Anionic [1,3] Sigmatropic Rearrangements of an Oxy-Cope System Incorporated in 8-Methylenebicyclo[3.2.1]oct-6-ene and Related Frameworks

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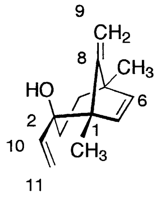
Treatment of an 8-methylene-endo-2-vinylbicyclo[3.2.1]oct-6-en-exo-2-ol with KH in THF gave mainly a [5-6] fused-ring compound via [1,3] sigmatropy with *retention of the configuration in the migrating group.*

Anionic oxy-Cope rearrangement of bridged polycyclic compounds has been closely investigated to refine a synthetic strategy of a natural product.[1-3] Preparation of such an oxy-Cope system is generally accompanied by the formation of the trans isomer. Little attention has been paid to a sigmatropic rearrangement of a trans oxy-Cope system.[2] In this paper we report an alkoxide accelerated [1,3] sigmatropic rearrangement of bridged bicyclic compounds **1** and **2**.

For the allyl alcohol **1**, we may point out several reaction courses such as a [1,3] migration giving a [5-5] fused-ring compound **3** via cleavage of the C(1)−C(2) bond and formation of a new bond between C-2 and C-6, a [1,3] migration giving a [5-6] fused-ring compound **4** via formation of a new bond between C-2 and C-9, and an oxy-Cope rearrangement to give a [5-7] fused-ring compound **5** via closure between C-6 and C-11. In addition to the regioselectivity, the stereochemistry of the migrating group should be investigated.

A desired substrate **1** was prepared from a ketone **6**.[4] Treatment of the ketone **6** successively with 1) LDA, iodomethane, 2) $KN(SiCH_3)_2$, allyl chloroformate, and 3) $Pd(OAc)_2$ in CH_3CN[5] gave a conjugated ketone **7**[6] in 59% overall yield. A composite reagent of methyl lithium and cerium trichloride[7] added to the α,β-unsaturated carbonyl system of **7** in a 1,2-manner to give the exo and endo alcohols in 62% and 30% yields, respectively. Pinacol-type rearrangements of both of them by treatment with 10 mol% of TsOH in boiling benzene gave a ketone **8** as the major product in more than 58% yields.[8] Treatment of the ketone **8** with a reagent derived from vinylmagnesium bromide and cerium trichloride in THF at -78 ℃ gave allyl alcohols **1** and **9** in 59% and 28% yields, respectively. By a manner similar to this transformation, the dihydro-derivative of **8** (**10**) was prepared from **6**. The ketone **10** was converted into allyl alcohols **2** and **11** in 51% and 36% yields, respectively.

The stereostructures of the endo alcohols **9** and **11** were defined by not only their spectral characteristics[9] but also their reactivities. A treatment of **9** with KH in THF at 0 ℃ for 20 min gave a ketone **12** in 99% yield. A similar reaction of **11** proceeded at 60 ℃ and a ketone **13** was derived in 83% yield. According to Paquette and his co-worker's report, a [3,3] sigmatropic rearrangement proceeds to form a [5-8] fused-ring compound in the case of an endo alcohol like **11**.[10]



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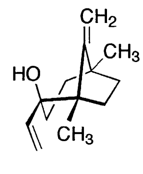

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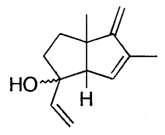

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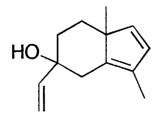

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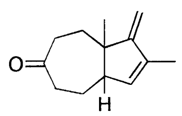

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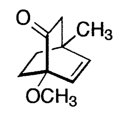

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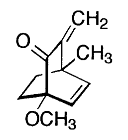

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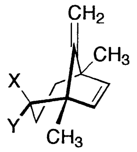
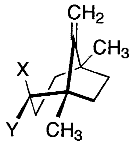


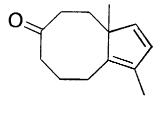
8 X, Y = O

9 X = CH=CH$_2$
Y = OH



10 X, Y = O

11 X = CH=CH$_2$
Y = OH



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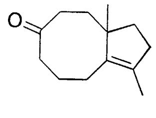

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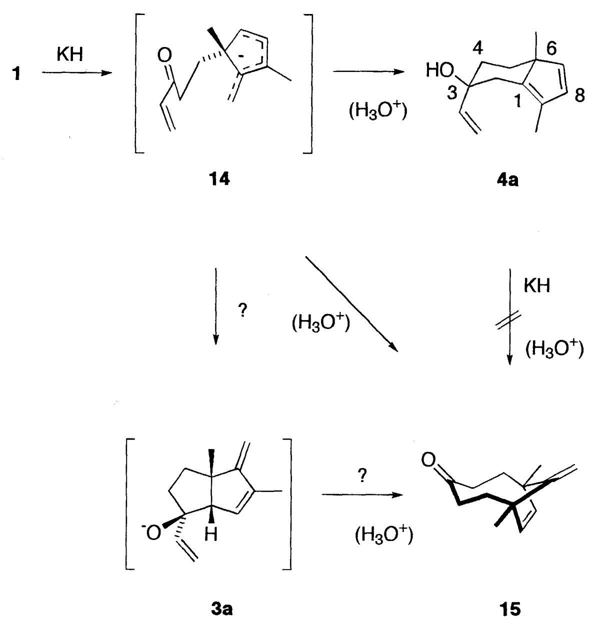
When the substrate **1** was treated with KH in THF at 0 ℃ for 20 min, a [5-6] fused-ring compound **4a** and a bicyclo[5.2.1]non-8-en-4-one **15** were derived in 77% and 15% yields, respectively as listed in Scheme 1. The stereostructure of **4a** was assigned as the depicted exo alcohol on the basis of its ^{1}H-NMR spectra.[11] This means that the [1,3] sigmatropic rearrangement is a suprafacial retention process.

