Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 46 (2005) 4883–4886
Tetrahedron Letters

Stereoselective synthesis of (*E*)-1-iodo-1-selenoalkenes via hydroalumination–iodination of 1-alkynyl selenides

Carlos Pérez-Balado, Fabio Lucaccioni and István E. Markó*

Université catholique de Louvain, Département de Chimie, Unité de Chimie Organique et Médicinale, Bâtiment Lavoisier, Place Louis Pasteur 1, B-1348 Louvain-la-Neuve, Belgium

Received 29 March 2005; revised 3 May 2005; accepted 12 May 2005
Available online 4 June 2005

Abstract—*syn*-Hydroalumination of 2,4,6-triisopropylphenylselanyl-1-alkynes **22** with DIBAL-H, followed by Al/I exchange with I_2, afforded selectively the corresponding (*E*)-1-iodo-1-selenoalkenes in good yields. The sterically hindered 2,4,6-triisopropylphenyl group proved to be mandatory and prevented the formation of undesired by-products.

During the course of the total synthesis of polycavernoside A,[1] a complex marine toxin, we required an expedient method for the stereoselective construction of the trisubstituted allylsilanes **1**. Whilst a few procedures exist for the assembly of **1**,[2] it was envisaged that the formal generation of an alkene-1,1-dianion such as **2**, followed by sequential, stereocontrolled, alkylations would lead to an efficient access to these useful allylating agents (Fig. 1). A number of alkene-1,1-dianion equivalents have already been reported in the literature.[3] However, they suffer from various shortcomings, including limited reactivity. It was thus thought that 1-iodo-1-selenoalkenes **3**, of defined geometry, could be interesting equivalents of dianion **2**.

Although a few methodologies for the preparation of 1-iodo-1-selenoalkenes **3** have been described,[4] they usually afford **3** with moderate *E*/*Z* selectivity or require several steps. In this letter, we wish to present some preliminary results on the establishment of a novel methodology for the stereoselective synthesis of (*E*)-1-iodo-1-selenoalkenes **3**, based upon the *syn*-hydrometallation of 1-alkynyl selenides **5**, followed by metal/iodine exchange with I_2.

At the onset of this work, the hydrozirconation of 1-phenylselanyl-hex-1-yne **6** was performed with $Cp_2Zr(H)Cl$.[5] The in situ generated 1-zircono-1-selenoalkene species **7** was subsequently captured with various electrophiles, affording the corresponding selenoalkenes in good to moderate yields (Scheme 1). Deuterolysis and protonolysis experiments demonstrated that the hydrozirconation of the C–C triple bond occurred in a *syn* manner and that the Zr residue was located on the carbon bearing the selenium moiety. Trapping of **7** with I_2 or NBS, at low temperature, provided a mixture of *E* and *Z* isomers of the corresponding 1-halo-1-selenoalkenes **8** and **11**, indicating that isomerisation of the C–C double bond takes place either during the Zr/halogen exchange or during the work-up. Although

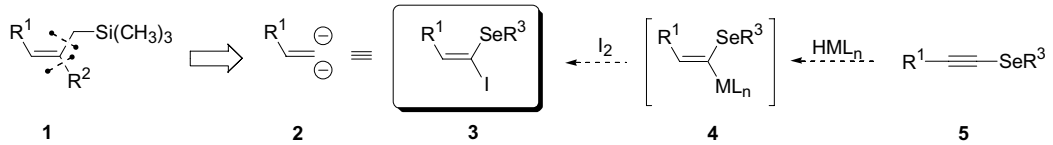
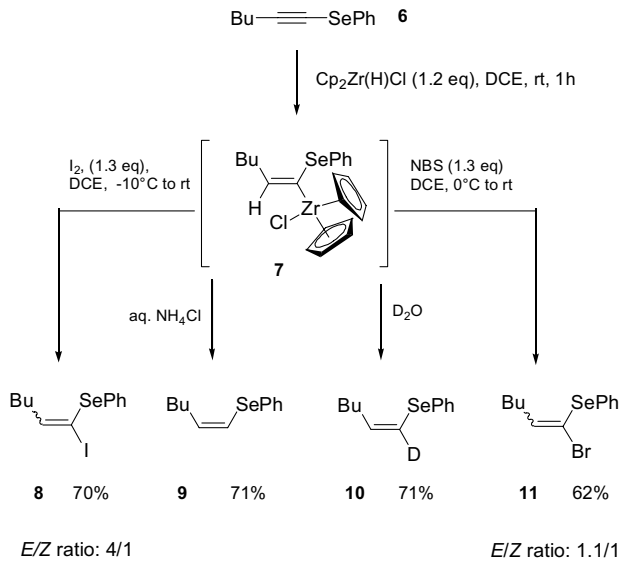


