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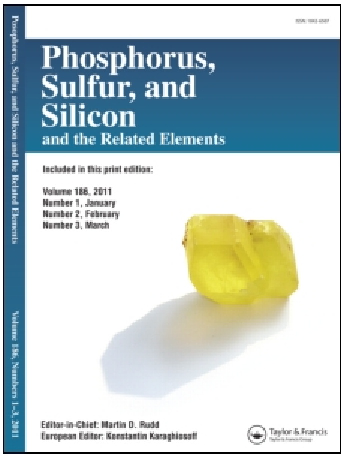

Phosphorus, Sulfur, and Silicon and the Related Elements

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Synthesis of Vinylic Chalcogenides (S, Se, Te) by Wittig and the Horner-Wittig Reactions

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An overview on the applications of the Wittig and Horner-Wittig reactions to the synthesis of vinylic sulfides, ketene dithioacetals, 1,3-dithioles, 1,4-benzodithiafulvenes, 1,4-benzodithiafulvenes, vinylic sulfoxides, vinylic sulfones, vinylic selenides, ketene selenoacetals, vinylic tellurides, ketene phenyltelluroacetals, ketene dithioacetal mono-S-oxides, ketene (S, Te) acetals and chalcogeno allenes is presented.

Keywords: Wittig reactions; Horner-Wittig reactions; vinylic chalcogenides; sulfur; selenium; tellurium; sulfoxides; sulfones

1. INTRODUCTION

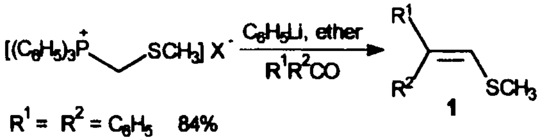
Among the derivatives of chalcogens, vinylic species have been widely studied and found widespread use in organic synthesis. Their usefulness arises from the combination of a carbon-carbon double bond that constitutes one of the simplest functional group with the reactivity of chalcogens. General methods of synthesis and the reactivity of vinylic selenides and tellurides have been recently revised,[1] but the sulfur counterparts did not receive so far this attention. Other review articles present only specific aspects on this chemistry, without a general scope.[2]

In this article we will present an overview of the most important methods for vinylic chalcogenides synthesis (sulfur, selenium and tellurium derivatives) by the Wittig and the Horner-Wittig reactions, in view of the importance of this reaction for organic synthesis. The review will cover the preparation of vinylic sulfides, vinylic selenides, vinylic tellurides, vinylic sulfoxides, vinylic sulfones, ketene acetals, etc.

2. PREPARATION OF SULFUR VINYLIC COMPOUNDS BY WITTIG AND HORNER-WITTIG REACTIONS

2.1. Vinylic Sulfides by Wittig

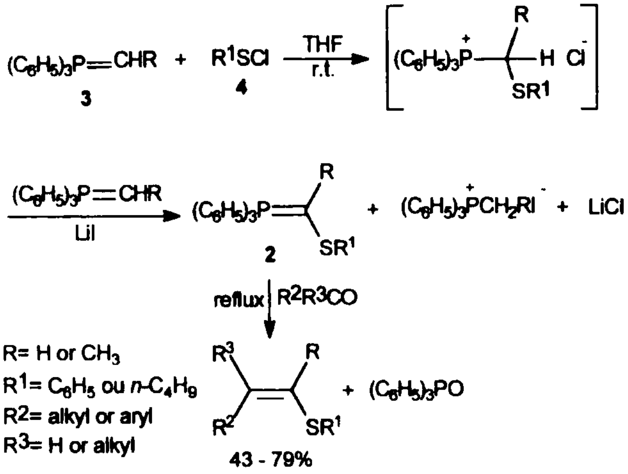
Vinylic sulfides were the first vinylic chalcogenides prepared by the Wittig reaction. Wittig and Schlosser,[3] in 1961, described the preparation of vinylic sulfides **1** from the corresponding α-methylthio phosphonium salts, by treatment with phenyllithium, followed by the addition of a carbonyl compound (scheme 1).



$R^1 = R^2 = C_6H_5$ 84%
$R^1 = C_6H_5$; $R^2 = H$ 70%

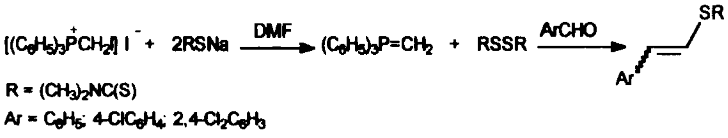
SCHEME 1

In 1968, Mukaiyama *et al.*[4] reported the preparation of vinylic sulfides, in good yields, by treating α-phenylmercaptoethylidene triphenylphosphorane **2** (R^1 = C_6H_5), formed from ethylidene triphenylphosphorane **3** and benzenesulfenyl chloride **4**, in a transilidation reaction, with aldehydes or ketones (Scheme 2). By using *n*-butanesulfenyl chloride **4** (R^1= *n*-C_4H_9), a more reactive phosphorane **2** (R^1= n-C_4H_9) toward carbonyl compounds would be prepared (reacting even with cyclohexanone) owing to the increased nucleophilic character of the phosphorane.



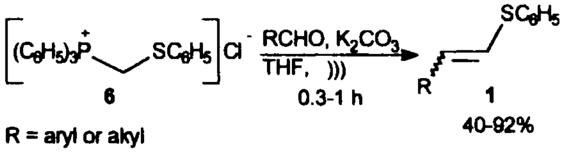
SCHEME 2

A modification of this methodology[5] involved the replacement of benzenesulfenyl chloride **4** by the disulfide **5** with a weak S-S bond, generated *in situ* by the reaction of a phosphonium salt with a dithiocarbamyl anion. The reaction performed in the presence of aldehyde in DMF led to the styryl sulfides (Scheme 3). The reaction of stabilized (by an ethoxycarbonyl group) sulfonyl phosphoranes with nitro-substituted aldehydes have also been described.[6]



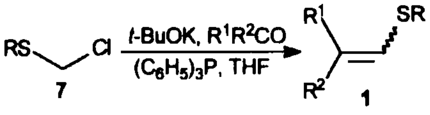
SCHEME 3

In another methodology,[7] vinylic sulfides **1** were obtained by using PTC and the sonication techniques in a short time reaction. Reactions were performed at room temperature and the inexpensive and convenient-to-handle K_2CO_3 was used as base, under very simple experimental procedures. The phenylsulfenylmethyl (triphenyl) phosphonium **6** reacted with aromatic and aliphatic aldehydes in order to give the corresponding vinylic sulfides **1** in good yields, with stereochemistry predominantly *E* (Scheme 4).



SCHEME 4

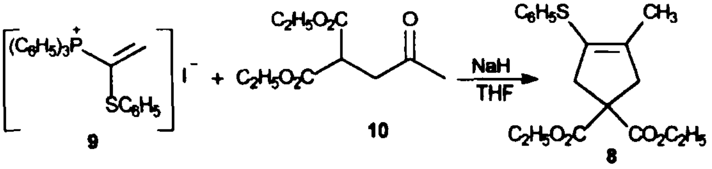
A simplified one-pot procedure was also described by Silveira *et al.*[8] This reaction was performed very easily by simply mixing of all the reagents at room temperature, giving the expected vinyl sulfides **1** in 46-84% yield. In this method, the triphenylphosphoranes are formed *"in situ"* by the reaction of chloromethyl phenylsulfide **7**, *t*-BuOK and triphenylphosphine. Reaction of the phosphorane with aldehydes or ketones affords the products **1** with preferential *Z*-configuration (Scheme 5). The corresponding 1-chloro-1-phenylthiosulfides have also been prepared by a similar methodology[9] or under phase transfer conditions.[10]



R = CH_3 or C_6H_5
R^1 = H or alkyl
R^2 = alkyl or aryl

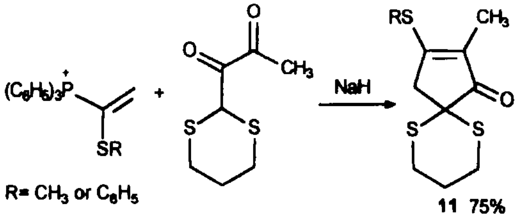
SCHEME 5

The cyclic vinylic sulfide **8** was prepared by Hewson[11] in a 90% yield. This reaction involved the addition of salt **9** to the enolate anion of the ketodiester **10** in THF, at room temperature (Scheme 6).



SCHEME 6

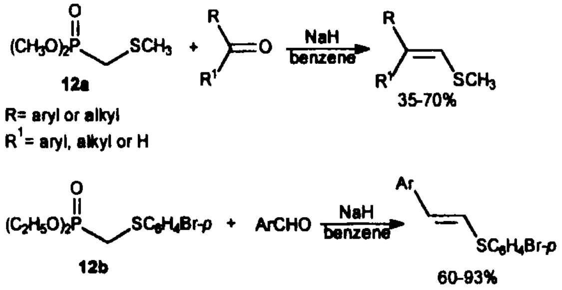
Later on detailed studies were published on the scope of this reaction leading to more functionalised cyclopentanes **11**, applicable to the synthesis of natural products.[12-14]



SCHEME 7

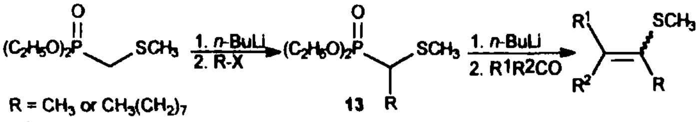
2.2. Vinylic Sulfides by Horner-Wittig

Vinylic sulfides have been obtained from dimethyl methylmercaptomethane phosphonate **12a**, which undergoes the Horner-Wittig reaction with aliphatic and aromatic aldehydes and ketones (Scheme 8).[15,16] The reaction is best carried out by the reaction of **12a** with sodium hydride in the presence of the aldehyde, otherwise lower yields are obtained. The reaction of **12a** with ketones is slower and can be accelerated by heating; however, using dimethylformamide as a solvent is preferable in this case. The vinylic sulfides derived from aldehydes possess the *E*-configuration. The phosphonate **12b** also suffers the same type of reaction.[17]



SCHEME 8

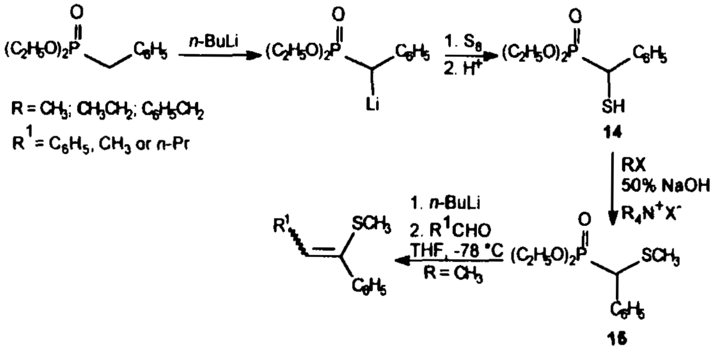
Similar results were described soon after by Corey and Shulman.[18] In this case, the preparation of more substituted vinylic sulfides was studied, by the alkylation of the anion derived from a phosphonate similar to **12a**, by treatment with *n*-BuLi and an alkylhalide. Sequential treatment of the phosphonates **13** with *n*-butyllithium and an aldehyde or ketone and heating at 50 °C eliminated diethyl phosphate monoanion to give vinyl sulfides of preferential *E*-configuration (Scheme 9). The lithio derivatives **13** could be formed either at -70 °C in THF or at 0 °C in cyclohexane.



