Palladium-Catalyzed Coupling of sp^2-Hybridized Tellurides

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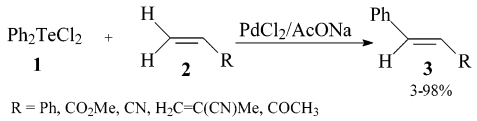
ABSTRACT

Vinylic tellurides are of importance due to their useful behavior as synthons and intermediates. Recently, the use of these compounds in place of vinylic halides or triflates in the palladium-catalyzed cross-coupling reaction has emerged as a powerful tool in the preparation of conjugated enyne and enediyne. In this way, vinylic tellurides can behave as aryl or vinyl carbocation equivalents. This review focuses on methods that involve the use of vinylic tellurides in palladium-catalyzed cross coupling reaction.

1. Introduction

Vinylic tellurides are useful intermediates in organic synthesis.[1] *Z*-Vinylic tellurides have been easily obtained by hydrotelluration of alkynes by either sodium tellurolate ($BuTeTeBu/NaBH_4/EtOH$)[2a] or lithium tellurolate (Te^0/BuLi/THF).[2b] On the other hand, *E*-vinylic tellurides have been obtained by stereospecific cis hydrometalation of the alkynes, followed by transmetalation of the *E*-vinylorganometalic complexes formed with organotellurenyl halide.[3] Of the two diastereoisomers, the *Z*-vinylic tellurides have been employed more frequently as intermediates because of their better availability. One of the most important reactions of vinylic tellurides is in transmetalation.[4] The vinyl organometallic obtained in this way can react with carbonyl compounds,[5] α,β-unsaturated systems,[6] or epoxides.[7] Recently a new application of vinylic tellurides utilizing palladium catalyzed cross-coupling has been described. In this case, they behave as aryl or vinyl carbocation equivalents. They react in a manner similar to vinylic halides or triflates in the Sonogashira,[8] Heck,[9] Suzuki,[10] and Stille[11] cross-coupling reactions with palladium as a catalyst.[12] In this way, there are some advantages to use vinylic tellurides instead of the other methods, such as the 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. Recently, we have described the synthesis of polyacetylenic acids isolated from *Heisteria acuminata* by using a vinylic telluride coupling reaction[13] to demonstrate the great applicability of these compounds in organic synthesis. Conversely, in the past decade there have been developments in Pd-catalyzed coupling systems for Heck, Suzuki, Stille, and Sonogashira reactions and others as a consequence of the great interest in the development of coupling substrates that are more both economical and readily accessible. Herein, we present all of the methods that involve the use of vinylic tellurides in palladium-catalyzed cross coupling reactions.

Scheme 1



2. Review

2.1. Reactions of Vinylic Tellurides with Alkenes—Heck-Type Reactions. *2.1.1. Carbodetelluration (Transmetalation) of Aryltellurium(IV) Compounds.* The history of the use of vinylic tellurides in palladium-catalyzed reactions began with the carbodetelluration of aryltellurium (IV) compounds.[14] The authors found that the reactions of diphenyltellurium (IV) dichloride **1** and palladium(II) chloride and sodium acetate with styrene in acetic acid at reflux afforded *E*-stilbene 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 **3**. The reaction was extended to other olefins **2**, and the compounds **3** were obtained in variable yields (3−98%), Scheme 1. The stereochemistry of the olefins **3** was trans except for those derived from acrylonitrile, which were obtained in a mixture of trans:cis = 74:26.

Gilson Zeni 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). Afterward he moved to the Federal University of Santa Maria, where he is now an Adjunct Professor. His current research interest centers around the synthesis and reactivity of chalcogen compounds and development of new synthetic methods and novel catalysts in cross-coupling reactions that involve vinylic tellurides.

Antonio Luiz Braga 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 currently he is still at the same place as Professor of Organic Chemistry. He carried out postdoctoral studies with Professor Ludger Wessjohann (Institute of Plant Biochemistry, Germany). His research interests mainly reside in the application of Chiral Chalcogen Compounds in Organic Synthesis.