Figure 1.

Keywords: Selenides; Hydroalumination; 2,4,6-Triisopropylphenyl selenide; Iodination.
* Corresponding author. Tel.: +32 10 47 87 73; fax: +32 10 47 27 88; e-mail: marko@chim.ucl.ac.be

0040-4039/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2005.05.052



Scheme 1.

the iodoalkene **8** could be obtained in good yield and with a reasonable *E*/*Z* ratio of 4 to 1, this was clearly not sufficient for our purposes. Hydroalumination of **6** with DIBAL-H was then explored.

The hydroalumination of phenylseleno-acetylenes, analogous to **6**, has been described by the groups of Al-Hassan and Dabdoub,[6] who showed that DIBAL-H also added in a *syn* manner to the C–C triple bond of these alkynyl selenides. They also demonstrated that the aluminium residue was positioned on the same carbon as the selenium substituent (Fig. 2). However, when the hydroalumination of 1-phenylselanyl-hex-1-yne **6** was performed with DIBAL-H, followed by quenching of the in situ generated 1-alumino-1-selenoalkene **13** with dilute HCl, the (*Z*)-alkenyl selenide **14** was obtained in a moderate 61% yield. Besides **14**, diphenyl diselenide **15** was isolated in 29% yield. The formation of diphenyl diselenide appears to proceed via the competitive cleavage of the (sp)C–Se bond of **6** by hydride attack on the selenium moiety. This generates phenylselenol and an alkynylalane. Phenylselenol is then deprotonated by the hydride to give phenylselenoate, which rapidly oxidises to diphenyl diselenide in the presence of oxygen during the work-up.[7]

The undesired formation of diselenide **15** was a serious drawback in this approach and, in order to establish a high yielding reaction, needed to be suppressed. We reasoned that the competitive (sp)C–Se bond cleavage could probably be prevented by selectively hindering the selenium atom, thereby inhibiting the coordination between the selenium substituent and the aluminium reagent and hence, the delivery of hydride on selenium. In order to verify our hypothesis, 2,4,6-triisopropylphenylselanyl 1-alkynes, bearing the voluminous 2,4,6-triisopropylphenyl (TIPP) group instead of the phenyl group, were prepared.

The 2,4,6-triisopropylphenylselanyl 1-alkynes **22** were synthesised in good yields from di-2,4,6-triisopropylphenyl diselenide **19** and the corresponding terminal alkynes.[8] Diselenide **19** was readily obtained from 1-bromo-2,4,6-triisopropylbenzene, by Br/Li exchange with 2 equiv of *t*-BuLi, followed by treatment with metallic selenium and final oxidation of the selenol to the diselenide (84% yield). Addition of Br_2 to **19** generated in situ the corresponding selenyl bromide **20**, which was reacted immediately with the lithium acetylides **21**, obtained by deprotonation of the corresponding terminal alkynes with *n*-BuLi at low temperature, to give the desired 1-alkynyl selenides in good yields (Scheme 2).

Much to our delight, when 1-(2,4,6)-triisopropylphenylselenylhex-1-yne **12** was treated with DIBAL-H, followed by quenching with dilute HCl (under the same conditions as **6**), the (*Z*)-alkenyl selenide **17** was obtained in 95% yield. Gratifyingly, the diselenide **19** could not be detected in the crude reaction mixture (Fig. 2). Thus, it transpires that the steric hindrance of the TIPP group dramatically influences the selectivity of the hydroalumination reaction by suppressing the competitive C–Se bond cleavage. The formation of the diselenide by-product is prevented and the hydrometallation of the C–C triple bond becomes essentially quantitative.

