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Hydroalumination of phenylthioacetylenes. Synthesis and reactions of (Z)- and (E)-1-butyltelluro-1-phenylthio-1-alkenes

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Abstract—Hydroalumination of phenylthioacetylenes with the Zweifel's reagent as reducing agent followed by the addition of C_4H_9TeBr afforded (*Z*)-telluro(thio)ketene acetals (*Z* >80–93%). The (*E*)-isomers were obtained with 100% stereoselectivity by reduction of thioacetylenes with DIBAL-H, followed by the addition of *n*-BuLi and subsequent treatment with C_4H_9TeBr . Reaction of the (*E*)-telluro(thio)ketene acetals with *n*-BuLi followed by the addition of valeraldehyde afforded the (*Z*)-phenylthio allylic alcohol as the main product and traces of the (*E*)-isomer, while the mixture of (*Z*)- and (*E*)-telluro(thio)ketene acetals under similar reaction conditions gave the (*E*)-phenylthio allylic alcohol exclusively. © 2001 Elsevier Science Ltd. All rights reserved.

Organotellurium compounds have been the subject of intense research due to their applications in organic synthesis.^{1,2} The chemistry of vinyl tellurides^{2–4} has received special attention because these compounds can be used as intermediates in carbon–carbon bond formation, resulting in carbon chain elongation by different processes such as transition metal-catalyzed cross-coupling reactions⁵ or by the stereo-retentive Te/metal exchange reactions like Te/Li,⁶ Te/Cu,⁷ Te/Zn,^{5c,d,8} or Te/Mg.⁹

Our group developed some methodologies for the synthesis of vinylic compounds containing two heteroatoms directly attached to the same carbon-carbon double bond as telluroketene acetals,¹⁰ (E)-telluro(stannvl)ketene acetals^{2b} and (E)-telluro(seleno)ketene acetals,¹¹ using bis(cyclopentadienyl) chloro zirconium hydride (Schwartz's reagent) as reducing agent. In a previous study (1999),¹² we published the synthesis of telluro(thio)ketene acetals by reaction of methylthio phosphonates with aryl (or butyl) tellurenyl halides and aldehydes under basic conditions. However, this methodology produced mixtures of (Z)-, (E)-telluro(thio)ketene acetals and vinyl sulfides as by-products. To date, this is the first and only known method for the synthesis of this kind of compounds. Of particular importance is the regio- and stereocontrol to obtain pure alkenes containing two different organochalcogene groups such as organotellurium and organosulfur moieties in their structure, with the aim to study the selectivity in the reactivity of each of these groups in different reactions like transmetallations, metal-catalyzed cross-coupling reactions and others. With this in mind, a novel methodology for the synthesis of disubstituted 1,2-dichalcogene alkenes with opposite regiochemistry to the telluro(thio)ketene acetals was recently developed by our group.^{4b} The hydrotelluration of thioacetylenes was performed, and the (Z)-1-butyltelluro-2-phenylthio-1-alkenes with total control on the regio- and stereochemistry were obtained in good yields.^{4b}

The reaction of selenoacetylenes with DIBAL-H followed by the addition of C_4H_9 TeBr results in the (*E*)-teluro(seleno)ketene acetal formation with total control of the regio- and stereochemistry, as described by us recently.¹³ However, the desired products were obtained in low to moderate yields (22–50%), probably because the Al/Te exchange reactions are less efficient in the vinyl alanes¹³ than in the corresponding ate complexes, as will be disclosed in the present communication.

Now, we devoted our efforts to the development of methodologies for the synthesis of telluro(thio)ketene acetals with high regio- and stereoselectivity. In this way, we envisioned two related routes for the synthesis of each isomer (E)- and (Z)-butyltelluro-1-phenylthio-1-alkene. First, we studied the reduction of phenyl-

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thioacetylenes **1a–d** with DIBAL-H which is a synstereospecific addition process, with the hydride and the organoaluminum moiety being added to the triple bond on the same side. It is noteworthy that the aluminum atom is exclusively attached to the sp^2 carbon bearing the phenylthio group, affording exclusively the α -aluminated phenylthio alkene intermediate **2** (Scheme 1). Subsequent addition of *n*-BuLi to the α -aluminum vinylsulfide intermediate **2** allows the generation of the corresponding ate complex **3** that is more reactive than **2** toward the Al/Te exchange reaction. In this way, the capture of **3** with C₄H₉TeBr gave the (*E*) compounds **4a–d**¹⁴ in good yields, with 100% regio- and stereoselectivity (Scheme 1; Table 1). On the other hand, the synthesis of (Z)-telluro(thio)ketene acetals with high stereoselectivity was performed employing the Zweifel's reagent as an *anti*stereoespecific reducing agent.¹⁵ The lithium di(*iso*butyl)-*n*-butyl aluminate hydride (Zweifel's reagent) was generated in situ by adding *n*-BuLi in hexanes to a solution of DIBAL-H in THF at 0°C. Thioacetylenes **1a-d** were reacted with the formed ate complex, resulting in an *anti*-addition of the hydride and the organoaluminum moiety with the last group being transferred to the sp^2 carbon bearing the phenylthio group, as depicted in the proposed structure for the lithium phenylthio vinyl alanate intermediate **5** (Scheme 2). This intermediate was trapped with C₄H₉TeBr and



Scheme 1.