R = CH_3 or $CH_3(CH_2)_7$
R^1 = alkyl, aryl or H
R^2 = alkyl or aryl

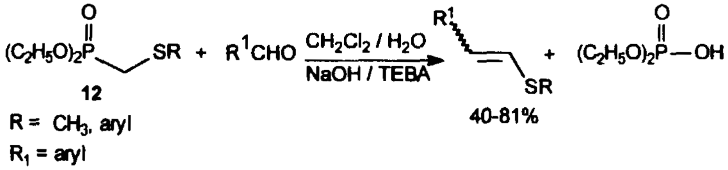
SCHEME 9

Improvements on this reaction were made by Mikolajczyk *et al.*,[19,20] who described the preparation of several substituted thiophosphonate by the addition of the elemental sulfur to the corresponding phosphonate carbanion, affording α-phosphoryl thiols **14**. The synthesis of these compounds, in conjunction with their alkylation, provides a new entry to variously substituted sulfides **15**, such as the one substituted by phenyl group at the α-position. The resulting lithio derivative of **15** reacts with aldehydes to give the corresponding vinyl sulfides, which on hydrolysis, gives access to aromatic ketones (Scheme 10).[20]



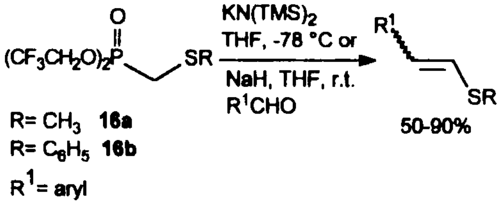
SCHEME 10

The Horner-Wittig reaction of α-phosphoryl compound **12** can be also performed in the two-phase catalytic system. The α-phosphoryl sulfides **12** give the corresponding vinylic sulfides[21] (3 examples described) in good yields, using TEBA as a phase-transfer catalyst (Scheme 11). The reaction can also be performed without addition of a typical phase-transfer catalyst.[21] However, the reaction was found to be specific to aromatic aldehydes. Ketones and aldehydes capable of enolisation are unreactive.



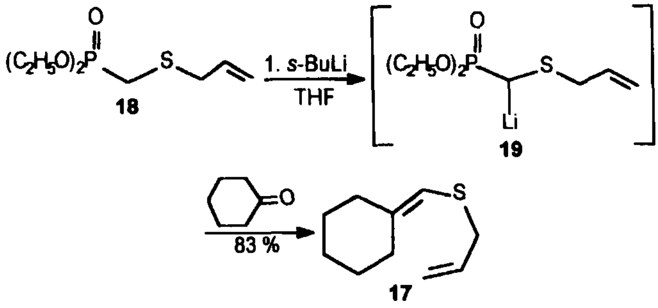
SCHEME 11

With the aim of preparing *cis*-vinylic sulfides, Kokin *et al.*[22] introduced a modified Horner-Wittig reaction, where the olefination was carried out using the trifluorphosphonate **16** and various aromatic aldehydes (Scheme 12). For example, the reaction of **16a** with benzaldehyde or *p*-tolualdehyde in the presence of NaH showed a preference for *E*-isomer. However, the use of **16b** and the $KN(TMS)_2$, as the base, reversed the selectivity, and the *Z*-isomer became predominant on reaction with benzaldehyde. Pure *Z*-vinylic sulfides could be obtained by the reduction of the corresponding *Z*-vinylic sulfoxides, obtained in higher isomeric purity by this route as it will be discussed bellow.



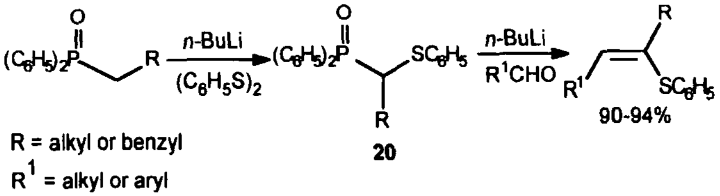
SCHEME 12

Allyl vinyl sulfides[23] can be prepared from the allythiomethylphosphonate **18**. A slow addition of *sec*-butyllithium in cyclohexane to a THF solution of **18**, at -78 °C afforded the anion **19**, which reacts with several ketones and benzaldehyde to give the desired allyl vinyl sulfides in good yields. Scheme 13 presents the product formed from the reaction with cyclohexanone.



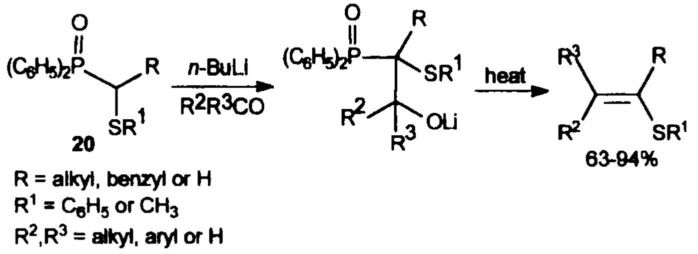
SCHEME 13

Warren and co-workers[24] reported the preparation, in high yields, of vinyl sulfides by the reaction of diphenylphosphinoxide **20** with *n*-butyllithium and aldehydes (Scheme 14). This method could also be applied to the synthesis of 1-phenylthiobutadienes[25] and masked 1,4-diketones by the reaction of a γ-phenylthio-γ-phosphinoyl ketal with aldehydes.[26]



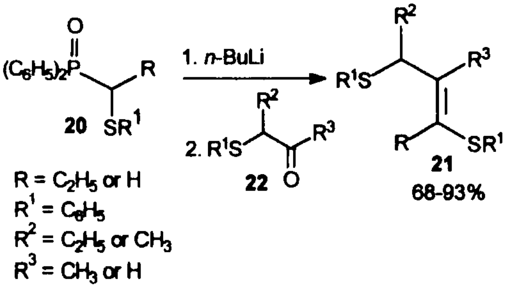
SCHEME 14

In another work,[27] Warren showed that ketones only react with diphenylphosphinoxide **20** when R= H and R^1= C_6H_5, affording vinyl sulfides in excellent yields. The substituted reagents **20** also react with ketones, if a methylthio instead of phenylthio group is present (R= alkyl and $R^1 = CH_3$), and the substituent (R) is not branched (Scheme 15). The reaction with aldehydes furnishes the corresponding vinylic sulfides in 90-94 % yield.



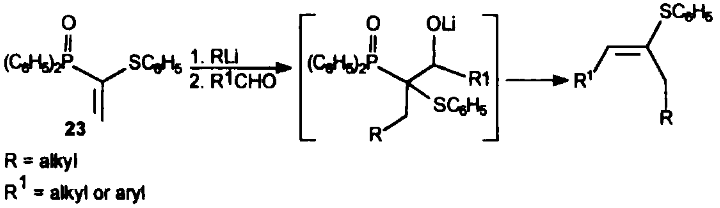
SCHEME 15

1-3-Bis(phenylthio)allyl ethers **21** have been prepared, in good yields, by the same route described above, starting from diphenylphosphinoxide **20** and reacting with the α-phenylthiocarbonyl compounds **22** (Scheme 16).[27]



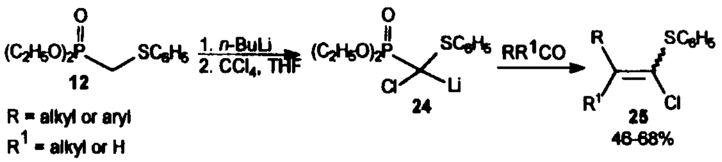
SCHEME 16

The addition of an alkyllithium to 1-(phenylthio)vinyldiphenyl phosphine oxide **23** produces the corresponding α-thio anion, which adds to an aldehyde to give vinyl sulfides in one step from **23**, albeit in low yields.[28] The vinyl sulfides are formed as mixtures of geometrical isomers (Scheme 17).



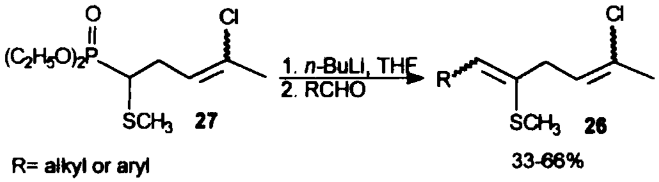
SCHEME 17

α-Chlorovinylic sulfides can also be prepared by the Horner-Wittig reaction. Coutrot *et al.*[29] found that the treatment of arylthiomethanephosphonates **12** with *n*-butyllithium, at low temperature, in THF and the subsequent chlorination by tetrachloromethane provides the intermediate phosphonate **24** (Scheme 18). The reaction of **24** with aldehydes and ketones has been employed for the preparation of phenyl 1-chloro-1-alken-1-yl sulfides **25** in moderate yields. Similar results were described using chloromethanephosphonate and *n*-BuLi as the base.[30]



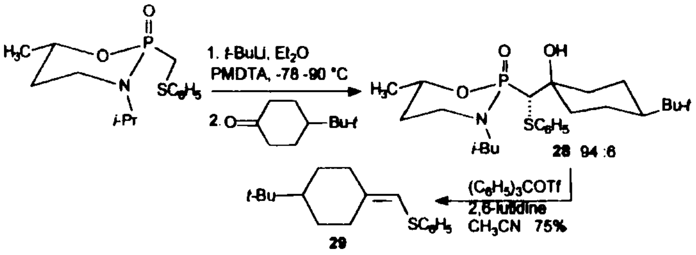
SCHEME 18

2-Chloro-5-methylthio-2,5-hexadienes[31] **26**, masked 1,4-diketones, were prepared by the Horner-Wittig reaction of aldehydes with diethyl (4-chloro-1-methylthio-3-pentenyl)phosphonate **27** (Scheme 19). The reaction of **27** with ketones were also examined, but the yields of the products were low (15-37%).



