Chem. Rev. **2006,** *106,* 1032–1076

Vinylic Tellurides: From Preparation to Their Applicability in Organic Synthesis

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Received August 3, 2005

Contents

1. Introduction

The first organotellurium compound was reported more than 150 years ago with the synthesis of diethyl telluride by Wöhler in 1840.[1] From its first discovery to the middle of the twentieth century, organotellurium chemistry remained the chemistry of a curious element and did not spark much interest from the scientific community. However, the explosive development of selenium chemistry has attracted attention to the potentiality of the still undeveloped chemistry of tellurium analogues. This renewed interest has resulted in

10.1021/cr0505730 CCC: \$59.00

Gilson Zeni was born in 1970 in Irai, Brazil. He received his M.S. degree from the Federal University of Santa Maria-RS (South Brazil) in 1996, working under the direction of Prof. A. L. Braga, and his Ph.D. (1999) under the direction of Professor J. V. Comasseto (the University of São Paulo). He then moved to the Federal University of Santa Maria, where he is now an Associate Professor. In 2003, he received a CNPq Postdoctoral Fellowship to work with Prof. R. C. Larock at Iowa State University. His current research interests center around the synthesis and reactivity of organochalcogen compounds, the development of new synthetic methods, and novel catalysts for cross-coupling reactions of vinylic tellurides.

Diogo Seibert Lüdtke was born in Cachoeira do Sul, RS, Brazil, in 1979. He received his B.S. in Chemistry in 2000 from the Federal University of Santa Maria (South Brazil). In 2005, he completed his Ph.D. at the same university under the supervision of Prof. Antonio L. Braga, working with the synthesis of chiral selenium-containing amino acid derivatives and peptides, as well as with catalytic enantioselective synthesis mediated by chiral selenium ligands. His research interests are focused on the design, preparation, and application of new chiral organochalcogen ligands in asymmetric catalysis.

Rodrigo Barroso Panatieri was born in 1973 in Piratini, Brazil. He received his B.S. degree in 2001 and his M.S. degree in 2002, from the Federal University of Santa Maria-RS (South Brazil), working under the direction of Prof. Gilson Zeni. After that, he started, in the same group, his Ph.D. studies on the synthesis of acetylenic tellurophene derivatives via Pd-catalyzed cross-coupling. His research interests are focused on the improvement of cross-coupling reactions using organochalcogen compounds.

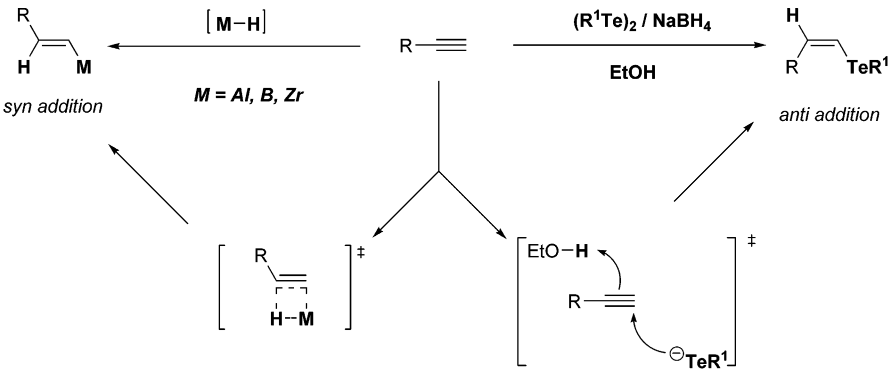
Antonio Luiz Braga was born in Tupã (SP State) and obtained his B.Sc. in 1982 from the Federal University of São Carlos (SP State). He received his M.S. and Ph.D. degrees from the University of São Paulo in 1984 and 1989, working under the direction of Prof. J. V. Comasseto in the field of organic selenium chemistry. In 1985, he obtained a position at the Federal University of Santa Maria-RS (South Brazil) as Assistant Professor, and he currently is still at the same place as Professor of Organic Chemistry. His research interests mainly reside in the catalytic applications of chiral organochalcogen compounds in asymmetric synthesis.

an impressive increase in the number of publications, which can be evidenced by the numerous review articles and books devoted to the various and different methodologies.[2] In fact, these many efforts and developments have transformed organotellurium chemistry into a very broad and exciting field with many opportunities for the research and development of applications.

Many different classes of organotellurium compounds have been prepared and studied to date, and vinylic tellurides are certainly the most useful and the most promising in view of their usefulness in organic synthesis. In addition to their utility in the field of organic chemistry, the toxicological and pharmacological aspects of organotellurium compounds have also been recently reviewed.[3]

However, the use of tellurium chemistry for synthetic organic chemists or as a tool in organic synthesis has been hampered due to a bad reputation related to the bad smell, toxicity, or instability of these compounds. In fact, these comments are true for a particular group of tellurium compounds, but it is not a rule for all tellurium compounds. In our lab, we have been using many different classes of tellurium compounds and have observed that tellurides or ditellurides bearing an alkyl group, with a low molecular weight, have a bad smell. However, when these alkyl groups present any additional substituent, the corresponding tellurides or ditellurides are practically odorless. Other tellurium compounds, such as organotellurium trihalides, diaryl tellurides, and ditellurides, are solids, very stable (can be stored in the lab, in a simple flask, for a long time), and completely odorless. In addition, the vinylic tellurides, one of the most used classes of tellurium compounds, containing either an aromatic or an aliphatic group with saturated or unsaturated chains, are all odorless compounds and can be easily prepared, purified, and stored as a common chemical used in the lab. Regarding toxicity, another reason that has

Scheme 1



hindered the development of organotellurium chemistry is that studies are still scarce in the literature. Some authors have described that organotellurium compounds are less toxic than their selenium derivatives,[2i] and others have indicated that organotellurium compounds are more toxic than organoselenium compounds.[3] We are sure, unlike most, that no highly specialized techniques are required in the handling of organotellurium compounds, and work with these compounds is very similar to work with any other class of chemical compounds, such as organoselenium, organosulfur, organotin, and organophosphorus.

During the preparation of this review, an excellent review by Professor N. Petragnani[4] appeared in the literature, which covered the advances in general organotellurium chemistry. Petragnani's article reviewed the methodologies for general organotellurium chemistry, and the specific class vinylic tellurides (synthesis and reactivity) was covered but not extensively discussed. Due to the growing importance and utility of vinylic tellurides in the field of organic synthesis, the fact that the last comprehensive review on the preparation and reactivity of this specific class of organotellurium compounds was published in 1997,[2s] and the many new remarkable findings and applications which have been published since then, this article is intended to critically and comprehensively review the several methods described for the preparation of vinylic tellurides. Furthermore, this article will also discuss vinylic telluride reactivity toward several different reaction conditions and the applicability of such transformations in organic synthesis. Finally, the use of vinylic tellurides in the synthesis of biologically active compounds will be covered. The synthesis and reactivity of aryl tellurides will not be discussed here, since it will be discussed in a chapter of the book by Professor J. V. Comasseto that will appear in the literature shortly.

2. Preparation of Vinylic Tellurides

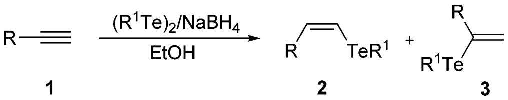
2.1. Preparation of Vinylic Tellurides by Nucleophilic Tellurium Species

2.1.1. Hydrotelluration of Alkynes

The hydrometalation of alkynes, such as hydroalumination,[5] hydroboration,[6] and hydrozirconation,[7] is a common method for the preparation of functionalized alkenes. Usually, the hydrometalation of an alkyne affords the *E*-alkene, by a *cis* addition of the hydrogen and the metal upon the triple bond in a four-membered transition state (Scheme 1). On the other hand, the hydrotelluration of alkynes is the most important and widely employed method for the preparation of vinylic tellurides.[8] It differs from the other hydrometalation reactions, since it proceeds in an *anti* fashion, as a result of an addition of an organotellurolate anion to the alkyne. This *anti* addition leads to the *Z*-vinylic telluride, which is stereochemically stable, since no isomerization to the *E* isomer has been reported to date. This characteristic makes the hydrotelluration reaction unique and a very important method for the generation of *Z*-alkenes, starting from alkynes, which are not easily accessible by other methodologies (Scheme 1).

The nucleophilic organotellurium species are most commonly generated *in situ* by the reduction of the corresponding diorganoditellurides with sodium borohydride in ethanol as solvent. Diorganoditellurides are used as precursors of tellurium anions due to the instability of the organotellurols, which cannot be isolated in the same way as the related selenols and thiols. The reduction of the diorganoditelluride can easily be visualized, since the initial dark red color of the solution disappears with the addition of sodium borohydride and a gas evolution is observed, resulting in a colorless solution at the end of the reduction. The exact structure of the species formed has yet to be determined. In view of the protic nature of the solvent, an equilibrium between the ionic species and the solvent can occur, suggesting that the most probable hydrotelluration agent is $(R^1Te)_2/NaBH_4$. The addition of the nucleophilic tellurium agent across the alkyne triple bond can give two regioisomeric products **2** and **3**, and the regioselectivity of the reaction is dependent on the nature of alkyne **1** (Scheme 2).[8]

Scheme 2



Although the first example of a reaction of a nucleophilic tellurium species with a terminal alkyne was reported in 1966,[9] this reaction has received little attention in the subsequent years, and only isolated examples were reported until the middle 1980s, when Comasseto and co-workers described a systematic study on the synthesis of vinylic tellurides, divinyl tellurides, and 1-(organyltelluro)-1,3-butadienes (Figure 1).[10]

Since this pioneering work, several different alkynes with different steric and electronic properties were subjected to hydrotelluration conditions, giving numerous different types of vinylic tellurides. Our aim here is to describe them, based on the structure of the starting alkyne, to discuss the differences in the reactivity of the substrates employed, and to comment on the regiochemistry and yields of the reactions.

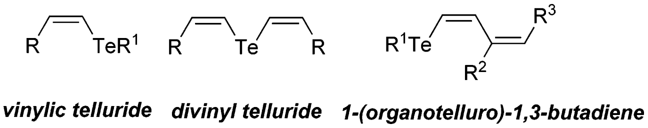
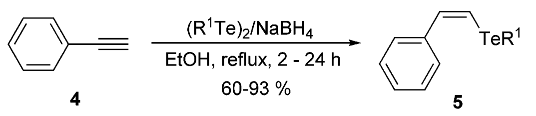


Figure 1.

2.1.1.1. Hydrotelluration of Alkynes via $(Rte)_2/NaBH_4$.

2.1.1.1.1. Hydrotelluration of Aryl and Alkyl Alkynes. Aryl alkynes are excellent substrates for the preparation of vinylic tellurides. For example, phenylacetylene (**4**) is hydrotellurated in very high yields with short reaction times, and it tolerates a variety of organotellurides containing different R^1 groups, such as butyl, phenyl, 4-methoxyphenyl, 2-thienyl, and vinyl (Scheme 3). The authors reported that alkynes bearing the aliphatic butyl group gave higher yields than those with an unsaturated group. In all cases, the reaction led to the 1,2-addition product **5** exclusively with *Z* stereochemistry.[10b,11]

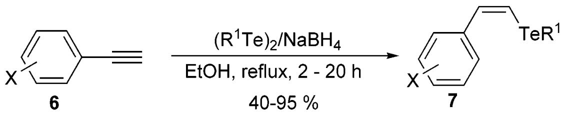
Scheme 3



R^1 = Bu, Ph, 4-MeOPh, 2-Th, $CH{=}CH_2$, $C(CH_3){=}CH_2$

Substituted aryl alkynes are suitable substrates for the preparation of *Z*-vinylic tellurides. The reaction is tolerant of several different functional groups in the alkyne, such as halogens (Cl, Br), alkyl groups, methoxy groups, and even more sensitive substituents, for example, carboxylic acids and esters (Scheme 4).[10b,12] In general, the electronic nature of the substituents at the aromatic ring does not have a significant influence on the yield of the reaction. Usually, the yields are high for both electron-donating and electron-withdrawing groups. Steric effects do not seem to exert a great influence, since similar yields are obtained with alkynes with substituents at all three possible positions on the aromatic ring. A decrease in the yield of the vinylic telluride **7** is observed when a free carboxylic acid[12a] or a nitro[12b] group is present in the starting alkyne **6**.

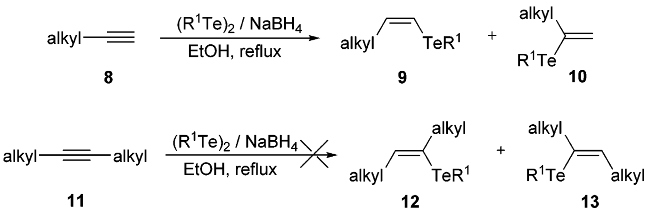
Scheme 4



X = Br, Cl, MeO, Me, NO_2, CO_2H, CO_2Et; R^1 = Me, Ph, $CH{=}CH_2$, $C(CH_3){=}CH_2$

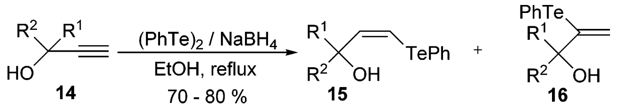
Conversely, alkyl-substituted alkynes **8** suffer from regioselectivity problems, as they give rise to two different regioisomeric vinylic tellurides, **9** and **10**. The 1,2-addition products predominate, whereas a lower amount (11−28%) of the 2,2-disubstituted product is formed. Vinylic tellurides **12** and **13** are not formed, since internal disubstituted alkyl alkynes **11** are not hydrotellurated (Scheme 5).[2d]

Scheme 5



2.1.1.1.2. Hydrotelluration of Hydroxy and Amino Alkynes. Hydroxy alkynes **14** are remarkable substrates for the hydrotelluration reaction, being that they furnish allylic alcohols, which are very important intermediates in organic synthesis. They can be further converted to a wide range of functional groups. Thus, the synthesis of allylic alcohols that contain stereodefined geometry of the double bond is of general interest in organic chemistry. Therefore, propargylic alcohols of different substitution patterns were subjected to hydrotelluration conditions and furnished the desired vinylic tellurides containing an allylic alcohol moiety (Scheme 6).[12a] The yields were typically good, and the regioselectivity of the reaction always favored product **15**. However, both regioisomeric tellurides **15** and **16** were easily separated by column chromatography.

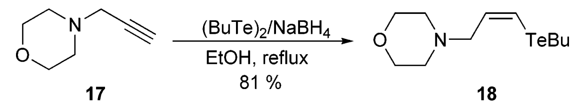
Scheme 6



15 : 16 *ratio:* 95-80 : 5-20; R^1 and R^2 = H, Me, *i*-Bu, cyclo-C_6H_{10}

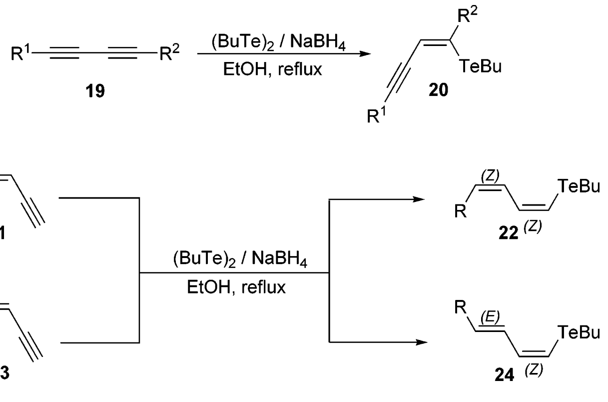
Similar to propargylic alcohols, propargylic amines can be hydrotellurated giving rise to allylic amines. For example, the morpholine-derived propargylic amine **17** was hydrotellurated with $(BuTe)_2/NaBH_4$, furnishing the *Z*-vinylic telluride **18**, containing an allylic morpholine, in 77% yield as a single isomer (Scheme 7).[10a]

Scheme 7



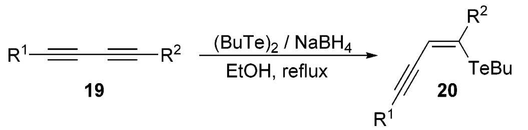
2.1.1.1.3. Hydrotelluration of Enynes and Diynes. Diynes **19** and enynes **21** and **23** can also be used as substrates for the hydrotelluration reaction (Scheme 8). These are very attractive precursors, since the product will be conjugated dienes **22** and **24** or enynes **20**, which can be further converted to highly unsaturated compounds with defined stereochemistry. In addition to their great utility in organic synthesis, enynes and diynes occur in numerous natural products.[13]

Scheme 8



One very relevant characteristic of this type of product is the possibility of obtaining stereodefined conjugated dienes in high yields with the *Z*,*Z* and *E*,*Z* combinations. This

Table 1. Hydrotelluration of Diynes



entry	R^1	R^2	time (h)	yield (%)
1	H	H	0.25	93
2	CH_2OH	CH_2OH	0.25	71
3	Me	Me	2.5	81
4	Ph	Ph	2.5	83
5	4-MePh	4-MePh	3	73
6	4-MeOPh	4-MeOPh	3	68
7	Ph	H	0.16	75
8	C_6H_{13}	H	0.28	79
9	Ph	Me	2	80
10	Ph	CH_2OH	0.25	76
11	Ph	Me_2COH	1	82
12	C_6H_{13}	CH_2OH	0.58	89
13[a]	Me_2COH	H	0.16	70

[a] A 88:12 mixture of regioisomers was obtained, favoring the 1,2-disubstituted product.

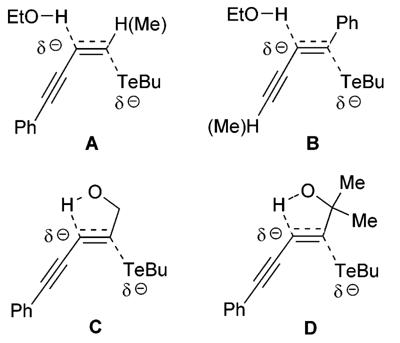


Figure 2.

represents a very important feature of the present methodology, because such conjugated systems are not easily obtained through other routes.[14]

Regarding the preparation of vinylic tellurides containing a triple bond, the reaction is usually very fast with symmetrical 1,3-diynes of different types. For instance, alkynes with substituents, such as propargyl alcohol, methyl, hydrogen, and aromatic rings, successfully react with the tellurium nucleophile, leading to the corresponding enynes functionalized with the organotellurium group in good to excellent yields (Table 1, entries 1−6). When the diyne carries aromatic substituents with an electon-donating group, the yield of the reaction is slightly lower than that for the parent phenyl substituent (compare entries 4 vs 5 and 6, Table 1).

Extending the above-mentioned studies, a remarkable paper has been published by Dabdoub and co-workers, in which they describe the chemioselective triple bond reduction of unsymmetrical butadiynes by treatment with the $(BuTe)_2$/$NaBH_4$ hydrotelluration system (Table 1, entries 7−13).[15] With the monosubstituted butadiynes, the reaction takes place exclusively at the terminal triple bond, leading to the *Z*-butyltelluro enynes in a very fast reaction and in good yields (Table 1, entries 7 and 8). The terminal triple bond is more reactive than the internal one, due to steric hindrance of the phenyl group, which hampers the attack of the telluride anion to the other triple bond. Further evidence of the influence that steric effects have on this system is the fact that when unsymmetrical disubstituted diynes are employed, for example, when the terminal hydrogen is replaced by a larger methyl group (Table 1, entry 9), the reaction is slower, taking 2 h for its completion. However, tellurium addition takes place exclusively at the methyl-substituted triple bond. A further explanation is given by the authors, who suggest that electronic effects are operating in the hydrotelluration of unsymmetrical diynes. The incipient negative charge, which is formed in the transition state at the adjacent carbon, is better stabilized by the phenylethynyl moiety (Figure 2, structure **A**) than by the ethynyl or propynyl groups (Figure 2, structure **B**).

In the case of propargylic substituents at one of the triple bonds, the reaction is faster than that with triple bonds bearing aryl or alkyl substituents. This fact is probably due to the formation of cyclic five-membered transition states of type **C** and **D** (Figure 2), which are trapped by hydrogen intramolecularly, rather than by hydrogen from the solvent. The more hindered the propargylic alcohol, the more difficult is the ring formation, explaining the longer reaction times when the two propargylic hydrogens are replaced by two methyl groups (Table 1, entries 10−12). In a single case (Table 1, entry 13), a mixture of regioisomers is obtained, where the attack of tellurium is favored at the terminal triple bond rather than at the propargilic position, resulting in an 88:12 regioisomeric mixture (Table 1, entry 13). On the basis of these data, the authors suggest the following order of reactivity for the butyltellurolate anion:

$$\text{terminal} > \text{propargylic} > \text{alkyl} > \text{aryl}$$

Another example of 1,3-diyne hydrotelluration was recently reported by Marino and Nguyen.[16] Unsymmetrical diyne alcohol **25** was selectively functionalized at the propargylic carbon−carbon triple bond (Scheme 9).

After several optimization studies, it was found that the stoichiometry as well as the reaction time were crucial for the outcome of the reaction. Thus, when 0.5 equiv of dibutyl ditelluride was employed and the reaction was stopped after 20 min at reflux, vinylic telluride **26** was obtained in high yield. However, when excess amounts of $(BuTe)_2$ and $NaBH_4$ were used with longer reaction times, the ditellurated product **27** was predominantly formed.

Moreover, tellurium-containing dienes are accessed by the hydrotelluration of enynes **28**.[10b,14a,b] The reaction takes place stereoselectively at the triple bond, yielding the corresponding tellurobutadienes **29** with the new double bond formed exclusively with *Z* stereochemistry (Table 2).

Only enynes bearing terminal alkynes are reactive toward the hydrotelluration conditions. Enynes with disubstituted triple bonds fail to react under the given conditions. An exception to this account is when the enyne **30** containing a propargyl alcohol is employed. In this case, the hydroxyl group at the propargyl position activates the butyltellurolate

Scheme 9

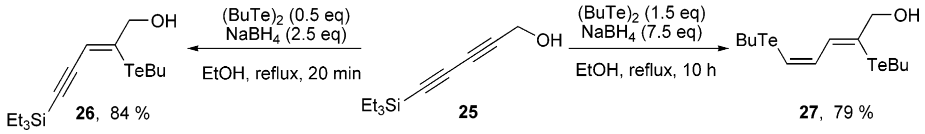
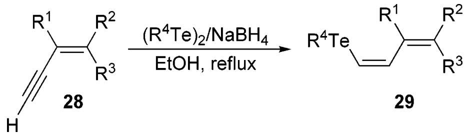


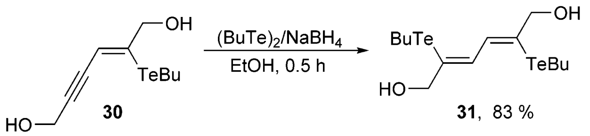
Table 2. Hydrotelluration of Enynes



entry	R^1	R^2	R^3	R^4	time (h)	yield (%)
1	H	H	OMe	Bu	28	50
2	Me	H	CH_2OH	Bu	2	69
3	H	H	TeBu	Bu	2	70
4	cyclo	$(CH_2)_4$	H	Bu	12	89
5	Me	H	CH_2OH	$C_{12}H_{15}$	5	80
6	Me	H	CH_2OH	4-MeOPh	5	70
7	Me	H	CH_2OH	4-MeOPh	5	91
8	Me	CH_2OH	H	$C_{12}H_{15}$	5	65
9	Me	CH_2OH	H	2-MePh	5	75
10	cyclo	$(CH_2)_4$	H	$C_{12}H_{15}$	5	60
11	cyclo	$(CH_2)_4$	H	4-MeOPh	5	53
12	Me	CH_2OTHP	H	Bu	4	83
13	H	CH_2OTHP	H	Bu	5	89
14	Me	H	H	Bu	5	75

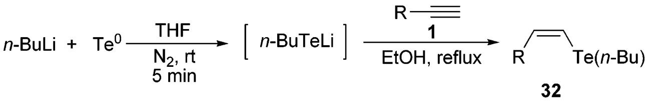
attack at the triple bond and affords the telluro butadiene **31** in 83% yield (Scheme 10).

Scheme 10



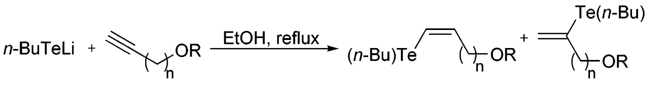
2.1.1.2. Hydrotelluration of Alkynes via BuLi/Te^0. Conversely, one of the major drawbacks of the hydrotelluration reaction is the use of dibutyl ditelluride as the precursor of the butyl tellurolate anion, since it is not commercially available. To circumvent this problem, an improved procedure to generate the butyl tellurolate anion was published in 2000.[17] This procedure consists of the reaction between butyllithium and elemental tellurium in THF at room temperature, which gives lithium butyl tellurolate, by the consumption of gray tellurium to form a pale yellow solution. To this solution, the alkyne dissolved in dry deoxygenated ethanol is added and refluxed (Scheme 11). The Z-vinylic tellurides **32** obtained by this newly developed method are obtained in similar yields to those observed by using the dibutyl ditelluride/$NaBH_4$ method. In addition, an intramolecular version of this hydrotelluration has been employed to prepare tellurium-containing heterocycles from terminal or internal alkynes. These studies indicated that this hydrotelluration affords both exo-*dig* and endo-*dig* cyclization products from moderate to good yields (Table 3).[18]

Scheme 11



2.1.1.2.1. Hydrotelluration of Hydroxy Alkynes. This method has been employed in regioselectivity studies on the hydrotelluration of hydroxy alkynes both of short and long chains (Scheme 12).[19] The best results in terms of regioselectivity were achieved when propargylic alcohol was hydrotellurated. The ratio of both products was 8:1, in favor of the 1,1-disubstituted vinylic telluride. In the case of the protected propargyl alcohol, this regioselectivity is lost, and the major product is the 1,2-disubstituted vinylic telluride, although with low selectivity (ratio 1.7:1). For the other hydroxy alkynes studied, the regioselectivity of the reaction is low, usually from 1.4 to 1.9:1, in favor of the 1,2-disubstituted product.

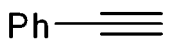
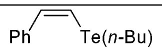
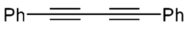
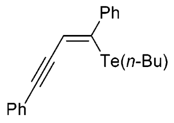
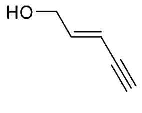
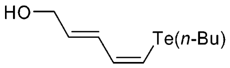
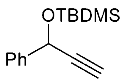
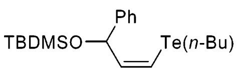
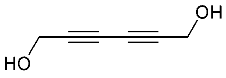
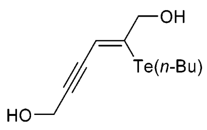
Scheme 12



R = H, THP; n = 1 - 9

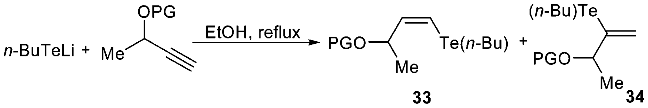
To circumvent this problem, a study of protection of the hydroxyl group of propargyl alcohols with different com-

Table 3. Hydrotelluration of Alkynes with the BuTeLi Method

Entry	Alkyne	Product	Time (h)	Yield (%)
1			4	88
2			8	75
3			6	77
4			8	72
5			7	80

monly used groups was described (Scheme 13).[20] It was found that the steric demand of the protective groups was decisive for the outcome of the reaction and the best choice was TBS protection, which virtually furnishes only product **33**, instead of the 1,1-disubstituted **34**.

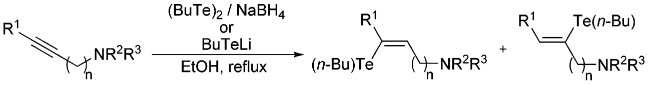
Scheme 13



		33 : 34
PG =	H	3 : 1
	THP	6 : 1
	Trityl	15 : 1
	TBS	>99 : <1

2.1.1.2.2. Hydrotelluration of Amino Alkynes. We have recently described a comparative study on the hydrotelluration of aminoalkynes, using two different methods for the generation of tellurium nucleophile.[21] In this article, the hydrotelluration of several aminoalkynes **35** of different substitution patterns at the amino group and with different chain lengths was tested (Scheme 14). Previous to this article, only isolated examples of the hydrotelluration of alkynes with amino groups as substituents had been published. There was still a lack of information about the reaction of this class of alkynes with tellurium nucleophiles.[10a,11a]

Scheme 14

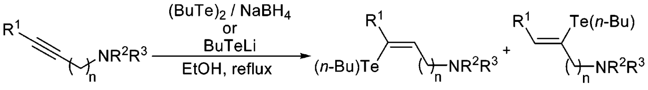


35

The reactions were performed using procedures for the generation of both nucleophilic tellurium species, BuTeTeBu/ $NaBH_4$ and BuLi/Te^0. The author observed that no significant difference in yields and regioselectivity was obtained.

The best results in terms of regioselectivity were obtained with trisubstituted amines. The pyrrolidine, piperidine, and morpholine derivatives exclusively gave product **36** in yields ranging from 57 to 71% (Table 4, entries 4−6). Interestingly, when an internal aminoalkyne, with one of the termini of the alkyne moiety, is substituted with a SMe group (Table 4, entry 7), complete reversal in the regiochemistry was observed. This fact is probably due to the high ability of the sulfur atom to stabilize a neighboring negative charge. In contrast, when selenium or alkyl analogues were treated under the same conditions, no reaction was observed. In the hydrotelluration of primary, secondary, and long chain aminoalkynes, a loss in the regioselectivity was detected.

Table 4. Hydrotelluration of Aminoalkynes

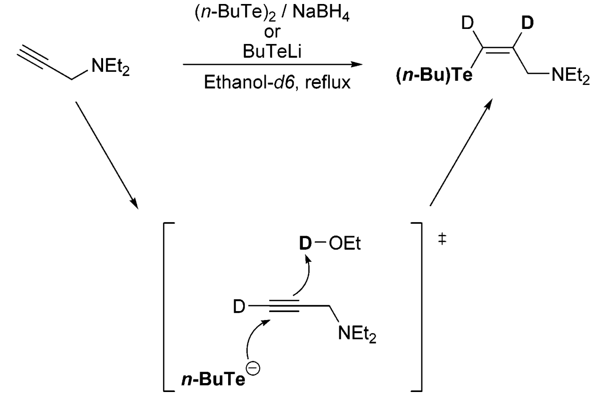


35 **36**

entry	R^1	R^2	R^3	*n*	yield (%)	ratio X:Y
1	H	Et	Et	1	60	1:0
2	H	H	H	1	50	2:1
3	H	H	Me	1	60	3:1
4	H	cyclo	$(CH_2)_4$	1	67	1:0
5	H	cyclo	$(CH_2)_5$	1	57	1:0
6	H	cyclo	$(CH_2)_2O(CH_2)_2$	1	71	1:0
7	MeS	Et	Et	1	50	0:1
8	H	H	H	5	35	1.4:1
9	H	Et	Et	5	55	1.6:1

An additional experiment was carried out to elucidate the mechanism of the reaction, in which deuterated ethanol was employed in order to determine if the hydrogen, which is added to the triple bond, comes from the solvent or from water. As observed by ^1H and ^{13}C NMR, the product was dideuterated alkene, and its formation is explained by the H−D exchange of the acetylenic hydrogen, followed by the hydrotelluration and capture of deuterium from the solvent (Scheme 15).

