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New Organometallic Reagents Using Highly Reactive Metals

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Contents

1 Introduction

In 1972, a general approach was reported for the preparation of highly reactive metal powders by the reduction of anhydrous metal salts in ethereal or hydrocarbon solvents using alkali metals as reducing agents, in conjunction with or without an electron carrier.[1] The reduction of metal salts in this manner produces finely divided metal slurries. These metal slurries are highly reactive, air sensitive, and are usually pyrophoric in the absence of solvent. In this report, these active metals are indicated as M*.

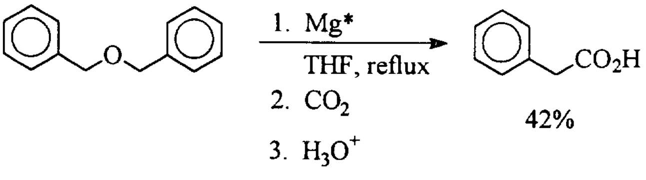
The choice of metal salt, reducing agent, and solvent can result in dramatic differences in the reactivity of the active metal. For the majority of the metals, the choice of lithium as reducing agent in conjunction with an electron carrier produces active metals with the highest reactivity. The anion of the metal salt in some metals can have a profound effect on the reactivity of the active metal. For most of the active metals, the reduction is most effectively performed using tetrahydrofuran as solvent. In some cases, the reduction of certain metals can cause the cleavage of ethereal solvents and the reduction therefore must be carried out in a hydrocarbon solvent, as in the formation of active uranium.[2]

In synthesis, the application of active metals as reagents for the preparation of organometallic intermediates is a well known and effective method. Due to the high reactivity of active metals, reactions are typically carried out more efficiently, under milder conditions, and with a wider array of substrates than with other current methods.

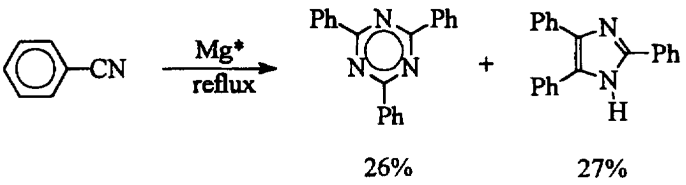
2 Active Magnesium

2.1 *Formation of Grignard Reagents From Active Magnesium*

The reduction of anhydrous magnesium salts produces a highly reactive form of magnesium. The reactivity of active magnesium is sufficient to oxidatively insert into a carbon-oxygen bond. Treatment of dibenzyl ether with active magnesium for five days at reflux gives a 42% yield of phenylacetic acid after quenching with carbon dioxide (Scheme 1).[3] Active magnesium displays reactivity toward nitriles similar to that of alkali metals. The reaction of active magnesium with benzonitrile in refluxing glyme produced 2,4,6-triphenyl-1,3,5-triazine and 2,4,5-



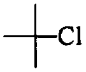
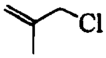
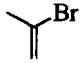
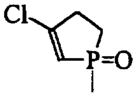
Scheme 1

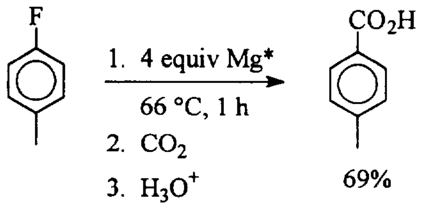


Scheme 2

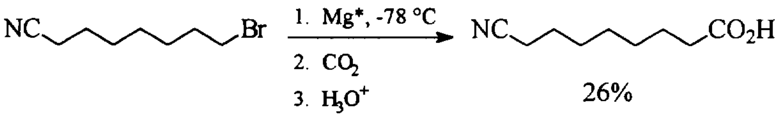
triphenylimidazole in 26% and 27% yields respectively (Scheme 2).[3] The high reactivity of active magnesium allows for the high yield preparation of Grignard reagents from a wide variety of alkyl, vinyl, and aryl halides (Table 1).[4] The oxidative addition of active magnesium proceeds under milder conditions towards halides than standard forms of magnesium. Active magnesium can react with aryl bromides at -78 °C in a few minutes to form the corresponding Grignard reagents,[4,5] where as Grignard reagents may even be formed from alkyl and aryl *fluorides* using active magnesium. *p*-Fluorotoluene reacts with active magnesium at 66 °C in 1 h, and upon trapping with carbon dioxide, gives the carboxylic acid in 69% yield (Scheme 3). The oxidative addition appears to be sensitive

Table 1. Preparation of Grignard Reagents by Active Magnesium

Halide	Mg*/halide	Temp. (°C)	Time (min.)	% Yield
	2	25	5	81
	2	25	60	52
	1.7	66	360	63
	2	25	60	82
	2	25	5	71
	2	66	390	40

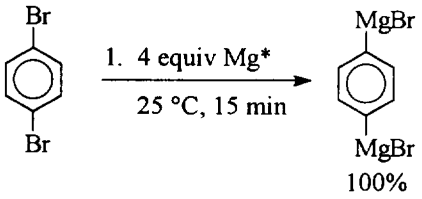


Scheme 3

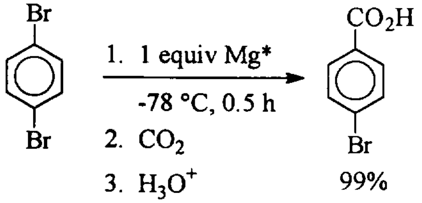


Scheme 4

to the coordination of the metal by various functional groups. At -78 °C, the cyano group coordinates to the magnesium surface and completely inhibits the oxidative addition. Aryl and alkyl bromides containing the cyano group failed to form the Grignard reagent. However, 8-bromooctanenitrile did produce the Grignard reagent when treated with active magnesium at low temperature (Scheme 4). Active magnesium is sufficiently reactive to form the diGrignard reagent from dibromobenzene at room temperature (Scheme 5).[4] However, the oxidative addition can be controlled at low temperature to give exclusively the mono-Grignard reagents from dichloro or dibromobenzenes (Scheme 6).[6]



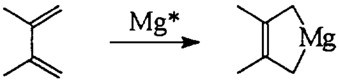
Scheme 5



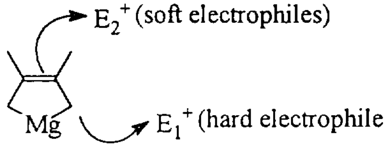
Scheme 6

2.2 *Formation and Reactivity of Magnesium-Diene Complexes*

The activity of active magnesium is also sufficient to form magnesium-diene complexes with 2,3-dimethyl-1,3-butadiene producing a novel bis-nucleophilic organometallic reagent in high yield (Scheme 7).[5b]



Scheme 7



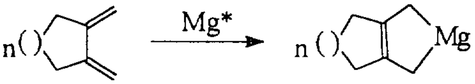
E_1^+ = silicon halide

E_2^+ = alkyl halides, esters, imines, lactone

Scheme 8

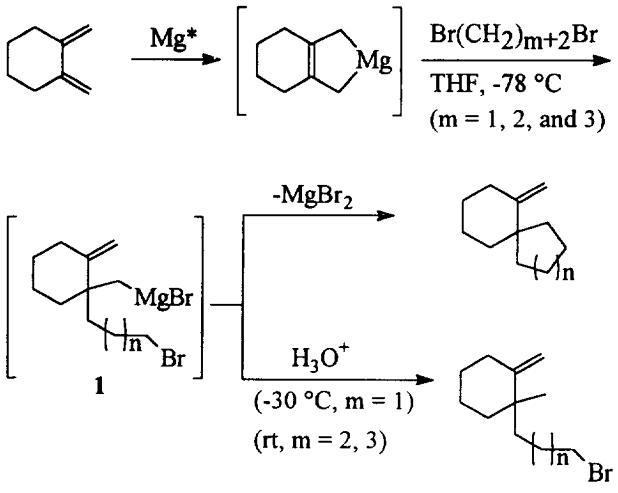
These reagents are unique and possess behavior unlike those of classical Grignard reagents. The 1,3-diene complexes react in the 2-position with soft carbon electrophiles (alkyl halides,[5b] esters,[7] imines,[8] and lactones,[9] Scheme 8). Where as with hard electrophiles (silicon, tin, boron halides), they react exclusively in the 1-position of the butadiene.[5]

Spirocyclic systems may be accessed by the reactions of bis-electrophiles with the magnesium complexes of 1,2-bis(methylene)cycloalkanes (Scheme 9).[10] The reaction of the diene-magnesium reagents with 1,*n*-dibromoalkanes produces spirocarbocycles containing an exocyclic double bond (Table 2). The second alkylation step on the bis-electrophile may be avoided by trapping intermediate 1 by protonation (Scheme 10). The reaction of 1,3-diene-magnesium complexes with bromoalkylnitriles leads to the generation of keto-functionalized spirocycles (Scheme 11).