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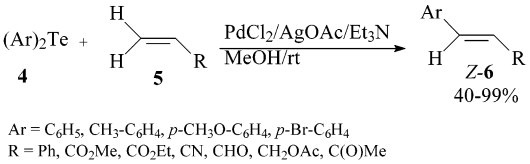
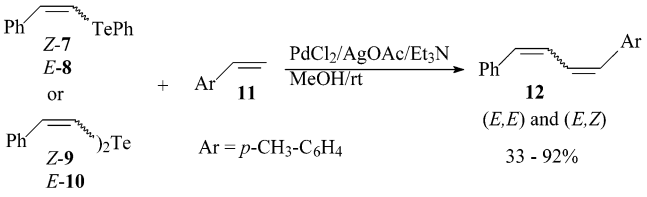
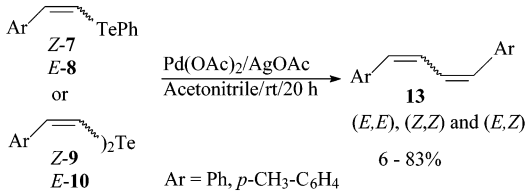
Scheme 2



Scheme 3



Scheme 4

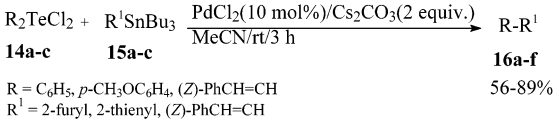


2.1.2. Cross-Coupling Reactions of the Aryl Tellurides with Alkenes. It has been reported that the cross-coupling reaction of diphenyl tellurides **4** with alkenes **5** in methanol at 25 °C in the presence of Pd^{II} catalyst, using Et_3N as base and an appropriate oxidant such as AgOAc, afforded the corresponding aryl-substituted *Z*-alkenes **6** in good yields (Scheme 2).[15] 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 when using oxidants such as ammonium hexanitratocerate, $CuCl_2$, and $K_2S_2O_8$.

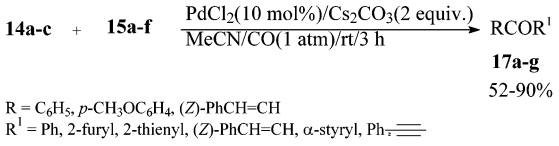
This method has been extended to several vinylic tellurides such as (*Z*)- and (*E*)-phenyl styryl tellurides **7** and **8**, (*Z*,*Z*)- bis-vinylic tellurides **9**, and (*E*,*E*)- bis-vinylic tellurides **10** with *p*-methylstyrene **11**. This cross-coupling reaction afforded the corresponding alkenylalkenes **12** in yields higher than 33% (Scheme 3). The entire process is highly stereoselective, and no *E*,Z-isomerization was observed during the reaction.

2.1.3. Homocoupling Reactions of the Vinylic Tellurides with Alkenes. The reaction of vinylic tellurides **7**−**10** 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*) **13**, 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 also proved 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 4 was found to be the use of $Pd(OAc)_2$ (0.05 mmol)/AgOAc (1 mmol), vinylic tellurides (**7**−**10**, 0.5 mmol), and acetonitrile (10 mL) at 25 °C for 20 h.[16]

