ORGANIC LETTERS

2007
Vol. 9, No. 22
4439−4442

Acid- and Pd(0)-Catalyzed Ring Opening of 1-(1-Cycloalkenyl)cyclopropyl Sulfonates

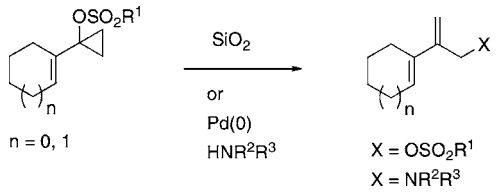
Long Guo Quan,[†] Hyung Goo Lee,[‡] and Jin Kun Cha*[,‡]

Department of Chemistry, Yanbian University, Yanji, 133002, Jilin, China, and Department of Chemistry, Wayne State University, 5101 Cass Avenue, Detroit, Michigan 48202

jcha@chem.wayne.edu

Received July 25, 2007

ABSTRACT



We report herein facile acid-catalyzed isomerization of 1-(1′-cycloalkenyl)cyclopropyl sulfonates under mild conditions. The remarkable ease of ring opening is attributed to the presence of a 1′-alkyl substituent. Also included is a palladium-catalyzed ring opening reaction of 1-(1′-cycloalkenyl)cyclopropyl tosylates for convenient preparation of substituted 1,3-dienylamines, which complements previously reported nucleophilic substitution reactions of (1-vinyl)cyclopropyl tosylates.

Solvolysis of cyclopropyl sulfonates (or halides) was extensively investigated and believed to involve a concerted ionization−ring opening process.[1] The cyclopropyl−allyl rearrangement is thus viewed as a concerted 2π-electrocyclic ring opening. Recent examples include synthetically useful preparations of 2-substituted allylic bromides by the action of magnesium bromide.[2,3] A ring-closed cyclopropyl cation can be trapped by a nucleophile in the presence of an α-substituent (e.g., cyclopropyl or phenyl) that is capable of stabilizing the developing positive charge. Surprisingly, the effects of a C1-vinyl substituent on C2−C3 ring opening or the intermediacy of the respective cyclopropyl cation have not been fully elucidated.[1] Additionally, it does not appear that effects exerted by a 1′-alkyl group of the C1-vinyl substituent were examined. We describe herein facile acid-catalyzed isomerization of 1-(1′-cycloalkenyl)cyclopropyl sulfonates under mild conditions. Also included are palladium-catalyzed ring opening reactions for convenient preparation of highly substituted 1,3-dienes.

A 1-(1′-cycloalkenyl)cyclopropyl sulfonate was first chosen as the substrate, in part, because the requisite cyclopropanol **2** was readily available by the Kulinkovich cyclopropanation of **1** (Scheme 1).[4−7] We also reasoned that, when

[†] Yanbian University.
[‡] Wayne State University.

(1) (a) Roberts, J. D.; Chambers, V. C. *J. Am. Chem. Soc.* **1951**, *73*, 5034. (b) Woodward, R. B.; Hoffmann, R. *J. Am. Chem. Soc.* **1965**, *87*, 395. (c) DePuy, C. H.; Schnack, L. G.; Hausser, J. W.; Wiedemann, W. *J. Am. Chem. Soc.* **1965**, *87*, 4006. (d) Howell, B. A.; Jewett, J. G. *J. Am. Chem. Soc.* **1971**, *93*, 798. (e) von R. Schleyer, P.; Sliwinski, W. F.; Van Dine, G. W.; Schoellkopf, U.; Paust, J.; Fellenberger, K. *J. Am. Chem. Soc.* **1972**, *94*, 125. For reviews, see: (f) Gibson, D. H.; DePuy, C. H. *Chem. Rev.* **1974**, *74*, 605. (g) Aksenov, V. S.; Terent'eva, G. A.; Savinykh, Y. V. *Russ. Chem. Rev.* (*Engl. Transl.*) **1980**, *49*, 549. (h) Salaün, J. Rearragements involving the cyclopropyl group. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley: New York, 1987; p 809. (i) Boche, G.; Walborsky, H. M. *Cyclopropane Derived Reactive Intermediates*; Wiley: New York, 1990; pp 117−173. (j) Jendralla, H. In *Houben-Weyl Methods of Organic Chemistry*; Thieme: Stuttgart, 1997; Vol. E17c, Chapter 2.4.1.3, pp 2313−2346.