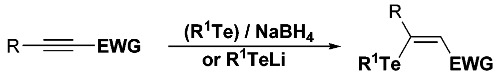
Scheme 15



2.1.1.3. Hydrotelluration of Alkynes Bearing an Electron-Withdrawing Group.

The hydrotelluration of alkynes bearing electron-withdrawing groups **37** is an attractive variation of the hydrotelluration reactions. This methodology will be discussed in a separate paragraph and organized according to the nature of the electron-withdrawing group present in the starting alkyne (Scheme 16).

Scheme 16



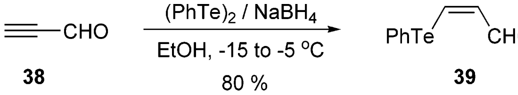
37

EWG = aldehyde, ketone, ester, phosphonate, phosphinoxide,
sulfone, sulfoxide, sulfide

2.1.1.3.1. Hydrotelluration of Alkynes Bearing Aldehyde and Ketone Groups. The hydrotelluration of propargyl aldehydes and ketones is scarcely studied. To the best of our knowledge, there are only a few reports dealing with the hydrotelluration of alkynes containing these functions.[22,23]

One of the examples is the preparation of β-phenyltelluro acrolein **39** by treating propargyl aldehyde **38** with phenyl tellurolate anion to yield the desired product in 80% yield (Scheme 17).[22]

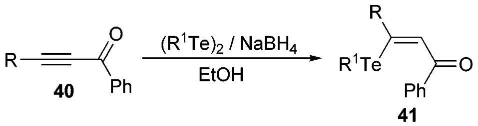
Scheme 17



38 **39**

The addition of tellurolates to alkynyl ketones **40** proceeds in a manner similar to that of aldehydes. Good yields of **41** are obtained with the substituents alkyl or aryl, and lower yields are achieved when the R substituent is a carboxyl group (Scheme 18).[23]

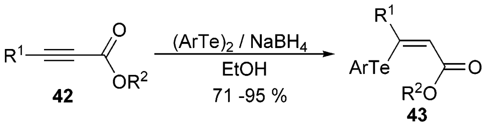
Scheme 18



R = CO$_2$H, R^1 = 2,4-MeOPh, 21 %
R = Bu, R^1 = 4-MeOPh, 68 %
R = Ph, R^1 = Ph, 86 %

2.1.1.3.2. Hydrotelluration of Alkynes Bearing Ester Groups. Acetylenic esters **42** are suitable substrates for the preparation of vinylic tellurides **43**. They underwent a smooth addition of the tellurolate anion to furnish the tellurium-containing acrylates in good to excellent yields (Scheme 19).[23,24] An exception to this tendency was observed when a free carboxyl group was present in the substrate, in which case the hydrotelluration product was obtained in only 21% yield. Regarding the electronic and steric nature of the substituent at the aryltellurolates, it seems that the electronic effects of the substituents on the aromatic ring do not significantly affect the time and yield of the reaction.

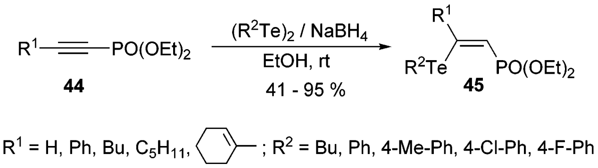
Scheme 19



R^1 = H, Ph, Me, 1-cyclohexanol; **R^2** = H, Me, Ph, *i*-Pr, COCH=C(TePh)(Ph); **Ar** = Ph, 4-MeCOPh, 2,4-MeOPh, 2-MePh, 3,5-MeOPh, 3-FPh, 3-MeOPh, 3-MePh, 4-FPh, 4-MeOPh, 4-MePh

2.1.1.3.3. Hydrotelluration of Alkynes Bearing Phosphonate and Phosphine Oxide Groups. The phosphonate group is well-known to be a good Michael acceptor.[25] Thus, the hydrotelluration of alkynyl phosphonates **44** proceeds in a Michael-type addition giving the β-organyltelluro vinyl phosphonates **45** in good yields with complete stereoselectivity in favor of the *Z* diastereoisomer.[26] The reaction has been performed at room temperature, and dibutyl and diaryl ditellurides have been used as the nucleophilic organyltellurium source. The reaction was also carried out with terminal and internal alkynyl phosphonates, and good results were obtained in both cases. Lower yields were achieved when the R^1 substituent at the β-position was 1-cyclohexenyl, probably due to the steric effect (Scheme 20).

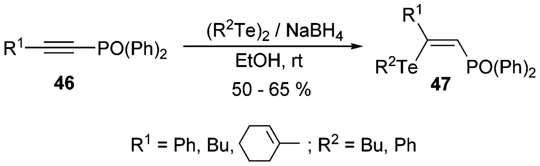
Scheme 20



With regard to the substitution pattern at the ditelluride, little influence on the yield has been observed. For example, the results obtained in the hydrotelluration of the same substrate with the following three different tellurolate precursors, each with substituents of different electronic properties, (4-Me-PhTe)$_2$, (4-Cl-PhTe)$_2$, and (PhTe)$_2$, showed no significant difference in the yields of the corresponding products (yields were 59, 63, and 61%, respectively).[26c]

We have successfully described the reaction between the nucleophilic tellurium species and 1-alkynylphosphine oxides **46**.[27] The phosphine oxide group behaves similarly to the phosphonates acting as a Michael acceptor, in that it reacts with the organotellurolate to give the corresponding β-organyltelluro vinyl phosphine oxide **47** in moderate yields (Scheme 21).

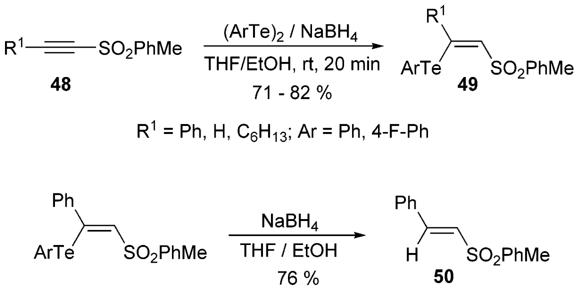
Scheme 21



When R^2 = Ph, all products were obtained with a *Z* geometry of the double bond. However, when the organic group attached to tellurium was a butyl group, the unexpected formation of a smaller amount of *E*-β-organyltelluro vinyl phosphine oxide was observed.

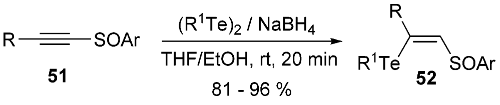
2.1.1.3.4. Hydrotelluration of Alkynes Bearing Sulfone and Sulfoxide Groups. β-Sulfonyl vinyl tellurides **49** with *Z* stereochemistry can be obtained by hydrotelluration of 1-alkynyl sulfones **48**.[26c] The addition of aryl tellurolate to the alkyne occurred smoothly in a mixture of THF and EtOH as solvent. The reaction was very fast, being completed in 20 min and furnishing the *Z*-2-aryltelluro-1-alkenyl sulfones in good yields (Scheme 22). No isomeric products were obtained, as determined by ^{1}H NMR. Interestingly, when the reaction was conducted for longer periods of time, the product was converted to *E*-vinyl sulfone **50**, free of tellurium. The authors suggest that this is the result of a reductive detelluration promoted by sodium borohydride.

Scheme 22



Recently, the same reactivity pattern was observed for alkynyl sulfoxides **51**.[28] The hydrotelluration reaction of these sulfoxides led to β-organotelluro vinyl sulfoxides **52** in good yields with very short reaction times (Scheme 23).

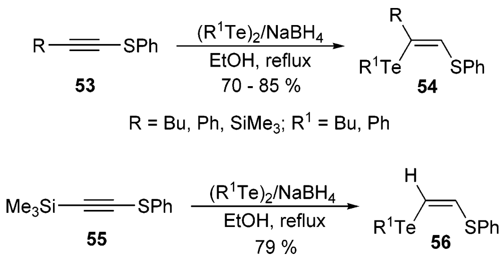
Scheme 23



R = H, C$_4$H$_9$, C$_5$H$_{11}$; R^1 = Ph, Bu; Ar = Ph, *p*-Tol

2.1.1.3.5. Hydrotelluration of Alkynes Bearing Sulfide Groups. Although the sulfide group is not exactly an electron-withdrawing group, alkynyl sulfides **53** react with organotellurium nucleophiles in a similar manner as do alkynyl esters, phosphonates, and sulfones. This is explained by the ability of the sulfur atom to stabilize an adjacent negative charge, allowing alkynyl sulfides to react in a Michael-type addition of the organotellurolate anion to yield the trisubstituted alkenes **54** in good yields (Scheme 24).[29] An attractive result was obtained when the group SiMe$_3$ was

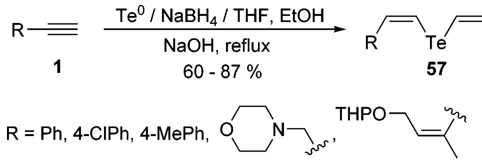
Scheme 24



attached at the triple bond as in **55**, giving the desilylated product **56** instead of trisubstituted olefin.

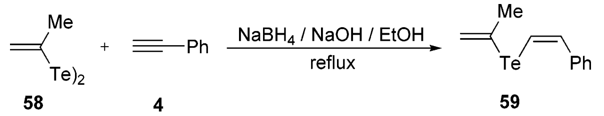
2.1.1.4. Preparation of Bis-vinylic Tellurides. Bis-vinylic tellurides **57** constitute a very attractive class of tellurium compounds in which the tellurium atom is attached to two alkene moieties. Such compounds were obtained in good yields by the reaction of M_2Te (generated by the reduction of Te^0 with $NaBH_4$) with 2 equiv of a terminal alkyne. The reaction was performed with several different alkynes (Scheme 25).[10b,11a]

Scheme 25



Unsymmetrical bis-vinylic tellurides **59** can also be prepared. The reaction between divinyltelluride **58** and sodium borohydride and the subsequent hydrotelluration of an alkyne lead to unsymmetrical bis-vinylic telluride **59** in good yields (Scheme 26). The presence of sodium hydroxide is crucial for the reaction since it converts tellurols to tellurolate anions, avoiding side reactions at the alkene moiety.

Scheme 26



2.1.2. Preparation of Vinylic Tellurides via Vinylic Substitution Reactions

The vinylic substitution reactions by the lithium butyltellurolate anion are a useful alternative which agreeably complements the hydrotelluration of alkynes in the synthesis of vinylic tellurides. This methodology allows the preparation of tri- and tetrasubstituted vinylic tellurides which are otherwise more difficult to prepare. Another advantage of this reaction is the availability of the starting materials, since *β*-dicarbonyl compounds **60** are used as precursors for the vinylic substrate (Figure 3).

The first report on a vinylic substitution promoted by a tellurium anion was reported by Comasseto and co-workers,[10a] in which they describe the reaction of *E*-*β*-bromostyrene **61** with the tellurium anion generated by the reduction of dibutyl ditelluride with lithium aluminum hydride. Subsequently, Uemura and Ohe published an analogous reaction using Na/HMPA for the reduction of ditelluride to tellurolate (Scheme 27).[30]

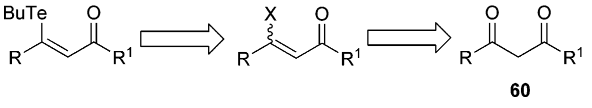
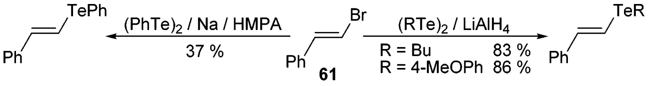


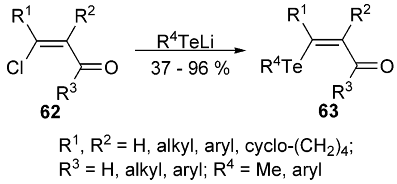
Figure 3.

Scheme 27



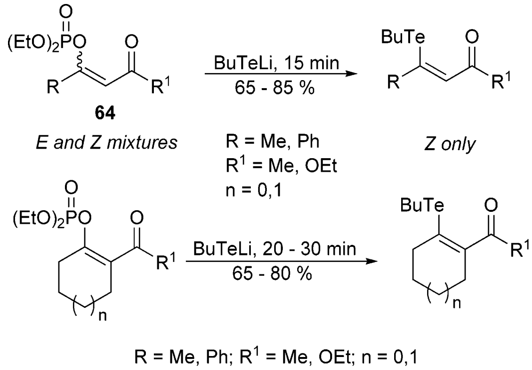
The reaction remained unexplored until the end of the 1990s, when Minkin published a systematic study on the preparation of functionalized vinylic tellurides by the substitution of activated vinylic halides **62**.[31] The reaction is tolerant to both aldehydes and ketones and furnishes vinylic tellurides **63** in moderate to good yields (Scheme 28). In all cases, the *Z* stereochemistry was obtained and the structure was confirmed by NMR and X-ray analyses.

Scheme 28

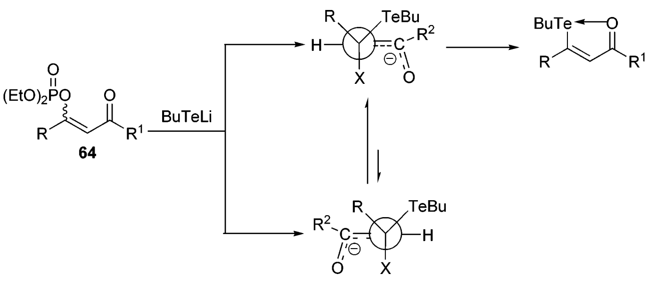


In an extension of their previous studies, Comasseto and co-workers disclosed, in 1999, a new approach for vinylic substitution by lithium butyltellurolate. This approach consists of the reaction of enol phosphates **64** instead of vinyl halides.[32] The advantages of this method are the easy availability of *β*-dicarbonyl compounds, which are the precursors for the enol phosphates, and the possibility to obtain a single isomer of vinylic telluride starting from a mixture of *E* and *Z* isomers of the enol phosphate (Scheme 29). The reaction is believed to proceed by an addition–elimination mechanism, since a tellurium–oxygen interaction is observed by X-ray, Raman, and IR analyses (Scheme 30).[33]

Scheme 29



Scheme 30

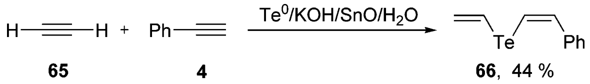


Additional studies on the reaction revealed that the organic moiety attached to tellurium can be varied; thus, several different organolithium reagents can be used to generate lithium tellurolate, showing that the reaction is general for a variety of organyltellurolates.[34] Furthermore, the nature of the leaving group was examined. Performing the reaction of lithium butyltellurolate with enol phosphate, tosylate, triflate, and acetate afforded the desired product in similar yields and within the same reaction times. In all cases, only *Z*-vinylic tellurides were obtained.

2.1.3. Preparation of Vinylic Tellurides from Elemental Tellurium with the KOH/SnO/H$_2$O System

Elemental tellurium is useful for the preparation of unsymmetrical divinyl tellurides by reaction under the KOH/SnO/H$_2$O system.[35] The reaction is conducted in the presence of both acetylene precursors in a one-pot procedure and in a single step. For instance, when Te, acetylene **65**, and phenylacetylene **4** react under these conditions, *Z*-styryl vinyl telluride **66** is synthesized in a moderate yield (Scheme 31).

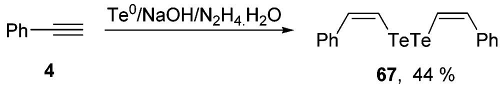
Scheme 31



2.1.4. Preparation of Vinylic Tellurides from Elemental Tellurium, Alkynes, and the NaOH/N$_2$H$_4$/H$_2$O System

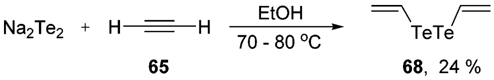
The reduction of elemental tellurium with hydrazine under basic conditions conveniently generates metal ditelluride.[35] The reaction between Na$_2$Te$_2$, prepared under these conditions, and phenylacetylene leads to the preparation of *Z,Z*-distyryl ditellurides **67** in 82% yield (Scheme 32).

Scheme 32



Accordingly, this procedure can be applied for the preparation of divinyl ditelluride **68**, although in low yields, due to the instability of the product. It is worth noting that ethanol is added to the reaction mixture, which is heated at 70−80 °C (Scheme 33).

Scheme 33



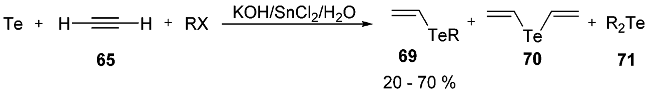
2.1.5. Preparation of Vinylic Tellurides from Elemental Tellurium, Alkynes, and Alkyl Halides

A convenient method for the preparation of vinylic tellurides by the direct reaction between elemental tellurium, acetylene, and alkyl halides has been described. The reaction is performed in the presence of the strongly basic and strongly reducing system KOH/SnCl$_2$/H$_2$O, according to the following equation:[36]

$$\mathrm{Te^0 + 6KOH + SnCl_2 \rightarrow K_2Te + 2KCl + K_2SnO_3 + 3H_2O} \quad (1)$$

The authors affirm that the nucleophilic tellurium species generated reacts initially with the acetylene to give a vinyl tellurium anion, which further reacts with the alkyl halide to afford the alkylvinyl tellurides **69**. When alkyl iodides were employed, the yields of the alkylvinyl telluride decreased and the dialkyltelluride was observed as a major product of the reaction. The major drawback of this methodology is the formation of a considerable amount of divinyltelluride **70** and dialkyltellurides **71** as byproducts (Scheme 34).

Scheme 34



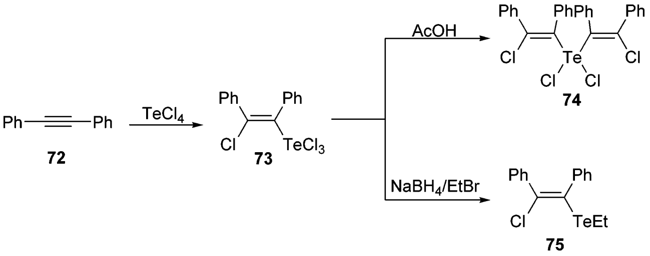
R = Me, Et, *n*-Pr, *i*-Pr, *n*-Bu, *t*-Bu, X = Cl, Br, I

2.2. Preparation of Vinylic Tellurides by Electrophilic Tellurium Species

2.2.1. Addition of Tellurium Tetrahalides to Alkynes

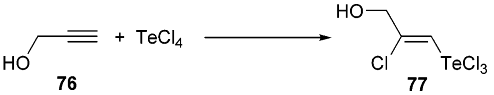
The electrophilic addition of tellurium tetrahalides to alkynes is one of the most traditional methods to prepare vinylic tellurides. It was first developed by Petragnani in the early 1960s. The author described the preparation of β-chlorovinyl tellurium trichloride **73** by the addition of tellurium tetrachloride to diphenylacetylene **72**.[37] Further treatment of the vinyl tellurium trihalide with AcOH or NaBH$_4$/EtBr leads to bis(β-chlorovinyl) tellurium dichloride **74** and to vinylic telluride **75**, respectively (Scheme 35).

Scheme 35



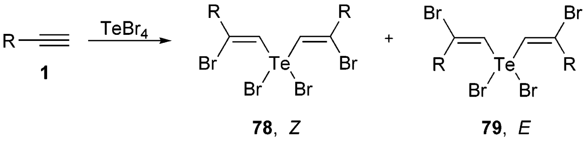
Propargyl alcohol **76** was successfully employed in such a reaction and furnished β-chlorovinyl tellurium trichloride **77** in good yield (Scheme 36).[38]

Scheme 36



Similarly, tellurium tetrabromide has been employed in this reaction, leading directly to the corresponding bis(β-bromovinyl) tellurium dibromides **78** and **79** in good yields (Scheme 37).[39] Mixtures of *Z* and *E* isomers were formed, and in all cases studied the *Z* isomer was formed as the major product.

Scheme 37

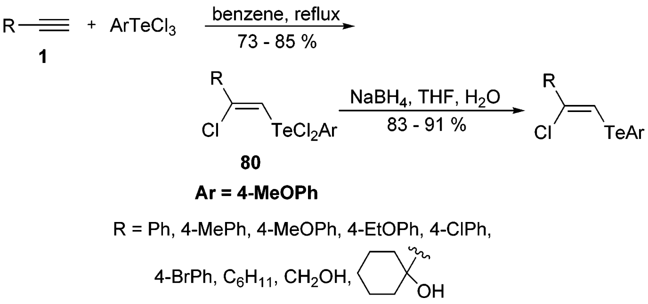


R = Ph 70 % *Z* : *E* 4.5 : 1
R = C$_5$H$_{11}$ 70 % *Z* : *E* 3.4 : 1

2.2.2. Addition of Organotellurium Halides to Alkynes

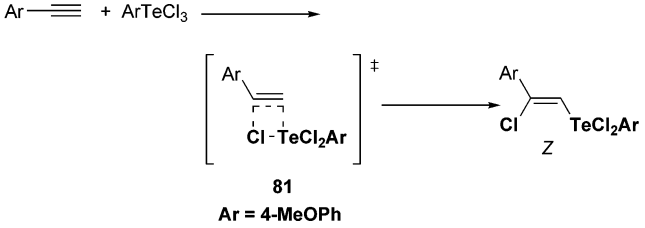
Organotellurium halides behave similarly to tellurium tetrahalides, acting as an electrophilic source of tellurium. In light of this, (*p*-methoxyphenyl)tellurium trichloride has been added to terminal alkynes to give 1-chloro-1-organyl-2-[dichloro(*p*-methoxyphenyl)telluro]ethenes **80** of a *Z*-configuration, which can be reduced to the corresponding vinylic tellurides by $NaBH_4$ in THF and H_2O (Scheme 38).[40]

Scheme 38



The reaction proceeds with high regio- and stereoselectivity, and the structure of the compounds is confirmed by their ^{13}C shifts and X-ray structures. A mechanistic rationale is proposed by the authors explaining the *Z* stereochemistry obtained as a result of a four-centered cyclic transition state **81** (Scheme 39).

Scheme 39

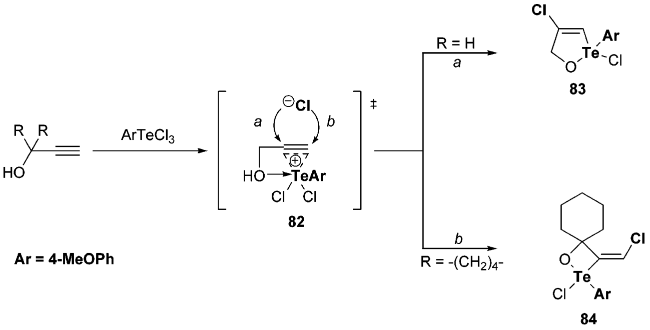


Further studies on the addition of *p*-methoxyphenyl tellurium trichloride to 3-hydroxy alkynes were later reported.[41] The influence of the hydroxyl group in the regio- and stereochemistry has been examined. X-ray product analysis from the reaction of propargyl alcohols with *p*-methoxyphenyl tellurium trichloride revealed that cyclic oxychlorides **83** and **84** were obtained instead of the desired acyclic tellurides. Different from simple alkynes (Scheme 34), propargyl alkynes gave the products through an *anti* addition pathway, via the formation of a telluronium ion **82**, coordinated with the hydroxyl group. Opening of the telluronium ion can proceed by paths *a* and *b*. Path *a* is favored over *b* when the propargylic position is unencumbered, leading to a five-membered oxychloride ring. On the other hand, with hindered propargylic alcohols, path *b* is favored and a four-membered oxychloride ring is formed (Scheme 40).

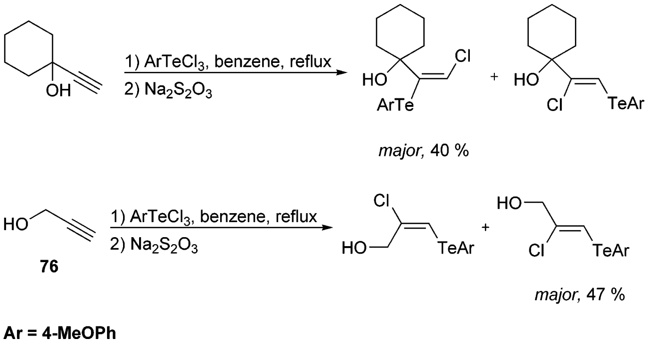
When propargyl alcohols are subjected to electrophilic tellurium addition with *p*-methoxyphenyl tellurium trichloride plus sodium bissulfite, the *β*-chloro vinylic tellurides were isolated in good yields instead of the oxychlorides (Scheme 41). This is explained by the direct reduction of the oxychlorides to the corresponding vinyl tellurides.

The analogous aryltellurium tribromide can be employed in a similar manner as their parent trichlorides. Huang and Wang have described the stereoselective synthesis of *Z*- and *E*-*β*-bromovinyl tellurides **85** and **86** by the addition of aryltellurium tribromides to terminal alkynes (Scheme 42).[42]

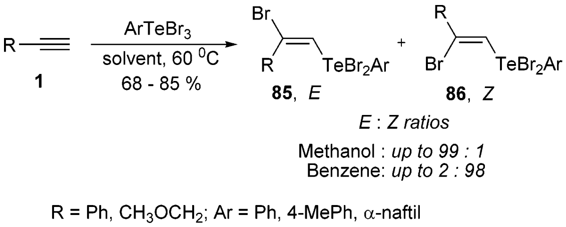
Scheme 40



Scheme 41



Scheme 42

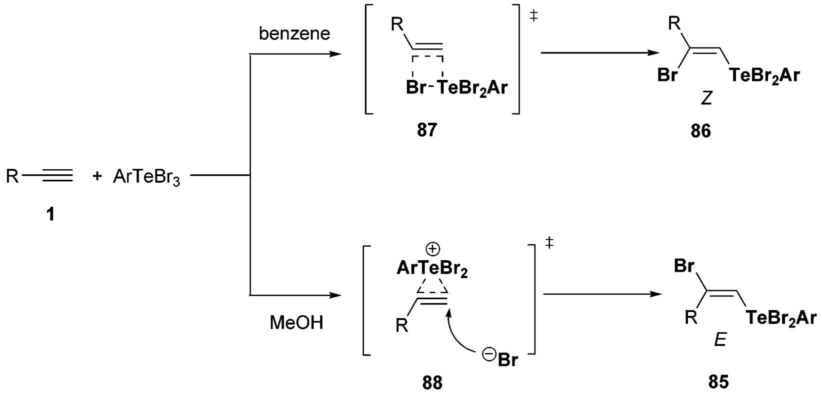


The reaction is highly regioselective, but the stereoselectivity is dependent on the polarity of the solvent. In methanol, tellurium ions **88** can be formed due to the more polar environment, predominantly giving the *anti* products **85**. On the other hand, when nonpolar benzene was used, the reaction proceeded through a four-membered transition state **87**, which led almost exclusively to the *Z* isomers **86** (Scheme 43).

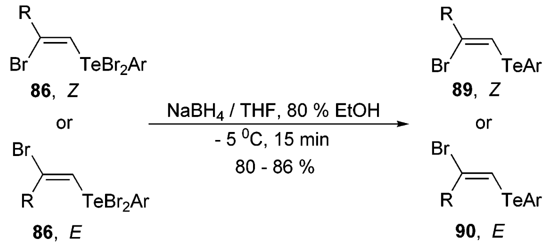
The dibromides **85** and **86** described in Scheme 43 can be further reduced to the corresponding vinylic tellurides **89** and **90** by debromination, leading to trisubstituted alkenes. Thus, this was achieved by the treatment of the *Z* or *E*-*β*-bromovinyl aryl tellurium dibromides with sodium borohydride, furnishing the desired compounds in good yields (Scheme 44).

Organotellurenyl bromides have been used to prepare vinylic tellurides.[43] The reaction between alkynes and bromide (prepared *in situ* from the reaction between diphenyl ditelluride and bromine) affords the vinylic tellurides, without the need for a reduction step for tellurium dihalides, which are obtained by the previously discussed method. However, the selectivity is lower when compared to the case of the addition of organotellurium trihalides, and the best result in terms of stereoselectivity is a 4.5 to 1 ratio, in favor of the *E* isomer **91** (Scheme 45). Interestingly, when propargyl

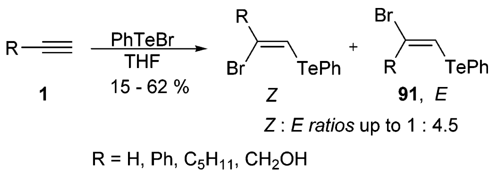
Scheme 43



Scheme 44



Scheme 45



alcohol was used, the opposite regioisomer was obtained with tellurium being attached to the internal carbon of the alkyne.

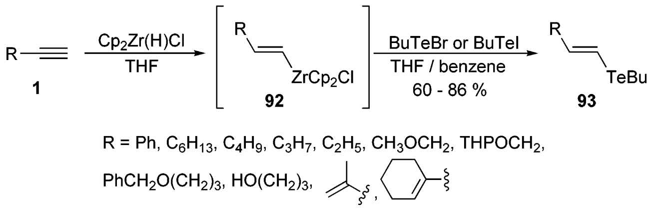
2.2.3. Preparation of Vinylic Tellurides by a Metal–Tellurium Exchange Reaction

2.2.3.1. Zirconium−Tellurium Exchange. The hydrozirconation of alkynes is a powerful approach to the preparation of several functionalized alkenes with high regio- and stereoselectivity.[44] Conversely, the preparation of *E*-vinylic tellurides has been much less studied in comparison to that of *Z* isomers. Thus, the well-known potential of the hydrozirconation reaction to stereoselectively produce *E*-organometallics has attracted the attention of many researchers. These vinylic zirconium intermediates can further undergo a zirconium−tellurium exchange reaction with an electrophilic tellurium source, such as organotellurenyl halides, to furnish *E*-vinylic tellurides.

