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Review

CARBOMETALLATION : ADDITION OF ORGANOMETALLIC COMPOUNDS TO ISOLATED MULTIPLE BONDS IN FUNCTIONALLY SUBSTITUTED COMPOUNDS

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CONTENTS

I. Introduction 2
II. Carbomagnesiation of isolated double bonds 2
1. Carbomagnesiation of alkenols 2
2. Mechanism of the reaction 4
3. Stereochemistry 5
4. Carbomagnesiation of isolated double-bonds 9
5. Effect of solvent and catalysis by transition metals 12
III. Carbomagnesiation of allenols and acetylenic compounds 13
1. Allenols 13
2. Acetylenic compounds 14
IV. Behaviour of other organomagnesium compounds 16
V. Organolithiation of isolated multiple-bonds 17
VI. Addition of other organometallic compounds to isolated multiple bonds 23
VII. References 26

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I. INTRODUCTION

After the discovery of organomagnesium compounds by Victor Grignard there were several reports on their tendency to add to a variety of polar functional groups [1,2]. Although there are reports on the addition of Grignard reagents to a double bond in fulvenes [3-5] and α,β-unsaturated carbonyl compounds [6-8] by using copper catalysis these were generally found to be unreactive towards unconjugated carbon - carbon multiple bonds.

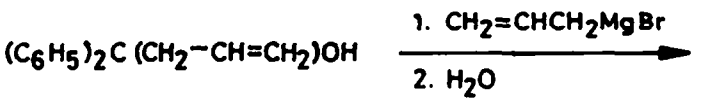
Podall and Foster [9] have reported that diethylmagnesium in diethyl ether reacted with ethylene at 50 atm. pressure and 100°C temperature to yield dibutylmagnesium. Later Shepherd [10] found that 1:1 adducts were formed between α-olefins (e.g., ethylene and isobutylene) and sec-alkyl, tert-alkyl or 2-alkenylmagnesium and trialkylaluminium compounds at temperatures of 100-150°C and pressures of 500-800 psi. Lehmkuhl [11-13] also found that addition of organomagnesium and -zinc compounds to 1-alkenes or 1,2- or 1,3-dienes to yield addition products. This reaction was found to be useful in the synthesis of various organic compounds [14-17] including natural products [18-20]. Recently this reaction has been reviewed [21]. The additions of organometallic compounds to multiple bonds intramolecularly (i.e., organomagnesium rearrangements) [22,23], to acetylenic compounds [24] and to enynes [25] have also been reviewed.

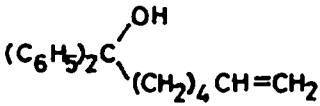
II. CARBOMAGNESIATION OF ISOLATED DOUBLE BONDS

1. Carbomagnesiation of alkenols :

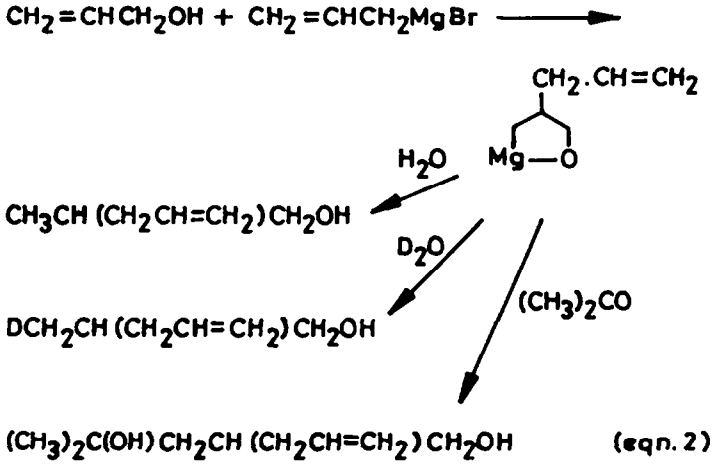
In 1965 Eisch and Husk [26] observed the addition of allylmagnesium bromide at the double bond of 1,1-diphenylbut-3-en-1-ol (eqn. 1) during the latter's preparation from benzophenone and allylmagnesium bromide.

The addition of C-Mg to a C-C multiple bond is termed as 'Carbomagnesiation'. In 1966 Cherest, Felkin, Frajerman, Lion, Roussi and Swierczewski [27] also reported the addition of reactive Grignard reagents (e.g., allyl and benzyl) to the double bond of





(eqn. 1)



(eqn. 2)

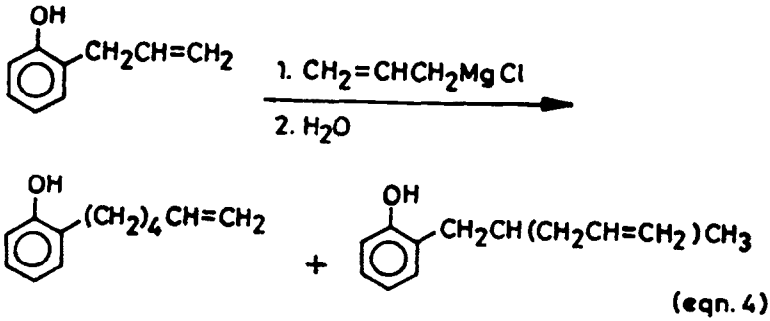
allyl alcohol (eqn. 2).

During kinetic studies [28] with cinnamyl alcohol, it was found that the reaction was strongly catalyzed by magnesium bromide and the alkyl substitution at the double bond was found to hinder the reaction. Allyl, benzyl and tert-butyl magnesium bromides were found to add to 1,1-diphenyl-alkenols of the type shown in eqn.3 (where n = 0, 1, 2 and 4) to yield the corresponding carbinols or olefin after hydrolysis, in which the R group of the Grignard reagent was principally attached to the ω carbon (eqn.3) [29,30]. The addition of crotylmagnesium chloride to an allylic alcoholate derived from the addition of acrolein to the crotylmagnesium chloride was also observed [31]. o-Allylphenol was found to react with allylmagnesium bromide or chloride to furnish 6-(o-hydroxyphenyl)-1-hexene and 4-methyl-5-(o-hydroxyphenyl)-1-pentene

$$(C_6H_5)_2C(OH)(CH_2)_nCH=CH_2 \xrightarrow[2.\ H_2O]{1.\ CH_2=CHCH_2MgBr} (C_6H_5)_2C=CH(CH_2)_{n-1}CH_2CH_2CH=CH_2$$

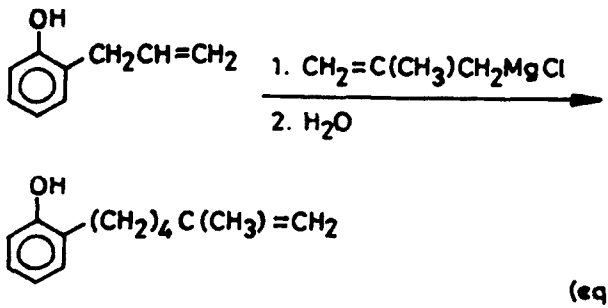
$(n=0,1,2)$ (eqn. 3)

products resulting from both possible orientations of addition (eqn. 4) [32].