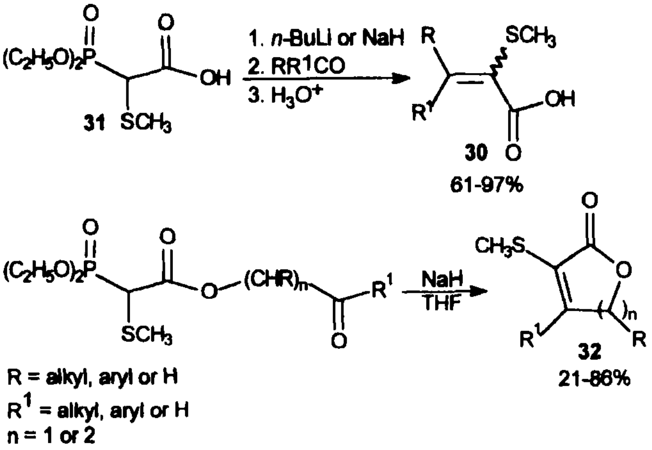
SCHEME 19

Denmark and Chen[32] recently reported an alkylidenation reaction for the highly selective synthesis of dissymmetric olefins, applicable to the synthesis of vinylic sulfides with very high stereospecifity. The route uses PMDTA (pentamethyl diethylene triamine) in Et_2O at -90 °C, to improve the diastereoselectivity of addition, to gives **28**. Trityl triflate-activated olefinations of **28** cleanly afforded the (phenylthio) methylidene **29** in very high optical purity (Scheme 20).



SCHEME 20

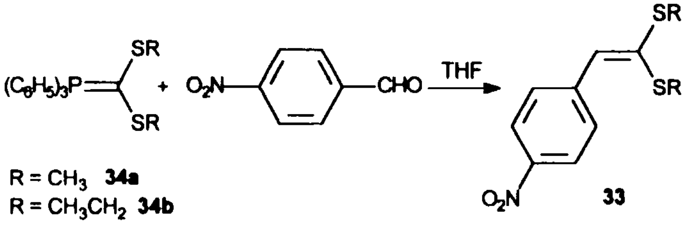
The synthesis of α-methylthio-α,β-unsaturated carboxylic acids **30** have been reported by Mikolajczyk and Midura.[33] These compounds, mixtures of ***E*** and ***Z*** isomers, were obtained by the reaction of the dianion derived from diethyl α-methylthio-phosphonoacetic acid **31** with carbonyl compounds, in high yields (Scheme 21). **31** was also converted to the corresponding α-methylthio lactones **32** in a two-step process involving an intramolecular Horner-Wittig reaction.



SCHEME 21

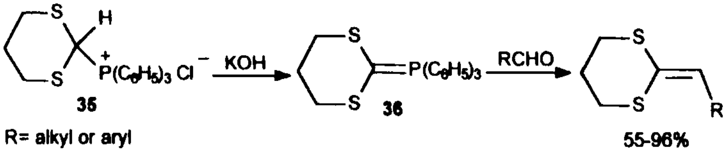
2.3. Ketene Dithioacetals by Wittig

Lemal and Banitt[34] described the first synthesis of the ketene dithioacetal **33** by a Wittig-type reaction, starting from **34a-b** (prepared by the reaction of the corresponding dithiocarbene and Ph_3P) and p-nitrobenzaldehyde in THF under reflux, yielding 64 and 71% of the products, respectively (Scheme 22).



SCHEME 22

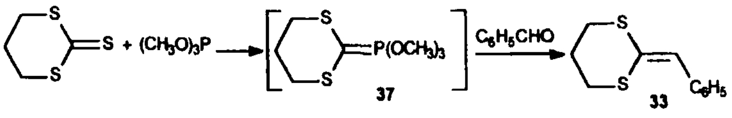
Ketene dithioacetals have been obtained from the triphenylphosphonium salt **35**, which was easily converted into ylide **36**. Thus, **36** in presence of aldehydes gave the corresponding products in high yields (Scheme 23).[35]



SCHEME 23

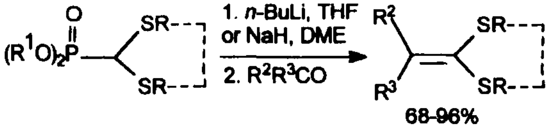
2.4. Ketene Dithioacetals by Horner-Wittig

Corey and Märkl[36] reported the preparation of ketene dithioacetal **33** with 90% yield, by the reaction of the ylide **37** and benzaldehyde (scheme 24). Other aldehydes also gave good results.[36,37] However, the ylide **37** did not react measurably with a number of ketones.



SCHEME 24

Mikolajczyk *et al.*[38,39] developed a general synthesis of ketene dithioacetals by Horner-Wittig reaction in yields from 68 to 96%. The approach is applicable to reactions with aromatic, acyclic and cyclic aldehydes and ketones. It is noteworthy that good results have been obtained with acetophenone and benzophenone, as well as with cyclic ketones like cyclopentanone and cyclohexanone (Scheme 25). The method is also applicable to the synthesis of O,S-thioacetals. The phase-transfer catalysis technique is also applicable for the Horner-Wittig reaction, using 50% aq. NaOH and TEBA-Cl as catalyst. However, it has been found that the range of carbonyl compounds is limited to aromatic aldehydes.



R = CH_3, $CH_2CH_2CH_2$, CH_2SCH_2 or benzyl

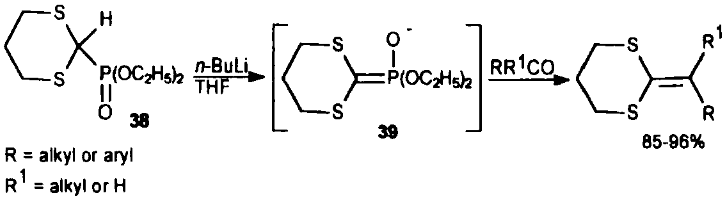
R^1 = CH_3 or CH_3CH_2

R^2 = alkyl, aryl or H

R^3 = alkyl, aryl or H

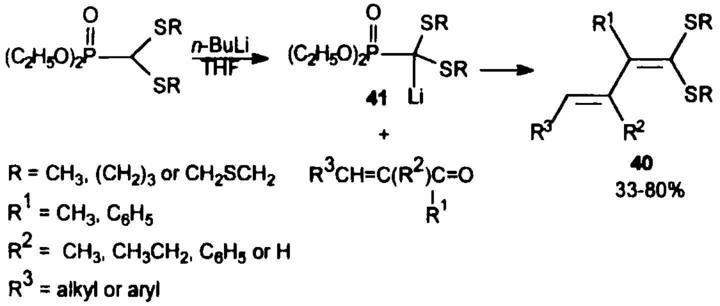
SCHEME 25

Ketene dithioacetals have also been obtained from diethylphosphonate **38**. Treatment of **38** with *n*-BuLi gives the ylide **39** that, in presence of aldehydes or ketones, furnishes the corresponding products in high yield (Scheme 26).[35]



SCHEME 26

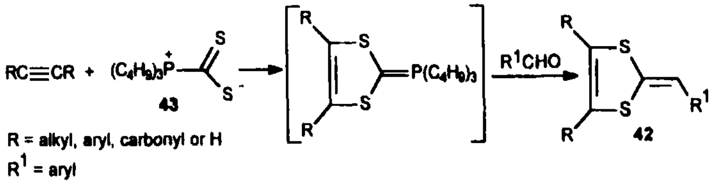
A general synthesis of conjugated ketene dithioacetals **40** was developed by Mikolajczyk and Balczewski.[40] α-Lithio-α-phosphoryl dithioacetals **41** react with aldehydes and ketones to give conjugated ketene dithioacetals **40** in moderate to good yields (Scheme 27). It was found that, in contrast to the reaction of **41** with α,β-unsaturated aldehydes, whose reaction it is fast, the reaction with ketones required much longer reaction time and should be carried out at room temperature, under strictly moisture and oxygen free conditions.



SCHEME 27

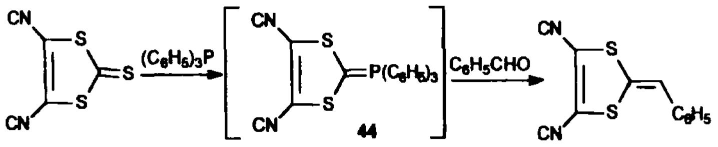
2.5. 1,3-Dithioles by Wittig

Hartzler[41] reported a general preparation of 2-benzylidene-1,3-dithioles **42** from the aliphatic phosphine-carbon disulfide complex **43**, with acetylenes and aromatic aldehydes, in non-specified yields (Scheme 28). This reaction has proved to be a general one for aldehydes, although requisite reaction conditions vary with the acetylene. Cava and co-workers also described a detailed study on the synthesis of 4,5-dicarbomethoxy-1,3-dithioles by a similar route.[42]



SCHEME 28

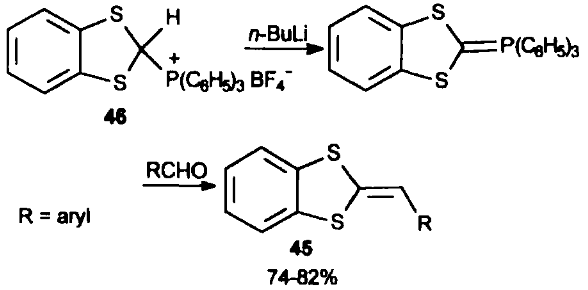
2-Benzylidene-4,5-dicyano-1,3-dithiole was also prepared[43] from the ylide **44** and benzaldehyde (Scheme 29).