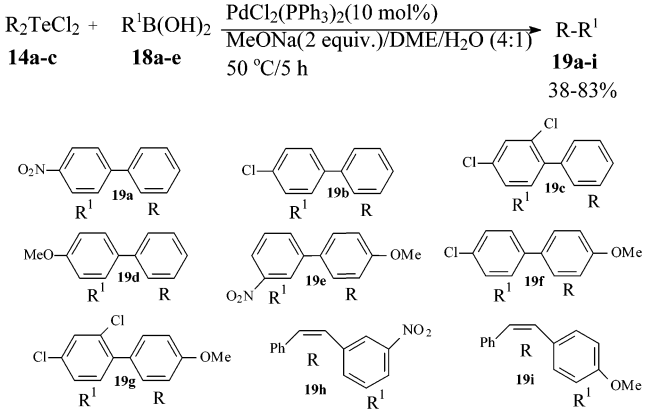
Scheme 5



Scheme 6



Scheme 7

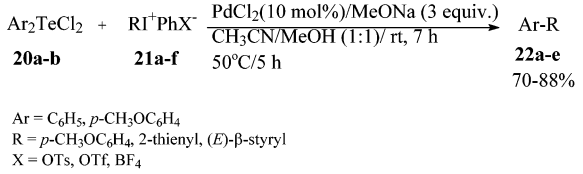


2.2. Cross-Coupling Reaction of the Organotellurium Compounds with Organostannanes—Stille-Type Reactions. Organostannanes have been successfully employed in cross-coupling reactions with diaryl- or divinyl-tellurium dichlorides. The reaction of organotellurium dichlorides **14a**−**c** with vinylstannane species **15a**−**c** in the presence of $PdCl_2$ with Cs_2CO_3 as the base and MeCN as the solvent afforded the cross-coupling products **16a**−**f** in good yields, as illustrated in Scheme 5. In this method, the authors tested other catalysts, such as $Pd(PPh_3)_4$, $Pd_2(dba)_3CHCl_3$, and $PdCl_2(PPh_3)_2$ The best results were obtained with $PdCl_2$. Concerning the bases used, Cs_2CO_3 was more efficient than K_2CO_3, Na_2CO_3, or MeONa.[17]

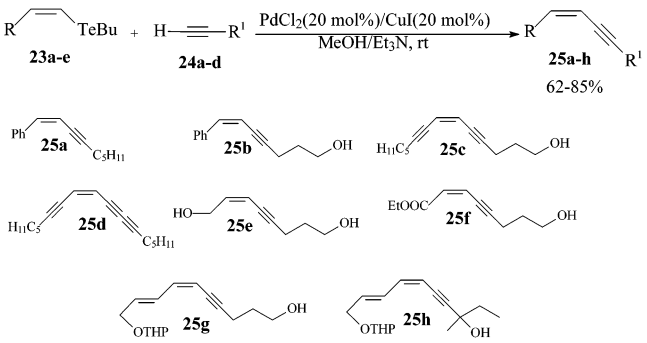
On the other hand, the authors also promoted detelluric cross-coupling carbonylations of diaryl- or divinyltellurium dichlorides **14a**−**c** by reaction with vinylstannanes **15a**−**f**. This cross-coupling reaction can be carried out using catalytic amounts of $PdCl_2$ (10 mol %), CO (1 atm) in MeCN, and Cs_2CO_3 as the base, affording ketones in 52−90% yield, Scheme 6.[17]

2.3. Cross-Coupling Reaction 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 formation of the carbon−carbon bonds.[18] An investigation of the palladium-catalyzed cross-coupling of diaryl and bis-vinyltellurium dichlorides with organoboronic acids has been reported recently.[19] As illustrated in Scheme 7, various diaryl or bis-vinyltellurium dichlorides **14a**−**c** were allowed to react with arylboronic acids **18a**−**e** in the presence of $PdCl_2(PPh_3)_2$ and NaOMe in DME/H_2O,

Scheme 8



Scheme 9

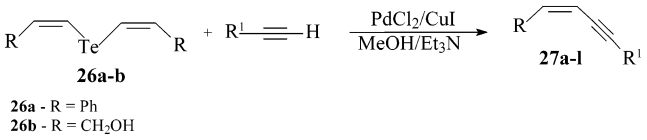


affording the coupled products **19a**−**i** in fair to good yields (Scheme 7).

2.4. Palladium-Catalyzed Cross-Coupling of Organotellurium Compounds with Hypervalent Iodonium Salts—Heck-Type Reactions. In another effort, Kang et al.[20] have shown that diaryltellurium dichlorides **20a**,**b** can be readily coupled with iodonium salts **21a**−**f** in the presence of palladium catalysts to give coupled products **22a**−**e**, Scheme 8. This method gives 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 gives the products in 70−88% yields.