Having found that the TIPP group allowed efficient hydroalumination of 1-alkynyl selenides, we next turned our attention to the preparation of stereodefined 1-iodo-1-selenoalkenes by iodination of the corresponding vinylalane intermediates **23**. Addition of I_2 to **23** afforded the corresponding 1-iodo-1-selenoalkenes **24** in excellent yields. In all cases, only the *E* isomer was obtained,[9] indicating that the replacement of Al by I takes place with retention of configuration of the C–C double bond (Table 1). The Al/I exchange requires careful control of the reaction conditions, in order for the iodination to be complete.[10] If the reaction mixture is

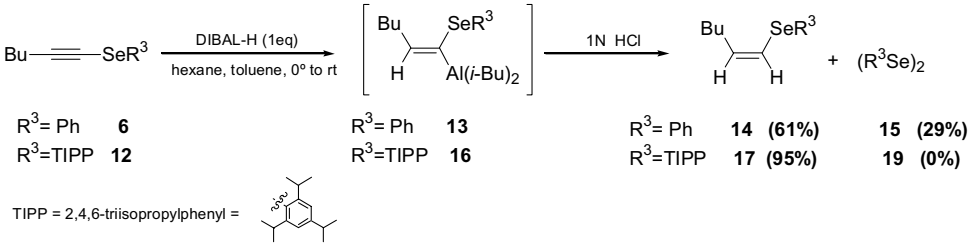
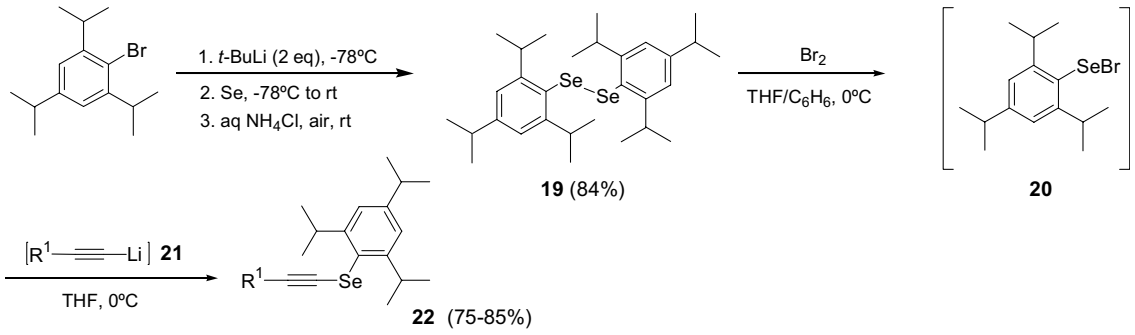
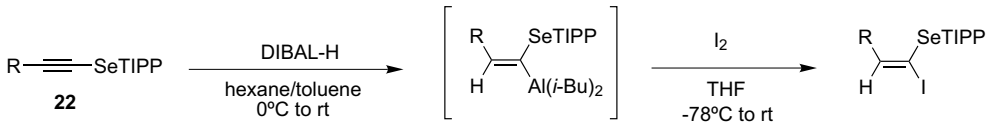


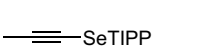
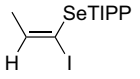
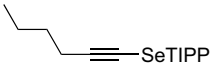
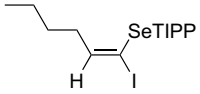
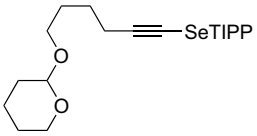
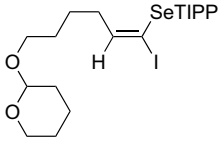
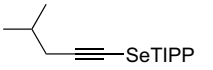
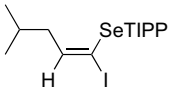
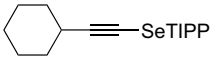
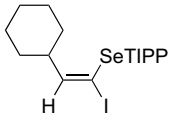
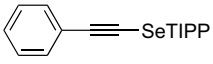
Figure 2.



Scheme 2.

