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Synthesis of 1-(2′-Phenyl)cyclopropyl-2,3-epoxypropan-1-ol as the Radical Precursor for the Kinetic Study of Oxiranylcarbinyl Radical

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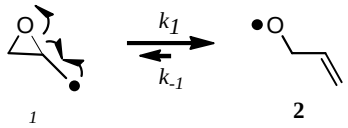
Abstract: We have successfully synthesized 1-(2′-phenyl)cyclopropyl-2,3-epoxypropan-1-ol **3**, which will be applied to the kinetics study of oxiranylcarbinyl radical.

Keywords: Synthesis, radical reaction, rearrangement.

The oxiranylcarbinyl radical can undergo rapid rearrangement to generate an allyloxy radical (**1** → **2**)[1]. This process has been found application in organic synthesis[2]. For example, Rawal developed a novel method leading to *cis*-fused bicyclic compounds based on tandem reactions of oxiranylcarbinyl radical ring opening - intramolecualr H abstraction - radical addition[2f].



1 **2**

On the other hand, the oxiranylcarbinyl radical rearrangement is so rapid that this radical species has never been directly identified spectroscopically[3]. There have been considerable efforts devoted to the study of kinetics of oxiranylcarbinyl radical rearrangement in recent years[1b,4,5]. We have been attempting the possibility to determine the rate constant of **1** → **2** with intramolecular competition method (**Scheme 1**)[4]. In this paper, we report the successful synthesis of 1-(2′-phenyl)cyclopropyl-2,3-epoxypropan-1-ol **3**, which is the precursor for generating radical **4**.

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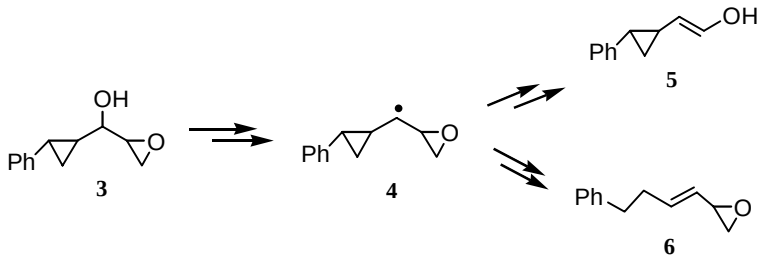
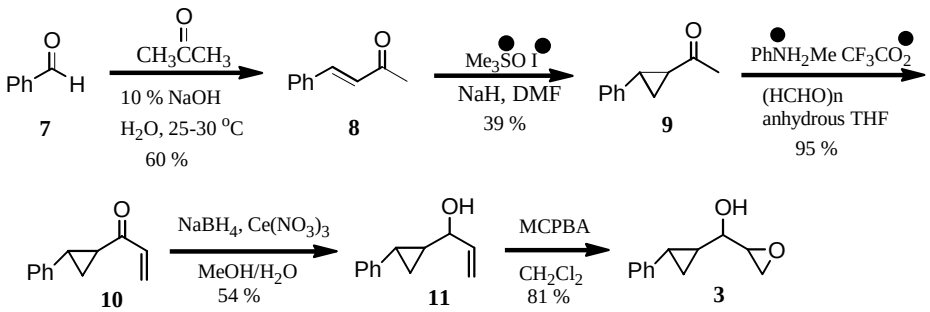
Scheme 1



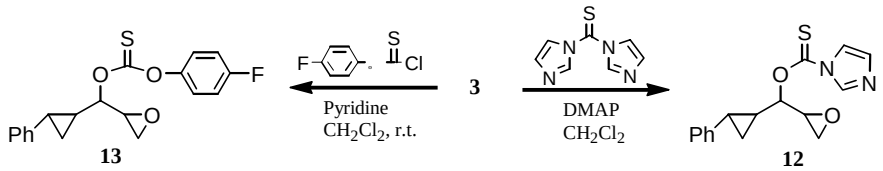
The synthetic pathway for **3** is shown in **Scheme 2**. Claisen-Schmidt reaction of benzaldehyde **7** with acetone under basic condition gave α, β–unsaturated ketone **8** in 60 % yield. In this reaction, excess amount of acetone is needed in order to avoid the further reaction of the product **8** with benzaldehyde to form dibenzylideneacetone[6]. Next step is the cyclopropanation of the double bond of **8**. This was originally attempted with Simmon-Smith reaction. However, the CH_2I_2-$Cu(OAc)_2$/Zn combination[7] did not provide the required product. Instead, a complex mixture was formed. We then tried dimethyloxosulfonium methylide generated from trimethyloxosulfonium iodide[8]. This reaction provided the expected product **9** in 39 % yield. The ketone **9** was converted to α–methylene ketone **10** with paraformaldehyde and *N*-methylanilinium trifluoroacetate[9].

Scheme 2



Selective reduction of the carbonyl group of the α, β–unsaturated carbonyl compound with $NaBH_4/Ce(NO_3)_3$[10] yielded a mixture of the diastereomeric alcohol, which was separated by column chromatography to give the major isomer **11** in 54 % yield. The allylic alcohol was oxidized with MCPBA[11] in CH_2Cl_2 at room temperature to give the target compound 1-(2′-phenyl)cyclopropyl-2, 3-epoxypropan-1-ol **3** in 81 % yield as diastereomeric mixture (~ 2 : 1)[12].