SCHEME 29

2.6. 1,4-Benzodithiafulvenes by Wittig

Akiba and co-workers[44] reported the synthesis of 1,4-benzodithiafulvenes **45** from phosphonium salts **46**. The deprotonation of **46** with *n*-BuLi in THF -78 °C and the treatment with aromatic aldehydes (5 example) gave the product with 74-82% yields (Scheme 30).



46

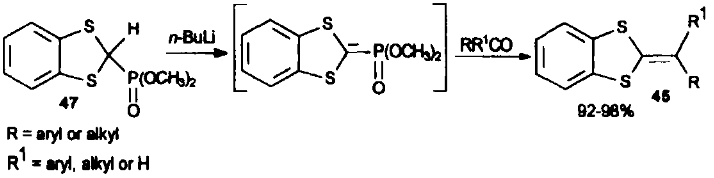
45

74-82%

SCHEME 30

2.7. 1,4-Benzodithiafulvenes by Horner-Wittig

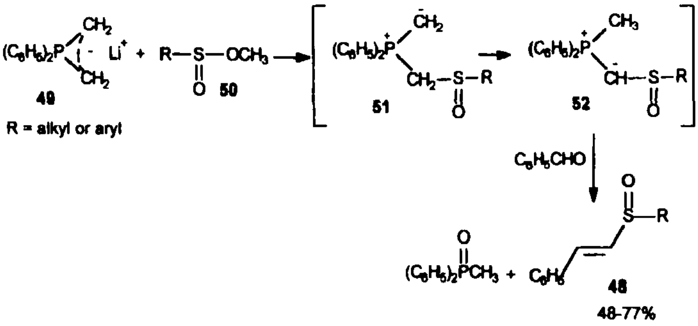
Akiba *et al.*[44] reported the synthesis of 1,4-benzodithiafulvenes **45** from dialkyl 1,3-benzodithiolylphosphonate **47**. The deprotonation of **47** with *n*-BuLi in THF at -78 °C, followed by addition of aromatic aldehydes and ketones (6 examples), gave the product in very high (92-98%) yields (Scheme 31). The same authors[45] also described a general method for the synthesis of benzo-1,4-dithiafulvalenes derived from cyclic ketones (8 examples), by a Wittig-Horner reaction. The products were obtained in good to high yields.



SCHEME 31

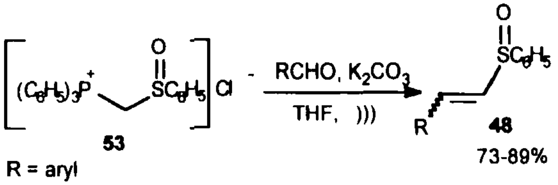
2.8. Vinyl Sulfoxides by Wittig

Mikolajczyk *et al.*[46,47] reported an efficient and highly *E*-stereoselective one-pot synthesis of vinyl sulfoxides **48**, using dimethyldiphenylphosphonium diylide **49** as a key reagent (Scheme 32). The reaction of this diylide with equimolar amounts of methyl or ethyl sulfinates **50**, carried out at *ca.* -20 °C in THF solution, gives the phosphonium ylide **51**, which after proton migration is transformed into more stable ylide **52**. Addition of benzaldehyde affords styryl sulfoxides **48** with *E*-stereoselectivity. By the use of the pure (-)-(*S*)-menthyl p-toluenesulfinate, (+)-(*R*)-styryl p-tolylsulfoxide was obtained in 72% yield and in good optical purity.[47]



SCHEME 32

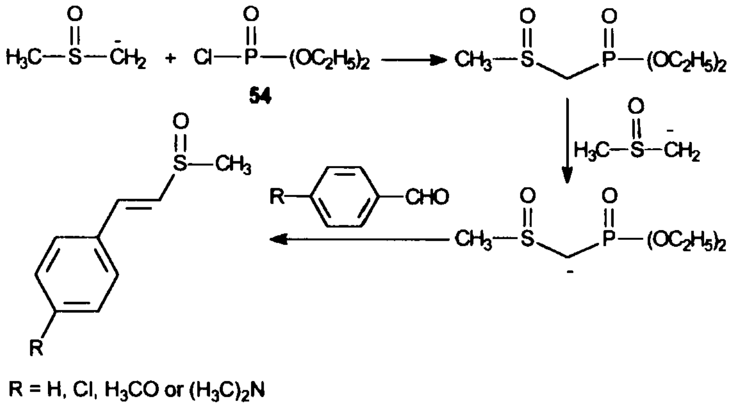
Silveira *et al.*[7] explored the sonication technique for preparing vinyl sulfoxides **48**. In this case, the phosphonium salts **53** were used, which react with aromatic aldehydes at room temperature and using K_2CO_3 as base, to give the products **48** in good yields, as a separable mixture of *Z* and *E* isomers (Scheme 33).



SCHEME 33

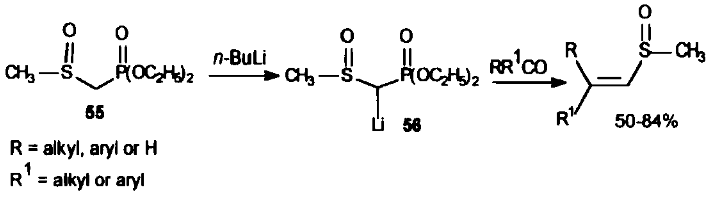
2.9. Vinyl sulfoxides by Horner-Wittig

Almog and Weissman[48] reported a one-step preparation of β-styryl methylsulfoxide from dimethyl sulfoxide. The reaction of methylsulfinyl anion with diethyl chlorophosphate **54** and aryl aldehydes, in dimethyl sulfoxide, at room temperature, gave the vinylic sulfoxides in yields higher than 60%. The products showed an exclusive *E*-configuration (Scheme 34).



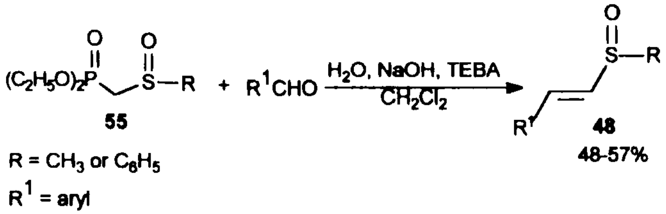
SCHEME 34

A more detailed study was described by Mikolajczyk,[49] using the sulfoxide **55** as a key compound for the Horner-Wittig reaction with carbonyl compounds (Scheme 35). Deprotonation of **55** with *n*-BuLi in THF at −78 °C, followed by the addition of aromatic aldehydes and ketones to **56**, gave vinylic sulfoxides (10 examples) in good yields. The use of aldehydes or unsymmetrical ketones furnishes the corresponding sulfoxides as mixtures of ***E*** and ***Z*** geometrical isomers.



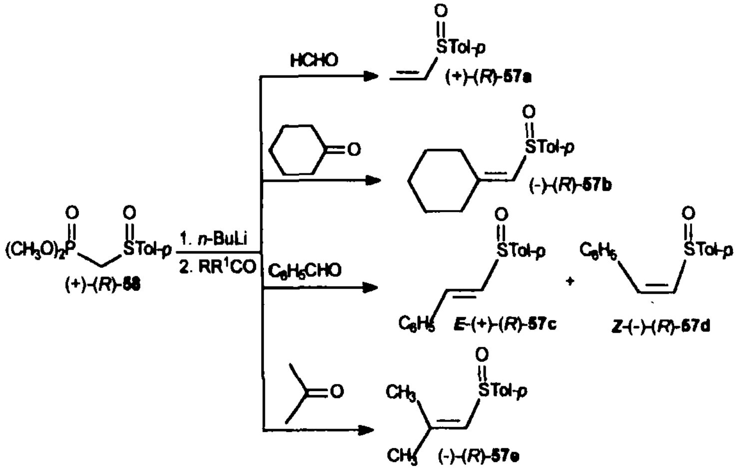
SCHEME 35

Mikolajczyk *et al.*[21] also reported the synthesis of vinyl sulfoxides **48** by the Horner-Wittig reaction in a two-phase system, catalyzed by quaternary ammonium salts and crown ethers, starting from α-phosphoryl sulfoxide **55** and aromatic aldehydes. The reaction affords mixtures of geometrical isomers in good yields (Scheme 36).



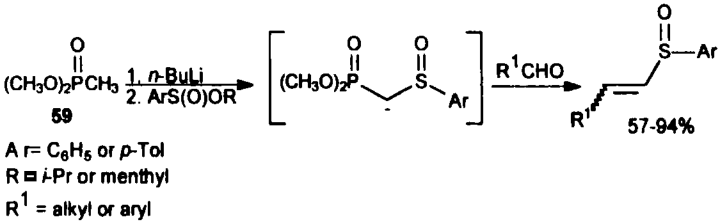
SCHEME 36

In another work, Mikolajczyk *et al.*[50] described the synthesis of optically active vinyl sulfoxides **57a-e**, starting from optically active *p*-tolyl sulfoxide **58**. Thus, treatment of **58** with *n*-BuLi and carbonyl compounds furnished **57** in good yields (Scheme 37). In the case of reaction with cyclopentanone, complete isomerization to the β,γ-isomer was observed. Partial isomerization (34 % of β,γ-unsaturated system) also occurred in the reaction with acetone.



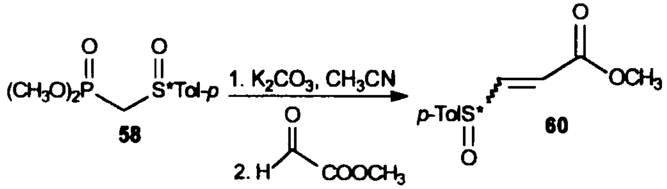
SCHEME 37

Recently, Craig *et al.*[51] modified this methodology performing a convenient one-pot procedure for the preparation of both racemic and homochiral vinylic sulfoxides (13 examples), via the Horner-Wittig reaction. The reaction started with dimethyl methanephosphonate **59**, which, by treatment with *n*-BuLi at −78 °C in THF, followed by addition of isopropyl benzenesulfinate or menthyl *p*-toluenesulfinate and aldehydes, gave the desired products (Scheme 38). The reaction generally exhibits a low *Z*-selectivity for aliphatic and unsaturated aldehydes and similarly low *E*-selectivity for aromatic aldehydes.



