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One-pot synthesis of mixed (*Z*)-1,2-bis(organylchalcogene)-1-alkenes precursors of the novel β-organylthio vinyllithium intermediates

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ABSTRACT

One-pot hydrochalcogenation of 1-phenylthioacetylenes using organylselenolate and organyltellurolate anions generated by the insertions of selenium and tellurium in *n*-organyl lithium produced (***Z***)-1,2-bis(organylchalcogene)-1-alkenes. The chemical reactivity of these mixed 1,2-bis(organylchalcogene)-1-alkenes was studied by Te/Li and Se/Li stereoretentive exchanges carried out with *n*-butyl lithium, furnishing the new intermediate species (***Z***)-β-organylthio vinyllithium anions, which were trapped with aldehydes, to give the (***Z***)-3-hydroxy vinyl thioethers with total control of the regio- and stereochemistry.

Stereocontrolled methodologies to prepare vinyl organylchalcogenide compounds and their applications in the construction of new carbon–carbon bonds via organometallic intermediates have been developed with the highest priority.[1] The hydrotelluration described by Buzilova and co-workers[2] stimulated a wide range of studies leading to the synthesis of (***Z***)-vinyl tellurides by addition of organyltellurolate anions to terminal and disubstituted alkynes containing Michael acceptor groups.[1f,3] The chemoselective reactions of sodium tellurolate,[4] selenolate,[5] and thiolate[6] anions occur in conjugated butadyine systems with total control of regio- and stereochemistry, furnishing the (***Z***)-1-organylchalcogene-1-buten-3-ynes. Moreover, (***E***)-vinyl organochalcogenides were obtained by the hydrozirconation of terminal and substituted alkynes using bis(cyclopentadienyl) zirconium (IV) chloride hydride as a reducing agent and subsequent Zr/Te[7], Zr/Se,[8] and Zr/S[9] exchanges. Recently, our group reported the synthesis of (***E***)-vinylsulfides by the hydroalumination of thioacetylenes with lithium di(isobutyl)-*n*-butyl hydride, followed by acid hydrolysis.[10]

Several methods to synthesize 1,1-bis(organylchalcogene)-1-alkenes such as telluroketene acetals,[11] telluro(seleno)ketene acetals,[11a,12] telluro(thio)ketene acetals,[13] and seleno(thio)ketene acetals[14] which could easily lead to the synthesis of trisubstituted olefins containing two heteroatoms attached in the same C-sp^2 position have been developed.

On the other hand, (***Z***)-1,2-bis(organylchalcogene)-1-alkenes were obtained by the hydrochalcogenation of thioacetylenes using the organyltellurolate (RTe$^-$) and organylselenolate (RSe$^-$) anions generated 'in situ' by the reduction of diorganyl ditelluride and diorganyl diselenide with sodium borohydride.[15] However, these diorganyl dichalcogenides are known to produce neuropathy to the central nervous system, teratogenic effects, and severe damage to the liver and kidneys.[16] Based on these facts and regarding the applications of (***Z***)-1,2-bis(organylchalcogene)-1-alkenes to the total synthesis of natural products[17] and functionalized alkynyl tellurides, which have shown an interesting antidepressive action.[18] We describe, herein, the one-pot hydrochalcogenation of 1-phenylthioacetylenes **1a–g** in THF/water, using the appropriated chalcogene nucleophilic species,[19] generated 'in situ' by the insertion of elemental tellurium[19a] or selenium[19b] in organyl lithium, avoiding the preliminary preparation and use of volatile, air-sensitive, odorous, and highly toxic diorganyl ditelluride and diorganyl diselenide.[16] The addition of (RSe$^-$Li$^+$) or (RTe$^-$Li$^+$) anions to thioacetylenes **1a–g** occurred at the β-position relative to the phenylthio group via the vinyl intermediate type **2** furnishing the mixed (***Z***)-1,2-bis(organylchalcogene)-1-alkenes **3a–m** in good yields (Table 1).