(eqn. 4)

But o-allylphenol and (2-methyl-2-propenyl)magnesium chloride gave only 6-(o-hydroxyphenyl)-2-methyl-1-hexene (eqn. 5).



(eqn. 5)

2. Mechanism of the reaction :

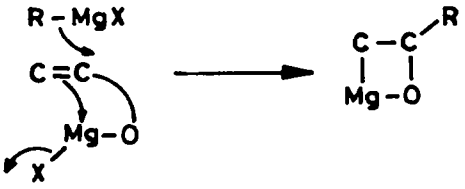
It has been established by many workers that the hydroxyl group plays a direct role in the addition of the allyl group to the double bond. The hydroxyl group promotes the addition of Grignard

reagents to isolated multiple bonds. The magnesium salt of the alkenol can react by either one of the two pathways proposed.

a) Intramolecular mechanism : Eisch and Husk [26] proposed that the reaction was facilitated by the proximity of the reacting bonds (eqn. 6).

(eqn. 6)

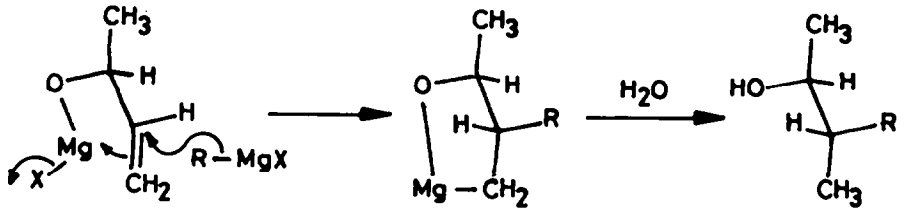
b) Intermolecular mechanism : Felkin and coworkers [27] suggested that the 'R' group adds from an external molecule of the organomagnesium compound (intermolecular nucleophilic attack), while -OMgX acts simultaneously as an internal electrophile (intramolecular electrophilic assistance) (eqn. 7).



(eqn.7)

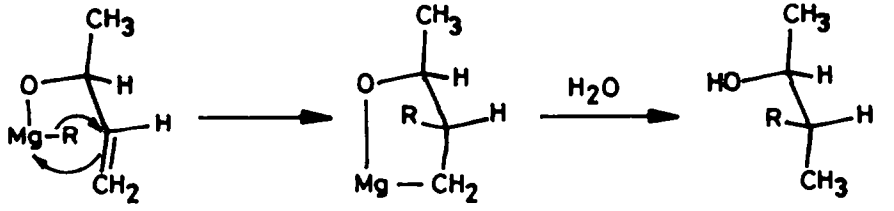
The intramolecular mechanism predicts syn addition of R and Mg to the face of the double bond nearest to the metalated hydroxyl group, whereas intermolecular mechanism predicts anti addition of R and Mg to the face of the double bond farthest from the hydroxyl group.

3. Stereochemistry : Felkin and coworkers [27] observed the formation of erythro- and threo-3-methyl-5-hexen-2-ols (8:1 ratio) from the reaction of allylmagnesium bromide and α-methallyl alcohol, which supports the intermolecular nature of the reaction (eqn. 8).



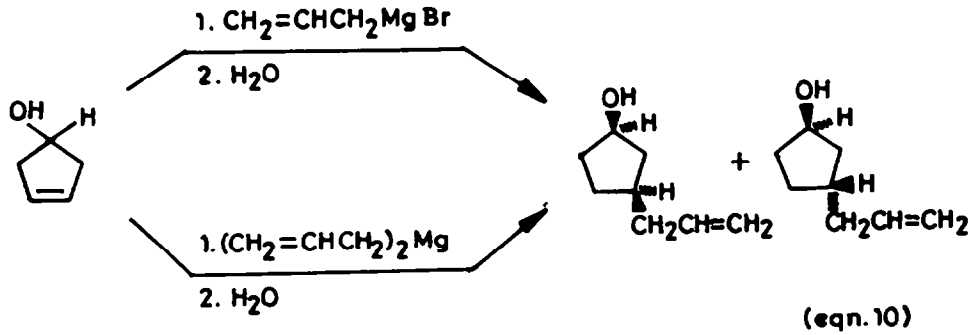
(eqn.8)

Intramolecular reaction would furnish probably the threo alcohol, since the pathway leading to the threo isomer keeps the bulky groups (CH_3 and CH_2) as far away as possible (Eqn. 9).



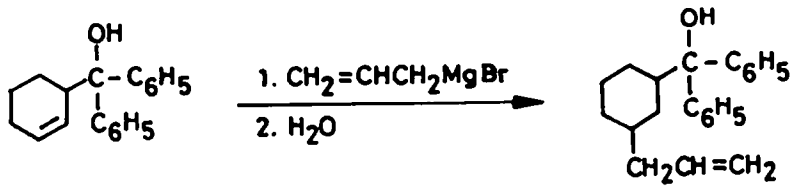
(eqn. 9)

Eisch, Merkley and Galle [33] during the stereochemical studies on carbomagnesiation found that 3-cyclopenten-1-ol with allylmagnesium bromide furnished a 4:1 mixture of cis- and trans-3-allylcyclopentanols. In contrast, the reaction with diallylmagnesium yielded only the cis- isomer (eqn. 10).