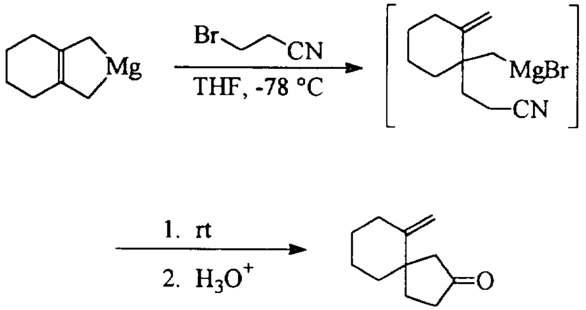


Scheme 9

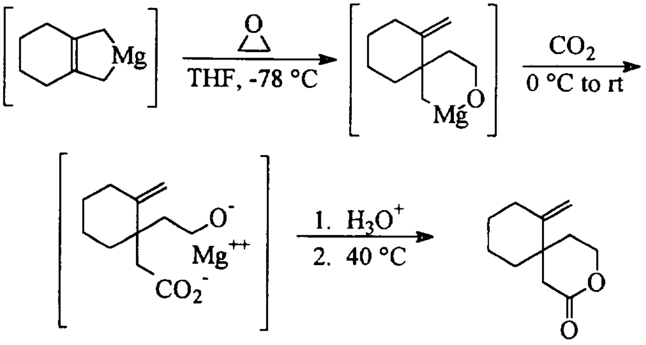
Spiro δ- or γ-lactones and alcohols can be obtained from magnesium-diene complexes by treating the



Scheme 10

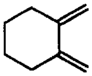
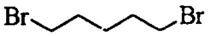
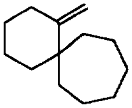
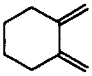
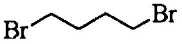
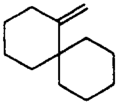
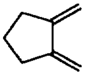
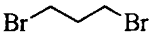
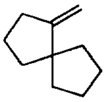
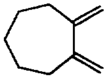
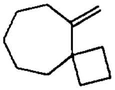


Scheme 11

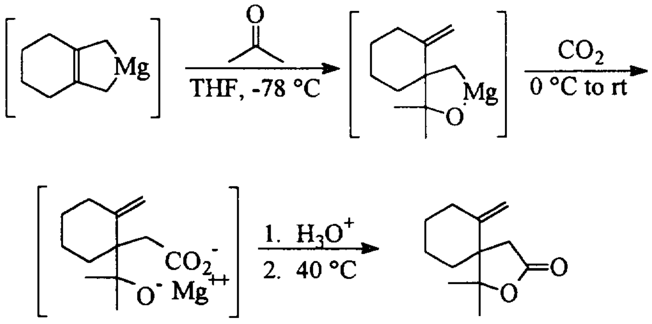


Scheme 12

Table 2. Reactions of Diene-magnesium Reagents with 1,n-dibromoalkanes

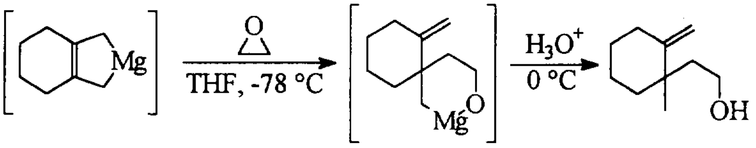
Diene	Electrophile	Product	% Yield
			45
			75
			60
			45

conjugated diene-magnesium reagents with epoxides followed by carbon dioxide (Scheme 12).[11] The use of ketones as the electrophile provides spiro γ-lactones after the initial adduct is exposed to carbon dioxide (Scheme 13).[12] If the initial adduct is hydrolyzed, alcohols are formed which contain both an olefin and a quaternary center (Scheme 14).

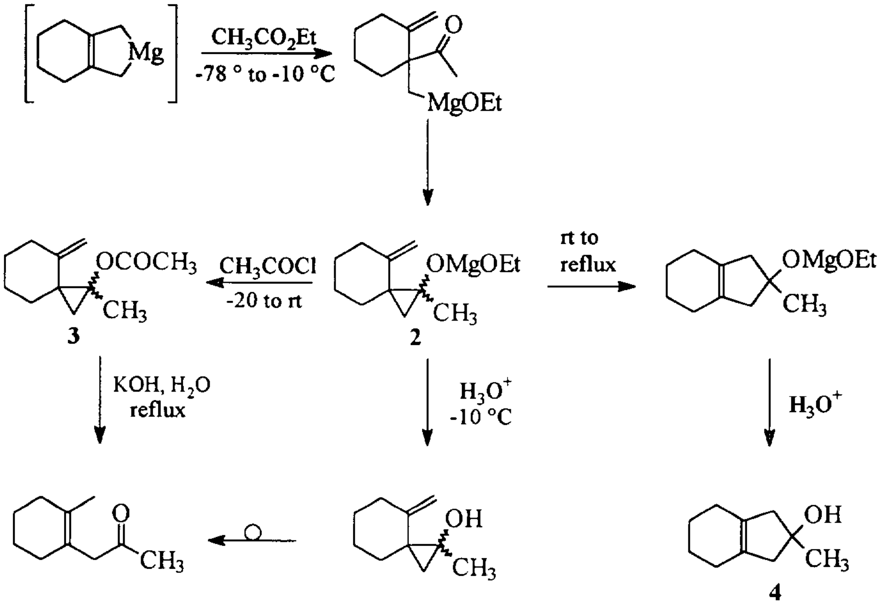


Scheme 13

Reaction of the magnesium complexes of 1,3-dienes with either esters or lactones produces the magnesium salt of a cyclopropanol (**2**)[9] which may be trapped as the cyclopropyl acetate (**3**), or as a substituted cyclopentenol (**4**) after heating (Scheme 15). When the alkoxide **2** is protonated, intramolecular rearrangement ensues to afford



Scheme 14



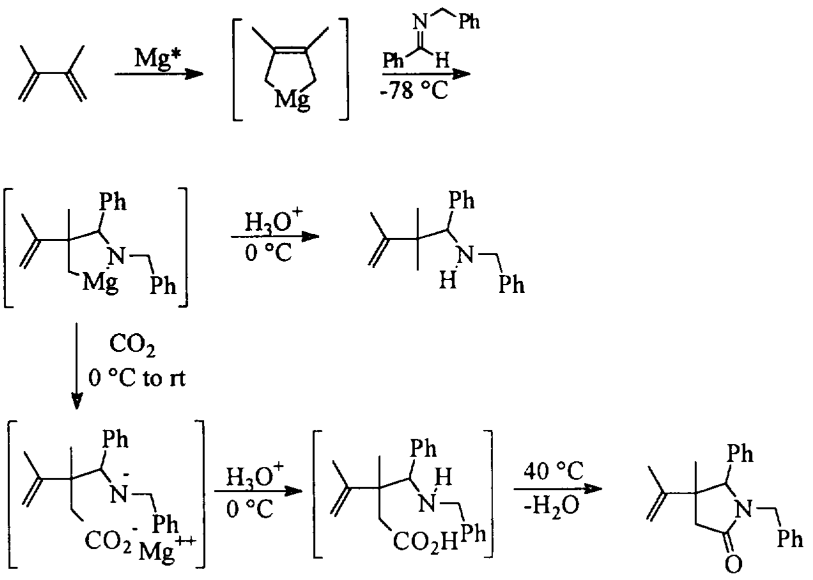
Scheme 15

β,γ-unsaturated ketones. This procedure can be used to prepare substituted cyclopentenols containing both primary and tertiary hydroxyl groups. Cyclic, acyclic, and unsymmetrical magnesium-diene complexes have been also shown to react with carboxylic esters and lactones. γ-Lactams can be formed by the sequential addition of imines and carbon dioxide to the magnesio cycloadducts (Scheme 16).[8]

Active calcium,[13] barium,[14] and strontium[14, 15] have also been employed to form diene complexes, and in some cases gave higher yields with electrophiles than the corresponding magnesium species.

