

Syn-epoxidation of Chiral (Z)-2-Methyl-3-alkenal Acetal
via Stereo-selective Bromohydrin Formation

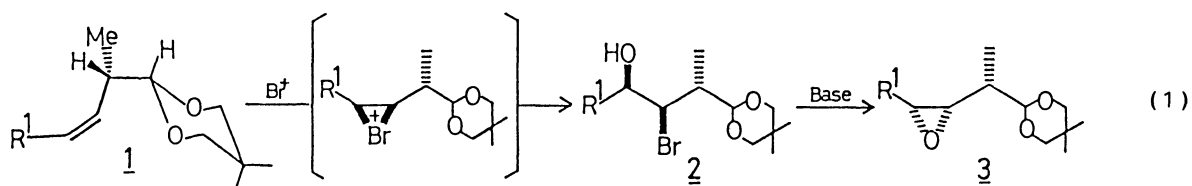
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Synthesis of syn-epoxide from chiral (Z)-2-methyl-3-alkenal acetal via stereoselective bromohydrin formation by using a reagent prepared from N-bromosuccinimide (NBS) and dimethyl sulfoxide (DMSO) under irradiation, and regioselective C-C bond formation were described.

Recently we have reported the highly anti-selective epoxidation of (Z)-alkenal acetal (1)¹⁾ via a metal catalyzed epoxidation using *tert*-butyl hydroperoxide (TBHP).²⁾ Hence it is very important to develop a synthetic procedure of the corresponding syn-epoxide. We interested in the control of stereo- and regio-selectivities by the practical use of the acetal group in acyclic systems.

Two-step conversion of an olefin to an epoxide via bromohydrin formation had been widely used. Dalton had reported a general procedure by using NBS in moist DMSO, and then proposed the mechanism where DMSO attacked to a bromonium ion and followed by hydrolysis.³⁾ We considered that 2,3-anti-bromonium ion would be generated stereoselectively by the hindrance of the methyl group, since the most stable conformation of 1 would be represented in Eq. 1. Then DMSO would attack at γ -position regioselectively by the hindrance of the methyl and the acetal groups to give 2,3-anti-bromohydrin (2), which would be easily converted into syn-epoxide (3).



The treatment of (Z)-1⁴⁾ with NBS (2 equiv.) in moist DMSO at 15 °C showed a little anti-selectivity (anti/syn=1.5, Table 1, entry 1). As the results of examinations, the selectivity was enhanced by the solvents in the following order diethyl ether > dichloromethane > acetonitrile (Table 1, entries 2,3,4). Moreover it was proven that bromohydrin formation did not proceed at low temperature without light, when bromine was generated to give dibromide as a by-product in the presence of water (entry 5). Typical procedure was as follows: Into NBS (4 mmol) in Pyrex vessel under an argon atmosphere, anhydrous diethyl ether (4 ml) and DMSO (10 mmol) were added at -18 °C. The mixture was irradiated by using a usual fluo-

rescent lamp, and the temperature was raised up until a precipitate (NBS) colored pale yellow. After irradiation for 15 min at $-18\text{ }^{\circ}\text{C}$, water (5 mmol) in THF (6 ml) was added. Into the obtained clear yellow solution, (Z)-1⁴⁾ (1 mmol) in diethyl ether (2 ml) was added in dark. After 2 h, an aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (4 equiv.) was added. The mixture was extracted with diethyl ether and evaporated at $0\text{ }^{\circ}\text{C}$. The residue was purified by silica-gel column chromatography to give 2 (Table 1, entries 7,8).

We assumed that a bromo radical generated by irradiation of NBS reacted with DMSO to give an unknown yellow compound,⁵⁾ which added to olefin to give an adduct or to water to give hypobromous acid. Bromohydrin (2) was treated with sodium hydride in DMF⁶⁾ to give syn-epoxide (3) in 85% yields (Fig. 1).

(2S, 3R, 4R)-Syn-epoxide (3) and (2S, 3S, 4S)-anti-epoxide (4)¹⁾ reacted at γ -position regioselectively with some nucleophiles. The treatment of 3 and 4 with MeLi (10 equiv.) - CuI (1 equiv.) gave (2S, 3R, 4S)-5 and (2S, 3S, 4R)-6 in 50% (recovered 46% of 3) and 85% yields, respectively. Thus all diastereomers can be prepared by the selection of R^1 , R^2 and the chirality of

1. Moreover the treatment of 5 and 6 with difluoro-(3-tetrahydropyranyloxy-1-propynyl)borane at $-78\text{ }^{\circ}\text{C}$ ⁷⁾ gave 6-alkyloxy-5-alkynes (7 and 8) in 96% yield in both cases (Fig. 1). They are useful chiral synthons for the synthesis of three and more-serial asymmetric centers in acyclic systems. The application of these methodologies to the synthesis of natural product is under current investigation.

Table 1. Bromohydrin formation of (Z)-1

Entry	R^1	NBS/equiv.	Solvent	Temp/ $^{\circ}\text{C}$	Yield/%	anti/syn
1	$\text{Ph}(\text{CH}_2)_3$	2.0	DMSO	$15^{\text{a)}$	90	60/40
2	"	"	MeCN	$-42 \rightarrow -20^{\text{a)}$	52	59/41
3	"	"	CH_2Cl_2	$-78 \rightarrow -42^{\text{a)}$	52	70/30
4	"	"	Et_2O	$-78 \rightarrow -12^{\text{a)}$	66	74/26
5	"	"	"	$-12,^{\text{b,c)}$	56	91/9
6	"	4.0	"	$-18,^{\text{c)}$	55	89/11
7	"	"	"	$-18,^{\text{c)}$	83	89/11
8	Me	"	"	"	86	84/16

a) In the natural light. b) with water. c) Irradiated.

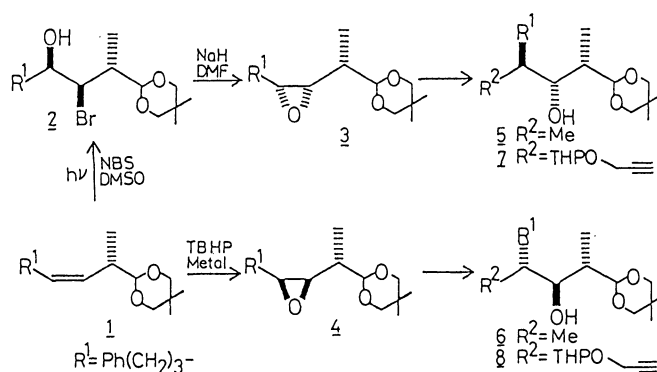


Fig. 1.

References

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- 2) Y. Honda, A. Ori, and G. Tsuchihashi, *Chem. Lett.*, **1986**, 1417.
- 3) D. R. Dalton and D. G. Jones, *Tetrahedron Lett.*, **1967**, 2875; D. R. Dalton, V. P. Dutta, and D. C. Jones, *J. Am. Chem. Soc.*, **90**, 5498 (1968).
- 4) (E)-Aldehyde acetal was also converted to a bromohydrin under the same conditions, but it was easily oxidized by NBS to give a corresponding ester.
- 5) This electrophile might be Br-O-SMe_2^+ .
- 6) The treatment of 2 with *t*-BuOK in *t*-BuOH gave 4-ketone (28%, Fig. 2) as a by-product besides 3 (72%) through hydride rearrangement.
- 7) M. Yamaguchi and I. Hirao, *Tetrahedron Lett.*, **24**, 391 (1983).

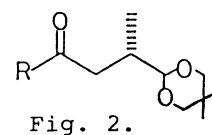


Fig. 2.

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