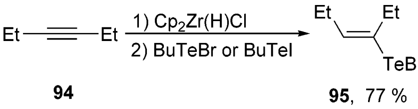
Two groups have independently reported the zirconium−tellurium exchange reaction for the preparation of *E*-vinylic tellurides.[45] The reaction is performed by the treatment of an alkyne with Schwartz's reagent, $Cp_2Zr(H)Cl$, where the vinyl zirconocene chloride **92** intermediate undergoes an exchange reaction with butyltellurenyl halide to exclusively give *E*-vinylic tellurides **93** in high yields (Scheme 46).

For the most part, terminal alkynes have been employed in this reaction, but internal alkynes can also be used. For instance, hex-3-yne (**94**) was successfully employed in the sequential hydrozirconation−tellurium exchange reaction and afforded the corresponding vinylic telluride **95** in 77% yield (Scheme 47).

Scheme 46

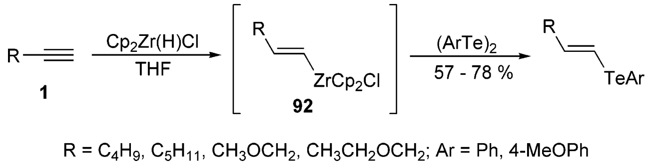


Scheme 47



A variation of the procedure described above employing diaryl ditellurides as the electrophilic tellurium source was published by Huang and co-workers.[46] The advantage of this new procedure is that it avoids the previous preparation of tellurenyl halides. On the other hand, half of the aryl tellurium starting material is lost in the reaction (Scheme 48).

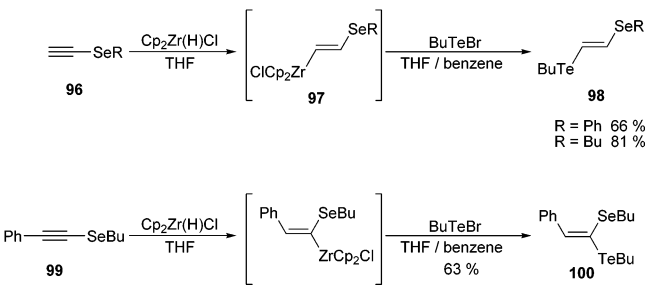
Scheme 48



A special interest has been devoted to the preparation of mixed chalcogene-containing alkenes, and further studies on the sequential hydrozirconation−tellurium exchange reaction directed to the synthesis of functionalized vinylic tellurides have been carried out. This methodology was applied from simple aryl- and alkyl-substituted alkynes to terminal and internal alkynyl selenides, and the regioselectivity of this process was also studied in detail.[47]

In addition, terminal selenoalkyne **96** was treated with Schwartz's reagent to afford the vinyl zirconate intermediate **97**, which was trapped with butyltellurenyl bromide, leading to the *E*-vinylic telluride **98** as the sole product in good yields. The reaction was performed with two different starting selenides, and the best results were achieved when R was the butyl group (Scheme 49). When an internal selenoalkyne **99** bearing an aromatic phenyl group was used, the regiochemistry observed was completely different from that of terminal selenoalkyne, affording only the ketene telluro-

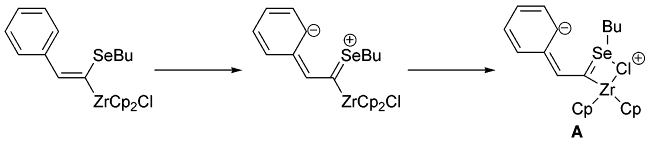
Scheme 49



(seleno) acetal **100**, which demonstrates that the reaction proceeds through a different pathway (Scheme 49).

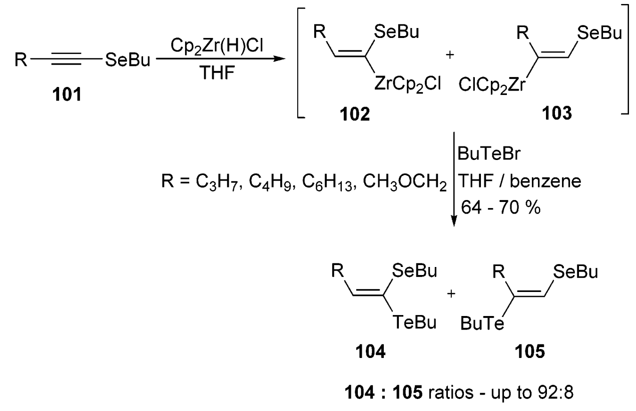
The authors suggest that an interaction between the chloro atom in **A** from the Schwartz's reagent and the organoselenium moiety is responsible for the change in the regioselectivity of the reaction (Scheme 50).

Scheme 50



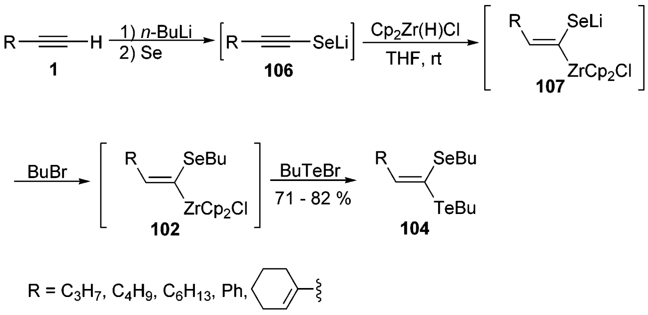
However, when selenoalkynes **101** bearing an alkyl group were submitted to the hydrozirconation reaction, a mixture of the regioisomers, α- and β-zirconated vinylselenides **102** and **103**, was obtained, which can be observed through the ratios of the products formed after trapping with BuTeBr. Different ratios of the regioisomeric products were obtained, and the major isomer was always the α-substituted product **104**. This indicates that the organoselenium moiety is partially responsible for zirconium's preference to attach to the α-position, although the formation of the cyclic intermediate proposed in Scheme 50 is less favored when compared to the alkyl-substituted selenoalkyne (Scheme 51).

Scheme 51

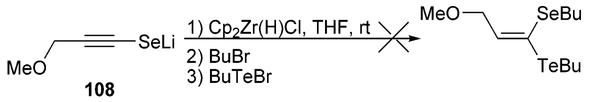


These problems of regioselectivity depicted in Scheme 51 were creatively circumvented in an additional study by the same authors, where they described the preparation of ketene telluro(seleno) acetal with total regio- and stereocontrol.[48] The strategy adopted in this work was the *in situ* generation of alkynylselenolate anions **106** instead of alkynylselenides. In this reaction, the hydrozirconation of both alkyl- and aryl-substituted alkynylselenolate anions, followed by trapping with butylbromide, exclusively furnished the α-zirconated vinyl selenide intermediates **107**, which, upon the Zr−Te exchange reaction with BuTeBr, led to the formation of the desired ketene telluro(seleno) acetals **104** in good yields as a sole product (Scheme 52). Interestingly, when the propargyl ether **108** derivative was employed as a starting material, no product was obtained (Scheme 53).

Scheme 52

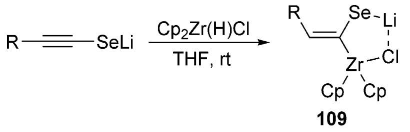


Scheme 53



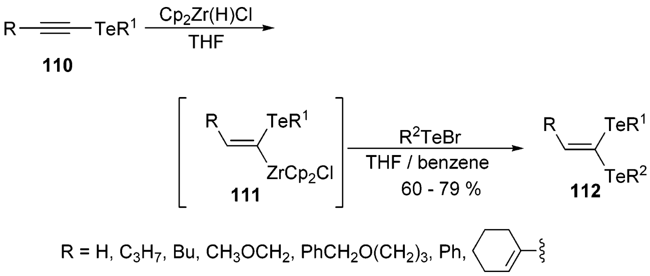
A plausible mechanism to explain the exclusive formation of the α-zirconated vinyl selenolate intermediate is the formation of a five-membered cyclic intermediate **109**, which is by far more efficient than the four-membered intermediate (Scheme 50) previously proposed for the alkynyl selenides (Scheme 54).

Scheme 54



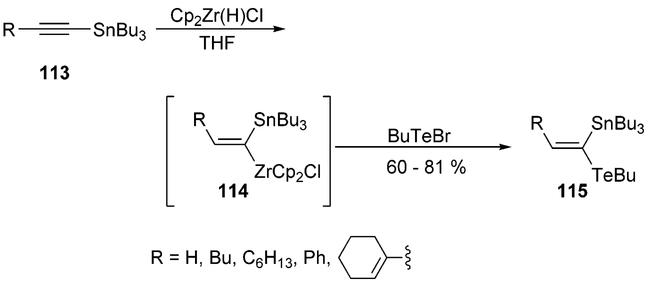
Telluroalkynes **110** have been evaluated under these reaction conditions and have proven to be suitable substrates for the sequential hydrozirconation−tellurium exchange reaction leading to the ketene telluro acetals **112**.[47,49] The only product obtained by the hydrozirconation of telluroalkynes was the α-zirconated intermediate **111**, regardless of the nature of the substituents in the starting material (Scheme 55). All ketene telluro acetals **112** were obtained in good yields, and no cleavage of the Csp−Te bond was observed under this condition.

Scheme 55



The hydrozirconation of trialkylstannyl acetylenes **113** has attracted attention due to the high regio- and stereoselectivity observed in the preparation of *Z*-vinylic stannanes.[50] Therefore, the hydrozirconation/telluration conditions were applied to stannylalkynes in an attempt to prepare ketene stannyl(telluro) acetals **115** (Scheme 56).[51] The reaction was shown

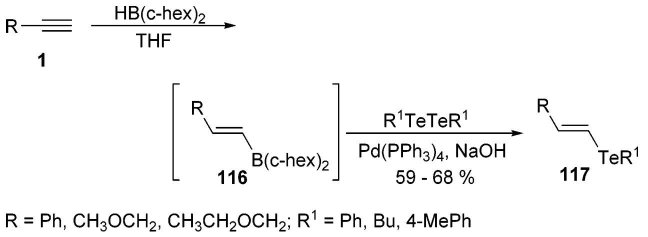
Scheme 56



to be 100% stereoselective, and the functionalized vinylic tellurides **115** were obtained in good to excellent yields. The reaction is completely regioselective, affording only the α-zirconated intermediate **114**, probably due to a complexation similar to that of the selenium and tellurium analogues.

2.2.3.2. Boron−Tellurium Exchange. Organoboranes offer a wealth of transformations in the C−B bond. In general, the Csp2−B undergoes reactions under mild conditions, such as Suzuki cross-coupling[52] or transmetalations to organozinc[53] or organocopper reagents.[54] Diorganoyl ditellurides can be applied as coupling partners with alkenyl boranes, in the presence of a palladium catalyst in a C−heteroatom coupling reaction. Thus, vinylic tellurides of an *E*-configuration **117** were prepared by this methodology, via a dicyclohexyl alkenyl borane intermediate **116** in the presence of a catalytic amount of $Pd(PPh_3)_4$ and a diorgano ditelluride (Scheme 57).[55] Only *E* isomers were obtained, indicating that the boron−tellurium exchange is stereoselective, with retention of the vinyl borane intermediate configuration.

Scheme 57



The authors propose a catalytic cycle for the Pd-catalyzed boron−tellurium exchange, where an oxidative addition of ditelluride to Pd(0) affords intermediate **A**, which is converted by transmetalation to intermediate **B**, followed by the reductive elimination to give the product, which in turn regenerates Pd(0) to the catalytic cycle (Figure 4). It is valid to comment that the reaction does not occur in the absence of the palladium catalyst.

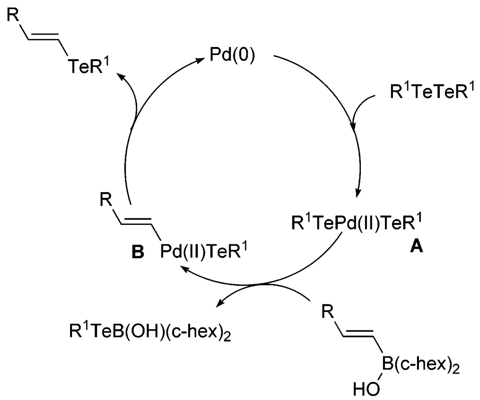
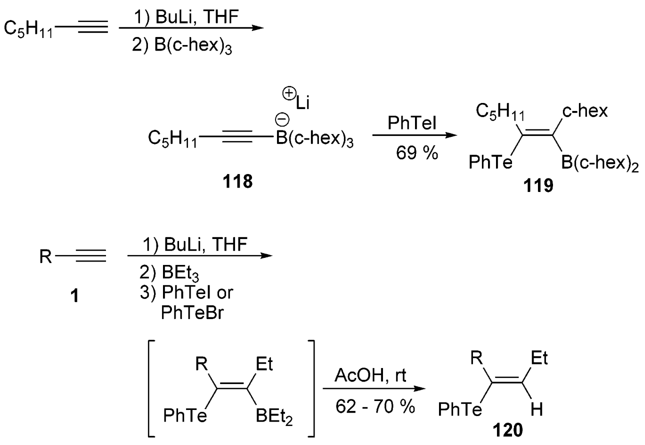


Figure 4.

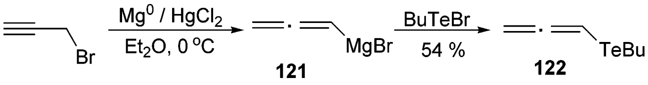
Further methodologies for the chemistry involving boron and tellurium species lie in the tellurium electrophile-induced rearrangement of 1-alkynyltrialkyl borates **118**.[56] One reaction can be carried out by the deprotonation of a terminal alkyne with BuLi and further trapping with a trialkylborane, furnishing the alkynyl trialkylborate **118** intermediate, which reacts with tellurenyl halide to afford vinyl telluride **119** in good yields. Another approach consists of the addition of acetic acid at the end of the reaction, to promote a protodeborylation, which yields trisubstituted vinylic telluride **120** (Scheme 58).

Scheme 58



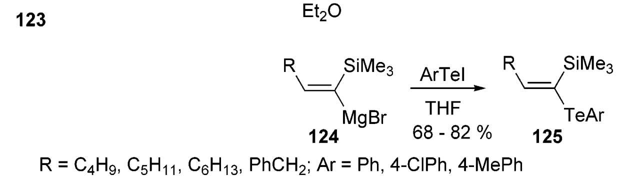
2.2.3.3. Magnesium−Tellurium Exchange. There are only a few reports dealing with the magnesium−tellurium exchange for the preparation of vinylic tellurides. In 1996, it was applied to the preparation of telluro allenes **122**.[57] The reaction consists of the generation of allenylmagnesium bromide **121** from propargyl bromide with $Mg/HgCl_2$ in diethyl ether. The reaction of the Grignard reagent with butyltellurenyl bromide furnished the butyltelluro allene **122** in 54% yield after purification (Scheme 59).

Scheme 59



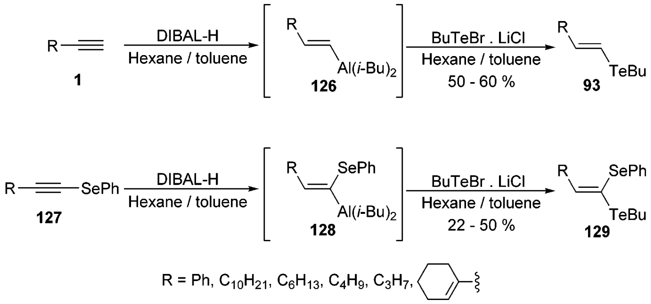
In addition to this work, a very recent paper concerning a hydromagnesiation of alkynyl silanes **123** has been published, in which vinylmagnesium reagent intermediates **124** were trapped by tellurium electrophilic reagents.[58] The reaction was performed using alkynyl silanes as starting materials which were hydromagnesiated with *i*-BuMgBr in the presence of a catalytic amount of Cp_2TiCl_2. The magnesium was attached exclusively to the same carbon as the silicon atom. The vinyl Grignard reagent **124** underwent the magnesium−tellurium exchange reaction with a complete retention of the double bond geometry, to afford the *E*-α-aryltellurenyl vinylsilanes **125** in good yields (Scheme 60).

Scheme 60



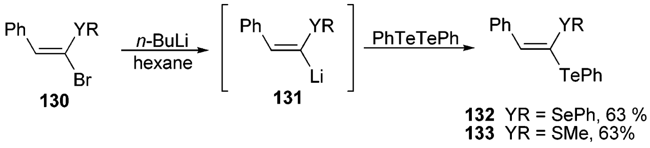
2.2.3.4. Aluminum−Tellurium Exchange. Vinyl alane **126** intermediates are produced by the hydroalumination of alkynes with DIBAL-H and react with tellurenyl halides to produce *E*-vinylic tellurides **93**.[59] The aluminum−tellurium exchange reaction occurs with total retention of the vinyl organometallic intermediate to exclusively afford the *E*-vinylic telluride **93**. The best results were obtained when the reaction was carried out in the presence of LiCl (Scheme 61). Moreover, the hydroalumination of alkynyl selenides **127** has been reported. The reaction produces the mixed ketene telluro(seleno) acetals **129** after the exchange of the vinyl alane intermediate **128** with butyltellurenyl bromide in the presence of lithium chloride (Scheme 61).[60]

Scheme 61



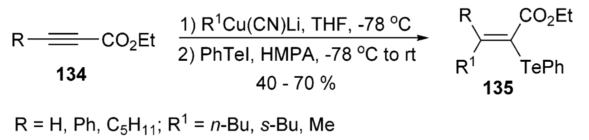
2.2.3.5. Lithium−Tellurium Exchange. Our group reported the lithium−tellurium exchange via generation of the reactive lithium species by treatment of α-bromo vinyl chalcogenides **130** with butyllithium in hexane.[61] The functionalized vinyllithium intermediates **131** readily react with diphenyl ditelluride to afford the vinylic tellurides **132** and **133** in good yields. It is noteworthy that no isomerization of the vinyllithium was observed under the conditions employed, and the reaction proceeded in a stereoconservative manner (Scheme 62).

Scheme 62



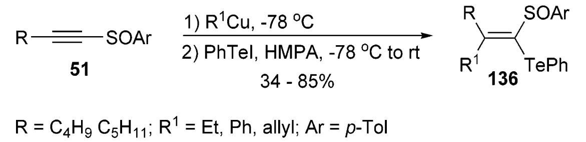
2.2.3.6. Copper−Tellurium Exchange. A copper−tellurium exchange was successfully applied in the synthesis of vinylic tellurides via carbocupration reaction of alkynes containing electron-withdrawing groups in conjugation. The carbocupration reaction of alkynes is of high synthetic interest since it allows the preparation of functionalized vinyl copper intermediates by a Michael-type addition. These intermediates can be further trapped by convenient electrophiles to give tri- or tetrasubstituted olefins. One approach to the synthesis of α-phenyltelluro-α,*β*-unsaturated esters **135** was described by Silveira and co-workers. The authors described the reaction of substituted ethyl propiolates **134** with organocuprates to generate the vinyl copper species that reacts with the tellurenyl iodide to afford the vinylic tellurides **135** in good yields (Scheme 63).[62] When R = Ph, a higher temperature is needed for the completion of the reaction. However, the increase in the temperature leads to a mixture of *E* and *Z* isomers. When another R, such as an H or an alkyl substituent, is present, only one isomer is obtained.

Scheme 63



The carbocupration of acetylenic sulfoxides **51** has recently been accomplished, where a monocopper reagent added regio- and stereoselectively in a Michael-type reaction in a *syn* fashion to give vinyl copper intermediates. These were efficiently trapped with PhTeI, affording the α-phenyltellurovinyl sulfoxides **136** in good to excellent yields. Allyl copper reagents were employed; however, lower yields were obtained (Scheme 64).[28]

Scheme 64

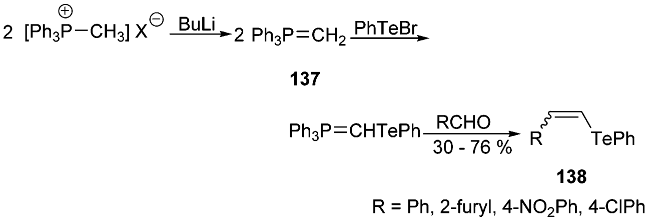


2.3. Preparation of Vinylic Tellurides by Wittig and Wittig−Horner Reactions[63]

2.3.1. Vinylic Tellurides by Wittig Reactions

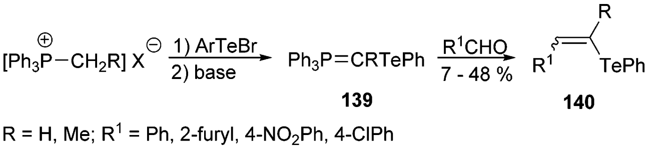
The preparation of vinylic tellurides by the Wittig reaction was accomplished by Silveira and co-workers in the 1990s.[64] Two different methods were developed; the first consists of the transylidation reaction between alkylidene triphenylphosphorane **137** and phenyltellurenylbromide. The subsequent reaction with aldehydes furnishes vinylic tellurides **138** in moderate to good yields in *E*/*Z* ratios of up to 1:8 (Scheme 65).

Scheme 65



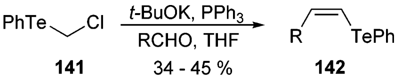
The second method consists of the generation of triphenylphosphonium tellurodihalotellurolates by the reaction of equimolar amounts of aryltellurenyl bromides and phosphonium salts. The reaction with a base produces the telluro-phosphoranes **139**, which upon reaction with aldehydes give vinylic tellurides **140** in moderate yields and good selectivity (up to 13:1) in favor of the *Z* isomer (Scheme 66).

Scheme 66



Vinylic tellurides **142** have been prepared by a one-pot procedure, exclusively in the *Z*-configuration, via addition of *t*-BuOK to a solution of chloromethyl phenyl telluride **141** and triphenylphosphine in THF, followed by addition of an aldehyde (Scheme 67).[65]

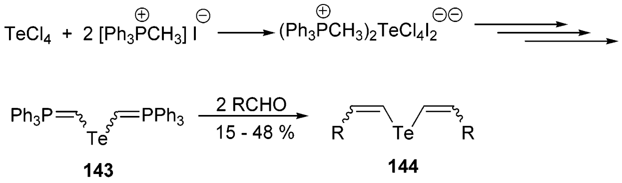
Scheme 67



R = Ph, 2-furyl, 4-NO_2Ph, 4-MePh

The same group has reported the preparation of symmetrical divinyl tellurides **144** by the reaction of intermediate **143** with aldehydes to generate bis-vinylic tellurides in a mixture of isomers in moderate yields (Scheme 68).[66]

Scheme 68

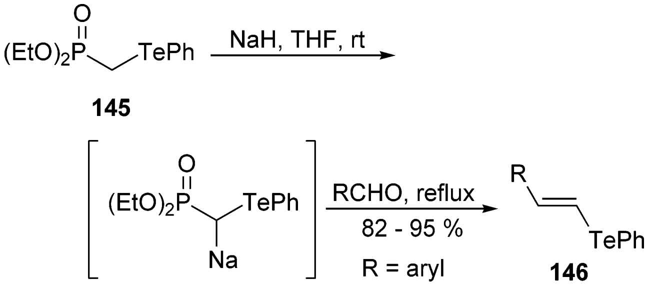


R = Ph, 2-furyl, 4-ClPh, 4-MePh, Me_2CH, $CH_3CH_2CH_2$

2.3.2. Vinylic Tellurides by Wittig–Horner Reaction

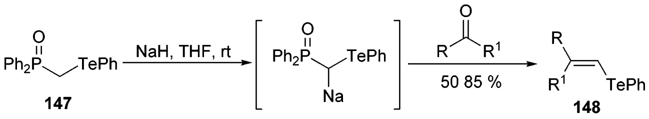
The preparation of *E*-vinylic tellurides by a Wittig−Horner reaction was accomplished by the deprotonation of 1-(phenyltelluro)methyl phosphonate **145** by sodium hydride, followed by the addition of aromatic aldehydes to afford the corresponding vinylic tellurides **146** in high yields exclusively with an *E*-configuration (Scheme 69).[67]

Scheme 69



Phenyltelluroalkylphosphine oxide **147** has recently been applied in the preparation of vinylic tellurides through a reaction with aldehydes or ketones. When aromatic aldehydes were employed, the formation of the *E* isomer was favored in a ratio of up to 15.6:1. However, with aliphatic aldehydes, the favored product was the *Z* isomer, though in lower diastereoselectivities. The reaction with ketones worked well, furnishing trisubstituted vinylic tellurides **148** in good yields (Scheme 70).[68]

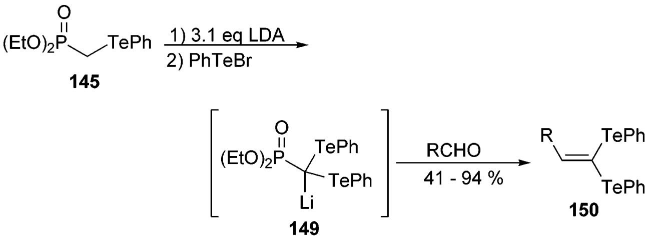
Scheme 70



R, R^1 = H, alkyl, aryl

The preparation of ketene telluro acetals **150** by the reaction of diethyl alkylphosphonates with LDA and the subsequent addition of phenyl tellurenyl bromide was described by Silveira and co-workers. The resulting intermediate **149** was treated with carbonyl compounds to furnish products **150** in good yields (Scheme 71).[69]

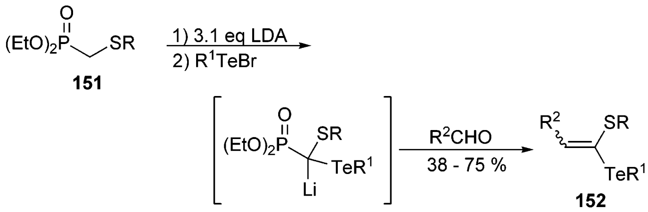
Scheme 71



R = Ph, 2-furyl, 4-NO_2Ph, Me_2CH, $CH_3CH_2CH_2$, $H_2C{=}CH$

The reaction of thiomethyl phosphonates **151** with aryl or butyl tellurenyl halides, under basic conditions, provides moderate to good yields of ketene thio(telluro) acetals **152**. Both aromatic and aliphatic aldehydes gave a mixture of *Z* and *E* isomers (Scheme 72).[70]

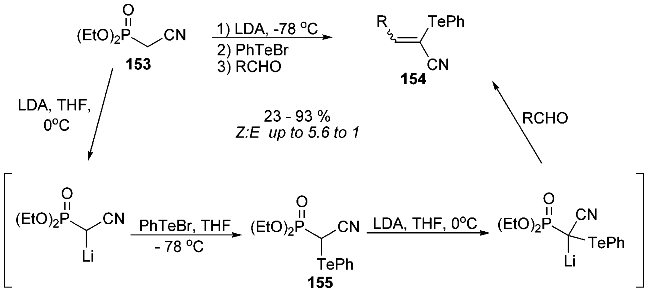
Scheme 72



R = Me, Ph; R^1 = Ph, Bu; R^2 = Ph, 2-furyl, 4-MePh,
4-ClPh, Me_2CH, $CH_3CH_2CH_2$, H

Phenyltelluro acrylonitriles **154** have been synthesized by an analogous reaction as described in Scheme 72. Cyanomethyl phosphonate **153** was treated with LDA, whose intermediate reacted with PhTeBr, affording an α-phenyltelluro(cyano) phosphonate intermediate **155**, which reacted with aldehydes to give acrilonitriles, typically, in good yields and in *Z*/*E* ratios ranging from 4.5:1 to 5.6:1. Lower yields were obtained when formaldehyde (R = H) was employed (Scheme 73).[71]

Scheme 73

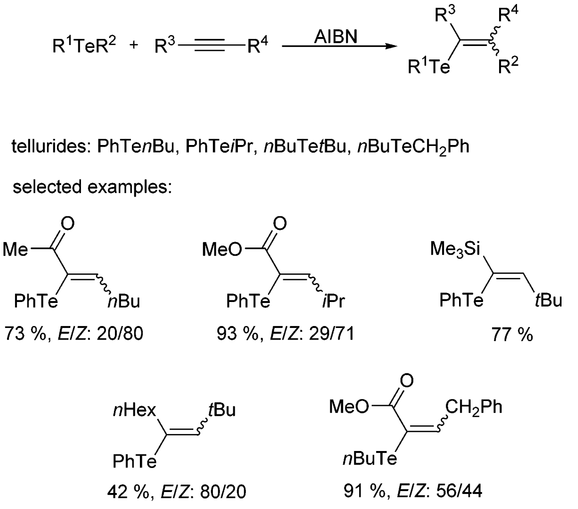


2.4. Preparation of Vinylic Tellurides by Free Radical Processes

2.4.1. Carbotelluration of Alkynes

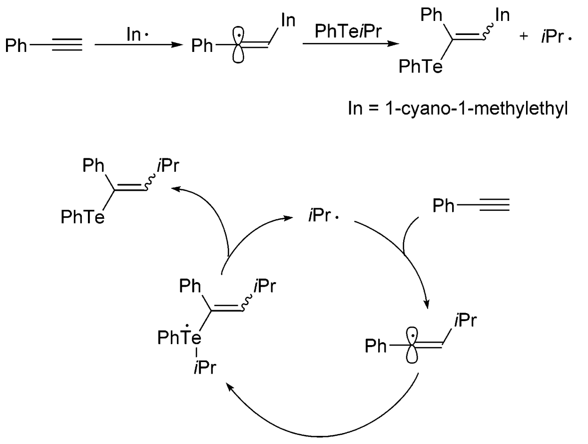
The carbotelluration of alkynes was described by Sonoda and co-workers.[72] Diorganyl tellurides add to alkynes regioselectively to afford alkenyl tellurides, as shown in Scheme 74. Primary, secondary, and tertiary alkyls and benzyl-substituted tellurides are suitable substrates for this carbotelluration, and good yields of the trisubstituted vinylic tellurides can be obtained in a range from poor to very good *E*/*Z* ratios.

Scheme 74



The mechanism of the reaction is believed to be a radical chain reaction initiated by the addition of 1-cyano-1-methylethyl radical (In•) to phenylacetylene, leading to the formation of *i*-Pr•, which then reacts with phenylacetylene to afford a vinylic radical. This species undergoes a reaction with diorganyl telluride, leading to the formation of vinylic telluride, and regenerates *i*-Pr• (Scheme 75).

