HClgas}}$$

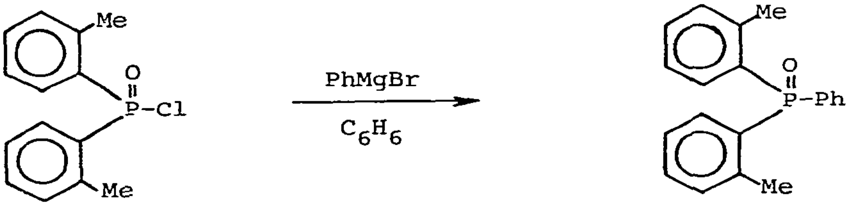
[549]

$$\text{Ar}_2\text{PCl} \xrightarrow{\text{RMgX}} \text{Ar}_2\text{PR}$$



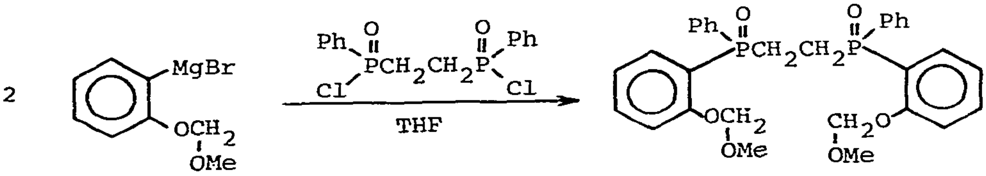
[58]

(54%)



[550]

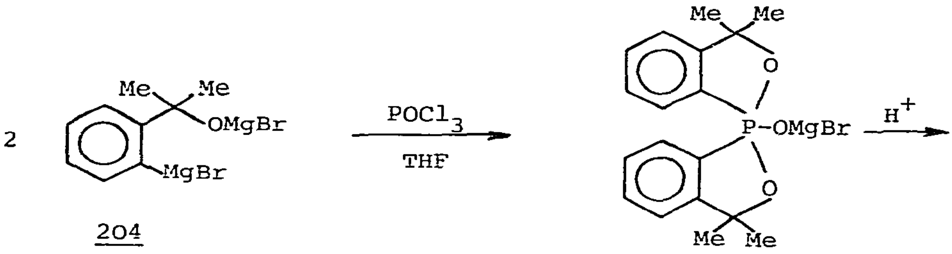
(72%)



[89]

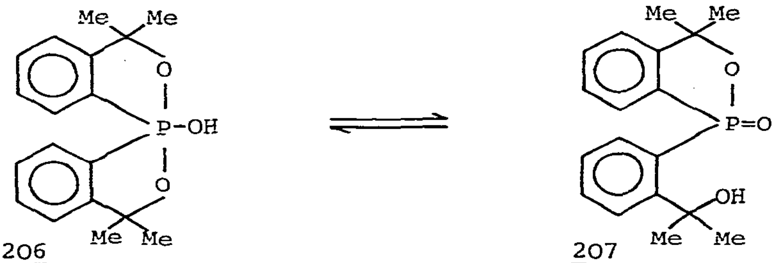
(50%)

The reaction between $POCl_3$ and the Grignard reagent 204 gives the phosphoranoxide anion 205, a stable model for the postulated intermediate in nucleophilic substitution at tetracoordinated phosphinoyl phosphorus. Protonation of 205 yields a tautomeric mixture of 206 and 207, decreasing temperature and basic solvents, such as pyridine, favouring the hydroxyphosphorane 206 relative to the open-chain tautomer 207 in the equilibrium mixture [76]:



204

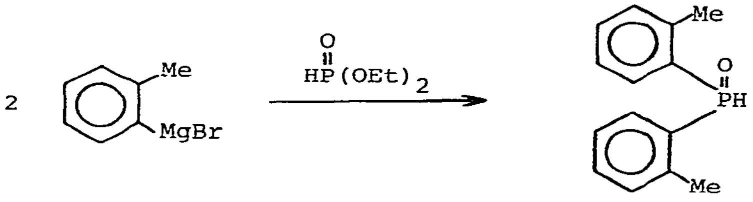
205



206

207

Alkoxy groups at phosphorus have also been replaced by Grignard reagents. e.g.



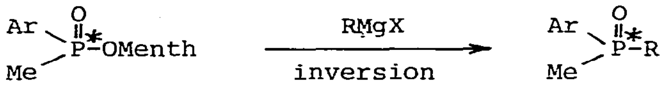
[550]

(57%)

$$\mathrm{ArMgBr} \xrightarrow[\mathrm{Et_2O}]{\mathrm{P(OMe)_3}} \mathrm{ArP(OMe)_2}$$

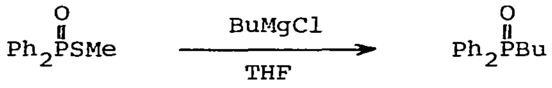
(40-46%) [551,552]

Starting from the pure diastereomeric menthyl esters 208 optically active phosphine oxides have been prepared [551]:



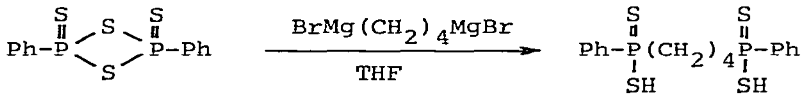
208

In contrast to the corresponding dithioate esters 200 which show $S_N2(S)$ reaction with Grignard reagents, 209 is mainly attacked at the phosporus atom by an $S_N2(P)$ mechanism [544]:



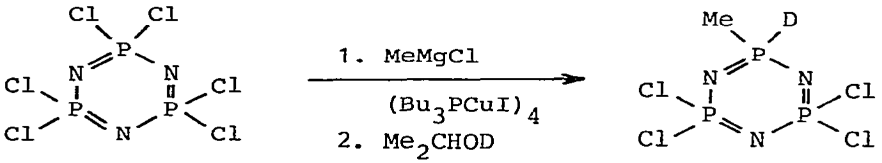
209 (93%)

The same is true for the reaction of perthiophosphonic anhydrides with di-Grignard reagents yielding bifunctional dithiophosphinic acids [158]: e.g.



(54%)

Finally an unusual reaction of MeMgCl with hexachlorocyclotriphosphazene 210 in THF in the presence of $(Bu_3PCuI)_4$ has been reported, which gave, after treatment with 2-propanol, high yields of an air- and moisture-sensitive crystalline product indentified as 211. Isotope-labeling studies using Me_2CHOD indicated that 211 is probably generated via a metallophosphazene intermediate [553]:



210 211 (76%)

E. Alkylation (displacement) at other elements

Because of the huge number of reactions reported, only some selected examples will be included here, along with general synthetic and mechanistic studies.

Group II metals. Several specially substituted zinc, cadmium, and mercury compounds have been synthesized by the Grignard procedure: e.g.

$$X(CH_2)_nMgCl \xrightarrow[Et_2O/THF]{ZnCl_2} [X(CH_2)_n]_2Zn \qquad [97]$$

(70%)

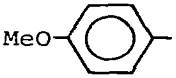
X = OMe, SMe, NMe_2
n = 3, 4

$$Me_3SiCH_2MgCl \xrightarrow[Et_2O]{CdI_2} (Me_3SiCH_2)_2Cd \qquad [170]$$

(53%)

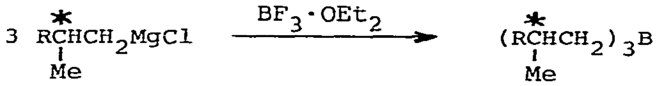
$$Ar_2CHCH_2MgBr \xrightarrow{HgBr_2} Ar_2CHCH_2HgBr \qquad [554]$$

(61%)

Ar = Ph, 

The reaction between zinc or cadmium halides and Grignard reagents was shown by voltammetric measurements to lead only to symmetrical organozinc or organocadmium compounds, whereas the corresponding reaction with methyllithium yields successively the symmetrical compound Me_2Zn or Me_2Cd and then an ate-complex such as Me_4ZnLi_2 or Me_4CdLi_2 [555].

Group III. Optically active trialkylboranes have been prepared by the reaction of the corresponding Grignard reagents with a slight excess of boron trifluoride diethyl etherate [556]:



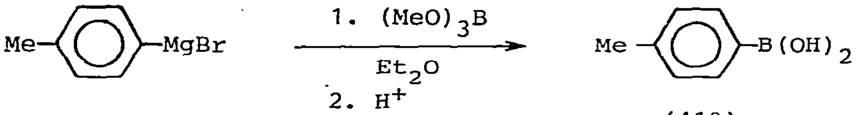
$$3\ R\underset{\substack{|\\ Me}}{\overset{*}{C}}HCH_2MgCl \xrightarrow{BF_3\cdot OEt_2} (R\underset{\substack{|\\ Me}}{\overset{*}{C}}HCH_2)_3B$$

(73%)

R = i-Pr, t-Bu

Grignard reagents RMgBr with a bulky group R, on the other hand, react with $BF_3\cdot THF$ to yield the complex compound $Mg(BF_3OH)_2(THF)_4$ with a trans-octahedral molecular geometry [557].

Starting with trimethyl borate, one or two methoxy groups can be replaced [558,559]. The synthesis of diphenylborinic acid, however, only worked in DME; attempts to carry out the reaction using Et_2O or THF as the solvent were unsuccessful [559]:



(41%)

$$2\ \mathrm{PhMgBr} \xrightarrow[\substack{\mathrm{DME} \\ 2.\ H^+}]{1.\ (MeO)_3B} Ph_2BOH$$

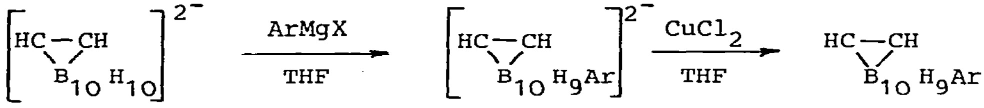
(80%)

Allyl(dialkyl)boranes have been prepared by adding allyl bromides and dialkylborinates simultaneously to magnesium turnings in a large amount of diethyl ether [560,561]: e.g.