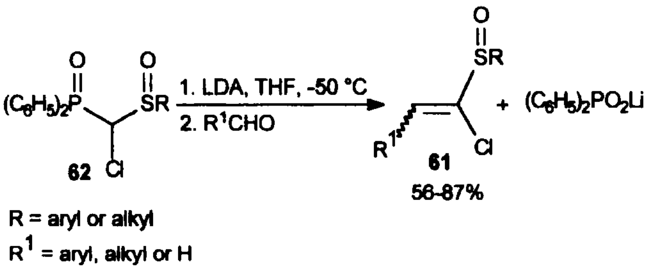
SCHEME 38

Naso and co-workers[52] studied the influence of the base in the enantioselectivity of the Horner-Wittig synthesis of chiral methyl *Z* and *E*-(3)-*p*-tolylsulfinylpropenoate **60**, starting from the *p*-tolyl sulfoxide **58** and reacting with methyl glyoxylate or pyruvate (Scheme 39). From all results, it could be inferred that it is possible to obtain optically pure *E* and *Z*-isomers in medium yields, if a suitable base/solvent system were used, for example K_2CO_3 in CH_3CN as show below.



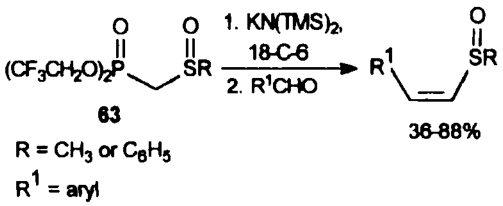
SCHEME 39

A Horner-Wittig synthesis of 1-chlorovinyl sulfoxides **61** was reported by van der Gen and co-workers,[53,54] by the direct transformation of aldehydes into homologous **61** from [(α-chloro)sulfinylmethyl]diphenylphosphine oxides **62** (Scheme 40). The products were obtained in good yields with aromatic as well as with aliphatic and α,β-unsaturated aldehydes (23 examples described). In most of the cases, the formation of 1-chlorovinyl sulfoxides **61** proceeded with excellent ***Z***-stereoselectivity. The synthesis of optically active α-chlorovinyl sulfoxides has been described by a strategy, including α-chloro-α-phosphoryl sulfoxides[55] and reaction with aldehydes. A racemic version of this strategy has also been described.[56]



SCHEME 40

Although vinyl sulfoxides are conveniently prepared by the Horner-Wittig reaction, the ***E***-isomers are preferentially formed, albeit in some cases in low geometrical selectivity. Kokin *et al.*[22] described a method for the ***Z***-selective synthesis of vinyl sulfoxides. The olefination was carried out using the fluorinated phosphonate **63** and various aromatic aldehydes in the presence of potassium bis(trimethylsilyl) amide and 18-crown-6. Reaction performed in THF showed a very good ***Z***-selectivity for most of aromatic aldehydes studied (Scheme 41). The reaction of **63** with saturated aliphatic aldehydes, such as *n*-octanal, showed no selectivity, and ***Z*** and ***E***-isomers were formed in almost equal amounts.



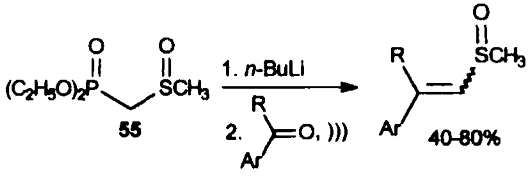
63

R = CH_3 or C_6H_5

R^1 = aryl

SCHEME 41

Furthermore, although the above procedure was largely applied to various aldehydes, few aliphatic, cyclic or aromatic ketones were used. Recently was reported[57] that the Wittig-Horner reaction of sulfinyl phosphonate 55 and aryl ketones may be carried out at room temperature, with *n*-BuLi, under ultrasonic irradiation, affording vinyl sulfoxides as *E* and *Z* mixtures, in low selectivity (Scheme 42).



55

R = CH_3, CF_3 or C_6H_5

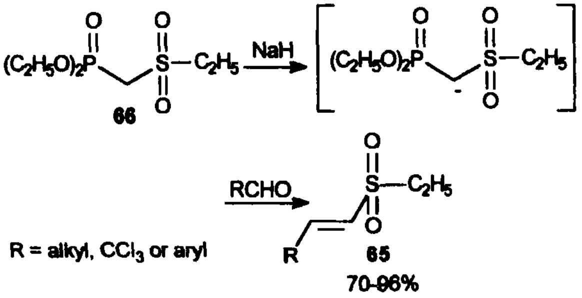
Ar = 4-$NO_2C_6H_4$; 4-FC_6H_4; 4-ClC_6H_4; 4-BrC_6H_4; C_6H_5; 4-$NO_2C_6H_4$; 4-$CH_3OC_6H_4$; 4-$CH_3C_6H_4$

SCHEME 42

2.10. Vinyl Sulfones by Horner-Wittig

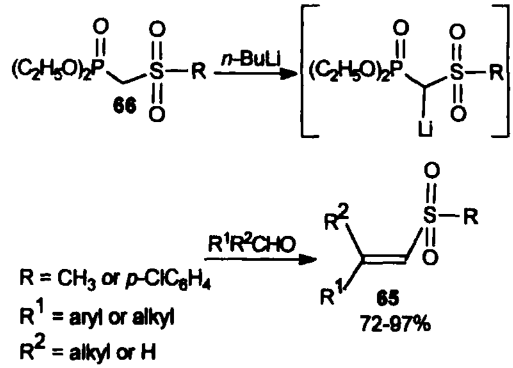
A convenient route to vinyl sulfones 65, starting with the carbanion of diethyl ethylsulfonylmethylphosphonate 66, aldehydes and

NaH as a base, was investigated by Popoff and co-workers[58] in a Horner-Wittig reaction (Scheme 43). The yields were good (70-96%). Similar results were described using dimethyl methylsulfonomethane phosphonate[16] and or diethyl arylsulfonomethanephosphonate.[17]



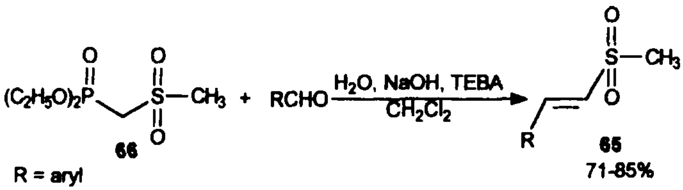
SCHEME 43

The Horner-Wittig reaction using NaH or sodium methoxide at room temperature, to generate the phosphonate anion has thus been limited to the preparation of arylidene sulfones. Posner and Brunelle[59] reported a modification of this procedure by using *n*-BuLi as base in THF, at -78 °C. The anion generated from **66** reacts not only with aryl aldehydes to form arylidene sulfones but also with aliphatic aldehydes and ketones, to give alkylidene sulfones **65** in high yield (Scheme 44). The *E*-vinyl sulfones are the exclusive product in reactions with aldehydes.



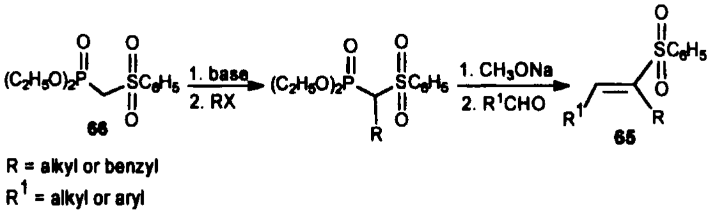
SCHEME 44

Mikolajczyk *et al.*[21] reported the synthesis of vinyl sulfones by the Horner-Wittig reaction in a two-phase system, catalyzed by quaternary ammonium salts and crown ethers. The reaction of α-phosphoryl sulfones **66**, aq. NaOH/TEBA and aromatic aldehydes gave the corresponding vinyl sulfones **65** in yields higher than 60% (Scheme 45). The products were obtained as pure *E*-isomers.



SCHEME 45

Ellingsen and Undheim[60] used the Horner-Wittig reaction between the α-alkylated phenylsulfonylmethylphosphonate, derived from **66**, and carbonyl compounds for the syntheses of α-aryl- and alkyl-vinyl sulfones **65** (Scheme 46). The reaction with aldehydes proceeded readily in methanolic sodium methoxide. The reaction in a two-phase system, catalyzed by tetrabutylammonium hydroxide, proceeded equally well. The products **65** from both methods were stereoisomeric mixtures; the *E*-isomer was favored in methanolic sodium methoxide and the *Z*-isomer favored under phase-transfer catalysis. Similar results were described, using diethylchloro-(benzenesulfonyl)-methanephosphonate and NaH as base, for the preparation of α-chlorovinyl sulfones (**65**: R=Cl; R^1=aryl; 6 examples, 77-90 % yield).[30]

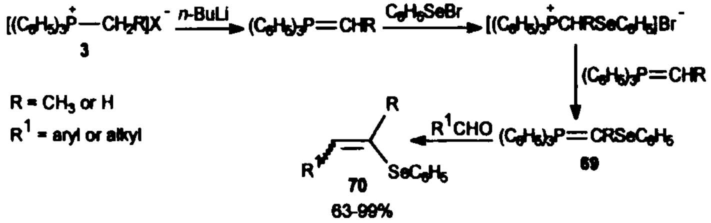


SCHEME 46

3. PREPARATION OF SELENIUM VINYLIC COMPOUNDS BY WITTIG AND HORNER-WITTIG REACTIONS

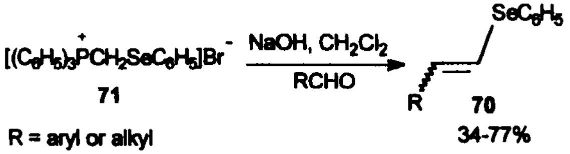
3.1. Vinylic Selenides by Wittig

Petragnani and co-workers[61,62] described, several years ago, the synthesis of vinylic selenides by a Wittig-type reaction. Thus, the transylidation reaction between C_6H_5SeBr and two equivalents of an alkylidenetriphenylphosphoranes **3** gave selenophosphoranes **69**, which reacts with aldehydes to give the expected vinylic selenides (10 examples) **70** (Scheme 47). The yields are very high for aromatic aldehydes and in the 65% range for aliphatic ones. A mixture of isomers was obtained in all reactions. The phenylseleno phosphoranes **69** could also be prepared by quaternization of triphenylphosphine with phenyl(bromoalkyl)selenides, followed by treatment with *n*-BuLi, at room temperature, in THF as the solvent.



