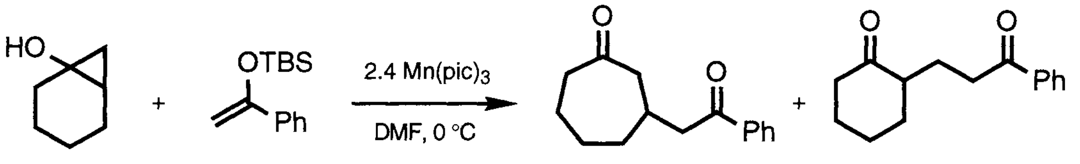
CHEMISTRY LETTERS, pp. 545-548, 1993.

Synthesis of Medium-Sized Bicyclic Compounds by Intramolecular Cyclization of Cyclic β-Keto Radicals Generated from Cyclopropanols Using Manganese(III) Tris(2-pyridinecarboxylate)

Nobuharu IWASAWA, Masahiro FUNAHASHI, Satoshi HAYAKAWA, and Koichi NARASAKA
Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

Bicyclic cyclopropanols having olefinic side chain are oxidized with Mn(pic)$_3$ to generate cyclic β-keto radicals with ring-expansion, which cyclize intramolecularly affording bicyclic radical intermediates. The cyclized radicals are trapped with various radical-trapping reagents such as electron-rich or -deficient olefins, tributyltin hydride and diphenyl diselenide to give the corresponding functionalized products.

In the previous papers, we reported that treatment of cyclopropanol derivatives with manganese(III) tris(2-pyridinecarboxylate) (Mn(pic)$_3$) generates β-keto radicals, which add to either electron-rich or electron-deficient olefins to give the corresponding intermolecular addition products in good yields.[1, 2] In this reaction, oxidation of 2-alkyl-substituted cyclopropanols produces preferentially β-keto radicals having more substituents. For example, treatment of bicyclo[4.1.0]heptan-1-ol (**1**) with Mn(pic)$_3$ in the presence of a silyl enol ether gave a ring-expanded cycloheptanone derivative **2** as a major product as shown in Eq. 1.[1]

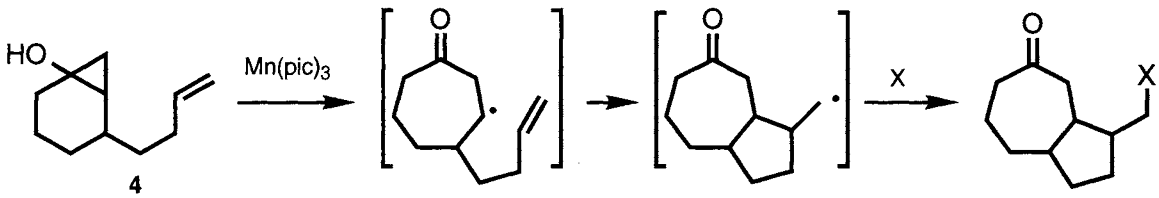


(1)

1 TBS = Bu^{t}Me$_2$Si **2** 77% **3** 5%

Application of the above reaction to the intramolecular reaction was examined to realize an efficient method for the construction of bicyclic carbon frameworks having medium-sized rings, which are commonly seen in the basic skeletons of natural products such as guaianolides and pseudoguaianolides. In this communication, we would like to report the preliminary accounts of this work.[3]

First, a bicyclo[4.1.0]heptan-1-ol derivative **4** having 3-butenyl group at C$_5$ position was chosen as a substrate.[4] As shown in Scheme 1, oxidation of this compound with Mn(pic)$_3$ is expected to produce a ring-

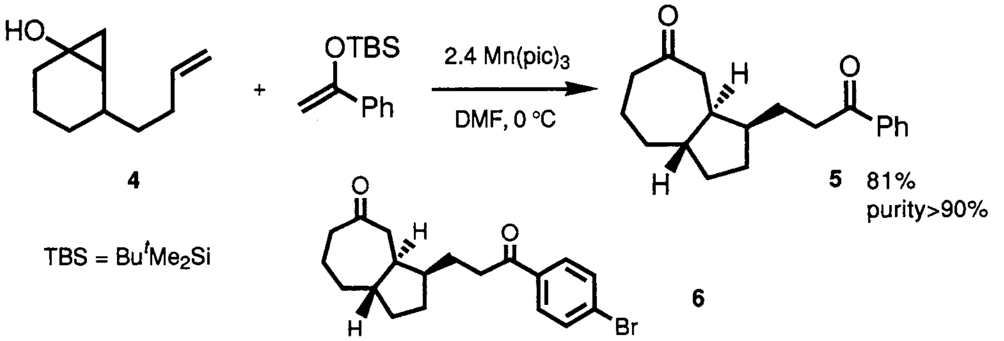


4 **A** **B** X = radical-trapping reagent

Scheme 1.