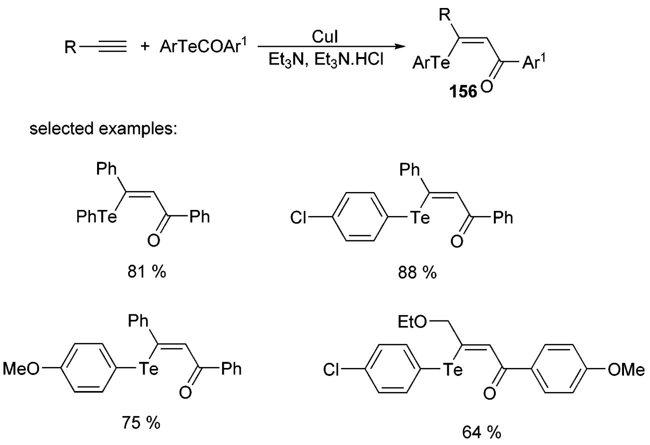
Scheme 75



2.4.2. Telluroacylation of Alkynes

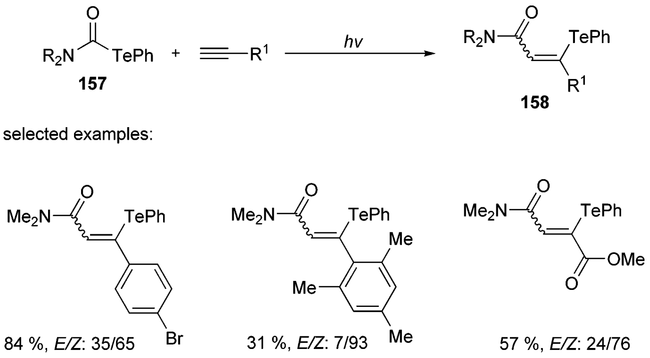
The telluroacylative addition of telluroesters to alkynes has been described. The reaction proceeded with the simultaneous introduction of the aryl tellurenyl and acyl groups to the organic molecule.[73] The reaction was performed in anhydrous dimethylformamide in the presence of cuprous iodide and triethylamine, and after exposure to air, the vinylic tellurides **156** were isolated in good yields (Scheme 76). It is worthy to mention that the reaction was highly stereoselective, and only *Z* adducts were isolated. Their configuration was confirmed based on differential NoE experiments.

Scheme 76



Carbamotelluroates **157** have been reported to add to acetylenes under irradiation of a visible light to form β-telluroacrylamides **158** in a regioselective manner.[74] The reaction proceeds via a radical chain mechanism comprising two processes: (i) the addition of carbamoyl radicals at the terminal carbon of the triple bond, giving vinylic radicals, and (ii) the S_N2 reaction on the Te atom caused by the attack of vinyl radicals to **157** (Scheme 77). The reaction typically occurs in good yields and with *E*/*Z* ratios of up to 7:93.

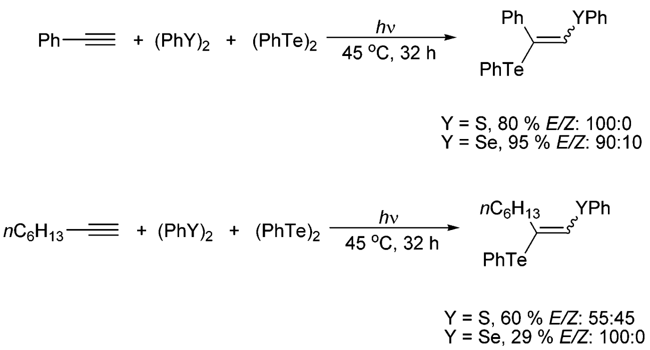
Scheme 77



2.4.3. Thio- and Selenotelluration of Alkynes

The thio- and selenotellurations of alkynes using a $(PhS)_2$ or $(PhSe)_2/(PhTe)_2$ binary system were reported by Ogawa and co-workers.[75] The reaction occurs with a visible light irradiation using equimolar amounts of diphenyl disulfide or diphenyl diselenide and diphenyl ditelluride, giving origin to the thio- and selenotelluration products in high yields and very good *E*/*Z* ratios for aromatic alkynes. Alkyl alkynes gave much poorer yields and selectivity for the thiotelluration system (Scheme 78).

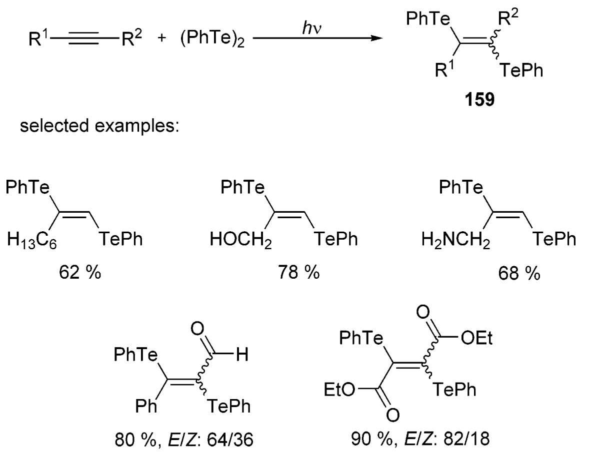
Scheme 78



2.4.4. Bistelluration of Alkynes

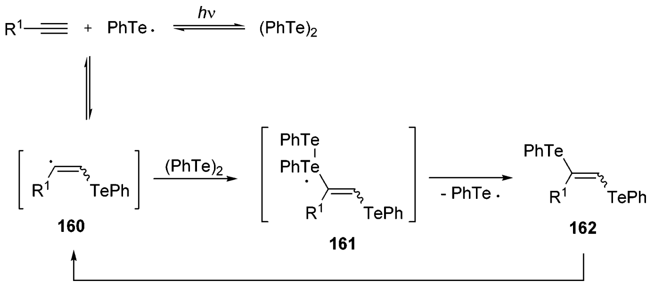
A method involving the photoinduced addition of diphenyl ditelluride to alkynes has also been developed, leading to the formation of bis(phenyltelluro) alkenes **159**.[76] The reaction was performed under a visible light irradiation (>400 nm), and a series of vicinal ditelluro alkenes **159** were produced in high yields and in good to excellent diasteroselectivities, with preferential formation of the *E* isomer (Scheme 79).

Scheme 79



The authors provided a mechanistic proposal which includes the addition of the phenyltelluro radical (PhTe•) to acetylenes to form the alkenyl radical intermediate **160** and the subsequent S_N2 reaction of **161** with $(PhTe)_2$, leading to 1,2-bis(phenyltelluro)alkenes **162** with a regeneration of PhTe• (Scheme 80).

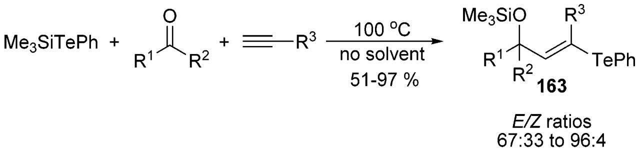
Scheme 80



2.4.5. Addition of Trimethylsilyl Phenyl Telluride to Alkynes

A three-component reaction of trimethylsilyl phenyl telluride, carbonyl compounds, and an alkyne was reported by Yamago and co-workers.[77] The reaction occurs at 100 °C without solvent. This reaction is applicable to a variety of carbonyl compounds and alkynes and seems to be useful for the diversity-oriented synthesis of allylic alcohols (Scheme 81). Aromatic ketones and aldehydes are more suitable substrates, since shorter reaction times are required and the product **163** is obtained in higher yields. The reaction is *E* selective, and ratios of up to 96:4 are obtained.

Scheme 81

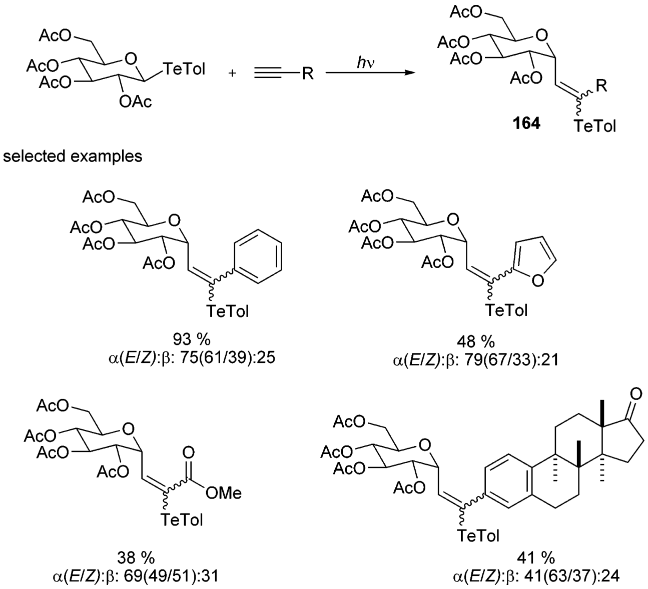


R^1, R^2 = Ph, *p*-MeOPh, *p*-Me_2NPh, *i*Pr, -$(CH_2)_3$-, H
R^3 = Ph, *p*-EtO_2CPh, *p*-BrPh, 3-pyridyl, 1-cyclohexenyl, CO_2Et

2.4.6. Radical Addition of Telluroglycosides to Alkynes

A very interesting paper on the preparation of a vinylic telluride with a glucosyl moiety has been published.[78] The reaction is applicable to a variety of aryl and heteroaryl alkynes in high yields, and it proceeds under neutral conditions, allowing the use of acid- and base-labile groups. Alkyl alkynes gave low yields of the product **164**, and internal alkynes did not react under the described conditions. In all cases, the α isomers were preferentially obtained over the *β* isomers (Scheme 82).

Scheme 82

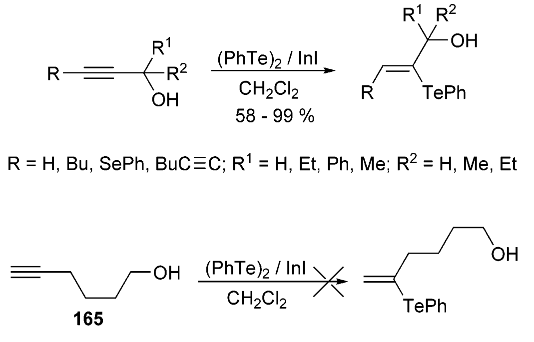


2.5. Miscellaneous

2.5.1. Preparation of Vinylic Tellurides via Indium Tellurolate

Recently, we have described a rigorous chemio-, regio-, and stereoselective protocol for the hydrotelluration of several propargyl alcohol derivatives using an indium(III) tellurolate.[79] Tellurium nucleophile is readily generated by the reaction of In(I)I with $(PhTe)_2$ in dichloromethane through an oxidative insertion of indium monoiodide to the Te−Te bond. The reaction of the indium tellurolate, generated *in situ*, with a range of propargyl alcohols furnishes Markovnikov adducts in good to excellent yields (Scheme 83). The reaction is efficient for a series of substituted substrates at R, R^1, and R^2 positions; however, when longer chain alcohols were employed, no product was obtained (Scheme 83).

Scheme 83



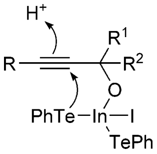


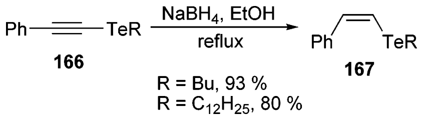
Figure 5.

We believe that the reaction occurs through the coordination of the propargyl alcohol hydroxyl group with indium tellurolate, indicating that this could be key for the high chemio-, regio-, and stereoselectivity obtained in the addition of a tellurium moiety to an alkyne. This observation can be used to explain why longer chain alcohols, such as **165**, do not react under these conditions (Figure 5).

2.5.2. Vinylic Tellurides from Acetylenic Tellurides

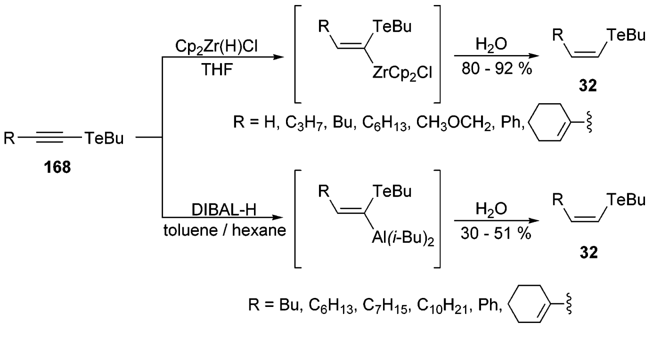
Acetylenic tellurides **166** are suitable substrates for the preparation of vinylic tellurides. Several different reducing agents were tested to reduce alkyne to alkene, leading to vinylic tellurides. However, many reagents, such as $LiAlH_4$ and hydrazine, fail to have success in this transformation, since only terminal alkynes and the corresponding ditellurides were obtained. The first successful method reported was the reduction of alkynyl tellurides **166** with sodium borohydride in ethanol, under reflux.[80] The reaction is believed to form acetylide and tellurolate anions by the cleavage of the Csp−Te bond. Next, the tellurolate attacks the triple bond in a hydrotelluration reaction to generate vinylic tellurides **167** in good yields (Scheme 84).

Scheme 84



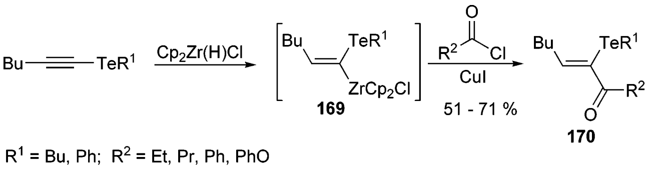
Another approach to the reduction of acetylenic tellurides **168** to produce vinylic tellurides **32** is the hydrometalation reaction followed by acidic quenching. The most commonly used metals are aluminum[59] and zirconium,[47] due to their ability to reduce the triple bond without cleaving the Csp−Te bond, which is very labile. Comparatively, hydrozirconation offers advantages over hydroalumination reactions, mainly because it is performed at room temperature and higher yields are significantly obtained. On the other hand, the use of DIBAL-H as a reducing agent results in a partial removal of the organotellurium moiety from the acetylenic tellurides **168**, explaining the lower yields of vinylic tellurides **32** (Scheme 85).

Scheme 85



In another example of hydrozirconation of acetylenic tellurides, the vinylzirconium intermediates **169** are trapped with acyl chlorides to give origin to a range of *Z*-α-organotelluro-α,*β*-unsaturated carbonyl compounds **170** (Scheme 86).[81] Regio- and stereocontrol of the reaction is well defined, and only the *Z* products are obtained. The reaction is assumed to pass though a Zr−Cu transmetalation with retention of the configuration at carbon.[82] Besides CuI, other copper salts, such as CuBr, CuCN, and $CuBr{\cdot}SMe_2$, gave similar results.

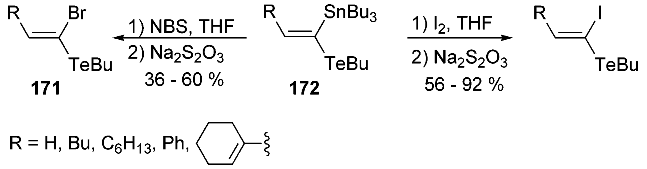
Scheme 86



2.5.3. Preparation of α-Halo Vinylic Tellurides from Ketene Stannyl(Telluro) Acetals

Halogen-functionalized vinylic tellurides have a great potential for organic synthesis. Their preparation has been described to occur through a Sn−halogen exchange reaction in mixed ketene stannyl(telluro) acetals.[51] The reaction was carried out under mild conditions, and the iodo derivatives were obtained upon treatment of the starting material **172** with 2.15 equiv of iodine in THF (Scheme 87). Other solvents and different amounts of iodine resulted either in lower yields or in partial isomerization of the double bond. Similarly, brominolysis was performed with NBS in THF; however, a mixture of products was obtained when Br_2 was used instead of NBS. Total retention of the double bond configuration was observed here, although the brominated products **171** were obtained in lower yields when compared to the case of iodinolysis (Scheme 87).

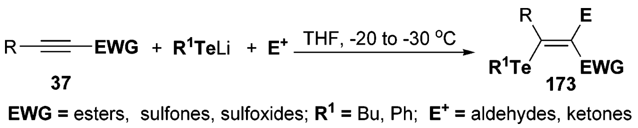
Scheme 87



2.5.4. Preparation of Vinylic Tellurides via Electrotelluration Reactions

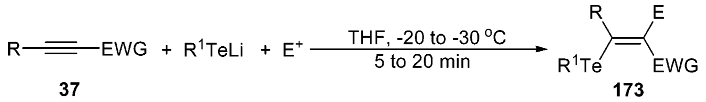
A new approach into the synthesis of vinylic tellurides has been recently described by Marino and Nguyen.[83] This reaction involves the addition of a lithium tellurolate anion to alkynes **37** containing an electron-withdrawing group, followed by the trapping of the incipient vinyl anion with electrophyles, such as aldehydes, ketones, and trialkylsilyl chlorides. This method leads to tri- and tetra-substituted alkenes **173** bearing an organotellurium group (Scheme 88).

Scheme 88

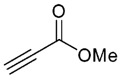
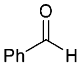
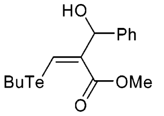
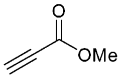
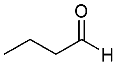
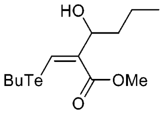
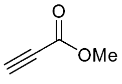
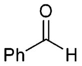
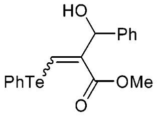
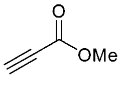
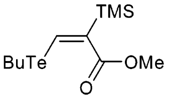
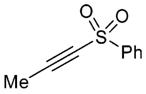
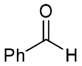
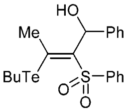
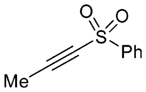
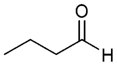
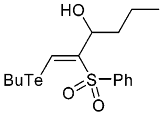
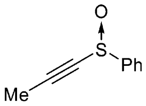
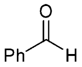
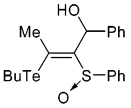
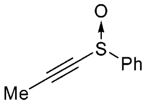
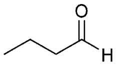
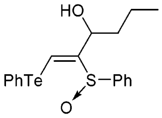


Initial tests of this reaction were performed with nonactivated alkynes, and no trapping of benzaldehyde was achieved. The attention was turned to the more activated alkynes, such as alkynyl esters, sulfones, and sulfoxides.

Table 5. Electrotelluration Reaction



37 **173**

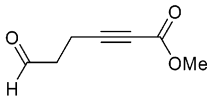
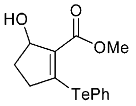
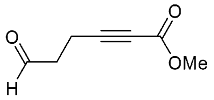
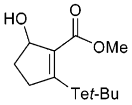
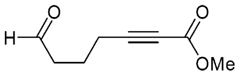
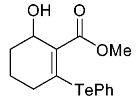
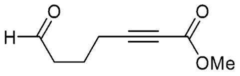
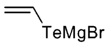
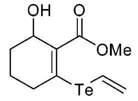
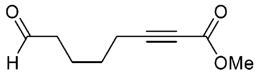
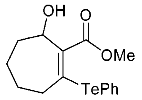
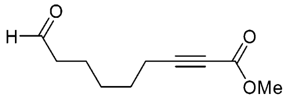
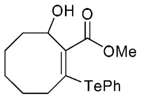
Entry	Alkyne	Nucleophile	Electrophile	Product	Yield (%)
1		BuTeLi			71
2		BuTeLi			46
3[a]		PhTeLi			84
4		BuTeLi	TMSCl		45
5		BuTeLi			69
6		BuTeLi			60
7		BuTeLi			65
8		PhTeLi			78

[a] A 1:13 ratio of *E*/*Z* isomers was obtained.

Several variations in the organic group attached to tellurium as well as the electrophile are tolerated. The authors observed that the aldehydes are very good electrophiles giving the products in very short reaction times (Table 5). Trimethylsilyl chloride was also employed as electrophile, which gave the vinylic tellurides, without any O-silylation product formation (Table 5, entry 4). The authors also described that the phenyl tellurolate is less reactive than the butyl tellurolate, allowing a *cis*/*trans* equilibration of the vinyl anion (Table 5, entry 3). Except for this case, all other examples with esters, sulfones, and sulfoxides afforded the *Z*-vinylic telluride in good yields.

Upon the success of this first attempt at the electrotelluration reaction, the intramolecular version of this method was studied. The reaction is analogous to the intramolecular Baylis–Hillman reaction,[84] with the advantage that the tellurium nucleophile is incorporated into the product after ring formation, and the product can then be further transformed into other functional groups. The reactions were performed mainly with lithium phenyl tellurolate due to the fact that its products demonstrated higher stability than those of lithium butyl tellurolate. The intramolecular electrotelluration was completed very quickly, and the cyclized products were obtained in moderate to good yields. Seven- and eight-membered rings were obtained in lower yields because the proton trapping of the vinyl anion intermediate was competitive with the intramolecular cyclization (Table 6, entries 5 and 6).

Table 6. Intramolecular Electrotelluration

Entry	Alkyne	Nucleophile	Product	Yield (%)
1		PhTeLi		72
2		*t*-BuTeLi		51
3		PhTeLi		80
4				74
5		PhTeLi		41
6		PhTeLi		48

3. Reactivity of Vinylic Tellurides

3.1. Stability of the Carbon–Tellurium Bond in Vinylic Tellurides

A remarkable paper was published by Comasseto and Rahmeier in 1997 that dealt with the stability of the carbon−tellurium bond in vinylic tellurides toward several different reagents frequently used in organic chemistry laboratories worldwide.[85]

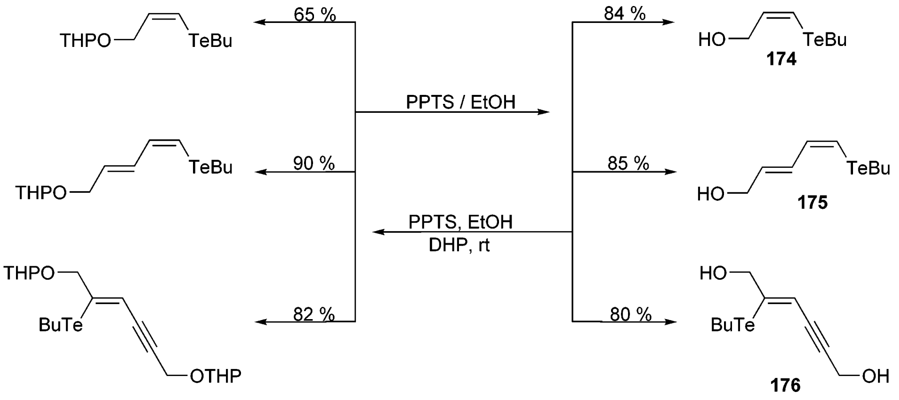
The authors studied both transmetalation reactions, which we will discuss in detail in the upcoming section, and the behavior of vinylic tellurides under several different conditions, such as acids, bases, and oxidizing and reducing agents.

First, the stability of the C−Te bond was studied in the presence of protection/deprotection conditions. Hence, three different vinylic tellurides, **174**, **175**, and **176**, containing a free hydroxyl group were protected as their THP ethers under acid catalysis of PPTS (Scheme 89). The hydrolysis of the THP ethers regenerated the vinylic tellurides with free hydroxyl groups and was performed under acidic conditions with PPTS/EtOH at 50 °C (Scheme 89). In the protection or deprotection reaction, neither removal of the tellurium group nor isomerization of the double bond was observed. When the reaction temperature was higher than 55 °C, dibutyl ditelluride was formed as a byproduct.

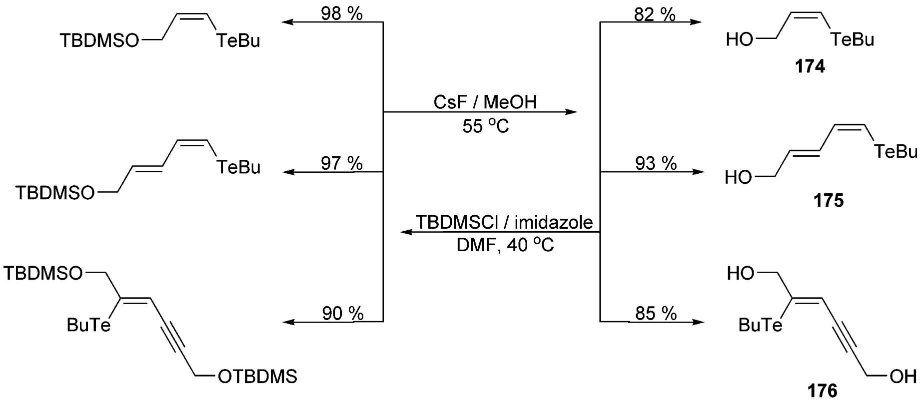
When TBDMS was used as a protecting group, under a basic catalysis of imidazole, high yields were obtained. Conversely, the deprotection of the corresponding tellurides with free OH groups was easily achieved by treatment with cesium fluoride in MeOH at 55 °C (Scheme 90). The C−Te bond has also proven to be stable under these reaction conditions.

Acetylation of vinylic tellurides was performed with acetic anhydride in pyridine giving the acetylated products, **177**,

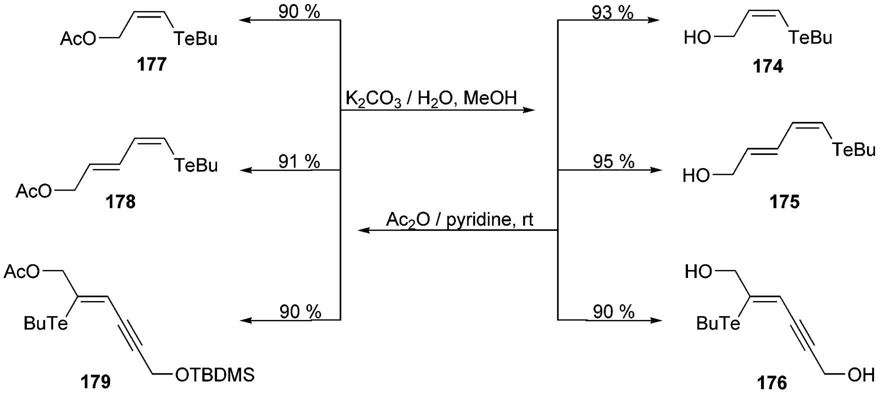
Scheme 89



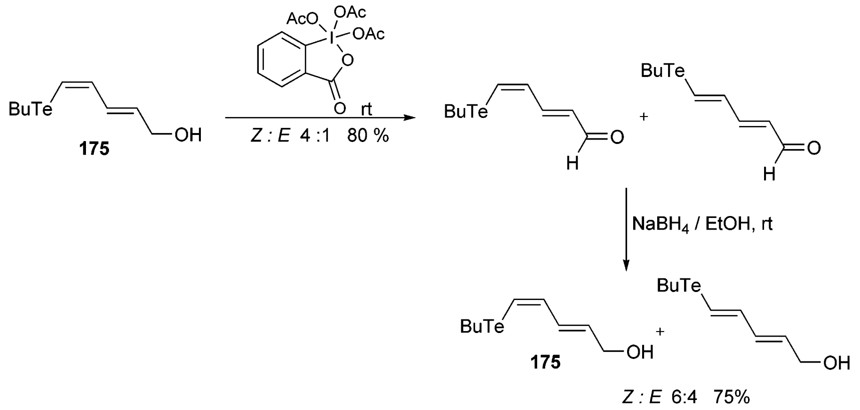
Scheme 90



Scheme 91



Scheme 92

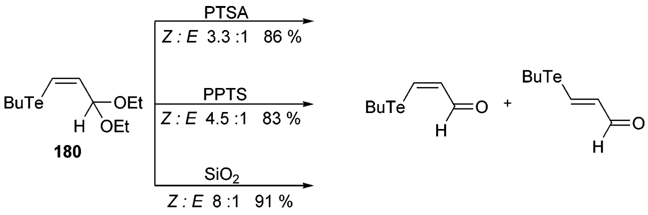


178, and **179**, in high yields. The corresponding hydrolysis of the acetylated products was performed under basic conditions, regenerating the vinylic tellurides in excellent yields (Scheme 91).

The studies have been further extended toward oxidizing and reducing conditions. In fact, it has been observed that telluride **175** was oxidized to the corresponding unsaturated aldehyde in 80% yield by treatment with Dess–Martin periodinane. However, the isomerization of the telluride carbon–carbon double bond took place and a 4:1 *Z*/*E* mixture was isolated. The reduction of this mixture with $NaBH_4$ resulted in vinylic telluride with a *Z*/*E* ratio of 6:4 (Scheme 92).

The hydrolysis of vinylic telluride **180** under several different conditions resulted in the formation of unsaturated aldehyde in good yield. However, under all conditions employed, isomerization of the double bond was observed. The best *Z*/*E* ratio (8 to 1) was obtained when SiO_2 in hexane was employed (Scheme 93).

Scheme 93



3.2. Transmetalation Reactions

One of the most powerful applications of vinylic tellurides is the ability to undergo tellurium–metal exchange reactions with several different commonly used, commercially available, or easily prepared organometallic reagents. This tel-

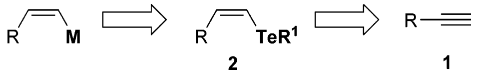


Figure 6.

lurium−metal exchange reaction proceeds very easily, giving origin to vinyl organometallics, which are very useful intermediates from the synthetic point of view. In addition to the ease of the exchange reaction, one unique feature of vinylic tellurides is that they give *Z*-vinyl organometallics by a simple hydrotelluration−transmetalation sequence (Figure 6).

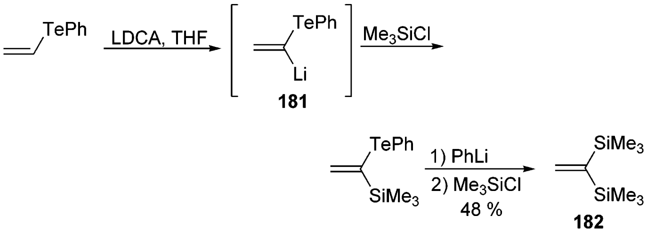
In this section we will discuss the nuances of the tellurium−metal exchange reactions, emphasizing their scope and generality for useful transformations in organic synthesis.

3.2.1. Tellurium–Lithium Exchange Reactions

The tellurium−lithium exchange is a very attractive transformation of vinylic tellurides, since it affords the corresponding vinyllithium species, which react with a wide range of electrophiles, providing funcionalized alkenes with a complete retention of the stereochemistry of the starting telluride.