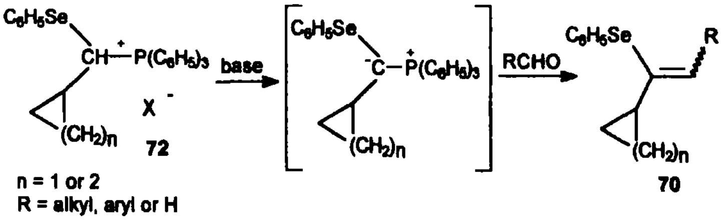
SCHEME 47

Comasseto and Brandt[63] performed the synthesis of vinyl selenides by the reaction between phenylseleno methyl(triphenyl) phosphonium bromide **71** and carbonyl compounds, using phase transfer conditions (Scheme 48). The reaction of **71** with aldehydes yielded the pure vinyl selenide **70** of predominantly ***Z*** configuration (5 examples). Ketones failed to react under these conditions. The same authors[64] employed these methods to develop an efficient route to 1-phenylselenobutadienes *via* phenylseleno alkenylidene phosphoranes.



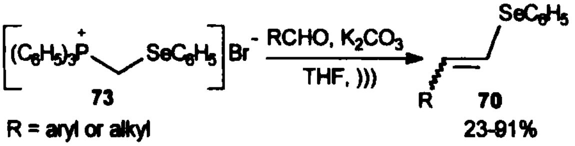
SCHEME 48

Minami *et al.*[65] reported the Wittig reaction of [cyclopropyl(phenylseleno) methyl]- and [cyclobutyl(phenylseleno) methyl] triphenylphosphonium salts **72** with aldehydes, *via* the corresponding phosphoranes. *Z*- and *E*-(1-cyclopropyl-1-phenylseleno)- and (1-cyclobutyl-1-phenylseleno)alkenes **70** were obtained in moderate to good yields (Scheme 49). The stereochemistry is dependent on the nature of the base used.



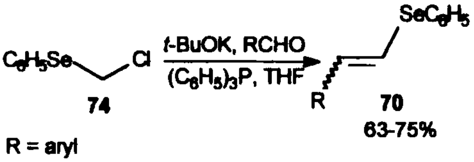
SCHEME 49

Silveira *at al.*[7] described the preparation of vinyl selenides from the reaction of phenyselenomethyl(triphenyl)phosphonium **73** and aldehydes under sonication conditions. The treatment of a THF solution of α-phosphoryl selenides with potassium carbonate furnishes the corresponding vinylic selenides **70** in good (for aromatic aldehydes) to medium (for the aliphatic series) yields (Scheme 50). Concerning to the stereochemistry, it was observed that, predominantly, the *Z*-vinylic selenides were produced, but with low stereoselectivity. Under these conditions, ketones failed to react.



SCHEME 50

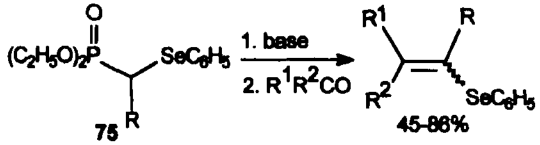
In another work, the same authors[8] described the preparation of vinyl selenides **70**, based on a very convenient one-pot procedure. The olefination reaction was performed by the addition of *t*-BuOK to a solution of chloromethylselenide **74** and triphenylphosphine in THF, followed by the addition of an aldehyde (Scheme 51). The reactions were performed very easily, by mixing all the reagents at room temperature, giving the expected vinylic selenides in good yields. The stereochemistry of the products shows an isomeric *Z*/*E*-mixture.



SCHEME 51

3.2. Vinylic Selenides by Horner-Wittig

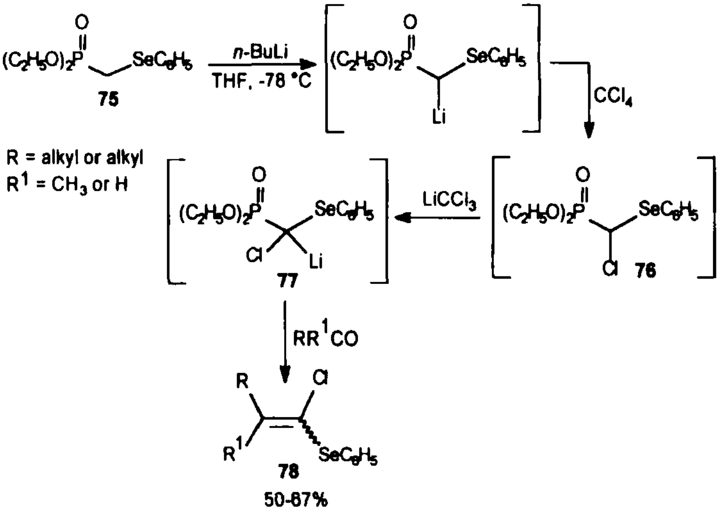
Comasseto and Petragnani[66] prepared vinyl selenides of predominantly *E* configuration by a Horner-Wittig reaction, using selenophosphonates **75**, *n*-BuLi or NaH as base and aldehydes or ketones (Scheme 52). The yields of the reaction are generally good in the case of aromatic aldehydes, decreasing from about 80% to about 50%, with increasing length of the chain R in **75**. The same reaction was performed under phase transfer conditions, but only aromatic aldehydes reacted.[63]



R = alkyl or H
R^1 = aryl or alkyl
R^2 = alkyl or H

SCHEME 52

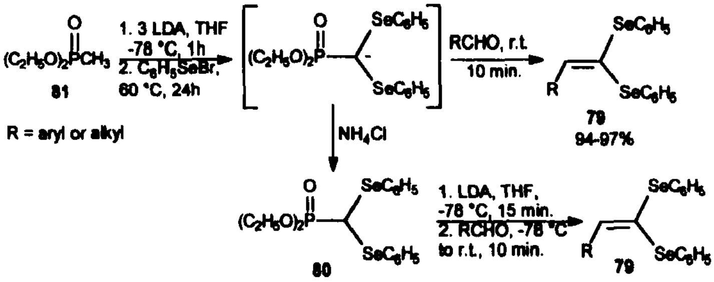
Coutrot *et al.*[67] reported that the lithium derivatives prepared from diethyl phenylselenomethanephosphonate **75** and *n*-BuLi, at low temperature, reacted with carbon tetrachloride to give the corresponding α-chlorinated phosphonate **76** and trichloromethyllithium. The latter deprotonates **76** *in situ* to give a new lithio derivative **77**, which reacts with carbonyl compounds (Scheme 53). These different steps took place in one pot and led to chlorovinyl phenyl selenides **78**. The reaction proved to be highly stereoselective with aromatic and aliphatic aldehydes to give one (not determined) stereoisomer. Reaction with butanone gave a 1:1 mixture of stereoisomers.



SCHEME 53

3.3. Ketene Selenoacetals by Horner-Wittig

Oh and co-workers[68] reported a mild and convenient synthetic method for the preparation of ketene selenoacetals **79** from aldehydes and diethyl 1,1-bis(phenylseleno)methylphosphonate **80** or diethylmethylphosphonate **81** (Scheme 54).

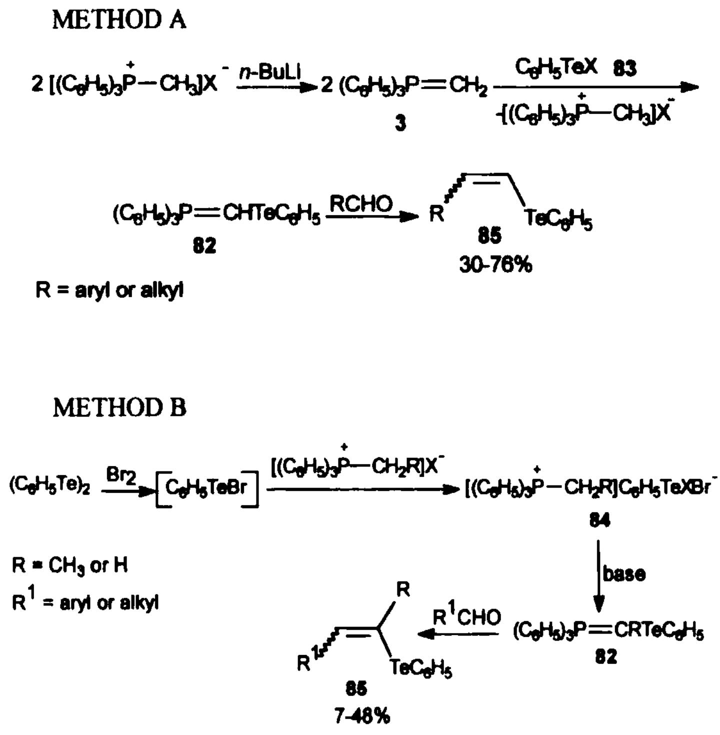


SCHEME 54

4. PREPARATION OF TELLURIUM VINYLIC COMPOUNDS BY WITTIG AND HORNER-WITTIG REACTIONS

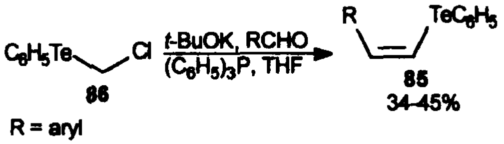
4.1. Vinylic Tellurides by Wittig

Silveira *et al.*[69] described the preparation of vinylic tellurides by the Wittig reaction. In this study, two methods were developed. Tellurophosphoranes **82** were obtained by a transylidation reaction between an alkylidenetriphenylphosphorane **3** and phenyltellurenyl bromides **83** (method A) and from triphenylphosphonium dihalotellurolate **84** on reaction with bases (method B). The tellurophosphoranes **82** reacted with aldehydes *in situ* to give vinylic tellurides **85**, with preferential ***Z*** stereochemistry by both methods (Scheme 55). Method A showed a small preference for ***Z***-isomers, whereas method B furnished a high preference for ***Z*** products.