Table 1. Hydroalumination–iodination of 1-(2,4,6)-triisopropylphenylselenyl-1-alkynes



Entry	Substrate	Product	Yield[a]
1			92%
2			95%
3			96%
4			82%
5			91%
6		—	0%

[a] Isolated yields after purification by column chromatography.

stirred longer than 1 h at room temperature, some degradation may occur, accompanied by the appearance of the *Z* isomer. In the case of the phenyl acetylene derivative (Table 1, entry 6), the addition of DIBAL-H to the C–C triple bond did not occur, even when the hydroalumination was performed in refluxing hexane. This lack of reactivity could be due to the generation of prohibitive steric repulsions between the aryl and SeTIPP groups during the addition of the aluminium hydride.

In sharp contrast, bromination of **23**, either with Br_2 or NBS, afforded a 1/1 mixture of (*E*) and (*Z*)-1-bromo-1-selenoalkenes. Although the yields were good (80–90%), the replacement of Al by Br occurred with complete scrambling of the configuration of the C–C double bond even under carefully controlled reaction conditions. This might be an indication that bromination and iodination of **23** follow different mechanistic pathways.

In summary, we have developed a novel, efficient and stereoselective methodology for the synthesis of (*E*)-1-iodo-1-selenoalkenes via hydroalumination of 1-alkynyl selenides, followed by Al/I exchange with full retention of configuration. Steric shielding of the selenium with a hindered 2,4,6-triisopropylphenyl substituent proved to be mandatory and prevented the formation of

undesired diselenides. The 2,4,6-triisopropylphenylselenyl 1-alkyne precursors are prepared in a straightforward manner, from readily available materials. Current efforts are now being directed towards exploring the reactivity of (*E*)-1-iodo-1-selenoalkenes as potential precursors for the stereocontrolled synthesis of trisubstituted alkenes.

Acknowledgements

Financial support of this work by Chirotech Technology Ltd., Cambridge, UK and the Université catholique de Louvain is gratefully acknowledged.