3 Active Zinc

The reduction of anhydrous zinc salts produces a highly reactive form of zinc. The early work used potassium metal in THF[16] and the reduction was found to be exothermic and required cooling (Scheme 17). This

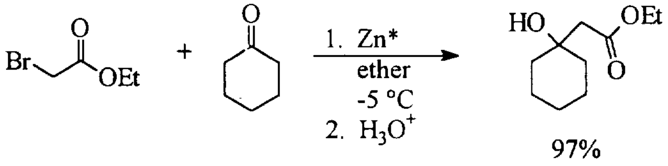


Scheme 16

form of active zinc has been quite efficient in the Reformatsky reaction. Thus, ethyl 2-bromoacetate reacted with active zinc in ether at -5 °C and with the corresponding chloroester at 10 °C. The Reformatsky reaction occurs rapidly and efficiently, with the suppression of side reactions, in near quantitative yields (Scheme 18).[17] This form of active zinc also reacted directly with alkyl and aryl *bromides* (Scheme 19)[16] and provided the first examples of this transformation. In 1991, an improved reduction method for the preparation of active zinc was reported.[18] Using lithium naphthalenide as the reducing agent, the resulting zinc was shown to be more reactive than that obtained from the reduction of zinc salts by potassium metal. (Scheme 20). It was also found that the reduction may be carried out using catalytic quantities of naphthalene.[19]

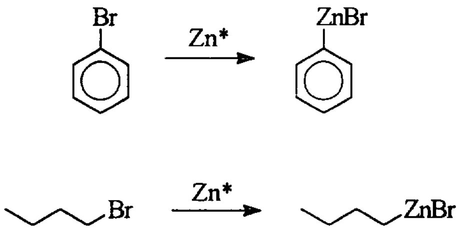
$$2\,K + ZnCl_2 \longrightarrow Zn^* + 2\,KCl$$

Scheme 17

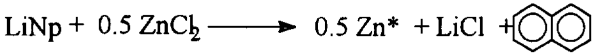


Scheme 18

This new form of active zinc reacts with alkyl iodides[20] instantaneously at room temperature and with alkyl bromides at room temperature over a period of several hours.[18] Aryl iodides react at room temperature, and aryl



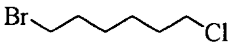
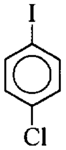
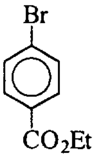
Scheme 19



LiNp = lithium naphthalenide

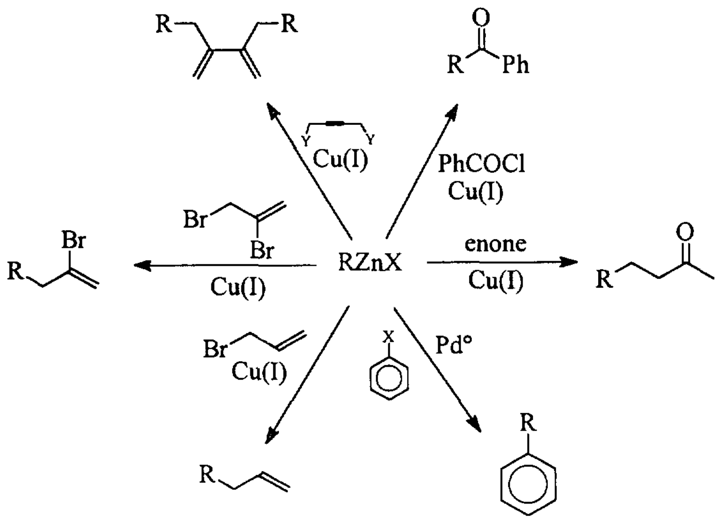
Scheme 20

Table 3. Reaction of Active Zinc with Organohalides

Organohalide	Equiv Zn*	Temp.	Time (h)	Yield (%)
	1.2	rt	4	100
	1.0	rt	1	100
	2.0	rt	3	100
	2.0	reflux	2	100

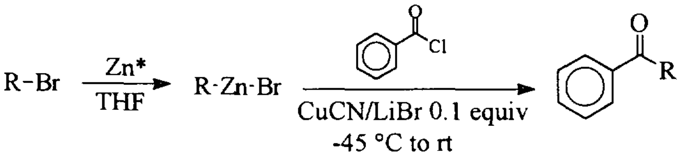
bromides react at refluxing temperatures (Table 3).[18] This metalation procedure was shown to tolerate nitrile, ester, ketone, and chloride in the produced organozinc halide. The organozinc halides prepared according to the present method, are capable of reacting with a variety of electrophiles in the presence of Cu(I) or Pd(0) (Scheme 21).[18, 21]

Although active zinc readily undergoes oxidative addition, it is also very mild. Active zinc readily yields



Scheme 21

alkylzinc bromides under mild conditions from the direct oxidative addition of active zinc to secondary and tertiary alkyl bromides.[22] The technique has proved useful for hindered and unhindered unactivated secondary and tertiary alkyl bromides as assessed by trapping with benzoyl chloride (Scheme 22). The oxidative addition occurs



R = secondary and tertiary alkyl

Scheme 22

rapidly for tertiary alkyl bromides at room temperature (Table 4). Adamantyl bromide, known[23] to be a difficult system in oxidative addition, gave the organozinc bromide in refluxing THF in good yield. The formation of secondary alkylzinc bromides was also facile from unactivated[21a] secondary alkyl bromides (Table 5), and was shown to accommodate remote functional groups including esters and nitriles (Table 6).

Active zinc has become a powerful tool in the generation of π-deficient heteroaromatic organometallics and in the oxidative addition to difficult aromatic halides to form organozinc reagents by readily inserting zinc into the carbon-halogen bond. The first example of 3-thienylzinc iodide was generated by direct, room temperature, oxidative addition into 3-iodothiophene to form the thermally stable species (Scheme 23).[24] This same procedure was used to prepare 3-indoylzinc iodide reagents (Scheme 24)[25] which cannot be prepared by metathesis of

Table 4. Tertiary Alkylzinc Bromides

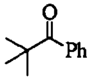
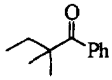
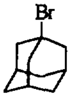
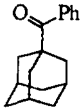
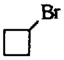
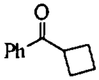
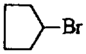
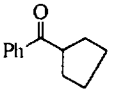
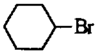
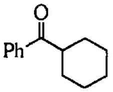
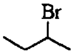
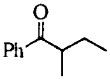
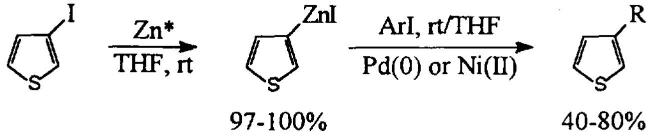
Bromide	RCOCl equiv	Product	Yield (%)
	0.7		75
	0.7		86
	0.7		72