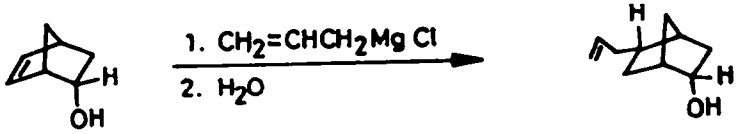
(eqn.10)

(2-Cyclohexenyl)diphenyl carbinol was also found to yield the cis-allyl derivative (eqn. 11). These results were ascribed due to the intramolecular rearrangement of an allylmagnesium alkoxide. The proximity of the allylmagnesium bond to the carbon-carbon π-bond brings about an electrophilic attack by the magnesium centre and hence a net syn addition.

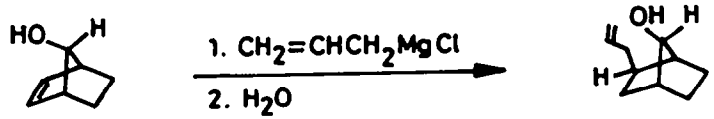


(eqn. 11)

Richey and coworkers [34,35] reported the stereochemistry of addition of allylic Grignard reagent to homoallylic alcohols, namely hydroxy bicyclo [2.2.1] heptenes. Reactions of endo-bicyclo [2.2.1] hept-5-en-2-ol and anti-bicyclo [2.2.1] hept-2-en-7-ol with allylmagnesium bromide or chloride yielded endo-5-allyl-bicyclo [2.2.1] heptan-2-ol (eqn. 12) and exo-2-allyl-syn-bicyclo-[2.2.1] heptan-7-ol (eqn. 13). All these results showed the



(eqn. 12)

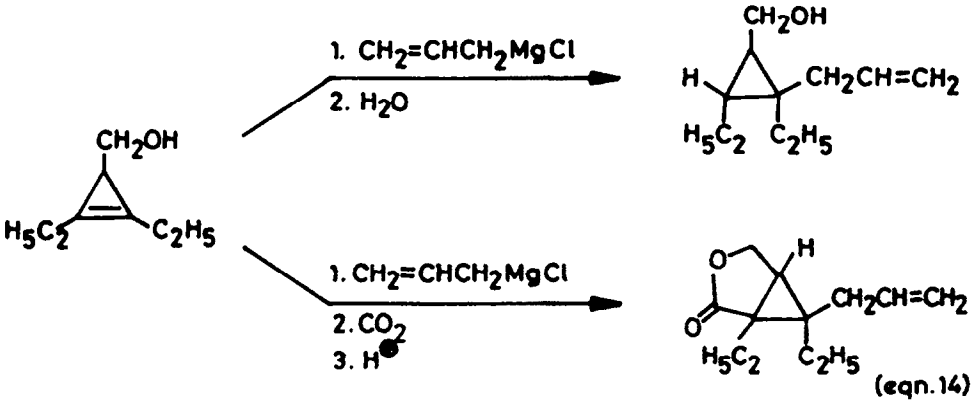


(eqn. 13)

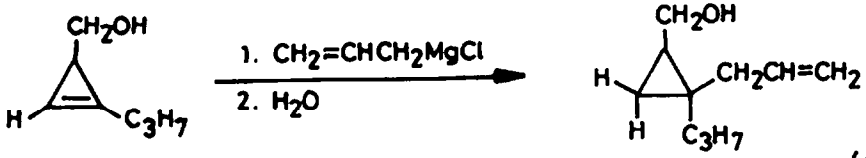
attachment of an allyl group to the face of the double bond nearest to the hydroxyl group, hence it was concluded that the intermolecular pathway is operative. These observations, however are

limited to allylic organomagnesium compounds and to homoallyl alcohols.

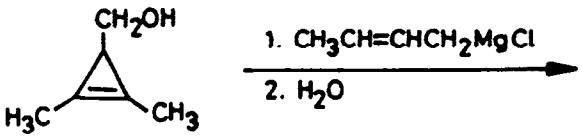
The stereochemistry of the addition of allylic Grignard reagents to the double bond of alkyl substituted 3-(hydroxymethyl)cyclopropenes was also studied [36]. In the products, both the allyl group and the group (H or COOH) replacing magnesium were cis to the hydroxymethyl group (eqn. 14). The new carbon-carbon bond was formed preferentially at the more substituted allylic carbon of the allyl group (eqn. 15) and at the more substituted carbon of the cyclopropene double bond (eqn.16).

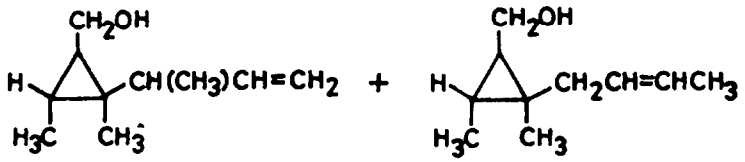


(eqn.14)



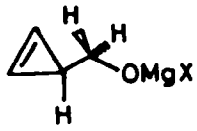
(eqn.15)





(eqn.16)

However only allyl Grignard reagents were found to be effective unlike cyclopropenes, which several Grignard reagents have been found to add under mild conditions [37-42]. It was detected that hydroxymethyl group retards the addition to cyclopropene. It was explained on the assumption that the geometry of the stable conformation of metalated 3-(hydroxymethyl)cyclopropene is such that in which -OMgX is farthest from the cyclopropyl ring.



4. Carbomagnesiation of double-bonded compounds bearing other functional groups :

The amine function can also promote addition of Grignard reagents to multiple bonds [43,44]. Thus allylmagnesium chloride adds to cinnamylamine, N,N-dimethylcinnamylamine and N-phenyl-allylamine to furnish allylated products (eqns. 17-19).

$$C_6H_5CH{=}CHCH_2NH_2 \xrightarrow[2.\ H_2O]{1.\ CH_2{=}CHCH_2MgCl} C_6H_5CH_2CH(CH_2CH{=}CH_2)CH_2NH_2 \qquad \text{(eqn. 17)}$$

$$C_6H_5CH{=}CHCH_2N(CH_3)_2 \xrightarrow[2.\ H_2O]{1.\ CH_2{=}CHCH_2MgCl} C_6H_5CH_2CH(CH_2CH{=}CH_2)CH_2N(CH_3)_2 \qquad \text{(eqn. 18)}$$

$$CH_2{=}CHCH_2NHC_6H_5 \xrightarrow[2\ H_2O]{1.\ CH_2{=}CHCH_2MgCl} CH_3CH(CH_2CH{=}CH_2)CH_2NHC_6H_5 \qquad \text{(eqn. 19)}$$

The promoting effect of a primary amino group is attributed to the presence of RNHMgX and RNHMgR species, which are isoelectronic with ROMgX and ROMgR species, presumably responsible for the effect of a hydroxyl group. Since tertiary amines cannot form analogous species, the promoting effect is attributed to the formation of complexes, in which -MgX or -MgR may have relationships to the double bond similar to those in ROMgX and ROMgR.

