Radical isomerization of borylated allylic sulfones

Erich Altenhofer, Michael Harmata

PII: S0040-4039(14)02101-7
DOI: http://dx.doi.org/10.1016/j.tetlet.2014.12.047
Reference: TETL 45571

To appear in: *Tetrahedron Letters*

Received Date: 22 November 2014
Revised Date: 8 December 2014
Accepted Date: 9 December 2014

Please cite this article as: Altenhofer, E., Harmata, M., Radical isomerization of borylated allylic sulfones, *Tetrahedron Letters* (2014), doi: http://dx.doi.org/10.1016/j.tetlet.2014.12.047

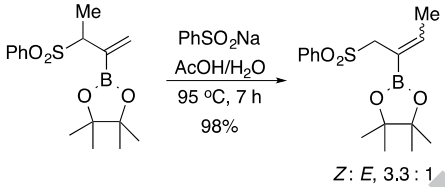
Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

Radical isomerization of borylated allylic sulfones

Leave this area blank for abstract info.

Erich Altenhofer and Michael Harmata



Z: *E*, 3.3 : 1

Tetrahedron Letters
journal homepage: www.elsevier.com

Radical isomerization of borylated allylic sulfones

Erich Altenhofer and Michael Harmata*

Department of Chemistry, University of Missouri-Columbia, 601 S. College Ave., Columbia, MO 65211 USA

ARTICLE INFO

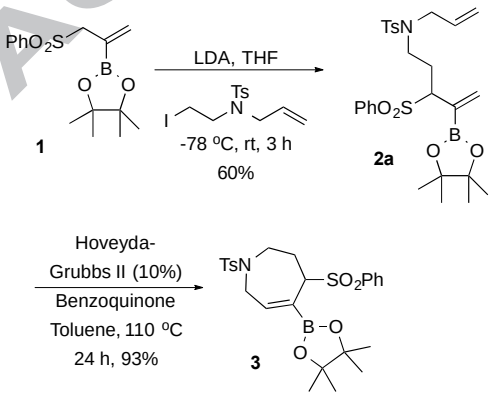
Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Sulfones
Boronates
Radicals
Isomerization
Allylic

ABSTRACT

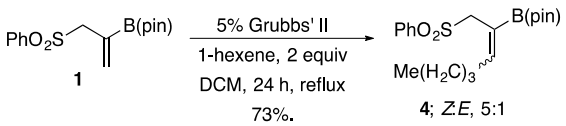
We report a preliminary study of the radical isomerization of borylated allylic sulfones to their more thermodynamically stable isomers. This reaction is important as it provides access to structurally unique vinyl boronates not easily accessible by other means.

We recently reported the alkylation of 2-boryl allylic sulfone **1** with a variety of alkyl halides, demonstrating that the boronic ester remains intact throughout the deprotonation/alkylation procedure.[1] This result was gratifying as boronic esters are Lewis acidic, and their survival in the presence of a sulfonyl anion was not unconditionally guaranteed.[2] The success of this chemistry opened the door for further exploration with this simple 2-boryl species in other processes. In a more recent publication, we demonstrated that alkylated products could undergo ring-closing metathesis with the Hoveyda-Grubbs 2nd generation catalyst, allowing for the synthesis of functionalized cyclic and polycyclic boronic esters.[3] In general, the formation of five- to seven-membered rings could be accomplished, including heterocyclic azepine **3** (Scheme 1).

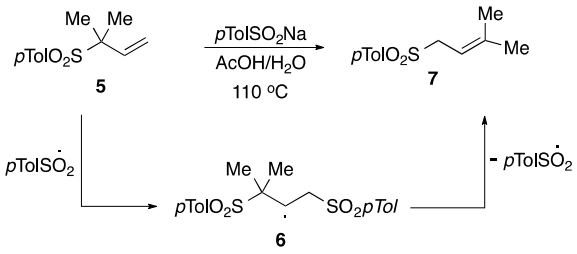


Scheme 1. Synthesis of functionalized cyclic boronates.

We also reported the intermolecular cross-metathesis reaction of **1,** but found that while the process worked with simple terminal alkenes, it failed with styrene and a selection of other terminal alkenes functionalized with heteroatoms at the allylic position (Scheme 2).



Scheme 2. Cross-metathesis reaction of **1**.