Table 5. Secondary Alkylzinc Bromides

Bromide	RCOCl equiv	Product	Yield (%)
	0.7		75
	0.9		84
	0.7		99
	1.0		95

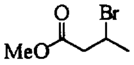
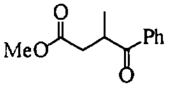
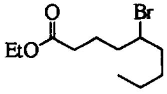
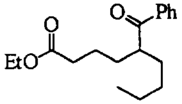
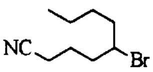
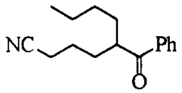


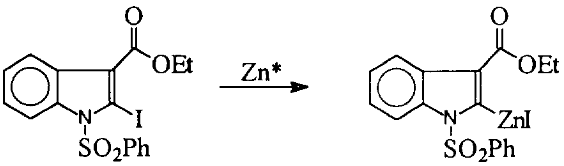
R = aryl

Scheme 23

organolithiums with zinc(II) chloride. These organometallics can only be obtained in high yield through the reaction of the 3-iodoindoles with active zinc. The later is also effective in the preparation of pyridinylzinc halide reagents from halopyridines,[26] and adds smoothly to iodo or bromo pyridines at room temperature forming the zinc reagents

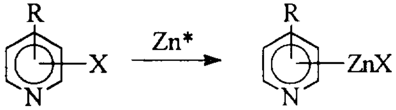
Table 6. Functionalized Secondary Alkylzinc Bromides

Bromide	RCOCl equiv	Product	Yield (%)
	0.7		75
	0.7		54
	0.7		60



Scheme 24

in high yields (Scheme 25). Coupling of aryl halides or benzoyl chloride using a palladium catalyst has also been observed. More heavily substituted systems can also be transformed into their zinc derivatives. Iodo-4,6-dimethyl-2-zinciopyrimidine and 3-quinolylzinc iodide are cases in point (Scheme 26).[27]

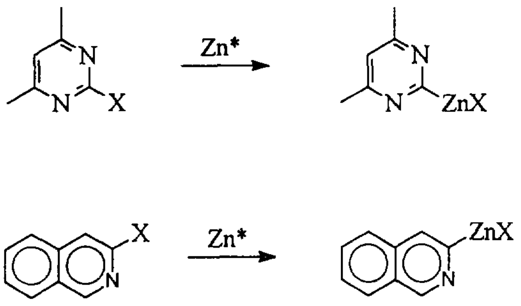


X, R = Br, H; I, H; I, 2,6-diMe

Scheme 25

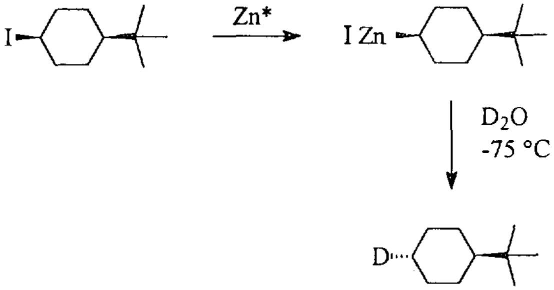
The active zinc may also lend itself toward the possibility of forming configurationally stable organometallics. For example, *cis*-4-*tert*- butylcyclohexyl iodide inserted zinc and was quenched with D_2O at low temperature to give the *trans*-deutero product (Scheme 27).[28]

Active zinc has been shown to be an effective mediator in intramolecular conjugate additions. A spirodecanone was formed from the 1,4-addition of the organozinc reagent which was readily available from a primary iodide (Scheme 28).[20] Other ring closures where also shown to occur (Scheme 29), and are thought to proceed by a mechanism that does not involve a free radical pathway.

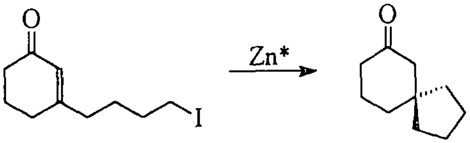


X = Br, I

Scheme 26

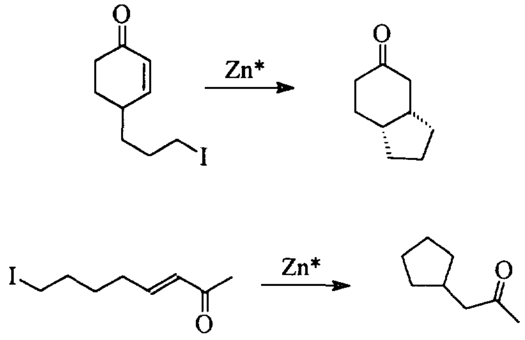


Scheme 27

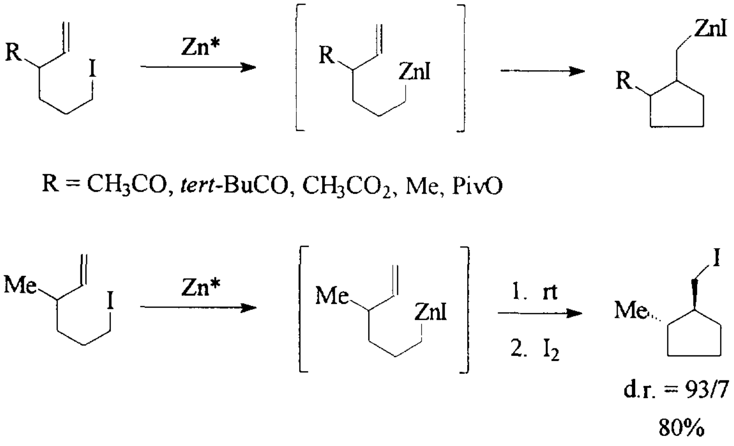


Scheme 28

The direct insertion of active zinc into the carbon-iodine bond of 6-iodo-3-functionalized-1-hexenes form the primary alkylzinc iodides which then undergo an intramolecular insertion of the olefin π-bond into the zinc-carbon bond to form methyl cyclopentanes (Scheme 30).[29] When R is methyl, the diastereoisomeric ratio was found to be high. This is a significant finding in that this is a regiospecific 5-exo-trig cyclization which can occur in the presence of functional groups providing an intermediate that can then be elaborated further with various electrophiles. This methodology can be extended to ω-alkenyl-*secondary*-alkylzinc reagents (Scheme 31).[30]



Scheme 29

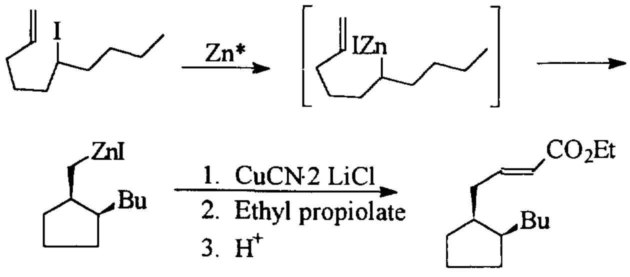


R = CH_3CO, *tert*-BuCO, CH_3CO_2, Me, PivO

d.r. = 93/7

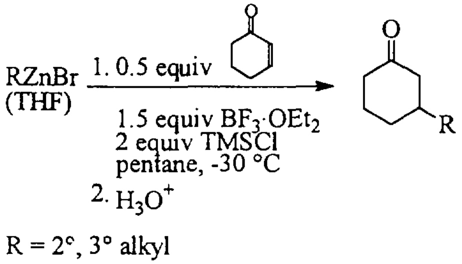
80%

Scheme 30



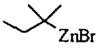
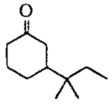
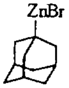
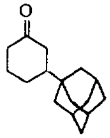
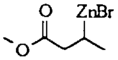
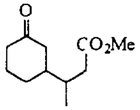
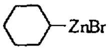
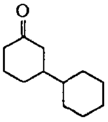
Scheme 31

