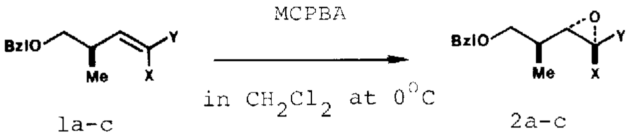
Tetrahedron Letters Vol. 21, pp 4229 - 4232
0040-4039/80/1029-4229$02.00/0

FURTHER STUDIES ON STEREOSPECIFIC EPOXIDATION OF ALLYLIC ALCOHOLS

Iltifat Hasan and Yoshito Kishi*
Department of Chemistry, Harvard University
12 Oxford Street, Cambridge, MA 02138, U. S. A.

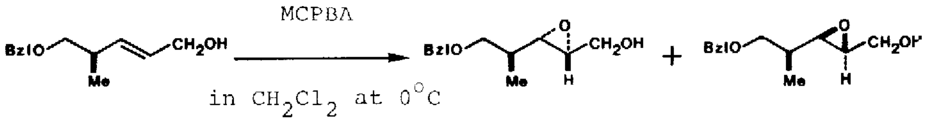
Abstract: A stereosepcific synthesis of the epoxides 4 and 12c is described

We have recently reported that epoxidation of allylic alcohols 1a-c with m-chloroperbenzoic acid yields the epoxides 2a-c exclusively in a practical sense, while 3 yields a 3:2 mixture of the two possible epoxides 4 and 5.[1] The dramatic difference in the degree of the stereoselectivity observed was attributed to the difference in the degree of relative stability of one eclipsed conformation over the other two with respect to the sp^3-sp^2 system.[1,2] Accepting



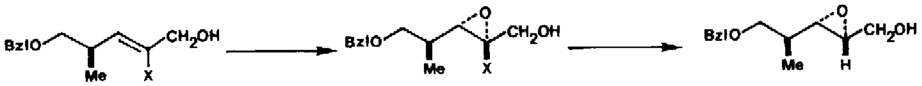
1a-c 2a-c

a: X = Me, Y = CH_2OH
b: X = CH_2OH, Y = Me
c: X = CH_2OH, Y = H



3 4 5

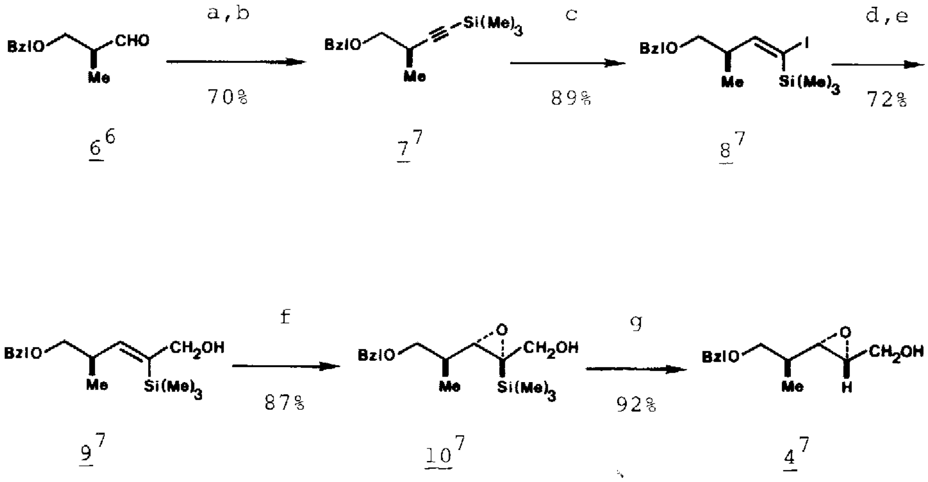
this explanation, a plan for a stereocontrolled synthesis of the epoxide 4 is depicted below. The substituent X, desirably bulky, will make one eclipsed conformation more stable than the other two, hence a highly stereoselective



epoxidation reaction might be expected. After the epoxidation, the C-X bond should be replaced by the C-H bond with retention of its stereochemistry. A current literature search made the choice of X = Si(Me)$_3$ seem obvious.