References and notes

1. (a) Yasumoto, T.; Yotsu-Yamashita, M.; Haddock, R. L. *J. Am. Chem. Soc.* **1993**, *115*, 1147; (b) Haddock, R. L.; Cruz, L. T. *Lancet* **1991**, *338*, 195; For total syntheses of polycavernoside A see: (c) Fujiwara, K.; Murai, A.; Yotsu-Yamashita, M.; Yasumoto, T. *J. Am. Chem. Soc.* **1998**, *120*, 10770; (d) Paquette, L. A.; Barriault, L.; Pissarnitski, D. *J. Am. Chem. Soc.* **1999**, *121*, 4542; (e) White, J. D.; Blakemore, P. R.; Browder, C. C.; Hong, J.; Lincoln, C. M.; Nagorny, P. A.; Robarge, L. A.; Wardrop, D. J. *J. Am. Chem. Soc.* **2001**, *123*, 8593.
2. For some selected reviews see: (a) Sarkar, T. K. In *Science of Synthesis, Houben–Weyl Methods of Molecular Transformations*; Georg Thieme: Stuttgart, 2002; Vol. 4, p 837; (b) Sarkar, T. K. *Synthesis* **1990**, 969, and 1101.
3. For selected reviews on alkene 1,1-dianion equivalents see: (a) Marek, I. *Chem. Rev.* **2000**, *100*, 2887; (b) Chinkov, N.; Chechik, H.; Majumdar, S.; Liard, A.; Marek, I. *Synthesis* **2002**, 2473; For alkene-1,2-dianion equivalents see: (c) Gerard, J.; Hevesi, L. *Tetrahedron* **2004**, *60*, 367; (d) Gerard, J.; Hevesi, L. *Tetrahedron* **2001**, *57*, 9109.
4. (a) Tingoli, M.; Tiecco, M.; Testaferri, L.; Temperini, A.; Pelizzi, G.; Bacchi, A. *Tetrahedron* **1995**, *51*, 4691; (b) Comasseto, J. V.; Menezes, P. H.; Stefani, H. A.; Zeni, G.; Braga, A. L. *Tetrahedron* **1996**, *52*, 9687; (c) Huang, X.; Ma, Y. *Synth. Commun.* **1997**, *27*, 2407; (d) Dabdoud, M. J.; Baroni, A. C. *J. Org. Chem.* **2000**, *65*, 54.
5. For hydrozirconation of 1-alkynyl selenides see: (a) Zhu, L.-S.; Huang, Z.-Z.; Huang, X. *Tetrahedron* **1996**, *52*, 9819; (b) Huang, X.; Zhu, L.-S. *Synthesis* **1996**, 1191; (c) Zhu, L.-S.; Huang, Z.-Z.; Huang, X. *J. Chem. Res.* **1996**, 112; (d) Dabdoud, M. J.; Begnini, M. L.; Guerrero, P. G. *Tetrahedron* **1998**, *54*, 2371; (e) Dabdoub, M. J.; Begnini, M. L.; Guerrero, P. G.; Baroni, A. C. *J. Org. Chem.* **2000**, *65*, 61.
6. (a) Al-Hassan, M. I.; Al-Naijar, I. M.; Ahmad, M. M. *Spectrochim. Acta, Part A.* **1986**, *45*, 1011; (b) Al-Hassan, M. I. *Synth. Commun.* **2001**, *31*, 3027; (c) Dabdoub, M. J.; Cassol, T. M.; Barbosa, S. L. *Tetrahedron Lett.* **1996**, *37*, 831.
7. Dabdoud, M. J.; Comasseto, J. V. *Organometallics* **1998**, *7*, 84.
8. Comasseto, J. V.; Silveira, C. C.; Ferreira, J. T.; Catani, V. *Synth. Commun.* **1986**, *16*, 283.
9. I/Li exchange of **24** (R = Me) with *n*-BuLi, followed by quenching with dilute acid afforded exclusively the (*Z*)-1-propenyl selenide (J_{CH-CH} = 8.8 Hz), thus confirming the (*E*)-geometry of the C–C double bond of **24**.
10. Typical experimental procedure: Preparation of (*E*)-2-(iodo-propenylselenyl)-1,3,5-triisopropyl-benzene [Table 1, entry 1]: DIBAL-H (26.4 mL, 39.6 mmol, 1.5 M in toluene) was added dropwise to a stirred solution of prop-1-ynyl selenide (12.1 g, 37.8 mmol) in hexane (80 mL) cooled at 0 °C, under an argon atmosphere. The reaction mixture was stirred for 1 h at 0 °C and then 2 h at rt. The resulting colourless solution was cooled to −78 °C and a solution of I_2 (24 g, 94.5 mmol) in THF (45 mL) was added dropwise via *cannula*. The mixture was allowed to slowly reach 0 °C. It was then stirred for 1 h at 0 °C and finally 45 min at rt. It was poured into a mixture of EtOH (215 mL)/EtOAc (215 mL)/H_2O (108 mL) and treated with $NaBH_4$ until the solution became colourless or slightly yellow. The solution was washed with aqueous 1 N HCl (130 mL), a saturated aqueous $Na_2S_2O_3$ solution (100 mL), brine (150 mL), dried over $MgSO_4$ and the solvents were removed under reduced pressure. The crude product was purified by chromatography on silica gel (hexane) to afford 15.6 g (92% yield) of the title compound as a reddish oil. ^1H NMR ($CDCl_3$, 300 MHz) δ_H (ppm): 7.04 (2H, s), 6.83 (1H, q, J = 6.9 Hz), 3.67 (2H, hep, J = 6.9 Hz), 2.91 (1H, hep, J = 7.0 Hz), 2.75 (3H, d, J = 6.9 Hz), 1.27 (6H, d, J = 7.0 Hz), 1.23 (12H, d, J = 6.9 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C (ppm): 153.0, 150.7, 140.7, 125.8, 121.9, 82.1, 34.2, 33.9, 24.2, 23.8, 20.2 IR (neat): 3041, 2959, 2926, 1701, 1462, 1382, 1361, 1168, 1069 cm^{-1}. MS (EI) *m/z* (%): 450 [M^+] (62), 324 [M^+–I] (73). Anal. Calcd for $C_{18}H_{27}ISe$: C, 48.12; H, 6.06. Found: C, 48.45; H, 6.23.