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Skeletal Rearrangement *via* Alkoxy Radical: Conversion of Epoxydecalin Thiocarbonylimidazolide to Bicyclo[6.3.0]undecanone and Bicyclo[5.3.1]undecanone

Atsushi Nishida,*[1] You-Ichirou Kakimoto, Yukie Ogasawara, Norio Kawahara, Mayumi Nishida,[†] and Hiroaki Takayanagi[‡]

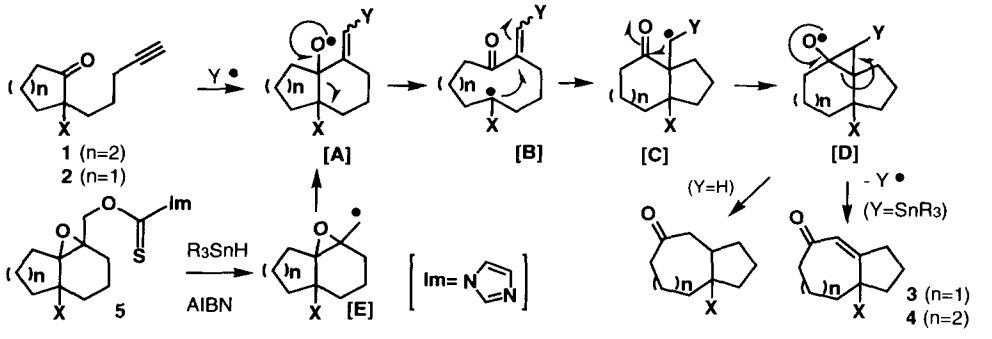
Hokkaido Institute of Pharmaceutical Sciences, 7-1 Katsuraoka, Otaru 047-02, Japan
[†]Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060, Japan
[‡]School of Pharmaceutical Sciences, Kitasato University, 5-9-1 Shirokane, Minato-ku, Tokyo 108, Japan

Abstract: The radical reaction of three epoxydecalin thiocarbonylimidazolides was investigated using nBu$_3$SnH and AIBN. Two types of rearrangement from a ten-membered cyclic carbon radical, which was formed by β-cleavage of alkoxy radicals, were observed. © 1997 Elsevier Science Ltd.

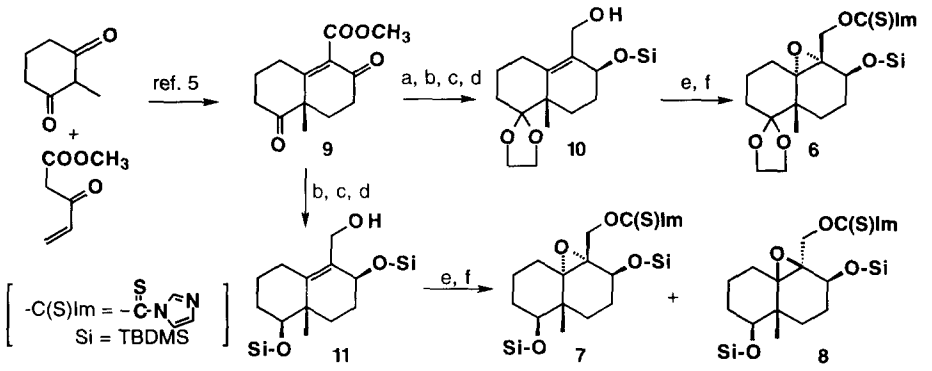
The β-cleavage reaction of alkoxy radicals has recently been recognized as a useful method for the transposition of radical centers, and sometimes occurs with skeletal rearrangement.[2] We previously reported the skeletal rearrangements of cycloalkanones (**1** and **2**) with a pentynyl side chain to bicyclic cycloheptenones **3** and cyclooctenones **4** (Scheme 1).[3] The bicyclic alkoxy radical intermediate [A], which was generated by the intramolecular addition of stannylalkenyl radical to a carbonyl group, caused this rearrangement. Pattenden also reported radical skeletal rearrangement from a related intermediate.[4]

However, in the reactions of **1** and **2**, the efficiency of the transformation was highly dependent on the structure of the substrate. The reaction proceeded smoothly when substituent X was a silyloxy group. However, when X was a carbon functionality, the yields of the rearranged products were less than 20%. Substituent X may affect the efficiency of the first step in cyclization through both electronic and steric effects. To obtain more information about these reactions, we examined the radical reaction of **5**, which should generate the same alkoxy radical [A] with defined stereochemistry *via* fragmentation of the epoxy-methyl radical [E]. We report here a radical skeletal rearrangement using epoxydecalin thiocarbonylimidazolides.