It is also noticed that the effectiveness of the metalated amino group is lower than the metalated hydroxyl group. This is due to the fact that the effectiveness in assisting additions increases with the decreasing basicity of the metalated assisting atom. Metalated primary amino group is more effective than by a tertiary amine function. Moreover it was observed that a metalated phenylamino group is more effective than a metalated primary amino group.

The addition of allyl Grignard reagents to the double bond of alkenylalkyl ethers [29,30] (e.g., 1-methoxy, 1,1-diphenyl-3-butene) and vinylpyridines [45] (e.g., 2- and 4-styrylpyridines) and anilines [29] (e.g., α-allylbenzhydrylaniline) were also reported.

Grignard reagents add to the double bond of vinylsilanes. The reaction is sensitive to the nature of substituents attached to the silicon atom and to the nature of the Grignard reagent [46]. Alkoxy and chloro groups were found to exert an activating effect to the extent that quantitative yields of addition products were frequently observed. Addition to β-carbon of the vinyl group was the major product (Table 1). The order of reactivity of Grignard reagents was found to be tertiary > secondary > primary. But phenylbenzyl- and allyl- Grignard reagents were found to afford only displacement products.

Aliphatic and aromatic Grignard reagents have been found to add

Table 1 : Addition of Grignard reagent with alkoxy silanes [46].

$$CH_2=CHSi\,R_{3-n}\,Y_n \xrightarrow{R'MgX} R'CH_2CH_2Si\,R_{3-n}Y_n + CH_3CHR'Si\,R_{3-n}Y_n$$

Vinyl silane		n	% Yield Addition products	% Yield Substitution Products
$CH_2=CHSi(Me)_{3-n}(OEt)_n$	i-PrMgCl	0	3	0
		1	100	0
		2	100	0
		3	71	29
$CH_2=CHSi(PhCH_2)_{3-n}(OMe)_n$	$C_6H_{11}MgBr$	1	100	0
		2	100	0
$CH_2=CHSi(Ph)_{3-n}(OMe)_n$	i-PrMgBr	1	100	0
	$C_6H_{11}MgBr$	2	100	0

across the double bond of fluoroolefins [47,48]. But the resulting adducts lose MgX_2 to give new fluoroolefins containing longer chain. The yields of the reaction was dependent on the structure of the Grignard reagent (eqns. 20-22).

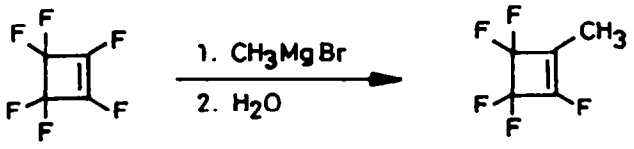
$$F_2C=CCl_2 + C_2H_5MgBr \longrightarrow [C_2H_5CF_2CCl_2MgBr] \longrightarrow C_2H_5CF=CCl_2 \quad \text{(eqn. 20)}$$

$$F_2C=CCl_2 + C_6H_5MgBr \longrightarrow C_6H_5CF=CCl_2 \quad \text{(eqn. 21)}$$

$$CF_3CF=CFI + CH_3MgBr \longrightarrow CH_3CF_2CF=CF_2 \quad \text{(eqn. 22)}$$

A similar reaction with perfluorocyclobutene and alkylmagnesium halide was also reported [49,50]. Thus methylmagnesium bromide

adds to perfluorocyclobutene and the resulting adduct loses MgFBr to afford 1-methylpentafluorocyclobut-1-ene (eqn. 23).



(eqn. 23)

5. Effect of solvent and catalysis by transition metals :

Although the donor coordination site on the olefin foster the carbomagnesiation reaction, too great a Lewis basicity of the coordination site on the substrate olefin or solvent strongly retards the reaction. This is due to the fact that if the magnesium is coordinated with a basic amine site or with THF molecules, its Lewis acidity towards an olefinic π-bond will be significantly lowered and hence its reactivity depressed (Table 2) [28].

Table 2 : Effect of solvent on the addition of allylmagnesium bromide to 1,1-diphenylbut-3-en-1-ol [28].

Solvent	Yield
Benzene	4%
Diethyl ether	60%
Tetrahydrofuran	1%

Temperature = RT Time = 95h

It was observed that nickelacetylacetonate fosters the carbomagnesiation reaction [28]. This is ascribed to the reactivity of π-allylnickel intermediates (eqn. 24) [51-53]. These nickel-allyls must be able to convert alkenoxymagnesium bromide into alkenoxy(allyl)nickel or magnesium reagents, which are capable of undergoing assisted allylation.

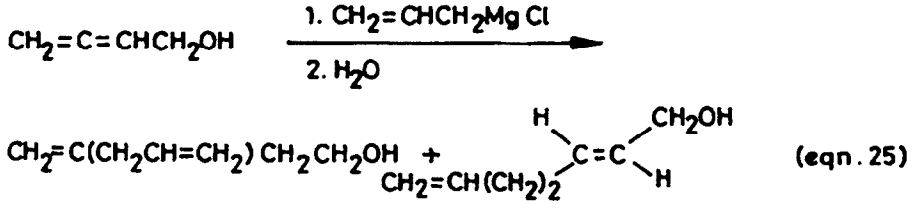
$$Ni(acac)_2 + 2CH_2{=}CHCH_2MgBr \longrightarrow$$

$$(\pi\text{-}CH_2CHCH_2)Ni + 2\,MgBr(acac) \qquad \text{(eqn. 24)}$$

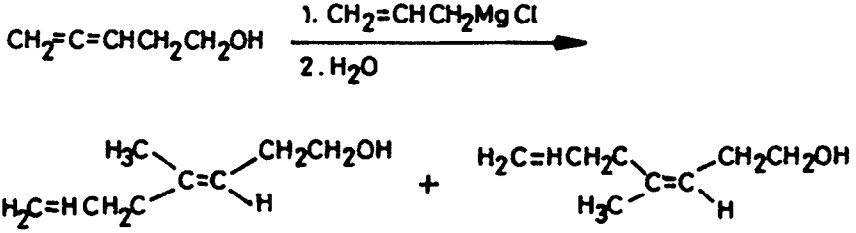
III. CARBOMAGNESIATION OF ALLENOLS AND ACETYLENIC COMPOUNDS

1. Allenols :

Richey and Szucs [54] observed that in the addition of allylmagnesium chloride to allenols bond formation occurs predominantly at the central carbon atom (eqn. 25,26).