2.5. Reactions of the Vinylic Tellurides with Alkynes—Sonogashira-Type Reactions. *2.5.1. 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.[21] 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.[22] 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.[23] The reaction has also been performed using bromoalkynes and vinylmetals, like vinyl boron,[24] copper,[25] zinc,[26] aluminum,[27] or magnesium.[28] The use of vinylic tellurides to obtain enynes and enediyne systems has been previously described using transmetalation with *n*-BuLi[29] and cyanocuprates.[30] 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.[31] We found that the optimum conditions for the coupling in Scheme 9 was the use of $PdCl_2$ (20 mol %)/CuI(20 mol %), MeOH (5 mL), (*Z*)-vinylic telluride **23** (1 mmol), the appropriate alkyne **24** (2 mmol) and Et_3N (1 mmol) at 25 °C. By extending the coupling reaction to other alkynes, various *Z*-enynes and *Z*-enediynes **25a**−**h** were obtained in good yields, Scheme 9. The reaction proceeds cleanly under mild conditions. Our approach represented an improvement over described methods, avoiding 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.[2a,2b,32]

Scheme 10



Scheme 11

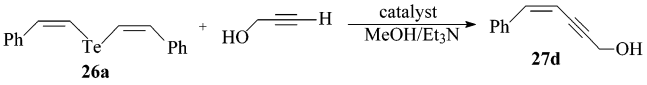


Table 1. Influence of the Ligands on the Palladium Complex

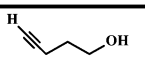
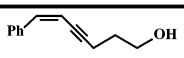
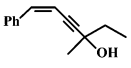
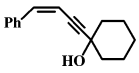
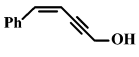
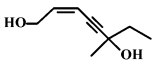
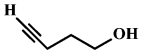
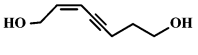
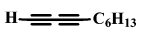
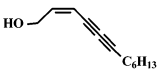
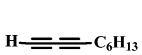
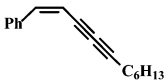
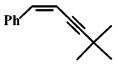
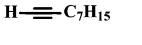
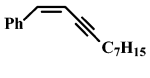
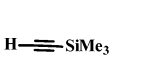
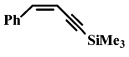
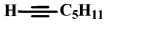
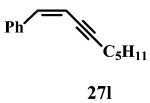
entry	catalyst (mol %)	time (h)	yield, **27d** (%)
1	$Pd(PPh_3)_4$/CuI (20)	48	0
2	$Pd(PPh_3)_4$ (20)	48	0
3	$PdCl_2/PPh_3$ (20)	20	8
4	$PdCl_2(PPh_3)_2$ (20)	20	5
5	$Pd(OAc)_2$ (20)	24	2
6	$PdCl_2(PhCN)_2$ (20)	20	5
7	$PdCl_2$/CuI (1)	24	23
8	$PdCl_2$/CuI (3)	24	30
9	$PdCl_2$/CuI (5)	24	47
10	$PdCl_2$/CuI (10)	6	85

2.5.2. 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 also investigated the stereospecific formation of (*Z*)-enyne **27a**−**l** systems by palladium catalyzed cross-coupling reactions of (*Z*)-bis-vinylic tellurides **26a**,**b** with 1-alkynes (Scheme 10).[33]

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 **26a** (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). As shown in Table 1, Pd-$(PPh_3)_4$ or $Pd(PPh_3)_4$/CuI did not exhibit catalytic activity in this reaction (entries 1 and 2), 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 **27d** (entries 3−6). The reaction yields were greatly enhanced by increasing the amount of $PdCl_2$/CuI from 1% to 10% (entries 7−10), where in the enyne **27d** was obtained in 85% isolated yield Table 1, entry 10.

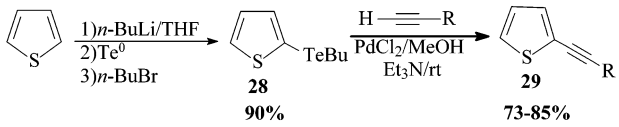
The nature of the amine was critical for the success of the coupling. Using pyrrolidine, piperidine or morpholine (1 equiv) as base, no reaction was observed. With Et_2NH,