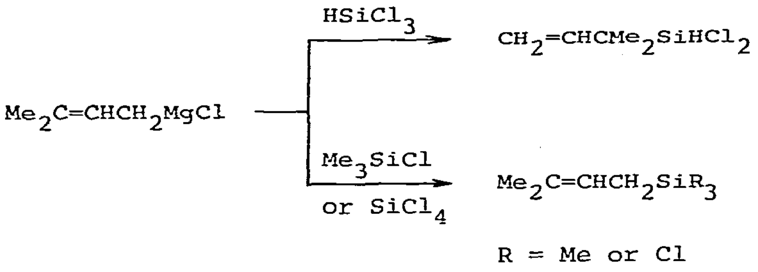
$$Bu_2BOC_6H_{13} \quad + \quad CH_2{=}CHCH_2Br \xrightarrow[Et_2O]{Mg} CH_2{=}CHCH_2BBu_2$$

(50%)

Dicarbadodecaborate(14) dianions interact with various arylmagnesium halides forming B-aryldianions, the oxidation of which with $CuCl_2$ produces B-aryl-o-carboranes. The reaction is nonselective yielding 3-, 4-, 8-, and 9-aryl-o-carboranes as well as polyarylated carboranes [562]:

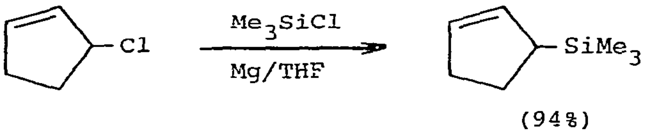


<u>Group IVa</u>. The course of the reaction of chlorosilanes with the Grignard reagent from 1-chloro-3-methyl-2-butene can be controlled by changing the substituents on the chlorosilane. Thus, with trichlorosilane, the Grignard reagent afforded regioselectively dichloro(α,α-dimethylallyl)silane while the reaction with tetrachlorosilane or trimethylchlorosilane gave only the corresponding γ,γ-dimethylallylsilanes [563]:

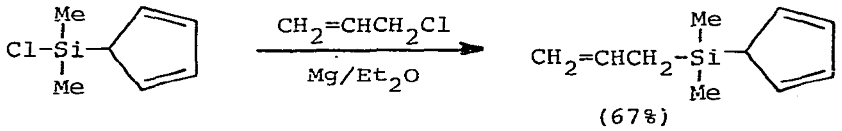


Other allylsilanes have been prepared by the Barbier procedure: e.g.

$$CH_2{=}CHCH_2Br \xrightarrow[Mg/THF]{Me_3SiCl} CH_2{=}CHCH_2SiMe_3 \quad (81\%) \qquad [564]$$

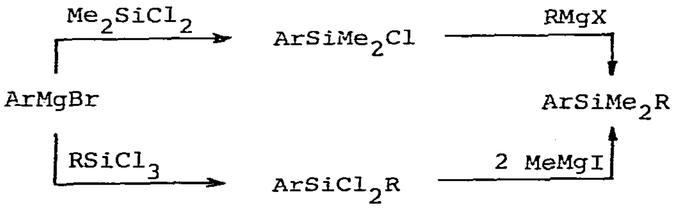


[565]



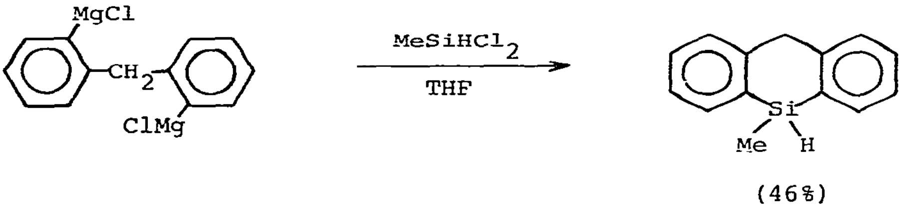
[566]

Alkylation and arylation of dichloro- and trichlorosilanes can be done selectively with sequential introduction of different groups [63,167,173,567]: e.g.

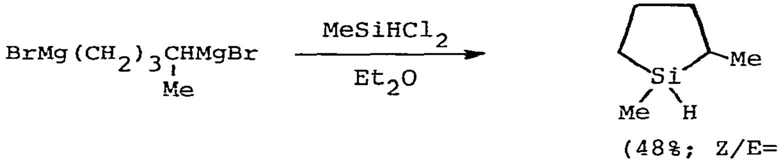


[567]

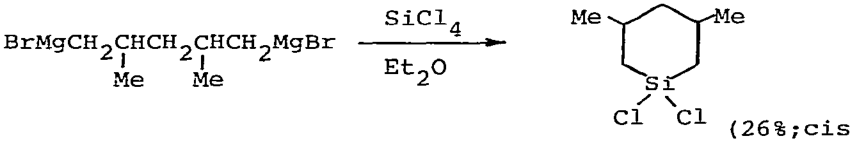
The corresponding reactions with bifunctional Grignard reagents have been used for ring formation: e.g.



[169]

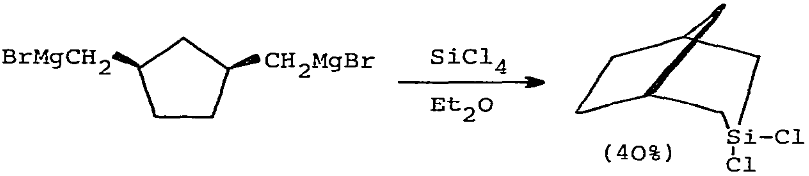


[159]



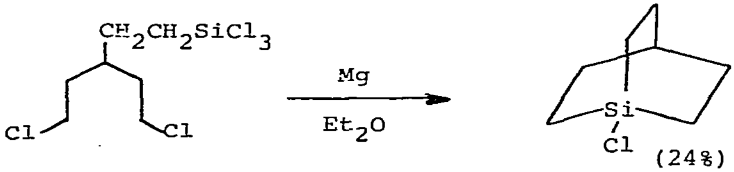
[161]

(26%;cis+trans)

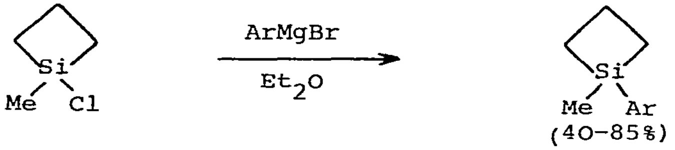


[161]

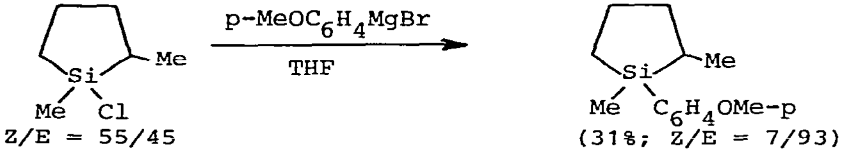
1-Chloro-1-silabicyclo[2.2.2]octane has been prepared by an internal Barbier reaction using 1,2-dibromoethane entrainment [93]:



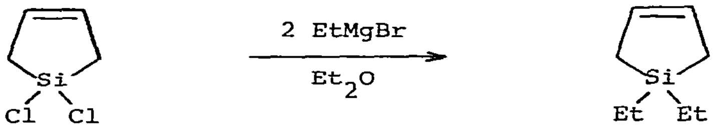
The remaining chloro atoms at the silicon of those cyclic silanes may be replaced by further Grignard reactions: e.g.



[568]

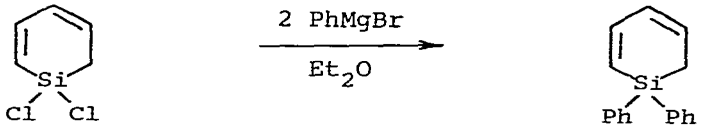


[159]



(78%)

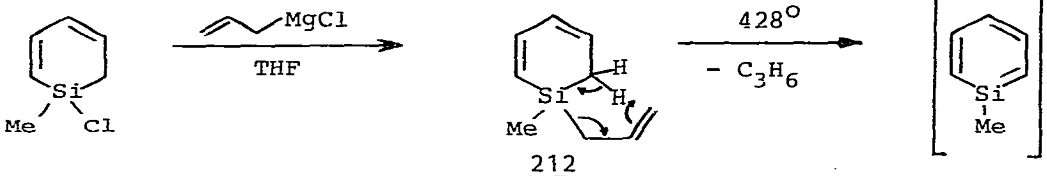
[569]



(43%)

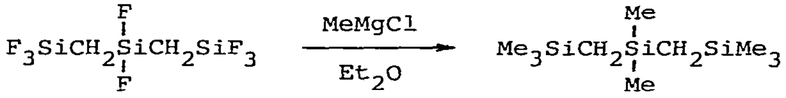
[570]

Pyrolysis of the allylsilacyclohexadiene 212 prepared in the same manner, generated 1-methylsilabenzene which could be trapped by a Diels-Alder reaction with acetylene [571]:



212

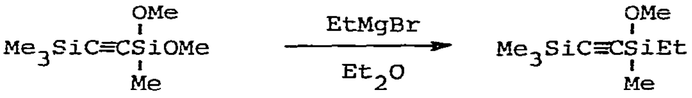
Other groups at the silicon atom like F [572,573], Br [574], OMe [165,575], SPh [574], and even H [576] can also be dispatched by Grignard reagents whereby the more polarizable group is specifically replaced [573]: e.g.



$$F_3SiCH_2\overset{F}{\underset{F}{Si}}CH_2SiF_3 \xrightarrow[Et_2O]{MeMgCl} Me_3SiCH_2\overset{Me}{\underset{Me}{Si}}CH_2SiMe_3$$

(60%)