Scheme 1



Scheme 2

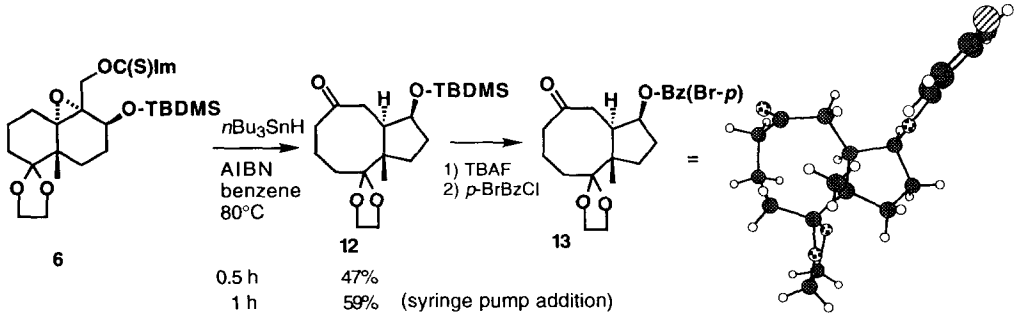


a) ethylene glycol, TsOH, b) $NaBH_4$, c) TBDMS-Cl, imidazole, d) DIBAH, e) mCPBA, f) 1,1'-thiocarbonyldiimidazole, Et_3N, $ClCH_2CH_2Cl$, reflux.

Three epoxydecalin thiocarbonylimidazolides, **6**, **7** and **8**, were prepared from known bicyclic diketoester **9**[5] (Scheme 2). Compound **9** was converted to **10** by monoketalization and sequential reduction of the α,β-unsaturated keto-ester functionality. Epoxidation of **10** using mCPBA gave a single epoxide whose stereochemistry was determined to be α-epoxide by X-ray analysis. This epoxide was converted to thiocarbonylimidazolide **6** in the usual manner. Sodium borohydride reduction of **9** at -78 °C gave two diols as diastereoisomers at the allylic stereo center (α:β=1:2). These could be separated after conversion to bissilylether. Separated β-alcohol was then converted to **11**, which was epoxidized by mCPBA to give two epoxides. These epoxides were separated and the stereochemistry of both epoxides was again determined by X-ray analysis (Scheme 6). Both epoxides were converted to radical precursors **7** and **8**.

When a mixture of **6**, nBu$_3$SnH (2 eq), and AIBN in benzene was heated for 0.5 h at 80 °C, the rearranged product **12** was obtained at a yield of 47% (Scheme 3). Slow addition of a solution of nBu$_3$SnH and AIBN using a syringe pump for 1 h improved the yield of **12** (59%).The structure of **12** was elucidated spectroscopically and finally determined by X-ray crystallographic analysis after conversion to **13**. The relative stereochemistry between the silyloxy group and the methyl group was retained, and the stereochemistry of the ring juncture was *trans*. No *cis* isomer was observed in this reaction.[4]

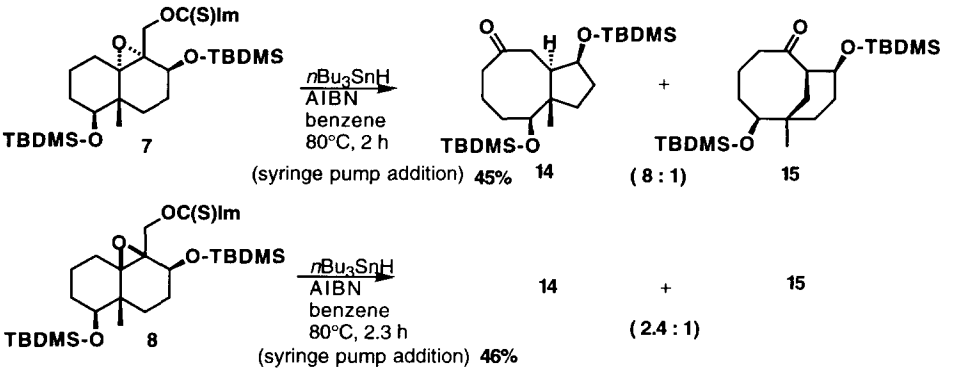
Scheme 3



The radical reaction of *trans*-bissilyl ether **7** gave two products, **14** and **15**, in a ratio of 8:1 in 45% yield (Scheme 4). Their structures were determined by X-ray crystallographic analysis after conversion to crystalline derivatives **16** and **17** (Fig. 1). The major product **14** had a *trans*-bicyclo[6.3.0]skeleton, and the relative stereochemistries of the starting material were retained. The minor product **15** was a bicyclo[5.3.1]-undecanone derivative. This is the first *endo*-cyclized product isolated and characterized in these radical reactions (Scheme 5).

If the conformation of the ten-membered cyclic carbon radical **18** can readily change before recyclization, both **7** and its stereoisomer **8** should yield the same products in the same ratio. However, *cis*-bissilyl ether **8** gave a mixture of **14** and **15** in a ratio of 2.4:1, in 46% yield. These results indicate that the ten-membered radical intermediates from **7** and **8** have different conformations which are imposed by the structures of **7** and **8**, and that they cyclize before attaining complete equilibrium (Scheme 6). It is unclear why **8** yielded more of the *endo*-cyclized product.