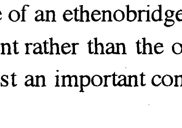
The ketone **15** is regarded as a ring-enlargement product by two carbons. One of feasible routes from **1** to **15** was a tandem one including an anion-assisted Cope rearrangement of **4a**, while



Scheme 1

the latter was recovered after treatment with KH in boiling THF for 4 h.[12] Another considerable route is tandem anionic oxy-Cope rearrangements via an alkoxide **3a**. However, the following experimental results seem to support a direct [1,3] sigmatropic migration rather than the tandem route.

The alcohol **2** was inactive, when it was treated with KH in THF under reflux for 15 h. The substrate was consumed by treatment with KH and 18-crown-6 in boiling THF for 5 h and a [5-6] fused-ring compound **16** and a bicyclo[5.2.1]non-8-en-4-one **17** were derived in 34% and 14% yields, respectively. Formation of **17** suffers doubts about the tandem route from **1** to the ketone **15** via the alkoxide **3a**.



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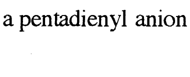

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Thus, anion-assisted sigmatropic rearrangements of **1** and **9** proceeded more easily than those of **2** and **11**, respectively. The presence of an ethenobridge accelerates the [1,3] sigmatropic rearrangement rather than the oxy-Cope rearrangement. This seems to suggest an important contribution of a pentadienyl anion structure like **14** for the rearrangement of **1**.

In conclusion, now we can prepare selectively both [5-8] fused-ring and [5-6] fused-ring compounds from 8-methylenebicyclo[3.2.1]oct-6-en-2-ones.

References and Notes

1 For reviews,' see: a) L. A. Paquette, *Synlett.*, **1990**, 67. b) L. A. Paquette, *Angew. Chem., Internat. Ed. Engl.*, **29**, 609 (1990).

2 For a review, see: S. R. Wilson, *Org. Reaction*, **43**, 93 (1993).

3 More recent work: a) L.A. Paquette and R. C. Thompson, *J. Org. Chem.*, **58**, 4952 (1993). b) L. A. Paquette, S. K. Huber, and R. C. Thompson, *J. Org. Chem.*, **58**, 6872 (1993). c) R. Guevel and L.A. Paquette, *J. Am. Chem. Soc.*, **116**, 1776 (1994). d) J. Doyon, W. He, and L. A. Paquette, *J. Org. Chem.*, **59**, 2033 (1994). e) J.-F. Devaux, I. Hanna, J.-Y. Lallemand, and T. Prange, *J. Org. Chem.*, **59**, 2349 (1994). f) K. Mori and Y. Matsushita, *Synthesis*, **1995**, 845.

4 a) D. A. Evans, W. L. Scott, and L. K. Truesudale, *Tetrahedron Lett.*, **1972**, 121. b) S. A. Monti,S.-C. Chen, Y.-L. Yang, S.-S. Yuan, and O. P. Bourgeois, *J. Org. Chem.*, **43**, 4062 (1978).

5 J. Tsuji, I. Minami, I. Shimizu, and H. Kataoka, *Chem. Lett.*, **1984**, 1133.

6 All new compounds reported here exhibit satisfactory spectral and analytical and/or HRMS characteristics.

7 We recommend more than 30 h of stirring and then 2 h of sonication of a dry $CeCl_3$ powder in THF, see: a) T. Inamoto, N. Takiyama, K. Nakamura, T. Hatajima, and Y. Kamiyama, *J. Am. Chem. Soc.*, **111**, 4392 (1989). b) N. Greeves and L. Lyford, *Tetrahedron Lett.*, **33**, 4759 (1992).

8 Pinacol-type rearrangement of 1-methoxybicyclo[2.2.2]oct-5-en2-ol via an allyl cation intermediate, see: T. Uyehara, T. Inayama, T. Furuta, T. Kato, Y. Yamamoto, M. Ueno, and T. Sato, *Bull. Chem. Soc. Jpn.*, in press.

9 For an example, ^{1}H-NMR studies of **9** revealed the presence of NOE (0.6%) between the signals due to one of the exomethylene protons and one of the vinyl methylene protons.

10 L. A. Paquette, S. Liang, and P. Glatsis, *Synlett.*, **1990**, 663.

11 Key interactions obtained from NOE difference spectra of **4a** are those between the signals due to the 5-endo-proton and the methine proton of the vinyl group (2.2% and 2.4%).

12 A reaction of **4a** with KH and 18-crown-6 in THF at room temperature for 30 h gave a mixture of many products and 4a. We found neither **12** nor **15** in the mixture.