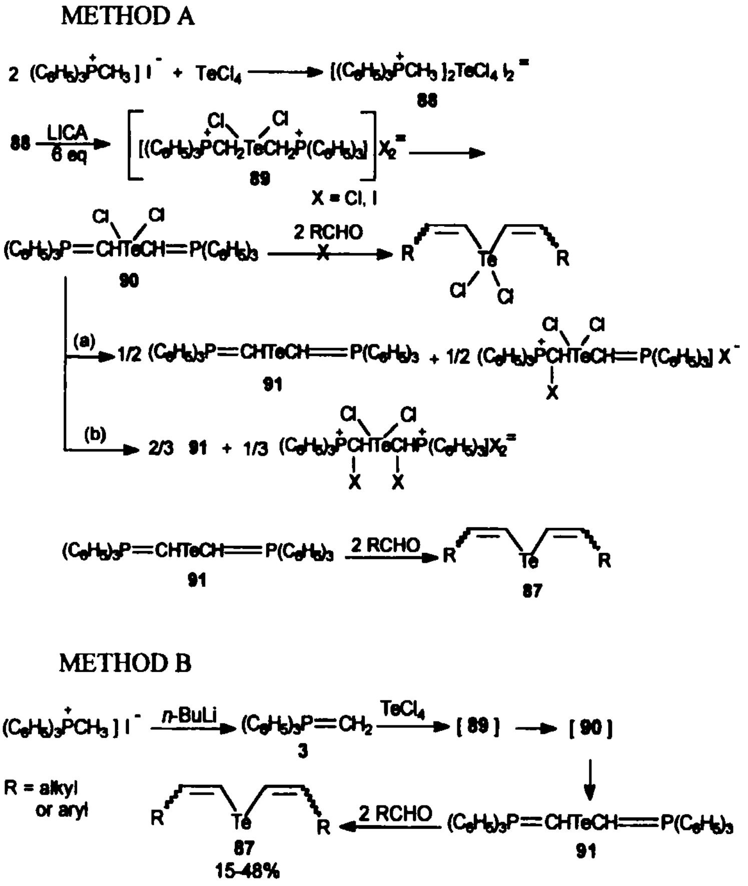
SCHEME 55

Vinylic tellurides **85** have also been prepared[8] by a one-pot procedure from chloromethylphenyltelluryde **86**, triphenylphosphine and *t*-BuOK as base, followed by addition of an aldehyde (Scheme 56). The corresponding vinylic tellurides obtained were of exclusive ***Z***-configuration.



SCHEME 56

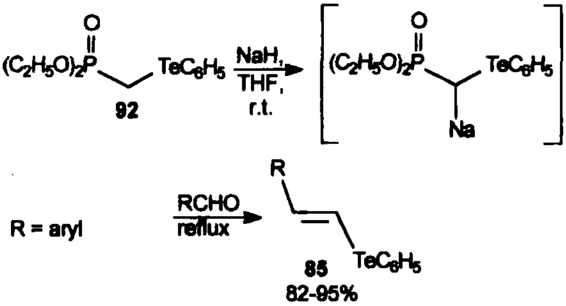
Recently was reported[70] the preparation of symmetrical divinyl tellurides **87** by sequential reaction of bis-(triphenylmethyl phosphonium) halotellurate **88** with base (**88**, after several consecutive steps, would generate the intermediate **91**, method A) or by the reaction of triphenylmethylidene phosphoranes **3** with $TeCl_4$ (method B), followed by the addition of aldehydes (Scheme 57). The reaction with aromatic aldehydes was not stereoselective, giving isomer mixtures, with a preferential ***E*** geometry (from the ***E,Z*** and ***E,E*** isomers). By performing the olefination reaction in the presence of 30% HMPA as a co-solvent, the ***Z,Z*** isomer becomes predominant. In the case of aliphatic aldehydes, the ***Z*** geometry (from the ***Z,Z*** and ***Z,E*** isomers) is preferred in both solvent systems. A metal salt and base dependence were observed both on the stereochemistry of divinyl tellurides, as well as on the yield (for the reaction with benzaldehyde). Using KH instead of *n*-BuLi in THF, the ***Z,Z***-product was formed almost exclusively, but in only 12% isolated yield. Possible intermediates involved in this reaction are presented on scheme 57.



SCHEME 57

4.2. Vinylic Tellurides by Horner-Wittig

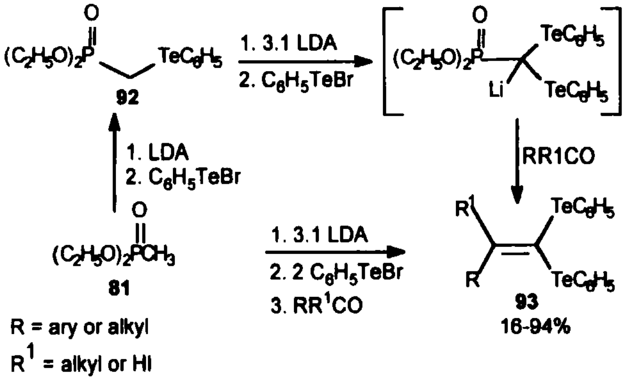
Reaction of the diethyl 1-(phenyltelluro)alkylphosphonates 92 with NaH in THF, followed by addition of aromatic aldehydes, gave the corresponding vinyl tellurides **85** in high yields (scheme 58).[71] All products were observed with exclusive *E* configuration.



SCHEME 58

4.3. Ketene Phenyltelluroacetals by Horner-Wittig

Silveira *et al.*[72] described the preparation of ketene phenyltelluroacetals **93**, by the reaction of diethyl methylphosphonate **81** or diethyl phenyltelluromethylphosphonate **92** with LDA, phenyltellurenyl bromide and then with a carbonyl compound (Scheme 59). The method permits easy access to compounds **93** in good to excellent yields with few exceptions. Reaction with ketones was also examined, but only reaction with cyclohexanone (16 % yield) was observed.

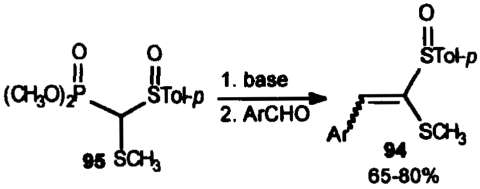


SCHEME 59

5. MISCELLANEOUS

5.1. Ketene Dithioacetal Mono-S-oxides by Horner-Wittig Reaction

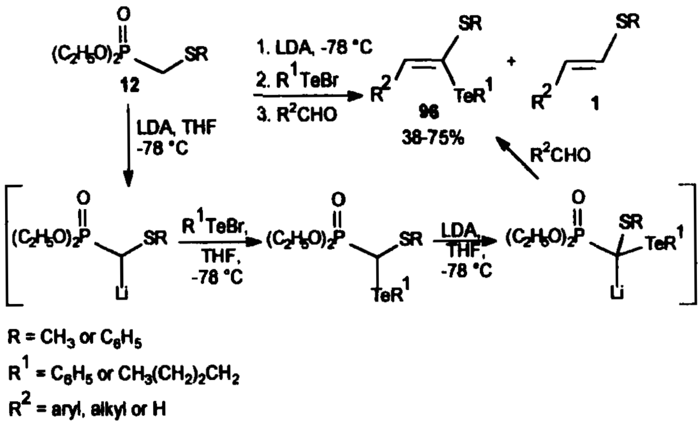
The sulfenylated α-phosphoryl sulfoxide **95** reacts with a base, yielding the appropriate α-phosphonate carbanion, that was used in the Horner-Wittig olefination with aromatic aldehydes to afford ketene dithioacetal mono-S-oxides **94** (Scheme 60).[73] This methodology was also used to obtain optically active ketene dithioacetal mono-S-oxides **94**, starting from optically active α-phosphoryl sulfoxides **95**.



SCHEME 60

5.2. Ketene (S, Te)Acetals by Horner-Wittig Reaction

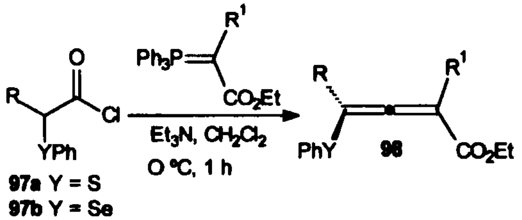
Reaction of thiomethyl phosphonates **12** with aryl (or butyl) tellurenyl halides and aldehydes under basic conditions provides moderate to good yields of ketene thio (telluro) acetals **96**. In some reactions, vinylic sulfides **1** were isolated as by products of this transformation (Scheme 61).[74] The products were obtained as a mixture of ***E*** and ***Z*** isomers and the yields were in 38-75% range. The reaction worked well for both aliphatic and aromatic aldehydes.



SCHEME 61

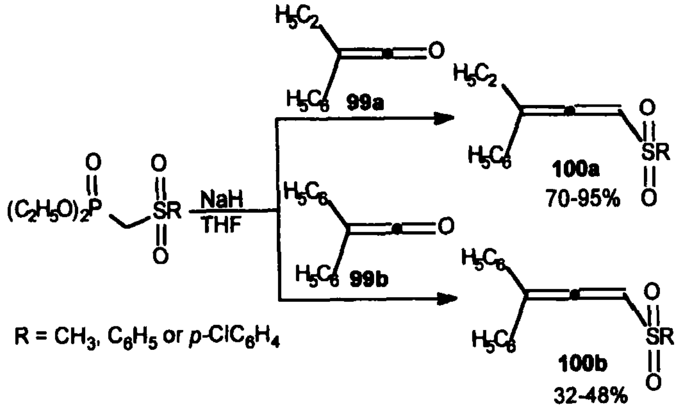
5.3. Chalcogeno Allenes

Few chalcogeno allenes have been prepared by methods involving the Wittig reaction. The synthesis of 4-phenylthio and 4-phenylseleno allenic esters **98** was recently described by the reaction of carboxyphosphoranes with α-phenylthio- and α-phenylseleno ketenes, generated *in situ* from the corresponding acid chlorides **97**, as described on scheme 62.[75]



SCHEME 62

Fillion *et al.*[76] have found that diethylmethyl(or aryl)sulfonyl methylphosphonate undergoes the Horner-Wittig reaction with both ethylphenylketene **99a** and diphenylketene **99b**, affording allenic sulfones **100a,b** (Scheme 63). The method affords high yields when **99a** used and lower with **99b**.