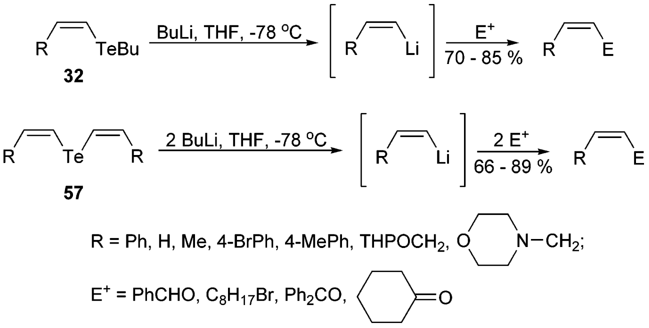
A significant study on the tellurium−lithium exchange was carried out by Kauffmann,[86] in an extension of a previous finding of Seebach,[87] in which organic tellurides were transformed into their lithium analogues by treatment with an organolithium reagent. The reaction of lithium intermediates **181** with trimethylsilyl chloride afforded the silylated product **182** in 48% yield (Scheme 94).

Scheme 94



A few years later, Comasseto and co-workers studied in detail the transmetalation of *Z*-vinylic **32** and *Z*,*Z*-bis-vinylic tellurides **57** with BuLi.[88] The reaction of the vinyllithium intermediates with several electrophiles, such as aldehydes, ketones, and alkyl bromides, was accomplished in good yields, leading to functionalized *Z*-alkenes with a complete retention of the original double bond geometry (Scheme 95).

Scheme 95



Moreover, when *Z*,*Z*-bis-vinylic tellurides **57** were employed, 2 equiv of vinyllithium was formed. The authors observed that when an aryl group (as in **142**) instead of a butyl group (as in **32**) was attached to the tellurium atom, a complex mixture of products was obtained. This can be explained by the fact that BuLi can attack two sites (the C_{vinyl}−Te and C_{aryl}−Te bonds), giving a mixture of lithium intermediates and, consequently, affording a mixture of products (Figure 7).

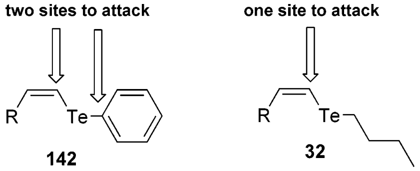
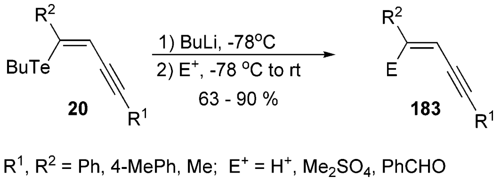


Figure 7.

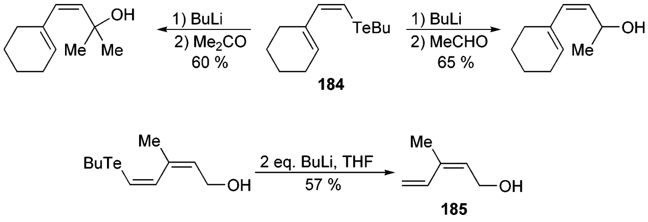
After these findings, many other classes of vinylic tellurides have been used to generate vinyllithium intermediates with a defined double bond geometry. Conjugated vinylic tellurides, such as those containing an enyne moiety **20**, were successfully transmetalated with BuLi, yielding enynes free of tellurium **183**.[14a] The reaction occurred with total retention of the double bond geometry, even when the temperature was raised from −78 °C to room temperature. This is noteworthy since the halogen−lithium exchange in conjugated systems, such as enynyl bromides and butadienyl bromides, occurs with a loss of the stereoselectivity of the double bond (Scheme 96).[89] The enynyllithium intermediates obtained by this method successfully react with benzaldehyde, dimethyl sulfate, and water in high yields and very short reaction times (ca. 30 min).

Scheme 96



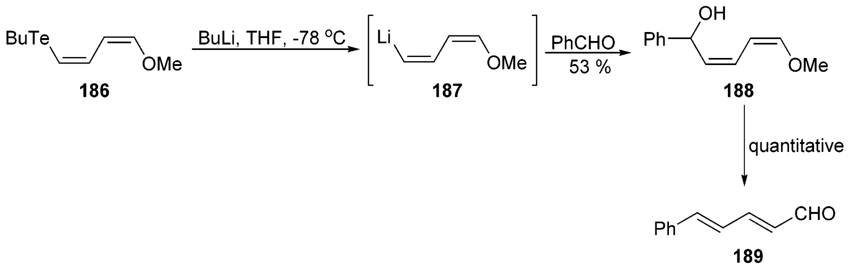
The conjugated diene system bearing a tellurium group deserves a particular interest in the transmetalation reactions, since it is an important structural feature of many natural products, such as insect pheromones.[90] This system is a highly valuable intermediate in organic synthesis, especially as a substrate for the Diels−Alder reaction.[91] The stereodefined functionalized dienes can be prepared by means of a Te−Li exchange of 1-butyltelluro-1,3-butadiene **184**.[14b] The transmetalation occurs smoothly at low temperatures, and the trapping of lithium intermediates by electrophiles, such as acetone and acetaldehyde, gives *Z*-allylic alcohols in good yields (Scheme 97). The reaction with water as a proton source readily furnishes the product free of the tellurium group **185** in moderate yield (Scheme 97).

Scheme 97



The reaction of (1*Z*,3*Z*)-1-butyltelluro-4-methoxy-1,3-butadiene (**186**) with BuLi at −78 °C generates the vinyllithium intermediate **187**, which reacts with benzaldehyde to afford allylic alcohol **188** in 53% yield. The product is spontaneously and quantitatively converted into the 5-phenyl

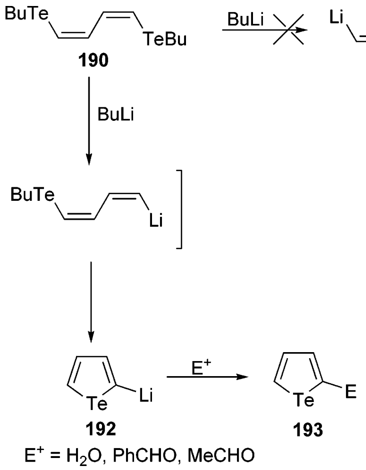
Scheme 98



pentadienal **189** with an *E*-configuration in the two double bonds (Scheme 98).

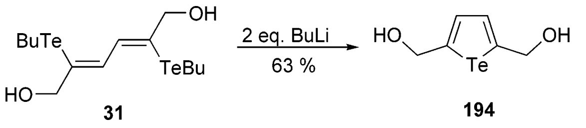
Furthermore, the reaction of butyllithium with 1,4-bis-(butyltelluro)-1,3-butadiene (**190**) did not afford the 1,4-dilithium species **191** as expected; rather, a ring closure to form tellurophene **192** was observed.[14b] The first tellurium exchange occurs, and before the second exchange takes place, the tellurium atom is intramolecularly attacked by the vinyl anion, and the aromatic heterocycle is formed. A second equivalent of butyllithium is assumed to deprotonate the α-position of tellurophene. This fact is supported by the addition of benzaldehyde to the reaction mixture, affording 2-substituted tellurophene **193** in 60% yield (Scheme 99).

Scheme 99



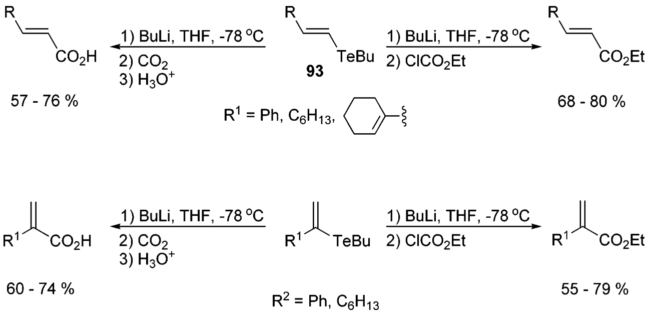
In addition, 2,5-disubstituted tellurophene **194** was prepared by the reaction of bis(butyltelluro)-1,3-butadiene **31** with butyllithium in THF in 63% yield (Scheme 100).

Scheme 100



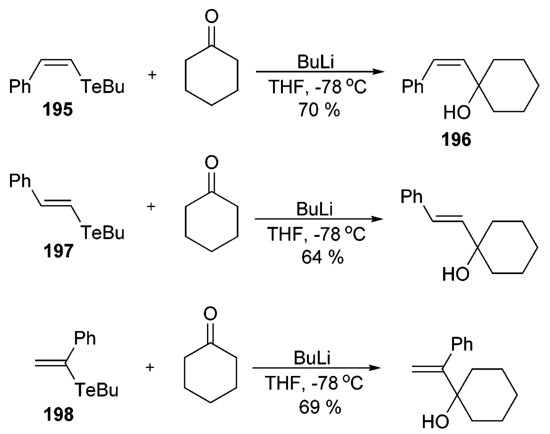
The *E* isomers of vinylic tellurides undergo a tellurium–lithium exchange in the same manner as the *Z* isomers. The synthetic potential of such a reaction was tested in the preparations of α,*β*-unsaturated acids and esters, which were accomplished in good yields by successive transmetalations and trapping of the incipient vinyl anion. Carboxylic acids were obtained by capture of the anion with CO_2 and acidic quenching in yields ranging from 55 to 79%. The parent esters were achieved in comparable yields (60–80%) by a similar protocol, just by changing the trapping agent to ethyl chloroformate (Scheme 101).[45b]

Scheme 101

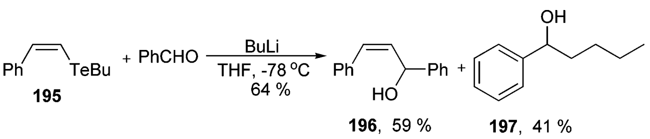


A very remarkable report on the reactivity of vinylic tellurides toward butyllithium describes the intermolecular competition between the tellurium–lithium exchange and the direct addition of the organolithium reagent to carbonyl compounds.[92] For this purpose, 1 equiv of BuLi was added at −78 °C to a solution of equal amounts of vinylic telluride and the carbonyl compound in THF. This study showed a remarkable reactivity profile for vinylic tellurides in comparison to carbonyl compounds and was useful to predict the reactivity of such systems in an intramolecular version of this reaction. The results of these experiments showed that when a ketone was employed, the reaction of *n*-BuLi took place exclusively at the vinylic telluride, giving the corresponding vinyllithium intermediate, which further reacted with cyclohexanone to afford allylic alcohol **196** in good isolated yields. The three different isomeric tellurides **195**, **197**, and **198** showed the same behavior and furnished the product in similar yields (Scheme 102).

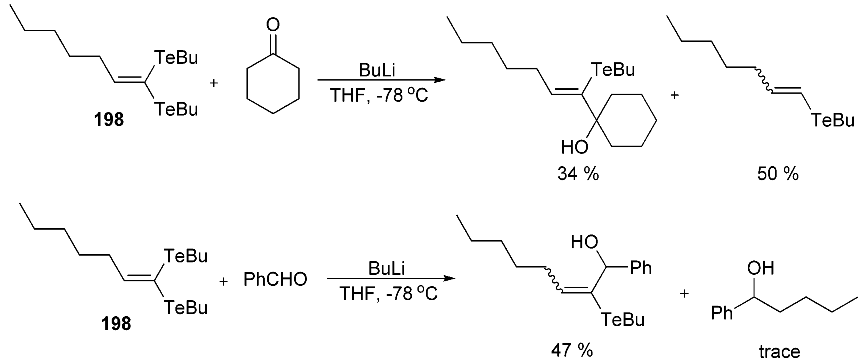
Scheme 102



Scheme 103



Scheme 104

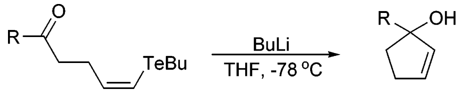


The same authors observed that when benzaldehyde is employed in the place of cyclohexanone, a competition between transmetalation and addition reactions is observed, since the products **196** and **197** were isolated. However, even when the more reactive aldehyde was used, the Te−Li exchange and further attack of the vinylic intermediate to benzaldehyde was the predominant pathway, since the major products were allylic alcohols (Scheme 103).

On the other hand, when ketene telluroacetal **198** was treated with the same reaction conditions described in Scheme 94, the Te−Li exchange occurred exclusively at one of the butyltelluro moieties. The reaction of the vinyl anion intermediate with carbonyl compounds takes place, but the products are isolated in low yields. This is probably due to the lower reactivity of the vinyl anion, as it is partially stabilized by the adjacent tellurium atom (Scheme 104).[92]

Taking advantage of the higher reactivity of the C−Te bond in the presence of a carbonyl functional group, an intramolecular reaction was performed and the cyclopentenols **199** were obtained in moderate yields (Scheme 105).[92]

Scheme 105

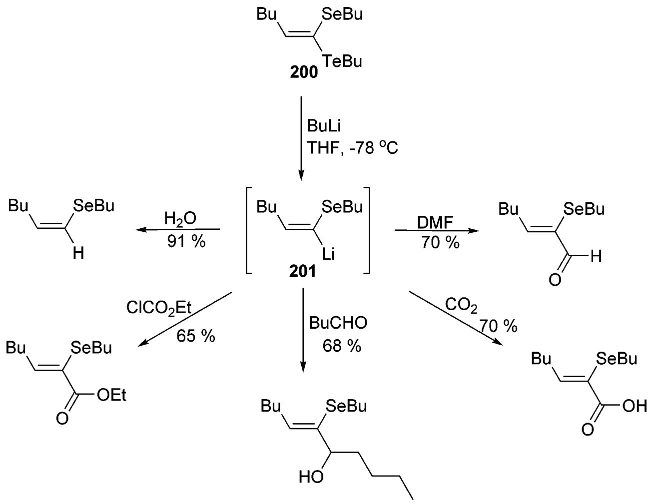


199
R = Me, 53 %
R = Et, 56 %

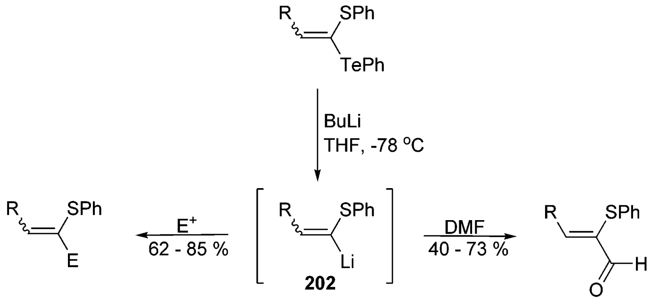
Reactions of ketene telluro(seleno) acetal **200** and telluro(thio) acetals with *n*-BuLi showed a regioselective removal of the organotellurium moiety and a formation of functionalized α-chalcogenide vinyllithium **201** and **202**. The posterior reaction of α-chalcogenide vinyllithium with several different electrophiles, such as water, DMF, ethylchloroformate, carbon dioxide, and aldehydes afforded the vinylic selenides, unsaturated aldehyde, ester, acid, and allylic alcohol in good yields with total retention of the double bond geometry (Scheme 106).[48] It is important to note that the Te−Li exchange occurs much faster than the Se−Li exchange.[93]

Similarly, ketene telluro(thio) acetals undergo the tellurium−lithium exchange, leading to the α-thio vinyllithium intermediates, which react with water, benzaldehyde, and methyl iodide to give the functionalized vinylic sulfides in good yields.[70] The reaction with DMF as the electrophile surprisingly affords almost only one isomer of the product, even if a mixture of *Z* and *E* isomers of the starting material is used (Scheme 107).

Scheme 106



Scheme 107



R = Ph, 4-ClPh, Pr; E^+ = PhCHO, H_2O, MeI

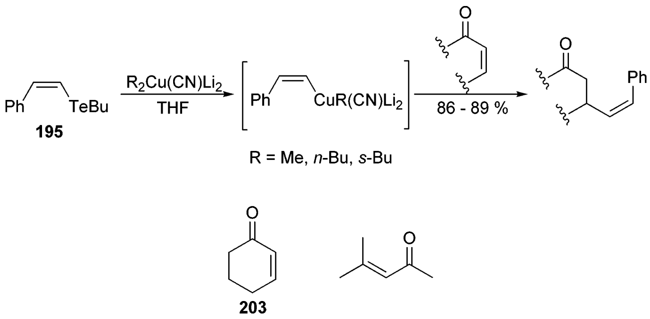
3.2.2. Tellurium–Copper Exchange Reations

The tellurium−copper exchange is probably the most important and promising of the tellurium exchange reactions, since it affords vinyl copper reagents of a *Z*-configuration, which can react with a variety of electrophiles and with complete retention of the double bond geometry.

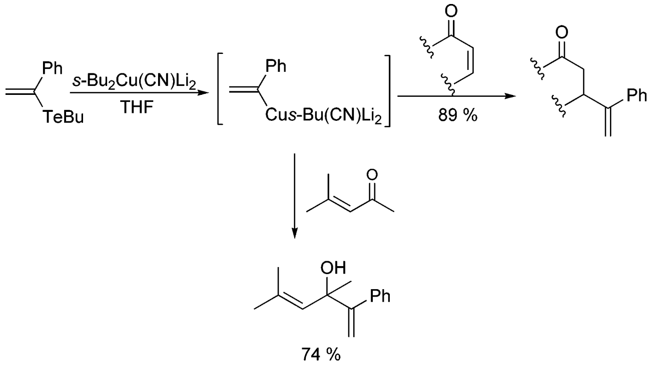
The landmark paper on the tellurium−copper exchange was published by Comasseto and Berriel in 1990 and opened outstanding new branches in the field of organotellurium chemistry.[94] The discovery of this new methodology to generate *Z*-vinyl copper reagents by a simple hydrotelluration−tellurium exchange sequence has allowed the exploration of several new features of tellurium chemistry that had not been envisaged before.

These new reactive alkenyl copper reagents have been successfully employed in conjugate additions to enones, leading to functionalized carbonyl compounds in high yields. The reaction is performed by adding vinylic telluride to the higher order cyanocuprate at room temperature. The ligand exchange reaction between vinylic telluride and the higher order cuprate occurs, followed by the addition of enone to the mixture at −78 °C. The nature of the R groups at the cuprate is important for the outcome of the reaction. No significant difference in the generation of the mixed cuprate was observed when an Me or *n*-Bu group was used, but sometimes a competition between the vinyl and butyl transfers can be observed (Scheme 108). However, when more crowded *s*-Bu or sterically hindered enones were employed, the 1,2-addition reaction took place instead of the 1,4-addition (Scheme 109). It is important to point out that if a phenyl, instead of a butyl group, is linked to tellurium at the vinylic telluride, a change in the selectivity of the transfer reaction of the phenyl group over the vinyl is observed.

Scheme 108

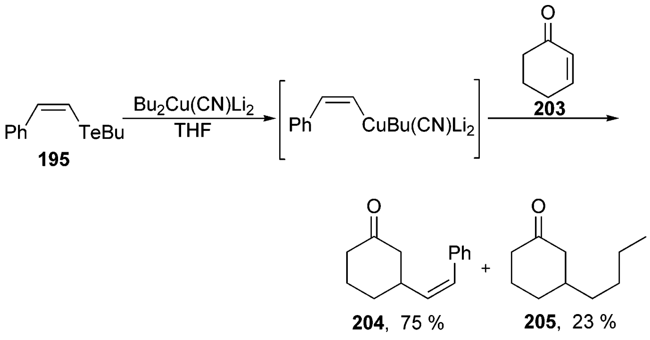


Scheme 109



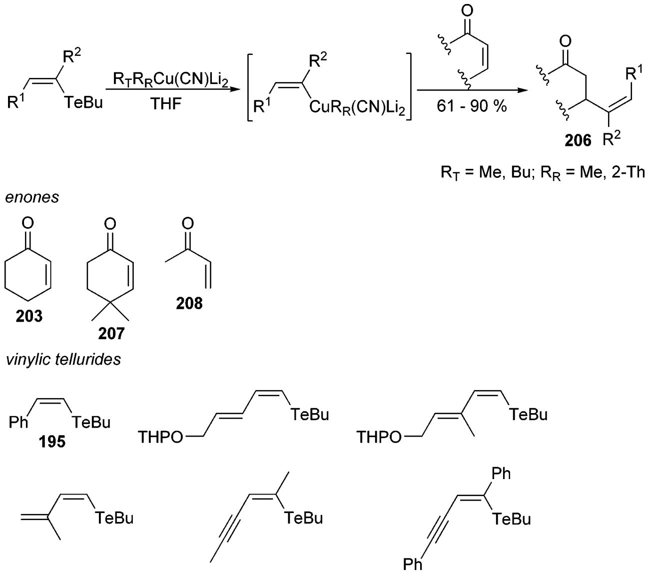
Later studies by same group have revealed that the reaction has been carried out with a wide range of enones using several different vinylic tellurides as precursors for the mixed cuprates.[11a,95] Detailed examination of the reaction conditions indicated that the butyl group was not the best residual ligand of the cuprate, since it led to a mixture of vinyl and butyl transfer products **204** and **205** (Scheme 110). The better results were achieved when the cuprate was formed from methyl, 2-thienyl (2-Th), or imidazoyl (Imid) cuprates, all of which exclusively gave the vinyl transfer product **204**. The cuprates most used were $Me_2Cu(CN)Li_2$ and Bu(2-Th)-$Cu(CN)Li_2$.

Scheme 110



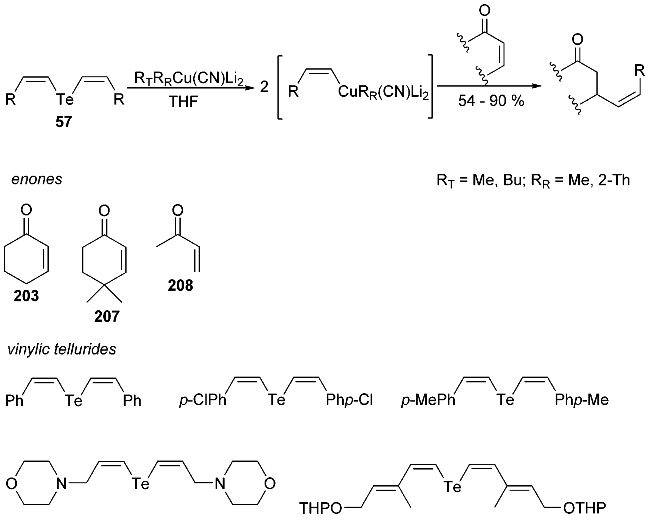
Three different enones were employed in this study, namely cyclohexenone **203**, 4,4-dimethylcyclohexenone **207**, and methyl vinyl ketone **208**. A range of vinylic tellurides was employed, and all of them were successfully transmetalated to the mixed higher order vinyl cyano cuprates, exclusively giving the alkenyl 1,4-addition products **206**. Several useful products have been achieved by this methodology, since stereochemically defined vinylic tellurides bearing diene or enyne moieties undergo the tellurium−copper exchange smoothly and are then transferred to the enones in good yields (Scheme 111). It is also noteworthy that no isomerization of the double bonds is observed. There is no great influence if the R_R group is changed from 2-Th to Me.[11a,95a,b]

Scheme 111

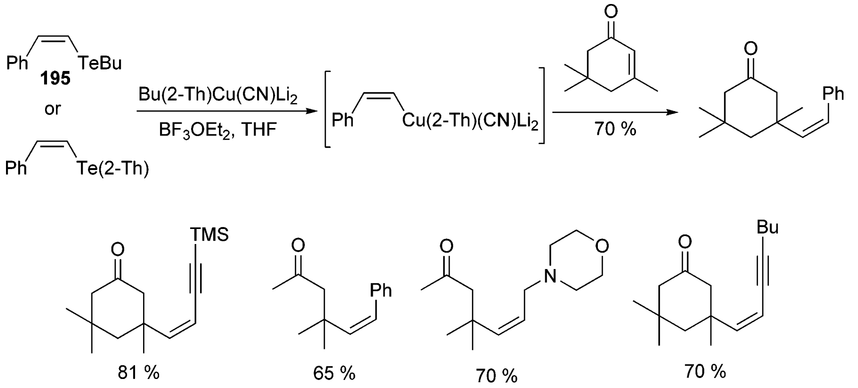


Moreover, bis-vinylic tellurides **57** are suitable substrates for the generation of the mixed cuprates with the advantage that 1 equiv of the bis-vinylic telluride can generate 2 equiv of the higher order vinyl cuprate. The reaction proceeds in

Scheme 112



Scheme 113



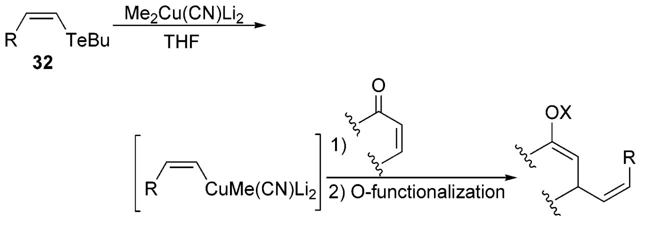
similar yields when compared to butyl vinyl tellurides, and the vinyl moiety is transferred exclusively, with complete retention of the stereochemistry of the starting telluride.[11a,95a,b]

The authors observed that hindered enones fail to react under the reaction conditions described in Scheme 112. To overcome this problem, changes in the reaction conditions were studied in order to make it possible to transfer vinyl copper reagents to more encumbered substrates. An efficient solution to this problem was to add $BF_3{\cdot}Et_2O$ to the reaction mixture, giving the 1,4-addition product in good yields with both THF and ether as solvents (Scheme 113).[96]

Additional studies on this reaction toward highly unsaturated systems have been developed. They explored the conjugate addition of an organocuprate followed by O-functionalization, leading to enol silanes, triflates, and phosphates.[97]

Several different vinylic tellurides of a *Z*-configuration, such as those containing diene and enyne moieties and bisvinylic tellurides, were employed in this reaction. The intermediate enolate was trapped with chlorotrimethylsilane, diethylchlorophosphate, and *N*-phenyltrifluoromethane-sulfonamide to generate the enolsilanes, phosphates, and triflates, respectively (Scheme 114).

Scheme 114



X = TMS, $P(O)(OEt)_2$, Tf

Highly unsaturated systems were assembled by this strategy, as depicted in Figure 8. The possibility of further extension of the chain with selective cross-coupling reactions at the OX group, leading to even more complex unsaturated conjugated systems, was devised. Similarly, a Negishi-type cross-coupling reaction catalyzed by Pd(0) was performed with *Z*-vinylzinc chloride **210**, generated by the transmetalation of vinylic telluride **209** with BuLi, followed by the treatment of the vinyllithium intermediate with zinc chloride. The reaction proceeded smoothly to afford the TMS-fuctionalized dienyne **212** in 80% yield. In addition, a Sonogashira reaction between propargyl alcohol and enol triflate **211** catalyzed by $Pd(PPh_3)_4$ was performed, giving the cross-coupled product **213** in high yield (Scheme 115).

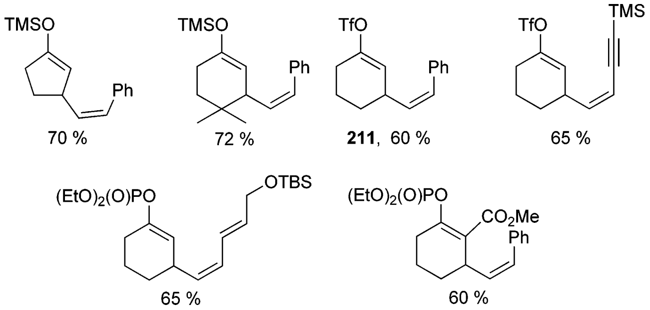
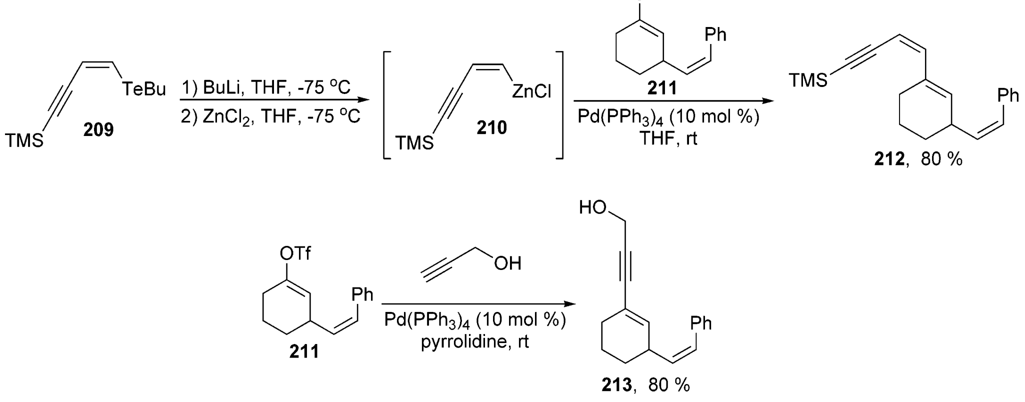


Figure 8.

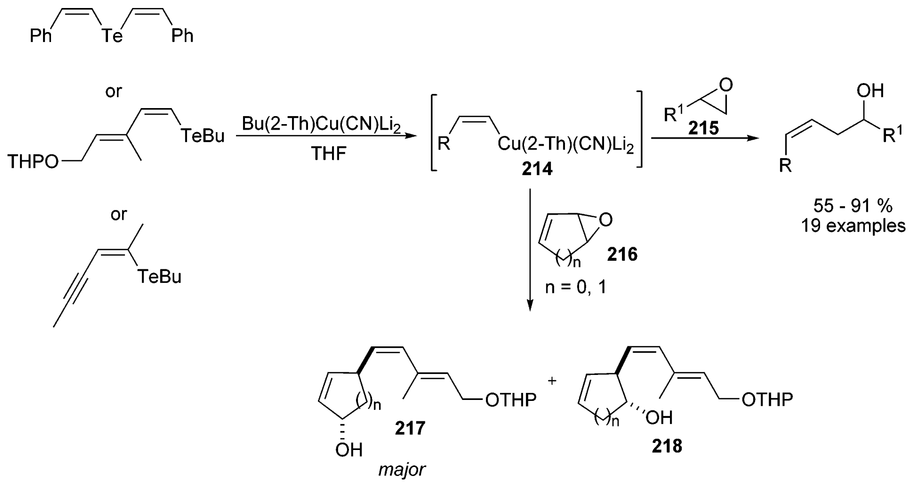
Besides α,*β*-unsaturated ketones, another class of electrophiles that have been used in reactions with the vinyl copper species generated by the tellurium−copper exchange reaction is epoxides.[11a,98]

Epoxide opening proceeds through a S_N2 mechanism, and in the particular case of a reaction with vinyl cuprates,

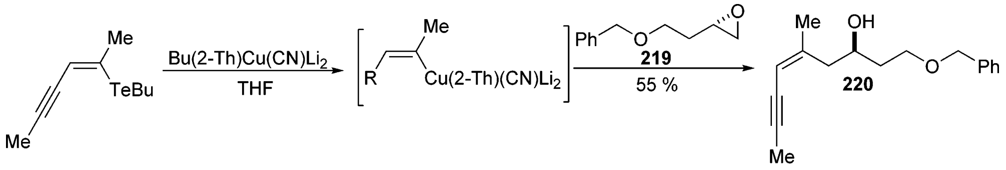
Scheme 115



Scheme 116



Scheme 117



homoallylic alcohols are formed as the major products. The importance of this transformation is highlighted by the fact that homoallylic alcohols are key intermediates in several total syntheses.[99]

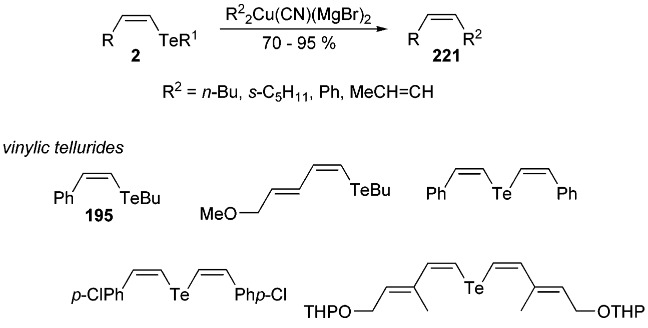
The higher order vinylic cuprates **214** which were employed in the epoxide openings were generated in the same manner as for the addition to enones. Hence, dilithio-2-thienylbutylcyanocuprate was chosen for the transmetalation reaction, since both $Me_2Cu(CN)Li_2$ and $Bu_2Cu(CN)Li_2$ demonstrated transfer competition between alkyl and vinyl groups.