(eqn. 25)



+ $CH_2=C(CH_2CH=CH_2)CH_2CH_2CH_2OH$

+ $CH_2=CHCH(CH_2CH=CH_2)CH_2\ CH_2OH$ (eqn. 26)

During the reaction of but-2,3-dien-1-ol with allylmagnesium chloride, the formation of 3-pentyn-1-ol and 4-pentyn-1-ol was also detected. The isomerization of allenol to alkynols was much more pronounced in THF rather than in diethyl ether. However, the major products (2-allyl-but-2-en-1-ol and 3-allyl-but-3-en-1-ol) obtained from the reaction of allylmagnesium chloride and 2-butyn-1-ol and 3-butynl-1-ol were not detected. Kinetic data also showed that the addition of allylmagnesium chloride to the allenol is at least 10-fold faster than the addition to 3-pentyn-1-ol. Intramolecular cyclisation of an allenic Grignard reagent was also reported [55].

2. Acetylenic compounds :

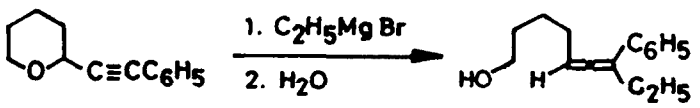
Vinylic or allylic Grignard reagents also add to alkynols [56], in which hydroxyl group promoting the addition as they do with alkenols. Acetylenic Grignard reagents were also found to undergo intramolecular cyclization [57]. Alkylmagnesium bromide were also found to add to the triple bond of 1,4-diamino-2-butynes (eqn. 27) [58], 1-alkoxy-4-amino-2-butynes (eqn. 28) [59], 4-(dialkylamino)-2-butyn-1-ols (eqn. 29) and tert-α-acetylenic alcohols and amines [60]. This is a method for the preparation of mono- or di-functional trisubstituted olefins.

$$H_2NCH_2C\equiv CCH_2NH_2 \xrightarrow[2.\ H_2O]{1.\ R^1MgBr} H_2NCH_2CH=CR^1CH_2NH_2 \qquad \text{(eqn. 27)}$$

$$H_2NCH_2C\equiv CCH_2OR^1 \xrightarrow[2.\ H_2O]{1.\ R^2MgBr} H_2NCH_2CH=CR^2CH_2OR^1 \qquad \text{(eqn. 28)}$$

$$R^1_2NCH_2C\equiv CCH_2OH \xrightarrow[2.\ H_2O]{1.\ R^2MgBr} R^1_2NCH_2CH=CR^2CH_2OH \qquad \text{(eqn. 29)}$$

It was concluded that the regioselectivity of the reaction depended on the nature of the functional groups located near the triple bonds and also on the nature of the substituents on the functional groups. Treatment of (2-phenylethynyl)-tetrahydropyran with ethylmagnesium bromide yielded 7-phenylnona-5,6-dien-1-ol



(eqn. 30)

quantitatively [61], providing a useful synthetic make to this compound (eqn. 30).

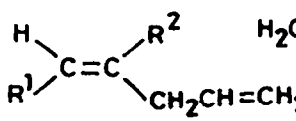
von Rein and Richey [62] studied the stereochemistry of the addition of Grignard reagents to alkynols. Usually trans-addition products, in which 'R' moiety of the RMgX near or farthest from the hydroxyl group were observed. However in some reactions trans-addition were accompanied by cis-addition products (Table 3).

Table 3 : Addition products from reactions of Grignard reagents with alkynols [62].

$R^1C{\equiv}CR^2 \xrightarrow[2.\ H_2O]{1.\ CH_2{=}CHCH_2MgX}$ Products

R_1	R_2	Time	Solvent	Hydrolysis products(% yield)		
				1	2	3
CH_3	CH_2OH	24	Ether	85	--	--
		48	THF	79	--	--
CH_3	$CH(OH)CH_3$	54	THF	22	--	--
CH_3	CH_2CH_2OH	120	THF	43	10	2
		120	Ether	50	25	--
CH_3	$CH_2CH(OH)CH_3$	48	THF	32	8	4
		48	Ether	45	14	16
C_2H_5	$CH_2CH(OH)CH_3$	168	THF	12	13	11
		72	Ether	3	24	--
CH_3	$(CH_2)_3OH$	72	THF	--	7	--

Reaction temperature = 50°C



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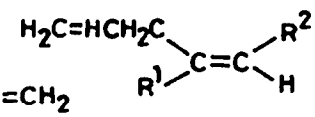

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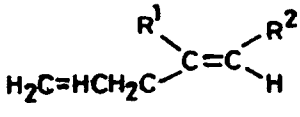
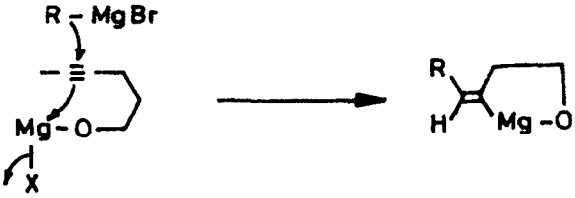


3

Formation of products arising from cis addition is attributed to the isomerization of alkynols to allenols. Moreover allenols were also noticed in small amounts in the reaction mixture. The products resulting from cis addition is observed during the addition of Grignard reagents to allenols [54]. This type of trans addition is expected if the reaction proceeds by a concerted mechanism (eqn. 31).