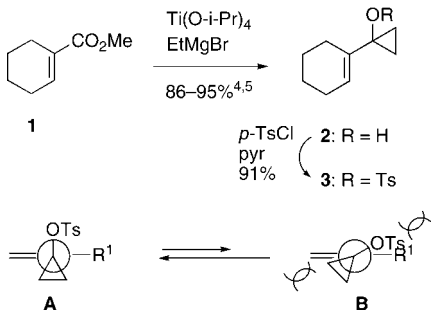
(2) (a) Kozyrkov, Y. Y.; Kulinkovich, O. G. *Synlett* **2002**, 443. (b) Kulinkovich, O. G.; Kozyrkov, Y. Y.; Bekish, A. V.; Matiushenkov, E. A.; Lysenko, I. L. *Synthesis* **2005**, 1713. (c) Kozyrkov, Y. Y.; Kulinkovich, O. G. *Synlett* **2004**, 344.

(3) See also: (a) Kirihara, M.; Kambayashi, T.; Momose, T. *J. Chem. Soc., Chem. Commun*. **1996**, 1103. (b) Kirihara, M.; Kakuda, H.; Tsunooka, M.; Shimajiri, A.; Takuwa, T.; Hatano, A. *Tetrahedron Lett.* **2003**, *44*, 8513.

(4) (a) Oh, H.-S.; Lee, H. I.; Cha, J. K. *Org. Lett.* **2002**, *4*, 3707. (b) Oh, H.-S.; Cha, J. K. *Tetrahedron: Asymmetry* **2003**, *14*, 2911.