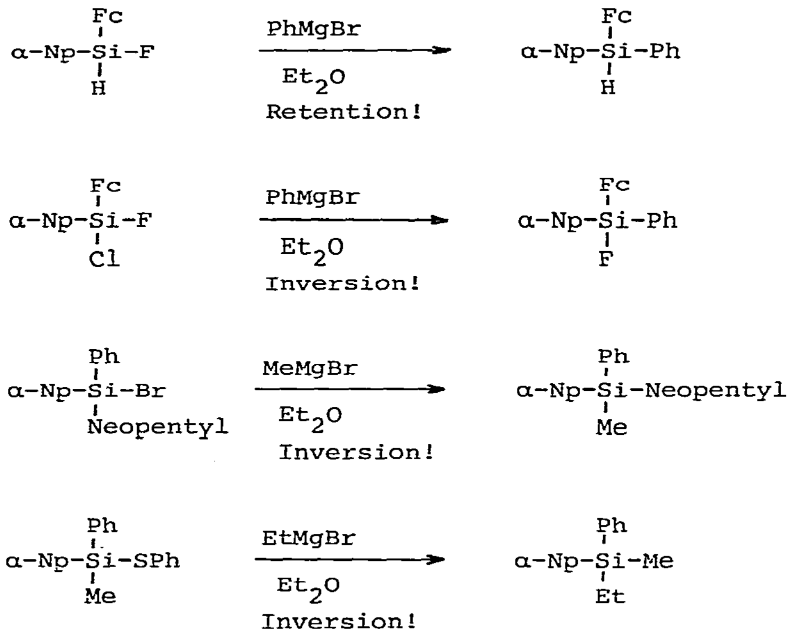
[572]



$$Me_3SiC{\equiv}C\overset{OMe}{\underset{Me}{Si}}OMe \xrightarrow[Et_2O]{EtMgBr} Me_3SiC{\equiv}C\overset{OMe}{\underset{Me}{Si}}Et$$

(71%)

[575]



$$\alpha\text{-Np-}\overset{\text{Fc}}{\underset{\text{H}}{\text{Si}}}\text{-F} \xrightarrow[\substack{\text{Et}_2\text{O}\\ \text{Retention!}}]{\text{PhMgBr}} \alpha\text{-Np-}\overset{\text{Fc}}{\underset{\text{H}}{\text{Si}}}\text{-Ph} \qquad [573]$$

$$\alpha\text{-Np-}\overset{\text{Fc}}{\underset{\text{Cl}}{\text{Si}}}\text{-F} \xrightarrow[\substack{\text{Et}_2\text{O}\\ \text{Inversion!}}]{\text{PhMgBr}} \alpha\text{-Np-}\overset{\text{Fc}}{\underset{\text{F}}{\text{Si}}}\text{-Ph} \qquad [573]$$

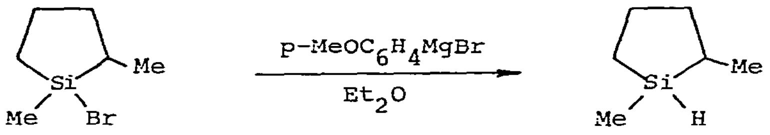
$$\alpha\text{-Np-}\overset{\text{Ph}}{\underset{\text{Neopentyl}}{\text{Si}}}\text{-Br} \xrightarrow[\substack{\text{Et}_2\text{O}\\ \text{Inversion!}}]{\text{MeMgBr}} \alpha\text{-Np-}\overset{\text{Ph}}{\underset{\text{Me}}{\text{Si}}}\text{-Neopentyl} \qquad [574]$$

$$\alpha\text{-Np-}\overset{\text{Ph}}{\underset{\text{Me}}{\text{Si}}}\text{-SPh} \xrightarrow[\substack{\text{Et}_2\text{O}\\ \text{Inversion!}}]{\text{EtMgBr}} \alpha\text{-Np-}\overset{\text{Ph}}{\underset{\text{Et}}{\text{Si}}}\text{-Me} \qquad [574]$$

Fc = Ferrocenyl; α-Np = α-Naphthyl

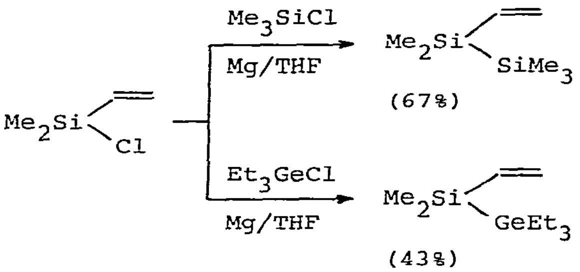
The stereochemistry of the nucleophilic substitution at silicon has been thoroughly studied [573,574,577]. Inversion of the configuration comes from an axial attack of the reactant and retention is explained by an equatorial attack [573]. The stereochemical outcome appears to depend primarily on the nature of the leaving group [574]. For a given leaving group the dominant influence on the stereochemistry at silicon is the electronic character of the attacking nucleophile: reagents which favour 1,2-addition to α-enones react with retention of configuration, whereas those which favour 1,4-addition react with inversion at silicon [577].

When silyl bromide <u>213</u> was reacted with p-anisylmagnesium bromide no anisyl product could be isolated, the predominant product being the SiH derivative <u>214</u> presumably via a silyl Grignard reagent formed by halogen-metal interconversion [159]:

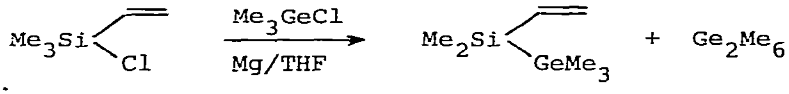


213 214 (50%)

A silyl Grignard reagent is probably also involved in the following Barbier reactions [180]:

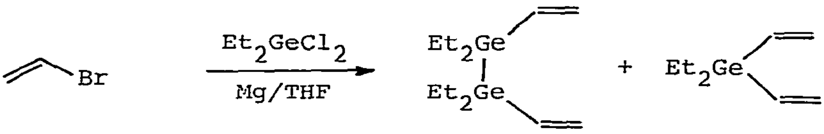


The corresponding reaction with Me_3GeCl yields a mixture of two products because this reagent - in contrast to Me_3SiCl and Et_3GeCl - can react with itself [180]:



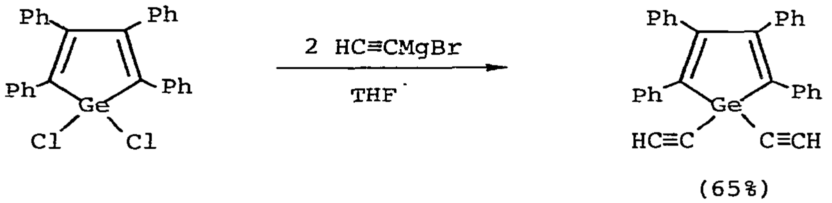
2 : 3

Treatment of vinyl bromide with Et_2GeCl_2/Mg/THF gives the digermane 215 together with diethyldivinylgermane [180]:

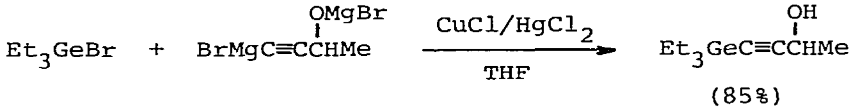


215 (30%) (8%)

Diethynylsilanes and -germanes have also been prepared [578]: e.g.

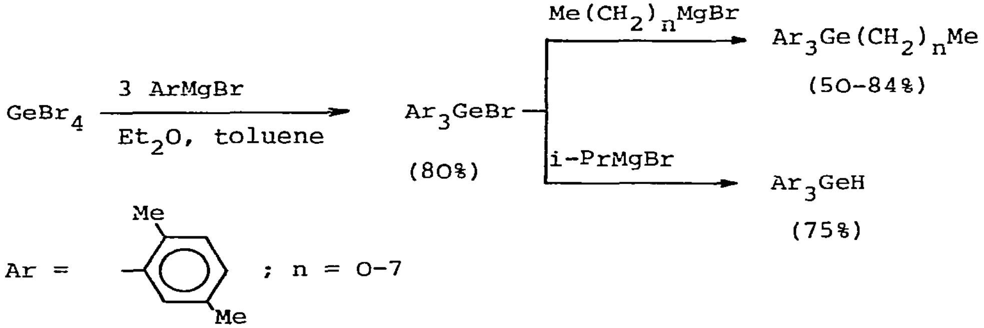


The following displacement reaction has be catalyzed by CuCl and $HgCl_2$ [78]:

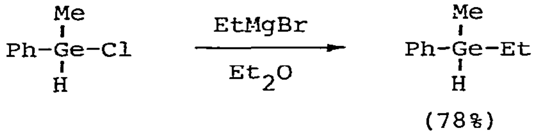


$$Et_3GeBr + BrMgC{\equiv}C\overset{OMgBr}{C}HMe \xrightarrow[THF]{CuCl/HgCl_2} Et_3GeC{\equiv}C\overset{OH}{C}HMe \quad (85\%)$$

Treatment with i-PrMgBr can lead to GeH derivatives [579]:



Other trisubstituted germanes have been prepared in the usual way [580]: e.g.



$$Ph\text{-}\underset{H}{\overset{Me}{Ge}}\text{-}Cl \xrightarrow[Et_2O]{EtMgBr} Ph\text{-}\underset{H}{\overset{Me}{Ge}}\text{-}Et \quad (78\%)$$

A mixture of halides has been obtained upon treating $GeCl_4$ with a molar amount of C_6F_5MgBr due to the readily occurring exchange of chlorine and bromine atoms in this system [53]:

$$GeCl_4 \xrightarrow[Et_2O/benzene]{C_6F_5MgBr} C_6F_5GeCl_nBr_{3-n}$$

$$(60\text{-}70\%)$$

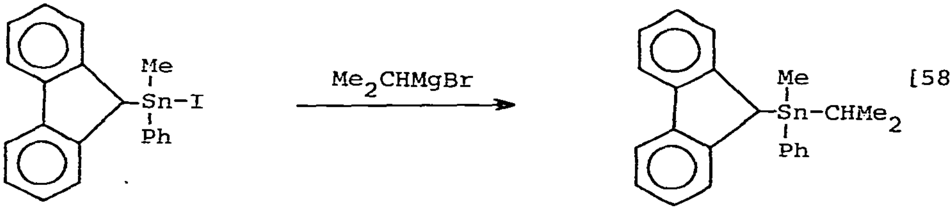
In the investigation of the alkylation reactions of halo(pentafluorophenyl)-germanes and -stannanes differences in reactivity between the germanium and tin derivatives have been observed. Whereas the halogermanes with EtMgBr give only the corresponding ethyl derivatives, in the case of the tin analogs the reactions are accompanied by the cleavage of the C_6F_5-Sn bond [53]: e.g.

$$(C_6F_5)_nGeX_{4-n} \xrightarrow{(4-n)EtMgX} (C_6F_5)_nGeEt_{4-n} \; + \; (4-n)MgX_2$$

$$\begin{tikzcd} (C_6F_5)_3SnBr \arrow[r, "EtMgBr"] & \underset{(14\%)}{(C_6F_5)_3SnEt} \arrow[r, "EtMgBr"] & {} \end{tikzcd}$$

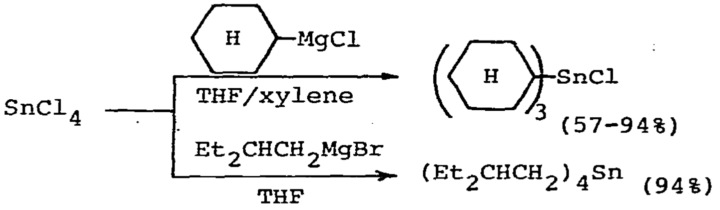
$$\begin{tikzcd} \underset{(50\%)}{(C_6F_5)_2SnEt_2} \arrow[d, "EtMgBr"] & + & C_6F_5MgBr \arrow[d, "(C_6F_5)_3SnBr"] \\ \underset{(8\%)}{C_6F_5SnEt_3} & & \underset{(21\%)}{(C_6F_5)_4Sn} \end{tikzcd}$$

New chiral organotin compounds have been prepared from suitable triorganotin halides and Grignard reagents [61,581,582]: e.g.