The intermolecular 1,4-addition to enones can be performed with secondary and tertiary alkylzinc bromides without the use of a copper(I) catalyst. The reaction is performed in a THF/pentane (1:9) solvent with $BF_3 \bullet Et_2O$ and TMSCl (Scheme 32). These conditions tolerate a variety of functional groups, and are also effective with bulky alkyl groups in the zinc species (Table 7).[31]



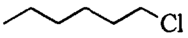
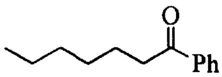
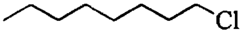
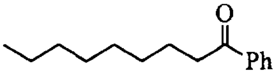
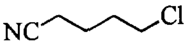
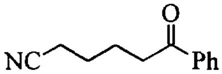
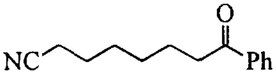
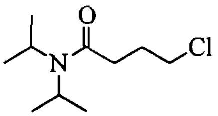
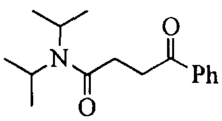
Scheme 32

Table 7. 1,4-Addition of Secondary and Tertiary Alkylzinc Bromides to Cyclohexenone without a Copper Catalyst

RZnBr	Product	Yield(%)
		74
		54
		51
		73

A highly active form of zinc may be prepared from the reduction of zinc cyanide utilizing lithium naphthalenide. This active zinc undergoes direct oxidative addition to alkyl chlorides.[32] Although some functional groups are inert, the zinc derivatives react with benzoyl chloride using a copper catalyst (Table 8).

Table 8. Reactions of Active Zinc Derived from Zinc Cyanide

Organohalide	$Zn^*_{(CN)}$: R-Cl	PhCOCl	Product	% Yield
	3:1	0.8		74
	4:1	0.8		65
	2:1	0.7		41
	2.5:1	0.9		68
	3:1	0.9		61

4 Active Indium

Active indium is prepared by the alkali metal reduction of anhydrous indium salts in hydrocarbon solvents under argon (Scheme 33).[33] This highly reactive form of indium exhibited a significant increase in reactivity towards alkyl iodides than commercially available indium metal. The later normally requires reaction times of a day or more, but active indium, as prepared above, reacted with methyl and ethyl iodide (2 h, 80 °C, xylene) to give the corresponding dialkylindium iodides. Diarylindium iodides may also be prepared from aryl iodides under the same conditions (Scheme 34).[34]

$$InCl_3 + 3\,M \longrightarrow In^* + 3\,MCl$$

M = K or Na

Scheme 33

$$2\,In^* + 2\,RI \longrightarrow R_2InI + InI$$

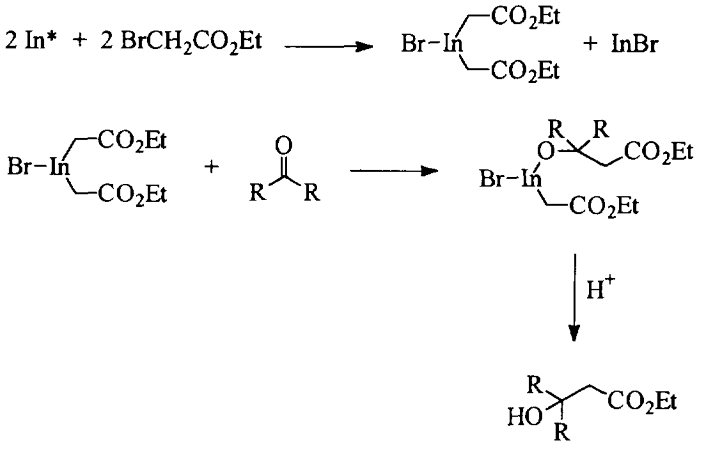
Scheme 34

The enhanced reactivity of active indium allowed the formation of triaryl and trialkyl indium compounds in quantitative yields from the diorganomercury compounds (Scheme 35).[35]

$$2\ \text{In*} + 3\ R_2Hg \longrightarrow 2\ R_3In + 3\ Hg$$

Scheme 35

Active indium is also effective in forming a Reformatsky-type reagent from α-halo esters that will add to ketones and aldehydes to give β-hydroxy esters (Scheme 36).[36]

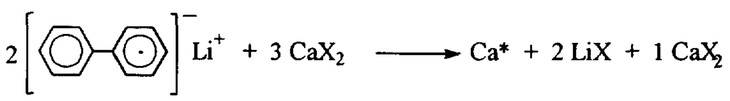


Scheme 36

5 Active Calcium

The direct oxidative addition involving calcium with organic substrates has been limited due to the poor reactivity of calcium metal. Organocalcium iodides are readily formed from organoiodides, but organobromides and chlorides are poor precursors to these derivatives.

An active form of calcium may be prepared by the lithium biphenylide reduction of calcium salts in THF.[37] This active calcium may be forming a complex with biphenyl, and is reasonably soluble in THF (Scheme 37). Alkyl



X = Br, Cl

Scheme 37

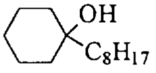
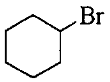
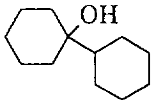
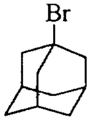
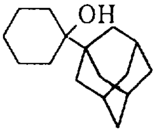
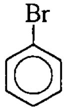
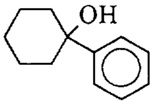
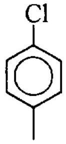
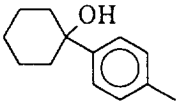
bromides and chlorides react with active calcium at -78 °C in THF to give the alkylcalcium halides in good yields (Scheme 38). Although arylbromides and chlorides react well, they require temperatures between -30 ° and -20 °C, respectively. Fluorobenzene reacted with active calcium at room temperature to give the phenylcalcium halide in excellent yield. The reaction of active calcium with adamantyl bromide gave a good yield of the adamantylcalcium bromide. The oxidative addition of magnesium turnings with this tertiary alkyl bromide is not effective.[23] These calcium reagents gave the 1,2-addition products with cyclohexanone efficiently (Table 9). The organocalcium halides used in conjunction with copper salts gave calcium cuprate reagents. These cross-couple with acid chlorides and also give the 1,4-addition products with enones (Scheme 39).

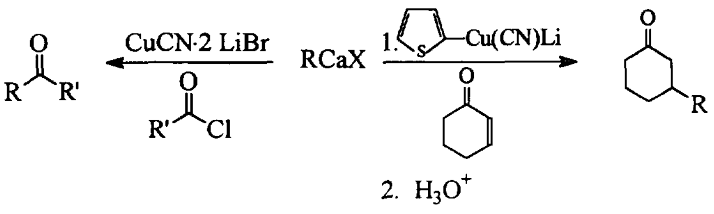
$$RX + Ca^* \longrightarrow RCaX$$

R = alkyl, aryl
X = Br, Cl, F

Scheme 38

Table 9. Formation of Organocalcium Halides and Addition to Cyclohexanone

Halide	CaX_2	Product	% Yield
n-octyl chloride	CaI_2		83
	$CaBr_2$		75
	$CaBr_2$		80
	CaI_2		85
	CaI_2		86



Scheme 39

6 Active Copper

6.1 Formation of Active Copper

The reduction of Cu(I) salts in the generation of active copper can produce active copper of varying reactivities and properties. These aspects are based on the type of solvent, choice of ligands, counter ions, and the reduction temperature. The simple reduction of Cu(I) salts with sodium or potassium using catalytic naphthalene as an electron carrier produced a grey black finely divided powder. This form of active copper was prone to sintering, and the reactivity was not sufficient to oxidatively add to organohalides at low temperatures in order to maintain the stability of the organocopper reagents. However, this form of copper did display a reactivity higher than that of copper-bronze in Ullmann coupling.[38]