Table 1. (Z)-Telluro(thio)ketene acetals obtained

Thioacetylene	Product ^a	Reaction time (min)	Yield (%) ^b
C_3H_7 SC ₆ H ₅ 1a	$C_{3}H_{7}$ $SC_{6}H_{5}$ $4a$ $TeC_{4}H_{9}$	60	75
C_4H_9 \longrightarrow SC_6H_5 1b	C_4H_9 SC_6H_5 $4b$ TeC_4H_9	60	80
C ₆ H ₅ SC ₆ H ₅ 1c	C_6H_5 SC_6H_5 4c TeC_4H_9	40	50
\sim	$ \begin{array}{c} & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & $	40	60

^a Fully characterized by NMR, MS, elemental analyses and IR.

^b Isolated yields and purified by PTLC.



Scheme 2.

Table 2. (Z)- and (E)-Telluro(thio)ketene acetals obtained

Thioacetylene	Products ^a	Ratio 6:4 ^b	Reaction time (min)	Yield (%) ^c
C_3H_7 \longrightarrow SC_6H_5 $1a$	$C_{3}H_{7} \xrightarrow{TeC_{4}H_{9}} C_{3}H_{7} \xrightarrow{SC_{6}H_{5}} + \underbrace{56a}_{SC_{6}H_{5}} + \underbrace{4a}_{TeC_{4}H_{9}} + \underbrace{56a}_{SC_{6}H_{5}} + \underbrace{56a}_{SC_$	93:7	60	63
C ₄ H ₉ — <u></u> SC ₆ H ₅ 1b	$C_{4}H_{9} \xrightarrow{TeC_{4}H_{9}} C_{4}H_{9} \xrightarrow{SC_{6}H_{5}} + \underbrace{5}_{6} $	85:15	60	65
C ₆ H ₅ SC ₆ H ₅ 1c	$C_{6}H_{5}$ $TeC_{4}H_{9}$ $C_{6}H_{5}$ C	80:20	40	57
$\sqrt{\frac{1}{1}}$ SC ₆ H ₅	$\begin{array}{c} & & \\$	90:10	40	60

^a Fully characterized by NMR, MS, elemental analyses and IR.

^b Ratio obtained by ¹H NMR.

^c Isolated yields and purified by PTLC.

mixtures of stereoisomers (Z)-telluro(thio)ketene acetals **6a–d** (major products; 80–93%) and (E)-telluro(thio)ketene acetals **4a–d** (by-products; 7–20%) were obtained in good yields (Scheme 2; Table 2).

Although the *syn*-hydroalumination reaction of common terminal alkynes using DIBAL-H have been extensively studied by others, the *anti*-hydroalumination employing the DIBAL-H/*n*-BuLi complex (Zweifel's reagent) have been scarcely studied to date¹⁵ and only in specific substrates. To the best of our knowledge neither *syn*- nor *anti*-hydroalumination of phenylthioalkynes to generate phenylthio vinyl aluminate complex intermediates **3** and **5** were ever reported.

The importance of the chemistry described here lies in the established synthetic utility of the vinyl tellurides^{1–11} and vinyl sulfides.^{11,16} The Te/Li exchange reaction is one of the most powerful tools for the regio- and stereocontrolled synthesis of olefinic systems.^{1a,6,10} However, only very few examples of this reaction employing trisubstituted vinyl tellurides have been described in the literature.^{4b} In the present communication, we also describe our preliminary results concerning the chemical reactivity of the trisubstituted 1-butyltelluro-1-phenylthio-1-alkenes obtained (4 and 6) and their synthetic applications. Employing a mixture of stereoisomers (Z)- and (E)-1butyltelluro-1-phenylthio-2-hexene 6b and 4b as a representative example, we studied the chemoselectivity in the reaction with *n*-BuLi at -78° C. To make possible the capture of the generated intermediates, they were subsequently treated with valeraldehyde and the (E)-6phenylthio-6-undecen-5-ol 9 was obtained exclusively in 77% yield. The reaction with n-BuLi produced exclusively the detellurated intermediates as a mixture of (Z)- and (E)- α -lithiated vinyl sulfides 7 and 8. After formation of these two intermediates, we believe that the steric interaction between the phenylthio and the butyl moieties in the (Z)- α -lithiated vinylsulfide 8 promotes the complete isomerization to the (E)- α -lithiated vinyl sulfide 7 which was trapped with valeraldehyde (Scheme 3).