10.1021/ol701653x CCC: $37.00
Published on Web 09/29/2007

Scheme 1

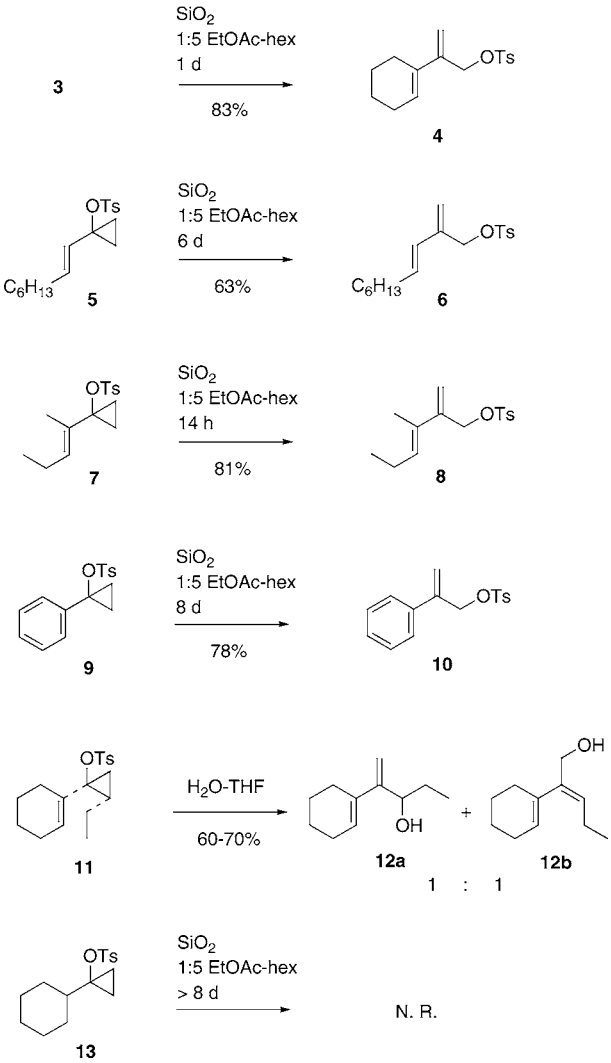


$R^1 \neq H$, minimization of allylic strain would lead to predisposition toward ring opening, as shown in conformer **A**. Despite extensive studies on solvolysis of cyclopropanol derivatives, known examples dealt with vinyl substituents where $R^1 = H$.

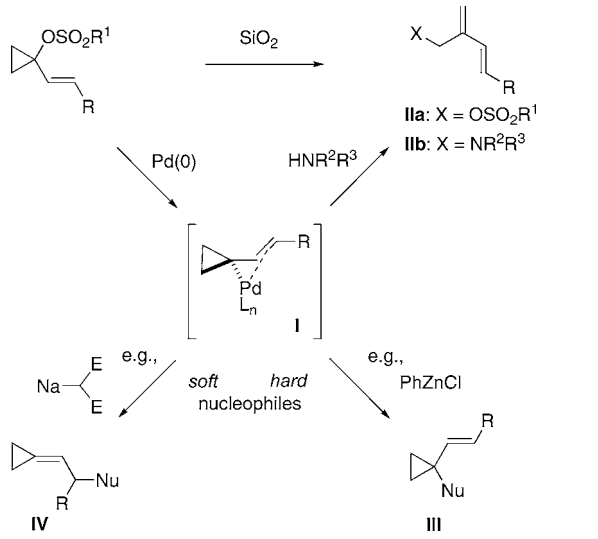
Cyclopropanol **2** was converted to tosylate **3** in excellent yield by standard methods (*p*-TsCl in pyridine). Upon exposure to SiO_2, **3** underwent facile ring opening at room temperature (within 1 day) to afford the ring-opened, allylic tosylate **4** cleanly (Scheme 2). No thermal rearrangement of **3** was observed (e.g., in a THF solution at reflux) in the absence of SiO_2. Several additional tosylates, **5**, **7**, **9**, **11**, and **13**, were next prepared to compare their reactivity toward the cyclopropyl−allyl rearrangement.[8] Both alkenyl and phenyl α-substituents promote solvolysis. More importantly, rate acceleration by an alkyl substituent at the 1′-position is conspicuous (**3** and **7** vs **5**). The presence of an alkyl group on the cyclopropane ring also quickens ring opening:[1] partial rearrangement of **11** was observed during aqueous workup. As expected, no solvolysis of **13** was observed under identical conditions.

These readily available tosylates (e.g., **4**, **6**, **8**, and **10**) are well suited for subsequent elaboration such as direct displacement and π-allylpalladium chemistry.[9] Remarkably facile ring opening of **3** (bearing a C1′-substituent) under mild acidic conditions prompted us to speculate that the π-allylpalladium complex derived from **3** could also undergo C2−C3 ring opening (e.g., **I** → **IIb**, Scheme 3). Such a

Scheme 2



Scheme 3



reaction pathway contrasts with leading contributions by Salaün and de Meijere on Pd(0)-catalyzed substitution

(5) (a) Lee, J.; Kim, H.; Cha, J. K. *J. Am. Chem. Soc.* **1995**, *117*, 9919. (b) Lee, J.; Kim, H.; Cha, J. K. *J. Am. Chem. Soc.* **1996**, *118*, 4198.