As a representative example of this protocol, we performed the hydrotelluration of 1-phenylthio-1-hexyne **1b** (1.5 equiv) with the lithium butyltellurolate anion [(C_4H_9TeLi),[19a] 1.5 equiv, generated 'in situ' by insertion of tellurium (1.5 equiv) in *n*-BuLi (1.5 equiv)] in THF (6.0 mL) followed by the addition of water (4.0 mL) and

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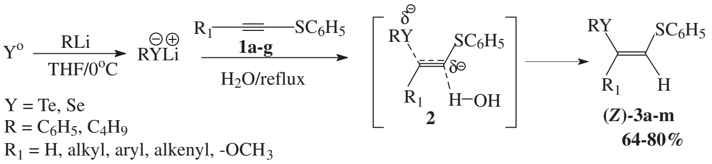
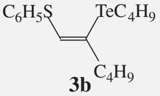
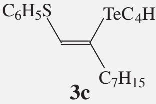
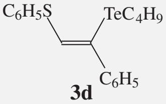
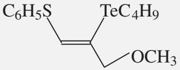
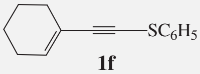
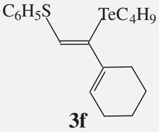
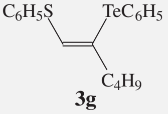
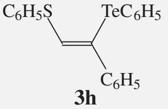
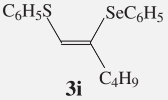
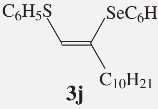
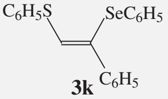
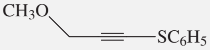
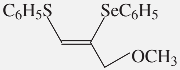
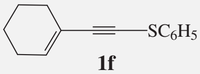
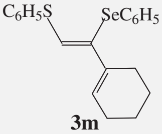
Table 1

Synthesis of (***Z***)-1,2-bis(organylchalcogene)-1-alkenes

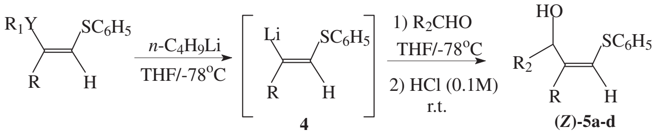


Entry	Thioacetylene	Nucleophile	Product[a]	Time (h)	Yield[b] (%)
1	$\mathrm{H}-\equiv-\mathrm{SC_6H_5}$ **1a**	C_4H_9TeLi	 **3a**	1.5	80
2	$\mathrm{C_4H_9}-\equiv-\mathrm{SC_6H_5}$ **1b**	C_4H_9TeLi	 **3b**	2.5	76
3	$\mathrm{C_7H_{15}}-\equiv-\mathrm{SC_6H_5}$ **1c**	C_4H_9TeLi	 **3c**	2.5	73
4	$\mathrm{C_6H_5}-\equiv-\mathrm{SC_6H_5}$ **1d**	C_4H_9TeLi	 **3d**	1.5	80
5	 **1e**	C_4H_9TeLi	 **3e**	1.5	75
6	 **1f**	C_4H_9TeLi	 **3f**	2.0	73
7	$\mathrm{C_4H_9}-\equiv-\mathrm{SC_6H_5}$ **1b**	C_6H_5TeLi	 **3g**	3.5	75
8	$\mathrm{C_6H_5}-\equiv-\mathrm{SC_6H_5}$ **1d**	C_6H_5TeLi	 **3h**	3.0	73
9	$\mathrm{C_4H_9}-\equiv-\mathrm{SC_6H_5}$ **1b**	C_6H_5SeLi	 **3i**	4.0	78
10	$\mathrm{C_{10}H_{21}}-\equiv-\mathrm{SC_6H_5}$ **1g**	C_6H_5SeLi	 **3j**	4.0	64
11	$\mathrm{C_6H_5}-\equiv-\mathrm{SC_6H_5}$ **1d**	C_6H_5SeLi	 **3k**	3.5	73
12	 **1e**	C_6H_5SeLi	 **3l**	4.0	70
13	 **1f**	C_6H_5SeLi	 **3m**	4.0	68

[a] Fully characterized by NMR (^{1}H, ^{13}C, gNOESY), MS, microanalysis data.