In the same way, the reaction of the isomerically pure (E)-1-butyltelluro-1-phenylthio-1-hexene **4b** with *n*-BuLi was performed in THF at -78° C, followed by the addition of valeraldehyde, and the (Z)-6-phenylthio-6-undecen-5-ol **10** was obtained in 76% yield as the major product. However, traces of the (E)-6-phenylthio-6-undecen-5-ol **9** were detected by ¹H NMR. We believe that in this case the reaction of *n*-BuLi with **4b** furnished initially the (Z)- α -lithiated vinyl sulfide interme-

diate 8. This intermediate undergoes a partial inversion of configuration due to the steric interaction between the phenylthio and the butyl groups, furnishing the (E)- α -lithiated vinyl sulfide 7. However, the reaction of the (Z)-8 intermediate with valeraldehyde occurs faster than the complete isomerization to 7, allowing the formation of 10 as the major product (Scheme 4).

Several attempt to transform intermediates 3b and 5b into compounds (Z)-10 and (E)-9, respectively, by direct condensation with valeraldehyde (up to 3.0 equiv.) failed completely. The major products obtained in these cases were the corresponding (Z)-11 or the (E)-12 phenylthio hexenes (Scheme 5), together with mixtures of saturated alcohols formed because the alkyl groups (from the aluminate intermediates) were preferentially transferred to the aldehyde.

As a consequence, it is important to mention that the whole routes described here to reach the stereodefined phenylthio allylic alcohols (Z)-10 and (E)-9 (from phenylthioacetylenes) are synthetically important even being necessary converting the aluminate intermediate to the tellurium compound, and then to a lithium compound before condensation.

In summary, as stated above, we have developed two new methodologies that permit the high stereoselective synthesis of (Z)- and (E)-telluro(thio)ketene acetals. The stereospecificity of tellurium compound formation





Scheme 5.

depends on that of the initial aluminate complexes that are described here for the first time. Our studies confirmed the expected highest reactivity of the butyltellurium group because the phenylthio group remained untouched in reactions of the telluro(thio)ketene acetals with n-BuLi. This last reaction allowed us to obtain the corresponding stereodefined phenylthio allylic alcohols. Other synthetic applications of these mixed 1,1-bis(organylchalcogeno)-1-alkenes are now under development in our laboratory.

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- 14. Typical procedure for the synthesis of (E)-1-butyltelluro-1-phenylthio-1-alkenes 4: To DIBAL-H (2.0 mL, 2.0 mmol, 1 M in hexanes) in hexanes (5.0 mL) under N₂, a solution of 1-phenylthio-1-hexyne (0.2 g, 1.0 mmol) in hexanes (2.0 mL) was added via syringe at rt. The reaction was refluxed for 60 min, then n-BuLi (1.53 mL, 2.0 mmol, 1.3 M in hexanes) was added dropwise at 0°C and stirring was continued for 30 min. A solution of C₄H₉TeBr/LiCl obtained in a different flask was transferred via syringe [4.0 mmol, obtained by the addition of Br_2 (0.32 g, 2.0 mmol) in benzene or CCl_4 (10 mL) to a solution of $(C_4H_9Te)_2$ (2.0 mmol, 0.73 g) in THF (10 mL) at 0°C, under stirring for 10 min followed by the addition of LiCl (1.3 g)]. Stirring was continued for an additional 30 min and the mixture was transferred to an Erlenmeyer flask and diluted with ethyl acetate (20 mL), 95% ethanol (10 mL) and water (20 mL). Butylbromide (0.64 mL, 6.0 mmol) and finally NaBH₄ (0.18 g, 6.0 mmol) were added to transform the $(C_4H_9Te)_2$ to the corresponding telluride, which is more easily removed by distillation. After the usual work-up the product was dried (MgSO₄) and the solvent evaporated under vacuum. The $(C_4H_9)_2Te$ was removed by distillation from the crude product using a Kugelröhr oven. The residue was purified by PTLC, using hexane as mobile phase. (E)-1-Butyltelluro-1-

phenylthio-1-hexene **4b**. Yield: 0.25 g (80%); CG/MS m/z 378 (27.23), 239 (11.90), 191 (30.59), 149 (100.00), 116 (25.19), 81 (57.69); ¹H NMR (300 MHz) (δ in CDCl₃) 0.86 (t, J=7.5 Hz, 3H), 0.90 (t, J=7.5 Hz, 3H), 1.16–1.46 (m, 8H), 1.70 (quint, J=7.5 Hz, 2H), 2.40 (q, J=7.5 Hz, 2H), 2.73 (t, J=7.5 Hz, 2H), 6.71 (t, J=7.5 Hz, 1H), 7.26 (m, 5H); ¹³C NMR 9.7, 13.4, 13.9, 22.3, 25.1, 31.1, 33.7, 36.4, 101.5, 126.3, 128.8, 129.4, 136.8, 152.9. Anal. calcd for C₁₆H₂₄TeS: C, 50.82; H, 6.40. Found: C, 50.82; H, 6.08.

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