(eqn.31)

Miller and Reichenbach [63] observed the addition of allylmagnesium chloride to propargyl alcohols (eqn. 32). They also observed an unusual addition of ethylmagnesium bromide to propargyl alcohol (eqn. 33).

$$RC\equiv CCH_2OH \xrightarrow[2.\ H_2O]{1.\ CH_2=CHCH_2MgCl} RCH=C(CH_2CH=CH_2)CH_2OH$$

$R = -CH_3, -Si(CH_3)_3$ (eqn.32)

$$HC\equiv CCH_2OH \xrightarrow[2.\ H_2O]{1.\ C_2H_5MgBr} H_2C=C(C_2H_5)CH_2OH$$

(eqn.33)

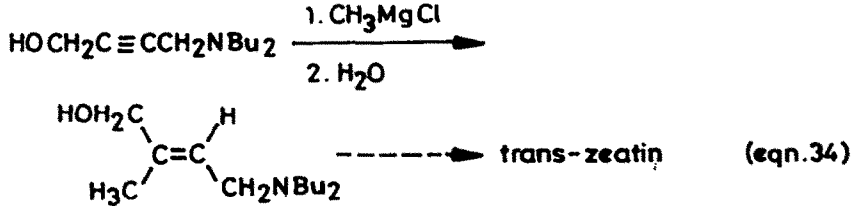
The addition of Grignard reagents to alkynols has been used in the synthesis of trans-zeatin (eqn. 34) [64].

IV. BEHAVIOUR OF OTHER ORGANOMAGNESIUM COMPOUNDS :

The literature shows that only active Grignard reagents such as benzyl, allyl and tert-butyl are capable of alkylating alkenols

but ordinary alkyl and aryl Grignard reagents are able to alkylate the multiple bonds except in a few instances [63,64]. Diallylmagnesium was also proved to be an effective allylating reagent [33].

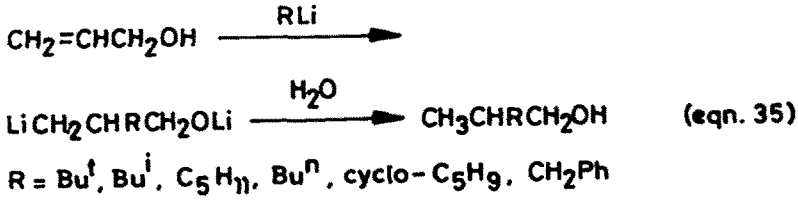
Eisch and Merkley [30] suggested that the greater the electron density available in the R-Mg bond, the more readily the group R would migrate to the olefinic bond. On this view, tert-butyl Grignard reagents owe their activity to the inductive electron release by the substituent methyl groups. Allyl and benzylic Grignard reagents are more reactive because electron delocalization will reduce the energy necessary to heterolyze the bond in the alkoxymagnesium salt.



(eqn.34)

V. CARBOLITHIATION OF ISOLATED MULTIPLE BONDS :

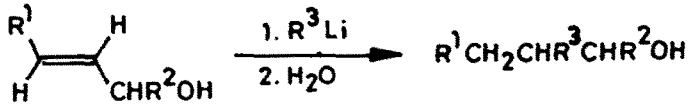
Organolithium reagents also add to the double bond of lithium salts of allylic alcohols in a regiospecific manner to give 2-substituted-1-propanols (eqn. 35) [65-67] as shown in Table 4.



(eqn. 35)

The yields of the products were found to increase in the presence of N,N,N',N'-tetramethylethylenediamine. The orientation of the addition is attributed to the greater stability of primary organolithium species produced compared to the secondary organolithium species that would have been formed by the alternate mode of addition. In a similar reaction Felkin and coworkers observed α-substituted alcohols to yield threo alcohols, which in contrary

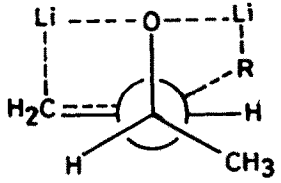
Table 4 : Addition of organolithium reagents to allyl alcohols



R^1	R^2	R^3	Temp °C	Time h	Hydrolysis products % yield in the absence of TMEDA	In the presence of TMEDA	Ref
H	C_6H_5	C_2H_5	RT	2.5	--	30	66
H	H	n-C_3H_7	RT	2.5	--	73	66
C_6H_5	H	n-C_3H_7	RT	2.5	--	70	66
H	CH_3	n-C_3H_7	RT	2.5	--	65	66
H	H	n-C_4H_9	RT	8.0	--	72	65
H	H	n-C_4H_9	97	2.5	5	--	65
H	H	iso-C_3H_7	97	2.5	48	--	65
H	H	iso-C_3H_7	97 RT	1.0 22.0	83	--	65
H	H	tert-C_4H_9	RT	7.0	17	--	65
H	H	tert-C_4H_9	RT	7.0	--	25	65
H	H	tert-C_4H_9	97	2.5	22	--	65
H	H	cyclopentyl	RT 79	4.0 1.5	--	68	65
H	H	C_6H_5	61	18.0	--	83	65
H	H	$C_6H_5CH_2$	65	11.0	--	83	65

to the carbomagnesiation of allyl alcohols to yield erythro alcohols [27]. The stereochemistry of the organolithiation reaction is due to the form of the transition state, in which the attacking organolithium reagent takes advantage of prior coordination at the lithium alkoxide function in order to add to the

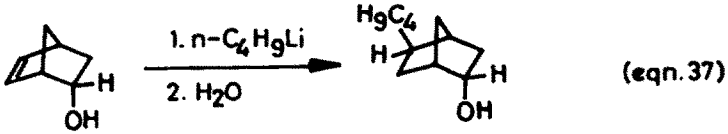
double bond by a cyclic mechanism.