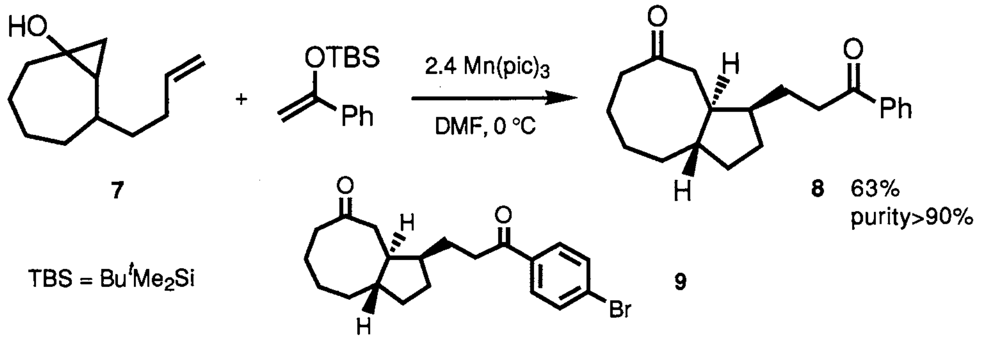
expanded β-keto radical **A**, which would add to the C-C double bond of the side chain in an exo manner intramolecularly[5)] to give a radical intermediate **B** having bicyclo[5.3.0]decan-3-one skeleton selectively. Finally, various functionalities could be introduced by the successive reaction of the radical **B** with various radical-trapping reagent **X** .

The reaction was carried out in the presence of an electron-rich olefin as a radical-trapping reagent. Thus, treatment of **4** with 2.4 mole amounts of Mn(pic)$_3$ in DMF in the presence of 2.5 mole amounts of α-(*tert*-butyldimethylsiloxy)styrene at 0 °C produced the desired ring-expanded bicyclo[5.3.0]decan-3-one derivative **5** in 81% yield in more than 90% purity. Two inseparable minor products were also detected in less than 5% respectively as judged by GC, ^{1}H NMR, and ^{13}C NMR, but **5** was isolated in pure form by recrystallization from hexane and ethyl acetate.[6)] The stereochemistry of **5** was deduced from the X-ray structural analysis of **6**[6)] synthesized from **4** and α-(*tert*-butyldimethylsiloxy)-4-bromostyrene, to have the relative stereochemistry as shown in Eq. 2.



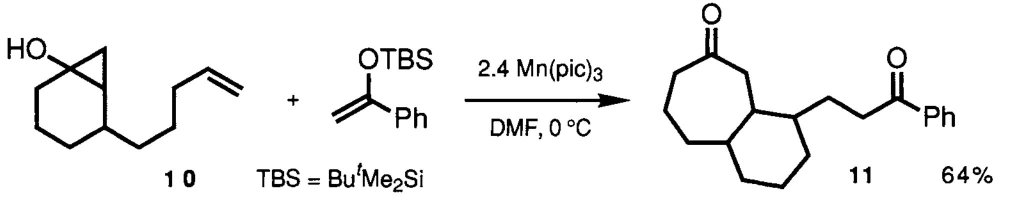
(2)

The same type of intramolecular cyclization with ring expansion proceeded in the case of a bicyclo[5.1.0]-octan-1-ol derivative **7**. The reaction of 6-(3-butenyl)bicyclo[5.1.0]octan-1-ol (**7**) with Mn(pic)$_3$ in the presence of α-(*tert*-butyldimethylsiloxy)styrene under the same conditions gave a bicyclo[6.3.0]undecan-3-one derivative **8** in the yield of 63%. In this case, **8** was also produced in more than 90% purity, and the stereochemistry of **8** was deduced from the X-ray structural analysis of **9**,[6)] which was prepared from **7** and α-(*tert*-butyl-dimethylsiloxy)-4-bromostyrene, to have the relative stereochemistry in Eq. 3.