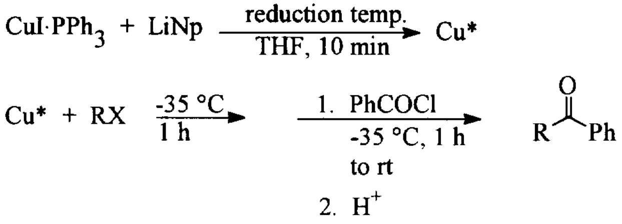
The temperature at which the copper salts are reduced has a pronounced effect on the reactivity of the resulting zero valent copper. For example, the reduction of copper iodide in the presence of tributyl or triphenylphosphine at low temperature (-78, -100 °C) produced copper of a highly reactive nature,[39] and the oxidative addition to organohalides proceeded at -35 °C, generating stoichiometric organocopper reagents. Additionally, the triorganophosphine present in the reaction mixture reduced homocoupling in the oxidative addition of alkyl halides. The CuCN•2LiX derived active copper[40] was slightly less reactive than the phosphine based active copper reagents. The advantage of using copper(I) cyanide was evident in product isolation as the product was free of phosphine. These forms of active copper are free of sintering.

There are five general procedures in making active copper. The reduction of copper(I) salts coordinated with a phosphine ligand, reduction of a soluble CuCN•2LiX complex, reduction of lithium 2-thienylcyanocuprate,[41] 2 equivalent reduction of copper(I) salts to form a formal copper anion,[42] and the sodium or potassium reduction of copper salts have all led to highly reactive coppers with unique chemical properties.

6.2 Reactions of Active Copper

The active coppers generated from the reduction of the complexes of Cu(I), $CuI{\bullet}PR_3$ (R = Ph, Bu)[39] (Tables 10, 11 respectively) and $CuCN{\bullet}nLiX$ (X = Cl or Br, n = 1 or 2)[40] (Table 12) readily undergo oxidative addition to alkyl iodides, bromides, and chlorides, as well as aryl iodides, bromides, and chlorides at low temperature. The oxidative addition to organohalides at low temperature reduces homocoupling of the alkyl halides and increases the efficiency of the oxidative addition. These forms of active copper can tolerate highly functionalized organohalides in the oxidative addition. This procedure may be used to form allylic copper reagents directly from allylic halides and acetates. The functional groups that can be present in the organocopper include ester, nitrile, ketone, alkene, epoxide, and halide (Table 13). These organocopper reagents cross-couple with alkyl halides, acyl halides, and allylic halides. They undergo 1,4-addition to enones and open epoxides (Scheme 40).

Table 10. Reactions of PPh_3-Based Active Copper



red. temp. (°C)	RX	% Yield RCOPh
0	*c*-hexyl bromide	25
-78	*c*-hexyl bromide	62
-100	*c*-hexyl bromide	82
0	*c*-hexyl bromide	46
-78	*c*-hexyl bromide	46
-100	*c*-hexyl bromide	69
0	PhCl	2
-60	PhCl	44
-100	PhCl	61

Np = naphthalene

Difunctional molecules, containing both an epoxide and a halide, can undergo intramolecular cyclization mediated by phosphine based active copper to form carbocycles. Treatment of 6-bromo-1,2-epoxyhexane with active copper at -78 °C formed 5,6-epoxyhexylcopper which cyclized upon warming to give a 1:6 mixture of the exo to endo product (Scheme 41). Epoxyarylcopper compounds also give intramolecular epoxide-opening

Table 11. Reactions of PBu_3-Based Active Copper

$$\mathrm{CuI{\cdot}PBu_3} + \mathrm{LiNp} \xrightarrow[\text{THF}]{\text{Condition A}} \mathrm{Cu^*}$$

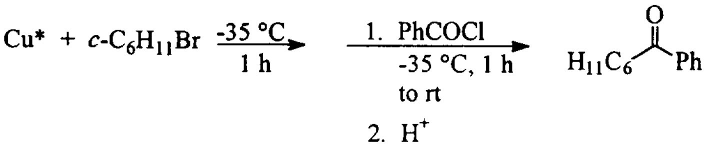
$$\mathrm{Cu^*} + \mathrm{RX} \xrightarrow[\text{2. H}^+]{\text{1. Condition B}} \mathrm{RH} + \mathrm{RX} + \mathrm{RR}$$

RX	A (°C, min)	B (°C, min)	%yield RH	%yield RX	%yield RR
n-octyl bromide	0, 20	-78, 20	65	5	25
n-octyl bromide	-78, 10	-78, 60	76	6	16
n-octyl bromide	-107, 10	-35, 60	76	0	17
n-octyl chloride	0, 20	-50, 80	23	71	0
n-octyl chloride	-78, 10	-50, 60	63	32	0
n-octyl chloride	-107, 10	-35, 60	64	31	0

Np = naphthalene

Table 12. Reactions of Copper Cyanide-Based Active Copper

$$\mathrm{CuCN{\cdot}nLiX} + \mathrm{LiNp} \xrightarrow[\text{THF, 10 min}]{\text{reduction temp.}} \mathrm{Cu^*}$$

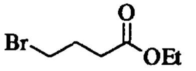
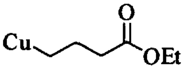
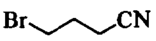
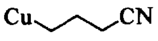
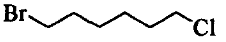
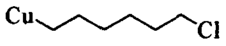
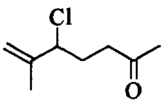
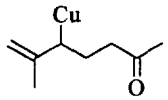
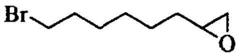
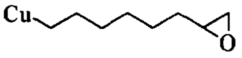
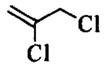
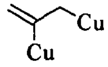
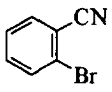
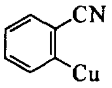
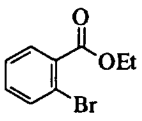
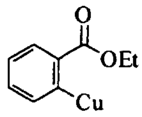
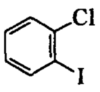
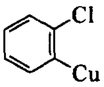


$$\mathrm{Cu^*} + c\text{-}\mathrm{C_6H_{11}Br} \xrightarrow[\text{1 h}]{-35\ ^\circ\mathrm{C}} \xrightarrow[\text{-35 °C, 1 h to rt; 2. H}^+]{\text{1. PhCOCl}} \mathrm{H_{11}C_6C(O)Ph}$$

n	LiX	red. temp. (°C)	% Yield
2	LiBr	-100	57
1	LiBr	-100	38
2	LiBr	-78	40
2	LiBr	-20	9
2	LiCl	-100	55
1	LiCl	-100	42
2	LiCl	-78	43

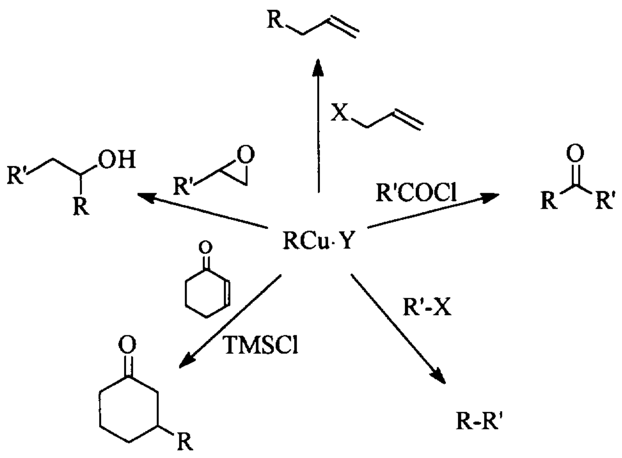
Np = naphthalene

Table 13. Formation of Functionalized Organocopper Reagents

Active Copper [a]	Organohalide	Cu*:R-X	Temp (°C)	[Organocopper]
A		1:0.25	-35	
A		1:0.25	-35	
A		1:0.25	-35	
A		1:0.4	-100	
C		1:0.21	-35	
A		1:0.25	-100	
B		1:0.5	0	
A		1:0.20	-35	
B		1:0.5	25	