SCHEME 63

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References

[1] J.V. Comasseto, L.W. Ling, N. Petragnani and H.A. Stefani, *Synthesis*, 373 (1997).
[2] O.I. Kolodiazhnyi, *Tetrahedron*, **52**, 1855 (1996).
[3] G. Wittig and M. Schlosser, *Chem Ber.*, **94**, 1373 (1961).
[4] T. Mukaiyama, S. Fukuyama and T. Kumamoto, *Tetrahedron Lett.*, 3787 (1968).
[5] R. Galli, *J. Org. Chem.*, **52**, 5349 (1987).
[6] H. Saikachi and S. Nakamura, *Yakugaku Zasshi*, **88**, 1039 (1968); *Chem Abstr.*, **70**, 11435 (1969).
[7] C.C. Silveira, G. Perin. and A.L. Braga, *J. Chem. Res. (S)*, 492 (1994).
[8] C.C. Silveira, M.L. Begnini, P. Boeck and A.L. Braga, *Synthesis*, 221 (1997),.
[9] C.C. Silveira, M.L. Begnini, P. Boeck and A.L. Braga, unpublished results.
[10] R. Galli, L. Scaglioni, O. Palla and F. Gozzo, *Tetrahedron*, **40**, 1523 (1989).
[11] A.T. Hewson, *Tetrahedron Lett.*, **19**, 3267 (1978).
[12] A.G. Cameron and A.T. Hewson, *J. Chem. Soc., Perkin Trans. 1*, 2979 (1983).
[13] A.G. Cameron, A.T. Hewson and M.I. Osamor, *Tetrahedron Lett.*, **25**, 2267 (1984).
[14] J.P. Marino and E. Laborde, *J. Org. Chem.*, **52**, 1 (1987); J.P. Marino, C.C. Silveira, J.V. Comasseto and N. Petragnani, *J. Org. Chem.*, **52**, 4139 (1987).
[15] M. Green, *J. Chem. Soc.*, 1324 (1963).
[16] I. Shahak and J. Almog, *Synthesis*, 170 (1969).
[17] I. Shahak and J. Almog, *Synthesis*, 145 (1970).
[18] E.J. Corey and J.I. Shulman, *J. Org. Chem.*, **35**, 777 (1970).
[19] M. Mikolajczyk, S. Grzejszczak, A. Chefczynska and A. Zatorski, *J. Org. Chem.*, **44**, 2967 (1979).
[20] M. Mikolajczyk, S. Grzejszczak and K. Korbacz, *Tetrahedron Lett.*, **22**, 3097 (1981).
[21] M. Mikolajczyk, S. Grzejszczak, W. Midura and A. Zatorski, *Synthesis*, 278 (1975); id, ibid. 396 (1976).
[22] K. Kokin, S. Tsuboi, J. Motoyoshiya and S. Hayashi, *Synthesis*, 637 (1996).

[23] E.J. Corey and J.I. Shulman, *J. Am. Chem. Soc.*, **92**, 5522 (1970).
[24] P. Blatcher, J.I. Grayson and S. Warren, *J. Chem. Soc., Chem. Commun.*, 547 (1976).
[25] P. Blatcher, J.I. Grayson and S. Warren, *J. Chem. Soc., Chem. Commun.*, 657 (1978).
[26] C.A. Cornish and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 2585 (1985).
[27] J.I. Grayson and S. Warren, *J. Chem. Soc., Perkin Trans 1*, 2263 (1977).
[28] S. Warren and A.T. Zaslona, *Tetrahedron Lett.*, **23**, 4167 (1982).
[29] P. Coutrot, C. Laurenco, J. Petrova and P. Savignac, *Synthesis*, 107 (1976).
[30] I. Yamamoto, T. Sakai, S. Yamamoto, K. Ohta and K. Matsuzaki, *Synthesis*, 676 (1985).
[31] J. Motoyoshiya, Y. Hongo, H. Tanaka and S. Hayashi, *Synth. Commun.*, **21**, 997 (1991).
[32] S.E. Denmark and C.T. Chen, *J. Am. Chem. Soc.*, **114**, 10674 (1992).
[33] M. Mikolajczyk and W.H. Midura, *Synlett*, 245 (1991).
[34] D.M. Lemal and E.H. Banitt, *Tetrahedron Lett.*, 245 (1964).
[35] C.G. Kruse, N.L.J.M. Broekhof, A. Wijsman and A. van der Gen, *Tetrahedron Lett.*, **18**, 885 (1977).
[36] E.J. Corey and G. Märkl, *Tetrahedron Lett.*, 3201 (1967).
[37] F.A. Carey and J.R. Neergaard, *J. Org. Chem.*, **36**, 2731 (1971).
[38] M. Mikolajczyk, S. Grzejszczak, A. Zatorski, B. Mlotkowska, H. Gross and B. Costisella, *Tetrahedron*, **19**, 3081 (1978).
[39] M. Mikolajczyk, S. Grzejszczak, A. Zatorski and B. Mlotkowska, *Tetrahedron Lett.*, **17**, 2731 (1976).
[40] M. Mikolajczyk and P. Balczewski, *Tetrahedron*, **48**, 8697 (1992).
[41] H.D. Hartzler, *J. Am. Chem. Soc.*, **93**, 4961 (1971).
[42] M. Sato, N.C. Gonella and M.P. Cava, *J. Org. Chem.*, **44**, 930 (1979).
[43] M.G. Miles, J.S. Wager, J.D. Wilson and A.R. Siedle, *J. Org. Chem.*, **40**, 2577 (1975).
[44] K. Ishikawa, K. Akiba and N. Inamoto, *Tetrahedron Lett.*, **17**, 3695 (1976).
[45] K. Akiba, K. Ishikawa and N. Inamoto, *Synthesis*, 861 (1977).
[46] M. Mikolajczyk, W. Perlikowska, J. Omelanczuk, H.J. Cristau and A. Perraud-Darcy, *Synlett*, 913 (1991).
[47] M. Mikolajczyk, W. Perlikowska, J. Omelanczuk, H.J. Cristau and A. Perraud-Darcy, *J. Org. Chem.*, **63**, 9716 (1998).
[48] J. Almog and B.A. Weissman, *Synthesis*, 164 (1973).
[49] M. Mikolajczyk, S. Grzejszczak and A. Zatorski, *J. Org. Chem.*, **40**, 1979 (1975).
[50] M. Mikolajczyk, W. Midura, S. Grzejszczak, A. Zatorski and A. Chefczynska, *J. Org. Chem.*, **43**, 473 (1978).
[51] D. Craig, K. Daniels, A. Marsh, D. Rainford and A.M. Smith, *Synlett*, 531 (1990).
[52] C. Cardellicchio, A. Iacuone and F. Naso, *Tetrahedron Lett.*, *36*, 6563 (1995); see also A. Guessous, F. Rouessac and C. Maignan, *Bull. Soc. Chim. Fr.*, 837 (1986).
[53] P.A. Otten, H.M.. Davies, J.H. van Steenis, S. Gorter and A. van der Gen, *Tetrahedron*, **53**, 10527 (1997).
[54] P.A. Otten, H.M. Davies and A. van der Gen, *Tetrahedron Lett.*, **36**, 781 (1995).
[55] M. Mikolajczyk, J.A. Krysiak, W.H. Midura, M.W. Wieczorek and J. Blaszczyk, *Tethahedron: Asymmetry*, **7**, 3513 (1996).
[56] T.H. Kim, E.J. Lee and D.Y. Oh, *Bull. Korean Chem. Soc.*, **17**, 4 (1996).
[57] H. El Fakih, F. Pautet, D. Peters and H. Fillion, *J. Prakt. Chem.*, **339**, 176 (1997).
[58] I.C. Popoff, J.L. Dever. and G.R. Leader, *J. Org. Chem.*, **34**, 1128 (1969).
[59] G.H. Posner and D.J. Brunelle, *J. Org. Chem.*, **37**, 3547 (1972).
[60] P.O. Ellingsen and K. Undheim, *Acta Chem. Scand. B*, **33**, 528 (1979).
[61] N. Petragnani, R. Rodrigues and J.V. Comasseto, *J. Organomet. Chem.*, **114**, 281 (1976).
[62] H.A. Stefani, M.M.C. Cavalheiro, J.V. Comasseto and N. Petragnani, *An. Acad. Bras. Cienc.*, **61**, 37 (1989).
[63] J.V. Comasseto and C.A. Brandt, *J. Chem. Research (S)*, 56 (1982).

[64] J.V. Comasseto and C.A. Brandt, *Synthesis*, 146 (1987).

[65] T. Minami, Y. Umezu, S. Shikita and Y. Okada, *Bull. Chem. Soc. Jpn.*, **62**, 3724 (1989).

[66] J.V. Comasseto and N. Petragnani, *J. Organomet. Chem.*, **152**, 295 (1978).

[67] P. Coutrot, C. Grison and M. Youssefi-Tabrizi, *Synthesis*, 169 (1987).

[68] W.S. Shin, K. Lee and D.Y. Oh, *Tetrahedron Lett.*, **33**, 5375 (1992).

[69] C.C. Silveira, G. Perin, A.L. Braga and N. Petragnani, *Synlett*, 58 (1995).

[70] C.C. Silveira, G. Perin, P. Boeck, A.L. Braga and N. Petragnani, *J. Organomet. Chem.*, **584**, 44 (1999).

[71] C.W. Lee, Y.J. Koh and D.Y. Oh, *J. Chem. Soc., Perkin Trans. 1*, 717 (1994).

[72] C.C. Silveira, G. Perin and A.L. Braga, *Tetrahedron Lett.*, **36**, 7361 (1995).

[73] M. Mikolajczyk, W.H. Midura, B. Wladislaw, F.C. Biaggio, L. Marzorati, M.W. Wieczorek and J. Blaszczyk, *Tetrahedron*, **53**, 2959 (1997).

[74] C.C. Silveira, G. Perin, A.L. Braga, M.J. Dabdoub and R.G. Jacob, *Tetrahedron*, **55**, 7421 (1999).

[75] C.C. Silveira, P. Boeck and A.L. Braga, *Tetrahedron Lett.*, **41**, 1867 (2000).

[76] H. Fillion, A. Hseine, M. Pera, V. Dufaud and B. Refouvelet, *Synthesis*, 708 (1987).