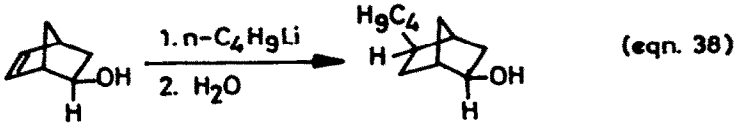
This transition state is more stable than the diastereomeric one with the H and CH_3 groups of the carbinol carbon interchanged. A similar hydroxyl group induced butylation of the double bond in α-vinylbenzyl alcohol in the presence of TMEDA in a highly stereospecific manner was also reported (eqn. 36) [68,69].

$$C_6H_5CH(OH)CH=CH_2 \xrightarrow[2.\ H_2O]{1.\ n\text{-}C_4H_9Li,\ TMEDA} C_6H_5CH(OH)CH(C_4H_9)CH_3 \qquad \text{(eqn. 36)}$$

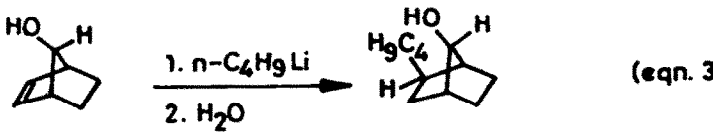
Addition of n-butyllithium to hydroxy bicyclo [2.2.1] heptenes was also reported [70], in which addition of the butyl group to the double bond occurs at the exo-position (eqns. 37-40).



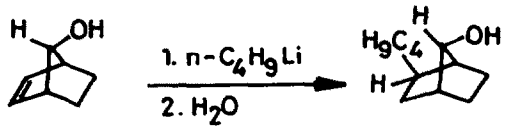
(eqn. 37)



(eqn. 38)

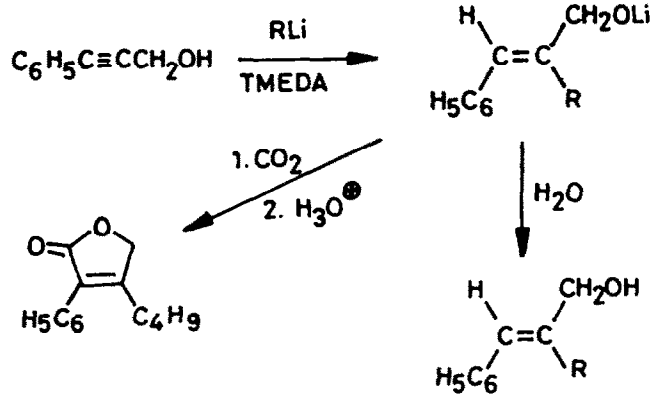


(eqn. 39)



(eqn. 40)

Alkyllithiums also add to the acetylenic alcohols [71,72]. Thus n-butyl-, benzyl-, and methyl-lithium add to phenylpropargyl alcohol to give the adduct in the E configuration (eqn. 41).



R= Bu, Me, CH_2Ph (eqn. 41)

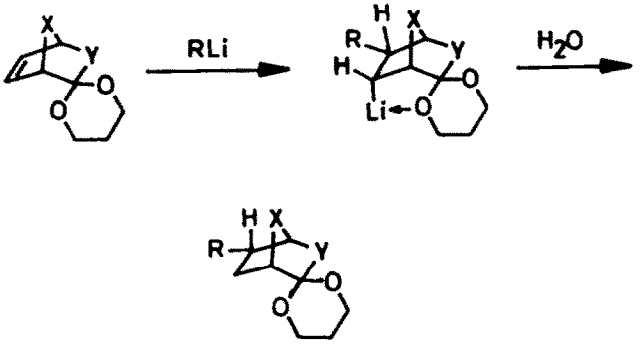
However it is not certain that the E configuration obtained is a direct result of the addition of organolithium to the substrate due to the rapid thermodynamic equilibrium of vinylic organolithium compounds [73,74]. A similar addition is facilitated by alkoxy, sulfide and amine groups also by coordination of heteroatom with lithium [75,76]. Isopropyllithium was found to add to the double bond of alkenyl ethers (e.g., allyl methyl ether, 2,2'-dimethyl-but-3-en-methyl ether, 2-methoxybicyclo [2.2.1] hept-5-ene). Isopropyl, tert-butyl and n-butyllithiums were also found to add to the unstrained unconjugated double bonds of alkenylamines e.g., N,N',2,2'-tetramethyl-but-3-en-1-amine, N,N'-dimethyl-bicyclo [2.2.2] oct-5-en-2-amine, 6-(N,N-dimethylamino)tricyclo-[3.2.0.$0^{2,4}$] non-8-ene and alkenyl sulfide (e.g., 1,1-dimethyl-prop-2-en methyl sulfide). Organolithium reagents also add to

allylamine to give α-substituted amines and ketones (eqn. 42) whereas tertiary amines yielded double bond addition products (eqn. 43) [45,77].

$$CH_2{=}CHCH_2NH_2 \xrightarrow[2.\ H_2O]{1.\ RLi} RCH_2CH_2\overset{O}{\overset{\|}{C}}R \qquad \text{(eqn. 42)}$$

$$C_6H_5CH{=}CHCH_2N(CH_3)_2 \xrightarrow[2.H_2O]{1.RLi} C_6H_5CH_2CHRCH_2N(CH_3)_2 \qquad \text{(eqn. 43)}$$

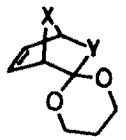
Kool and Klump [78] reported the addition of alkyllithiums to 2-alkenyl-1,3-dioxanes, which are of synthetic significance (eqn. 44)(Table 5).



(eqn. 44)

A similar reaction with open-chain 1,3-dioxanes was also reported. In all cases initial complexation of RLi to the functional group (-OH, -OR, $-NR_2$, -SR) is considered to be the cause for the stereo and regio selectivities of the reactions. Stabilization of the addition products by intramolecular chelation (as shown in eqn. 44) is supposed to be another factor for the rate enhancement. Isopropyllithium adds to the double bond of 7-tert-butoxynorbornadiene to give 7-tert-butoxy-2-isopropylnorborn-5-ene [79].

Table 5 : Addition of alkyllithiums to alkenyl-1,3-dioxanes [78].



Alkyllithium	X	Y	Addition Product Yield %
n-BuLi	$(CH_2)_2$	Nil	100
iso-Pr	$(CH_2)_2$	Nil	100
tert-Bu	$(CH_2)_2$	Nil	100
iso-Pr	$(CH_2)_2$	CH_2	75
n-Bu	$(CH_2)_2$	CH_2	20
iso-Pr	$(CH_2)_2$	CH_2	100
tert-Bu	$(CH_2)_2$	CH_2	90
n-Bu	$(CH_2)_3$	CH_2	60
iso-Pr	$(CH_2)_3$	CH_2	90
tert-Bu[a]	$(CH_2)_3$	CH_2	100

Temperature of the reaction = 25°C. In some cases minor products were also detected, which are not indicated here.
[a]Temperature of the reaction = 0°C

Organolithium reagents also add to the double bond of triphenylvinylsilane and the reaction depends on relative reactivity and structure of organolithium reagent (Table 6) [80]. But triethylvinylsilane affords trans-products with organolithium reagents by addition-elimination sequence (eqn. 45) [81].

