



Hydrochalcogenation of phenylthioacetylenes. Synthesis of mixed (Z)-trisubstituted 1,2-bis(organylchalcogeno)-1-alkenes[†]

Miguel J. Dabdoub,* Vânia B. Dabdoub and Marco A. Pereira

Laboratório de Síntese de Compostos Organocalcogênicos, Departamento de Química, FFCLRP, Universidade de São Paulo, Av. Bandeirantes, 3900, Ribeirão Preto, SP, Brazil

Received 21 November 2000; accepted 13 December 2000

Abstract—The treatment of 1-phenylthioacetylenes with phenylselenolate and butyl or phenyltellurolate anions generated by the reaction of the corresponding dichalcogenide with NaBH₄ in aqueous ethanol results in the formation of mixed 1,2-bis(organylchalcogeno)-1-alkenes of Z configuration. The phenylthio group acts as a directing and activating group for the nucleophilic addition of the chalcogenate anions © 2001 Elsevier Science Ltd. All rights reserved.

Hydrotelluration of mono- and disubstituted alkynes containing Michael acceptors like acetylenic ketones,¹ esters,² aldehydes² and acids² using sodium tellurolate anions, was described for the first time by Buzilova and co-workers.^{1,2} This reaction was later extended by different groups to other activated terminal acetylenic compounds.³ It has also been established that the addition of sodium tellurolate anions to terminal alkynes conjugated with aromatic groups, double or triple bonds occur with complete regio- and stereocontrol to afford the disubstituted vinylic species of Z-configuration.³ On the other hand, when the diisobutylaluminum tellurolate anion is used, complete inversion of the regiochemistry takes place affording exclusively the 1,1-disubstituted vinylic tellurides.⁴ Despite of a large number of disubstituted vinylic tellurides that are readily accessible, only a few examples of trisubstituted vinylic tellurides or selenides have been obtained by the hydrochalcogenation reaction,^{1,2,5} including the butyltellurobutenyne synthesized by the addition of sodium butyltellurolate on disubstituted butadiynes.^{6,7} In these cases the disubstituted triple bond needs to be conjugated to an activating group like a ketone,¹ ester,² aldehyde,² carboxylic acid² or another triple bond.^{6,7} Although the addition of sodium tellurolate anions seems to be generally applicable to terminal monoacetylenes and conjugated dimeric acetylenes, a lack of the regiocontrol is observed when alkyl mono-

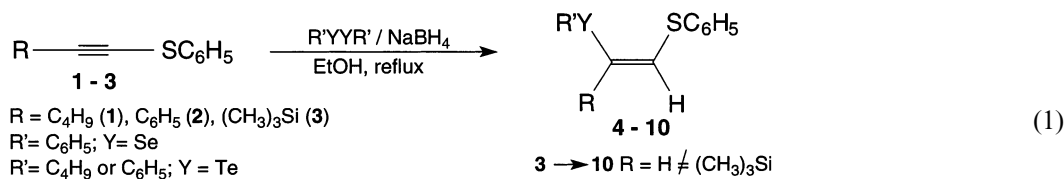
substituted acetylenes are used, affording mixtures of regioisomers.^{8–10} In the present study we observed that the reaction completely fails with internal monoacetylenes such as diphenylacetylene and 3-hexyne.

On the basis of our previous works,^{11–13} we expected the reactivity of the organotellurium (or selenium) functional group to be higher than the reactivity of the organosulfur group attached to the adjacent carbon of the same double bond, especially in the chalcogen/lithium exchange reaction^{11,12} and also in the formation of new carbon–carbon bonds in transition metal-catalyzed cross-coupling reactions.¹³ Because of our interest in the total synthesis of natural products containing trisubstituted olefins employing versatile vinylic tellurides or selenides as precursors, we examined the hydrochalcogenation of phenylthioacetylenes with chalcogenate anions (RTe[−] and ArSe[−]) and our preliminary results are described herein.

The studied reactions involve the treatment of phenylthioacetylenes 1–3 in ethanol with the organyl tellurolate or selenolate anions generated in situ by the reaction of the appropriate diorganyldichalcogenide with NaBH₄ in 95% ethanol. All the reactions were performed¹⁴ under reflux for the time indicated in Table 1. Addition of the chalcogen nucleophile (1.0 equiv.) afforded the previously unknown ‘Michael adduct’ 4–10 of Z configuration (100% for C₄H₉Te[−] and >98% for C₆H₅Te[−] and C₆H₅Se[−] as determined by ¹H NMR analysis), with the incorporation of the organotellurium (or organoselenium) moiety at the β-position relative to the phenylthio group as depicted in Eq. (1).

* Corresponding author. E-mail: migjodab@usp.br

[†] Dedicated to Professor Hans Viertler for his efforts to build a stronger Brazilian Chemical Society (SBQ).