Table 2. Enynes 27 Prepared According to Scheme 10

Entry	(*Z*)-bis-vinylic telluride **26**	Alkyne	Enyne **27**	Yield (%)
1	**26a**		 **27a**	82
2	**26a**		 **27b**	78
3	**26a**		 **27c**	83
4	**26a**		 **27d**	85
5	**26b**		 **27e**	70
6	**26b**		 **27f**	75
7	**26b**		 **27g**	84
8	**26a**		 **27h**	80
9	**26a**		 **27i**	85
10	**26a**		 **27j**	77
11	**26a**		 **27k**	73
12	**26a**		 **27l**	75

n-PrNH$_2$ or *n*-BuNH$_2$, moderate yields were observed (15 to 28%). However, with Et$_3$N, the enyne **27d** was obtained in 85% isolated yield and the reaction was completed within 6 h. The stereoisomeric purities of the enynes **27a**−**l** were similar to that of starting bis-vinylic tellurides **26**, indicating a complete retention of configuration in this type of reaction. The stereochemistry of the obtained enynes was easily established. Thus, the optimum conditions for the coupling in Scheme 10 were found to be the use of PdCl$_2$(10 mol %)/CuI(10 mol %), MeOH (10 mL), (*Z*)-bis-vinylic telluride **26a**,**b** (1 mmol), the appropriate alkyne (2 mmol), and Et$_3$N (1 mmol) at 25 °C. Extending

Scheme 12



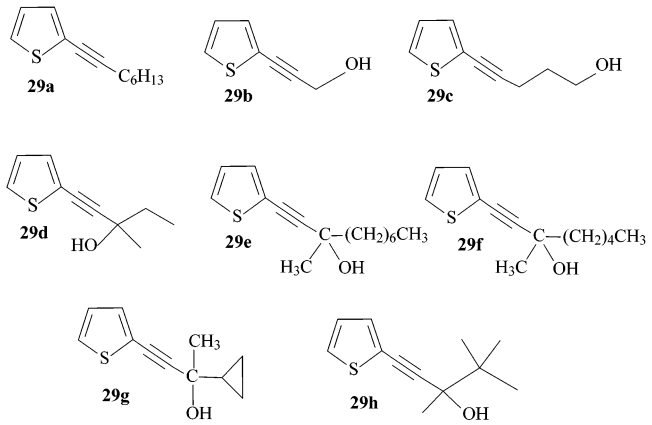
the coupling reaction to other alkynes, various *Z*-enynes **27** were obtained in good yields (Table 2).

2.5.3. Palladium-Catalyzed Cross-Coupling of 2-(Butyltelluro)thiophene or 2-(Butyltelluro)furan with 1-Alkynes. Several thiophene derivatives have been found to show nematocidal,[34] insecticidal,[35] antibacterial,[36] antifungal,[37] and antiviral[38] activity. Recently, we have investigated the antiinflammatory activity of acetylenic thiophene derivatives synthesized via a Pd-catalyzed coupling reaction of 2-(butyltelluro)thiophene with 1-alkynes.[39] In this study the following were evaluated: (a) influence of the nature of the catalyst, (b) effect of the nature of the amine, and (c) antiinflammatory activity of acetylenic thiophene derivatives prepared. The starting material required for the synthesis, 2-(butyltelluro)thiophene **28** (Scheme 12), was obtained from the metalation of thiophene with *n*-butyllithium[40] followed by treatment of 2-thienyllithium with elemental tellurium. Subsequent addition of 1-bromobutane gave the 2-(butyltelluro)thiophene **28** 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 **28** with 1-alkynes in methanol using PdCl$_2$ as the catalyst and triethylamine as the base at room temperature gave the acetylenic thiophenes **29** in 73−85% yield after purification (Scheme 12).