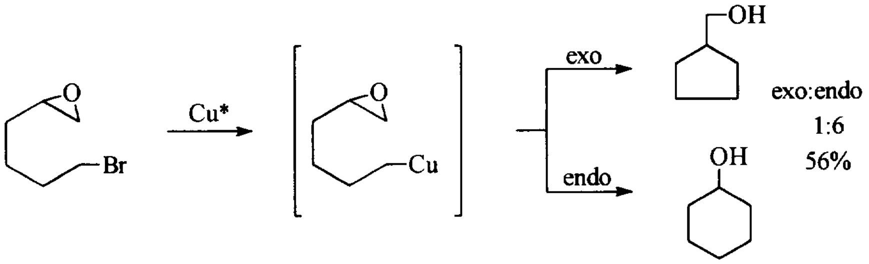
a) Active copper derived from the reduction of: A, CuCN ·2LiX; B, CuI·PBu_3; C, CuI·PPh_3

reactions. The regioselectivity is affected by the substitution pattern, reaction solvent, and the copper iodide-phosphine complex used to generate the active copper. Electron withdrawing groups in the benzene ring led to exo attack. Electron donors in the benzene ring produced mixtures of exo to endo products with the exo dominating (Scheme 42).



Y = PEt3, PPh3, or [(CN)Li·LiX]

Scheme 40

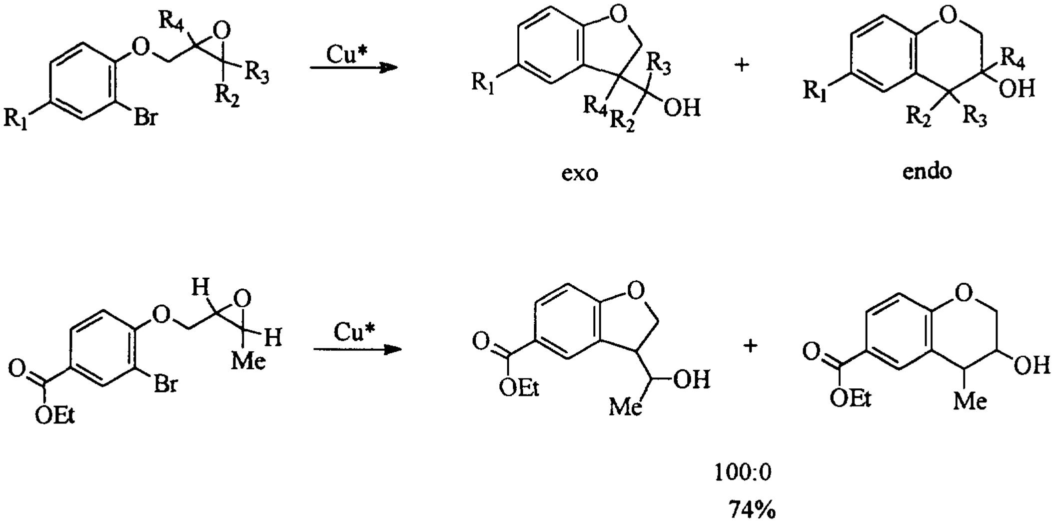


Scheme 41

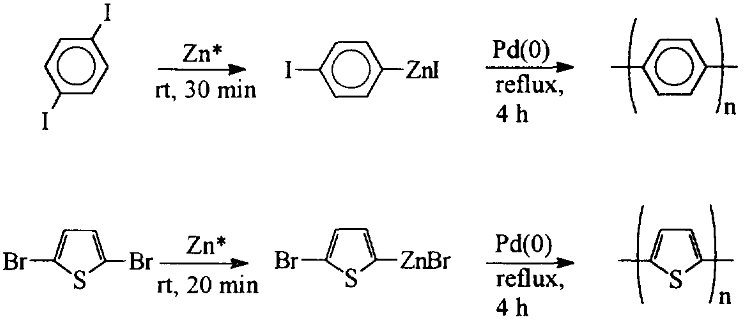
7 Active Metals in the Preparation of Polymers

Monoorganozinc arylenes were generated by the reaction of active zinc with dihaloarylenes. These reactions were totally chemoselective for the mono organozinc arylenes. The $Pd(PPh_3)_4$ catalyzed polymerization gave a quantitative yield of polyarylenes (Scheme 43).[43]

A temperature dependence for the regioselectivity in the oxidative addition of active zinc to 2,5-dibromo-3-alkylthiophenes can be used to obtain 97 to 98% of 2-bromo-5-(bromozincio)-3-alkylthiophene 5.[43, 44] The lower the initial temperature of the oxidative addition, the higher the regioselectivity (Table 14). These substrates also



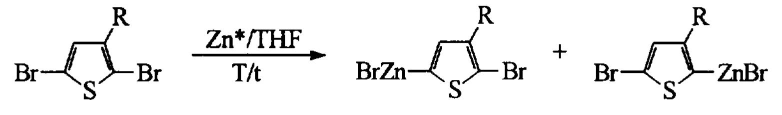
Scheme 42



Scheme 43

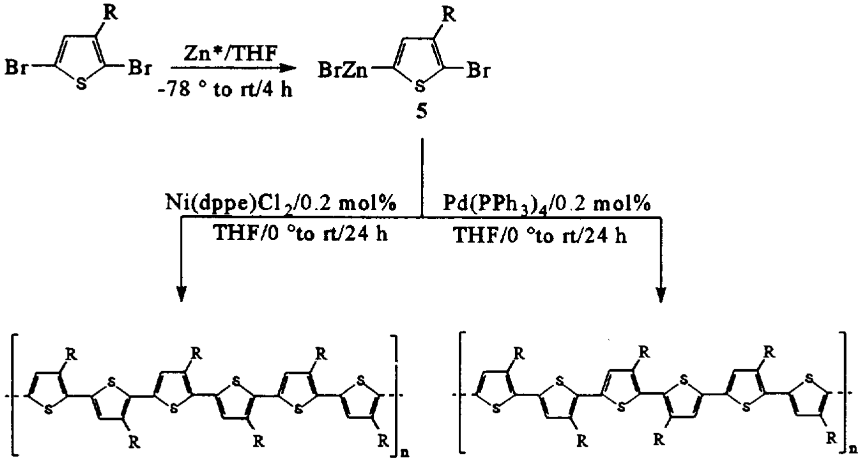
displayed high chemoselectivity in the oxidative addition. Compound **5** was polymerized with Ni(dppe)Cl_2 ([1,2-bis-(diphenylphosphino)ethane]nickel(II) chloride) to afford a completely regioregular head-to-tail poly-3-alkylthiophene **6**. A totally regiorandom polymer (**7**) was obtained using $Pd(PPh_3)_4$ as the catalyst. The regioregular head-to-tail poly-3-alkylthiophenes were characterized as a class of polymers with regiospecific head-to-tail configuration, markedly extended conjugation length, self-organized structure of polymer chain, low bandgap, and a polycrystalline texture. The average molecular weight of the polymers was 4×10^4 with an average molecular number of 3×10^4 and a polydispersity index of 1.4. The regioregular poly-3-alkylthiophenes had considerably higher neutral and doping conductivities than those of the regiorandom polymers.