(3)

As described above, the reactions proceeded stereoselectively when the ring-expanded radicals added to the olefinic part of the side chain in an exo manner to form a five-membered ring. Then, the reaction of a bicyclo-[4.1.0]heptan-1-ol derivative **10** having 4-pentenyl group at C$_5$ position was examined. In this case, it is expected that bicyclo[5.4.0]undecan-3-one skeleton would be formed by the attack of the ring-expanded β–keto radical on the olefinic part of the side chain in an exo manner. The reaction of 5-(4-pentenyl)bicyclo[4.1.0]-heptan-1-ol (**10**) gave almost equal amounts of two isomeric ring-expanded products **11** in 64% yield. Although these two products were determined to have the expected bicyclo[5.4.0]undecan-3-one skeletons from NMR spectra, the relative stereochemistry of these products **11** could not yet be established by spectroscopic methods.

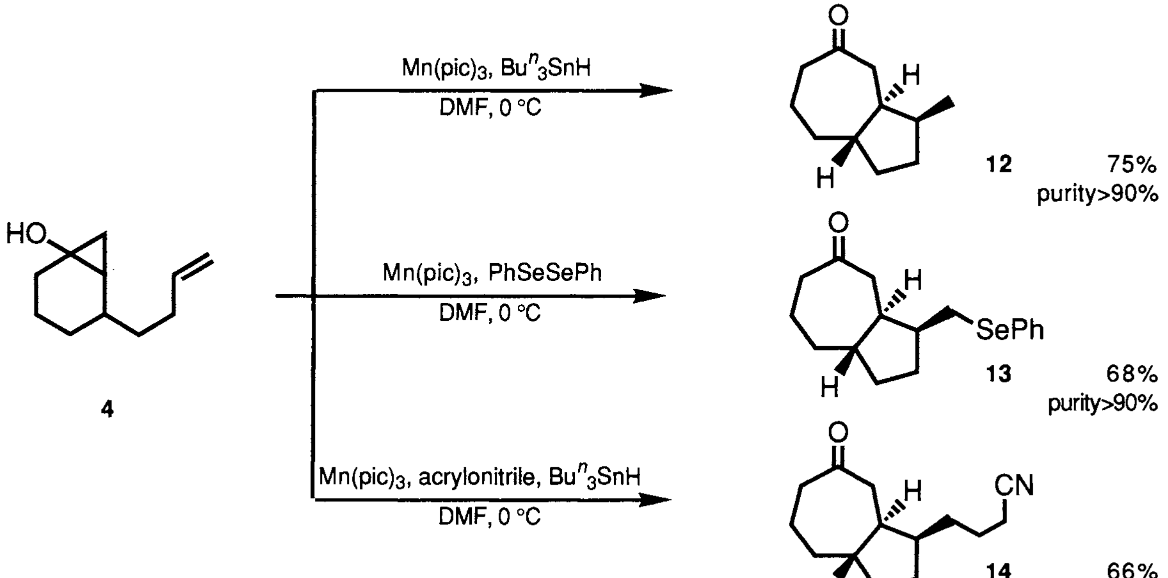


(4)

Next, employing **4** as a substrate, the reactions using some other radical-trapping reagents were examined to introduce various functionalities onto the side chain at C_{10} position. We have already reported that β-keto radicals oxidatively generated from cyclopropanols using Mn(pic)$_3$ can be directly trapped by PhSeSePh to give β-seleno ketones, or can add to electron-deficient olefins such as acrylonitrile by carrying out the reaction in the presence of $Bu^n{}_3SnH$.[2)]

When 5-(3-butenyl)bicyclo[4.1.0]heptan-1-ol (**4**) was treated with Mn(pic)$_3$ in DMF at 0 °C in the presence of 1.5 mole amounts of $Bu^n{}_3SnH$ as a radical-trapping reagent, a bicyclo[5.3.0]decanone derivative **12** of which side chain at C_{10} position is methyl group was produced in the yield of 75% with hydrogen atom abstraction of the radical intermediate **B** from $Bu^n{}_3SnH$. The same reaction in the presence of 0.75 mole amounts of PhSeSePh instead of $Bu^n{}_3SnH$ afforded the corresponding cyclized product **13** containing a selenomethyl group at C_{10} position in 68% yield. Furthermore, by carrying out the reaction in the presence of 1.5 mole amounts of $Bu^n{}_3SnH$ and 3.0 mole amounts of acrylonitrile as an electron-deficient olefin, the addition product **14** was obtained in the yield of 66%.