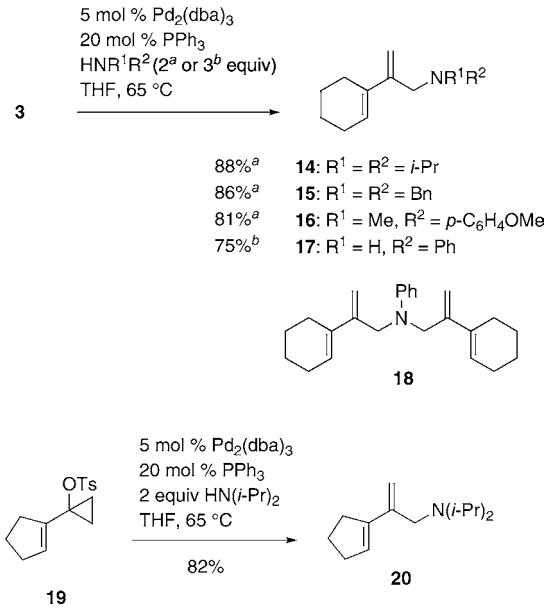
(6) For reviews on the Kulinkovich reaction, see: (a) Kulinkovich, O. G.; de Meijere, A. *Chem. Rev.* **2000**, *100*, 2789. (b) Sato, F.; Urabe, H.; Okamoto, S. *Chem. Rev.* **2000**, *100*, 2835. (c) Kulinkovich, O. G. *Eur. J. Org. Chem.* **2004**, 4517.

(7) In contrast to (1-cycloalkene)carboxylates, acyclic α,β-unsaturated esters are poor substrates for the titanium-mediated cyclopropanation reaction: (a) Racouchot, S.; Ollivier, J.; Salaün, J. *Synlett* **2000**, 1729. (b) Racouchot, S.; Sylvestre, I.; Ollivier, J.; Kozyrkov, Y. Y.; Pukin, A.; Kulinkovich, O. G.; Salaün, J. *Eur. J. Org. Chem.* **2002**, 2160.

(8) (a) The respective cyclopropanols were prepared (a) by the Kulinkovich cyclopropanation (in the case of **7**, **9**, **11**, and **13**) or (b) via the cyclopropanone hemiacetal (in the case of **5**). (b) Other acids (e.g., PPTS, *p*-TsOH) or Lewis acids are also effective for ring opening. (c) Tosylates were used in this study because of their crystalline properties, whereas other sulfonates also gave comparable results.

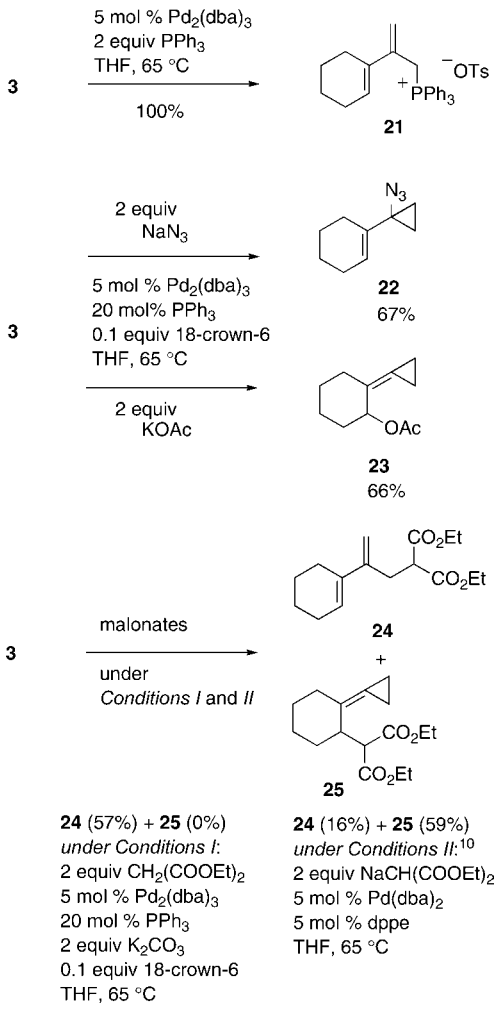
reactions, which proceed with retention of the three-membered ring with excellent regioselectivity (**I** → **III** and **I** → **IV**) depending on the nature of the nucleophiles.[10,11] In subsequent mechanistic studies, a hindered amine was chosen as the nucleophile to preclude side reactions due to small amounts of acidic impurities.[12] Under original conditions reported by Salaün and de Meijere, i.e., 2−5 mol % of $Pd(dba)_2$/dppe (1:2) as catalyst in THF at reflux, the starting tosylate **3** remained unchanged with formation of only trace amounts of **14** in the presence of diisopropylamine (2 equiv). By employing 5 mol % of $Pd_2(dba)_3$ and 20 mol % of Ph_3P in refluxing THF, **14** was obtained as the sole product in 88% yield (Scheme 4). Use of other amines also provided