[b] Isolated yields after purification by chromatography using silica gel (230–400 mesh) and hexane as the mobile phase in all cases.

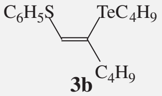
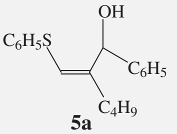
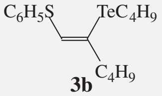
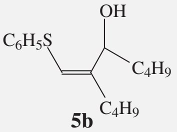
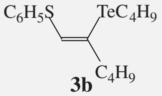
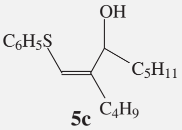
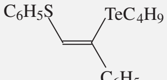
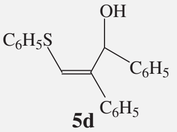
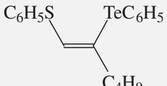
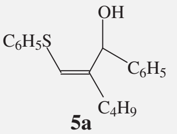
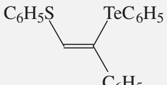
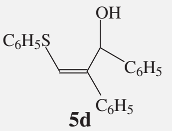
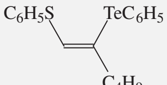
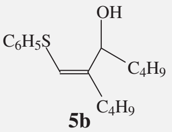
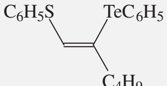
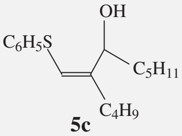
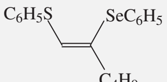
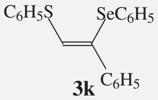
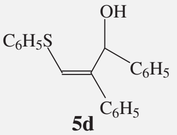
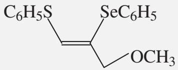
Table 2
Synthesis of (***Z***)-3-hydroxy vinyl thioethers



4

(Z)-5a-d
50-67%

R = Aryl, alkyl, Y = Te. R = Aryl, Y = Se
$R_1 = C_4H_9$, Y = Te. $R_1 = C_6H_5$, Y = Se
R_2 = Aryl, Alkyl

Entry	(***Z***)-1,2-Bis(organylchalcogene)	Electrophile	Product[a]	Yield[b] (%)
1	 **3b**	C_6H_5CHO	 **5a**	64
2	 **3b**	C_4H_9CHO	 **5b**	65
3	 **3b**	$C_5H_{11}CHO$	 **5c**	67
4	 **3d**	C_6H_5CHO	 **5d**	55
5	 **3g**	C_6H_5CHO	 **5a**	63
6	 **3h**	C_6H_5CHO	 **5d**	53
7	 **3g**	C_4H_9CHO	 **5b**	60
8	 **3g**	$C_5H_{11}CHO$	 **5c**	58
9	 **3i**	C_4H_9CHO	No reaction	–
10	 **3k**	C_6H_5CHO	 **5d**	50
11	 **3l**	C_6H_5CHO	No reaction	–

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[a] Fully characterized by NMR (^1H, ^{13}C), MS, microanalysis data.

[b] Isolated yields after purification by chromatography using silica gel (230–400 mesh) and a mixture of ethyl acetate/hexane (2:8 v:v) as the mobile phase in all cases.