Table 14. Regioselectivity of Active Zinc



5

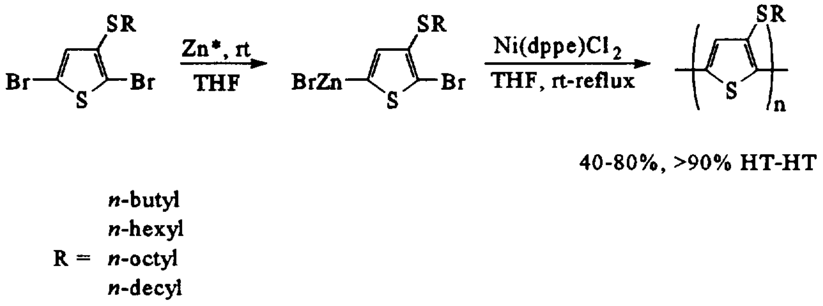
R	T (°C)/t (h)	5-(bromozincio):2-(bromozincio) (%)
n-hexyl	rt/1 h	90:10
n-hexyl	-45 to rt/4 h	93:7
n-hexyl	-78 to rt/4 h	97:3
n-butyl	-78 to rt/4 h	94:6
n-octyl	-78 to rt/4 h	98:2
n-tetradecyl	-78 to rt/4 h	98:2



(6a-f)
HT-HT linkage only

(7a-c)
HT-HT:HT-HH:TT-HT:HH-TT = 1:1:1:1

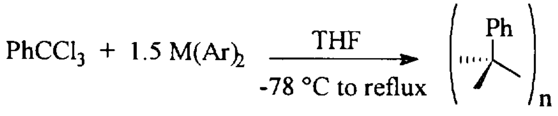
R		a: *n*-butyl	b: *n*-hexyl	c: *n*-octyl	d: *n*-decyl	e: *n*-dodecyl	f: *n*-tetradecyl
Yield (%)	6	80	82	79	77	71	67
	7	99	98	98			



Scheme 44

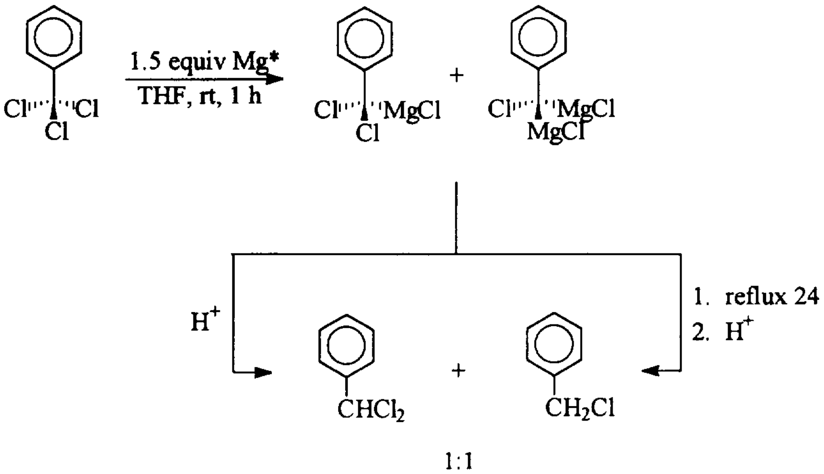
The synthesis of head-to-tail poly[3-(alkylthio)thiophenes] in which the sulfur atom of the substituent is directly connected to the 3-position of the thiophene ring can be achieved through 2,5-dibromothiophenes. The regioselectivity of the oxidative addition is >95% for the 5-position at rt.[45] Polymerization of the 2-bromo-5-(bromozincio)-3-(alkylthio)thiophenes was performed with Ni(dppe)Cl$_2$ (0.5%) to produce polymers in 40-80% yields (Scheme 44). Poly[3-(alkylthio)thiophenes] are soluble in carbon disulfide at rt, but are hardly soluble in other solvents at rt. The iodine doped polymer films range in conductivities from 450 to 750 S/cm. These polymers are polycrystalline and self-orienting.

Poly(phenylcarbyne) can be obtained in good yield from the reaction of group(II) active metals with α, α, α-trichlorotoluene (Scheme 45).[46] The active metals Ba*, Ca*, Sr* are effective reagents for this polymerization. The insoluble metal, Mg*, did not facilitate the formation of polymer. The products from the reaction upon workup were α-chlorotoluene and α, α-dichlorotoluene (Scheme 46). This result suggests a free-radical mechanism in the polymerization to form poly(phenylcarbyne) mediated by homogeneous metals (Scheme 47). The polymerization is assumed to proceed by free radical coupling generated by a single-electron transfer between M(biphenyl)$_2$ and the carbon-chlorine bond[47] followed by extrusion of a chlorine anion.

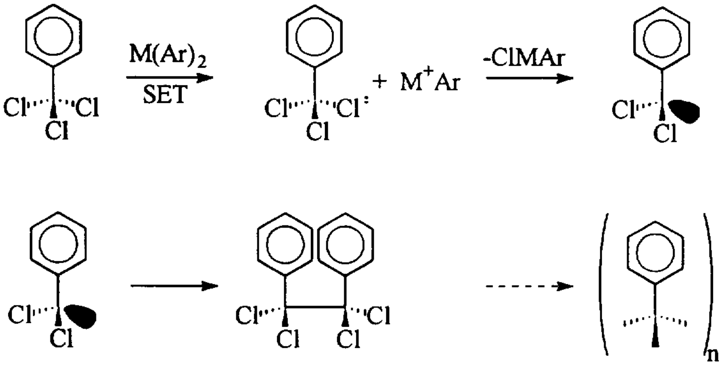


M = Ca, 46%; M = Sr, 42%; M = Ba, 42%

Scheme 45



Scheme 46



Scheme 47

8 Conclusion

The above survey displayed recent and novel advances in active magnesium, zinc, indium, calcium, and copper. The above mentioned methods of metal preparation have been applied to a number of other metals including Ni,[48] Al,[49] Co,[48b, 48d, 50] Fe,[48b, 48c] Pt,[48a, 48b] Pd,[48a, 48b] Cd,[51] Th,[52] Mn,[53] and Cr.[54] The scope of this report does not lend itself to a complete discussion of these additional metals.

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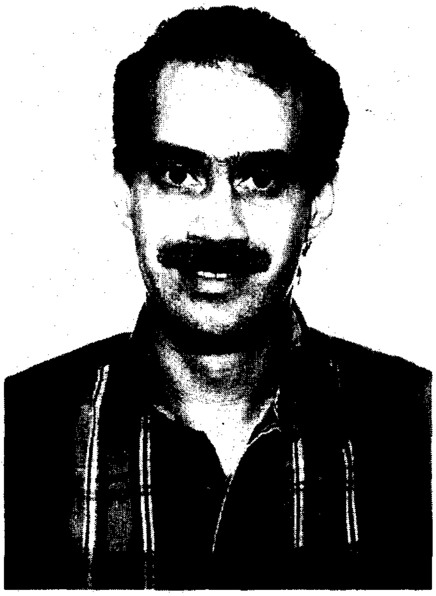
Biographical Sketch

Reuben D. Rieke



Mark V. Hanson

Reuben D. Rieke grew up in Fairfax, Minnesota. He received a Bachelor of Chemistry degree from the University of Minnesota-Minneapolis, doing undergraduate research with Professor Wayland E. Noland. He received a Ph.D. from the University of Wisconsin-Madison in 1966 under the direction of Professor Howard E. Zimmerman. He then did postgraduate work with Professor Saul Winstein at UCLA. He taught at the University of North Carolina at Chapel Hill from 1966 to 1977 and at North Dakota State University in Fargo from 1976 to 1977. He is currently Howard S. Wilson Professor of Chemistry at the University of Nebraska-Lincoln. His present research interests include the development and utilization of novel organometallic reagents derived from highly reactive metals. He also is interested in the synthesis of novel polymers using highly reactive metals.

Mark Hanson was born in Ft. Riley, KS in 1962. He received his B.S. (1989) in chemistry from the University of South Dakota and his M.S. (1992) from the University of Minnesota-Duluth. He obtained his Ph.D. in organic chemistry from the University of Nebraska-Lincoln (1996) working under Professor Reuben D. Rieke. He is currently a postdoctoral fellow at Iowa State University.