Addition of phenyllithium to allyl chloride was also reported [82]. But the adduct (resulting from C attack) undergoes an

Table 6 : Addition of organolithium reagents to triphenylvinylsilane [80].

$$(C_6H_5)_3SiCH=CH_2 + RLi \longrightarrow (C_6H_5)_3SiCH_2CH_2R$$

R	Time h	% Yield
n-butyl	44	67
Phenyl	6	84
p-tolyl	16	27
o-tolyl	6	17
α-naphthyl	10	8
p-dimethylaminophenyl	18	7

intramolecular reaction resulting cyclopropane (eqn. 46). This constitutes a synthetic method for the preparation of phenylcyclopropanes.

$$(C_2H_5)_3SiCF=CF_2 + RLi \longrightarrow$$

$$(C_2H_5)_3SiCF=CFR$$

R = Ph, Vinyl, allyl, Bu^n (eqn. 45)

$$CH_2=CHCH_2Cl \xrightarrow{PhLi} PhCH_2CH=CH_2 + Ph\text{-}\triangleleft \quad \text{(eqn. 46)}$$

VI. ADDITION OF OTHER ORGANOMETALLIC COMPOUNDS TO ISOLATED MULTIPLE BONDS

Organozinc compounds also found to add to carbon-carbon double bond [83-85]. Allylzinc bromide adds to 1-butenyldiethylamine to furnish allylated product in 60% yield (eqn. 47) [86].

$$CH_2=CHCH_2CH_2N(C_2H_5)_2 \xrightarrow[2.\ H_2O]{1.\ CH_2=CHCH_2ZnBr} CH_2=CH(CH_2)_5N(C_2H_5)_2 \qquad \text{(eqn. 47)}$$

Addition reactions of allylzinc compounds with unsaturated amines (ethylenic, acetylenic and allenic) were also studied. It was shown that this reaction constitutes a general method of synthesis of mono and diethylenic amines [87]. Allylzinc bromide adds to pent-2-en-4-yn-1-ol to give good yields of products resulting from mono and bis addition products in proportion depending on the reaction conditions [88] whereas allylmagnesium bromide gives 1-allylpent-4-yn-1-ol and 2-allylpent-3,4-dien-1-ol and allyllithium yields only 1-allylpent-4-yn-1-ol (eqns. 48-50).

$$HC\equiv CCH=CHCH_2OH \xrightarrow[2.\ H_2O]{1.\ CH_2=CHCH_2Li} HC\equiv CCH_2CH(CH_2CH=CH_2)CH_2OH \qquad \text{(eqn. 48)}$$

$$HC\equiv CCH=CHCH_2OH \xrightarrow[2.\ H_2O]{1.\ CH_2=CHCH_2MgBr} HC\equiv CCH_2CH(CH_2CH=CH_2)CH_2OH + CH_2=C=CHCH(CH_2CH=CH_2)CH_2OH \qquad \text{(eqn. 49)}$$

$$HC\equiv CCH=CHCH_2OH \xrightarrow[2.\ H_2O]{1.\ CH_2=CHCH_2ZnBr} HC\equiv CCH_2CH(CH_2CH=CH_2)CH_2OH + CH_2=C(CH_2CH=CH_2)CH=CHCH_2OH + CH_3-C(CH_2CH=CH_2)=CHCH=CHCH_2OH \qquad \text{(eqn. 50)}$$

Recently the addition of organometallic compounds to enzymes has been reviewed thoroughly [25].

The addition of unsaturated zinc bromides to various propargylic alcohols, propargyl amines and propargyl methyl ethers were studied (Table 7) [89,90]. Both mono and bis addition products were observed and their ratio was dependent on the reaction time and temperature. The ratios were explained in terms of the reversibility of the reaction.

Allylzinc bromide was found to add to the triple bond of organomagnesium or -zinc to afford mono- or di-allylated products (eqn. 51). A similar reaction of allylzinc bromide to vinyl Grignard to afford ∝-olefins was also reported [91].

$$CH_2=CHCH_2ZnBr + C_6H_5C\equiv CMBr \longrightarrow$$

$$CH_2=CHCH_2C(C_6H_5)=C(ZnBr)MBr$$

$$+ (CH_2=CHCH_2)_2CH(C_6H_5)C(ZnBr)MBr \qquad \text{(eqn. 51)}$$

Table 7 : Addition of unsaturated zinc bromide to acetylenic compounds [90].

$$HC\equiv CY \xrightarrow[2.\ H_2O]{1.\ RCH=CHCH_2ZnBr}$$

$$H_2C=C(CHRCH=CH_2)CH_2Y +$$

1a

$$H_2C=C(CH_2CH=CHR)CH_2Y$$

1b

R	Y	Time h	Temp °C	Hydrolysis products Yield % 1a + 1b	1a	1b
CH_3	CH_2OH	3	20	93	100	0
$CH_2=CH$	CH_2OH	24	20	70	99	1
		3	65	86	99	1
$CH_2=CH$	CH_2OH	24	20	77	72	28
		24	65	66	66	34

C_6H_5	CH_2OH	3	20	26	93	7
		3	65	35	84	16
		24	20	92	82	18
		24	65	67	74	26
C_6H_5	$CH(OH)CH_3$	24	20	63	42	58
		24	65	57	37	63
C_6H_5	$C(OH)(CH_3)_2$	24	65	34	30	70
CH_3	OCH_3	24	20	82	97	3
		8	65	46	92	8
		15	65	52	85	15
$CH_2=CH$	OCH_3	24	20	89	65	35
		24	65	81	53	47
C_6H_5	OCH_3	24	20	88	75	25
		24	65	58	64	36
CH_3	$N(CH_3)_2$	24	20	50	95	5
		8	65	30	90	10
$CH_2=CH$	$N(CH_3)_2$	24	20	22	66	34
		24	65	36	64	36
C_6H_5	$N(CH_3)_2$	24	20	69	81	19
		24	65	34	22	78

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