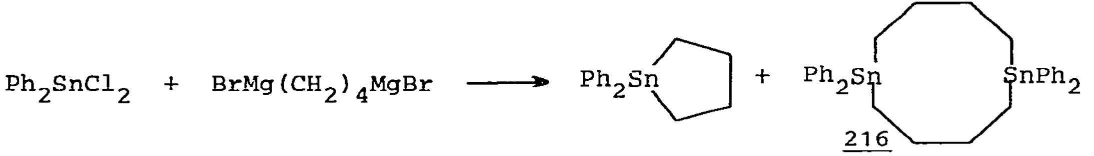


[582]

Starting from tin tetrachloride three [583,584] or four [585,586] chlorine atoms can be replaced all at once: e.g.

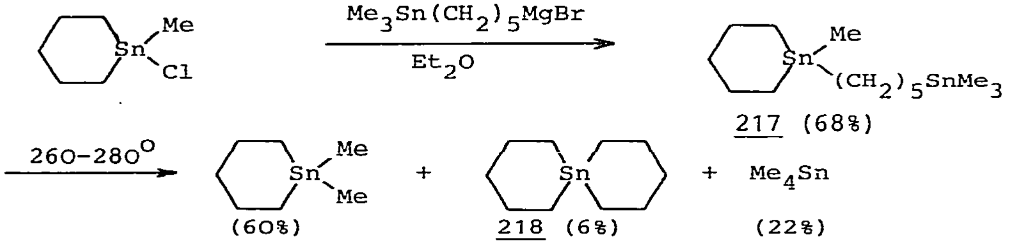


The reaction of butane 1,4-dimagnesium bromide with diphenyltin dichloride gives 1,1-diphenylstannacyclopentane already known and the new dimer 216, the structure of the latter compound has been shown by single-crystal X-ray diffraction to be of the "boat-chair-boat" type, similar to that of cyclodecane [155]:



216

Thermolysis of the stannacyclohexane derivative 217 prepared by a Grignard procedure yields 6% of the interesting tin spirocycle 218 [175]:



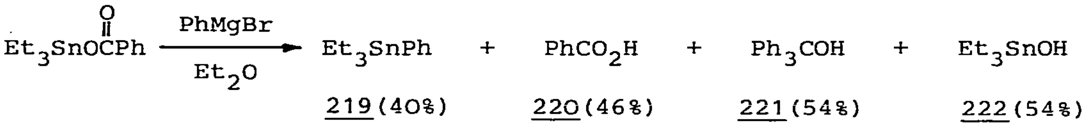
217 (68%)

(60%)

218 (6%)

(22%)

The reaction of triorganotin carboxylates with Grignard reagents were found to yield 219 and 220, derived from Sn attack of the reagent as well as 221 and 222 which were formed by attack on the carbonyl group. The factors controlling the reaction site was influenced by steric and inductive effects of the alkyl substituent on the tin atom, the basicity of the Grignard reagent as well as by solvation and association of the substrate [587]: e.g.



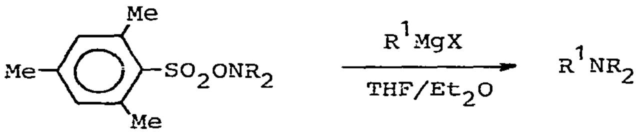
$$\mathrm{Et_3SnO\overset{\overset{\displaystyle O}{\|}}{C}Ph} \xrightarrow[\mathrm{Et_2O}]{\mathrm{PhMgBr}} \underset{\underline{219}\,(40\%)}{\mathrm{Et_3SnPh}} + \underset{\underline{220}\,(46\%)}{\mathrm{PhCO_2H}} + \underset{\underline{221}\,(54\%)}{\mathrm{Ph_3COH}} + \underset{\underline{222}\,(54\%)}{\mathrm{Et_3SnOH}}$$

The lead-Grignard reagent 223 prepared from t-BuMgCl and lead dichloride upon treatment with tert-butyl bromide yielded 17% hexa-tert-butyldiplumbane 224 [588]:

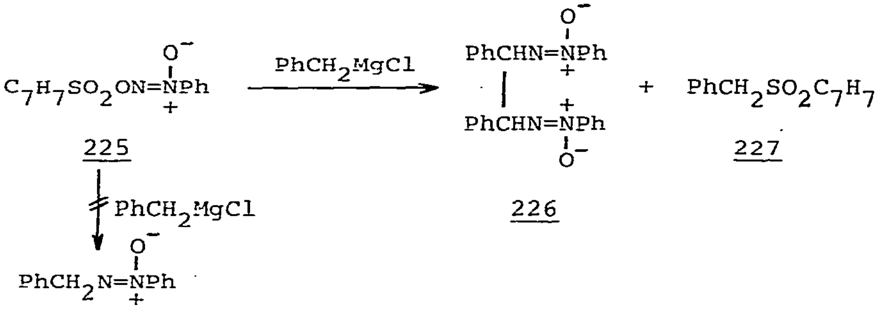
$$\mathrm{PbCl_2} \xrightarrow[\mathrm{THF}\,(-60^{\circ})]{3\ \mathrm{t\text{-}BuMgCl}} \underset{\underline{223}}{\mathrm{t\text{-}Bu_3PbMgCl}} \xrightarrow[-\mathrm{t\text{-}BuMgCl}]{\mathrm{t\text{-}BuBr}} \mathrm{t\text{-}Bu_3PbBr} \xrightarrow{\mathrm{t\text{-}Bu_3PbMgCl}}$$

$$\mathrm{t\text{-}Bu_6Pb_2}\quad \underline{224}\,(17\%)$$

Group Va. N,N-Dialkyl-O-mesityl-sulfonylhydroxylamines, easily obtainable from mesitylsulfonyl chloride and the corresponding hydroxylamines, may be used as reagents for the electrophilic amination of Grignard reagents. This mild procedure allows the synthesis of tertiary amines which are not available by nucleophilic substitution, as e.g. the amines of strained carbocycles [589]:



The tosyl derivative of cupferron 225 reacted with excess benzylmagnesium chloride in Et_2O/dioxane to give 226 and the sulfone 227 instead of the expected diazene oxide 228. A radical mechanism is proposed to explain these results [590]:



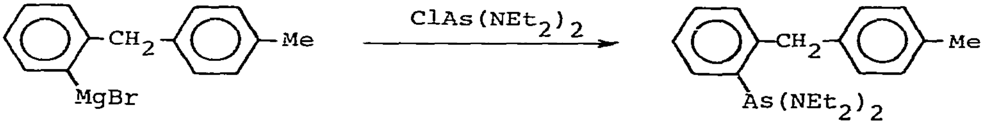
225

226

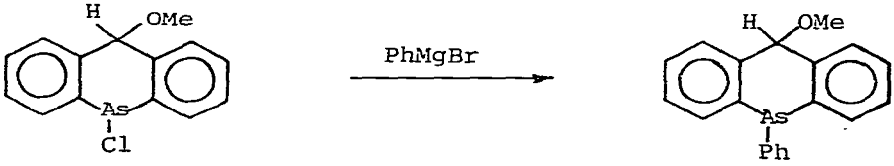
227

228

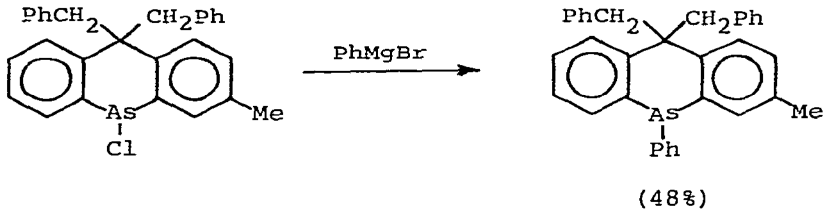
Displacements at trivalent arsenic [591] and antimony [592] have also been reported:



(61%)



(87%)



$$\text{t-BuMgCl} \xrightarrow[\text{Et}_2\text{O}(-40^\circ)]{\text{SbCl}_3} \underset{(38\%)}{\text{t-BuSbCl}_2} \xrightarrow[\text{THF}(30^\circ)]{\text{Mg}}$$

$$\underset{(30\%)}{(\text{t-BuSb})_4} + \underset{(37\%)}{\text{t-Bu}_3\text{Sb}} + \text{Sb} + \text{MgCl}_2$$

The following monoalkylation procedure yielded a substantial quantity of unexpected alkyldiiodostibine [593]:

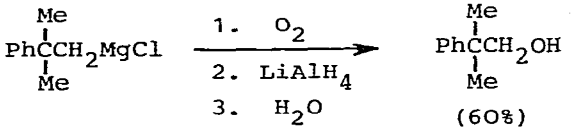
$$\text{RMgI} \xrightarrow[\text{Et}_2\text{O}]{\text{SbCl}_3} \underset{(20\%)}{\text{RSbI}_2}$$

R = Me, Et

Oxygen, peroxides, and selenium. The peroxide obtained by treating *tert*-butyl-magnesium chloride with dry oxygen was suggested as an initiator for the polymerization of methyl methacrylate and styrene [594]:

$$\text{t-BuMgCl} \xrightarrow[\text{Et}_2\text{O}(-75^\circ)]{\text{O}_2} \text{t-BuOOMgCl}$$

The reaction of Grignard reagents with oxygen was also used to prepare alcohols [154,492]: e.g.



$$\text{Ph}\overset{\text{Me}}{\underset{\text{Me}}{\text{C}}}\text{CH}_2\text{MgCl} \xrightarrow[\substack{2.\ \text{LiAlH}_4 \\ 3.\ \text{H}_2\text{O}}]{1.\ \text{O}_2} \underset{(60\%)}{\text{Ph}\overset{\text{Me}}{\underset{\text{Me}}{\text{C}}}\text{CH}_2\text{OH}}$$ [492]

The oxidation of Grignard reagents with molybdenum pentoxide is selective only in HMPT as the solvent [595]: e.g.

$$\text{n-}C_6H_{13}MgBr \xrightarrow[\text{2. } H_2O]{\text{1. } MoO_5\cdot HMPT} \text{n-}C_6H_{13}OH \quad (65\%)$$

An ionic mechanism is proposed for this system. In Et_2O, THF or pentane the yields are much lower (25-36%) due to a number of radical side reactions.