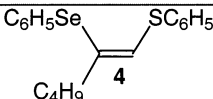
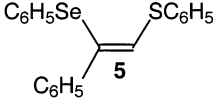
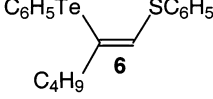
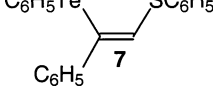
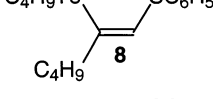
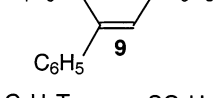
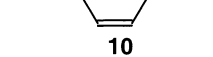
When the 2-trimethylsilyl-1-phenylthioacetylene **3** was used, the desilylated terminal phenylthioacetylene was generated in situ and underwent hydrotelluration affording exclusively the disubstituted 1-butyrtelluro-2-phenylthioethene **10** in 79% isolated yield (Table 1, entry 7). The results summarized in Table 1 show that the phenylthio group acts as a directing and activating group for the nucleophilic addition of the chalcogenate anion.

The regiochemistry of the obtained compounds was readily determined by the multiplicity of the vinylic hydrogen signal of compounds **4**, **6** and **8** that appeared in the ^1H NMR spectra (400 MHz; CDCl_3) as a singlet at 6.61 ppm in all three cases. In the case of the phenylsubstituted olefins **5**, **7** and **9**, the singlet corresponding to the olefinic hydrogens appeared at 7.25 ppm for **5**, 7.13 ppm for **7** and at 6.90 ppm for **9**. The NOE measurements in the ^1H NMR spectra of compounds **4**, **6** and **8** indicated that the products have the anticipated stereochemistry (Table 1). An enhancement of the allylic hydrogens was observed as the vinylic proton was irradiated confirming a *cis* relation between them.

The importance of the chemistry described here lies in the established synthetic utility of the vinylic tellurides,^{3,10,15} vinylic selenides^{16–18} and vinylic sulfides.^{12,19–21} The Te/Li exchange reaction occurs with total retention of configuration as first established by Sonoda's group.²² This process is one of the most powerful tools for the regio- and stereocontrolled functionalization of olefinic systems^{3,11,23,24} and it has been used in the synthesis of natural products in combination with the hydrotelluration of acetylenes.^{10,15}

With the (*Z*)-1,2-bis(organylchalcogeno)-1-alkenes in hand, we set out to study the differences in the reactivity between vinylic tellurides (or selenides) and vinylic sulfides toward butyllithium. Our preliminary studies confirm the expected highest reactivity of the butyllithium group because the phenylthio group remained untouched when compounds **8** and **9** were treated with 1.0 equivalent of butyllithium²⁵ in THF (-78°C ; 15 min). In these cases, after water addition to the reaction mixtures, the (*E*)-1-phenylthio-1-hexene and the (*E*)-1-phenylthio-2-phenyl ethene were obtained in 81 and 72% isolated yields, respectively.

Table 1. Trisubstituted (*Z*)-organyltellurium (or selenium)-2-phenylthio-1-alkenes obtained

Entry	Phenylthioacetylene	Product	Reaction time (h) ^a	Yield %
1	$\text{C}_4\text{H}_9\text{C} \equiv \text{CSC}_6\text{H}_5$ 1	 4	3.0	88
2	$\text{C}_6\text{H}_5\text{C} \equiv \text{CSC}_6\text{H}_5$ 2	 5	3.0	81
3	$\text{C}_4\text{H}_9\text{C} \equiv \text{CSC}_6\text{H}_5$ 1	 6	3.0	85
4	$\text{C}_6\text{H}_5\text{C} \equiv \text{CSC}_6\text{H}_5$ 2	 7	3.5	70
5	$\text{C}_4\text{H}_9\text{C} \equiv \text{CSC}_6\text{H}_5$ 1	 8	2.0	81
6	$\text{C}_6\text{H}_5\text{C} \equiv \text{CSC}_6\text{H}_5$ 2	 9	2.5	82
7	$(\text{CH}_3)_3\text{SiC} \equiv \text{CSC}_6\text{H}_5$ 3	 10	0.75	79

^aReaction monitored by TLC. ^bIsolated yields. ^cProducts purified by column chromatography using hexane as eluent.

On the other hand, it was observed that the 1-phenyl-1-phenylseleno-2-phenylthioethane **5** underwent the Se/Li exchange reaction when treated with butyllithium in THF (−78°C; 30 min), leading to the corresponding *E*-vinyl sulfide after treatment of the intermediate with water (59% yield). By reacting compound **4** with butyllithium under similar conditions we confirmed that the Se/Li exchange reaction is less efficient than the Te/Li exchange reaction. In this case, most of the starting material was recovered, and the expected (*E*)-1-phenylthio-1-hexene was isolated in only 38% yield. However, in all these cases the initial geometry of the double bonds was retained. More detailed studies on the generation of the β -phenylthiovinyl lithium intermediates from vinyl tellurides of types **8** and **9** and their reactions to form carbon–carbon bonds are underway in our laboratory.

In summary, we disclosed here the first highly efficient regio- and stereocontrolled hydrochalcogenation of disubstituted alkynes that does not contain unsaturated conjugated groups.