Several different epoxides were opened under these conditions. Usually, monosubstituted epoxides **215** gave the product of attack to the less-substituted position in good yields. Disubstituted epoxides failed to react, even if a Lewis acid was introduced to the reaction medium. It is remarkable to note that cyclic vinyl epoxides **216**, such as cyclopentadiene and 1,3-cyclohexadiene monoxide, yielded preferentially the 1,4-addition product **217** over the 1,2-addition product **218**, although in moderate regioselectivities (Scheme 116). Again a remarkable feature of the reaction is the complete retention of the stereochemistry of vinylic telluride during the vinyl transfer process.

Chiral epoxides, such as **219**, were employed in such transformations since the chiral homoallylic alcohol **220** was isolated without any loss of its optical purity, as determined by ^{19}F NMR spectroscopy of its Mosher's ester (Scheme 117).

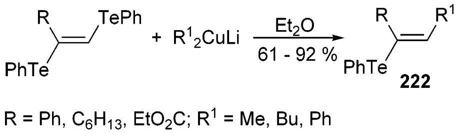
A dramatic change in the reactivity pattern is observed when the counterion of a higher order cyanocuprate is changed from the usual lithium to magnesium bromide.[100] The presence of the MgBr counterion favors the coupling reaction instead of the transmetalation reaction, affording the tellurium moiety substitution product **221** in good yields (Scheme 118). The reaction failed to furnish the product with a vinylic telluride containing an enyne moiety, which exclusively gave the transmetalation product.

Scheme 118



In contrast to the transmetalation reactions, which occur when a vinylic telluride reacts with a dilithio higher order organocuprate, the reaction of vinylic tellurides with lower order organocuprates furnished the coupling product instead. The coupling reaction proceeds stereoselectively with retention of the configuration of the starting telluride, and only the terminal TePh group undergoes a substitution reaction with the organocuprate.[101] Several different cuprates were successfully employed in this process, isolating the products **222** in high yields (Scheme 119). The reaction is assumed to proceed through an oxidative addition resulting in a Cu(III) intermediate **223**, which suffers reductive elimination to afford the coupled product (Figure 9).

Scheme 119



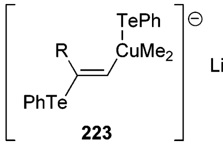
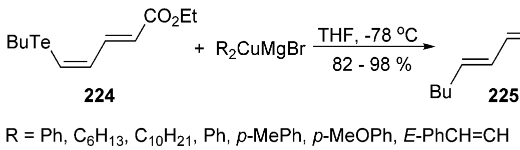
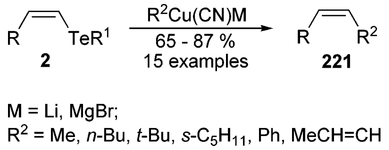


Figure 9.

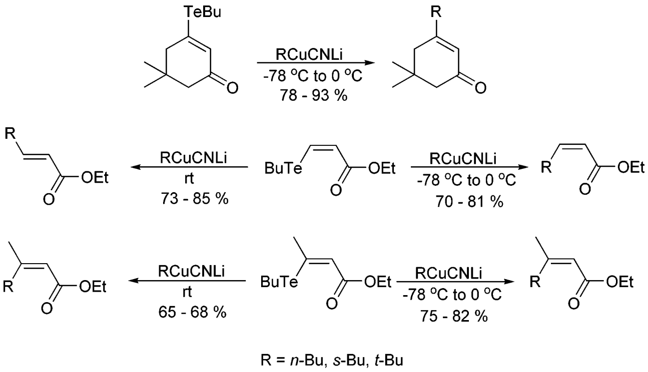
Scheme 120



Scheme 121



Scheme 122



Another report on the coupling reaction with lower order cuprates describes the substitution reaction of a butyltelluro group with several different copper reagents to give ethyl 5-telluro-(2*E*,4*Z*)-pentadienoate **224**.[102] The reaction was highly selective, and when cuprates of type $R_2CuMgBr$ were used, the substitution of the organotellurium group was accomplished with an almost exclusive preference of the 1,4- over the 1,6-addition to the unsaturated ester. The reaction proceeded with a complete inversion of the configuration of the double bond where the tellurium atom is attached, giving in all cases the products as a 2*E*,4*E* isomer in a ratio of >98:2 (Scheme 120). The authors assume that the telluride was first attacked by the organocopper reagent to form an "ate complex", followed by a 1,6-additon elimination reaction, furnishing the thermodynamically more stable product **225**, through a substitution reaction to give the detellurated product.

Lower order cyano cuprates were employed to effect such a transformation.[103] Several vinylic tellurides were employed in these studies, such as those containing aryl, ester, and morpholine groups. Bis-vinylic and β-chlorovinylic tellurides can also be employed in the coupling reactions. The influence of the counterion at the cuprate was also examined, showing that both Li and MgBr performed well. In the case of β-chlorovinylic tellurides, the reaction occurs selectively at the organotellurium group without modifying the chlorine atom. The advantage of the employment of cyanocuprates over dialkylcuprates is that only 1 equiv of the lithium or Grignard reagent is required for the formation of the copper reagent (Scheme 121).

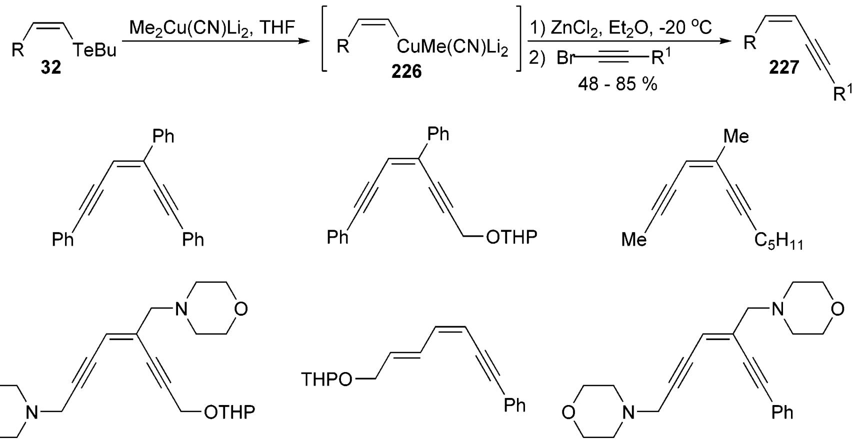
Another application of the coupling reaction of vinylic tellurides with lower order cyano cuprates is the reaction with functionalized tellurides to obtain detellurated products.[104] When the reaction was performed at room temperature, inversion of the configuration of the double bond or, in some cases, a mixture of isomers was obtained. However, when the temperature was lowered, the reaction took place with complete retention of the geometry of the double bond (Scheme 122). The results in the preparation of such systems gave better diastereoselective results than the direct substitution reaction between cuprates and β-keto enolphosphates.

The synthesis of enynes and enediynes was achieved by taking advantage of the tellurium−copper exchange.[105] The reaction was performed by an initial transmetalation of a vinylic telluride with a higher order cyano cuprate, resulting in vinylic cuprates **226**. These intermediates were transmetalated to the vinylic zinc chlorides, which were coupled with several bromoalkynes, resulting in the enynes and enediynes **227** in good yields (Scheme 123).

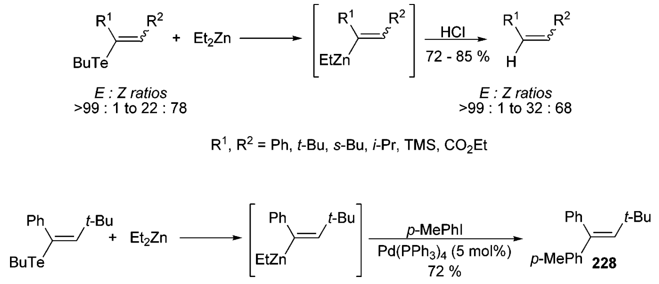
3.2.3. Tellurium–Zinc Exchange Reactions

The tellurium−zinc exchange reaction was reported by Sonoda and Kambe, who have described that vinylic tellurides can undergo a transmetalation reaction when treated with diethylzinc in THF.[106] When the reaction was carried out in $MeCCl_3$ as solvent, a dramatic decrease in the yield was observed, suggesting that the exchange reaction is accelerated by coordinating solvents. Different mixtures of *E* and *Z* isomers of the starting tellurides were used in the reaction. The stereochemistry has been shown to be fairly well retained during the reaction outcome, and the yields were from moderate to good. An advanced application of this tellurium−zinc exchange consists of a further cross-coupling reaction catalyzed by palladium with *p*-iodotoluene. The cross-coupling product **228** was isolated in 72% yield as a single isomer (Scheme 124).

Scheme 123



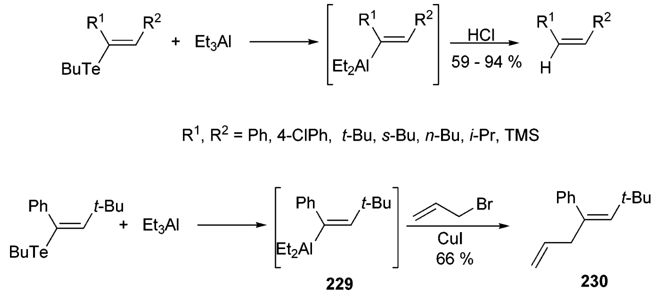
Scheme 124



3.2.4. Tellurium–Aluminum Exchange Reactions

Vinyl aluminum reagents can be prepared by tellurium−aluminum exchange.[107] The exchange reaction is carried out by treating the vinylic tellurides with an excess of triethylaluminum. The reaction proceeds efficiently with complete retention of the double bond geometry, in polar and noncoordination solvents such as $MeCCl_3$, $CHCl_3$, or CH_2Cl_2. Coordinating or apolar solvents dramatically reduce the product formation, suggesting that the coordination of aluminum to tellurium is essential for the exchange reaction. A synthetic application of this methodology was carried out using the copper-catalyzed coupling of the vinylaluminum reagent **229** with allyl bromide, to give **230** in 66% yields, as a sole isomer (Scheme 125).

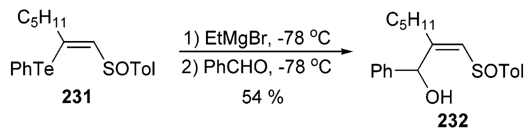
Scheme 125



3.2.5. Tellurium–Magnesium Exchange Reactions

The tellurium−magnesium exchange has been scarcely studied; in fact, only one example of such a transformation has been reported in the literature by Huang and co-workers. The authors described the reaction of a vinylic telluride containing a sulfoxide substituent **231**, which undergoes a tellurium−magnesium exchange reaction at low temperatures by treatment with EtMgBr. The vinylmagnesium intermediate was trapped with benzaldehyde to afford allylic alcohol **232** in 54% yield (Scheme 126).[28]

Scheme 126



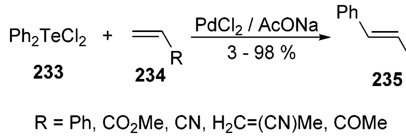
3.3. Cross-Coupling Reactions of Vinylic Tellurides

3.3.1. Palladium-Catalyzed Cross-Coupling Reactions[108]

Recently, a new application of vinylic tellurides employing palladium-catalyzed cross-coupling has been described.[109] In this case, they behave as aryl or vinyl carbocation equivalents. They react in a manner similar to vinylic halides or triflates in Sonogashira,[110] Heck,[111] Suzuki,[112] and Stille[113] cross-coupling reactions with palladium as the catalyst.[114] Therefore, there are some advantages to using vinylic tellurides, such as easy access, by stereoselective reactions, to either (*Z*)- or (*E*)-vinylic tellurides, no isomerization of the double bond, and the enhanced stability of these compounds. In addition, the use of vinylic tellurides in cross-coupling reactions tolerates many sensitive functional groups and mild reaction conditions. Conversely, in the past decade there have been developments in Pd-catalyzed coupling systems for Heck, Suzuki, Stille, Sonogashira, and other reactions, as a consequence of the great interest in finding coupling substrates that are both more economical and more readily accessible.

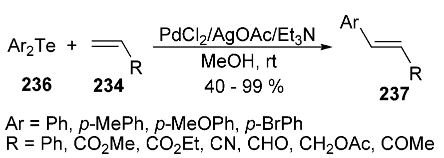
3.3.1.1. Reactions of Vinylic Tellurides with Alkenes−Heck-Type Reactions. *3.3.1.1.1. Carbodetelluration of Aryltellurium(IV) Compounds.* The history of the use of vinylic tellurides in palladium-catalyzed reactions began with the carbodetelluration of aryltellurium(IV) compounds.[115] The authors found that the reaction between diphenyltellurium(IV) dichloride **233** and styrene, catalyzed by palladium(II) chloride, using sodium acetate as base and in acetic acid at reflux afforded *E*-stilbene **237** in 54% yield. This reaction was very sensitive to the nature of the catalyst. Similar reactions with palladium black, palladium(II) acetate, and ruthenium(III) or ruthenium(II) chloride gave unsatisfactory yields of the desired product **235**. The reaction was extended to other olefins **234**, and the olefins **235** were obtained in variable yields (3−98%) (Scheme 127). The stereochemistry of the olefins **235** was *trans* except for those derived from acrylonitrile, which were obtained in a mixture of *trans*/*cis* = 74:26.

Scheme 127



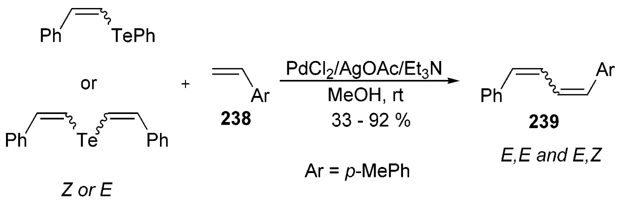
3.3.1.1.2. Cross-Coupling Reactions of the Vinyl Tellurides with Alkenes. It has been reported that the cross-coupling reaction of diphenyl tellurides **236** with alkenes **234** in methanol at 25 °C, in the presence of a Pd^{II} catalyst, using Et_3N as base and an appropriate oxidant, such as AgOAc, afforded the corresponding aryl-substituted *Z*-alkenes **237** in good yields (Scheme 128).[116] The experimental results indicated that no catalytic activity was observed using other solvents, such as tetrahydrofuran, benzene, or acetic acid. The coupling reaction was also unsuccessful using oxidants, such as ammonium hexanitratocerate, $CuCl_2$, and $K_2S_2O_8$.

Scheme 128



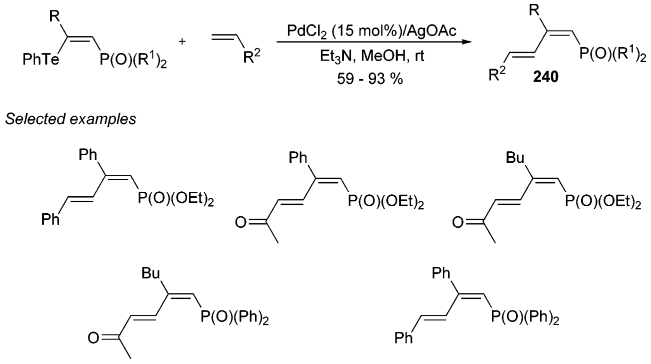
This method has been extended to several vinylic tellurides, such as (*Z*)- and (*E*)-phenyl styryl tellurides, (*Z*,*Z*)-bis-vinylic tellurides, and (*E*,*E*)-bis-vinylic tellurides, with *p*-methylstyrene **238**. This cross-coupling reaction afforded the corresponding alkenylalkenes **239** in yields higher than 33% (Scheme 129). The entire process was highly stereoselective, and no *E*, *Z* isomerization was observed during the reaction.

Scheme 129



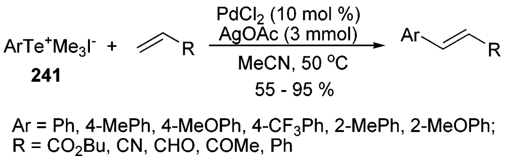
We have recently disclosed a regio- and stereospecific synthesis of phoshono-(1*Z*,3*E*)-dienyl compounds **240** from *β*-phenyltelluro-vinylphosphonates and -vinylphosphine oxides in a Heck-type reaction.[117] Several different reaction conditions were evaluated in this reaction, such as solvent, base, and the nature of the reoxidant employed. We have found that the best results were obtained using methanol as solvent, triethylamine as base, and silver acetate as the reoxidant agent. The presence of the latter is of crucial importance, since it allows us to employ the palladium salt in catalytic amounts. The reaction has proven to be efficient for vinyl phosphonates, phosphine oxides, styrenes, and methyl vinyl ketones. The regio- and stereochemistry of all dienes obtained were readily established by ^{1}H NMR spectroscopy, and the stereochemistry of the newly formed double bond was *E* in all cases. There was no evidence of the presence of the *Z* isomer probing the highly stereoselective character of the coupling reaction. Moreover, the reaction proceeds with retention of the stereochemistry of the original double bond of the starting telluride (Scheme 130).

Scheme 130



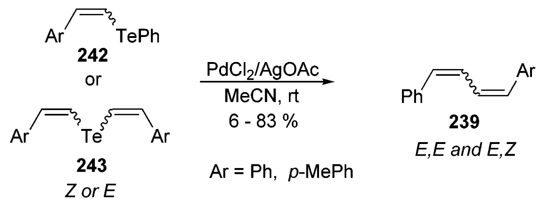
Telluronium salts **241** have been employed as suitable substrates for the Heck-type reaction with alkenes.[118] The major advantage in the employment of this class of tellurium compounds is their high stability in comparison to tellurides. Pd(OAc)$_2$, PdCl$_2$, and PdCl$_2$(PPh$_3$)$_2$ have been evaluated as the palladium source, and it was found that palladium chloride was the best choice in association with silver acetate as reoxidant and acetonitrile as solvent. Good yields of the products were obtained, and either electron-donating or electron-withdrawing groups can be present in the telluronium salt. The alkene reactant can also be varied, giving good results with substituents, such as aldehydes, ketones, esters, and nitriles (Scheme 131).

Scheme 131



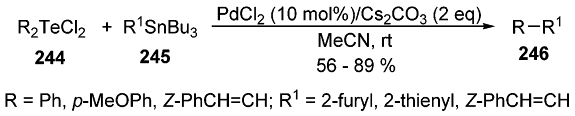
3.3.1.1.3. Homocoupling Reactions of Vinylic Tellurides. The reaction of vinylic tellurides **242**−**243** in the presence of catalytic amounts of Pd(OAc)$_2$ afforded the isomeric homocoupling products 1,4-diphenyl-1,3-butadienes (*E*,*E*; *E*,*Z*; and *Z*,*Z*) **239** in good to moderate yields. The presence of a reoxidant was critical for the success of the coupling, and the reaction rate was greatly enhanced by the addition of AgOAc as the reoxidant. The nature of the solvent was also proven to be very important to the success of this reaction, and the best results were obtained with methanol and acetonitrile. Benzene and tetrahydrofuran furnished the product in lower yields. Thus, the optimum condition for the coupling in Scheme 132 was found to be the use of Pd(OAc)$_2$ (0.05 mmol)/AgOAc (1 mmol), vinylic tellurides (**242**−**243**, 0.5 mmol), and acetonitrile (10 mL) at 25 °C for 20 h.[119]

Scheme 132



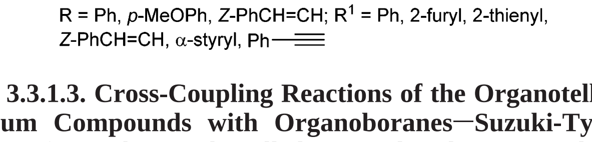
3.3.1.2. Cross-Coupling Reactions of the Organotellurium Compounds with Organostannanes—Stille-Type Reactions. Organostannanes have been successfully employed in cross-coupling reactions with diaryl- or divinyltellurium dichlorides. The reaction of organotellurium dichlorides **244** with vinylstannane species **245** in the presence of PdCl$_2$ with Cs$_2$CO$_3$ as the base and MeCN as the solvent afforded the cross-coupling products **246** in good yields as illustrated in Scheme 133. In this method, the authors tested other catalysts, such as Pd(PPh$_3$)$_4$, Pd$_2$(dba)$_3$CHCl$_3$, and PdCl$_2$(PPh$_3$)$_2$. The best results were obtained with PdCl$_2$ as catalyst. Concerning the bases used, Cs$_2$CO$_3$ was more efficient than K$_2$CO$_3$, Na$_2$CO$_3$, or MeONa.[120]

Scheme 133



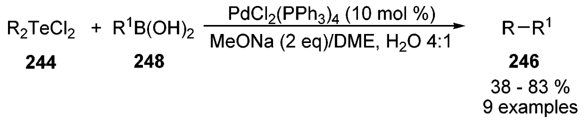
Similarly, the authors promoted detelluric cross-coupling carbonylations of diaryl- or divinyl-tellurium dichlorides **244** through a reaction with vinylstannanes **245**. This cross-coupling reaction can be carried out using catalytic amounts of PdCl$_2$ (10 mol %), CO (1 atm) in MeCN, and Cs$_2$CO$_3$ as the base, affording ketones **247** in 52−90% yields (Scheme 134).[120]

Scheme 134



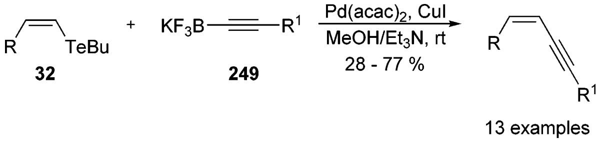
3.3.1.3. Cross-Coupling Reactions of the Organotellurium Compounds with Organoboranes—Suzuki-Type Reactions. The Suzuki palladium-catalyzed cross-coupling reaction between arylboronic acids and aryl halides or triflates has proven to be a very popular and versatile method for the formation of carbon−carbon bonds.[52] An investigation of the palladium-catalyzed cross-coupling of diaryl and bis-vinyltellurium dichlorides with organoboronic acids has recently been reported.[121] As illustrated in Scheme 135, various diaryl or bis-vinyltellurium dichlorides **244** were allowed to react with arylboronic acids **248** in the presence of $PdCl_2(PPh_3)_2$ and NaOMe in DME/H_2O, affording the coupled products **246** in fair to good yields (Scheme 135).

Scheme 135



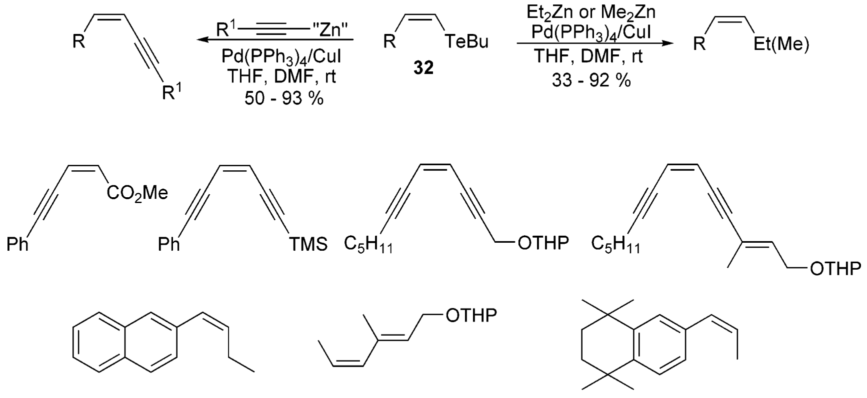
In addition to the reaction of bis-vinyltellurium dichlorides with organoboronic acids, a protocol for the synthesis of 1,3-enynes via a Suzuki-type reaction of vinyl tellurides **32** with potassium alkynyltrifluoroborate salts **249** was recently published.[122] $Pd(acac)_2$ furnished better results than other palladium salts, such as $PdCl_2$, $Pd(dba)_3$, $PdCl_2(PhCN)_2$, and $[Pd(allyl)Cl_2]$. Several bases were also studied, and the best yields were achieved with triethylamine, which furnished the product in better yields than cesium carbonate, sodium hydroxide, potassium *tert*-butoxide, and potassium carbonate. The reaction tolerates several functional groups, such as free alcohols groups, esters, dienes, and enynes; however, it fails to promote the coupling product when an amine functionality is present in the vinylic telluride (Scheme 136).

Scheme 136



3.3.1.4. Cross-Coupling Reactions of the Organotellurium Compounds with Organozinc Reagents—Negishi-Type Reactions. Cross-coupling reactions of organozinc reagents are a versatile and very useful tool in modern organic synthesis, because of their known ability to tolerate many functional groups.[123] In this context, Dabdoub and Marino have described efficient routes to promote the palladium-catalyzed coupling of alkylzinc[124] or alkylnylzinc[125] reagents with vinylic tellurides. The reaction is efficiently accomplished in the presence of catalytic amounts of $Pd(PPh_3)_4$ and 1 equiv of copper iodide. The use of DMF as a cosolvent together with THF has substantially increased the yields of coupled products. In the absence of the palladium catalyst, only the detellurated product was isolated. Copper iodide also plays an important role in the outcome of the process, since the consumption of the starting material was incomplete in its absence.

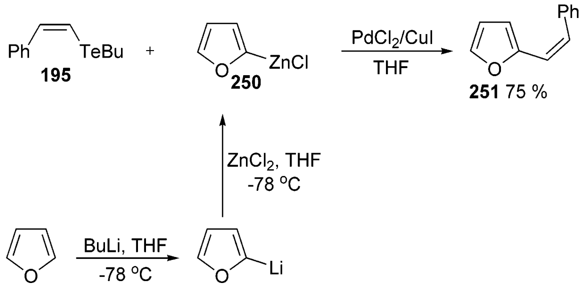
Scheme 137



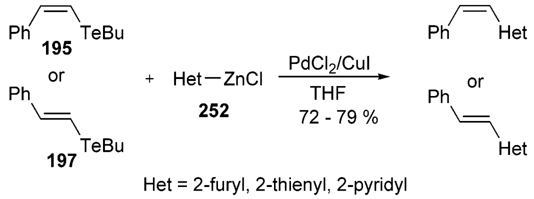
Polyfunctional unsaturated compounds have been prepared by this methodology, as this function is present in either vinylic telluride or alkynylzinc reagents. Thus, several enediyne structures were prepared in good yields (Scheme 137).

In addition to the achievements described by these authors, our group has concentrated efforts for the development of organozinc-based protocols to promote the cross-coupling of vinylic tellurides.[126] In fact, we have recently described the coupling of vinylic tellurides of a *Z*- or *E*-configuration **195** and **197** with heteroaromatic zinc reagents **252**, namely 2-furyl-, 2-thienyl-, and 2-pyridylzinc chlorides. Optimized conditions were achieved with *Z*-vinylic telluride **195** and 2-furylzinc chloride **250**, which was prepared *in situ* from 2-furyllithium and zinc chloride, to yield product **251** (Scheme 138). The best reaction conditions employed a catalytic amount of $PdCl_2$ and 1 equiv of CuI. The reaction has been further extended to the other isomer of vinylic telluride and to different heteroaromatic zinc reagents, demonstrating that this is an efficient method for the preparation of vinyl heterocycles in good yields (Scheme 139).

Scheme 138

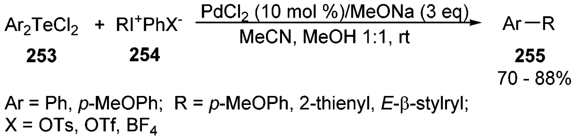


Scheme 139



3.3.1.5. Palladium-Catalyzed Cross-Coupling of Organotellurium Compounds with Hypervalent Iodonium Salts—Heck-Type Reactions. Kang and co-workers[127] have shown that diaryltellurium dichlorides **253** can be readily coupled with iodonium salts **254** in the presence of palladium catalysts to give coupled products **255** (Scheme 140). This method gave the best yields when the iodonium salts were allowed to react with diaryltellurium dichlorides in the presence of $PdCl_2$ (10 mol %) and MeONa (3 equiv), in CH_3CN/MeOH (1:1) at room temperature for 7 h. This protocol gave the products in 70−88% yields.