The corresponding reaction of MoO_5/Pyridine/HMPT with bornyl and norbornyl Grignard reagents proceeds with retention of configuration which suggests the utility of this complex for stereoselective syntheses [596].

The reaction of Grignard reagents with selenium yields selenomagnesium halides [516,597] which can be used to prepare alkyl aryl selenides [597]:

$$PhCH_2MgCl \xrightarrow{Se} PhCH_2SeMgCl \xrightarrow{Ar\overset{+}{N_2}Cl^-} ArSeCH_2Ph$$

$$Ar = Ph,\ p\text{-}BrC_6H_4,\ p\text{-}O_2NC_6H_4$$

A convenient synthesis of aromatic selenonium compounds uses the reaction of Grignard reagents with selenium oxychloride treating the reaction mixture with aqueous HBr [598]: e.g.

$$3\ PhMgCl \xrightarrow[THF(66^{o})]{SeOCl_2} Ph_3SeOMgCl \xrightarrow[H_2O]{HBr} \underset{(56\%)}{Ph_3Se^+Br^-} + \underset{(39\%)}{Ph_2Se}$$

The yield of selenonium compounds decreases in the order:

$$ArMgCl > ArMgBr \gg ArMgI$$

Transition elements. Trivalent titanium complexes internally coordinated by O or S atoms have been prepared [96]:

$$Cp_2TiCl \xrightarrow{MeZ(CH_2)_nMgCl} Cp_2Ti(CH_2)_nZMe \quad (6\text{-}22\%)$$

$$Z = O,\ S; \quad n = 3,\ 4$$

The extremely unstable tribenzyltitanium has been obtained not only starting from titanium trichloride [599] but also from the corresponding acetylacetonate [600]:

$$2\ \mathrm{Ti(acac)_3} \quad + \quad 3\ \mathrm{(PhCH_2)_2Mg} \xrightarrow[-50^{\circ}]{\mathrm{Et_2O}}$$

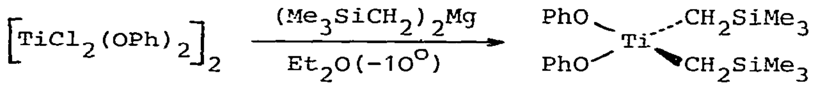
$$2\ \mathrm{(PhCH_2)_3Ti{\cdot}nEt_2O} \quad + \quad 3\ \mathrm{Mg(acac)_2}$$

Benzylation of the trivalent vanadium and chromium acetylacetonates, on the other hand, leads only to monosubstitution products [600]: e.g.

$$2\ \mathrm{V(acac)_3} \quad + \quad \mathrm{(PhCH_2)_2Mg} \xrightarrow[20^{\circ}]{\text{hexane}}$$

$$2\ \mathrm{PhCH_2V(acac)_2{\cdot}Mg(acac)_2}$$

Tetracyclohexyltitanium has been prepared by reaction of $TiCl_4$ or $Ti(OBu\text{-}n)_4$ with dicyclohexylmagnesium in pentane or ether at -30° [601]. Also one [51] and two [177,602] halogens in titanium(IV) derivatives were replaced selectively by Grignard procedures: e.g.

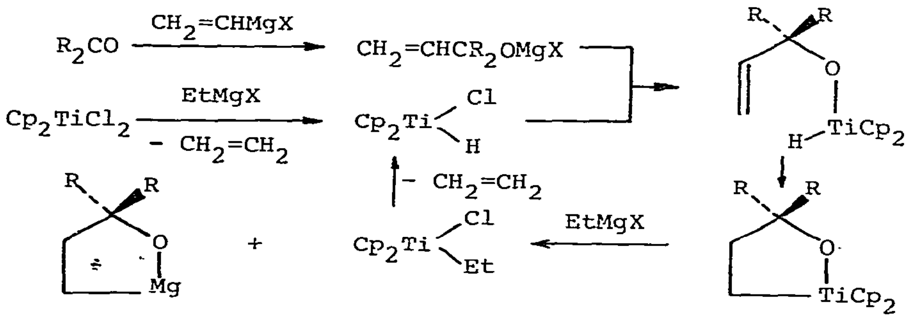


$$\left[\mathrm{TiCl_2(OPh)_2}\right]_2 \xrightarrow[\mathrm{Et_2O(-10^{\circ})}]{\mathrm{(Me_3SiCH_2)_2Mg}} \mathrm{(PhO)_2Ti(CH_2SiMe_3)_2}$$

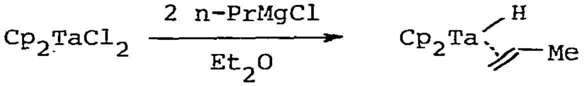
[177]

(20%)

Titanium hydride derivatives are probably involved in hydromagnesiation of alkenols by ethylmagnesium bromide [36]:

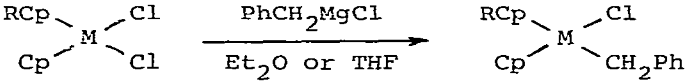


Similarly the reaction of Cp_2TaCl_2 with RMgCl (R = n-Pr, i-Pr, n-Bu, s-Bu, n-C_5H_{11}, and C_5H_9) give tantalum hydride π-olefin complexes [603]: e.g.



(60%)

Upon treatment of corresponding zirconium and hafnium derivatives with benzylmagnesium chloride one or both chlorines may be displaced. This way the first chiral dicyclopentadienyl compounds of zirconium(IV) and hafnium(IV) have been prepared [604]:



M = Zr, Hf

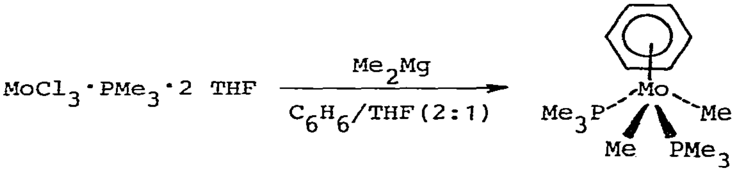
Similarly chiral rhodium(III) complexes of the type $CpRh(CNC_6H_{13})(C_6Cl_6)Cl$ have been obtained [67].

Benzylation of vanadium trichloride-tris-tetrahydrofuran gave only dibenzylvanadium chloride or a complex of benzylvanadium dichloride with benzylmagnesium chloride, no tribenzylvanadium could be obtained [605]:

$$VCl_3\cdot 3\ THF \xrightarrow[Et_2O]{PhCH_2MgCl} (PhCH_2)_2VCl\cdot MgCl_2\cdot 2\ THF \quad \text{or}$$

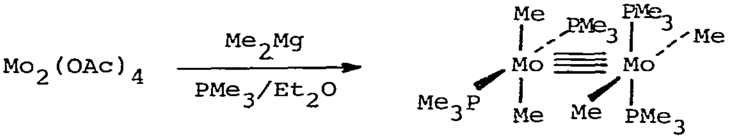
$$PhCH_2VCl_2\cdot PhCH_2MgCl\cdot 2\ THF$$

Treatment of $MoCl_3\cdot PMe_3\cdot 2$ THF with dimethylmagnesium in the presence of arenes yield methyl-arene complexes of molybdenum(II) containing two tertiary phosphines in trans position [606]: e.g.



(15-25%)

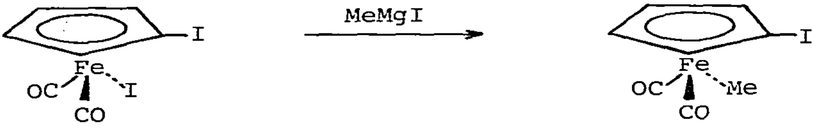
Magnesium dialkyls MgR_2 (R = Me, Me_3SiCH_2, Me_3CCH_2) also react with binuclear transition metal acetates $M_2(OAc)_4$ (M = Cr, Mo, Rh) and $Ru_2(OAc)_4Cl$ in the presence of PMe_3 to give monomeric or dimeric alkyls. In the latter case the metal-metal bond is retained [176]: e.g.



(69%)

Similarly binuclear acetate-bridged alkyls of rhenium(III) containing strong Re-Re quadruple bonds have been obtained [178].

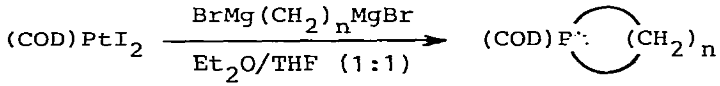
Displacement of halogen in iron(II) [607], cobalt(II) [608, 609], and nickel(II) [52] compounds using Grignard reactions have also been reported: e.g.