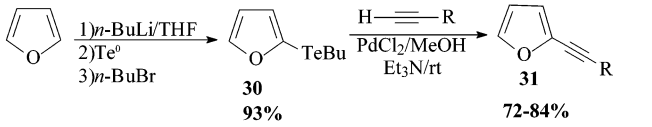
Of the compounds tested, Pd(PPh$_3$)$_4$ or Pd(PPh$_3$)$_4$/CuI did not exhibit catalytic activity in this reaction, and Pd(II) compounds such as PdCl$_2$/PPh$_3$, PdCl$_2$(PPh$_3$)$_2$, Pd(OAc)$_2$, and PdCl$_2$(PhCN)$_2$ gave unsatisfactory yields of the desired acetylenic thiophenes. However, by using 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 reaction was observed. The use of Et$_2$NH, *n*-PrNH$_2$ or *n*-BuNH$_2$ gave the desired product in low yield (5−8%). However, by using Et$_3$N, the acetylenic thiophene derivatives were obtained in good yield. We also found that the yields of acetylenic thiophene were markedly decreased using DMF, CH$_3$CN, THF, or CH$_2$Cl$_2$, instead of MeOH as the solvent. Thus, the optimum condition for the coupling in Scheme 12 was found to be the use of PdCl$_2$ (10 mol %), MeOH (5 mL), 2-(alkyltelluro)thiophene **28** (1 mmol), the appropriate 1-alkyne (2 mmol), and Et$_3$N (1 mmol) at 25 °C. Moreover, the coupling reaction was extended to other alkynes. The acetylenic thiophenes obtained are summarized in Scheme 13.

The acetylenic thiophenes **29a**−**c** obtained were screened for anti-inflammatory activity using the carrageenin-induced paw edema method.[41] This method is customarily used for the screening of new pharmacologically active compounds. The best results were obtained

Scheme 13

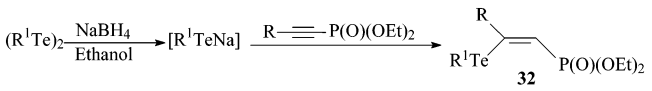


Scheme 14



31a - R = CH_2OH
31b - R = $CH_2(CH_2)_2OH$
31c - R = $C(OH)(CH_3)CH_2(CH_2)_3CH_3$
31d - R = $C(OH)(CH_3)CH_2(CH_2)_5CH_3$
31e - R = $C(OH)(CH_3)CH_2CH_3$
31f - R = *cyclo*-OH-C_6H_{10}
31g - R = CO_2Et
31h - R = $SiMe_3$

Scheme 15



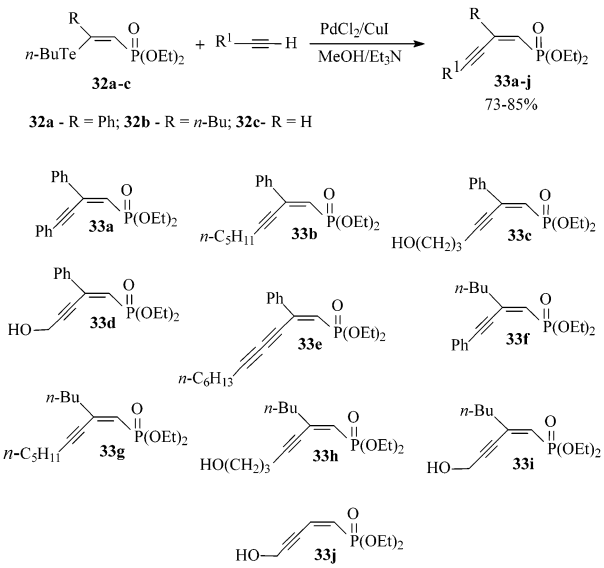
R = Ph; *n*-Bu; cyclohexenyl
$\mathbf{R^1}$ = Ph and n-Bu

using the acetylenic thiophene **29c** (50% of the edema inhibition at a dose of 250 mg/kg; i.p), demonstrating significant potential to reduce the carrageenin-paw edema when compared to acetylsalicylic acid (100 mg/kg, i.p., $p < 0.05$).

We also applied the method described above to prepare acetylenic furan derivatives (Scheme 14).[42] We found that direct coupling of 2-(alkyltelluro)furan **30** with 1-alkynes in the presence of palladium dichloride as the catalyst in methanol and triethylamine affords the desired acetylenic furan derivatives **31a**−**h** in good yields (72−84%). The obtained acetylenic furans **31a**−**c** were also screened for antiinflammatory activity. The acetylenic furan **31c** (100 mg/kg; i.p.) inhibited 40% of the edema ($p < 0.05$ by Duncan's multiple range test), induced by carrageenin when compared to control. Compound **31c** (250 mg/kg; i.p.) inhibited paw edema formation with greater potency than acetylsalicylic acid (100 mg/kg, i.p.), 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.