All of these reactions proceeded in high stereoselectivity to afford the corresponding products in more than 90% purity. The stereochemistry of these compounds is not established unambiguously, but it is assumed that these compounds have the same relative stereochemistry as that of **6**.



Scheme 2.

Quite recently, the same type of radical cyclization reaction was reported using $FeCl_3$ as an oxidant,[7)] in which the cyclized radical intermediates were trapped by chlorine atom and other radical-trapping reagents were not employed.[8)] On the contrary, the present reaction employing Mn(pic)$_3$ as an oxidant enables the use of a variety of radical-trapping reagents and makes it possible to introduce various functionalities onto the side chain of the product.

The present work was partially supported by the Sumitomo Foundation and Grant-in-Aid for Scientific Research on Priority Areas (Multiplex Organic Systems) from the Ministry of Education, Science and Culture. The authors would like to thank Drs. A. Kobayashi and Y. Hayashi at the University of Tokyo, and Dr. H. Ichida at Institute for Molecular Science for the performance of X-ray analysis.

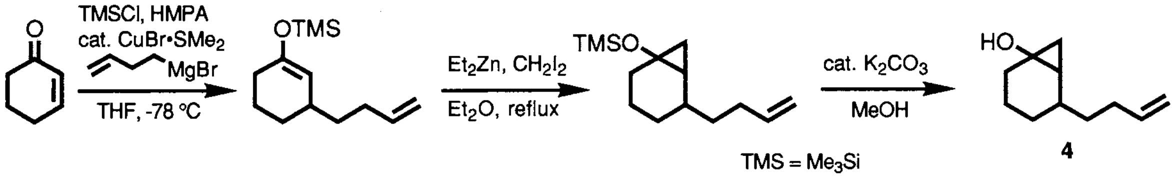
References

1) N. Iwasawa, S. Hayakawa, K. Isobe, and K. Narasaka, *Chem. Lett.*, **1991**, 1193.

2) N. Iwasawa, S. Hayakawa, M. Funahashi, K. Isobe, and K. Narasaka, *Bull. Chem. Soc. Jpn.*, in press.

3) M. Funahashi, N. Iwasawa, and K. Narasaka, 63rd National Meeting of the Chemical Society of Japan, Osaka, March 1992, Abstr., No. 3E305

4) The substrate **4** was easily prepared from 2-cyclohexen-1-one in 3 steps in 70% overall yield; that is, i) a copper(I) catalyzed conjugate addition of 3-butenyl magnesium bromide to 2-cyclohexen-1-one in the presence of trimethylsilyl chloride; ii) Simmons-Smith cyclopropanation with diiodomethane and diethylzinc; iii) methanolysis catalyzed by potassium carbonate. The other cyclopropanols **7** and **10** were prepared in the same manner.

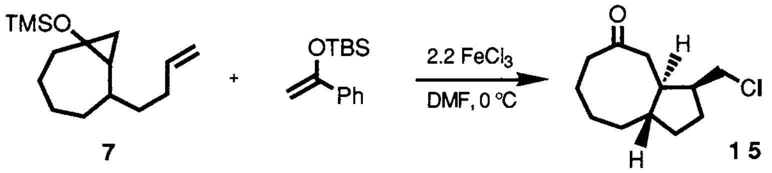


5) A. L. J. Beckwith, *Tetrahedron*, **37**, 3073 (1981).

6) Melting points of **5**, **6**, and **9** were 98 °C, 94 °C, and 79 °C respectively.

7) K. I. Booker-Milburn, *Synlett*, **1992**, 809.

8) The reaction of a trimethylsilyl ether of cyclopropanol **7** with $FeCl_3$ in the presence of α-(*tert*-butyldimethylsiloxy)styrene was attempted according to Ref. 7. However, the addition product **8** was not obtained at all, and a chlorinated product **15** was obtained in 33% yield.



(Received December 28, 1992)