Scheme 140



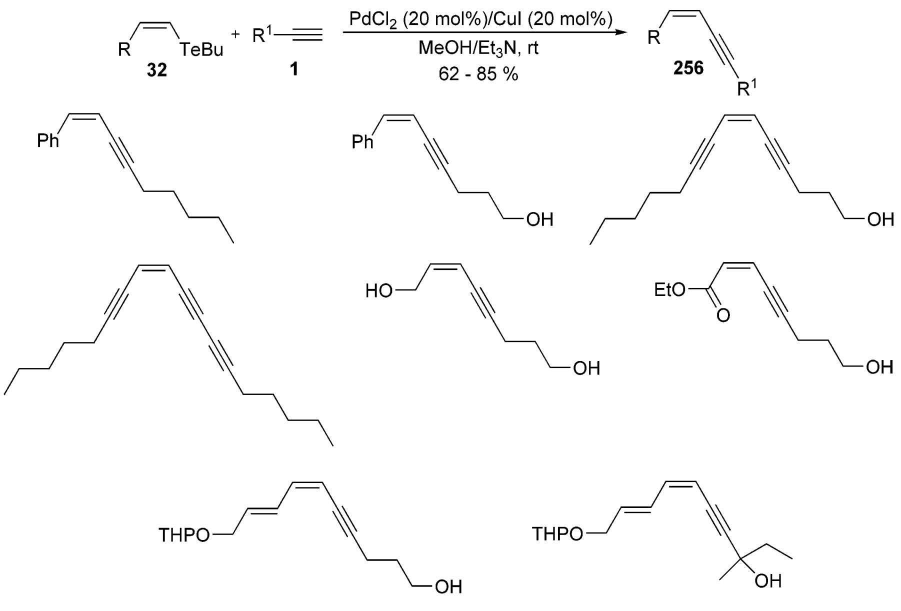
3.3.1.6. Reactions of the Vinylic Tellurides with Alkynes—Sonogashira-Type Reactions.[128] *3.3.1.6.1. Synthesis of Enynes and Enediyne Systems via Palladium-Catalyzed Cross-Coupling of Vinylic Tellurides with 1-Alkynes.* Calicheamycins, esperamycins, and dynemycins are a class of antibiotic molecules that emerged some years ago.[129] Among them are some of the most potent antitumor agents known to date. The synthesis of enynes and enediynes has received special interest during the last 20 years, and a variety of methods based on palladium-catalyzed reactions have been developed.[130] The cross-coupling reaction of vinyl bromides, iodides, chlorides, and triflates with monosubstituted acetylenes has been achieved in the presence of a Pd^0 or Pd^{II}/CuI catalyst.[131] The reaction has also been performed using bromoalkynes and a vinyl boron,[132] copper,[133] zinc,[134] aluminum,[135] or magnesium reagent.[136] The use of vinylic tellurides to obtain enyne and enediyne systems using transmetalation with *n*-BuLi[15] and cyanocuprates[97a] has been previously described. Nonetheless, the cross-coupling of vinylic tellurides with 1-alkynes was unknown. Initially, we described the stereospecific formation of (*Z*)-enynes and (*Z*)-enediynes in a palladium-catalyzed cross-coupling reaction of (*Z*)-vinylic tellurides with 1-alkynes.[137] We found that the optimum conditions for the coupling in Scheme 141 were the use of $PdCl_2$ (20 mol %)/CuI (20 mol %), MeOH (5 mL), (*Z*)-vinylic telluride **32** (1 mmol), the appropriate alkyne **1** (2 mmol), and Et_3N (1 mmol) at 25 °C. By extending the coupling reaction to other alkynes, various *Z*-enynes and *Z*-enediynes **256** were obtained in good yields (Scheme 141). Our approach represented an improvement over previously described methods, in that it avoids both the preparation of vinylmetals and haloalkynes and the protection of functional groups, such as alcohols. Another advantage of this method is the easy access and stability of (*Z*)-vinylic tellurides.

More recently, the scope of the cross-coupling reaction of vinylic tellurides with 1-alkynes has been extended to *E*-vinylic tellurides **93**.[138] Although several different conditions, including other palladium catalysts and different solvents and bases, were examined, the $PdCl_2$/CuI system has still proven to be the most effective for the coupling reaction, giving the *E*-enynes **257** in high yields (Scheme 142). Similar to the reaction of the *Z* isomers, no isomerization of the starting double bond was observed during the reaction.

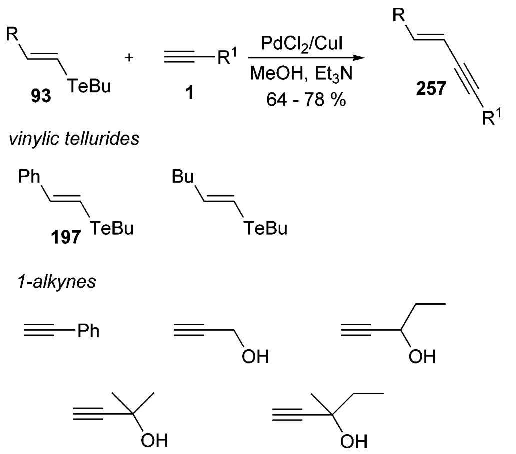
Another alternative to vinylic tellurides as starting materials for the synthesis of enynes is the use of the corresponding organotellurium dichlorides **258**, which are much more stable to air oxidation than their parent vinylic derivatives.[139] Again, the $PdCl_2$/CuI system furnished the best results and the reaction was tolerant to several functional groups, such as amines, phosphonates, and free alcohols without previous protection (Scheme 143).

3.3.1.6.2. Palladium-Catalyzed Cross-Coupling of Bis-vinylic Tellurides with 1-Alkynes. Along with the exploration of the synthetic potential of the Pd-catalyzed cross-coupling reaction with vinylic tellurides, we have also investigated the stereospecific formation of (*Z*)-enyne **256** systems by palladium-catalyzed cross-coupling reactions of (*Z*)-bis-vinylic tellurides **57** with 1-alkynes (Scheme 144).[140] Initial research efforts were dedicated to the development of a good catalytic system, and the influence of the ligands in the palladium complex was investigated. Thus, (*Z*)-bis-vinylic telluride **57** (1 equiv) was treated in methanol at room temperature with 2-propyn-1-ol (2 equiv) in the presence of different catalysts and Et_3N (1 equiv) as the base (Scheme 11). $Pd(PPh_3)_4$ or $Pd(PPh_3)_4$/CuI did not exhibit catalytic

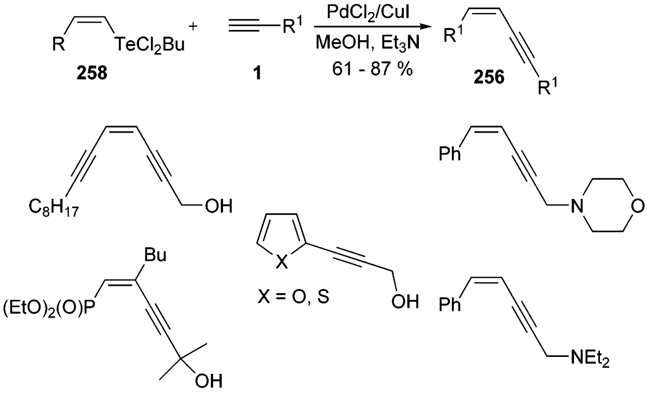
Scheme 141



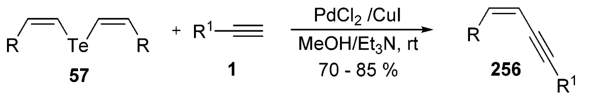
Scheme 142



Scheme 143



Scheme 144



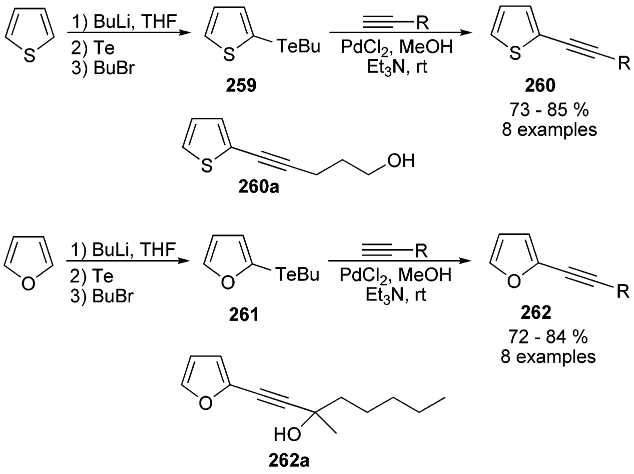
R = Ph, CH_2OH; R^1 = C_5H_{11}, C_7H_{15}, t-Bu, TMS, CH_2OH, $(CH_2)_3OH$, C(Me)(Et)OH, 1-cyclohexanol, ≀—≡—C_6H_{13}

activity in this reaction, and Pd(II) catalysts, such as $PdCl_2/PPh_3$, $PdCl_2(PPh_3)_2$, $Pd(OAc)_2$, and $PdCl_2(PhCN)_2$, gave unsatisfactory yields of the desired enyne **256**. The reaction yields were greatly enhanced by increasing the amount of $PdCl_2$/CuI from 1 to 10%, where the desired enyne **256** was obtained in 85% isolated yield.

The nature of the amine was critical for the success of the coupling. Using pyrrolidine, piperidine, or morpholine (1 equiv) as base, no reaction was observed. With Et_2NH, *n*-$PrNH_2$, or *n*-$BuNH_2$, moderate yields were observed (15−28%). However, with Et_3N, the enyne **256** was obtained in 85% isolated yield and the reaction was completed within 6 h. The stereoisomeric purities of the enynes **256** were similar to that of the starting bis-vinylic tellurides **57**, indicating a complete retention of the configuration in this type of reaction. Extending the coupling reaction to other alkynes, various *Z*-enynes **256** were obtained in good yields (Scheme 144).

3.3.1.6.3. Palladium-Catalyzed Cross-Coupling of 2-(Butyltelluro)thiophene or 2-(Butyltelluro)furan with 1-Alkynes. Several thiophene derivatives have been found to show nematocidal,[141] insecticidal,[142] antibacterial,[143] antifungal,[144] and antiviral[145] activity. Recently, we have investigated the anti-inflammatory activity of acetylenic thiophene derivatives synthesized via a Pd-catalyzed coupling reaction of 2-(butyltelluro)thiophene with 1-alkynes.[146] In this study, our research group evaluated: (a) the influence of the nature of the catalyst, (b) the effect of the nature of the amine, and (c) the anti-inflammatory activity of the acetylenic thiophene derivatives prepared. The starting material required for the synthesis, 2-(butyltelluro)thiophene (**259**) (Scheme 145), was obtained from the metalation of thiophene with *n*-butyllithium[147] followed by the treatment of 2-thienyllithium with elemental tellurium. Subsequent addition of 1-bromobutane gave the 2-(butyltelluro)thiophene (**259**) in good yield. This compound is stable and can be chromatographed and stored in the dark at room temperature for several days. Treatment of 2-(butyltelluro)thiophene (**259**) with 1-alkynes in methanol using $PdCl_2$ as the catalyst and triethylamine as the base at room temperature gave the acetylenic thiophenes **260** in 73−85% yield after purification (Scheme 145).

Scheme 145



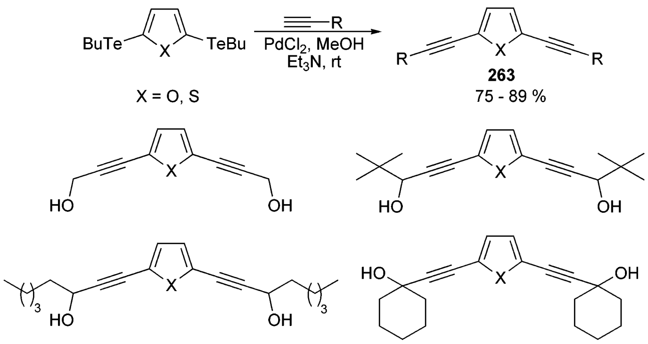
Of the catalysts tested, $Pd(PPh_3)_4$ and $Pd(PPh_3)_4$/CuI did not exhibit catalytic activity in this reaction and Pd(II) catalysts, such as $PdCl_2/PPh_3$, $PdCl_2(PPh_3)_2$, $Pd(OAc)_2$, and $PdCl_2(PhCN)_2$, gave unsatisfactory yields of the desired acetylenic thiophenes. However, by using $PdCl_2$ (10 mol %), the acetylenic thiophene was obtained in improved yields. The nature of the amine was also very important, because when the reaction was performed using pyrrolidine, piperidine, or morpholine (1 equiv), no product was obtained. The use of Et_2NH, *n*-$PrNH_2$, or *n*-$BuNH_2$ gave the desired products in low yields (5−8%). However, by using Et_3N, the acetylenic thiophene derivatives were obtained in good yields. We also found that the yields of acetylenic thiophenes were markedly decreased using DMF, CH_3CN, THF, or CH_2Cl_2, instead of MeOH as the solvent. Thus, the optimum condition for the coupling in Scheme 145 was the use of $PdCl_2$ (10 mol %), MeOH (5 mL), 2-(alkyltelluro)thiophene (**259**) (1 mmol), the appropriate 1-alkyne (2 mmol), and Et_3N (1 mmol) at 25 °C. Moreover, the coupling reaction was extended to other alkynes. The acetylenic thiophenes obtained are summarized in Scheme 145.

The acetylenic thiophenes **260** obtained were screened for anti-inflammatory activity, using the carrageenin-induced paw edema method.[148] This method is customarily used for the screening of new pharmacologically active compounds. The acetylenic thiophene **260a** ($p < 0.05$, 50% of the edema inhibition at a dose of 250 mg/kg; ip) demonstrated significant potential to reduce the carrageenin-paw edema when compared to acetylsalicylic acid (100 mg/kg, ip).

We also applied the method described above to prepare acetylenic furan derivatives **262** (Scheme 145).[149] We found that direct coupling of 2-(alkyltelluro)furan **261** with 1-alkynes in the presence of palladium dichloride as the catalyst in methanol and triethylamine affords the desired acetylenic furan derivatives **262** in good yields (72−84%). The obtained acetylenic furans were also screened for anti-inflammatory activity. The acetylenic furan (100 mg/kg; ip) inhibited 40% of the edema ($p < 0.05$ by Duncan's multiple range test) induced by carrageenin when compared to control. Compound **262a** (250 mg/kg; ip) inhibited paw edema formation with greater potency than acetylsalicylic acid (100 mg/kg, ip), a classical anti-inflammatory agent. The synthetic methods described represent a general and efficient protocol for carrying out the synthesis of acetylenic furans and thiophene derivatives with potential biological activities.

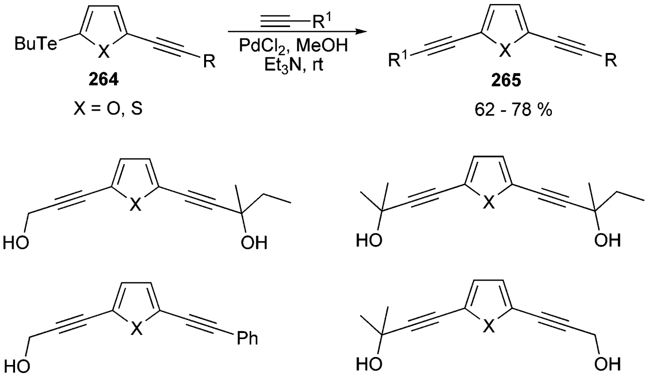
With the success in the synthesis and biological evaluation of acetylenic furan and thiophene derivatives, we turned our attention to the preparation of bis-acetylenic heteroaromatic compounds **263**, as an extension of our previous findings. Thus, the reaction of 2,5-bis(butyltelluro) furan[150] and thiophene[151] proceeded under mild conditions of palladium catalysis in the presence of an excess of 4 equiv of the terminal alkyne to afford the 2,5-bis-acetylenic product **263** in good yields (Scheme 146).

Scheme 146



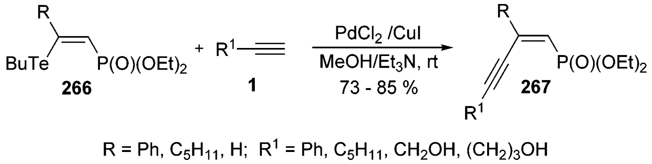
In a further attempt, we reduced the amount of the alkyne employed in the cross-coupling reaction to 1 equiv, and the solvent was changed to THF; thus, we were able to isolate the 2-(butyltelluro)-5-(acetylenic) thiophenes and furans **264**, which are suitable candidates for the next cross-coupling reaction, leading to unsymmetrical 2,5-bis(acetylenic) heterocycles **265** in high yields (Scheme 147).

Scheme 147



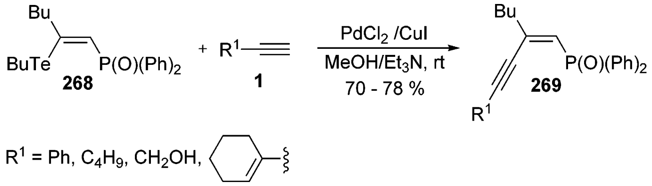
3.3.1.6.4. Enynephosphonates via Palladium-Catalyzed Cross-Coupling of β-Organotelluro Vinylphosphonates with Alkynes. Unsaturated phosphorus compounds represent an important class of synthetic intermediates. Many of these compounds have attracted attention because of their antibacterial, antiviral, antibiotic, pesticidal, anticancer, and enzyme inhibitory properties.[152] The synthetic methods for producing the C−P bond have been extensively reviewed.[153] However, so far, only one method of enynephosphonate preparation has been disclosed, which utilizes palladium-mediated cross-coupling reactions of α-iodo-vinylphosphonates with 1-alkynes.[154] Recently, we have shown that β-organochalcogeno vinylphosphonates **266**, prepared by the hydrochalcogenation of 1-alkynylphosphonates, are suitable substrates for the preparation of enynephosphonates **267** via cross-coupling reactions with alkynes.[155] Thus, the optimum condition for the coupling, described in Scheme 148, was found to be the use of $PdCl_2/CuI$ (20 mol % each), methanol (10 mL), β-organotelluro vinylphosphonates **266** (1 mmol), the appropriate 1-alkyne (2 mmol), and Et_3N (1 mmol) at room temperature. Using this method, several enynephosphonates **267** were prepared in good yields (Scheme 148). The stereoisomeric purities of **267** were equal to those of the starting β-organotelluro vinylphosphonates **266**, indicating complete retention of the configuration in this type of reaction.

Scheme 148



Similar reactions were developed in the preparation of enynephosphine oxides.[27] We found that the coupling reaction of compounds **268** with appropriate alkynes, under the same cross-coupling conditions described before, afforded the β-alkynyl vinylphosphine oxides **269** in 70−78% yields (Scheme 149).

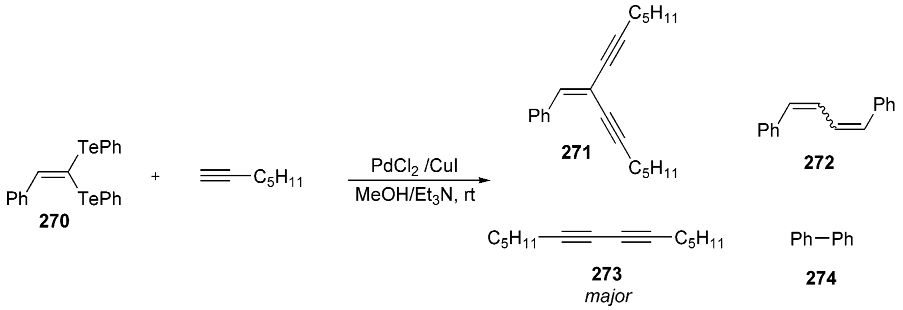
Scheme 149



3.3.1.6.5. Synthesis of Cross-Conjugated Geminal Enediynes via Palladium-Catalyzed Cross-Coupling Reaction of Ketene Butyltelluroacetals. The interest in developing palladium-mediated synthetic methods stimulated us to examine the reactivity of ketene telluroacetals (vinylic tellurides) with terminal alkynes to obtain conjugated and cross-conjugated enediynes via palladium-catalyzed cross-coupling reactions.[156]

Initially, efforts were focused on the reactivity of ketene phenyltelluroacetal **270** in a cross-coupling reaction with 1-alkynes (Scheme 150). Thus, ketene phenyltelluroacetal **270** (1 equiv) was treated in methanol at room temperature with 1-heptyne (2 equiv) in the presence of $PdCl_2$ (20 mol %)/CuI (20 mol %) and using Et_3N (1 equiv) as base. Under these conditions, the corresponding enediyne **271** was obtained as the minor product, but the major product **273**

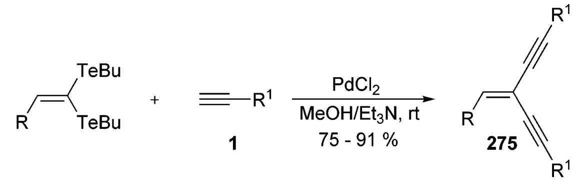
Scheme 150



and a small amount of homocoupling products **272** and **274** were also isolated (Scheme 150).

The reaction between ketene phenyltelluroacetal **270** in methanol at room temperature and 1-alkynes in the presence of $PdCl_2$ as catalyst and Et_3N as base in the absence of CuI was investigated. Under these conditions, diyne **273** was not observed. However, the cross-coupling reaction still proceeded unsatisfactorily, providing **271** contaminated with **272** and **274**. Thus, the optimum conditions for the coupling, as described in Scheme 151, were the use of $PdCl_2$ (20 mol %), MeOH (5 mL), ketene butyltelluroacetals (1 mmol), the appropriate 1-alkyne (4 mmol), and Et_3N (1 mmol) at 25 °C. In the next stage, the generality of the method was explored, extending the coupling reaction to other 1-alkynes, obtaining the enediynes **275** in good yields (Scheme 151). The reaction conditions tolerate the use of functionalities, such as hydroxyl and labile acetylenic trimethylsilyl groups.

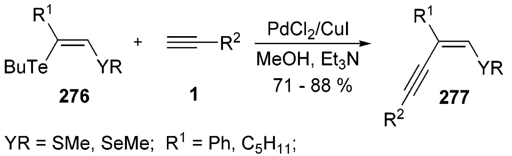
Scheme 151



R = Ph, C_3H_7, C_5H_{11}; R^1 = C_5H_{11}, TMS, CH_2OH, $(CH_2)_3OH$, C(Me)(Et)OH

3.3.1.6.6. Synthesis of Chalcogenoenynes by Palladium-Catalyzed Cross-Coupling Reactions. The coupling reaction of 1,2-bis(organoylchalcogeno)alkenes **276** with terminal alkynes was accomplished smoothly in the presence of the $PdCl_2$/CuI system to afford the chalcogenoenynes in good yields.[157] The stereochemistry of the products **277** was determined by NOE experiments, and the complete retention of the configuration of the double bond was observed. The reaction was efficient for a wide range of terminal alkynes, and the chalcogenoenynes **277** were obtained in yields ranging from 71 to 88% (Scheme 152).

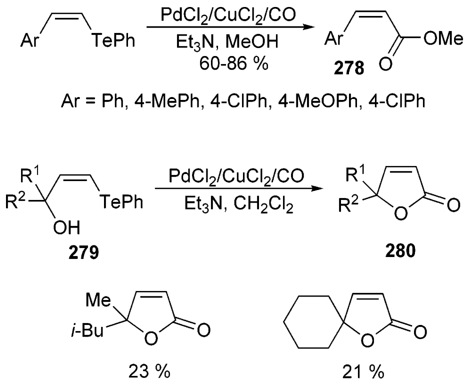
Scheme 152



YR = SMe, SeMe; R^1 = Ph, C_5H_{11};
R^2 = CH_2OH, $(CH_2)_3OH$, CMe_2OH, C(Me)(Et)OH

3.3.1.6.7. Palladium-Catalyzed Carbonylation of Vinylic Tellurides with Carbon Monoxide. The carbonylation of vinylic tellurides in the presence of a catalytic amount of palladium dichloride and carbon monoxide was described.[11b] The reaction is carried out in methanol as solvent, and the corresponding α,*β*-unsaturated esters **278** are isolated in good yields from a wide range of vinylic tellurides with different substitution patterns at the aromatic ring (Scheme 153). All products **278** were obtained in a *Z*-configuration of the double bond, which accounts for a stereoconservative reaction, as the starting tellurides were also of *Z*-configuration. This chemistry can also be extended to the synthesis of butenolides **280** by the carbonylation of tellurides containing an internal hydroxyl group **279**. The reaction takes place in low yields in dichloromethane as solvent (Scheme 153).

Scheme 153



Ar = Ph, 4-MePh, 4-ClPh, 4-MeOPh, 4-ClPh

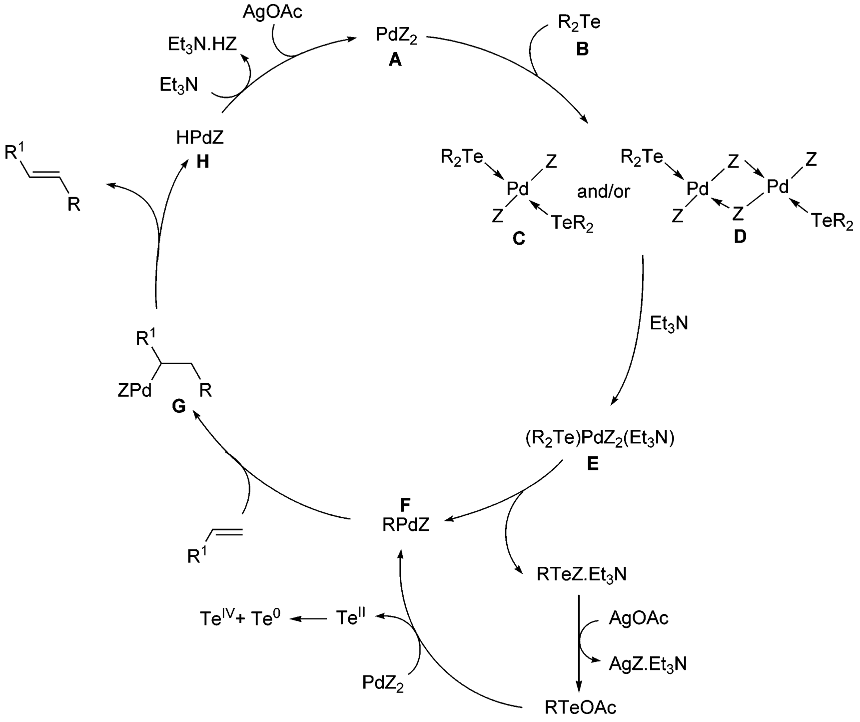
3.3.2. Mechanistic Considerations of Palladium-Catalyzed Cross-Coupling Reactions

The palladium-catalyzed cross-coupling reaction of vinylic tellurides has become one of the most exciting and promising in the field of organic tellurium chemistry, and there is still much to be discovered and understood about the subject, especially, in respect to the generality of substrates and their behavior toward different reaction conditions.[109]

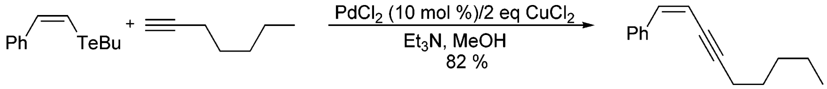
Regarding the mechanism of the reaction, some attempts have been made in order to clarify what occurs when an organic telluride reacts in the presence of a palladium salt. The first mechanistic proposal for this reaction was made by Uemura and co-workers for their palladium-catalyzed Heck-type reaction of organic tellurides with alkenes.[116,119]

They initially proposed that a complex between organic telluride and palladium(II) is formed at the initial stage, and it can exist in either a monomeric **C** or a dimeric **D** form. After the formation of this complex, aryl or alkenyl migration occurs to give aryl- or alkenyl-palladium species **F**, which reacts with alkenes to give arylalkenes of alkenylalkenes. The species produced, RTeZ, may react with PdZ_2 to give an organopalladium species, RPdZ, and an inorganic Te(II) species; the latter disproportionates to Te^0 and an inorganic Te(IV) species. Both Et_3N and AgOAc played an important role for this catalytic coupling reaction. Et_3N may act in the formation of a new monomeric species from **C** and/or **D**. It

Scheme 154



Scheme 155



also may be responsible for the capture of HZ from HPdZ (**H**), assisting in the rapid formation of palladium(0). Silver acetate works as the oxidant of Pd(0) to Pd(II) species, forming the active catalytic species required (Scheme 154).

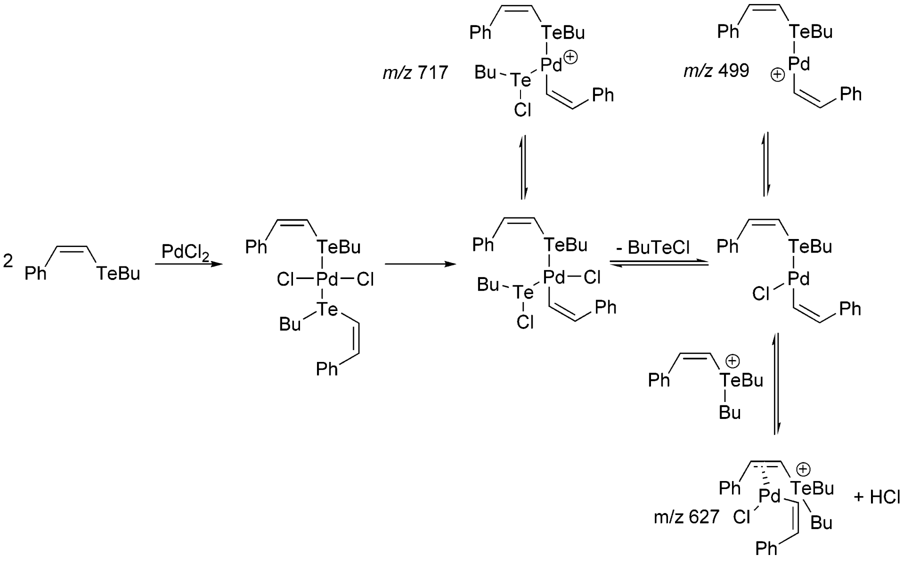
More recently, an elegant study described by Comasseto, Eberlin, and co-workers evaluated the mechanistic details of the coupling of vinylic tellurides with alkynes promoted by palladium dichloride.[158] To determine the advanced intermediates of the reaction, the authors used mass spectrometry techniques.

First, they developed a new protocol for the cross-coupling reaction, which employed 10 mol % $PdCl_2$ and 2 equiv of $CuCl_2$ as a reoxidizing agent in the presence of Et_3N and MeOH as solvent (Scheme 155).