[607]

(34%)

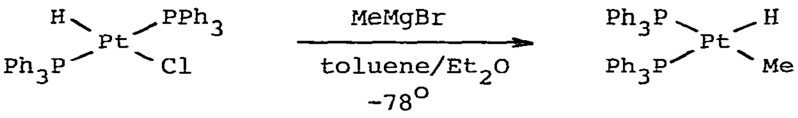
The preparation of Bis(alkenyl) platinum from $PtCl_2$ and RMgX (R = allyl, methallyl, crotyl) was improved by treating the reaction mixture with alcohol or aqueous alcohol [610]. Treatment of $(COD)PtI_2$ with EtMgI in Et_2O yields 48% (COD)PtIEt rather than $(COD)PtEt_2$, the product reported in 1973 from this reaction [611]. On the other hand, the same starting material with bifunctional Grignard reagents give platinum(II) metallacycles [157]:



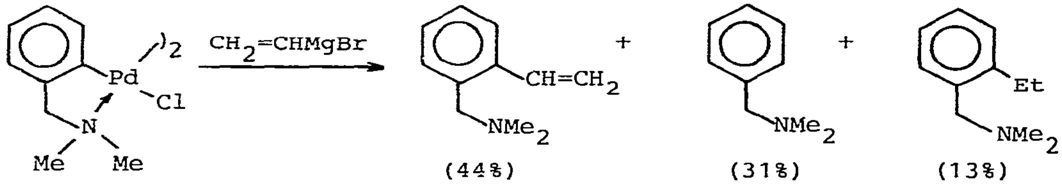
(65-79%)

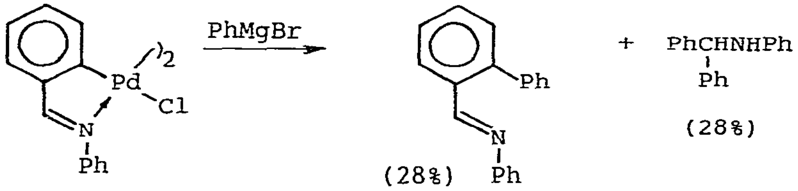
n = 4, 5

Treatment of a toluene solution of trans-$[PtHCl(PPh_3)_2]$ with MeMgBr at -78^{o} was found to yield cis-$[PtHMe(PPh_3)_2]$ quantitatively which on warming to -25^{o} decompose with the evolution of CH_4 [612]:



Similarly the reaction of cyclometalated palladium complexes with Grignard reagents in the presence of triphenylphosphine leads to Pd-C bond cleavage, a useful method for selective ortho alkylation of tertiary benzylic amines and benzaldehydes [613]: e.g.





The products are assumed to be formed via a nucleophilic attack of the Grignard reagent on the phosphine-coordinated palladium monomer followed by reductive coupling [613].

Finally the preparation of bis(pentamethylcyclopentadienyl) actinide dichlorides from thorium and uranium tetrachlorides has been reported [23]:

$$\mathrm{MCl_4} \xrightarrow[\text{toluene}(100^{\circ})]{2\ \mathrm{Me_5CpMgCl}} (\mathrm{Me_5Cp})_2\mathrm{MCl_2}$$

(70-90%)

M = Th, U

F. Reaction as a base; metallation

Preparation of a number of organomagnesium compounds by proton removal from an organic substrate has been discussed in section II.B. and II.C.

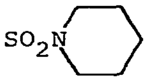
Additional reactions involving magnesium acetylids or similarly stabilized carbanion derivatives formed by deprotonation are:

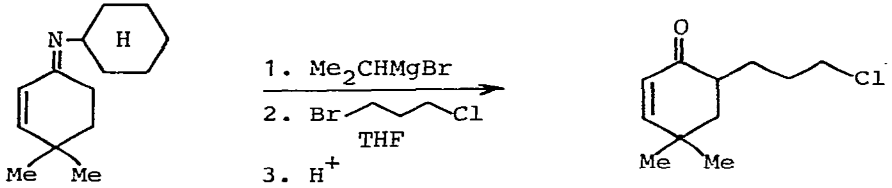
$$HC{\equiv}C(CH_2)_3R \xrightarrow[\substack{CuI/HMPT \\ 2.\ HC{\equiv}CCH_2Br}]{1.\ EtMgBr} HC{\equiv}CCH_2C{\equiv}C(CH_2)_3R \quad (51\text{-}55\%)$$

[614]

$$\xrightarrow[\substack{CuI/HMPT \\ 2.\ Me(CH_2)_4C{\equiv}CCH_2C{\equiv}CCH_2I}]{1.\ EtMgBr} Me(CH_2)_4C{\equiv}CCH_2C{\equiv}CCH_2C{\equiv}CCH_2C{\equiv}C(CH_2)_3R \quad (81\text{-}97\%)$$

R = CO_2H,

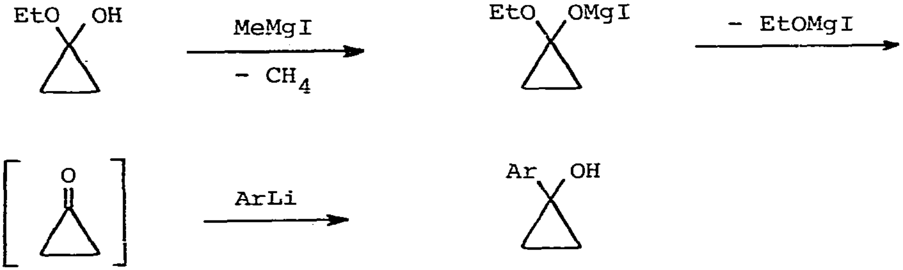




(32%)

[615]

Treatment of 1-ethoxycyclopropanol with aryllithiums failed to provide the desired 1-aryl-1-cyclopropanols. However, in the presence of 1 molar equivalent of MeMgI the reaction readily takes place presumably because the intermediate magnesium salt breaks down into cyclopropanone, whereas the corresponding lithium salt does not [616]:

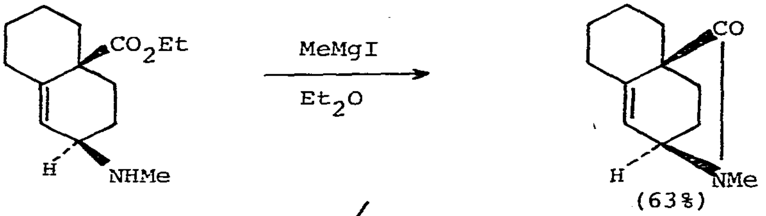


(50-75%)

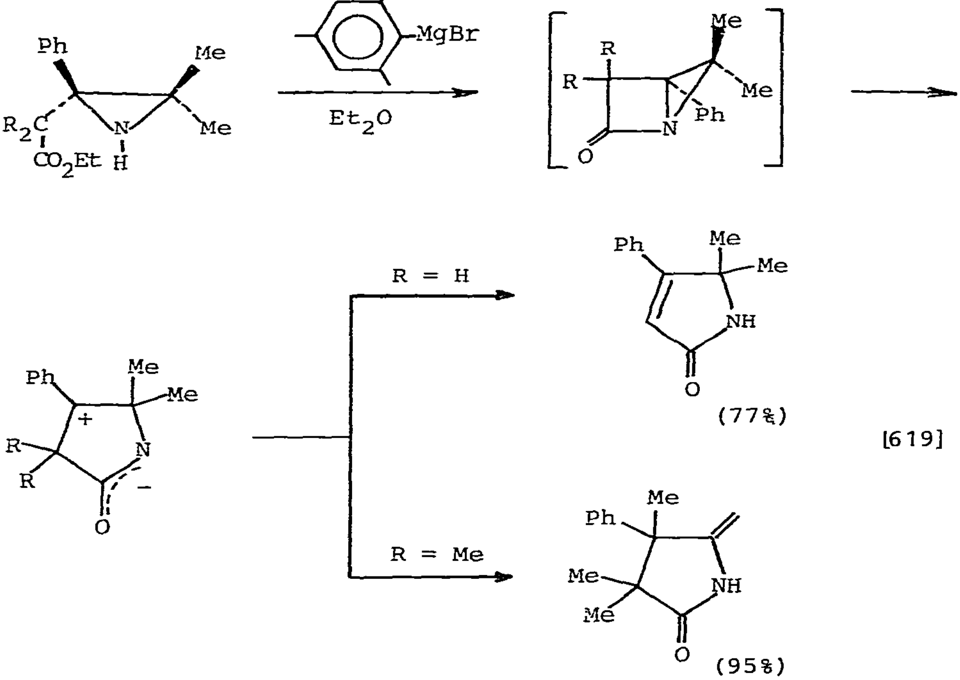
Primary amines can even be deprotonated by magnesium metal in the presence of acetic anhydride and catalytic amounts of $Cu(OAc)_2$ yielding N,N-diacetylamines [617]:

$$RNH_2 + 2\ (MeCO)_2O \xrightarrow{Mg} RN(COMe)_2 + Mg(OCOMe)_2 + H_2$$

Other reactions initiated by proton abstraction by a Grignard reagent include:

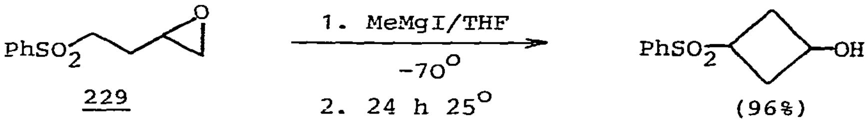


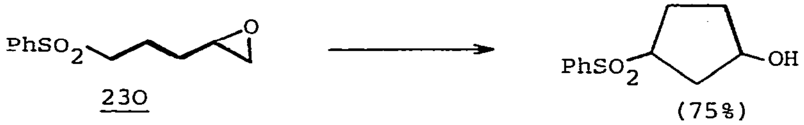
[618]



[619]

Epoxysulfones of the type 229 or 230 react with about 2 equivalents of MeMgI in THF to give 3-phenylsulfonylcyclobutanols and 3-phenylsulfonylcyclopentanols in good to excellent yields [25]:

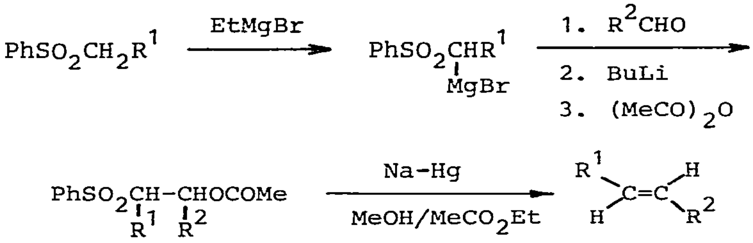




230

(75%)

Deprotonated alkyl phenyl sulfones are starting materials for a highly stereoselective synthesis of trans-olefins [24]:



$$\mathrm{PhSO_2CH_2R^1} \xrightarrow{\mathrm{EtMgBr}} \underset{\mathrm{MgBr}}{\mathrm{PhSO_2CHR^1}} \xrightarrow[\mathrm{2.\ BuLi}\quad \mathrm{3.\ (MeCO)_2O}]{\mathrm{1.\ R^2CHO}}$$

$$\underset{\mathrm{R^1\quad R^2}}{\mathrm{PhSO_2CH{-}CHOCOMe}} \xrightarrow[\mathrm{MeOH/MeCO_2Et}]{\mathrm{Na{-}Hg}} \mathrm{R^1(H)C{=}C(H)R^2}$$

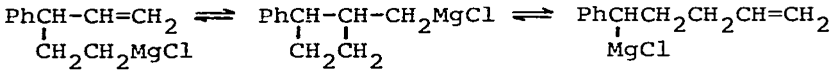
Previous instances in this review where the basicity of organomagnesium compounds has figured include elimination of HCl from terminal propargylic chlorides to generate an allene carbene-zwitterion intermediate [73] (section II.C.I.), elimination of HCN from α-cyano enamines with the formation of ketenimines [375], formation of cycloalkyl phenyl ketones from ω-alkoxynitriles and phenylmagnesium bromide [376] as well as aziridine-formation from oximes [377] (section V.A.).