subsequent reflux which furnished (***Z***)-1-phenylthio-2-butyltelluro-1-hexene **3b** in 76% yield (entry 2, Table 1). The regio- and stereochemistry of the mixed (***Z***)-1,2-bis(organylchalcogene)-1-alkenes **3a–m** were determined by NMR experiments. The vinylic hydrogen multiplicity of the alkylsubstituted olefins **3b** and **3i** observed in the ^{1}H NMR (400 MHz) spectra was detected as a singlet in 6.65 ppm and 6.61 ppm, respectively. The gNOESY experiments of **3b** and **3i** in the ^{1}H NMR showed an enhancement of the allylic hydrogens' signals when the vinylic hydrogens were irradiated. No correlations were observed involving the vinylic hydrogens and the hydrogens from the butyltelluro group for **3b** and CH (aromatic) attached to the selenium atom for **3i**. Therefore, the NOE experiments confirmed that the organylchalcogenes groups are situated between them in a cis relationship. Considering the ***Z***-configuration of the 1,2-bis(organylchalcogene)-1-alkenes **3a–m**, we believe that the mechanism involved in the hydrochalcogenation of thioacetylenes is similar to that observed for the hydrochalcogenation of activated acetylenes.[4b,6c,20] The addition of the RTe$^-$ or RSe$^-$ anions at the thioacetylene triple bond occurs in synchrony with the generation of the incipient carbanion intermediate onto C-sp^2 attached to phenylthio group **2**, which promptly abstracts the hydrogen of the water in an anti fashion mechanism (Table 1).

The pioneer study reported by Sonoda and co-workers which describes the first stereoretentive Te/Li transmetallation[21] emerged as a versatile alternative to prepare molecules with interesting biological activity[22] such as (−)-gymnodimine[22a] and conjugated polyene systems found in sex pheromones from marine algae.[22b]

Moreover, carbanions, stabilized by organylchalcogenes groups, as well as α-organylthio[23] and α-organylselenium[12a] vinyllithium are useful intermediates applied for the functionalization of trisubstituted olefins. We previously reported the stereoselective synthesis of (***Z***)- and (***E***)-2-hydroxy vinyl thioethers via condensation of aldehydes with α-phenylthio vinyllithium anions, generated by Te/Li[13] and I/Li[10] exchanges in telluro(thio)ketene acetals and thio(iodo)ketene acetals, respectively. However, to the best of our knowledge the preparation of (***Z***)-β-organylchalcogene vinyllithium anions has not yet been reported.

We describe herein for the first time the regio-specific generation of (***Z***)-β-organylthio vinyllithium **4** through the reaction of (***Z***)-1,2-bis(organylchalcogene)-1-alkenes **3** (1.5 equiv) in THF (10 mL) with *n*-BuLi (1.5 equiv) at −78 °C. The anions generated were then reacted with aldehydes (1.5 equiv), furnishing the (***Z***)-3-hydroxy vinyl thioethers **5a–d** in moderate to good yields (Table 2). In all cases, the highest reactivity of the butyltellurium group was observed while the phenylthio group remained intact toward *n*-BuLi. Reacting the (***Z***)-1-phenylseleno-1-phenyl-2-phenylthio ethene **3k** with *n*-BuLi under similar conditions, followed by trapping with benzaldehyde, led to (***Z***)-1-phenylthio-2,3-diphenyl-3-hydroxy-1-propene **5d**. In this case, we believe that the phenyl group must stabilize the β-phenylthio vinyllithium anion by the resonance effect. However, the reaction of compounds **3i** and **3l** with *n*-BuLi failed, and the starting materials were recovered intact. This demonstrated that the Se/Li exchange is less efficient than Te/Li transmetallation because of the weaker Csp^2-Te bond to 1,2-bis(organylchalcogene)-1-alkenes **3**, confirming our preliminary results.[15a] Studies to apply (***Z***)-3-hydroxy vinyl thioethers as a key intermediate to synthesize bioactive molecules are actually under investigation in our laboratory.

In summary, we describe herein the one-pot hydrochalcogenation of thioacetylenes to give mixed (***Z***)-1,2-bis(organylchalcogene)-1-alkenes which were applied to generate the not yet prepared β-phenylthio vinyllithium anion intermediates.

Acknowledgments

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Supplementary data

Supplementary data (the detailed experimental procedure, characterization data for all new compounds and respective copies of ^{1}H NMR, ^{13}C NMR, and mass spectra) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.07.112.

References and notes

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