Scheme 4



15−**17** in good yields. In the case of aniline, use of 3 equiv was beneficial. When 2 equiv was employed, **17** was isolated in 66% yield, along with the bisalkylation product **18** (11%). Similarly, **20** was prepared in comparable yield from **19**. When Ph_3P was employed as the nucleophile in place of an amine, the phosphonium salt **21** was obtained in quantitative yield (Scheme 5).[13] Use of the sulfonates precluded the

Scheme 5



potential complication due to the otherwise facile ring expansion pathway (i.e., the cyclopropylcarbinyl → cyclobutyl rearrangement) that could be induced by Pd(II) or acidic impurities.[4,14−16]

Other nucleophiles, which the Salaün and de Meijere groups had used,[10] were next examined for comparison studies: the nature of nucleophiles and the ligands (e.g., monodentate vs bidentate) also affected the reaction course. Pd(0)-catalyzed reactions with NaN_3 or potassium acetate

(9) For example, treatment of **4** with sodium malonate or KOAc under typical π-allylpalladium reaction conditions yielded the corresponding displacement products in excellent yields.

(10) (a) Stolle, A.; Salaün, J.; de Meijere, A. *Tetrahedron Lett.* **1990**, *31*, 4593. (b) Stolle, A.; Ollivier, J.; Piras, P. P.; Salaün, J.; de Meijere, A. *J. Am. Chem. Soc.* **1992**, *114*, 4051. (c) Aufranc, P.; Ollivier, J.; Stolle, A.; Bremer, C.; Es-Sayed, M.; de Meijere, A.; Salaün, J. *Tetrahedron Lett.* **1993**, *34*, 4193. (d) Atlan, V.; Racouchot, S.; Rubin, M.; Bremer, C.; Ollivier, J.; de Meijere, A.; Salaün, J. *Tetrahedron: Asymmetry* **1998**, *9*, 1131. (e) Lecornué, F.; Charnay-Pouget, F.; Ollivier, J. *Synlett* **2006**, 1407.

(11) For a review, see: Salaün, J. *Chem. Rev.* **2005**, *105*, 285.

(12) In view of lability of **3** toward SiO_2, no silica gel column chromatography was undertaken for purification. Instead, an aqueous workup procedure, followed by trituration or recrystallization, was used to secure **3**: experimental details are given in the Supporting Information.

(13) Wittig olefination of **21** with octanal in the presence of *n*-BuLi took place smoothly to give the corresponding triene (structure not shown) as a 6:1 mixture of *E*- and *Z*-isomers in 68% (unoptimized) yield.

(14) (a) Trost, B. M. *Top. Curr. Chem.* **1986**, *133*, 3. (b) Trost, B. M.; Brandi, A. *J. Am. Chem. Soc.* **1984**, *106*, 5041. (c) Trost, B. M.; Lee, D. C. *J. Am. Chem. Soc.* **1988**, *110*, 6556. (d) Trost, B. M.; Chen, D. W. C. *J. Am. Chem. Soc.* **1996**, *118*, 12541.