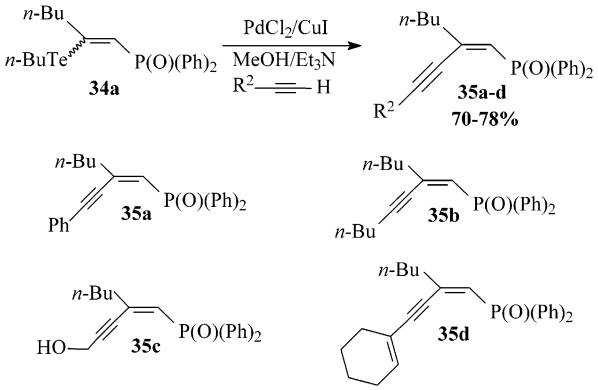
2.5.4. Enynephosphonates via Palladium Catalyzed Cross-Coupling of β-Organotelluro Vinylphosphonates with Alkynes. Unsaturated phosphorus compounds represent an important class of synthetic intermediates. Many of these compounds have attracted attention because of their antibacterial, antiviral, antibiotic, pesticidal, anti-cancer, and enzyme-inhibitory properties.[43] The synthetic methods for producing the C−P bond have been extensively reviewed.[44] However, so far, only one method of preparation of enynephosphonates has been disclosed utilizing palladium-mediated cross-coupling reactions of α-iodovinylphophonates with 1-alkynes.[45] Recently, we have shown that 1-alkynylphosphonates can be used to prepare β-organochalcogeno vinylphosphonates **32**[46] by hydrochalcogenation, (Scheme 15) and enynephosphonates **33** (Scheme 16) from cross-coupling reactions between β-organotelluro vinylphosphonates and alkynes.[47] Thus, the optimum condition for the coupling as described in Scheme 16 was found to be the use of $PdCl_2$/CuI (20 mol % each), methanol (10 mL), β-organotelluro vinylphosphonates **32** (1 mmol), the appropriate 1-alkyne (2 mmol), and Et_3N (1 mmol) at room temperature. Using this method, several enynephosphonates **33a**−**j** were prepared in good yields, Scheme 16. The stereoisomeric purities of

Scheme 16

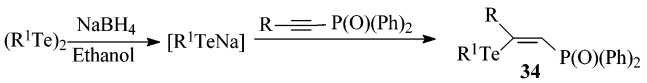


32a - R = Ph; **32b** - R = *n*-Bu; **32c**- R = H

Scheme 17

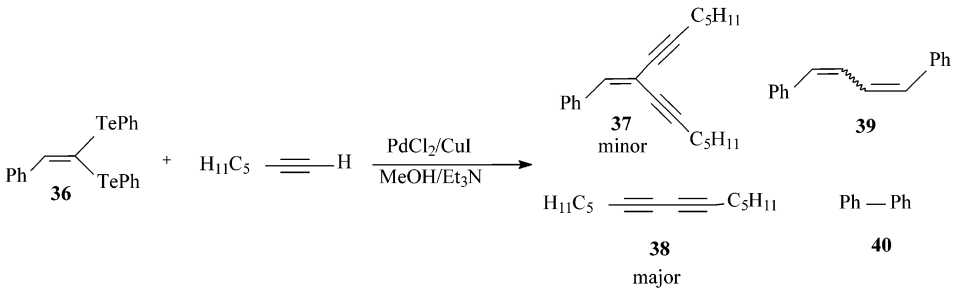


Scheme 18



$\mathbf{R^1}$= Ph and *n*-Bu
R = Ph; *n*-Bu; cyclohexenyl

Scheme 19



33a−**j** were equal to those of the starting β-organotelluro vinylphosphonates **32**, indicating complete retention of configuration in this type of reaction.

