Selective Ring-expansion of Oxirane into Tetrahydropyran and Tetrahydrofuran by Reagent-controlled Conditions

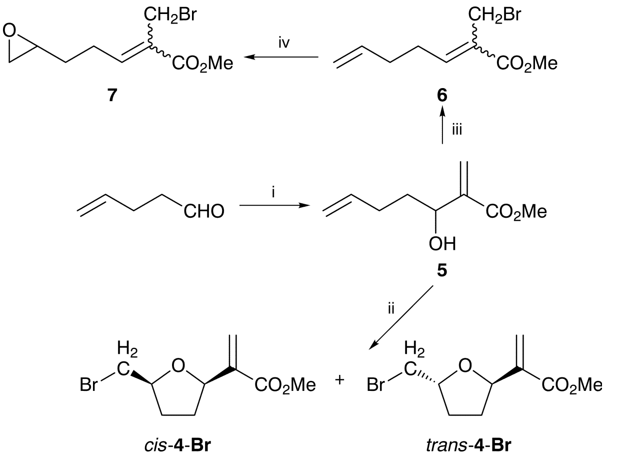
J. Chem. Research (S),
1998, 500–501
J. Chem. Research (M),
1998, 2217–2236

Munetaka Tokumasu, Asami Sasaoka, Yoshikazu Hiraga and Katsuo Ohkata*

Department of Chemistry, Faculty of Science, Hiroshima University, 1-3-1 Kagamiyama, Higashi-Hiroshima, 739-8526, Japan

Ring-expansion of methyl 2-bromomethyl-5-oxiranylpent-2-enoate (**7**) with various acids was studied; treatment with Lewis acids ($TiBr_4$, $MgBr_2$ and $ZnBr_2$) afforded the tetrahydrofuran derivative **4-Br** as a major product, while reaction with silver salt ($AgNO_3/KPF_6$), which is known to have a high halide affinity, gave preferentially the tetrahydropyran **3-ONO₂** derivatives as the major products.

Oxygenated heterocycles are frequent and important targets for synthesis either as final products or as useful synthetic intermediates.[1,2]



Scheme 3 *Reagents and conditions*: i, methyl acrylate, DABCO, r.t., 2 weeks, 78%; ii, TBCO, MeCN, r.t., 1 h, 79% (*cis*/*trans* 38:62); iii, Ph_3P. CBr_4, CH_2Cl_2, r.t., 30 min, 52%; iv, *m*-CPBA, CH_2Cl_2, r.t., 48 h, 85%

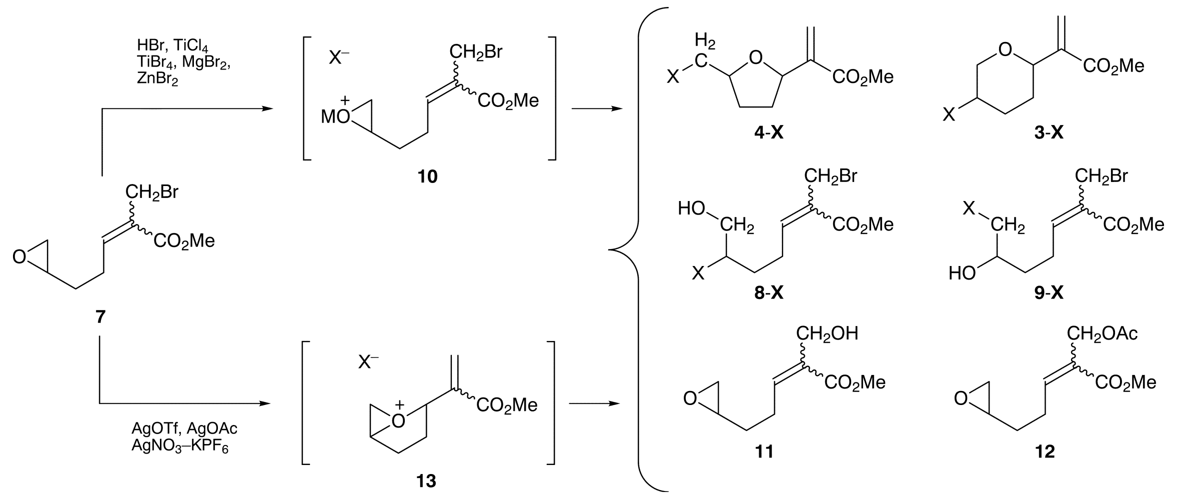
Baylis-Hillman reaction of pent-4-enal with methyl acrylate afforded the corresponding ester **5** in 78% yield.[5] Treatment of **5** with 2,4,4,6-tetrabromocyclohexa-2,5-dienone (TBCO) furnished the tetrahydrofuran derivatives **4-Br** (Scheme 3).