(15) For a review, see: (a) Salaün, J. *Top. Curr. Chem.* **1988**, *144*, 1. Cf. (b) Boontanonda, P.; Grigg, R. *J. Chem. Soc., Chem. Commun.* **1977**, 583. (c) Clark, G. R.; Thiensathit, S. *Tetrahedron Lett.* **1985**, *26*, 2503. (d) Nemoto, H.; Shiraki, M.; Fukumoto, K. *Synlett* **1994**, 599. (e) Mitchell, D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1990**, *112*, 291. (f) Larock, R. C.; Reddy, C. K. *Org. Lett.* **2000**, *2*, 3325. (g) Yoshida, M.; Sugimoto, K.; Ihara, M. *Org. Lett.* **2004**, *6*, 1979.

(16) To exclude the possible intermediacy of the allyl tosylate **4** by an initial rearrangement, a control experiment was performed without a palladium catalyst, in which the starting tosylate **3** was recovered unreacted. Additionally, aromatic and alkyl cyclopropyl tosylates **9** and **13** were stable under these conditions. The selective formation of **23** is in accord with the intermediacy of a π-allylpalladium complex, and an alternate cyclopropyl−allyl rearrangement induced by a Pd(II) species might be ruled out.

in the presence of 18-crown-6 displayed the regioselectivity (i.e., **22** and **23**) identical to literature results.[10,16,17] On the other hand, the cognate reactions with malonates hinged upon reaction conditions: use of diethyl malonate, K_2CO_3, and 18-crown-6 (conditions I) gave **24** in 57% yield. Adaptation of Salaün and de Meijere's conditions (conditions II) afforded a 1:3.4 mixture of **24** and **25** in 75% yield. These results contrast with exclusive formation of 2-cyclopropylidene esters from acyclic 1-(1′-vinyl)cyclopropyl sulfonates.[10,11] Although full elucidation of key factors that control the reaction pathways must await further studies, the π-allylpalladium complexes derived from 1-(1′-cycloalkenyl)-cyclopropyl sulfonates seem to be predisposed toward ring opening. This propensity toward ring opening might be attributed to minimization of allylic strain (see **A** in Scheme 1).[18]

In summary, the acid- and palladium-catalyzed ring opening reactions of 1-(1′-cycloalkenyl)cyclopropyl sulfonates were investigated for the facile preparation of highly substituted 1,3-dienes. The ease of acid-catalyzed ring opening is particularly noteworthy and could be attributed to quite large accelerating effects of 1′-substitution on ring opening. The palladium-mediated ring opening of 1-(1′-cycloalkenyl)cyclopropyl tosylates presents an interesting contrast to nucleophilic substitutions of (1-vinyl)cyclopropyl tosylates with retention of the three-membered ring. Since the starting (1′-cycloalkenyl)cyclopropanols are readily available by the Kulinkovich reaction of cycloalkene carboxylates, the present method provides convenient access to functionalized 1,3-dienes starting from esters.

Acknowledgment. We thank the National Institutes of Health (GM35956) and the National Science Foundation (CHE-0615604) for generous financial support.

Supporting Information Available: Additional examples of palladium-catalyzed reactions of 1-(1′-alkenyl)cyclopropyl tosylates, along with experimental details and spectroscopic data for key intermediates. This material is available free of charge via the Internet at http://pubs.acs.org.

OL701653X

(17) Allylic azides are known to undergo facile equilibration by [3,3]-sigmatropy, which complicates mechanistic analysis: (a) Vander Werf, C. A.; Heisler, R. Y.; McEwen, W. E. *J. Am. Chem. Soc*. **1954**, *76*, 1231. (b) Gagneux, A.; Winstein, S.; Young, W. G. *J. Am. Chem. Soc*. **1960**, *82*, 5956. (c) Feldman, A. K.; Colasson, B.; Sharpless, K. B.; Fokin, V. V. *J. Am. Chem. Soc*. **2005**, *127*, 13444.

(18) Additional comparison studies are available in the Supporting Information.