VII. OTHER REACTIONS OF ORGANOMAGNESIUM COMPOUNDS

A. Rearrangements

Nucleophilic eliminative ring fissions including organomagnesium ring-chain rearrangements have been reviewed [4].

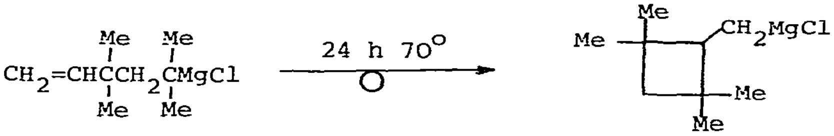
A cyclobutylmethyl intermediate is probably involved in the following rearrangement of the Grignard reagent 134 formed from cinnamylmagnesium chloride and ethylene upon heating at 85°C under ethylene pressure. From the equilibrium constant it can be calculated that the difference in free bond enthalpy between Mg-C_{prim} and Mg-C_{benzyl} bond is -0.4kcal·$\mathrm{mol^{-1}}$ [388]:



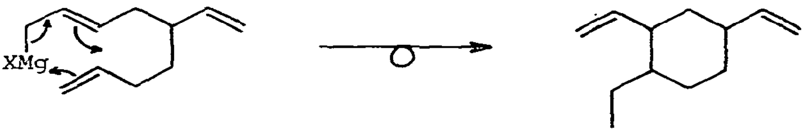
$$\underset{\mathrm{CH_2CH_2MgCl}}{\mathrm{PhCH{-}CH{=}CH_2}} \rightleftharpoons \underset{\mathrm{CH_2CH_2}}{\mathrm{PhCH{-}CH{-}CH_2MgCl}} \rightleftharpoons \underset{\mathrm{MgCl}}{\mathrm{PhCHCH_2CH_2CH{=}CH_2}}$$

134

(2,2,4,4-Tetramethylcyclobutyl)methylmagnesium chloride, on the other hand, is stable and can be prepared on heating the corresponding open-chain Grignard reagent without solvent to 70° [620]:

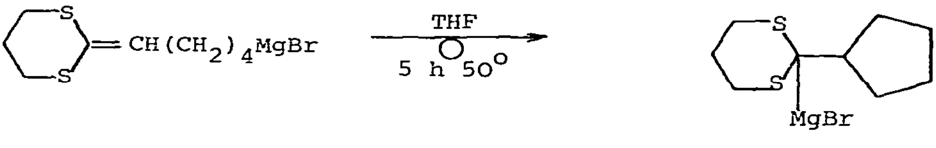


The 1:2-addition products of allyl Grignard reagents with butadiene 231 undergo fast intramolecular cyclization to the 2,4-divinylcyclohexylmethyl compounds 232. 1:2-Adducts with isoprene and 1:3-addition products of other Grignard reagents with excess butadiene react similarly [389].

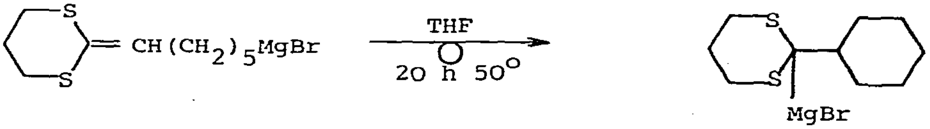


231 232

On heating the following ketene dithioacetal Grignard reagents cyclization to the six-membered ring proceeded more slowly than to the corresponding five-membered ring [488].

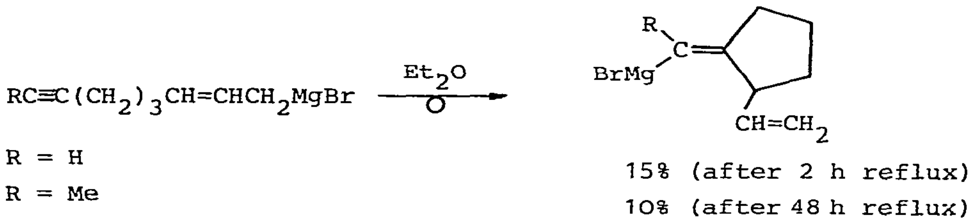


(74%)



(40%)

The intramolecular addition of an allylmagnesium bond to a C-C triple bond with allylic rearrangement, has also been reported. The reaction, however, is more facile with the corresponding organozinc compound [71]:



$RC\equiv C(CH_2)_3CH=CHCH_2MgBr \xrightarrow{Et_2O}$

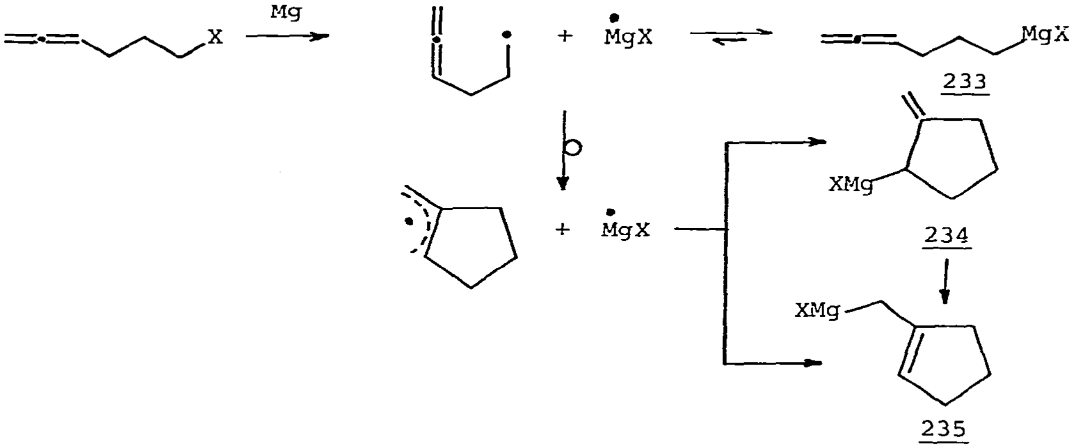
R = H

R = Me

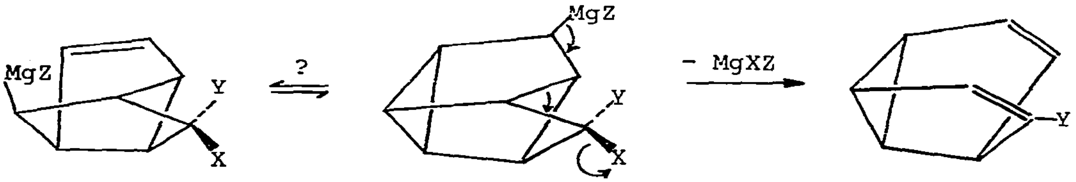
15% (after 2 h reflux)

10% (after 48 h reflux)

The cyclization accompanied by the reaction of γ-halogenoallenes with magnesium is strongly dependent on the solvent. A solution in ether contains exclusively the open-chain Grignard reagent 233, whereas solutions in THF consist of 233 and 235 in approximately equal amounts. The observed results are in agreement with the irreversible cyclization of the initially formed radical which is much better stabilized in THF than in diethyl ether [378]:



No Grignard equlilibrium was observed with the following tetracyclic system a semibullvalene derivative being rather formed [621]:



B. Catalysis of polymerization and other reactions

An undergraduate Grignard reaction experiment for polymerization of ethylene and propylene using a PhMgCl-$TiCl_4$ catalyst has already been noted in the introduction [10].

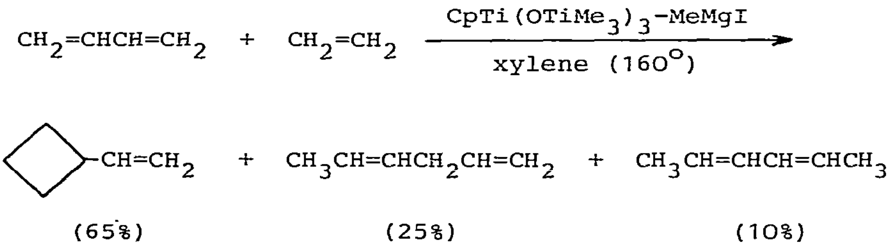
The year continued to see great activity in the patent literature in catalysis of alkene polymerization by multicomponent formulations which include an organomagnesium compound. For polymerization of ethylene and propylene the catalyst usually is formed by interaction of the organomagnesium compound with titanium tetrachloride and an aluminium trialkyl. Commonly a siloxane and an alcohol, ester or other Lewis base is also a partof the catalyst combination [622-627] (Because of the numerous patents involved, only the appropriate chemical abstract numbers are listed.) Thus a reaction product of EtMgCl, $TiCl_4$, Et_3Al, methylpolysiloxane, ethyl benzoate, and methyl p-toluate was used as a catalyst to prepare isotactic polypropylene [626].

