Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters 47 (2006) 5867–5868
Tetrahedron Letters

Selective one-pot synthesis of *Z*-iodoallylic iodides from propargyl alcohols

Govindaswamy Manickam,[a] Umesh Siddappa[a] and Yong Li[b,*]

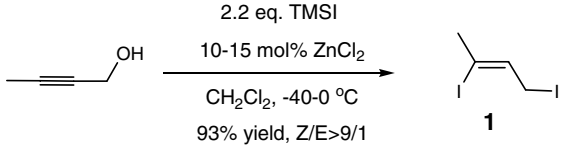
[a]*Syngene International Pvt. Ltd., 20th KM Hosur Road, Electronics City, Bangalore 560 100, India*
[b]*Kosan Biosciences Inc., Hayward, CA 94545, USA*

Received 7 June 2006; revised 13 June 2006; accepted 14 June 2006

Abstract—A selective one-pot procedure was developed for the production of *Z*-iodoallylic iodides from the corresponding propargyl alcohols.

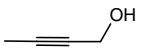
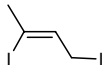
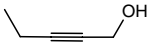
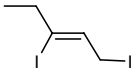
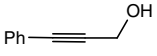
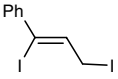
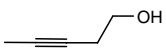
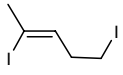
Iodides are useful building blocks in organic synthesis, particularly allylic and vinyl iodides. Most synthetically useful allylic vinyl diiodides are made from propargyl alcohols via multi-steps sequences[1] because direct conversion leads to mixtures in low yields.[2] Here we report that *Z*-iodoallylic iodides can be obtained in good yields from propargyl alcohols in a one pot procedure.

In association with one of our projects, large quantities of diiodide **1** were required. Although **1** can be prepared via a three-step, two-pot sequence from propargyl alcohol,[1a] a useful one-pot procedure was preferred. We envisioned that a Lewis acid catalyzed addition of HI across the triple bond of 2-butyn-1-ol followed by iodination of the resulting allylic alcohol would fulfill the requirement. To our delight, when zinc chloride was used as a catalyst, the reaction proceeded smoothly to produce diiodide **1** in high yield (Eq. 1).[3] Only a catalytic amount of zinc chloride (10–15 mol %) and slight excess of trimethylsilyl iodide (2.2 equiv) were required. The *Z*/*E* ratio of the double bond was greater than 9/1.



(1)

Table 1. Conversion of alkynols to diiodides

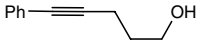
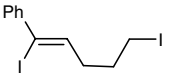
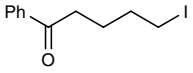
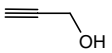
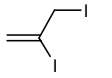
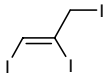
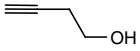
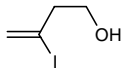
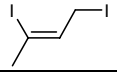
Entry	Starting material	Products	Yield (%)	*Z*/*E* ratio[c]	Product ratio[d]
1			93[a]	9.2/0.8	
2			80[b]	9/1	
3			80[b]	9.5/0.5	
4			65[b]	7/3	

(*continued on next page*)

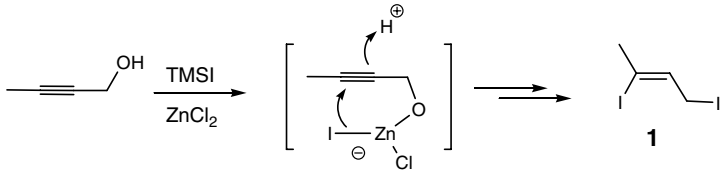
* Corresponding author. Tel.: +1 510 731 5203; fax: +1 510 732 8401; e-mail: li@kosan.com

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.06.081

Table 1 (*continued*)

Entry	Starting material	Products	Yield (%)	*Z*/*E* ratio[c]	Product ratio[d]
5		**A**  **B** 	A: 35[a] B: 45[a]		A/B 4.4/5.6
6		**A**  **B** 	A: 25[b] B: 50[b]		A/B 3.3/6.7
7		**A**  **1** 	A: 62[b] **1**: 19[b]		A/**1** 7.5/2.5

[a] Purified by vacuum distillation.
[b] Purified by silica gel chromatography.
[c] *Z*/*E* ratio was determined by ^{1}H NMR of crude reaction mixtures.
[d] Product ratios are based on purified materials.



Scheme 1.

Having succeeded in generating **1** from 2-butyn-1-ol, we then examined several other alkynyl alcohols to probe the generality of the reaction (Table 1). Similar results were observed with ethyl and phenyl substituted propargyl alcohols (entries 2 and 3). Extending the method to homo-propargyl alcohol led to decreased, but respectable, yield and *Z*/*E* selectivity (entry 4). Additional deterioration in selectivity was observed as the hydroxyl group is further removed away from the triple bond (entry 5). The formation of product **B** in entry 5 could occur via cyclization to a dihydropyran intermediate followed by acid catalyzed ring-opening. The methodology cannot be applied to terminal alkynyl alcohols, since unexpected mixtures were obtained (entries 6 and 7).

Although a mechanistic basis for the role zinc chloride plays remains to be determined, it is reasonable to speculate that an iodozincate complex is responsible for hydroxyl-directed iodide addition to the triple bond (Scheme 1).

In conclusion, we have developed a simple and economical procedure for the generation of *Z*-iodoallylic or *Z*-iodo-homoallylic iodides from the corresponding alkynyl alcohols.

References and notes

1. (a) Chappell, M. D.; Stachel, S. J.; Lee, C. B.; Danishefsky, S. J. *Org. Lett.* **2000**, *2*, 1633; (b) Kagechika, K.; Ohshima, T.; Shibasaki, M. *Tetrahedron* **1993**, *49*, 1773; (c) Sato, Y.; Nukui, S.; Sodeoka, M.; Mikiko, S.; Shibasaki, M. *Tetrahedron* **1994**, *50*, 371.
2. Gras, J.-L.; Chang, K. W.; Bertrand, M. *Tetrahedron Lett.* **1982**, *23*, 3571.
3. Trimethylsilyl iodide was purchased from Lancaster Chemical Co. and was used directly. Zinc chloride was purchased from Aldrich Chemical Co. and fused prior to use. Experimental procedure: To a solution of 2-butyn-1-ol (45 g, 0.64 mol) in dry dichloromethane (500 mL) was added freshly fused zinc chloride (13 g, 0.096 mol) under nitrogen atmosphere. The reaction mixture was cooled to −40 °C, and trimethylsilyl iodide was then introduced slowly under dark over a period of 30 min. The reaction mixture was slowly warmed to 0 °C and stirred for 1 h. It was filtered over a bed of celite and concentrated. The crude residue was subjected to vacuum distillation to give diiodide **1** as a brown oil (bp 59–62 °C/0.1 mm Hg, 184 g, 93%).