Scheme 4



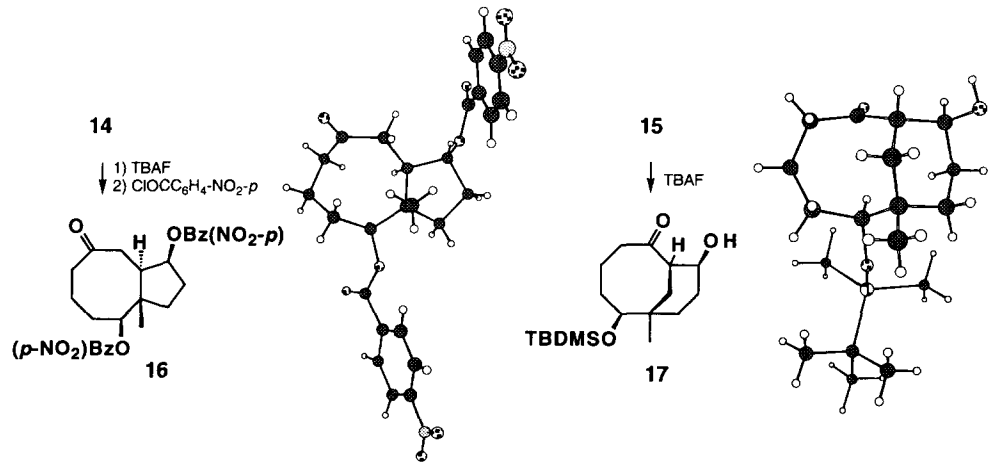
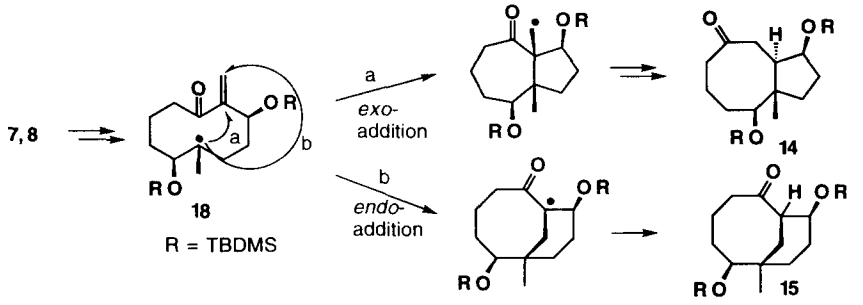
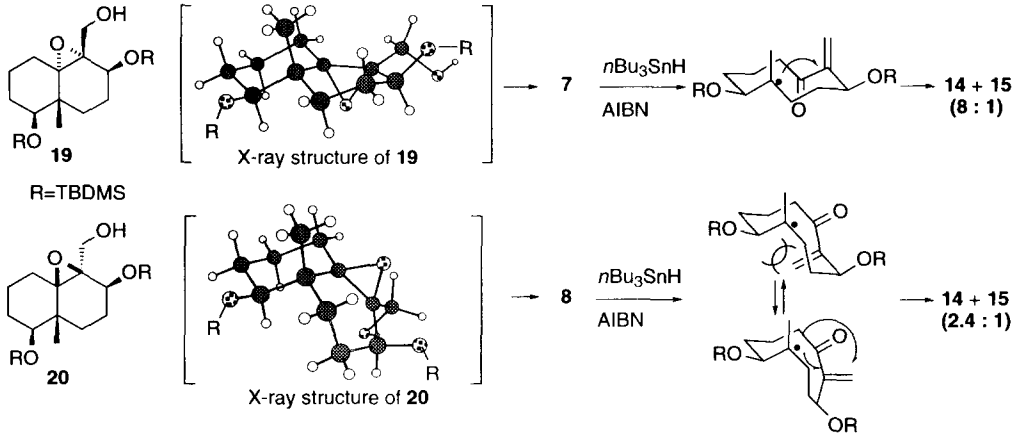


Figure 1. X-ray structures of **16** and **17**.

Scheme 5



Scheme 6



References and Notes

1) Present address: Faculty of Pharmaceutical Sciences, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba-shi 263, Japan, e-mail: nishida@p.chiba-u.ac.jp.

2) Dowd P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091-2115.

3) a) Nishida, A.; Takahashi, H.; Takeda, H.; Takada, N.; Yonemitsu, O. *J. Am. Chem. Soc.* **1990**, 112, 902-904, b) Nishida, A.; Ogasawara, Y.; Kawahara, N.; Nishida, M. *Tetrahedron Letters*, **1995**, *36*, 3015-3018.

4) a) Elwood, C. W.; Pattenden, G. *Tetrahedron Letters*, **1991**, *32*, 1591-1594, b) Mowbray, C. E.; Pattenden G. *Tetrahedron Letters*, **1993**, *34*, 127-130.

5) Pelletier, S. W.; Chappell, R. L.; Parabbakar, S. *J. Am. Chem. Soc.* **1968**, 90, 2889-2895.

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