Ethylmagnesium alkoxides prepared from Et_2Mg and alcohols were used as catalysts for the stereospecific polymerization of methacrylates at -78^o in toluene. While normal primary alkoxides had no stereospecific tendencies, alkoxides from 2-monosubstituted primary alcohols produced isotactic polymers. The isotacticity decreased with temperature increase. Secondary and tertiary alkoxides, on the other hand, afforded syndiotactic polymers without a pronounced temperature effect [628]. Starting with a chiral alcohol and Et_2Mg asymmetric selection was observed in the polymerization of (RS)-α-methylbenzyl methacrylate [629]. The same is true for a (−)sparteine/cyclohexylmagnesium chloride complex which at -78^o in toluene yielded a polymer with 86% optical purity. The optical purity was lower at -40^o and when cyclohexylmagnesium bromide or iodide or n-BuMgCl were used. With increasing asymmetric selectivity the isotacticity of the polymer also increased [630]. This high selectivity was ascribed to the fact that an (S)-elective center having a high selectivity was formed preferentially in the initial reaction and an (R)-elective center was formed after $>80\%$ (S)-α-methylbenzylmethacrylate had been consumed [631]. With the same catalyst asymmetric-selective polymerization of 2,3-epoxypropyl methacrylate was achieved yielding a highly isotactic product. Almost all epoxy groups remained unreacted during polymerization [632].

The kinetics of polymerization of methyl methacrylate initiated by alkylmagnesium halides in THF, dioxane, and toluene has also been studied. The activity of the catalyst increased in the sequence Bu $<$i-Bu $<$t-Bu and the bromides were more active than the corresponding chlorides and iodides. Again isotactic material was obtained [633]. In THF the molecular weight distributions were polymodal with peak positions that were independent of the THF concentration in the polymerization mixture, whereas the peak heights and the tacticities of the samples varied with the THF concentration. The results were discussed in terms of an eneidic pseudoanionic polymerization mechanism involving propargation by the formation of a monomer-complex at the growth site which proceeds via a four-center orientation to insert into a covalent Mg-C bond [634].

Highly isotactic poly(acrylic acid esters) were also obtained with ortho-substituted phenylmagnesium halides as catalysts. Thus isopropyl acrylate and mesitylmagnesium bromide at -78° in toluene yielded 61% of a polymer with isotacticity $>$95% [635].

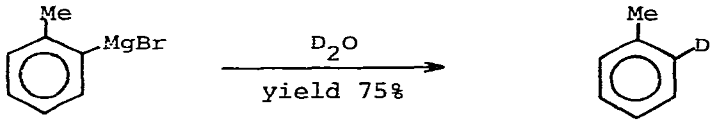
Codimerization of 1,3-butadiene and 1,3-pentadiene with ethylene in the presence of the catalytic system $CpTi(OSiMe_3)_3$-MeMgI selectively afforded vinylcyclobutanes [636]. e.g.



The total yield of codimers was 85%; using Et_3Al as cocatalyst in place of MeMgI lowered the yield to 60-65% [636].

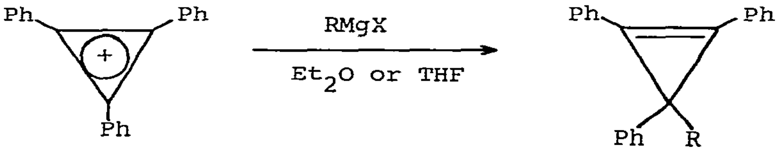
C. Miscellaneous reactions

Deuterated compounds with up to 87% deuterium incorporation have been prepared by treating Grignard reagents with D_2O [103,637,638]: e.g.



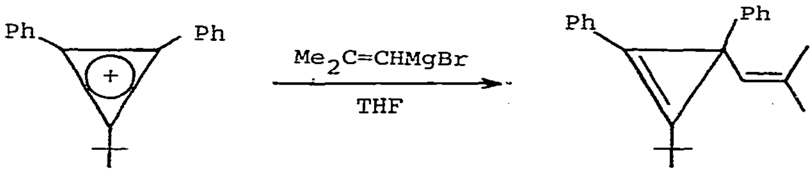
(87% pure d_1)

The reaction of triphenylcyclopropenium salts with phenyl, benzyl, allyl, and vinyl Grignard reagents yielded the corresponding 3-substituted 1,2,3-triphenylcyclopropenes: e.g.



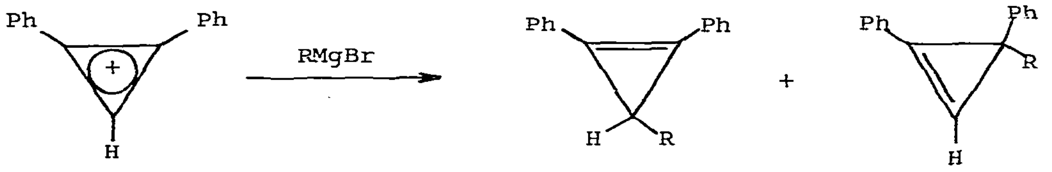
R = Ph;	X = Br	95%	[639]
R = $PhCH_2$;	X = Cl	87%	
R = $CH_2{=}CHCH_2$;	X = Br	70%	[640]
R = $CH_2{=}CH$;	X = Br	75%	
R = $Me_2C{=}CH$;	X = Br	63%	[33]
R = $CH_2{=}CPh$;	X = Br	48%	

A single product was also obtained starting from 1,2-diphenyl-3-*tert*-butyl-cyclopropenium bromide [33]:



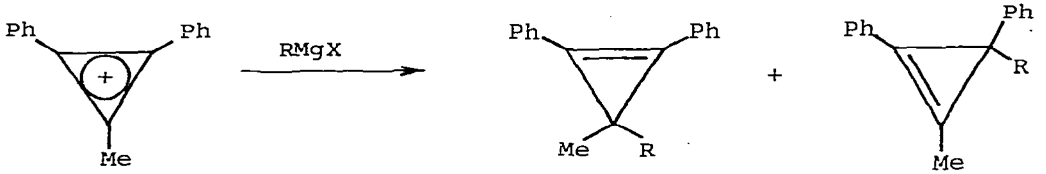
(46%)

Diphenylcyclopropenium perchlorate, on the other hand, yields one product with vinylmagnesium bromide but two products with allylmagnesium bromide [640]:



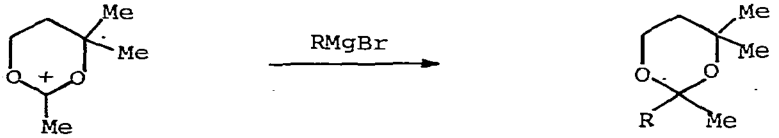
R = $CH_2{=}CH$	65%	—
R = $CH_2{=}CHCH_2$	41%	20%

Finally with 1,2-diphenyl-3-methylcyclopropenium perchlorate always a mixture of two products has been obtained, the ratio strongly depending on the nature of the Grignard reagent [640] :

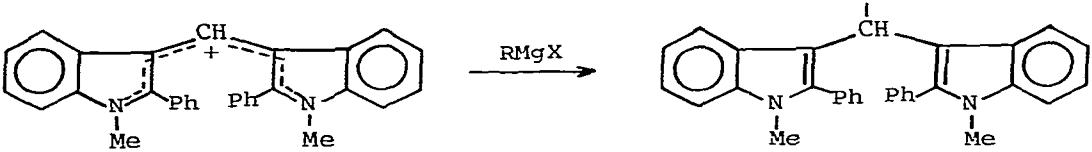


R = $PhCH_2$; X = Cl	27%	60%
R = $CH_2{=}CHCH_2$; X = Br	55%	31%
R = $CH_2{=}CH$; X = Br	65%	9%

Coupling of Grignard reagents with other carbocations has also been reported: e.g.



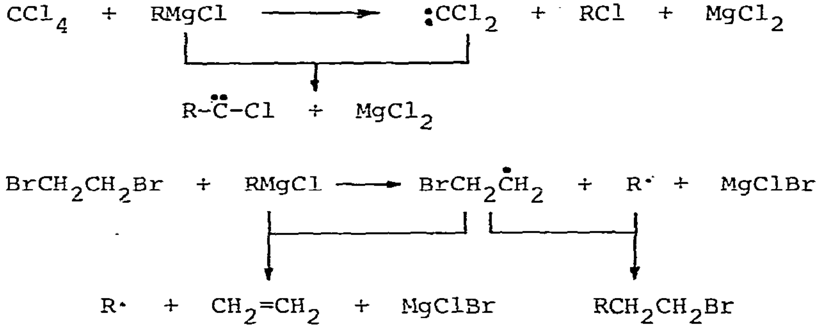
[641]



R = Me, Et, Ph

[642]

The reaction of neophylmagnesium chloride with carbon tetrachloride and 1,2-dibromoethane has been investigated in some detail. While CCl_4 which is a very reactive halide towards Grignard reagents reacts via an ionic pathway, with the less reactive dibromoethane electron transfer seems to take place to yield neophyl radicals. The reaction products are in agreement with the following mechanistic conception [643]:

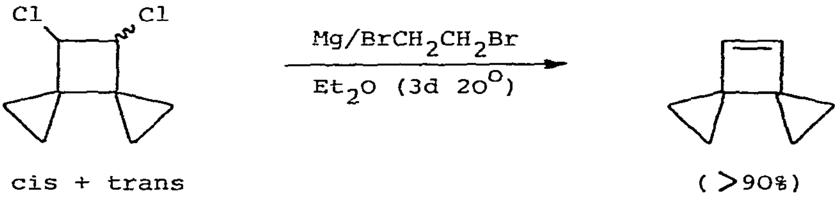


R = $PhCMe_2CH_2$

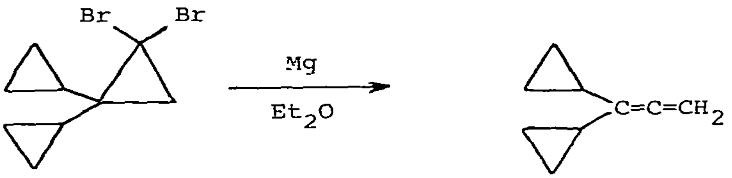
Free radicals are also involved in the reaction of 2- or 3-halogenoalkoxysilanes with magnesium which does not lead to stable organomagnesium derivatives [644]: e.g.

$$\underset{}{Me_3SiOCH_2CH_2Br} \xrightarrow[Et_2O]{Mg} \underset{(60\%)}{CH_2{=}CH_2} + \underset{(27\%)}{Me_3SiO(CH_2)_4OSiMe_3}$$

Other intramolecular displacement reactions using magnesium metal include:



[645]



[646]

(33%)

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