Similar reactions were developed in the preparation of enynephosphine oxide.[48] We found that the coupling reaction of compounds **34a** with appropriate alkynes under the same cross-coupling conditions as described before affords the β-alkynyl vinylphosphine oxides **35a**−**d** in 70−78% yield, Scheme 17.

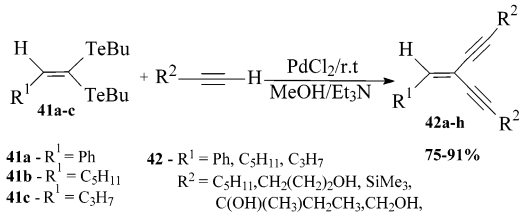
The starting materials, β-organotelluro vinylphosphine oxides **34**, were prepared by addition of alkynylphosphine oxides to a solution of sodium organyl tellurolate, prepared by reduction of ditellurides with sodium borohydride in ethanol at room temperature, Scheme 18.

2.5.5. Synthesis of Cross-Conjugated Geminal Enediynes via Palladium Catalyzed Cross-Coupling Reaction of Ketene Butyltelluroacetals. Interest in the development of synthetic methods based on palladium catalysis stimulated an examination of the reactivity of ketene telluroacetals (vinylic tellurides) with terminal alkynes to obtain conjugated and cross-conjugated enediynes via palladium catalyzed cross-coupling reactions.[49]

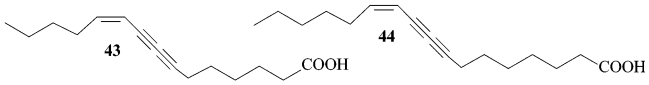
Initially, efforts were focused on the reactivity of ketene phenyltelluroacetal **36** in the cross-coupling reaction with 1-alkynes (Scheme 19). Thus, ketene phenyltelluroacetal **36** (1 equiv) was treated in methanol at room temperature with 1-heptyne (2 equiv) in the presence of $PdCl_2$ (20 mol %)/CuI (20 mol %), and Et_3N (1 equiv) as base. Under these conditions, the corresponding enediyne **37** was obtained as a minor product, but **38** (major) and a small amount of homocoupling products **39** and **40** were also isolated (Scheme 19).

The reaction between ketene phenyltelluroacetal **36** 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 **38** was not observed. However, the cross-coupling reaction still proceeded unsatisfactorily, providing **37** contaminated with **39** and **40**. Thus, the optimum conditions for the coupling as described in Scheme 20 were found to be 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 and observing that enediynes **42a**−**h** were obtained in good yield, Scheme 20. The reaction conditions tolerate the use

Scheme 20



Scheme 21



of functionalities such as hydroxy and labile acetylenic silyl trimethyl groups.

3. Recent Progress and Perspectives

The use of vinylic tellurides in the preparation of conjugated enyne and enediyne systems of natural products with biological activity using palladium-catalyzed cross-coupling has been described previously.[13] In that work, the synthesis of polyacetylenic acids isolated from *Heisteria acuminata*, namely, *Z*-hexadec-11-en-7,9-diynoic acid **43** and *Z*-octadec-12-en-7,9-diynoic acid **44**, was reported (Scheme 21).

Considering that vinylic tellurides can undergo similar reactions as vinylic halides and triflates are easily accessed and have great stability, we can expect that soon the development of more synthetic transformations and applications involving these reagents will be reported. Concerning toxicity, inorganic and organic tellurium compounds are highly toxic to the CNS of rodents.[50] The importance of occupational exposure to and environmental issues of tellurium are growing rapidly, but the biochemistry and clinical significance of such exposure are poorly understood. In fact, studies dealing with the distribution of Te and its concomitant toxicology are scarce in the literature. Consequently, we believe there will be impressive an increase in the toxicity and environmental studies in this area.

4. Conclusion

This report focuses on the use of vinylic tellurides in the preparation of conjugated diene, enyne, and enediyne systems using palladium-catalyzed cross-coupling reactions. The reactions proceed cleanly under mild condi-

tions, tolerate sensitive functional groups, and are highly diastereoselective, since only products with retention of configuration of the double bond are detected. Finally, this work describes the first application of vinylic tellurides in the synthesis of products with biological activity by a cross-coupling reaction.

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