Bromination of **5** with $Ph_3P–CBr_4$, followed by epoxidation with *m*-CPBA, gave epoxybromide **7** in 44% yield. Treatment of **7** with various acids afforded ring expansion-products (**4-X** and **3-X**) and ring-opening products (**8-X** and **10-X**) as shown in Scheme A.

Treatment of **7** with 47% aq. HBr or $TiCl_4$ gave a mixture of the ring-opened products **8** (11, 49%) and **9** (57, 47%), respectively. Reaction of **7** with $TiBr_4$ afforded the tetrahydrofuran derivative **4-Br** (46%, *cis*/*trans* 0.4:1) and the ring-opened products **8-Br** (14%) and **9-Br** (32%). Reaction of **7** with $MgBr_2$ and $ZnBr_2$ gave the tetrahydrofuran derivative **4-Br** in 52 and 64% yields, respectively.

For proton acid (HBr) and Lewis acids such as $TiCl_4$, $TiBr_4$, $MgBr_2$ and $ZnBr_2$, the acid reacts with the epoxy group to give intermediate **10** in the initial step, followed by inter- or intra-molecular nucleophilic attack to give **4-X**, **8-X** and **9-X** (Scheme A).

Reaction of **7** with silver triflate gave a mixture of six- and five-membered heterocycles **4-Br** (24%) and **3-Br** (25%). Treatment of **7** with silver acetate in aqueous medium gave a mixture of six- and five-membered heterocycles **4-OH**



Scheme A Ring-expansions and ring-openings of epoxybromo ester derivative **7** with various acids

---

*To receive any correspondence.

(19%) and **3-OH** (27%), respectively, along with alcohol *E*-**11** and acetate *E*-**12**. Treatment of **7** with a mixed reagent ($AgNO_3$–KPF_6) in CH_2Cl_2 afforded selectively the tetrahydropyran derivative **3-ONO$_2$** (56%).

The silver salt might be expected to eliminate bromide ion initially, followed by intramolecular nucleophilic attack of the epoxy group to give intermediate **13** (Scheme A).[4] Then, *endo*-attack to the intermediate **13** by nucleophile (NO_3^-) would produce the 2-tetrahydropyranylacrylate derivative **3-X**.[1–3]

The synthetic methodology shown above should be applicable to synthesis of various natural products containing five- and six-membered *O*-heterocycles.[1,2]

NMR and MS measurements were obtained on JEOL JNM-GSX270/LA500 and JEOL JMS-SX102A instruments, respectively, at the Instrument Center for Chemical Analysis, Hiroshima University.

Techniques used: ^1H and ^{13}C NMR, MS

References: 9

Tables: 4

Schemes: 5

Received, 12th May 1998; Accepted, 22nd May 1998
Paper E/8/03552K

References cited in this synopsis

1 S. J. Danishefsky, H. G. Selnick, M. P. De Ninno and R. E. Zelle, *J. Am. Chem. Soc.*, 1987, **109**, 1572; T. R. Hoye and S. A. Jenkins, *J. Am. Chem. Soc.*, 1987, **109**, 6196; S. T. Russell, J. A. Robinson and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1987, 351; I. Paterson, I. Boddy and I. Mason, *Tetrahedron Lett.*, 1987, **28**, 5205.

2 K. C. Nicolaou, C. V. C. Prasad, P. K. Somers and C.-K. Hwang, *J. Am. Chem. Soc.*, 1989, **111**, 5330; J. M. Betancort, V. S. Martin, J. M. Padrón, M. A. Ramírez and M. A. Soler, *J. Org. Chem.*, 1997, **62**, 4570; T. Hudlicky and G. Barbieri, *J. Org. Chem.*, 1991, **56**, 4598; I. Paterson, R. D. Tillyer and J. B. Smaill, *Tetrahedron Lett.*, 1993, **34**, 7137; C. Mukai, Y. Sugimoto, Y. Ikeda and M. Hanaoka, *Tetrahedron Lett.*, 1994, **35**, 2183.

3 M. Tokumasu, A. Sasaoka, R. Takagi, Y. Hiraga and K. Ohkata, *Chem. Commun.*, 1997, 875; N. Hayashi, K. Fujiwara and A. Murai, *Chem. Lett.*, 1996, 341; N. Hayashi, K. Fujiwara and A. Murai, *Tetrahedron Lett.*, 1996, **37**, 6173.

4 L. A. Paquette and M. K. Scott, *J. Am. Chem. Soc.*, 1972, **94**, 6760.

5 A. B. Baylis and M. E. D. Hillman, *Ger. Pat.*, 2155113, 1972 (*Chem. Abstr.*, 1972, **77**, 34174q); D. Basabaiah, P. D. Rao and R. S. Hyma, *Tetrahedron*, 1996, **52**, 8001; H. M. R. Hoffmann and J. Rabe, *J. Org. Chem.*, 1985, **50**, 3849; J. M. Brown, I. Cutting, P. L. Evans and P. J. Maddox, *Tetrahedron Lett.*, 1986, **27**, 3307.