To test the feasibility of this plan, allylic alcohol 9 was stereospecifically synthesized as summarized in Scheme 1. As expected, epoxidation of 9 did yield exclusively[4] the epoxide 10. On treatment with fluoride anion, the carbon-silicon bond of 10 was cleanly replaced with the carbon-hydrogen bond,

Scheme 1

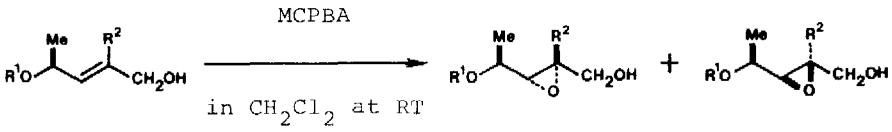


Reagents: a. CBr$_4$/(C$_6$H$_5$)$_3$P/CH$_2$Cl$_2$/0°C. b. n-BuLi/THF/-78°C, and then (Me)$_3$SiCl. c. DIBAL/heptane-ether/RT,[8] and then I$_2$ at -78°C. d. n-BuLi/THF/-78°C, and then ClCO$_2$Me. e. DIBAL/CH$_2$Cl$_2$-C$_6$H$_5$CH$_3$/-78°C. f. MCPBA/CH$_2$Cl$_2$/0°C. g. (n-Bu)$_4$NF/DMF/RT.[5]

which is known to take place with retention of its stereochemistry.[5] The overall stereoselectivity from 9 to 4 was excellent; no signals due to the diastereomeric epoxide 5 were detected in the NMR spectrum of the crude product.

The generality of this method was examined in one additional system. The results of epoxidation of the allylic alcohols 11a-d, synthesized stereospecifically from ethyl lactate,[9] are summarized in Table 1. The structure of the epoxides 12a-d was established chemically.[10] Once again, the substituent $R^2 = Si(Me)_3$ was found important in realizing the high degree of stereoselectivity (compare the case of 11d with that of 11c). It should be pointed out that the cooperative effect observed for 11b is not as pronounced as that for the previous examples.[1] On treatment with fluoride anion ($\underline{n}$-Bu_4NF/MeCN/RT), the trimethylsilyl group of the epoxide 12d was smoothly removed, to yield the epoxide 12c. The overall stereoselectivity from 11d to 12c was excellent; no signals due to the diastereomeric epoxide 13c were detected in the NMR spectrum of the crude product.

Table 1



11a-d[7]	12a-d[7]		13a-d[7]
a: $R^1 = CH_2C_6H_5$, $R^2 = H$	1	:	1[4]
b: $R^1 = CH_2C_6H_5$, $R^2 = Si(Me)_3$	3	:	1[4]
c: $R^1 = H$, $R^2 = H$	1	:	1[4]
d: $R^1 = H$, $R^2 = Si(Me)_3$	25	>	1[4]

Successful applications of the method described in this communication as well as those reported previously[1] for various synthetic problems will be presented elsewhere.

Acknowledgment Financial assistance from the National Institutes of Health (NS 12108), National Science Foundation (CHE-78-06296), and Hoffmann-La Roche Inc. is gratefully acknowledged.

References and Footnotes

1. a. M. R. Johnson, T. Nakata, and Y. Kishi, Tetrahedron Lett., 4343 (1979).
   b. M. R. Johnson and Y. Kishi, Tetrahedron Lett., 4347 (1979).
2. Y. Kishi, Aldrichimica Acta, in press.
3. For a review on conformational problems of sp^3-sp^2 systems, see G. J. Karabatsos and D. J. Fenoglio, "Topics in Stereochemistry", ed. E. L. Eliel and N. L. Allinger, Vol. 5, page 167 ff, Wiley-Interscience, New York, 1970.
4. This ratio was estimated by analysis of the NMR spectrum of the crude product
5. T. H. Chan, P. W. K. Lau, and M. P. Li, Tetrahedron Lett., 2667 (1976).
6. This aldehyde is readily available in racemic as well as optically active form; see footnote 5 of reference 1b.
7. Satisfactory spectroscopic data was obtained for this substance.
8. K. Uchida, K. Uchimoto, and H. Nozaki, J. Org. Chem., 41, 2215 (1976).
9. Ethyl lactate was benzylated ($C_6H_5CH_2Br$/NaH/DMF-THF), reduced ($LiAlH_4/Et_2O$), and oxidized (PCC/CH_2Cl_2) to yield the aldehyde, which was converted to 12b by the same sequence of reactions as summarized in Scheme 1. Deprotection of 12b (Li/liq. NH_3) gave 12d. Wittig reaction on the above aldehyde ($(C_6H_5)_3P{=}CHCO_2Et/C_6H_6$), followed by reduction ($DIBAL/CH_2Cl_2$-$C_6H_5CH_3$), yielded 12a, the deprotection of which (Li/liq. NH_3) gave 12c.
10. The epoxide 12a was converted to pentan-2,3-diol diacetate in 4 steps, i.e. 1. TsCl/Py, 2. $LiAlH_4/Et_2O$, 3. Li/liq. NH_3, and 4. Ac_2O/Py. The diacetate was found identical with the diacetate of the pentan-2,3-diol prepared from trans-2-pentene by osmium tetroxide oxidation. Chemical correlation among the epoxides 12a-d was subsequently carried out.

(Received in USA 8 August 1980)