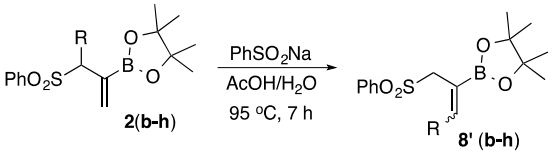


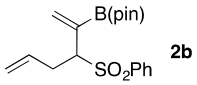
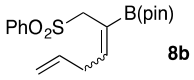
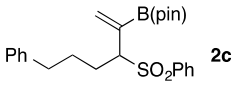
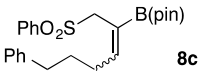
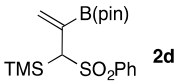
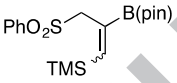
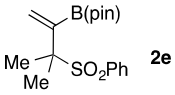
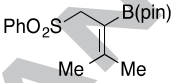
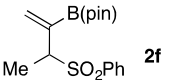
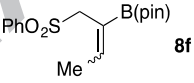
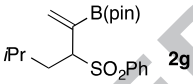
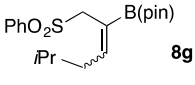
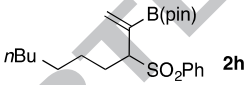
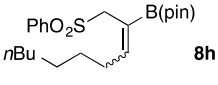
Scheme 3. Isomerization of allylic sulfones.

This problem inspired us to seek an alternative to metathesis that would result in similar products, but would be more general. It had been known for quite some time that the isomerization of allylic sulfones could be accomplished via a radical process. For example, Whitham and co-workers demonstrated that treatment of allylic sulfone **5** with sodium *p*-tolylsulfinate in hot acetic acid

* Corresponding author. Tel.: +001-573-882-1097; fax: +001-573-882-2754; e-mail: harmatam@missouri.edu

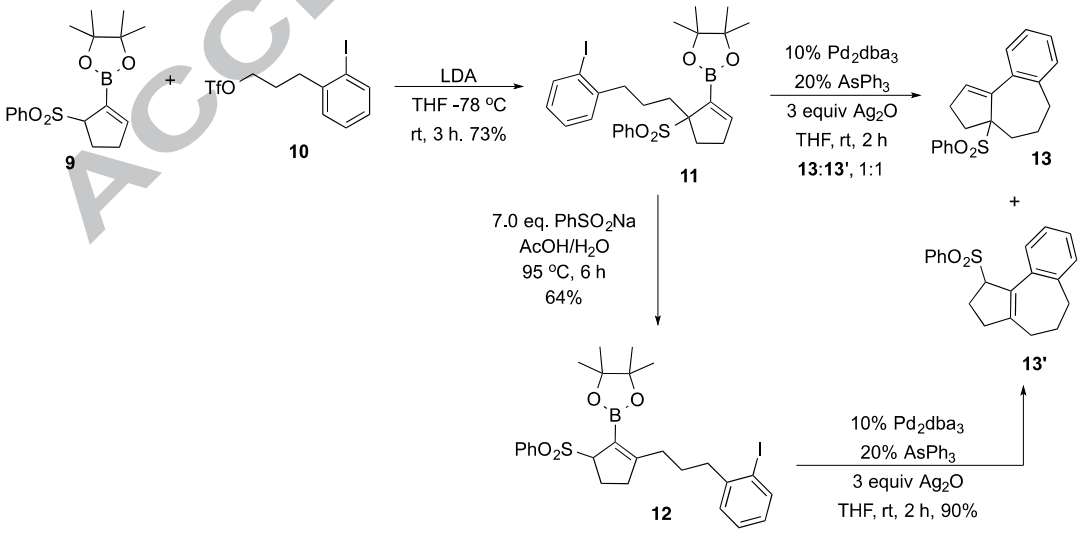
Table 1. Isomerization of borylated allylic sulfones.



Entry	Starting Material	Product	Yield % (*Z*:*E* ratio)[a]
1	 **2b**	 **8b**	89 (2.7:1)
2	 **2c**	 **8c**	80 (2.2:1)
3	 **2d**	 **8d**	0[b]
4	 **2e**	 **8e**	80
5	 **2f**	 **8f**	98 (3.3:1)
6	 **2g**	 **8g**	90 (1.8:1)
7	 **2h**	 **8h**	73 (1.7:1)

[a]Stereochemistry was by NOESY NMR.

[b]Compound **1** was isolated in 45% yield.



Scheme 4. Isomerization and intramolecular Suzuki coupling of a borylated, cyclic allylic sulfone.

resulted in the formation of sulfone **7** (Scheme 3).[4] The proposed mechanism involved the addition of a sulfinyl radical to the double bond of **5** followed by elimination of the other *p*-tolylsulfinate group to continue the chain. The driving force was simply the formation of the product with the more substituted double bond. We thus wondered if alkylation products of **1** might engage in the same type of chemistry.

Initially, we were concerned whether sulfone **1** would remain intact under the acidic conditions used for its analog **5**. We thought that the boronic ester might be deborylated under these conditions. However, it turned out that boronic ester **1** is stable in acetic acid at 95 °C. In general, alkyl substrates could be isomerized to the more thermally stable olefins and isolated products were recovered with the boronic ester intact (Table 1). Substrate **2b** was found to undergo isomerization uneventfully to form **8b** in 89% yield (entry 1). However, this and other examples exhibited little stereoselectivity, as the product was produced as a 2.7:1 mixture of *Z*:*E* isomers, respectively. Substrate **2d** underwent desilylation rather than simple isomerization, though it is not clear if isomerization preceded desilylation (entry 3). Substrate **2e** formed **8e** smoothly in excellent yield (entry 4).