Scheme 3



With the alcohol **3** in hand, we proceeded to convert it to **12**, from which radical **4** could be generated by treating with Bu_3SnH[13]. Preliminary investigation of **12** indicated that it was unstable at room temperature. It decomposed considerably in column chromatography. However, the esterification of a simple alcohol gave the corresponding ester as a stable compound. Further work is under the way to study the ester **12** in detail and also to look for other esters, such as **13**[14], which can be converted to radical **4**.

Acknowledgment

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References and Notes

1. For recent study on Oxiranylcarbinyl radicals, see:
   (a) D. M Smith, A. Nicolaides, B. T. Golding, *J. Am. Chem. Soc.*, **1998**, *120*, 10223.
   (b) L. Grossi, S. Strazzari, B. C. Gibert, A. C. Whitwood, *J. Org. Chem.*, **1998**, *63*, 8366.
   (c) F. E. Ziegler, A. K. Petersen, *ibid*, **1995**, *60*, 2666.
2. For examples, see:
   (a) D. A. Corser, B. A. Marples, R. K. Dart, *Synlett*, **1992**, 987.
   (b) F. E. Ziegler, A. K. Petersen, *J. Org. Chem.*, **1994**, *59*, 2707.
   (c) M. J. Begley, N. Housden, A. Johns, J. A. Murphy, *Tetrahedron*, **1991**, *47*, 8417.
   (d) H. –S. Dang, B. P. Roberts, *Tetra. Lett.*, **1992**, *33*, 6169.
   (e) H. Suginome, J. B. Wang, *J. Chem. Soc., Chem. Commun.*, **1990**, 1629.
   (f) V. H. Rawal, R. C. Newton, V. Krishnamurthy, *J. Org. Chem.*, **1990**, *55*, 5181.
3. D. Laurie, D. C. Nonhebel, C. J. Suckling, J. C. Walton, *Tetrahedron*, **1993**, *49*, 5869.
4. K. W. Krosley, G. J. Gleicher, *J. Phys. Org. Chem.*, **1993**, *6*, 228.
5. V. Krishnamurthy, V. H. Rawal, *J. Org. Chem.*, **1997**, *62*, 1572.
6. N. L. Drake, P. Allen, Jr. *Organic Synthesis*, *Coll. Vol. 1*, **1941**, 77.
7. J. M. Conia, J. C. Limasser, *Tetra. Lett.*, **1965**, *35*, 3151.
8. E. J. Corey, M. Haykovsky, *J. Am. Chem. Soc.*, **1965**, *87*, 1353.
9. J. –L. Grass, *Tetra. Lett.*, **1978**, *24*, 2111.
10. A. L. Geneal, J. L. Luche, *J. Am. Chem. Soc.*, **1981**, *103*, 5454.
11. a) B. E. Rossiter, T. R. Verhoeven, K. B. Sharpless, *Tetra. Lett.*, **1979**, *49*, 4733.
    b) E. D. Mihelich, *ibid*, **1979**, *49*, 4729. c) M. R. Johnson, Y. Kishi, *ibid*, **1979**, *49*, 4347.
12. ^{1}H NMR (400 MHz, $CDCl_3$) data for new compounds. **9**: δ 1.29 (m, 1H), 1.66 (m, 1H), 2.29 (s, 3H), 2.51 (m, 1H), 7.08 (m, 2H), 7.22 (m, 1H), 7.28 (m, 2H); **10**: δ 1.46 (m, 1H), 1.76 (m, 1H), 2.43 (m, 1H), 2.58 (m, 1H), 5.82 (d, 1H, *J* 10.5 Hz), 6.28 (d, 1H, *J* 17.4 Hz), 6.49 (dd, 1H, *J* 10.5, 17.4 Hz), 7.11 (m, 2H), 7.22 (m, 1H), 7.28 (m, 2H); **11**: δ 0.97 (m, 2H), 1.35 (m, 1H), 1.97 (m, 1H), 3.78 (m, 1H), 5.16 (dt, 1H, *J* 1.4, 10.4 Hz), 5.30 (dt, 1H, *J* 1.4, 17.1 Hz), 5.99 (ddd, 1H, *J* 5.8, 10.5, 17.2 Hz), 7.09 (m, 2H), 7.16 (m, 1H), 7.26 (m, 2H); **3,** major isomer: 0.99 (m, 2H), 1.36 (m, 1H), 2.11 (m, 2H), 2.76 (dd, 1H, *J* 2.5, 4.9 Hz), 2.83 (dd, 1H, *J*

3.9, 4.9 Hz), 3.17 (m, 2H), 7.08 (m, 2H), 7.15 (m, 1H), 7.25 (m, 2H).
13. a) D. H. R. Barton, S. W. McCombie, *J. Chem. Soc., Perkin Trans 1*, **1975**, 1574.
    b) D. H. R. Barton, W. B. Motherwell, A. Stange, *Synthesis*, **1981**, 743.
14. D. H. R. Barton, D. O. Jang, J. C. Jaszberenyi, *Synlett*, **1991**, 435.

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