In a second stage, they investigated the coupling reaction using mass spectrometry. Electrospray ionization (ESI-MS) and tandem electrospray ionization (ESI-MS/MS)[159] were the techniques of choice for these studies, since they were applied to fish the Pd- and Te-containing cationic intermediates, which are directly involved in the reaction, from the reaction medium to the gas phase for ESI-MS and ESI-MS/MS measurements.[160]

Among the several data that could be obtained by mass spectrometry, the most relevant for the proposal of a catalytic

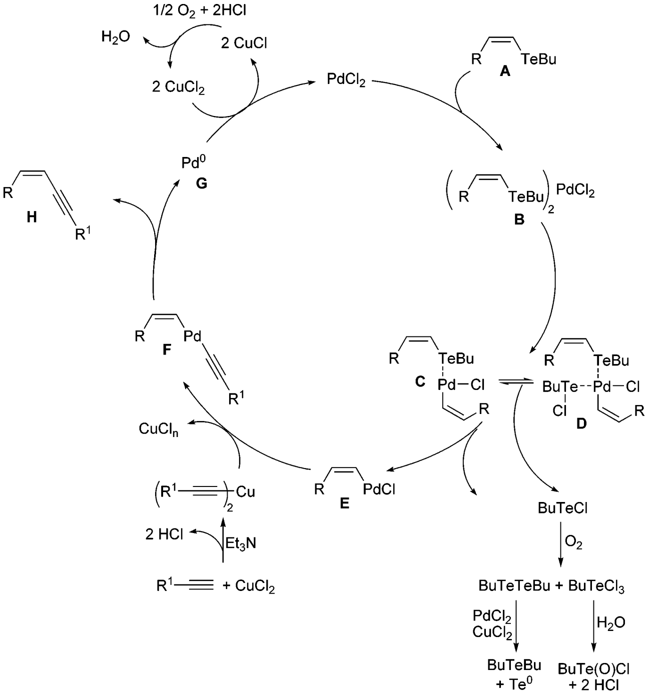
Scheme 156



cycle were those shown in Scheme 156, which are Te- and Pd-containing cationic complexes with *m*/*z* 717, *m*/*z* 627, and *m*/*z* 499. The authors have inferred that the detection of species *m*/*z* 717 and *m*/*z* 499, in their cationic forms, by ESI fishing suggests a solution equilibrium between them in the palladium insertion process. BuTeCl acts as a ligand that stabilizes the *m*/*z* 717 species, which is formed by the coordination of two styryl butyl tellurides with $PdCl_2$, followed by transmetalation.

An expanded catalytic cycle, depicted in Scheme 157, is proposed by the authors based on mass spectrometry measurements. The key aspects of this proposal involve the formation of the Te- and Pd-containing complexes **C** and **D**, which suffer a posterior insertion of the Pd atom into the C sp^2−Te bond to afford intermediate **E**, which upon transmetalation leads to the alkyne complex **F**. Reductive elimination delivers the enyne product and Pd(0), which is reoxidized to the active Pd(II) by reaction with $CuCl_2$ and then returns to the catalytic cycle (Scheme 157).

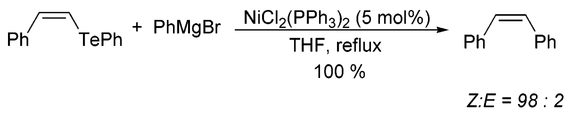
Scheme 157



3.3.3. Nickel-Catalyzed Cross-Coupling Reactions

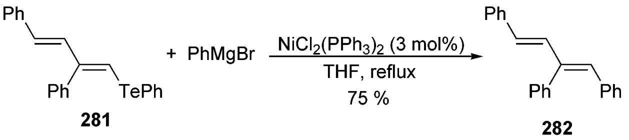
Nickel complexes are effective in catalyzing coupling reactions of vinylic tellurides. The first report on this subject was described by Uemura and Fukuzawa in 1982.[11b] They described the cross-coupling reaction of a vinylic telluride with an excess of a Grignard reagent catalyzed by $NiCl_2(PPh_3)_2$ in THF (Scheme 158). When the reaction was performed at room temperature, lower yields and a *Z*/*E* ratio of 90:10 in favor of the *Z* isomer were obtained. An increase of the temperature to reflux resulted in improved yields and an almost exclusive formation of the *Z* isomer. When the nickel catalyst was changed to $NiCl_2(dppp)$, poor *Z*/*E* selectivities were achieved, while alkyl Grignard reagents gave much lower yields of the corresponding alkenes.

Scheme 158



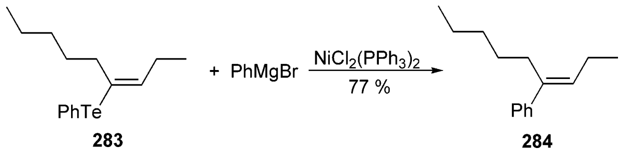
Another extension of this method was described for the preparation of unsaturated hydrocarbon **282** with loss of the tellurium group.[161] The tellurobutadiene **281** reacted with PhMgBr in the presence of a catalytic amount of $NiCl_2(PPh_3)$ in THF with retention of the configuration of both double bonds (Scheme 159).

Scheme 159



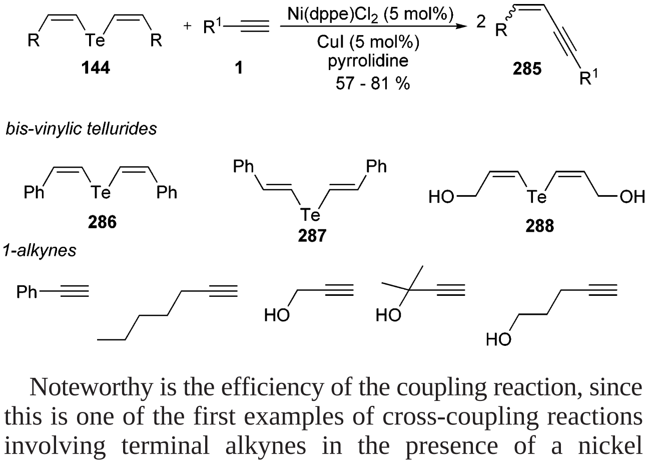
Trisubstituted olefin **284** was also prepared by a cross-coupling reaction of vinylic telluride **283** with PhMgBr, mediated by a nickel complex, in good yield with excellent regio- and stereocontrol (Scheme 160).[162]

Scheme 160



We have recently described a general approach to the preparation of *Z* and *E* enynes, through a nickel-catalyzed cross-coupling reaction of (*Z*,*Z*)- and (*E*,*E*)-bis-vinylic chalcogenides **144** with 1-alkynes.[163] By this method, the transfer of both vinyl groups linked to the tellurium atom was accomplished, which constitutes an attractive feature of the process. Initial efforts have employed $Ni(PPh_3)_2Cl_2$ as catalyst; however, the enynes **285** were obtained in low yields. When $Ni(dppe)Cl_2$ was used in the presence of CuI, an improvement was achieved and the desired products **285** were obtained in high isolated yields. The influence of the solvent was also evaluated, but we did not observe any further improvement by using THF, DMF, MeCN, CH_2Cl_2, benzene, MeOH, or mixtures of them. Thus, the best conditions were established to be $Ni(dppe)Cl_2$ (5 mol %), CuI (5 mol %), and pyrrolidine as the solvent at room temperature. The reaction has been successfully applied to both (*Z*,*Z*) and (*E*,*E*) isomers (**286** and **287**) and extended to telluride-containing free hydroxyl groups **288** (Scheme 161).

Scheme 161

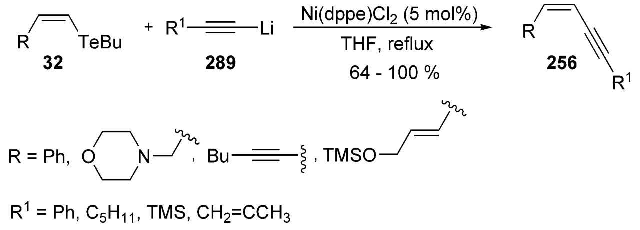


Noteworthy is the efficiency of the coupling reaction, since this is one of the first examples of cross-coupling reactions involving terminal alkynes in the presence of a nickel catalyst. Other advantages of this nickel-based system include air stability, low cost, and ease of preparation of the catalyst, all of which are important in considering the scale-up of a reaction.

Another remarkable fact is that, if the reaction is performed with pure (*Z*,*Z*) and (*E*,*E*) isomers, pure *Z*- or *E*-enynes are isolated in all cases.

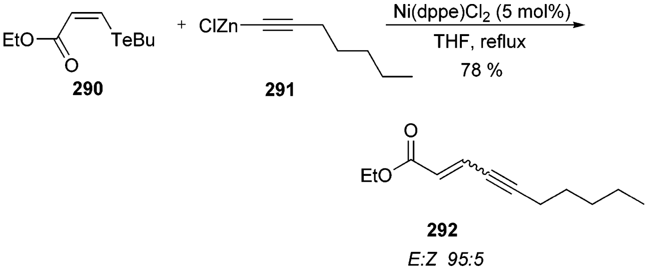
A variation of the above methodology was developed, which consists of the synthesis of enynes **256** by the coupling of vinylic tellurides with an excess of the alkynyllithium anion **289**, in the presence of Ni(dppe)$_2$Cl$_2$ (5 mol %) and in the absence of CuI.[164] The reaction was carried out in THF at reflux, giving the products in high yields with retention of the double bond configuration (Scheme 162).

Scheme 162



However, when the telluride functionalized with an ester group **290** was submitted to the reaction conditions, addition of the alkynoate to the reactive ester group occurred. To circumvent this problem, transmetalation to the less reactive alkynylzinc chloride **291** was performed to give the desired product **292** in 78% yield, preferentially in the *E*-configuration (Scheme 163). The authors observed that the reduction of the catalyst and the alkynoate amounts resulted in a drop of the yield. When a telluride containing a TBS-protected alcohol was employed, the reaction failed to give the expected products.

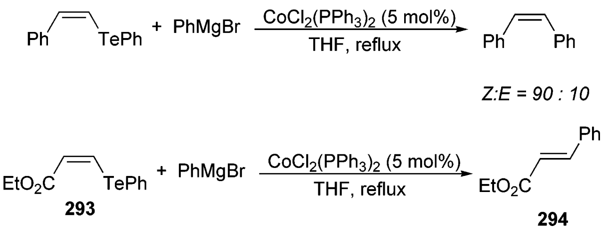
Scheme 163



3.3.4. Cobalt-Catalyzed Cross-Coupling Reactions

Cobalt(II) has appeared as a catalyst for the cross-coupling of vinylic tellurides with Grignard reagents.[165] The reaction works for PhMgBr; however, the yields were greatly decreased for aliphatic Grignard reagents, due to a sluggish reaction (Scheme 164). The *Z* isomer is obtained preferentially in a 90:10 ratio.

Scheme 164



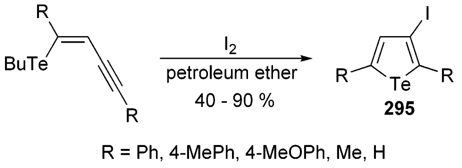
A completely different result was obtained when telluride **293** was used. Though it started from the *Z*-vinylic telluride, the isolated product **294** was the *E* isomer, with no traces of the formation of the *Z* isomer.

3.4. Miscellaneous

3.4.1. Iodocyclization of Butyltelluroenynes

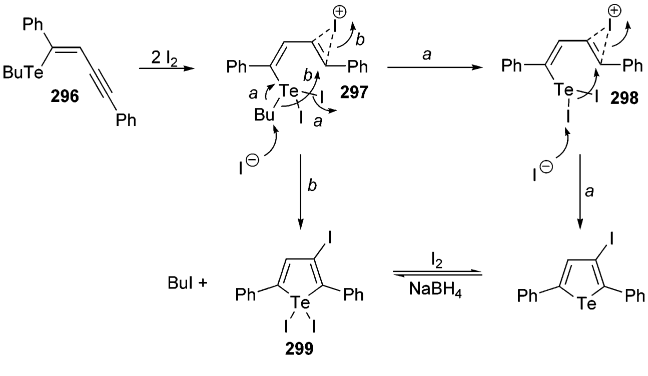
Tellurobutenynes are one of the most important classes of vinylic tellurides. By studying the chemistry and application of these classes of compounds, Dabdoub and co-workers have discovered that they undergo cleavage of the Te−Csp^3 bond by reaction with iodine, to produce 3-iodo tellurophenes **295** as main products.[166] The reaction is applicable to a series of tellurobutenynes, and the corresponding 3-iodo tellurophenes **295** are isolated in good to excellent yields (Scheme 165).

Scheme 165



A mechanistic proposal has been provided by the authors, which consists of an initial reaction of butyltelluroenyne **296** with iodine to generate the iodonium intermediate **297**. The reaction with iodide gives origin to iodobutane and tellurenyl iodide **298**, which undergoes attack by an iodide at the iodo atom, followed by ring closure through opening of the iodonium ion (pathway *a*, Scheme 166). In another possibility, a direct ring closure can happen to give the dihalogenated tellurophene **299** and iodobutane (pathway *b*, Scheme 166).

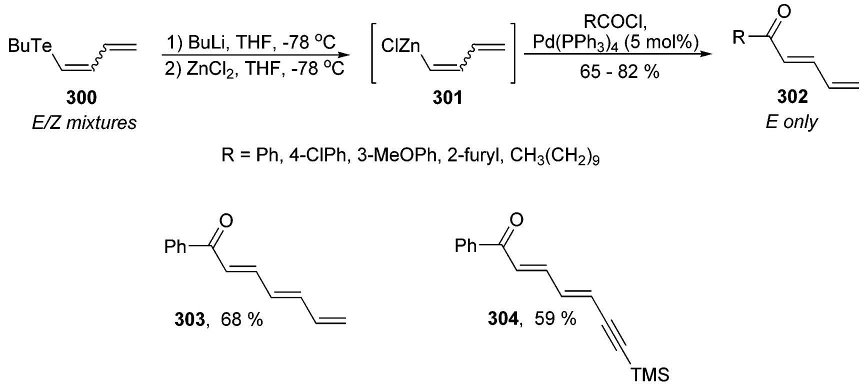
Scheme 166



3.4.2. Stereoselective Preparation of Conjugated Polyenic Ketones

A sequential transmetalation/cross-coupling reaction of vinylic tellurides, which aims to prepare conjugated polyenic ketones, has appeared in the literature.[167] The reaction consists of the treatment of a vinylic telluride **300** with BuLi, followed by the transmetalation of the vinyllithium intermediate to a vinylzinc reagent **301**, which is coupled with acyl chlorides to afford the conjugated polyenic ketones **302** with high stereoselectivity. Important to note is the fact that *E*/*Z* mixtures of the vinylic telluride can be employed in the reaction, and the product **302** is always isolated with only the *E*-olefin geometry, without a trace of the *Z* isomer (Scheme 167).

Scheme 167

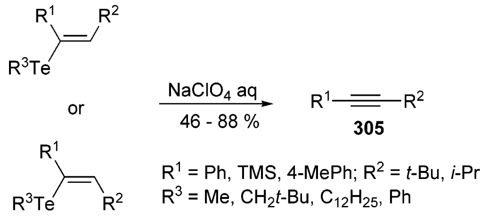


The best catalyst for this transformation was found to be $Pd(PPh_3)_4$, although $Pd(PPh_3)_2Cl_2$/*i*-Bu_2AlH (1:2) can also be used. This procedure allows the synthesis of other highly unsaturated conjugated systems, such as trienones **303** and dienyl-6-yl ketones **304**, with high stereoselectivity (Scheme 167).

3.4.3. Internal Acetylenes from Vinylic Tellurides

Vinylic tellurides, having no β-hydrogen on a sp^3 carbon, were quicky transformed into internal alkynes **305** when treated with aqueous sodium hypochlorite solution. Similar results have been achieved when the oxidizing agent was changed to H_2O_2 or *t*-BuOOH. The internal acetylenes **305** were obtained in good isolated yields (Scheme 168).[168]

Scheme 168



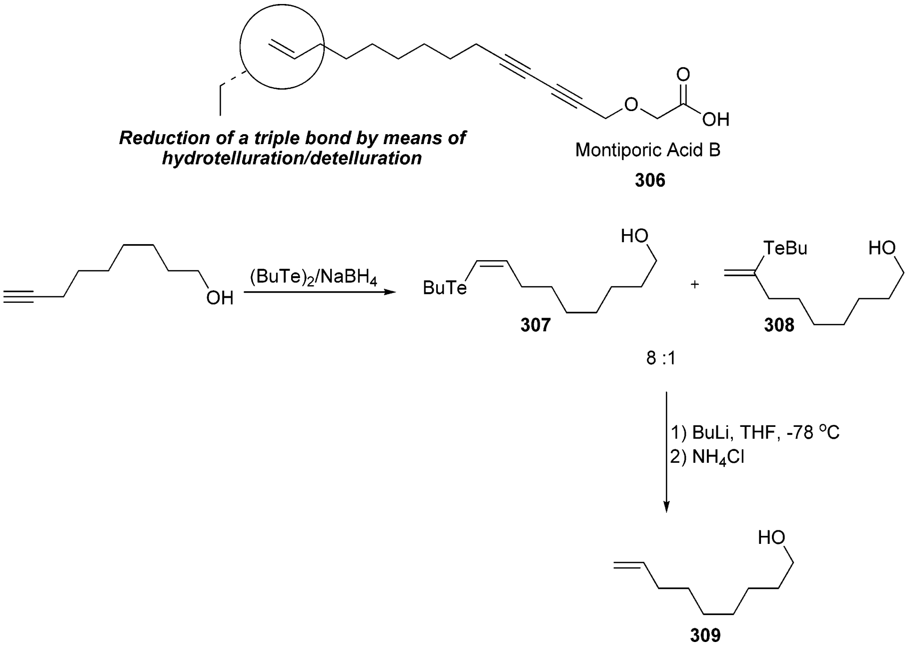
4. Applications to the Synthesis of Natural Products

4.1. Synthesis of Montiporic Acid B

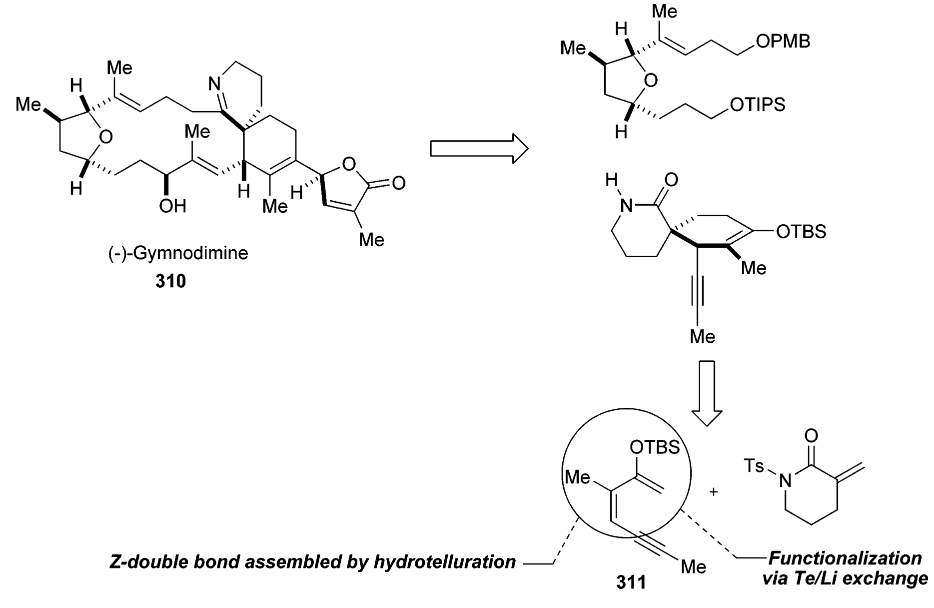
Two new polyacetylenic acids, namely Montiporic Acids A and B, were isolated from the eggs of scleractinian hard coral *Montipora digitata*, a hermaphroditic coral, by Fusetani.[169] The bioassays of these acids show that both exhibited antibacterial activity against *Escherichia coli* and cytotoxicity against P-388 murine leukemia cells (IC_{50} values of 5.0 and 12.0 μg/mL).

The total synthesis of both acids was accomplished in 1999, using vinylic telluride chemistry.[170] Montiporic Acid B (**306**) has a terminal double bond, which has been proven to be the major challenge in the synthesis of the compound. After several attempts to convert a terminal alkyne to the desired alkene, the reduction by means of a hydrotelluration reaction followed by a detelluration reaction through a Te−Li exchange proved to be a successful means of overcoming this difficulty. The hydrotelluration was performed under $(BuTe)_2/NaBH_4$ conditions and furnished two regioisomeric vinylic tellurides, **307** and **308**, in an 8:1 ratio in favor of the 1,2-*Z*-product **307**. This mixture was then treated with *n*-BuLi in THF, to give the intermediate vinyllithium, which

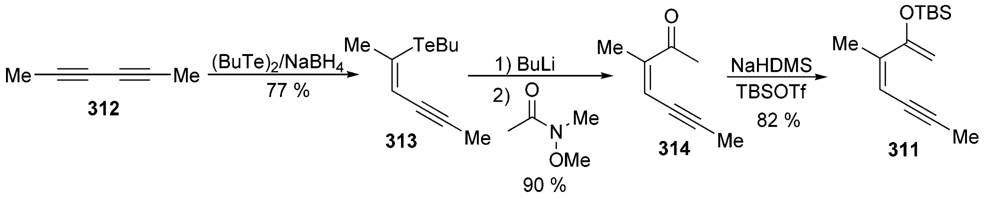
Scheme 169



Scheme 170



Scheme 171



is protonated by quenching with NH_4Cl to furnish the desired alkene **309** in 97% yield (Scheme 169). It is important to point out that this approach gave better results than the common Lindlar reduction.

4.2. Studies toward the Synthesis of (–)-Gymnodimine

Gymnodimine (**310**) is a member of a class of recently isolated marine toxins that possess unusual spirocyclic imines within macrocycles that also contain an ether or polyether subunit.[171] The relative or absolute stereochemistry of gymnodimine was determined by X-ray analyses.[172] An approach toward the total synthesis of (−)-gymnodimine (**310**) was described by Romo and co-workers, in which they envisioned the use of a Diels−Alder strategy to access the spirocyclic moiety of the molecule as a key step of the synthesis (for retrosynthesis, see Scheme 170).[173]

The required diene **311** for the Diels−Alder reaction was prepared by taking advantage of the unique features of tellurium chemistry. A hydrotelluration of propyne dimer **312** furnished vinylic telluride **313** with a *Z*-configuration of the double bond. The posterior Te−Li exchange reaction followed by the capture of the vinyl anion by the Weinreb amide gave the corresponding ketone **314**, which upon treatment with base and *tert*-butyldimethylsilyl triflate, under carefully controlled conditions, furnished enol ether **311** without isomerization. It is noteworthy that the tellurium−lithium exchange proceeded with complete retention of the geometry of the double bond. In this study, it is relevant that the diene was prepared on a large scale (∼5 g) (Scheme 171).

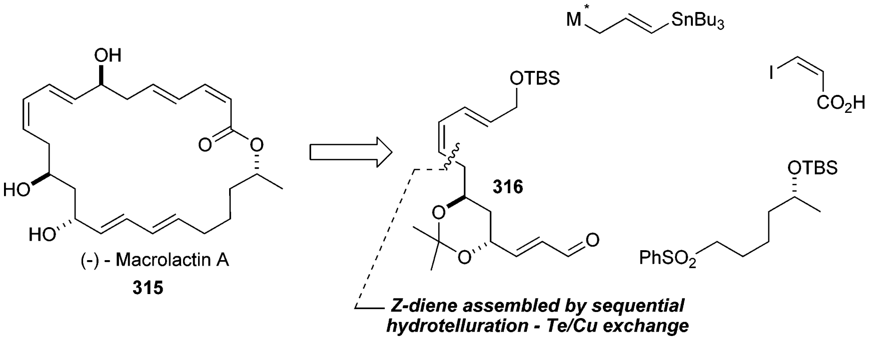
4.3. Synthesis of (–)-Macrolactin A

The macrolactins are a class of secondary metabolites isolated from a deep-sea bacterium.[174] Macrolactin A (**315**) exhibits a broad spectrum of activity with significant antiviral and cancer cell cytotoxic properties, including the inhibition of B16-F10 murine melanoma cell replication with an *in vitro* IC_{50} value of 3.5 μg/mL. It also has implications for controlling human HIV replication and for inhibiting *Herpes simplex* types I and II. Stereochemical assignments for Macrolactin A were made through the comparison of spectral data with those already established for Macrolactins B and F[175] and the first total synthesis developed by Smith and Ott.[176]

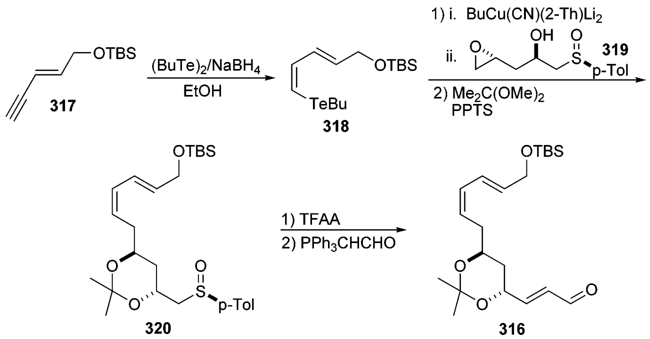
In another total synthesis, developed by Marino and Comasseto, the retrosynthetic analysis of the molecule involved the construction of a key fragment containing a diene moiety using tellurium chemistry (Scheme 172).[177]

Initially, the *Z*-diene moiety **316** was assembled by a hydrotelluration reaction of terminal enyne **317** via $(BuTe)_2$/$NaBH_4$ in ethanol, which exclusively afforded *Z*-vinylic telluride **318** in 92% yield. Further transmetalation with a higher order cyano cuprate resulted in *Z*-vinylic cuprate, which reacted with chiral epoxides **319** to furnish a 1,3-*anti*-diol, which is protected as the acetonide derivative **320**. Later, a Pummerer reaction at sulfoxide delivered the corresponding aldehyde. Wittig homologation resulted in the desired diene fragment **316** as a single stereoisomer (Scheme 173). It is noteworthy that both hydrotelluration and the Te−Cu exchange occurred with complete control of the stereochemistry and without formation of the *E*-diastereoisomer of the double bond.

Scheme 172



Scheme 173



4.4. Synthesis of Polyacetylenic Acids Isolated from *Heisteria acuminata*

The linear polyacetylenic acids **321** and **322** were isolated from the bark of *Heisteria acuminate* by bioassay-guided fractionation.[178] These compounds were found to have potent anti-inflammatory activity by the inhibition of cyclooxygenase (COX) and 5-lipoxygenase (5-LO).[179] Polyacetylenes have been previously reported in the literature as potent inhibitors of the arachidonic acid metabolism.[180] Therefore, it may be inferred that these compounds are, at least in part, responsible for the anti-inflammatory activity of *Heisteria acuminate* bark preparations used in folk medicine.

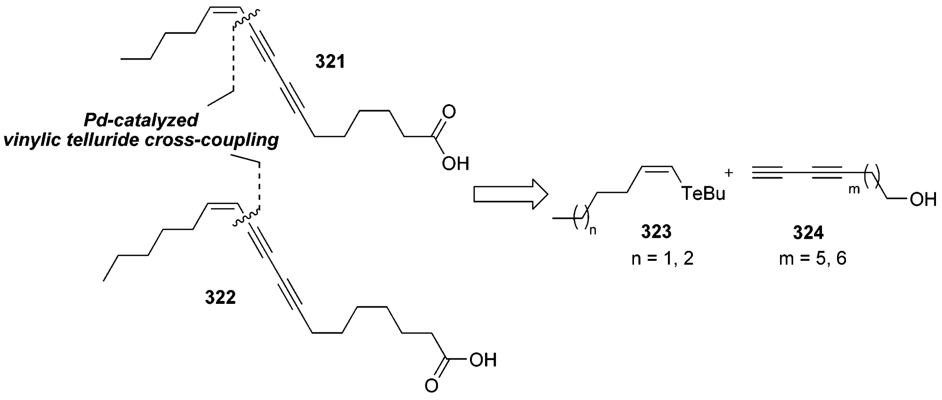
Their unusual structure, attractive biological activities, and scarce natural availability prompted us to synthesize them.[181] The retrosynthesis of both acids shows that the key *Z*-enediyne skeleton of the structure could be constructed by a palladium-catalyzed cross-coupling reaction of a *Z*-vinylic telluride **323** with the appropriate diyne alcohol **324** (Scheme 174).

Thus, the synthesis of vinylic telluride **323** was accomplished by the hydrotelluration of a terminal alkyne **325** through a reaction with BuTeLi, generated *in situ*, to afford the vinylic telluride **323** in a 6:1 mixture of regioisomers, in favor of the *Z*-1,2-vinylic telluride. Both isomers were easily separated by column chromatography, and the major product was obtained in 48% yield. The tellurides were then coupled with the appropriate alkynes **324** under $PdCl_2$/CuI conditions to exclusively afford enediyne alcohol **326** with the desired *Z*-configuration (Scheme 175).

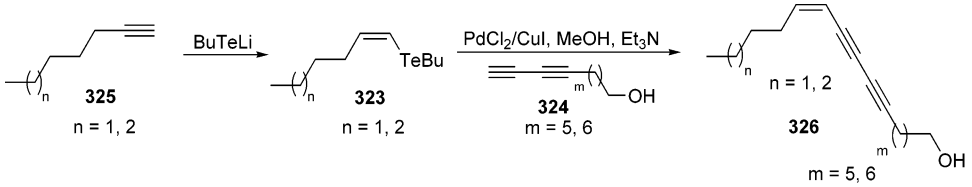
5. Conclusions

Recently, an impressive increase in the number of publications in the vinylic tellurides field has appeared in the literature. In fact, the many efforts and developments have transformed vinylic tellurides chemistry into a very broad and exciting field with many opportunities for research and development of applications. However, the use of vinylic tellurides by synthetic organic chemists or as a tool in organic

Scheme 174



Scheme 175



synthesis, mainly in the application to total synthesis, has been hampered due to a bad reputation related to these compounds. We have observed that many researchers prefer to use other vinyl halides and triflates, instead of vinylic tellurides. Thus, we hope with this review that we have demonstrated vinyl tellurides as valuable tools in synthetic strategies. We honestly wish that this article might help some chemists to look at tellurium chemistry from a different point of view and begin to consider vinyl tellurides as useful tools in future research projects.

Definitely, further developments in the synthesis and reactivity of vinylic tellurides, mainly in the study of the double bond functionalized, carbon−carbon bond formation, and their use in transition-metal-catalyzed coupling reactions are expected as well as studies on the toxicological and pharmacological aspects of vinylic tellurides, and perhaps, as was the case for organoselenium compounds 40 years ago, it is possible that the bad reputation, as toxic compounds, will fade. Thus, all of these considerations may add a new dimension to the field of polyvalent tellurium chemistry.

6. Acknowledgments

We are pleased to thank our collaborators, whose names appear in the references, for their dedicated and devoted contributions to our own work described herein. We are also grateful to CAPES, CNPq, and FAPERGS for financial support of our research. D.S.L. and R.B.P. thank CAPES and CNPq, respectively, for Ph.D. fellowships. G.Z. and A.L.B. are recipients of CNPq fellowships.

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CR0505730