The stereochemistry of the major isomerized products was determined via Nuclear Overhauser Effect Spectroscopy (NOESY). As a representative example, a portion of the two-dimensional ^{1}H-^{1}H NOESY spectrum for the diastereomeric mixture of **8g** is shown in Figure 1. The triplets appearing between 6.0 - 7.0 ppm on the horizontal axis correspond to the vinylic protons of **8g**, H_a and H_b, and the singlets around ~ 4 ppm on the vertical axis correspond to the α-sulfonyl protons. The vinylic hydrogen that is spatially close to α-sulfonyl hydrogens displays an overlap signal on the two-dimensional spectra, corresponding to the *E* isomer. The absence of any signal at the intersection of the two red lines verifies that the isomer in larger population, H_a, corresponds to the *Z* isomer.

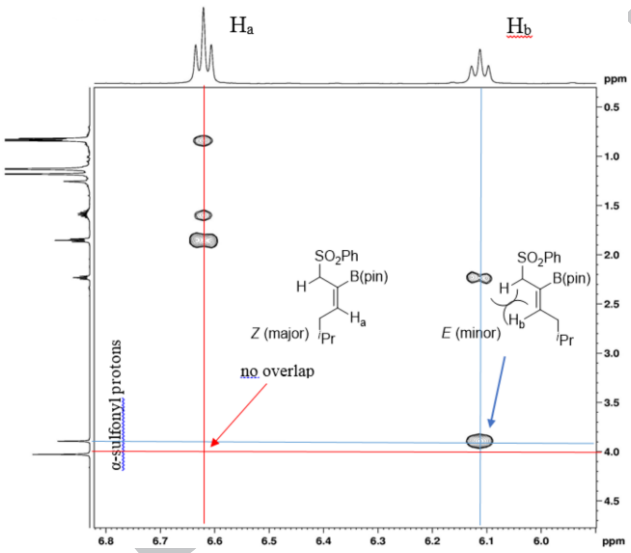


Figure 1. NOESY spectrum of *E*/*Z*-**8b**.

This procedure is convenient, yet is not as stereoselective as the metathesis procedure and further work will be necessary to enhance stereoselectivity. However, the methodology could find good use in certain contexts, as exemplified below.

We are interested in using functionalized boronates as lynchpins in the preparation of polycyclic systems. To that end, boronate **9** was deprotonated and alkylated with triflate **10**, affording **11** in 73% yield. An intramolecular Suzuki coupling using a procedure developed by Kishi[5] afforded a 1:1 mixture of products **13** and **13'**. In an effort to circumvent the formation of isomers, compound **11** was isomerized to **12** in 64% yield using the procedure detailed herein. Intramolecular Suzuki coupling afforded **13'** as the sole product in 90% isolated yield.

In summary, we have shown that borylated allylic sulfones can be isomerized under mildly acidic conditions to their more stable counterparts. For acyclic systems, the stereoselectivity is low. However, a single example of isomerization in a cyclic system demonstrated the utility of the method. Further studies are in progress. Results will be reported in due course.

Acknowledgments

This work was sponsored by the US National Science Foundation and the Department of Chemistry at the University of Missouri-Columbia. We thank Frontier Scientific for a gift of starting material used in the synthesis of **1**. We thank Ms. Carissa S. Hampton (University of Missouri-Columbia) for assistance in preparing this manuscript.

References and notes

1. Altenhofer, E. F.; Harmata, M. *Chem. Commun*. **2013**, *49*, 2365.
2. However, see: (a) Whiting, A. *Tetrahedron Lett.*, 1991, **32**, 1503. (b) Curtis, A. D. M. ; Whiting, A. *Tetrahedron Lett.*, 1991, **32**, 1507. (c) Mears, R. J.; Whiting, A. *Tetrahedron*, 1993, **49**, 177. (d) Curtis, A. D. M. ; Mears, R. J.; Whiting, A. *Tetrahedron*, 1993, **49,** 187.
3. Altenhofer, E.; Harmata, M. *Org. Lett*. **2014**, *16*, 3-5.
4. Knight, D. J.; Lin, P.; Whitham, G. H. *J. Chem. Soc., Perkin Trans. 1***1987**, 2707.
5. Uenishi, J.; Beau, J-M.; Armstrong, R. W.; Kishi, Y. *J. Am. Chem. Soc*. **1987**, *109*, 4756.

Supplementary Material

Supplementary material associated with this article can be found in the online version at: http://dx.doi.org/……