Acknowledgements

This work was supported by grants from FAPESP and CNPq. Thanks are due to Professor Antonio Gilberto Ferreira (UFSCar) for providing NMR facilities.

References

- Buzilova, S. R.; Sadekov, I. D.; Lipovich, T. V.; Filipova, T. M.; Vereshchagin, L. I. *Zh. Obshch. Khim.* **1977**, *47*, 1999.
- Buzilova, S. R.; Vereshchagin, L. I.; Sadekov, I. D.; Minkin, V. I. *Zh. Obshch. Khim.* **1976**, *46*, 933.
- Petragnani, N. *Best Synthetic Methods—Tellurium in Organic Synthesis*; Academic Press: London, 1994.
- Dabdoub, M. J.; Cassol, T. M. *Tetrahedron* **1995**, *51*, 12971.
- Detty, M. R.; Murray, B. J.; Smith, D. L.; Zumbulyadis, N. *J. Am. Chem. Soc.* **1983**, *105*, 875.
- Dabdoub, M. J.; Dabdoub, V. B. *Tetrahedron* **1995**, *51*, 9839 and references cited therein.
- Dabdoub, M. J.; Dabdoub, V. B.; Pereira, M. A.; Zukerman-Schpector, J. *J. Org. Chem.* **1996**, *61*, 9503 and references cited therein.
- Diisobutylaluminum tellurolate reacts with aryl or alkyl substituted terminal acetylenes in a general and 100% regiocontrolled process. See Ref. 4.
- Takahashi, H.; Ohe, K.; Uemura, S.; Sugita, N. *Nippon Kagaku Kaishi*. **1987**, 1508.
- Stefani, H. A.; Costa, I. M.; Zeni, G. *Tetrahedron Lett.* **1999**, *40*, 9215 and references cited therein.
- Dabdoub, M. J.; Begnini, M. L.; Guerrero, Jr., P. G.; Baroni, A. C. M. *J. Org. Chem.* **2000**, *65*, 61.
- Silveira, C. C.; Perin, G.; Braga, A. L.; Dabdoub, M. J.; Jacob, R. G. *Tetrahedron* **1999**, *55*, 7421.
- Dabdoub, M. J.; Dabdoub, V. B.; Marino, J. P. *Tetrahedron Lett.* **2000**, *41*, 433.
- Typical procedure: To a 100 mL flask, containing a mixture of the appropriate 1-phenylthioacetylene (5.0 mmol), NaBH₄ (0.236 g; 6.25 mmol) and 95% ethanol (25 mL) under a nitrogen atmosphere with vigorous stirring, the appropriate dichalcogenide (2.5 mmol) in ethanol (25 mL) was added dropwise (very slowly) at rt. The dark red color of the ditelluride or the yellow color of the diselenide became colorless in the course of the addition. The resulting solution was refluxed for the time indicated in Table 1, then it was allowed to reach room temp., diluted with ethyl acetate and washed with saturated aqueous NH₄Cl solution (2×) and brine (2×). The organic layer was dried over MgSO₄, filtered and concentrated using a rotary evaporator. The product was purified by column chromatography on silica gel (hexanes), to give the pure compound.
- Yang, J.; Cohn, S. T.; Romo, D. *Org. Lett.* **2000**, *2*, 763.
- Tingoli, M.; Tiecco, M.; Testaferri, L.; Temperini, A. *Tetrahedron* **1995**, *51*, 4691.
- Huang, X.; Ma, Y. *Chin. J. Chem.* **1998**, *16*, 483.
- Potapov, V. A.; Amozova, S. V. *Zh. Org. Khim.* **1996**, *32*, 1142 and references cited therein.
- Fianddanese, V.; Marchese, G.; Naso, F.; Ronzini, L. *J. Chem. Soc., Perkin Trans. 1* **1985**, *1*, 1115.
- Waters, M. S.; Cowen, J. A.; McWilliams, J. C.; Maligres, P. E.; Askin, D. *Tetrahedron Lett.* **2000**, *41*, 141.
- Gridnev, I. D.; Miyamura, N.; Suzuki, A. *J. Org. Chem.* **1993**, *58*, 5351.
- Hiroy, T.; Kambe, N.; Ogawa, A.; Miyoshi, N.; Murai, S.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1987**, *99*, 1221.
- Ogawa, A.; Tsuboi, Y.; Obayashi, R.; Yokoyama, K.; Ryu, I.; Sonoda, N. *J. Org. Chem.* **1994**, *59*, 1600.
- Dabdoub, M. J.; Begnini, M. L.; Cassol, T. M.; Guerrero, Jr., P. G.; Silveira, C. C. *Tetrahedron Lett.* **1995**, *36*, 7623.
- Typical procedure: To a solution of compound **9** (2.0 mmol) in THF (20 mL), BuLi (2.0 mmol) was added at −78°C under a nitrogen atmosphere. After 15 minutes, water was added (4.0 mL) and the product was isolated following the usual extraction procedure.¹¹